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ECTRIMS 2025 ePoster

Clinical Aspects of MS & Related Diseases - Diagnosis and differential diagnosis

P1000
Reassessing Dissemination in Space: The Role of Spinal Cord Lesion Burden in Early Multiple Sclerosis Diagnosis

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Introduction: According to current diagnostic criteria for MS, the presence of at least one brain lesion must be present at the time of diagnosing transverse myelitis to satisfy the criterion of dissemination in space (DIS).
Objectives/Aims: This study aimed to evaluate whether the presence of more than one spinal cord lesion at the onset of the first clinical event increases the risk of developing relapsing-remitting MS (RRMS), and whether this finding alone might be sufficient to satisfy the DIS criterion.
Methods: We performed a retrospective analysis of clinical and radiological data in patients who presented with myelitis. Only spinal cord lesions involving <3 vertebral segments were considered. Patients were excluded if they exhibited brain lesions typical of MS, neuromyelitis optica spectrum disorder (NMOSD), MOG antibody-associated disease (MOGAD), or presented with features suggestive of an alternative diagnosis. Clinical and paraclinical variables were compared between patients who converted to RRMS during follow-up (M-MS) and those who did not (M-nMS). Differences between groups were assessed using non-parametric tests, and Cox regression analysis was adjusted by age in accordance with the study objectives.
Results: Eighty-five patients were included: 33 in the M-MS group and 52 in the M-nMS group. The median age was 35 years (IQR:30–39) and 42 years (IQR:32.5–51), respectively (p=0.03). Women predominated in both groups (73% and 58%, p=0.1). At onset, multiple spinal cord lesions were observed in 51.1% of M-MS vs. 21% of M-nMS (p=0.004). Oligoclonal bands (OCB) in cerebrospinal fluid were significantly more frequent among patients who converted to MS (58% vs. 15%, p<0.001).
In univariable analysis, each variable was significantly associated with RRMS conversion. A multivariable Cox regression model demonstrated that the presence of multiple spinal cord lesions at onset was independently associated with increased risk conversion to RRMS, (HR=2.2, 95%CI=1.1–4.4, p=0.02). The coexistence of OCB positivity and multisegmental myelitis was associated with a markedly increased risk (HR=2.6, 95%CI=1.3–5.4, p=0.008).
Conclusion: Multisegmental spinal cord lesions at onset were more frequent among patients who subsequently developed MS, particularly when combined with OCB. These findings suggest that multiple spinal cord lesions may fulfill DIS criteria, even without brain lesions. Further prospective studies are warranted to validate these findings.

Disclosure of interest: The authors have not disclosures related to this abstract

P1001
The Implication of the Blood-Brain Barrier integrity on serum Neurofilament Light Chain levels as a marker for neuro-axonal injury

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Introduction: The blood-brain barrier (BBB) is critical for central nervous system homeostasis, and its dysfunction is linked to various neurological disorders. Neurofilament Light Chain (NfL), a biomarker for neuroaxonal damage, is detectable in cerebrospinal fluid (CSF) and serum. However, the effect of BBB integrity on serum NfL levels is not fully understood.
Objectives/Aims: This study investigates how BBB disruption influences the correlation between CSF and serum NfL levels using two different analytical platforms.
Methods: We analyzed NfL levels in paired CSF and serum samples from 77 patients categorized by BBB integrity. The CSF/serum albumin quotient (Q_{Alb}) was used to evaluate BBB integrity (intact: N=34, disrupted: N=43). NfL concentrations were measured using the HD-X (Single Molecule Array) and Lumipulse G600 II (Chemiluminescent Enzyme Immunoassay) platforms.
Results: For HD-X, CSF NfL levels in the intact BBB group were 434.00 pg/ml (IQR: 274.50–1175.00), and in the disrupted group, 1117.00 pg/ml (IQR: 538.50–3009.00), p<0.001. Serum NfL was 9.42 pg/ml (IQR: 6.25–23.07) in the intact group and 22.15 pg/ml (IQR: 11.38–43.43) in the disrupted group, p=0.003. Using Lumipulse, CSF NfL in the intact BBB group was 323.50 pg/ml (IQR: 207.00–1189.50), and 915.00 pg/ml (IQR: 519.50–2426.50) in the disrupted group, p<0.001. Serum NfL was 12.20 pg/ml (IQR: 8.95–30.78) in the intact group and 32.56 pg/ml (IQR: 15.35–62.28) in the disrupted group, p=0.004.

Correction (September 2026): This paper has been updated to correct the sentence "Among those treated with DMTs, the conversion rate was 16.7%, compared to 41.5% in untreated patients"

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Correlation analyses between CSF and serum NfL levels revealed strong positive correlations in the intact BBB group for both HD-X (r=0.82, p<0.001) and Lumipulse (r=0.86, p<0.001). In the disrupted BBB group, the correlations were moderate but still significant for both platforms: HD-X (r=0.72, p<0.001) and Lumipulse (r=0.69, p<0.001).
Conclusion: Our study confirms a strong correlation between CSF and serum NfL levels. However, BBB integrity may influence NfL levels, with higher and more variable serum NfL in the BBB disrupted group. These findings highlight that in certain cases of particularly severe BBB disruption, BBB status should be considered when interpreting NfL measurements.

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P1002
Influence of tobacco smoking on disease activity parameters in patients with relapsing forms of multiple sclerosis initiating disease-modifying therapy

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Introduction: Tobacco smoking (TS) is associated with an increased risk of disease activity and disability worsening in patients with relapsing forms of multiple sclerosis (RRMS).
Objectives/Aims: To assess the impact of TS on clinical and radiological measures of disease activity in RRMS patients initiating disease-modifying therapy (DMT).
Methods: A retrospective longitudinal study was conducted within a prospective cohort of RRMS patients. Between 2015 and 2021, a tobacco use survey was administered, collecting data on smoking habits and demographics at DMT initiation. Patients were followed during 24 months to evaluate the occurrence of relapses, relapse-associated worsening (RAW), progression independent of relapse activity (PIRA), interval MRI activity (⩾1 new T2 or contrast-enhancing lesion [CEL]), and EDSS trajectories. At baseline (DMT initiation), descriptive statistics summarized demographic and clinical data, and group comparisons were performed using parametric and non-parametric tests. Associations between smoking status at DMT initiation (smokers [s-DMT] vs. non-smokers [ns-DMT]) and outcomes at 24 months were analyzed with logistic regression. Linear mixed models assessed EDSS trajectories. All models were adjusted for baseline age, DMT class, EDSS, annualized relapse rate (ARR), and CEL count, as appropriate.
Results: A total of 1242 patients were included (68% female; median [IQR] follow-up 8.06 [5.26–14.14] years), of whom 1074 had comparative MRI data. At baseline, 42% initiated injectable therapies, 31% oral therapies, and 27% monoclonal antibodies. No significant differences were observed in age, EDSS, CEL and ARR between s-DMT and ns-DMT. At 24 months, s-DMT was independently associated with increased relapse (OR 1.65, 95% CI 1.19–2.27; p=0.002), PIRA (OR 1.94, 95% CI 1.35–2.80; p<0.001), and interval MRI activity (OR 1.94, 95% CI 1.41–2.69; p<0.001) occurrence. No significant association was found with RAW (OR 1.77, 95% CI 0.70–4.54; p=0.2). Compared to ns-DMT, s-DMT exhibited a significantly steeper EDSS increase (β=0.006; p<0.001), particularly among patients initiating oral therapies (β=0.007; p=0.012) and monoclonal antibodies (β=0.013; p<0.001), but not among those on injectable therapies (β=−0.002; p=0.476).
Conclusion: Smoking at the time of DMT initiation is associated with significantly worse clinical and radiological outcomes, reflecting both inflammatory and neurodegenerative disease activity in RRMS patients.

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clinical fellow; in the past three years he has received travel expenses for scientific meetings from Roche, Merck, and Genzyme; compensation for consulting services or participation on advisory boards from Amgen, Merck, Biogen-Idec, Sanofi and Novartis; lecture fees from Novartis, Merck, Sanofi, Janssen, Lumex pharma and Biogen-Idec; and research support from Biogen-Idec and Novartis. M Marrodan has received fees for educational presentations and/or conference attendance from Merck-Serono Argentina, Biogen-Idec Argentina, Novartis Argentina, Gador, Astra-Zeneca, Raffo and Roche Argentina. G Arrambide received compensation for consulting services, speaking honoraria or participation in advisory boards from Roche, Horizon Therapeutics, and Bristol Myers Squibb; and travel support for scientific meetings from Novartis, Roche, ECTRIMS, and EAN. She serves as editor for Europe of the Multiple Sclerosis Journal – Experimental, Translational and Clinical journal; and as a member of the editorial and scientific committee of Acta Neurológica Colombiana. She is a member of the International Women in Multiple Sclerosis (iWiMS) network executive committee, the European Biomarkers in Multiple Sclerosis (BioMS-eu) steering committee, the MOGAD Eugene Devic European Network (MEDEN) steering group, and the Platform Adaptive Trial for remyelination and neuroprotection in mUltiple Sclerosis (PLATYPUS) steering committee. She is a recipient of grants PI19/01590 and PI22/01570, awarded by the Instituto de Salud Carlos III (ISCIII), Ministerio de Ciencia e Innovación de España. C Tur is currently being funded by a Miguel Servet contract, awarded by the Instituto de Salud Carlos III (ISCIII), Ministerio de Ciencia e Innovación de España (CP23/00117). 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R Carvajal is currently being funded by a grant, awarded by the Instituto de Salud Carlos III (ISCIII), Ministerio de Ciencia e Innovación de España (FI/2400299). In 2023 he was awarded with a Research Training Programme from the European Charcot Foundation. In 2023, he received a grant by "Vall d'Hebron Institut de Recerca." In 2021, he received an ECTRIMS Fellowship training performed during 2021–2022. He has also received speaking honoraria from Roche, Novartis, Biogen, Merck, and Sanofi. A Casallas is currently an ECTRIMS clinical fellowship awardee for 2024-2025 and receives support from ECTRIMS. In 2022 she was awarded with a grant from the European Charcot Foundation for MSM program. She has also received speaking honoraria from Roche, Novartis, Biogen, Merck, and Sanofi. S Otero-Romero has received speaking and consulting honoraria from Genzyme, Biogen- Idec, Novartis, Roche, Excemed and MSD; as well as research support from Novartis. 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P1003
Clinical Performance of Mass Spectrometry-based Oligoclonal Banding for the Diagnosis of Multiple Sclerosis Compared to Traditional Methods

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Introduction: Multiple sclerosis (MS) is an inflammatory demyelinating disease characterized by the intrathecal synthesis of immunoglobulins that accumulate in the cerebrospinal fluid (CSF). Detection of these CSF-restricted oligoclonal immunoglobulin (IgG) bands (OCB) is an important laboratory marker for the diagnosis of MS and has been part of the McDonald criteria as a substitute for dissemination in time. Recent revisions of the diagnostic criteria have included measuring kappa free light chains (kFLC) in CSF as an alternative to the gold standard OCB. Matrix-Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF) mass spectrometry methodologies have been increasingly used in the detection of monoclonal immunoglobulins and are currently limited to the diagnosis and management of monoclonal gammopathies.
Objectives/Aims: This feasibility study aimed to assess the ability of the EXENT system (The Binding Site [TBS], part of Thermo Fisher Scientific) to detect oligoclonal peaks in paired serum and CSF samples and to evaluate the clinical performance of mass spectrometry-based OCB detection compared to traditional OCB testing and K index for the diagnosis of MS.
Methods: Paired CSF and serum samples from 20 multiple sclerosis patients (comprising 16 with relapsing-remitting MS (RRMS), 2 with secondary progressive MS (SPMS), and 2 with primary progressive MS (PPMS)) and 20 non-MS patients (including 8 with non-MS inflammatory neurological diseases (NMS-IND), 8 with non-inflammatory neurological diseases (NIND), and 4 neurologically normal (NN)) were analyzed using the EXENT System and by isoelectric focusing. In addition, kFLC and albumin concentrations were determined with the Optilite Freelite Kappa Mx kit and the Optilite Low Level Albumin kit (TBS), and the K index was calculated. Oligoclonal banding was deemed positive when $\geqslant$2 unique IgG CSF bands were present (pattern type 2 and 3), whereas pattern type 1 and 4 were categorized as negative. Patient diagnoses were assigned based on the 2024 McDonald criteria.
Results: The diagnostic sensitivity of MALDI-TOF mass spectrometry OCB was 90% with a specificity of 95%, compared to the 95% sensitivity and 85% specificity of traditional OCBs and the 95% sensitivity and 74% specificity of the K index.
Conclusion: These results demonstrate that MALDI-TOF mass spectrometry may offer a potentially sensitive alternative method to aid in the diagnosis of MS and can demonstrate similar clinical performance when compared to current state-of-the-art diagnostic methodologies.

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P1004
Clinical Implementation of Central Vein Sign and Revised Diagnostic Criteria at a University Teaching Hospital

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Introduction: The central vein sign (CVS) has been included in the revised diagnostic criteria, however there is a reported 17-year implementation gap from scientific research through to clinical implementation. As a CVS research centre, where CVS analysis has been performed clinically since 2020, we sought to investigate the process of CVS implementation over this time and its impact on clinical care.
Objectives/Aims: Investigate (1) the change in CVS reporting over time, before and after the 2024 revised criteria were announced, (2) the clinical indications for scans with CVS reporting, (3) the difference in CVS reporting by internal and external radiologists and (4) where CVS analysis contributed to clinical management.
Methods: Retrospective review of MR head scans with dedicated susceptibility-weighted sequence (Jan 2020-Mar 2025,

Nottingham, n=412). We recorded if CVS was documented in requests/reports, MR indication, and whether the radiologist was from our centre or an external provider. Comparison was between imaging up to and following Sep 2024, to align with the revised diagnostic criteria. Medical notes were reviewed for patients between Jan–Nov 2024 (n=70) to investigate if CVS reporting influenced clinical practice.
Results: Clinicians requested CVS analysis in 16% scans up to Sep 2024 and 43% following. CVS radiologist reporting was 25% up to Sep 2024 and 39% after. Suspicion of misdiagnosis was indication for 4% scans. External radiologists reported CVS at a lower rate than internal radiologists, 17% vs 28%. Subgroup analysis (n=70) showed CVS contributed substantially to clinical decision making in 94% of patients. No patients underwent LP following CVS analysis.
Conclusion: Even at a leading CVS research centre, the adoption of CVS analysis has taken years to progress. This change dramatically accelerated following the announcement of the revised diagnostic criteria. CVS analysis greatly contributes to clinical decision making and efforts must be made to support implementation.

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P1005
Performance of the 2024 McDonald diagnostic criteria for multiple sclerosis

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Introduction: Diagnostic criteria for multiple sclerosis (MS) have undergone numerous revisions, with their most recent revision announced in 2024.
Objectives/Aims: This study aimed to compare the 2024 McDonald diagnostic criteria with their earlier iterations with respect to time to MS diagnosis, MS phenotype and disability.
Methods: The eligible patients attended the Royal Melbourne Hospital Neuroimmunology Centre between 2013 and 2022 with clinically or radiologically isolated syndrome (CIS, RIS). Inclusion criteria were age at CIS/RIS between 18 and 50 years, first visit within 6 months of CIS/RIS and a brain MRI within 6 months of first visit. The primary outcome was reaching the diagnosis of MS according to the 2024 criteria, in comparison to the 2017 McDonald criteria. Secondary outcomes included time to MS diagnosis and disability assessed using the MS Severity Score (MSSS) during follow-up. These outcomes were compared separately among patients diagnosed with CIS/RIS before year 2017 and between 2017 and 2022. In addition, the 2010 McDonald were also evaluated in the pre-2017 group. Additionally, we applied the 2024 criteria to patients with CIS after the publication of 2024 MS criteria.
Results: A total of 163 patients were included. The mean age at CIS/RIS was 31.4 years, and 72% were female. Based on the 2024 criteria, 133 (81.6%) patients fulfilled the criteria of MS at baseline compared to 122 (74.9%) based on the 2017 McDonald criteria. Among the subgroup assessed with the 2010 McDonald criteria, 38 (49.4%) reached the diagnosis of MS at baseline.
The mean time to MS diagnosis was shorter when applying 2024 criteria (6.5 months) compared to 2017 and 2010 criteria (7.8 months and 10.9 months, respectively).
Patients diagnosed with MS at baseline according to the 2024 and 2017 McDonald criteria, showed lower MSSS during follow-up compared to those diagnosed with 2010 criteria. Since the announcement of 2024 criteria, 13 patients were enrolled and 11 (85%) fulfilled the diagnostic criteria of MS at baseline.
Conclusion: At the time of first clinical/radiological presentation of MS, the application of the 2024 revised diagnostic criteria of MS resulted in an increased sensitivity to diagnose MS and a shorter time to diagnosis compared to the previous revisions of the McDonald criteria. The criteria were also more efficient at identifying patients with MS with a milder disease course.

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P1006
In Multiple Sclerosis, Acute Clinical Events with Stable MRI Exhibit Distinct Clinical Characteristics Compared to Events with Active MRI

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Introduction: Recent studies have reported that acute clinical events with stable MRI (ACES) occur in patients with Multiple Sclerosis (MS), particularly in those treated with anti-CD20 therapies or Natalizumab. These relapses, which lack corresponding radiological activity, remain insufficiently studied.
Objectives/Aims: To identify factors associated with relapses without new MRI lesions (ACES) in comparison to relapses with active MRI (RAM).
Methods: MS relapses were identified from the French OFSEP database at Bordeaux University Hospital, including patients who had received at least one injection of an anti-CD20 therapy since 2008. Each relapse was manually reviewed in the clinical files and categorized as either ACES or RAM. Data collected included the presence of new neurological location on clinical examination, treatment type, EDSS score, and other clinical variables. Multivariate logistic regression was used to determine factors associated with ACES.
Results: Among 2,524 clinical events reviewed, 553 relapses in 232 patients were included: 279 were classified as ACES and 274 as RAM. ACES were more frequent in patients receiving high-efficacy monoclonal antibody therapies (HET): 95 (34.1%) vs. 21 (7.7%) in RAM, $p < 0.001$. ACES were also less likely to involve a new neurological territory: 131 (63.6%) vs. 87 (41.4%) in RAM, $p < 0.001$. Patients with ACES had a longer disease duration (mean 9.9 vs. 8.9 years, $p = 0.022$) and a higher EDSS score prior to relapse (mean 2.9 vs. 2.3, $p < 0.001$). In multivariate analysis, ACES were significantly associated with treatment with HET (OR 4.56; 95% CI [2.18–10.00], $p < 0.001$), absence of new neurological location (OR 1.84; 95% CI [1.14–3.00], $p = 0.013$), higher EDSS score prior to relapse (per 1-point increase: OR 1.24; 95% CI [1.05–1.48], $p = 0.013$).
Conclusion: Relapses without new MRI lesions (ACES) are significantly more likely in patients treated with high-efficacy therapies, with no new neurological territory affected, and higher baseline disability. These findings suggest that ACES represent a distinct clinical phenotype that warrants specific diagnostic and therapeutic considerations.

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P1007
MS Prodrome from the Patient's Perspective

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Introduction: Increasing evidence suggests that individuals with Multiple Sclerosis (MS) experience a prodromal phase marked by non-specific symptoms before clinical onset. This study aimed to investigate the nature, frequency, and healthcare interactions associated with these early symptoms in a real-world MS cohort.
Objectives/Aims: To identify common physical, mental, and emotional symptoms experienced before MS diagnosis, and to assess patient experiences with primary care during the prodromal period.
Methods: A structured questionnaire was distributed to patients under the Wessex MS service, collecting demographic data, MS type, family history, other medical diagnoses, and symptom history prior to MS diagnosis. Quantitative data were analyzed descriptively.
Results:

- **Demographics**: 193 respondents; 75.6% female, most aged 36–65. The majority had Relapsing Remitting MS (71.4%).
- **Symptom Onset**: 67.4% reported symptoms over one year before diagnosis; 32% experienced symptoms over six years prior.
- **Common Prodromal Symptoms:**
  - Physical: numbness/tingling (68), fatigue (61), limb weakness (50), dizziness (27), bladder issues (33), and visual disturbances (27).
  - Mental/Emotional: anxiety (85), low mood (75), memory problems (73), and concentration difficulties (68).
- **Healthcare Engagement:**
  - 71.7% consulted a GP; 27.8% did not recall or seek help.
  - Among those who saw a GP, 40% visited 3+ times.
  - Only 32.4% were referred to Neurology within one year of symptom onset; 41.6% waited over one year or were not referred by their GP.
- **Diagnosis and Treatment:**
  - 70.6% believed their early symptoms were MS-related in hindsight.
  - Median time to treatment post-diagnosis was within 3–6 months for most.

Conclusion: This study highlights that a significant proportion of MS patients experienced early symptoms—often emotional, cognitive, or subtle neurological issues—years before diagnosis. Many sought medical advice, but delays in specialist referral were common. Improved awareness of MS prodromal features among primary care providers may support earlier identification and intervention.

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P1008
Clinical Characteristics and Disease Progression in Multiple Sclerosis: A Comparison of Late Middle-Age Onset vs Late Adulthood Onset

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Introduction: The age at which multiple sclerosis (MS) presents can impact the disease's progression and long-term outcomes. Late middle age onset MS (LMOMS) and late adulthood onset MS (LAOMS) are considered distinct subgroups within the MS spectrum, but the rationale for selecting specific age thresholds for comparison remains underexplored.
Objectives/Aims: This study aimed to investigate clinical differences, including disability level, relapse frequency, and MS type, between patients diagnosed with LMOMS and LAOMS.
Methods: Patients with MS were grouped into two categories based on the age of onset: LMOMS (onset between 50 and 60 years) and LAOMS (onset after 60 years). Data regarding the Expanded Disability Status Scale (EDSS) scores, demographic information, disease duration, and relapse frequency were retrospectively collected and analyzed.
Results: A total of 89 patients with MS were included: 12 in the LMOMS group and 77 in the LAOMS group. The mean age at diagnosis was significantly higher in the LAOMS group compared to the LMOMS group (68.25 ± 3.77 vs. 57.34 ± 4.20, $p<0.001$), and the mean age of patients was also higher in LAOMS (78.00 ± 7.19 vs. 68.32 ± 4.78, $p<0.001$). However, no significant differences were observed between the groups regarding disease duration, EDSS scores at the first and last visit, total number of relapses, or relapses per year. MS subtypes were similarly distributed across both groups: LMOMS (RRMS: 44, SPMS: 12, PPMS: 21), and LAOMS (RRMS: 5, SPMS: 1, PPMS: 6).
Conclusion: Although patients with LAOMS were older and diagnosed later than those with LMOMS, there were no significant differences in disability progression, relapse frequency, or MS subtype distribution. These findings suggest that the age of onset beyond 50 years does not substantially alter the clinical course of MS, underscoring the importance of individualized care regardless of onset age.

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P1009
Clinical Integration Of Brain And Cord Mri Features Improves Differential Diagnosis Of Multiple Sclerosis

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Introduction: Accurate diagnosis of multiple sclerosis (MS) requires early recognition and careful exclusion of alternative conditions. Advances in understanding MS differential diagnoses have improved the identification of magnetic resonance imaging (MRI) features that help distinguishing MS from other mimicking conditions.
Objectives/Aims: To explore the role of brain and spinal cord MRI features in differentiating patients with suspected central nervous system (CNS) inflammatory diseases.
Methods: Prospective data from 125 patients undergoing diagnostic evaluation, including 1.5T brain and spinal cord MRI scans from February 2021 and March 2024 were analyzed. The cohort comprised 91 patients with MS, 15 with other inflammatory neurological diseases (OIND), and 19 with non-inflammatory neurological diseases (NIND). Brain and spinal cord lesion topographies and morphological features were evaluated to identify MRI features discriminating MS from OIND and NIND.
Results: Random forest analysis identified key MRI features supporting MS diagnosis over OIND: absence of longitudinally extensive transverse myelitis (relative importance [RI]=100%), presence of ⩾1 Dawson's finger (RI=55.3%), ⩾1 cortical lesion (RI=42.6%), and ⩾1 brain T2-hyperintense white matter (WM) lesion (RI=36.4%). After excluding the presence of ⩾1 brain T2-hyperintense WM lesion, fulfilling ⩾2 of the 3 selected criteria distinguished MS from OIND patients with a sensitivity of 0.59 and a specificity of 0.80. For distinguishing MS from NIND, relevant MRI features included ⩾1 T2-hyperintense spinal cord lesion (RI=100.0%), ⩾1 Dawson's finger (RI=84.3%), ⩾1 cortical lesion (RI=61.4%), ⩾1 cerebellar peduncle lesion (RI=52.2%) and ⩾3 central vein sign-positive lesions (RI=27.8%). Fulfilling ⩾2 of the 5 selected criteria identified MS patients with a sensitivity of 0.64 and a specificity of 0.84.
Conclusion: Integrating specific MRI features in the diagnostic work-up of patients with suspected CNS inflammatory disease improves differentiation between MS, OIND, and NIND, reducing the risk of misdiagnosis.

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P1010
Clinical characteristics, diagnostic accuracy, and outcomes of anti-NMDAR encephalitis: Experience from a Latin American tertiary centre

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Introduction: Anti-N-methyl-D-aspartate receptor encephalitis (NMDARE) is the most prevalent autoimmune encephalitis, predominantly affecting young females. Despite established diagnostic criteria, its clinical heterogeneity, especially in non-Western, Educated, Industrialized, Rich, and Democratic (WEIRD) populations, poses diagnostic and therapeutic challenges.
Objectives/Aims: This study aimed to characterize the demographic, clinical, and radiological features of NMDARE in a Latin American tertiary referral centre, with a focus on age-related-differences between paediatric and adult patients.
Methods: We conducted a retrospective cohort study, of patients with NMDARE between January 2016 and December 2024. Cases were included if anti-NMDAR antibodies were confirmed. Demographic, clinical, and paraclinical data were extracted from clinical records. Comparative analyses between paediatric (⩽18 years) and adult patients (> 18years) were performed using parametric and non-parametric statistical tests based on data distribution.
Results: Among 1026 screened patients, 58 tested positive for anti-NMDAR antibodies,
with 49 meeting inclusion criteria (paediatrics n=23, adults n=26). Median age at onset
was 20 years (IQR: 4.5–33.5); female predominance was higher in adults (61.5% vs.
30.4%; p=0.03). Adults presented more frequently with confusion (57.7% vs. 13%; p=0.003), mood disturbances (61.5% vs. 26.1%; p=0.03), cognitive impairment (76.9% vs. 36.1%; p=0.001), and dysautonomia (19.2% vs. 0%; p=0.04). In contrast, paediatric patients exhibited a higher prevalence of speech disturbances (56.5% vs. 34.6%; p=0.02). EEG alterations were more frequent among paediatrics (69.6% vs. 42.3%; p=0.01). No significant differences were observed in hospitalization duration, rates of intensive care unit (ICU)admission or and treatment responses. Across the entire cohort, CSF pleocytosis (> cells/mm^3) was associated with an increased likelihood of ICU admission (OR=11, p=0.01). Relapses occurred in 10% of patients.
Conclusion: NMDARE presents distinct age-related clinical phenotypes. While current diagnostic criteria remain broadly applicable, the observe differences underscore the need for age-adapted diagnostic and management strategies. The predominance of EEG abnormalities in paediatrics patients and psychiatric manifestations in adults may guide more tailored clinical approaches.

Disclosure of interest: The authors have nothing to disclose related to this abstract

P1011
The value of oligoclonal bands in multiple sclerosis compared to other neurological disorders: a retrospective data analysis from an Austrian tertiary center

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Introduction: Cerebrospinal fluid (CSF) analysis is key to diagnosing multiple sclerosis (MS). In particular, the presence of CSF-specific oligoclonal bands (OCB) is examined alongside differential diagnostic aspects.
Objectives/Aims: This study aims to investigate the diagnostic value of OCB in MS compared to other neurological disorders.

Methods: Patients who presented to the Department of Neurology of the Medical University of Vienna between January 1, 2004, and December 31, 2020, due to neurological complaints and underwent lumbar puncture (LP) for diagnostic purposes were included in this retrospective analysis. Exclusion criteria were incomplete laboratory data and/or a missing final diagnosis.
Results: Of 5,744 patients who underwent LP, 5,225 were available for analysis. Of these, 745 (14.3%) were diagnosed with MS whereby CSF-specific OCB showed a sensitivity of 92.8% and a specificity of 90.4%. While the positive predictive value (PPV) was merely 61.5%, the negative predictive value (NPV) yielded 98.7%. In comparison, OCB displayed low sensitivity rates for most other neurological disease groups. Of note, neuroborreliosis (n=66) had a relatively high OCB positive rate of 70%, followed by central nervous system human immunodeficiency virus infections (n=32) with 62.5%.
Conclusion: CSF-specific OCB have a high sensitivity and specificity and a very high NPV for diagnosing MS. However, the PPV was lower in this cohort. These findings must be carefully considered when diagnosing MS and interpreting OCB, especially in the context of differential diagnostic workup.

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P1012
Investigating the diagnostic challenges of Multiple Sclerosis in Iran: Insights from clinicians

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Introduction: MS diagnosis can be delayed due to a variety of barriers encountered by both healthcare providers and patients. Timely diagnosis is critical for disability prevention through initiation of disease-modifying therapy. Previous studies have demonstrated that regional differences, including availability of healthcare resources and cultural factors, may influence access to early MS diagnosis and suggest the need for identifying country-specific barriers to MS diagnosis.
Objectives/Aims: The objective of this study is to identify the barriers to MS diagnosis in Iran from the perspective of neurologists.
Methods: A cross-sectional study was conducted implementing a questionnaire adapted from the MS International Federation (MSIF) Atlas of MS, 3rd Edition, and the MSIF 2024 Topical Survey, with the addition of questions relevant to MS diagnosis in Iran. The questionnaire was made available to the Iranian neurology community through an online social media platform. Data were collected from April 1 to June 30, 2024.
Results: The survey was completed by 103 neurologists (34.1% response rate), including 64 general neurologists (GN) and 39 MS specialists (NMS). Participants were 47.4 ± 9.6 years old on average, and most (58.3%) were employed at educational institutions. Eighty percent of respondents reported at least one

major barrier to early MS diagnosis. These comprised a lack of public awareness of MS symptoms (43.7%), inadequate awareness among healthcare practitioners (37.9%), and patient unwillingness to undergo diagnostic testing due to social stigma (77.3%). While magnetic resonance imaging (MRI) was widely accessible and frequently used by physicians, there were differences in access to other paraclinical tests for diagnosing MS, such as optical coherence tomography (OCT), myelin oligodendrocyte glycoprotein immunoglobulin G (MOG-IgG) testing, visual evoked potentials (VEP), and aquaporin-4 immunoglobulin G (AQP4-IgG) testing. The majority of respondents (98.05%) stated that they followed national MS diagnostic guidelines; however, 16% of GNs and 4% of NMSs stated they did not utilize the McDonald criteria for MS diagnosis due to a lack of awareness or training.

Conclusion: Barriers to timely MS diagnosis in Iran are diverse, and suggest unmet needs for public awareness, healthcare professional education, and access to critical resources. Addressing these barriers through targeted education and improved infrastructure may ultimately improve clinical outcomes in patients with MS in Iran.

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P1013
Diagnostic clues in etiologic diagnosis of longitudinally extensive transverse myelitis, a retrospective study

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Introduction: Longitudinal extensive transverse myelitis (LETM) is defined as a spinal cord lesion extending across three or more vertebral segments. In routine neurological practice, establishing the correct diagnosis can be challenging due to the wide range of potential etiologies.

Objectives/Aims: The aim of this study is to review the etiologies of LETM and describe the clinical presentation associated with each etiology.

Methods: A retrospective review was performed of patients diagnosed with LETM at a tertiary centre between 2012 and February 2025. Recorded variables included demographic data, etiologies, clinical and radiologic presentation, lumbar puncture, autoimmune panels, treatments administered and the clinical evolution. Data were compared between etiological groups.

Results: A total of 47 patients with LETM were included (mean age 51 years, 53% female). The most common diagnosis was idiopathic LETM in 13 patients (28%), followed by neuromyelitis optica (NMO) in 10 (21%), infectious causes, tumour-related, and dural arteriovenous fistula in 4 each (9%), lupus (LES)-associated in 3 (6%), anti-myelin oligodendrocyte glycoprotein (MOG) antibody-associate disease and sarcoidosis in 2 each (4,1%), and single cases of multiple sclerosis, venous infarction, ischemia, nutritional deficiency and glial fibrillary acidic protein (GFAP) astrocytopathy (2% each).

Clinical features varied by etiology. Conus involvement was present in 100% of anti-MOG and in 75% of fistula cases, but only 20% of NMO cases. Subacute onset was more common in fistula, tumour-related and sarcoidosis (median time to nadir of 123, 195 and 317 days, respectively), whereas inflammatory causes such as NMO, infectious, MOG and LES-related LETM presented acutely (median nadir $<$30 days).

Tumor-associated LETM had the longest median lesion length (18 vertebral segments), followed by anti-MOG (14.5 segments). Contrast enhancement was observed in 100% of tumor- and fistula-related cases.

NMO had the poorest prognosis, with only 10% of patients achieving complete or near-complete recovery. In contrast, patients with LES-associated and anti-MOG disease showed complete recovery in 100% of cases. Sphincter involvement was seen in all patients with anti-MOG and fistula-related LETM.

Conclusion: In patients with new-onset LETM, the most frequent diagnosis was idiopathic, followed closely by neuromyelitis optica. Clinical presentation can provide important diagnostic clues and should be carefully considered in the evaluation of LETM.

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P1014
Optic neuritis characterization in a Colombian specialized institution: 10 years of experience

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Introduction: Optic neuritis (ON) is caused by diverse diseases frequently leading to vision loss. Differentiating its etiology is crucial for diagnosis, treatment, and prognosis.
Objectives/Aims: To characterize patients diagnosed with ON at the Neurological Institute of Colombia from January 2014 to January 2023.
Methods: A retrospective observational study was conducted on adult patients with possible or definitive ON according to the 2022 criteria. We evaluated sociodemographic data, clinical manifestations, etiology and MRI findings. A comparative analysis between the main CNS autoimmune causes of ON and other etiologies, as well as between MS-ON and AQP4+NMOSD (aquaporin-4 positive neuromyelitis optica spectrum disorder)-ON was performed.
Results: 204 patients were included in the study. The main ON etiologies were idiopathic (39.7%), MS (23.6%), and AQP4+NMOSD (22.6%). Comparison between the main CNS (central nervous system) autoimmune causes of ON (MS, NMOSD, MOGAD, ADEM) and other etiologies of ON shows: younger age at diagnosis (36 vs. 45 years, $p<0.001$), less headache (40.4% vs. 59.6%, p=0.02), less optic disc edema (36.5% vs. 63.5%, p=0.008), higher CSF pleocytosis (81.8% vs. 18.2%, $p<0.001$), higher proportion of oligoclonal bands (78.6% vs. 21.4%, $p<0.001$), and a higher recurrence rate (71.4% vs. 28.6%, $p<0.001$). In a subgroup analysis, MS-ON versus AQP4+NMOSD-ON demonstrates: older age at diagnosis ($p<0.001$), milder visual impairment (82.1% vs. 17.9%, $p<0.001$), higher proportion of oligoclonal bands (90.9% vs. 9.1%, $p<0.001$), less proportion of nerve contrast enhancement (44.9% vs. 55.1%, p=0.025), absence of longitudinally extensive lesions (0% vs. 100%, p=0.048), more posterior involvement (71.4% vs. 28.6%, p=0.014), and less intraorbital involvement (37.1% vs. 62.9%, p=0.023) in patients with MS-ON.
Conclusion: Idiopathic ON, MS, and AQP4+ NMOSD were the most common causes of ON in our cohort, consistent with international data. Our study identified distinct clinical and radiological features that can help differentiate MS-related ON from NMOSD-related ON, which can aid in diagnosis and inform treatment decisions in clinical practice.

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P1015
When Ockham's Razor Does Not Apply: Ischemic Retinopathy in a Patient with Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS) is a neurodegenerative, inflammatory disease of the central nervous system, with multifactorial etiology and chronic progression. The clinical presentation at onset depends on the location of the demyelinating lesions. Optic neuritis occurs as the first presentation in approximately 25% of cases.
Objectives/Aims: -
Methods: -
Results: A 59-year-old man, previously diagnosed with MS, presented with a painless decrease in visual acuity in the right eye, noted upon waking, although reporting prior nonspecific visual changes over the past two months. On initial evaluation, notable findings included inferior nasal quadrantopsia and relative afferent pupillary defect on the right eye, without dyschromatopsia or papilledema on fundoscopy. The ophthalmological examination of the right eye revealed scotoma in the inferior nasal field and retinal pallor in the superior temporal arc. The etiological investigation revealed: a sedimentation rate below the reference value (8 mm/1st hour), dyslipidemia; magnetic resonance imaging of the neuroaxis showed subtle T2 FLAIR hyperintensity in the intracanalar segment of the right optic nerve, with no enhancement with gadolinium, of uncertain chronology, and no new demyelinating lesions in the brain or spinal cord, as well as no imaging signs compatible with activity in previously existing lesions; cervical and transcranial Doppler ultrasound showed no significant abnormalities; transesophageal echocardiography showed a patent *Foramen Ovale* and an aneurismatic interauricular septum. The diagnosis of ischemic retinopathy in the right eye was made, and secondary prevention for stroke was initiated. There

was also an existing optic nerve lesion, likely chronic, unrelated to the acute symptoms.
Conclusion: This case emphasizes the need to maintain a high clinical suspicion for alternative diagnoses, even when the clinical presentation appears consistent with an exacerbation of a known chronic disease. In MS-related optic neuritis, the fundoscopic examination is typically unremarkable. Therefore, the presence of retinal abnormalities - such as retinal pallor, as seen in this case - is atypical and should prompt evaluation for other possible underlying causes.

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P1016
Glial Fibrillary Acidic Protein Astrocytopathy: Clinical Presentations, MRI Features, and Treatment Responsiveness based Based on a Two-center Chinese Cohort Study

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Introduction: Glial fibrillary acidic protein astrocytopathy (GFAP-A) is a recently defined nosological form belonging to the class of autoimmune inflammatory disorders affecting the central nervous system (CNS).
Objectives/Aims: Here we report the clinical and MRI characteristics, treatment, and prognosis of a GFAP-A cohort from two centers in China.
Methods: We retrospectively analysed the data from 42 adult patients diagnosed with GFAP-A between June 2019 and September 2024. Clinical features, semi-quantitative antibody test results, MRI features, treatment approaches, and prognosis were collected.
Results: Among the 42 patients, 27 were male and the median age at disease onset was 47.5 years. The clinical phenotype included myelitis (23.8%), encephalomyelitis (28.6%), encephalitis (19%), meningoencephalomyelitis (16.7%), meningitis/spinal meningitis (9.5%), and peripheral neuropathy (2.4%). In enhanced MRI images, 5 (11.9%) of the patients showed enhancement of the cerebral meninges, 2 (4.8%) had enhancement of the ependyma, and 6 (14.3%) had enhancement of the spinal cord pia mater. 76.9% of the patients responded to the glucocorticoid treatment while 69% had a monophasic course. Spearman correlation analysis showed that the presence of oligoclonal bands in CSF significantly correlated with 1-year relapse (CI=0.65, P = 0.001).
Conclusion: The clinical manifestations of GFAP-A are highly diverse, encompassing encephalitis, myelitis, and meningitis, including spinal meningitis. The enhancement of the spinal pia mater and ependyma on MRI were confirmed. Most patients exhibit a positive response to glucocorticoid therapy. The presence of oligoclonal bands in CSF could potentially serve as an indicator for predicting recurrence.

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P1017
The Kappa Free Light Chain index has a high diagnostic accuracy and concordance with Oligoclonal Bands when tested prospectively in suspected cases of Multiple Sclerosis

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Introduction: The 2024 McDonald criteria include the kappa free light chain index (κFLCi) as interchangeable with oligoclonal bands (OCB). The 6.1 cut-off has been suggested as appropriate but a prior consensus recommended additional OCB testing in case of κFLCi values in a grey zone between 2.4 and 20.0.
Objectives/Aims: To assess the concordance between the κFLCi 6.1 cut-off and OCB in suspected MS, to test other κFLCi cut-off within the grey zone and to compare different platforms/assays.
Methods: Observational study including patients with suspected MS from two centres. κFLCi and OCB were tested using

the same paired CSF and serum samples through turbidimetry (Barcelona) or nephelometry (Lisbon). Concordance between κFLCi and OCB was evaluated using Cohen's kappa. McNemar's test was used to assess cut-offs in the grey zone. Diagnostic performance was assessed using ROC curves.

Results: Of 203 patients were included, 70.4% were female, mean age was 43.08 (±14.42) years and median follow-up 14.0 (IQR 11.5) months. At baseline, 136 (67.0%) had ⩾1 demyelinating attack, 21 (10.3%) objective progression and 46 (22.7%) incidental MRI findings. MS was diagnosed in 105 (51.7%) patients according to the 2024 McDonald criteria; 14 (6.9%) had findings suggestive of MS but did not meet the criteria; 50 (24.6%) had other inflammatory conditions and 34 (16.8%) had non-inflammatory conditions. Concordance between the κFLCi 6.1 cut-off and OCB was substantial (87.7%, kappa=0.747, $p<0.001$). Non-concordant cases (n=25, 12.3%) predominantly showed negative OCB (n=18, 72.0%). Of these, 6 had MS, 3 had findings suggestive of MS but did not meet the diagnostic criteria, 5 had other inflammatory conditions and 4 had non-inflammatory diseases. Of 7 (28.0%) non-concordant cases with positive OCB, 6 met MS diagnosis and 1 was seronegative NMOSD. Both OCB and κFLCi had a sensitivity of 87.6% while specificity was 78.6% and 67.4%, respectively. McNemar's test showed no difference between 6.1 and other tested cut-offs in the grey zone ($p>0.05$). Nephelometry showed slightly lower sensitivity (85.2%) and higher specificity (70.0%) compared to turbidimetry (90.2% and 65.5%, respectively). ROC curves revealed AUCs of 0.860 for nephelometry and 0.828 for turbidimetry, with overlapping confidence intervals.

Conclusion: The 6.1 cut-off for κFLCi shows comparable diagnostic performance to OCB in MS diagnosis. Nephelometry and turbidimetry methods perform similarly, proving that κFLCi provides reliable information across methods for MS diagnosis.

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Sclerosis (BioMS-eu) steering committee, the MOGAD Eugene Devic European Network (MEDEN) steering group, and the Platform Adaptive Trial for remyelination and neuroprotection in mUltiple Sclerosis (PLATYPUS) steering committee. She is a recipient of grants PI19/01590 and PI22/01570, awarded by the Instituto de Salud Carlos III (ISCIII), Ministerio de Ciencia e Innovación de España.

P1018
Slow Learning or Memory Deficit? Survival Analysis of Episodic Memory Performance in MS

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Introduction: Episodic memory impairments are common in people with multiple sclerosis (pwMS), and their link with slowed information processing speed (IPS) has been documented. However, a key challenge remains: distinguishing true memory dysfunction from performance deficits driven primarily by slowed IPS. Traditional neuropsychological assessments often fail to disentangle these mechanisms, as they rely on fixed trial structures that do not account for individual differences in learning speed.
Objectives/Aims: This study contributes to the existing literature by investigating the impact of IPS on episodic memory performance in MS using a survival analysis approach. Rather than focusing solely on how much is learned, we examine how long it takes pwMS to reach a learning criterion. Survival analysis can highlight differences in the rate of progress toward the learning goal (i.e., learning trajectories).
Methods: We retrospectively analyzed data from 157 persons with MS (pwMS, 66 RRMS, 57 SPMS, 40 PPMS) and 109 healthy controls (HC) who completed the Selective Reminding Test (SRT). Learning efficiency was assessed using time-to-event (survival) analysis, measuring the number of trials required to achieve two consecutive full recalls of a word list (SRT-goal). Additionally, pwMS were classified as having preserved or impaired IPS based on standardized IPS assessments.
Results: PwMS required significantly more trials to reach the SRT-goal than HC (mean: 10.23 vs. 8.52 trials, $p < .001$). IPS played a critical role in learning success: only 12.7% of IPS-impaired pwMS achieved the SRT-goal compared to 59.3 % of those with preserved IPS. The log-rank test indicates significant differences between the groups ($\chi^2 = 27.78$; $p < .001$, $\phi = 0.45$), confirming that the difference in survival distributions is statistically significant. Comparing MS-subtypes, 60% of relapsing-remitting MS (RRMS) patients reached the SRT goal, whereas only 15.8% of secondary progressive MS (SPMS) and 15% of primary progressive MS (PPMS) patients did.
Conclusion: Survival analysis provides new insights into the learning dynamics of pwMS and highlights IPS as a key factor in episodic memory impairment. These findings underscore the need for assessment tools that distinguish memory deficits from slowed IPS and suggest potential targets for cognitive rehabilitation strategies in MS.

Disclosure of interest: B.Degraeve: Nothing to disclose

P1019
Diagnostic Evaluation of Patients with Suspected Atypical Demyelinating Diseases: A Comprehensive Analysis of Differential Diagnoses

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Introduction: Atypical demyelinating syndromes (ADS) differ from multiple sclerosis (MS) in clinical presentation, treatment response, and MRI findings. Accurate differential diagnosis is essential, as infectious, vascular, and neoplastic conditions can mimic ADS, potentially leading to misdiagnosis and inappropriate treatment. Neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are key entities within the ADS spectrum, with distinct clinical and biomarker profiles.
Objectives/Aims: To characterize the differential diagnoses of patients referred for suspected ADS over a 10-year period at a Brazilian tertiary center, and to evaluate the frequency of demyelinating and non-demyelinating conditions, inflammatory and non-inflammatory etiologies, and disease recurrence.
Methods: This retrospective observational study reviewed medical records from patients referred between 2015 and 2025 to the Atypical Demyelinating Diseases Clinic at Hospital das Clínicas da Faculdade de Medicina da USP. Inclusion criteria were adults with suspected ADS; MS cases diagnosed prior to referral were excluded. Final diagnoses were based on clinical, radiological, and laboratory data, including antibody testing for AQP4-IgG and MOG-IgG using a cell-based assay.
Results: Of 1,590 patients screened, 564 met inclusion criteria. NMOSD was the most common diagnosis (53.7%), followed by MOGAD (9.4%), and atypical MS (8.2%). Inflammatory causes accounted for 94.7%, with demyelinating diseases comprising 91.8% of cases. Infectious mimics (1.2%) included neuroschistosomiasis, arboviruses, and HTLV-1. Vascular mimics (3.7%) included ischemic myelopathy and arteriovenous fistulas. Only one neoplastic case was identified. Most patients (67.2%) had recurrent disease. Antibody testing timing was critical for accurate diagnosis, especially in MOGAD.
Conclusion: ADS encompass a wide range of disorders, predominantly inflammatory and demyelinating. NMOSD and MOGAD were the most frequent diagnoses. Correct and timely diagnosis is crucial to guide treatment, particularly in regions with high infectious disease prevalence and limited access to antibody testing. Multidisciplinary evaluation enhances diagnostic precision.

Disclosure of interest: Nothing to disclose

P1020
Early Clues and Prognostic Insights in Double-Seronegative Longitudinally Extensive Transverse Myelitis (dsLETM)

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Introduction: Double-seronegative longitudinally extensive transverse myelitis (dsLETM) is a rare and heterogeneous inflammatory spinal cord disorder defined by lesions extending over three vertebral segments with negative myelin oligodendrocyte glycoprotein (MOG) and Aquaporin-4 (AQP4) antibodies (Ab) at onset and throughout follow-up. Its ethiology encompasses a broad differential diagnosis with varying long-term risk of disability.
Objectives/Aims: This study aimed to describe demographic and clinico-radiological features and to assess treatment response and outcomes.
Methods: Retrospective observational study with prospective data collection from two European Neuroimmunology Units. Patients with LETM and persistently negative MOG/AQP4-Ab were included. Alternative causes were excluded.
Results: Twenty-six patients (53.8% male; 69.2% Caucasian; median age 43.5 years [IQR 30–48]) were included. A monophasic course was observed in 77%. Isolated spinal cord involvement was present in 88.5%, while 11.5% had multifocal CNS relapses.
Ethiology was unclear in most cases: idiopathic (53.8%), parainfectious (26.9%) or post-vaccinal (3.8%). A well-supported diagnosis was reached in 15%: CNS-vasculitis, Systemic lupus erythematosus-Sjögren overlap, Neurosarcoidosis and Primary Progressive MS. All patients presented subacutely. At nadir: 7.7% had mild (EDSS 0–2), 2.1% moderate (EDSS 3–4) and 61.5% severe (EDSS >5) disability. Moderate-to-severe motor impairment occurred in 57.7%, including lower limb weakness (61.5%) and tetraparesis (11.5%). At nadir, 7.7% required walking aids and 53.8% were bed-bound. Sensory level was present in 61.5% and 88.5% had sphincter dysfunction.
CSF was inflammatory in 57.7% (median cells 22 [IQR 3.75–38], 70% mononuclear). MRI showed a median of 10 vertebral segments affected (IQR 6–18.5); gadolinium enhancement in 61.5%. Thoracic vertebral segments were involved in 76.9%, cervical in 61.5%, and the entire spinal cord in 30.8%.
All received acute treatment: 87% intravenous steroids, 30.8% plasmapheresis, 7.7% intravenous immunoglobulin and 11.5% other immunosuppressant (IS); 70% responded, 27% free of disabling symptoms. 77% remained on long-term IS. After a median follow-up of 43.5 months (IQR 19–90), median EDSS was 4 (IQR 2.1–5.9) and 50% remained ambulatory.
Worse neurological outcomes (EDSS >4) were significantly associated with male sex (p=0.043), higher number of vertebral segments affected (p=0.046, r=0.56), motor severity at onset (p=0.04), and suboptimal acute-phase response (p=0.016 for EDSS; p=0.05 for ambulation).
Conclusion: dsLETM may represent a clinical manifestation within a broader spectrum of systemic and neurological disorders rather than a distinct entity. Early clinic-radiological features, as nadir motor impairment and extension of spinal cord lesion, and response to acute treatment may offer valuable prognostic insights.

Disclosure of interest: Nothing to disclose

P1021
Long-term follow-up of patients with radiologically isolated syndrome: a report from Iran

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Introduction: Evidence regarding MS conversion rates and risk factors in patients with radiologically isolated syndrome (RIS) is still limited, and no consensus is made regarding the initiation of disease-modifying therapies (DMTs) for these patients.
Objectives/Aims: We aim to provide real-world data on our neurologists' approaches to RIS patients and their outcomes.
Methods: We searched in the medical records of patients referred to the Sina Clinic of Demyelinating Disorders. A total of 66 patients diagnosed with RIS were found until November 20th, 2023. Patients who did not return for follow-up visits were excluded, resulting in 53 patients entering analysis. Two trained medical doctors extracted patients' clinical and demographic characteristics into record sheets, including imaging reports, conversion to MS, visit dates, and DMTs. The information in the record sheets was checked with the patients' corresponding neurologists. Follow-up duration was defined in months, from their first to their last visits. Quantitative variables are reported as median ([interquartile range], range).
Results: The median age at diagnosis was 32.0 ([27.0 - 36.0], 13:58) years old, and 43 (81.1%) were female. The median follow-up duration was 93 months ([63.0-108.0], 2:195). Fifteen patients (28.3%) had a family history of MS, and nine patients (17.0%) had a history of autoimmune diseases. A total of 19 patients (35.8%) experienced conversion to MS. Out of 41 (73.4%) RIS patients that did not receive medical treatment, 17 (41.5%) converted to MS, 4 (9.8%) experienced asymptomatic new T2 MRI lesions, and 20 (48.8%) remained stable. The other 12 RIS patients (22.6%) received DMTs. Seven patients (13.2%) were prescribed DMTs upon diagnosis. An additional five patients (9.4) received DMTs at follow-up appointments due to new demyelinating changes in their brain MRIs. Of the 12 RIS patients on DMTs, two (16.7%) converted to MS, one (8.3%) had new T2 lesions on follow-up, and 9 (75%) remained stable. Patients were prescribed low-efficacy DMTs except for two patients who were given Fingolimod. Additionally, one patient under treatment with dimethyl fumarate was switched

to rituximab due to new T2 lesions. The Median time to MS transition and time under treatment with DMTs were 36.0 ([20.5 – 63.0], 2:101) and 55.5 ([35.3 – 94.5], 2:108) months, respectively.
Conclusion: The overall conversion rate of RIS patients to MS was 35.8%. Among those treated with DMTs, the conversion rate was 16.7%, compared to 41.5% in untreated patients. However, the design of this study is descriptive, and future comparative studies are warranted to further explore these findings.

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P1022
Distinct Features Of Patients With Scleroderma Associated Autoantibodies And Cns Demyelinating Disease Compared To Ms

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Introduction: Although screening for antibodies (Abs), related to systemic autoimmune diseases (SAD), is often performed in patients with CNS demyelination to exclude mimickers and confirm MS diagnosis, systemic sclerosis (SSc) associated Abs are rarely reported in this context.
Objectives/Aims: To describe patients with CNS demyelination and SSc Ab reactivity and their distinct features compared to MS patients, negative for SAD-associated Abs.
Methods: Among 758 patients evaluated for CNS demyelination, over 6 years, we detected 34 (4.5%) cases with SSc associated Abs (anti-Scl70, anti-CENPB and anti-PM-Scl100), via immunoblot testing (EUROIMMUN) (SSc-Ab group). 249 consecutive, treatment-naive, MS patients served as controls.
Results: SSc-Ab patients were predominantly females (73.5%), with a median age of 41 years and with a higher incidence of hyperlipidaemia/hypertension compared to MS (27.3% vs 8.7%, p:0.002 and 24.2% vs 7.4%, p:0.002 respectively). SSc-Ab group showed a higher prevalence of bowel/bladder and cortical clinical signs vs MS (27.3% vs 13.8% p:0.44 and 9.1% vs 1.2% p:0.004 respectively). Radiologically, SSc-Ab patients presented more frequently combination of small vessel disease (SVD) and typical MS lesions compared to MS (20.6% vs 4.4% p:$<$0.0001). Contrarily, lesions exclusively typical for MS were observed less often in SSc-Ab vs MS patients (70.6% vs 85.2% p:0.031). Moreover, SSc-Ab cases had lower 25-OH-vitamin-D levels, higher serum angiotensin-converting enzyme levels and longer activated partial thromboplastin time vs MS [median (IQR)] [(15.1(13.8) vs 22.8(11.4) ng/mL p:0.016, 41.8(20.2) vs 28.7(23.3) U/L p:0.022 and 27.5(4.5) vs 25.7(4.0) sec p:0.001 respectively]. Sicca, arthralgias and rash were the main clinical autoimmune features (33.3%, 30.0% and 23.3% respectively). One patient was diagnosed with undifferentiated connective tissue disease but none with SSc.
Conclusion: SSc associated Abs are detected in a minority of patients with CNS demyelination and linked to distinct features, involving vascular pathology. Their pathogenetic role and possible correlation with underlying autoimmunity remain to be elucidated.

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P1023
A Multimodal Approach to Identify relevant biomarkers in MS: May we distinguish different phenotypes at the time of diagnosis?

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Introduction: Multiple sclerosis (MS) is a heterogeneous disease with variable clinical outcomes.
Objectives/Aims: In this study we aimed to build a prediction model that combines Principal component analysis (PCA) and cluster analysis for identifying sets of biomarkers associated with MS at the time of diagnosis and for characterizing, if any, distinct MS phenotypes.
Methods: In this monocentric, cross-sectional study MS patients naïve to therapy were evaluated at the time of MS diagnosis. Clinical, laboratory, and neuroimaging data were gathered, including optical coherence tomography (OCT) for retinal layer assessment and serum neurofilament light (NFL) measurements. We first applied PCA to reduce data dimensionality and reveal key biomarker correlations. Subsequently, K-means clustering was used to classify patients into distinct phenotypic groups.
Results: A total cohort of 71 patients with MS was enrolled, mean age 35.7 years (SD=9.8). PCA yielded five components with eigenvalues greater than 1.0, collectively accounting for 68.12% of the total variance in the dataset. Component 1 was characterized by strong negative coefficients for retinal thickness measurements (GCIPL: -0.82, pRNFL: -0.79, mRNFL: -0.75) and a moderate positive coefficient for serum NFL (0.45), suggesting an inverse relationship between retinal integrity and neurodegeneration. Component 2 was primarily characterized by high positive coefficients for NFLs, in both cerebrospinal fluid (CSF NFL: 0.88) and serum (sNFL: 0.56). This indicates that patients with elevated NfLs tend to share a common patterns independently from other variables.
K-means clustering of the PCA-transformed data identified two distinct patient subgroups (Cluster 0: n=38; Cluster 1: n=33).

Between-cluster comparisons revealed significant differences in several key variables. Cluster 1 patients exhibited significantly thicker retinal layers (GCIPL: 72.4 vs. 64.8 μm, p=0.003; mean pRNFL: 98.3 vs. 89.7 μm, p=0.002) and better cognitive performance (mean SDMT z-score: -0.31 vs. -0.89, p=0.01; mean BVMT-R z-score: -0.22 vs. -0.76, p=0.008) compared to Cluster 0. Notably, Cluster 1 patients also displayed significantly higher serum NFL levels (mean: 18.6 vs. 12.3 pg/mL, p=0.007), despite their better structural and cognitive profiles.
Conclusion: The ordered application of PCA and clustering highlights possible MS phenotypes at the time of diagnosis. The numerical differences in retinal thickness and NFL levels underscore the potential of this multimodal biomarker approach to enhance early diagnosis and guide personalized treatment strategies. Future longitudinal studies will further validate these findings.

Disclosure of interest: All the authors have nothing to disclose related to the submitted manuscript

P1024
MRI features of central nervous system involvement in 104 Moroccan patients with Neuro-Behcet's disease

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Introduction: Behçet's disease (BD) is a recognized as a chronic relapsing heterogeneous multisystem inflammatory disorder and a vasculitis of unknown origin which has a peculiar epidemiology. Neurologic involvement has been reported to be less common than other systemic manifestations, but can cause substantial disability.
Objectives/Aims: Our purpose is to determine the magnetic resonance imaging (MRI) patterns in patients with neuro-Behçet's disease (NBD) who had neural parenchymal involvement and cerebral venous thrombosis (CVT).
Methods: This is a retrospective study of 104 patients presenting with BD and neurological involvement, collected over a period of 23 years. The MRI neurobehçet's disease (NBD) patients, associated with parenchymal involvement in 86 cases (82.7%) and CVT in 18 cases (17.3%) were reviewed. In this series, we studied the anatomic-radiologic location and the distribution of the lesions, in order to define the MRI patterns of neurological involvement.
Results: 86 (82.3%) patients had parenchymal and 18 (17.3%) had non-parenchymal NBD. Concerning parenchymal CNS pattern, brain MR imaging (MRI) showed hypointense lesions on T1-weighted and hyperintense lesions on T2 and FLAIR-weighted images, involving mostly the brainstem (84.8%), basal ganglia (68.6%), cerebral white matter (53.4%), internal capsule (47.6%) and thalamus (46.5%). The most common imaging finding in NBD patients who had neural parenchymal involvement was the mesodiencephalic region in 67 (77.9%) patients, the capsulo-diencephalic region in 34 patients (39.5%) and the pontobulbar region in 18 (20.9 %) patients. For the extraparenchymal pattern, the brain MRI results of our series showed that the venous involvement was isolated superior sagittal sinus (SSS) thrombosis in 8 patients (44.4%), isolated lateral sinus (LS) thrombosis in 4 patients (22.2%), and concomitant SSS and right lateral sinus thrombosis in 3 patients (16.6%). CVT resulted in a spontaneous hyperintense aspect of the sinus on MRI with the absence of secondary changes such as venous infarct or hemorrhagic transformation in all of our patients, and the MRV confirmed the diagnosis in all of our 18 patients by the absence of sinus visualization.
Conclusion: Brain MRI study including contrast and MR angiography (MRA) especially MR venography (MRV), are mandatory in categorizing the neurological involvement and both should be used routinely in cases of suspected NBD. This commonly demonstrates characteristic features especially in acute/sub-acute parenchymal involvement and differentiates NBD from other CNS inflammatory disorders that mimic NBD patterns.
Key words: Behçet's, parenchymal, venous, thrombosis, MRI.

Disclosure of interest: nothing to disclose

P1025
Prevalence of Multiple Sclerosis misdiagnosis in two referral centers in Iran

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Introduction: MS symptoms and MRI findings overlap with other conditions, complicating diagnosis and increasing the risk of misdiagnosis. Little is known about the prevalence and causes of misdiagnosis of MS in Iran, and such data could improve patient outcomes.
Objectives/Aims: This study aims to determine the prevalence of MS misdiagnosis in two referral centers in Tehran, Iran.
Methods: We retrospectively reviewed medical records. A random sample of 2,000 patients referred for MS diagnosis or treatment was selected from 17,000 records. Each record was reviewed by MS experts to classify patients as correctly diagnosed or misdiagnosed. Demographic, clinical, laboratory, and radiologic data were collected.
Results: Of 2,000 patients, 47.45% were referred for diagnostic confirmation and 52.55% for treatment. MS was confirmed in 1,816 (90.8%) patients, while 184 (9.2%) were misdiagnosed. The mean age of MS patients was 32.83 years (SD = 10.30), and 75.82% were female. In the misdiagnosed group, 127 (69%) were female, with a mean age of 36.53 years (SD = 11.50) for females and 37.61 years (SD = 10.53) for males. The average duration of misdiagnosis was 2.8 years (SD = 3.68) for females and 2.4 years (SD = 3.29) for males. A family history of MS was reported in 7.2% of patients. The most common alternative diagnoses were vascular diseases (20.3%), neuromyelitis optica (14.8%), and migraine (6.0%). Other diagnoses included hereditary spastic

paraparesis, patent foramen ovale, and psychogenic disorders. The most frequent clinical symptoms were paresthesia (39.7%), blurred vision and headache (20.1% each), and vertigo (12.0%). MRI findings showed nonspecific white matter lesions in 56.5%, multiple T2 hyperintense lesions in 16.3%, and juxtacortical lesions in 17.4%. Longitudinally extensive transverse myelitis (LETM) was seen in 9.2% of cases. Laboratory findings revealed NMO-IgG positivity in 38.5% of cases tested.
Conclusion: The MS misdiagnosis rate at two referral centers in Iran was 9.2%, aligning with global estimates (5-18%). Overlapping symptoms with vascular diseases, NMO, and migraine, along with nonspecific MRI findings, contributed to misdiagnoses. These results highlight the need for better diagnostic protocols and clinician training.

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P1026
OCT and OCT angiography in differential diagnosis of MS: the retina as a window on the CNS

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Introduction: MS is an inflammatory-demyelinating disease of the central nervous system (CNS) often misdiagnosed due to overlapping clinical and radiological features with other MS-like disorders, a mistake that generate both MS overdiagnosis and overtreatment. Syndromes with an MS-like course and a low of perivenular brain lesions (PVL) frequency on T2* MRI may include distinct disease entities, potentially involving primary arteriolar damage, which can be evaluated through non-invasive imaging techniques of the retina and optic nerve and of the retinal vascular network.
Objectives/Aims: To explore the contribution of Optical Coherence Tomography (OCT) and OCT angiography (OCT-A) in differential diagnosis of MS-like syndromes, this study aims to evaluate structural and vascular retinal differences among patients with typical MS, MS with red flags of better explanation (MSplus), and not-MS (nMS) diseases involving the CNS with distinct pathogenetic mechanisms.
Methods: OCT and OCT-A are non-invasive imaging techniques used to assess the structural characteristics of the retina and optic nerve, as well as the retinal vascular network.
Results: MS (n=42, typical MS n=34 and MSplus n=8) and nMS (n=15) were included. nMS: MOGAD (n=2), NMOSD (n=1), Susac Syndrome (n=2), Primary CNS lymphoma (n=2), vascular leukoencephalopathy (n=2), leukoencephalopathy in Psoriasic Arthritis (n=2), leukoencephalopathy in Sjogren Syndrome (n=2), leukoencephalopathy in antiphospholipid syndrome (n=2), and myelitis (n=2). The mean age of the whole population is 38,4 years (SD 11,4) with a mean disease duration of 9,6 years (SD 13,1). A subgroup of 19 pts (MS n=10 MSplus n=3 nMS n=6) received Central Vein Sign (CVS) analysis (CVS+ representing PVL>50% of all white matter lesions). OCT revealed thickness reduction of the retinal nerve fiber layer (RNFL) in the temporal zone in MS compared to MSplus/nMS ($p<0.001$). OCT-A didn't show differences in vessel density between eyes with history of optic neuritis and unaffected eyes; whereases, a reduction of the vascular plexus density was observed in both the superficial and deep capillary plexuses (inner and outer zones) in MSplus/nMS compared to MS ($p<0.001$). In the subgroup of CVS analysis, the retinal vessel density in the inner and outer zones of both the superficial and deep capillary plexuses was remarkably reduced in CVS- compared to CVS+ ($p<0.001$) showing high concordance between CVS+ and superficial capillary plexus status ($p<0.001$).
Conclusion: MS show different patterns of retinal vascular involvement. In particular, MSplus and nMS exhibited a reduced macular perfusion in the absence of structural retinal damage, a marker of primary microvascular involvement. Further studies are ongoing to validate the use of ophthalmological imaging as a reliable tool for early differential diagnosis among MS-like syndromes and characterization of the probably non-demyelinating pathogenic mechanism(s) underlying these.

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P1027
Bridging the Support Gap: Translating Pan-European Patient Journey Insights into Practice through a Comprehensive MS Patient Support Programme

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Introduction: Multiple Sclerosis (MS) patients across Europe navigate complex healthcare journeys, facing unmet needs that lead to anxiety, uncertainty, and reduced quality of life. Addressing these gaps is essential to enhance patient experiences and outcomes.
Objectives/Aims: To map the MS patient journey across the UK, Ireland, Germany, Spain, and Italy; identify key pain points and unmet needs; and translate these insights into developing a patient support programme (PSP) to enhance patient care.

Methods: In-depth interviews were conducted with 70 MS patients from five European countries (15 UK, 10 Ireland, 15 Germany, 15 Spain, 15 Italy). Analysis utilised the behavioural models COM-B and Theoretical Domains Framework to understand psychological influences on patient experiences and support needs.
Results: Unmet needs in emotional, informational, and practical domains were common across all countries. Significant support gaps between healthcare touchpoints—particularly post-diagnosis, during treatment decision-making, pre-first infusion, post-treatment, and between infusions exist. Patients can often feel unsupported, hindering decision-making and adherence. Despite cultural and systemic differences, consistent themes highlighted the necessity for tailored support. These insights present opportunities for a PSP to provide tailored assistance, enhance patient–healthcare professional communication, and improve treatment adherence across diverse European contexts.
Conclusion: Translating these pan-European insights into a sustainable PSP can address critical unmet needs. Such a programme can enhance patient experiences, engagement, and clinical outcomes across different healthcare systems. This initiative demonstrates effective translation of research into practice, aligning with collective aims of accelerating evidence implementation and sustainability in MS care throughout Europe.

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P1028
Evaluation of the Association of Rheumatological Disease and Autoantibodies on Patients with Multiple Sclerosis: A Single Cen

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Introduction: Multiple sclerosis (MS) is a chronic immune-mediated disease of the central nervous system. It has been suggested that there may be common genetic/environmental factors between MS and other autoimmune diseases.
Objectives/Aims: The main purpose of our study is to evaluate the autoantibody positivity and the frequency of rheumatological diseases accompanying MS in MS patients followed up in a single center.
Methods: The files of a total of 1800 patients followed up with a diagnosis of MS and a total of 468 patients data included. Rheumatological tests; ANA, ds-DNA, ENA subgroups, anti-cardiolipin antibodies (AKA), lupus anticoagulant (LAK), ACE level, RF, Anti-CCP levels, complement levels, p-ANCA and C-ANCA levels recorded. Patients with autoantibody positivity and patients with a rheumatological disease diagnosis accompanying MS were separately evaluated.
Results: The mean age of the patients was 37.5±0.9 years (71% female). The median follow-up period was 6 (1-15) years. ANA was found to be significantly positive in 39 and ds-DNA in 5 patients. ANA median value was 640 (160-2560), anti-dsDNA median value was 26.5 (10-160). Significant antiphospholipid antibody (aFL) positivity was present in 21 patients, AKA IgM was found in 5 patients, AKA IgG was found in 4 patients, and LAK was found in 16 patients. Anti-SSa positivity was present in 4 patients and Anti-SS-B positivity was present in 2 patients. Hypocomplementemia was present in 4 patients. RF was found in 18 patients. Two patients were positive for c-ANCA and two patients were positive for HLA-B27. When rheumatologic diseases accompanying MS were examined, 4 patients had Behçet's disease (one was neuro-Behçet), 5 patients had Familial Mediterranean Fever, 5 patients had Sjögren's syndrome, 3 patients had Rheumatoid arthritis, 4 patients had Psoriatic arthritis, 3 patients had Ankylosing spondylitis, 1 patient had Systemic sclerosis, 1 patient had Undifferentiated connective tissue disease, and 1 patient had Systemic lupus erythematosus. 1 patient was being followed up with both FMF and Ankylosing spondylitis diagnoses. In addition to MS treatment, 2 patients were using ixekizumab, 1 patient was using secukinumab, 2 patients were using rituximab, 1 patient was using anakinra as a biological modifier. In addition, 1 patient was using azathioprine, 3 patients were using mycophenolate mofetil, and 5 patients were using hydroxychloroquine.
Conclusion: We observed a significant association between autoimmune rheumatologic diseases, serological markers, and MS, suggesting that MS should be considered not merely a diagnosis of exclusion but potentially a comorbid autoimmune condition.

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Clinical Aspects of Ms & Related Diseases – NMOSD & MOGAD

P1029
Factors associated with MOG-IgG Serostatus change

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Introduction: MOG-IgG is a diagnostic biomarker of myelin oligodendrocyte glycoprotein antibody disorder (MOGAD). Factors associated with serostatus change are not known.
Objectives/Aims: We aim to determine the frequency and factors associated with MOG-IgG serostatus change.
Methods: All patients followed at a tertiary referral center tested for MOG-IgG by live Fluorescence-Activated Cell

Sorting cell-based assay (live-CBA) or fixed-CBA from 2017-2025 with serial testing (⩾2 tests) were included.
Kaplan-Meier curves estimated the seroconversion/seroreversion-free probability. An event was defined as the first serostatus change. Subjects were censored at the date of their last test.
Results: Of 4,351patients, 288 had serial MOG-IgG testing.
Of 56/288 initially MOG-IgG+, 42 patients remained positive (75%; 100% adults; median duration 239 days).
Of those initially MOG-IgG+, 14/56 seroreverted (25%, 12 adults, 2 children; median duration 504 days, range 44-1710 days). In 13 both tests were done by live-CBA (96%). 1 had the initial test done by fixed-CBA, and second test by live-CBA. Diagnoses include MOGAD (7), MS (1), CIS (3), migraine (1), POTS (1), epilepsy (1). Initial titers were 1:10 (1), 1:20 (5), 1:40 (4), 1:100 (3), 1:1000 (1). Treatments at seroreversion include rituximab (3), IVIg (2), none (9). A third test in 3 was positive in 2 (1:100, 1:20), negative in 1. None had further relapses (median duration from seroreversion 532 days). Seroreversion-free probability at 1 year was 88% (95% CI: 78% - 99%), 74% at 2 years (95% CI: 60%-91%).
Of 232/288 initially MOG-IgG-, 228 remained negative (98%, 100% adults; median duration 139 days).
Of those initially MOG-IgG-, 4/232 seroconverted (2%, 100% adults; median duration 248 days, range 30-2181 days). 3 had both tests by live-CBA (75%), while 1 had both tests by fixed-CBA. All 4 presented with optic neuritis and have diagnosis of MOGAD. Titers at seroconversion were 1:20 (1), 1:100 (2), and 1:1000 (1). Treatment at initial test were steroid (3), none (1). Seroconversion-free probability at 1 year and 4 years was 97% (95% CI: 94%-100%).
Conclusion: Seroreversion occurred in 25%, where 70% had titer <1:100, 50% had diagnosis other than MOGAD, and none had further relapses. Seroconversion was uncommon (2%), occurring in a few treated with steroids at the time of initial testing. These results suggest serial testing of patients initially MOG-IgG+ is useful, but for those initially MOG-IgG- serial testing is low yield unless there is concern for treatment masking seroreactivity.

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P1032
Frequency of MRI abnormalities in MOG-IgG-associated disease (MOGAD) at presentation: a cohort of Latin American patients

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Introduction: The 2023 diagnostic criteria for MOG-IgG-associated disease (MOGAD) incorporated typical MRI findings.
Objectives/Aims: We aimed to investigate the frequency of MRI features in a Latin American (LATAM) cohort at disease presentation.
Methods: We retrospectively reviewed the medical records and MRI characteristics of 144 LATAM MOGAD patients (Chile: 40, Peru: 36, Argentina: 31, Brazil: 26, Colombia: 8, and Ecuador: 3) during their first documented attack. All patients met the 2023 MOGAD criteria. Demographic and clinical

characteristics, including relapse type, and MRI scans performed within 30 days of the first clinical manifestation were evaluated.
Results: Among the 144 MOGAD patients, 117 (81.2%) had MRI scans available from their first attack. The most frequent clinical manifestations were as follows: unilateral optic neuritis (ON) in 39 patients (30 MRI scans, 76.9%) with perineural enhancement in 17 (56.7%), longitudinal compromise in 9 (30%), optic disc edema in 7 (23.3%) and 7 (23.3%) ill defined lesions in white and/or gray brain matter; bilateral ON in 37 patients (26 MRI scans, 70.3%) with perineural enhancement in 19 (73.1%), longitudinal compromise in 16 (61.5%), and ill-defined lesions in white/gray matter in 6 (23.1%); finally, isolated myelitis in 24 patients (20 MRI scans, 83.3%), showing longitudinal compromise in 15 (75%), conus involvement in 1 (5%), and H sign in 9 (45%); additionally, 5 patients (25%) had ill-defined lesions in white/gray matter. Notably, 24 patients (20.5%) did not show any of the typical MRI findings described in the 2023 diagnostic criteria.
Conclusion: This study highlights the variability of MRI findings in MOGAD patients at disease presentation, particularly within this LATAM cohort. While the 2023 diagnostic criteria provide valuable guidance, a significant proportion of patients (20.5%) do not exhibit the typical MRI features, emphasizing the need for a comprehensive approach to diagnosis.

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P1033
Distribution of Cerebral Lesions in Neuromyelitis Optica Spectrum Disorder and Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) share overlapping clinical and radiological features.
Objectives/Aims: This study aimed to characterize the distribution of cerebral lesions in patients with NMOSD and MOGAD.
Methods: Brain MRI axial FLAIR lesions were manually segmented using ITK-SNAP software. Sequences were coregistered to T1 images and normalized to the ICBM MNI-152 atlas via SPM12. Lesion density heat maps were created with MRIcroGL.
Results: We included 67 NMOSD (50F/17M) and 32 MOGAD (20F/12M) patients. Median age was 35 in NMOSD and 32 in MOGAD. Initial symptoms in NMOSD were spinal (38.8%) and optic neuritis (37.3%), while MOGAD predominantly presented with optic neuritis (62.5%) (p=0.04). Bilateral optic neuritis was observed in 20.8% of NMOSD and 15.6% of MOGAD (p=0.5). Median disease duration was longer in NMOSD (9 years) than in MOGAD (5 years; p=0.01). Monophasic course occurred in 19.4% of NMOSD and 25% of MOGAD (p=0.5). Relapse rates were 53.7% in NMOSD vs. 34.3% in MOGAD (p=0.07). Heat map analysis of 48 patients with NMOSD and 24 patients with MOGAD who had cerebral lesions revealed similar patterns of cortical, periventricular, and infratentorial involvement (p=0.3). However, the distribution of brainstem lesions differed significantly: NMOSD lesions predominantly clustered in the lower pons and medulla, whereas MOGAD lesions were primarily located in the upper pons (p=0.05).
Conclusion: Although general lesion patterns were comparable, the differing brainstem topography between NMOSD and MOGAD may reflect distinct pathogenic mechanisms. These findings highlight the relevance of lesion mapping for disease differentiation and warrant further studies in larger cohorts.

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P1034
Real-world experience with Rituximab in a Colombian Cohort of Patients with Neuromyelitis Optica Spectrum Disorders (NMOSD)

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Introduction: Neuromyelitis optica spectrum disorders (NMOSD) are a group of severe, autoimmune, chronic demyelinating and inflammatory diseases, characterized by recurrent

attacks such as optic neuritis or extensive longitudinal myelitis (1). Rituximab (RTX) has been widely used in NMOSD (2). Some guidelines recommend RTX as the first-line disease-modifying therapy for patients who are positive for aquaporin-4 IgG (AQP4)(3).
Objectives/Aims: To describe RTX use and clinical response to RTX in a Colombian cohort of NMOSD patients at a specialized center from August 2014-January 2025.
Methods: A retrospective cohort study of patients with NMOSD according to IPDN 2015 criteria(4). Treatment failure to RTX was defined as any new clinical or imaging inflammatory event in the central nervous system despite proper treatment. Quantitative variables were summarized with median and interquartile range (IQR), and qualitative variables were presented using frequencies and percentages. Median differences were evaluated with Mann-Whitney with a p-value <0.05 as statistically significant.
Results: 428 NMOSD patients who received RTX at any point during their disease course were included. The cohort comprised 82.0%(351) women, with a median age at diagnosis was 42.3 years (IQR 32.4-51.9). The median treatment duration was 2.9 (IQR 1.8-5.7) years while for disease duration was 6.5 years (IQR 3.5-10.1). Anti-AQP4 antibodies were tested in 237 patients using cell-based assay or indirect immunofluorescence; 72.9%(173) tested positive, while 27.0%(64) tested negative. Anti-myelin oligodendrocyte glycoprotein-MOG antibodies were assessed in 26 patients, of whom 11.5%(3) were positive and 88.4% (23) negative. Regarding current treatment, 96.5% (413) of patients were receiving RTX, 1.9%(8) satralizumab, 0.9%(4) tocilizumab, and 0.7%(3) were not on treatment. Rituximab was the most commonly used first-line therapy in 38.5%(15/39) of patients. Treatment failure with RTX occurred in 2.3%(10) of cases, with 80%(8) switching to satralizumab, while 20%(2) remained on RTX. In terms of patient-reported outcomes, at program entry, 61.0%(216) reported an optimal quality of life, which increased to 71.7% (254) at the last evaluation. For EDSS, 5.4%(23) initially had severe disability, which decreased to 4.6%(20) at the last evaluation.
Conclusion: RTX is considered an effective treatment option for disease management in this cohort with a very low rate of treatment failures, supported by an increment in optimal quality of life and improvement in EDSS scores.

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P1035
Visual Loss in Paediatric Leber Hereditary Optic Neuropathy (LHON) vs Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD): Diagnostic Clues and Prognostic Implications

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Introduction: Leber hereditary optic neuropathy (LHON) can be difficult to distinguish from acquired demyelinating syndromes in children, particularly as subacute presentations can occur in both conditions, and some patients may have extraocular manifestations.
Objectives/Aims: We aimed to compare the presenting features and outcomes of LHON and Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD) patients presenting with visual loss.
Methods: This retrospective observational cohort study included paediatric patients (<18 years old) from Great Ormond Street Hospital, UK, between 2011 and 2025. Clinical and paraclinical data were extracted and compared between patients LHON and MOGAD presenting with reduced visual acuity.
Results: A total of 28 patients were included (9 with LHON, 19 with MOGAD). The median age at onset was similar between groups (LHON: 8.2 years; MOGAD: 9.6 years; $p = 0.394$). The duration from symptom onset to visual nadir was longer in LHON (mean 112.2 days vs. 6.95 days in MOGAD; $p = 0.003$). MOGAD patients were more likely to have a preceding illness (0/9 LHON vs. 7/19 MOGAD; $p = 0.046$). Headaches and eye pain were seen only in the MOGAD group (0/9 LHON vs. 15/19 MOGAD; $p = 0.0001$ and 0/9 LHON vs. 13/19 MOGAD; $p = 0.0007$ respectively).
MRI abnormalities were found in 4/6 LHON patients and 15/19 MOGAD patients ($p = 0.539$) with optic nerve signal changes ($p = 0.042$) and optic nerve enhancement ($p = 0.013$). All MOGAD patients received steroid treatment, compared to only one LHON patient ($p = 0.0001$). Relapses occurred exclusively in MOGAD patients (26.3%; $p = 0.09$). Over a median follow-up of 1 year (IQR: 0–3.25), vision improvement was observed in both groups, but it was more pronounced in MOGAD (LHON: 4/8, MOGAD: 18/18, $p = 0.001$). Over the same period, LogMAR improved in the worst eye by a median of 0.96 points (IQR: 0.77–1.72) in MOGAD, and 0.12 points (IQR: -0.005–0.235) in LHON ($p = 0.003$). Time to visual recovery was longer in LHON (mean 121 days vs. 15 days in MOGAD; $p = 0.0001$). Only 2 out of 8 LHON patients recovered to normal vision, compared to 14 out of 18 MOGAD patients at the last follow-up ($p = 0.01$).
Conclusion: Both LHON and MOGAD present with visual loss, but MOGAD symptoms typically follow infections and are more likely to be accompanied by headache and eye pain. Interestingly, both groups may show visual recovery, with or without treatment. Compared to LHON, patients with MOGAD generally demonstrate more rapid recovery and more favorable visual outcomes.

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P1036
Characterizing Autoimmune Comorbidities in MOGAD: A single-center cohort study

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Introduction: In contrast with neuromyelitis optica spectrum disorders (NMOSD) in which autoimmune overlap is well-documented, increased prevalence of autoimmune disorders in association with myelin oligodendrocyte glycoprotein antibody disease (MOGAD) has not been consistently reported.
Objectives/Aims: This study aims to investigate the overall and sex-specific prevalence of autoimmune comorbidities in MOGAD patients, and to compare these rates to general population estimates.
Methods: Data from 239 confirmed MOGAD patients (143 female, 93 male) were extracted from the Mass General Brigham REDCap-based MOGAD database and analyzed using R statistical software. The database was previously constructed via retrospective chart review by neuroimmunology specialists. The prevalence of major comorbidities was calculated, with specific attention to autoimmune conditions. Observed proportions were compared to estimates from epidemiological literature using one-sample proportional z tests. Sex-specific analyses were conducted to examine differences between male and female patients.
Results: Autoimmune diseases were the most frequently reported comorbidity category, affecting 46 of 239 patients (19.2%) including 38 of 143 women (26.6%) and 7 of 93 men (7.5%). The most common autoimmune conditions were thyroid disease (18 patients, 7.5%), type 1 diabetes (4 patients, 1.7%), systemic lupus erythematosus (4 patients, 1.7%), and psoriasis (3 patients, 1.3%). Compared to population estimates (ranging from 3–8% depending on source), the overall prevalence of autoimmune disease in the MOGAD cohort represents an approximate 2–6-fold increase. In sex-specific analyses, women with MOGAD had significantly elevated rates of lupus (16.3-fold), and type 1 diabetes (10-fold) compared to general female population estimates (all $p<0.001$). No significant increases were seen in men.
Conclusion: Nearly 20% of individuals with MOGAD had at least one autoimmune comorbidity, with more than a quarter of female patients affected—substantially exceeding general population estimates. These findings suggest a potential enrichment of autoimmune disease in MOGAD, particularly among women. However, limitations include the modest sample size and the use of heterogeneous literature-based estimates, which vary by population and methodology. Future studies using matched case-control or population-based approaches are needed to validate these findings and better characterize autoimmune risk in MOGAD

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P1037
Headache associated with MOGAD Optic Neuritis: Clinical Patterns and Magnetic Resonance Imaging findings

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Introduction: Headache (HA) as a different symptom than periocular pain in patients with MOGAD-related optic neuritis (MOGAD-ON) has been reported. Its underlying mechanisms and relationship with optic nerve inflammation are still to be determined.
Objectives/Aims: To characterize HA in MOGAD-ON and describe its association with complementary test findings.

Methods: A multicenter cross-sectional study including patients fulfilling the 2023 MOGAD diagnostic criteria with ON and available HA data. Clinical and paraclinical ON-related information was collected from the medical records of 4 hospitals in Chile. Results are presented as frequency (%) and median (range).
Results: Among 95 patients diagnosed with MOGAD, 48 (51%) presented at onset with ON. HA data were available for 40 (83%) of these patients, of whom 20 (39%) had a previous history of HA. HA concomitant with ON was reported in 29 patients (60%), among whom ON was bilateral in 15 (52%) and unilateral in 14 (48%). HA preceded visual symptoms in 16 (55%) of cases and was concomitant in 11 (38%), with a median prodromal interval of 5 days (range 2–30). Retro-orbital pain was the most common location (62%), followed by migraine-like HA (14%) and hemicrania HA (7%). CSF was inflammatory in 4 (16%) patients, and OCB was positive in 4 (16%). MRI showed that patients with HA had a higher frequency of longitudinally extensive ON (68% vs. 55%), anterior lesions (40% vs. 22%), perineuritis (68% vs. 55%), and gadolinium enhancement (84% vs. 77%) compared to those without HA. Nonetheless, these differences were not statistically significant.
Conclusion: HA is a common and early symptom in MOGAD-ON, often retro-orbital and preceding vision loss. Although inflammatory MRI findings were more frequent in patients with HA, no clear association was established, highlighting the need for further investigation into its underlying mechanisms.

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P1038
Patient and carer perspectives related to research priorities and clinical trials in MOG antibody-associated disease: a survey and focus group study

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Introduction: Research involving the lived experience of patients affected by myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is limited. There are no studies providing Class I evidence related to therapeutic efficacy in MOGAD.
Objectives/Aims: We sought to evaluate research priorities and perceptions related to participation in randomised controlled trials from adult patients, and parents of children with MOGAD.
Methods: An online survey was developed in collaboration with three international consumer-led support groups, and distributed by their social media platforms. Three focus groups were moderated by a clinician-researcher in MOGAD.

Results: 105 respondents (81 adult patients, 24 parents of children with MOGAD) responded to an online survey. The top five research priorities were ranked in descending order of importance: finding a cure, identifying best treatment options, understanding aetiology, alleviating symptoms and preventing relapses. 35/105 (33%) of respondents would participate in a placebo-controlled trial. This increased to 69/105 (66%, $p<0.0001$), with knowledge that trial participation included close monitoring of disease activity and rapid treatment in an expert centre if a relapse occurs. The shift in response was primarily driven by adult patients (30/81, 37% to 56/81, 69%, $p<0.0001$; parents of children with MOGAD 6/25, 35% to 13/24, 59%, $p=0.2$). Outcome measures related to therapeutic efficacy were ranked: being able to see (91%), not having relapses (89%), being able to walk (88%), not having pain (75%), identifying biomarkers for prediction of severity/treatment response (68%), and being able to work/go to school (64%). 95% agreed or strongly agreed that clinical review, blood tests, and patient interviews across four visits, and two MRIs/yr was an acceptable trial burden. Focus groups identified thematic observations including the need for a clear pathway to manage an on-trial relapse, a greater focus on functional impairment, and accessibility and affordability of treatment, as key in trial acceptability.
Conclusion: Patients and parents of patients with MOGAD should be engaged to guide and codesign research priorities and trials. Parents of children with MOGAD may show greater hesitancy towards placebo-controlled trials than adult patients. Outcome measures which evaluate therapeutic efficacies should prioritise functional impact. This survey was critical in the development of the STAR-MOG protocol, the first international investigator-led phase III RCT in MOGAD.

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P1039
Co-occurrence of EBV Infection and MOGAD: A Series of Case Reports

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an antibody-mediated inflammatory demyelinating disorder of the central nervous system (CNS). Increasing evidence supported the association between Epstein-Barr virus (EBV) and the pathogenesis of multiple sclerosis (MS), whereas no evidence shows its effect on MOG-IgG induction, and the potential mechanisms linking EBV to the onset of MOGAD remain to be elucidated. We reported five cases with simultaneously detection of EBV activation and the newly onset of MOGAD manifested as encephalitis, which might provide clue for the potential pathogenic mechanism.
Objectives/Aims:
Methods:
Results: Five patients (24–46 years, 4 males, 1 female) showed common clinical features: initial symptoms of encephalitis with headache, fever, psychiatric abnormalities, and seizure. Then two cases developed CNS demyelinating manifestations with optic nerve damage, spinal cord symptoms and cognitive impairment shortly. Interestingly, all patients showed signs of EBV infection. Specifically, human herpesvirus 4 were detectable in the CSF by next - generation sequencing, and the serology result showed positive of EBV-related antibodies. All cases were positive for MOG-IgG (live-cell CBA) in the serum. Regarding treatment response, three patients showed transient improvement in CSF parameters after the initial anti-infective therapy. However, all of the patients achieved great improvement only

after corticosteroid treatment (high-dose pulse or low-dose), with refractory cases requiring additional intravenous immunoglobulin (IVIG) or tocilizumab.
Conclusion: All of the newly onset MOGAD cases showed concurrent EBV reactivation, which got symptomatic relived after immunosuppressive (corticosteroid) therapy. It suggested a potential causal link between EBV infection and MOGAD onset. EBV reactivation could trigger immune responses against CNS myelin via mechanisms such as molecular mimicry, aberrant B-cell activation, or epitope spreading in MS. The possibility of inducing MOG antibody production cannot be excluded. In our cases, the therapeutic efficacy of corticosteroid therapy further corroborates the hypothesis. Future epidemiological and experimental studies are needed to shed light on the relation between EBV and MOGAD, while providing therapeutic target for MOGAD management.

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P1040
Consistent Detection of AQP4 Antibodies: A Comparative Analysis Between Fixed and Live Cell-Based Assays

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Introduction: In recent years, live cell-based assay (LCBA) has been increasingly adopted in serological antibody detection due to its superior preservation of antigen conformational integrity. Comparative studies have shown that LCBA exhibits a moderately higher sensitivity when compared to fixed cell-based assays (FCBA). As of the 2023 international consensus criteria for MOG antibody-associated disease (MOGAD), LCBA is recognized as the gold-standard method for detecting myelin oligodendrocyte glycoprotein autoantibodies (MOG-IgG). However, the clinical necessity of prioritizing LCBA for the detection of aquaporin-4 autoantibodies (AQP4-IgG) in neuromyelitis optica spectrum disorder (NMOSD) remains unclear, especially when compared to its established role in diagnosing MOGAD.
Objectives/Aims: This study therefore undertakes a systematic evaluation of the consistency in AQP4-IgG detection between live cell-based assays using immunofluorescence (LCBA-IF) and fixed cell-based assays using immunofluorescence (FCBA-IF).
Methods: We compared the performance of LCBA-IF and FCBA-IF in detecting AQP4-IgG in 90 cases of NMOSD meeting 2015 International Panel for NMO Diagnosis (IPND) criteria, alongside 40 controls (8 healthy controls and 32 disease controls). Additionally, we further investigated the relationship between AQP4-IgG titers as measured by LCBA-IF and FCBA-IF and clinical parameters in NMOSD patients.
Results: No significant differences in age or gender were identified between the NMOSD cohort (n=90) and the control group ($n = 40$), ensuring comparability ($p > 0.05$). Among 130 paired serum samples analyzed using LCBA-IF and FCBA-IF, 78 samples tested positive while 48 tested negative across both methodologies, resulting in an overall agreement of 96.9% (Cohen's $\kappa = 0.935$, 95% CI: 0.872–0.998). The Spearman correlation coefficient was 0.977 ($p < 0.001$). For samples with discrepant results, instances where one assay returned a negative result corresponded to titers of 1:10 from the other assay. Both methods demonstrated 100% specificity, with LCBA-IF showing slightly higher sensitivity compared to FCBA-IF. Within LCBA-IF-tested groups, statistically significant differences in annualized relapse rates (ARR) were observed across all pairwise comparisons (low-titer vs. moderate-titer, low-titer vs. high-titer, and moderate-titer vs. high-titer; all $p < 0.05$). In contrast, within FCBA-IF-tested groups, no significant difference was found between the low-titer and moderate-titer subgroups; however, other comparisons reached significance ($p < 0.05$).
Conclusion: Overall, there is a strong concordance between LCBA-IF and FCBA-IF in detecting AQP4-IgG, with only minor discrepancies observed in low-titer samples, where LCBA-IF shows slightly higher sensitivity. Furthermore, our analysis suggests a potential link between elevated AQP4-IgG titers and an increased risk of relapse, a correlation that appears more pronounced when using LCBA-IF. For suspected NMOSD cases, LCBA is recommended as the preferred method for AQP4-IgG detection when available, while FCBA remains a reliable alternative in settings where LCBA is not accessible.

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P1041
Rheumatoid Factor IgM influence NMOSD and MOGAD cell-based assay quantitation

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Introduction: Neuromyelitis optica (NMO) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are autoantibody-mediated demyelinating diseases sharing the presence of glial antibodies. Complement is a prominent pathomechanism of NMO, and we have shown its likely contribution to MOGAD pathology as well. Though IgG autoantibodies are the diagnostic isotype in these conditions, it is understood that IgM are highly complement competent antibodies in humans. Cell-based assays (CBAs) suggest the presence of serum IgM; however, a prominent NMO study showing IgM deposition in patient lesions found AQP4-specific IgM to be elusive.
Objectives/Aims: We hypothesize that some NMO and MOGAD patients harbor rheumatoid factor IgM, or IgM antibodies binding the IgG Fc, which can influence the quantitative results of diagnostic CBAs and may contribute to pathology.
Methods: We employed commercial RF-IgM enzyme-linked immunosorbent assays (ELISAs), live flow cytometry-based CBAs, and effector function assays.
Results: We observed that 38% of our NMO cohort (n=51) were RF-IgM+, similar to the healthy donor cohort (n=37) at 37%. Surprisingly, an elevated 54% of our MOGAD cohort (n=46) were RF-IgM+. To assess the influence of RF-IgM on CBAs, we combined IgG monoclonal antibodies (mAbs) for the neurologic antigens – aquaporin-4 (AQP4)-specific mAb58 for NMO and myelin oligodendrocyte glycoprotein (MOG)-specific 8-18C5 for MOGAD – with varying concentrations of commercial serum RF-IgM or RF-IgM mAb and performed live CBAs, assaying for bound IgG and IgM. The addition of RF-IgM rendered the CBAs IgM positive, despite the lack of IgM specific for the neurologic antigens, confirming RF-IgM binding to IgG autoantibodies. Surprisingly, RF-IgM also influenced CBA IgG quantitation: the AQP4 CBA exhibited elevated IgG with the addition of RF-IgM; however, the MOG CBA exhibited reduced IgG. When NMO and MOGAD patient-derived IgG were supplemented with RF-IgM, both IgG and IgM CBA read-outs were elevated. The magnitude of this increase varied between individuals, suggesting differential RF-IgM binding capacities to serum IgG. Given the elevated RF-IgM+ patients in our MOGAD cohort, we assessed the influence of RF-IgM on cytotoxic IgG effector functions. At the highest concentration of RF-IgM tested (30 IU/mL), the addition of RF-IgM enhanced complement-dependent cytotoxicity (CDC) and reduced antibody-dependent cellular phagocytosis (ADCP). When RF-IgM were added to MOGAD serum IgG, there were variable effects on CDC (n=10, $p>0.1$). However, the addition of RF-IgM significantly reduced ADCP capacity of the serum IgG ($p=0.0089$). We similarly found that RF-IgM reduced ADCP capacity of mAb58 IgG and NMO serum IgG (n=11, $p=0.02$).
Conclusion: Patients with NMO and MOGAD can harbor RF-IgM that influence the IgG and IgM quantitation of diagnostic CBAs as well as the cytotoxic effects of IgG autoantibodies, even at very low concentrations.

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P1042
Paroxysmal symptoms in Neuromyelitis Optica spectrum disorder

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Introduction: The differential diagnosis of neuromyelitis optica spectrum disorder (NMOSD) against the domain of

demyelinating disease has been made simpler as a result of the breadth of new information emerging in recent years regarding this group of pathologies. Paroxysmal symptoms (PS) are defined as short-lasting, stereotyped and recurrent symptoms in NMOSD, and research into PS is still lacking in spite of their relatively high incidence.
Objectives/Aims: Our goal was to categorize and determine the incidence of different PS whilst examining the potential correlation with MR imaging and other important biomarkers of the disease.
Methods: This retrospective study included patients diagnosed with NMOSD from 2017 up until April 2025 in the University clinical centre of Serbia. Data regarding the type and frequency of PS, EDSS scores, duration of disease, and other basic demographic information were extracted from the national NMOSD disease registry of Serbia, and analysed using relevant statistical methods.
Results: Our cohort numbered 83 patients with a strong female predominance (84.3%). The mean age was 49.3 ±13.8 whilst the duration of disease on last follow-up was 6.9 ±7.2. EDSS at last follow-up was 4 ±2.6. Paroxysmal symptoms were present in a majority of patients (87.8%) whilst 95% had 3 or PS. Most frequent PS was numbness (N=53, 63.9%), followed by visual disturbance (N=50, 60.2%), painful tonic spasms (N=40, 48.2%), bladder and sphincter dysfunction (N=37, 44.6%; N=36, 43.4% respectively). Myoclonus was present in 20 patients (24.1%), who were more likely to experience said symptoms with previous myelitis (75%, OR 17.3, CI: 5.0-59.6). Tremor was present in 32.9% of patients and there was no correlation between tremor and lesions of the cerebellum or cerebellar peduncle demonstrated using MRI (p=3.465). Other PS like secondary restless leg syndrome (RLS) (14.6%) and focal dystonia (19.3%) were less common. Aquaporin- 4 (AQ-4) antibodies did not influence the presence of PS, as 90% of seropositive and 84% of seronegative patients displayed PS (p=0.484). Patients were responsive to symptomatic treatment in half of cases.
Conclusion: Little is known of paroxysmal symptoms in NMOSD. PS are often painful and, as such, negatively affect the quality of life of patients with NMOSD. High diversity and incidence of PS accentuate the need for further research with larger cohorts regarding this topic.

Disclosure of interest: Nothing to disclose

P1043
Depression, Anxiety Disorder and ADHD in Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease

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Introduction: Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD) is a recently defined inflammatory demyelinating disease of the central nervous system in adults and children. To date, little is known about mental health and psychiatric comorbidities in patients with MOGAD.
Objectives/Aims: To analyze the psychiatric comorbidities of depression, anxiety disorder and attention deficit hyperactivity disorder (ADHD) in MOGAD patients.
Methods: In this cross-sectional retrospective study, Mayo Clinic electronic medical records from patients referred to Mayo Clinic between 01/01/1992 and 03/01/2025 who fulfilled MOGAD diagnostic criteria, were reviewed for current or past diagnoses of depression, anxiety disorder, or ADHD.
Results: Among 394 MOGAD patients identified, 148 (37.6%) had depression, 187 (47.5%) had an anxiety disorder, and 40 (10.2%) were diagnosed with ADHD. A total of 216 patients (54.8%) had at least one of the three psychiatric conditions. In adolescent MOGAD patients, (age of 13-17 years), depression had a frequency of 31.8% (n=7/22), anxiety occurred in 40.9% (n=9/22), and ADHD in 27.3% (n=6/22). Psychiatric comorbidities were most frequent in young adults between the ages of 18 and 30, where 37% (n=27/73) were diagnosed with depression, 56.2% (n=41/73) with anxiety disorder, and 20.6% (n=15/73) with ADHD. In adult patients over 30 years of age (median: 50, interquartile range: 40-63), 39.1% (n=113/289) had depression and 46.7% (n=135/289) had anxiety disorder, and 6.6% (n=19/289) had ADHD. Adult patient over 30 years of age with a relapsing disease course of MOGAD were more likely to experience depression, anxiety or ADHD compared to those with a monophasic disease course (p=0.004, Odd's ratio 2.0, 95% confidence interval 1.22-3.29).
Conclusion: Psychiatric comorbidities are very frequent in MOGAD patients across all age groups. In adolescents and young adults with MOGAD, ADHD is frequently diagnosed while adult MOGAD patients over 30 years of age often have depression or anxiety, particularly those with a relapsing disease course. Further studies are needed to understand the underlying factors influencing the high frequency of psychiatric comorbidities in MOGAD.

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from MedImmune /Viela Bio; grants, personal fees, and non-financial support from Genentech, Roche; grants from Adimune, and personal fees for consulting from UCB, Astellas and Arialys and Sage Therapeutics. He has two patents issued (8889102; application 12-678350; Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia; and 9891219B2; application 12-573942; Methods for Treating Neuromyelitis Optica [NMO] by Administration of Eculizumab to an individual that is Aquaporin-4 [AQP4]-IgG Autoantibody positive) for which he has received royalties. SJP also has patents pending for IgGs to the following proteins as biomarkers of autoimmune neurological disorders: septin-5, kelch-like protein 11, GFAP, PDE10A, and MAP1B. He works at Mayo Clinic, which offers commercial MOG-IgG and AQP4-IgG testing. He receives no royalties from the sale of tests done at the neuroimmunology Laboratory at Mayo Clinic. Eion P. Flanagan: served on advisory boards for Alexion, Genentech and Horizon Therapeutics. He has received speaker honoraria from Pharmacy Times. He received royalties from UpToDate. Dr Flanagan was a site primary investigator in a randomized clinical trial on Inebilizumab in neuromyelitis optica spectrum disorder run by Medimmune/Viela-Bio/Horizon Therapeutics. Dr Flanagan has received funding from the NIH (R01NS113828). Dr Flanagan is a member of the medical advisory board of the MOG project. Dr Flanagan is an editorial board member of the Journal of the Neurological Sciences and Neuroimmunology Reports. A patent has been submitted on DACH1-IgG as a biomarker of paraneoplastic autoimmunity.

P1044
Assessing Walking Disability in People with NMOSD and MOGAD: The Applicability of the MSWS-12 as a Patient-Reported Outcome Measure

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) and Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) are rare demyelinating diseases. Tools for objective and subjective assessments (including Patient-Reported Outcome Measures, PROM) are usually adapted from Multiple Sclerosis (MS). Walking and gait abnormalities are frequent in both these disorders, and it is unclear whether MS tools fully capture disability in NMOSD or MOGAD patients.
Objectives/Aims: To evaluate the applicability of the 12-item Multiple Sclerosis Walking Scale (MSWS-12) in assessing walking disability in NMOSD and MOGAD patients.
Methods: Cross-sectional observational study in two tertiary hospitals, including patients diagnosed with either NMOSD with AQP4 antibodies (NMOSD-AQP4), MOGAD or double seronegative NMOSD. Clinical and demographic data were collected, including total MSWS-12 and EDSS scores. Construct validity was assessed using Spearman's correlation between MSWS-12 and EDSS. Discriminative validity was tested by comparing MSWS-12 scores between patients with and without myelitis, and between patients grouped by EDSS ($\leqslant$4.0 vs. $>$4.0), using the Mann–Whitney U test.
Results: A total of 40 patients were included, 28 female (70%), with an average age at diagnosis of 43.5 ($\pm$18.3) years and a median follow-up (FUP) time of 7.0 (4-13) years. NMOSD-AQP4 was found in 18 patients (45%), MOGAD in 12 (30%), and 10 were seronegative (25%). Past history of myelitis was present in 23 patients (57.5%). At the time of MSWS-12 assessment, 26 patients (65%) were under ongoing treatment (including 13 under rituximab and 10 under azathioprine). The median EDSS was 1.0 (0-3) and the median MSWS-12 was 23 (14-39). Spearman's correlation between MSWS-12 and EDSS was moderate (ρ=0.523; $p<0.001$), supporting construct validity. Patients with EDSS$>$4.0 had higher MSWS-12 scores than those with EDSS $\leqslant$ 4.0 (median (IQR) 60(53-60) vs 21(13-29), $p<0.001$). Patients with history of myelitis had higher MSWS-12 scores, but the difference was non-significant (p=0.062).
Conclusion: In a small group of NMOSD and MOGAD patients, MSWS-12 total scores correlate with EDSS, suggesting it may be a useful tool for assessing subjective walking disability. By capturing the patient's perspective, the MSWS-12 can complement existing clinical measures and help bridge the gap in PROMs for rare demyelinating diseases.

Disclosure of interest: Nothing to disclose

P1045
Residual Sequelae of Transverse Myelitis in MOG Antibody-Associated Disease: A survey based study of residual symptoms in MOGAD patients

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Introduction: Transverse myelitis is inflammatory injury to the spinal cord, a shared mechanism between several demyelinating and non-demyelinating disorders including neuromyelitis optica (NMOSD), multiple sclerosis and myelin oligodendrocyte

glycoprotein (MOG) antibody-associated disorder (MOGAD) in particular. While severe at nadir, patients with MOGAD generally have improved recovery based on EDSS compared to NMOSD and MS counterparts, although due to a predilection for conus lesions, patients with MOGAD are more likely to have ongoing sphincter dysfunction.
Objectives/Aims: MOGAD patients frequently have residual sensory and sphincter dysfunction that is less well characterized. We polled 118 MOGAD patients to assess for rates of motor, sensory, pain, sphincter, and sexual dysfunction amongst those with prior TM.
Methods: 118 anonymous MOGAD patients from the MOG project, Guthy Jackson Charitable Foundation (GJCF) and MGH Neuroimmunology clinic completed an anonymous survey geared towards patient-related outcome measures of ongoing motor, sensory, and sphincter function. Survey responses were uploaded to Mass General Brigham REDCap-based MOGAD database and analyzed using R statistical software.
Results: 58.5% of respondents reported ongoing weakness following TM. Out of those that responded, 35 /50 (70%) described improvement in their level of weakness compared to onset. 74.6% reported ongoing sensory deficits following TM, and of those that responded 60% reported improved sensation compared to onset. Another 71.8% reported ongoing pain/discomfort following TM with 52.9% of those responding reporting improvement in pain since onset. 44% (52/118) reported ongoing gait impairment post-TM with 55.8% of those responding reporting an improvement compared to onset. 55.1% reported persistent cramping/stiffness while only 43.1% reported improvement of this symptom. 30% reported persistent banding. 55.1% report occasional or persistent urinary retention while 65% reported occasional or frequent urinary urgency.
Conclusion: A majority of polled MOGAD patients reported ongoing weakness, sensory, bladder and sexual dysfunction following TM. Of those that responded, the majority did note improvement in these parameters following TM, except for the category of cramping/stiffness, where only 43.1% noted an improvement of these symptoms with time. Overall, close to three quarters of polled MOGAD TM patients reported ongoing sexual dysfunction (73.5%), decreased sexual desire (59.6%), sensory deficits (74.6%), cramping and pain. We found higher rates for bladder and sexual dysfunction than previously reported in the literature although this may be due to confirmatory bias. Further work needs to be completed to better characterize which patients are potentially most at risk for these sequelae post-TM with an aim of providing targeted therapies.

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P1046
Satralizumab treatment in adults with aquaporin-4 antibody positive neuromyelitis optica spectrum disorder: a single center experience

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a rare immune-mediated and inflammatory central nervous system disease commonly associated with antibodies against aquaporin-4 (AQP4 Ab). In addition to other complex disease mechanisms, interleukin-6 (IL-6)- mediated pathways play a significant role in NMOSD immunopathogenesis. Safety and efficacy of satralizumab, a humanized monoclonal recycling antibody that targets the IL-6 receptor, has been confirmed in pivotal NMOSD trials, but real-world data are limited.
Objectives/Aims: To present real-world data on satralizumab use in adult patients with AQP4 Ab-positive NMOSD.
Methods: We reviewed demographic and clinical information of 10 patients with AQP4 Ab-positive NMOSD who have been treated at the University of North Carolina School of Medicine Department of Neurology, Chapel Hill, North Carolina, United States of America (USA); and have received satralizumab at any time point since the satralizumab regulatory approval for NMOSD in the USA in 2020 until April 2025.
Results: Female/male ratio was 9:1; 70% of patients were African Americans, 30% Caucasians. Median age at NMOSD onset was 28.5 years (range, 14-76 years), and median age at last follow-up visit was 44 years (range, 24-81 years). Satralizumab was the first NMOSD maintenance treatment in 6 out of 10 patients. The remaining 4 patients were switched to satralizumab from: eculizumab (n=1 patient), rituximab (n=2) and mycophenolic acid (n=1). Median duration of satralizumab treatment in our cohort has been 1.9 years (range, 0.3-4.3 years). Four patients discontinued satralizumab treatment due to: death caused by metastatic breast cancer (cancer was diagnosed prior to starting satralizumab treatment in a patient with paraneoplastic NMOSD, n=1), pregnancy (n=1), injection site reactions (n=1) and post-injection severe headaches (n=1). No clinically significant laboratory abnormalities were observed during treatment that were considered related to satralizumab. All patients who remained on satralizumab have been NMOSD relapse free until the last follow-up.
Conclusion: Satralizumab shows good efficacy and safety profile in our NMOSD cohort. Given the rarity of NMOSD, real-world data from multiple centers on satralizumab efficacy and long-term safety are warranted.

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P1047
Latin American Consensus Recommendations for management and treatment of adult MOGAD patients in clinical practice

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Introduction: Recent advancements in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) have led to new diagnostic criteria, emerging biomarkers, and a better understanding of clinical phenotypes and treatment strategies. These developments have made managing MOGAD patients in Latin America (LATAM) more complex.

Objectives/Aims: This consensus aims to evaluate best practices for MOGAD management in LATAM to improve long-term outcomes.

Methods: A panel of LATAM neurologists specializing in demyelinating diseases convened virtually from 2023 to 2024 to develop consensus recommendations for MOGAD management. A questionnaire with 59 statements was distributed across five categories: 1) Diagnosis and serological tests, 2) Imaging and complementary tests, 3) Prognostic factors, 4) Acute treatment, and 5) Long-term treatment. The RAND/UCLA modified Delphi process was used to achieve formal consensus.

Results: All statements achieved strong or relative agreement in the first round, with no further rounds necessary. The panel discussed diagnosis, differential diagnoses, disease prognosis, personalized treatment strategies, and identifying inadequate responses to treatment, incorporating both published evidence and expert opinions.

Conclusion: These consensus recommendations aim to optimize MOGAD management in LATAM, providing tailored treatment protocols to improve long-term patient outcomes.

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P1048
Chinese Delphi Consensus for the Multidisciplinary Management of NMOSD

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) predominantly affects women of childbearing age and is frequently associated with systemic autoimmune comorbidities. In China, the coexistence of hepatitis B virus (HBV) or tuberculosis infection in NMOSD patients is not uncommon, posing significant challenges to long-term immunosuppressive therapy. With the recent approval of novel biologic agents including inebilizumab, satralizumab and eculizumab, there has been increasing emphasis on comprehensive multidisciplinary management for NMOSD patients across both acute and remission phases.
Objectives/Aims: we convened an expert panel encompassing neurology, ophthalmology, pharmacy, rheumatology, infectious diseases, and radiology to establish a consensus on the multidisciplinary management of NMOSD, aiming to optimize evidence-based clinical practice.
Methods: The consensus-building process commenced with a systematic literature review to draft preliminary recommendations. These proposals underwent an iterative Delphi-based voting protocol. Panel members independently voted on each recommendation, with dissenting opinions requiring written justifications. The structured voting comprised a maximum of three rounds: 1) Round 1: Recommendations achieving unanimous approval (100% consensus) were directly adopted. 2) Round 2: Proposals without initial unanimity were revised through panel discussions and re-voted, requiring a supermajority consensus threshold (⩾75%). 3) Round 3: Persistently contentious items underwent final modifications and voting under the same ⩾75% threshold. Only recommendations fulfilling these consensus criteria were incorporated into the final guidelines.
Results: A multidisciplinary panel of 22 Chinese experts developed 32 evidence-based recommendations through a modified Delphi protocol. During the first voting round, 5 recommendations failed to attain unanimous consensus and were subsequently revised through iterative expert feedback. This refinement process yielded 29 finalized statements meeting the predefined ⩾75% consensus criteria, categorized as follows: 4 on acute-phase treatment, 7 on the maintenance therapy, 10 on the infection risk assessment and management, 1 on the concurrent systemic autoimmune diseases, 1 on the pregnancy or lactation considerations; 1 on the vaccination strategies, 5 on the long-term follow-up protocols.
Conclusion: Evidence-based consensus guidelines for the multidisciplinary management of NMOSD were systematically developed through an iterative Delphi protocol integrating contemporary clinical evidence and real-world practice insights from multiple tertiary medical centers. These guidelines provide actionable algorithms for 1) standardization of immunotherapy regimens across acute/remission phases, 2) risk-stratified management of comorbid infections (HBV, tuberculosis, etc.), 3) clinical workflow integration among neurology, ophthalmology, and allied specialties.

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P1049
Prevalence of Obesity in NMOSD: Insights from a Large Real-World Database

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Introduction: Obesity is a rising public health issue and has been increasingly recognized for its role in promoting systemic inflammation and immune dysregulation. These effects have been implicated in the development and progression of several autoimmune and neuroinflammatory diseases. While emerging research points to possible links between obesity and neuroimmune conditions, the prevalence and significance of obesity in NMOSD remain poorly understood.
Objectives/Aims: To evaluate the prevalence of obesity among NMOSD patients relative to a non-NMOSD cohort stratified by age using a large-scale electronic health record (EHR) database.

Methods: We conducted a cross-sectional analysis using TriNetX EHR data. NMOSD patients were identified via ICD-10 code G36.0, excluding those with multiple sclerosis, sarcoidosis, or immune checkpoint inhibitor exposure. Obesity was defined using ICD-10 code E66.0 (obesity due to excess calories) to exclude secondary causes of obesity. A matched control group without NMOSD was used for comparison across age groups.
Results: The analysis included 5,505 NMOSD patients and 113,621,041 non-NMOSD individuals. Across all age groups, obesity prevalence was higher in NMOSD patients compared to the control cohort (total prevalence: 8.28% vs. 3.80%, $p < 0.0001$). However, the degree of difference varied by age. The most pronounced differences were observed in younger and middle-aged individuals, particularly those aged 30-39, where the prevalence ratio was 4.40 (30-34 years, $p < 0.0001$) and 2.63 (35-39 years, $p < 0.0001$). As age increased, the difference between NMOSD and control groups diminished, with no significant difference observed after age 70 (e.g., 70-74 years: prevalence ratio $= 1.04$, $p = 0.841$). A slight resurgence in obesity prevalence was noted in the 90+ age group, though this finding may be influenced by survivor bias or sample size limitations (prevalence ratio $= 7.13$, $p < 0.0001$).
Conclusion: Our findings confirm a significantly higher prevalence of obesity in NMOSD patients compared to the general population, particularly in younger and middle-aged individuals. The magnitude of this association weakens with age, potentially due to disease-related factors such as spinal cord atrophy, reduced mobility, and nutritional decline in later life. Notably, the elevated obesity rates observed even in pediatric NMOSD patients support the notion that obesity may be a risk factor for NMOSD rather than merely a consequence of chronic disease. Further longitudinal studies are needed to explore the causal relationship between obesity and NMOSD onset, progression, and clinical outcomes.

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P1050
Predictive Value of Billing Codes for Identifying Relapse Hospitalizations in NMOSD

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is marked by inflammatory relapses resulting in severe neurologic injury. While relapses often lead to hospitalization, patients with NMOSD may also be hospitalized for pseudo-relapses, treatment-related adverse events (e.g., infection), and unrelated comorbidities (e.g., cardiac events). Real-world studies frequently assume that hospitalization diagnostic codes accurately reflect clinical events, yet few validate claims codes for this purpose. We assess the predictive value of NMOSD-related hospital billing codes to differentiate between relapse and non-relapse hospitalizations.
Objectives/Aims: To calculate the predictive value of hospitalization billing data in distinguishing relapse from non-relapse hospitalizations in patients with NMOSD.
Methods: Patients meeting the 2015 diagnostic criteria for NMOSD who were hospitalized within the Mass General Brigham (MGB) system (consisting of 12 hospitals) between January 2016 and March 2025 were included. Relapse hospitalizations were defined as admissions for a core NMOSD demyelinating event with documented or retrospectively described supportive clinical examinations. Non-relapse hospitalizations included admissions with clear alternate etiologies and/or without new clinical signs or imaging evidence of relapse. Admitting and primary ICD-10 and ICD-9 billing codes were examined. The sensitivity, specificity, positive predictive values (PPVs), and negative predictive values (NPVs) of billing codes for NMOSD (ICD-10 G36.0, ICD-9 341) alone; NMOSD in combination with optic neuritis (ON; ICD-10 H46x, ICD-9 377) or transverse myelitis (TM; ICD-10 G37.3, ICD-9 341.2); and NMOSD or ON or TM were evaluated.
Results: We identified 53 patients – median age of 53 years (range 24-97), 77% female, 84% seropositive – with a total of 120 MGB hospitalizations: 47 (39.2%) relapses and 73 (60.8%) non-relapses. NMOSD billing codes showed a sensitivity of 78.7%, specificity of 72.6%, PPV of 64.9%, and NPV of 84.1% for an adjudicated relapse hospitalization. Combining NMOSD codes with one of either ON or TM codes had a sensitivity of 36.1%, specificity of 95.9%, PPV of 85.0%, and NPV of 70.0%. Using a diagnostic code of either NMOSD or ON or TM yielded a sensitivity of 91.5%, specificity of 67.1%, PPV of 64.2%, and NPV of 92.5%.
Conclusion: Admitting and primary NMOSD billing codes alone have a low positive predictive value in identifying relapse hospitalizations. A combination of NMOSD with either ON or TM billing codes increases the specificity and positive predictive value of relapse hospitalizations but severely reduces sensitivity. Considering NMOSD or ON or TM billing codes yielded a high sensitivity and negative predictive value, but poor specificity and positive predictive value. This observed variability underscores the need to validate diagnostic codes as predictors of relapse hospitalization to facilitate accurate real-world NMOSD research.

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P1051
Impact of First Demyelinating Event Severity on Long-Term Disability in Neuromyelitis Optica Spectrum Disorder: A Retrospective Cohort Study

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is characterized by relapsing demyelinating events of the central nervous system that can range from mild to severely disabling or even life-threatening. Although inflammatory activity is a hallmark of NMOSD, the relationship between the severity of the first demyelinating event and long-term clinical outcomes remains unclear.
Objectives/Aims: To investigate whether the severity of the first demyelinating event in NMOSD is associated with subsequent relapse activity and long-term disability.
Methods: This retrospective cohort study included 57 patients diagnosed with NMOSD. The severity of the initial demyelinating episode was categorized based on the Expanded Disability Status Scale (EDSS): mild (0–3.0), moderate (3.5–5.5), and severe (⩾6.0). Demographic and clinical data -including age at onset, follow-up duration, EDSS at the last visit, number of relapses after the first event, treatment type, and treatment duration- were analyzed using appropriate statistical methods.
Results: A total of 57 patients (73.6% female; mean age: 36.67 ± 13.64 years) were included. Aquaporin-4 antibodies were positive in 24 patients, MOG antibodies in 2, and 31 seronegative patients. The first demyelinating event was classified as mild in 35 patients, moderate in 11, and severe in 11. No significant differences were observed among the severity groups in terms of gender, age, total follow-up duration, treatment type or duration, or NMOSD subtype ($p > 0.05$). Relapse rates following the first event were also similar across the three groups ($p > 0.05$). However, the EDSS score at the last visit remained significantly higher in those with initially moderate or severe relapses (median [IQR]: severe: 6.0 [2.5], moderate: 1.5 [1.5], mild: 1.0 [2.0]; $p < 0.01$).
Conclusion: Although the severity of the first demyelinating event was not associated with future relapse rates, it was significantly related to long-term disability in NMOSD patients. This suggests that even a single severe attack may have lasting consequences on neurological function. Therefore, early identification of severe initial episodes and timely initiation of effective immunotherapy are crucial for minimizing irreversible damage and optimizing long-term outcomes. These findings highlight the importance of individualized treatment strategies based not only on serostatus and relapse frequency but also on the clinical severity of disease onset.

Disclosure of interest: Ergi Kaya: Nothing to disclose, Yasemin Simsek: Nothing to disclose, Serkan Ozakbas: Nothing to disclose

P1052
Impact of Aquaporin-4 Serostatus on Disease Activity and Disability in NMOSD: A Five-Year Comparative Study

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a rare, relapsing demyelinating disease of the central nervous system. It includes aquaporin-4 antibody-positive (AQP4+) NMOSD, myelin oligodendrocyte glycoprotein antibody-associated disease, and seronegative NMOSD (SN-NMOSD). Although these subtypes may exhibit similar clinical presentations, comparative data on their prognosis are still limited.
Objectives/Aims: To investigate the clinical and prognostic differences between AQP4+ and SN-NMOSD patients during the first five years following diagnosis.
Methods: This retrospective cohort study included 70 NMOSD patients (37 AQP4+, 33 SN-NMOSD). Data collected comprised age at diagnosis, sex, time from first symptom to diagnosis, localization of the first symptom, baseline Expanded Disability Status Scale (EDSS) scores, baseline relapse count, treatment type and duration, total relapse count and EDSS scores at 2 and 5 years, radiological activity during follow-up, and No Evidence of Disease Activity-3 (NEDA-3) status at the second and fifth years. Comparative analyses were performed using appropriate statistical methods.
Results: Among the 70 participants (81.4% female; mean age 38.4 ± 12.9 years), no significant differences were found between the AQP4+ and SN-NMOSD groups in terms of age at diagnosis, sex, time to diagnosis, first symptom localization, treatment type, or treatment duration ($p > 0.05$). However, the AQP4+ group had significantly higher baseline EDSS scores, and relapse counts compared to the SN-NMOSD group (EDSS: median 3.0 [IQR 2.75] vs. 2.0 [IQR 0.75], $p = 0.003$; baseline relapse count: 2.0 [IQR 2.0] vs. 2.0 [IQR 1.0], $p = 0.046$). No significant differences were observed between groups in relapse count, MRI activity, or NEDA-3 status at 2 and 5 years ($p > 0.05$). Nonetheless, a trend toward greater long-term disability persisted in the AQP4+ group.
Conclusion: Although relapse frequency and radiological activity during the five-year follow-up were comparable, AQP4+ NMOSD patients demonstrated a more aggressive disease course at baseline, with higher relapse burden and disability scores compared to those with SN-NMOSD. These findings

highlight the importance of early diagnosis and appropriate treatment strategies tailored to serostatus to mitigate long-term disability, particularly in AQP4+ patients.

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P1053
Cell Type-Specific Immune Regulation in MOG Antibody-Associated Disease Revealed by Single-cell RNA Sequencing

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Introduction: The pathogenesis of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) remains elusive. A subset of patients experiences frequent relapses, and the underlying mechanisms driving recurrence require elucidation.
Objectives/Aims: This study aims to elucidate the alterations in immune cell subsets and their functional dynamics during both the acute and remission phases in patients with MOG antibody-associated disease (MOGAD).
Methods: Peripheral blood mononuclear cells (PBMCs) and cerebrospinal fluid (CSF) samples from six MOGAD patients were subjected to single-cell RNA sequencing (scRNA-seq) to delineate immune functional dynamics across disease phases. Flow cytometry and histopathological analysis of central nervous system (CNS) lesions were employed to validate critical cell subsets and functional pathways.
Results: MOGAD exhibited marked activation of adaptive immunity (T cells, B cells, NK T cells) coupled with relative suppression of innate immunity (myeloid cells, NK cells). In relapsing patients, peripheral T cell activation drove B cell activation, clonal expansion, class-switching, and secretion of autoantibodies and cytokines. Subsets of T and B cells expressing high levels of migration-related genes infiltrated the CNS, synergizing with myeloid cells to amplify localized inflammatory cascades. Active MHC-II-mediated presentation of myelin antigens activated $CD4^+$ T cells, establishing a self-sustaining feedback loop. During remission, a relapse-primed cellular reservoir persisted, wherein memory T cells promoted B cell survival via low-level CD40L signaling, preserving autoantibody reserves for rapid reactivation upon antigen re-exposure. Notably, newly diagnosed patients exhibited robust immunoregulatory activity in peripheral T and B cells. Flow cytometry confirmed significant expansion of key subsets in MOGAD patients, with substantial infiltration of $CD4^+$ T cell subsets and foam cells within CNS lesions.
Conclusion: MOGAD follows a sequential immune response pattern of "peripheral initiation, central amplification, metabolic adaptation, and quiescent latency." Critical cellular subsets identified herein may serve as therapeutic targets for disease control.

Disclosure of interest: None

P1054
Evaluating the Pre-Test Probability of MOG Antibody Testing in Paediatric Patients

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Introduction: Paediatric cases constitute about 50% of myelin oligodendrocyte glycoprotein (MOG) antibody associated disease (MOGAD) cases. MOGAD can manifest as optic neuritis, acute disseminated encephalomyelitis (ADEM), transverse myelitis, cerebral monofocal or polyfocal deficits, or cortical encephalitis. Serum testing is rapidly available in many institutions and is now a routine test for evaluation of acute neurological or psychiatric conditions.
Objectives/Aims: To evaluate the pre-test probability (PTP) of serum antibody testing against MOG in a cohort of paediatric patients at a single institution presenting with a clinical picture concerning for MOGAD.
Methods: Retrospective chart review was performed on paediatric patients at Texas Children's Hospital on patients 18 or younger who received MOG antibody serum testing from 1 January 2023 to 31 December 2023.
Results: In 2023, 194 patients were tested for MOG antibodies, with 21 testing positive, and 174 testing negative. The overall pre-test probability of a positive result in this cohort was 10.8%. The PTP increased to 20% if there was radiographic evidence of demyelinating disease based on the 2023 MOGAD criteria. In patients presenting with concerns for ADEM, the PTP was 6.8%. In patients presenting with myelitis concerns, the PTP was 0.125%. Optic neuritis was higher, with a PTP of 25%. Finally, the PTP of those presenting with focal neurologic deficits was 14.3%. All patients with solely psychiatric symptoms had a negative MOG antibody test.
Conclusion: This retrospective study demonstrates that the PTP of MOG antibody positivity varies significantly based on clinical presentation in paediatric patients but can increase if there is radiographic evidence of demyelination. Among those tested, the highest yield was seen in patients with signs of optic neuritis, followed by focal neurologic deficits. In contrast, cases concerning myelitis or ADEM showed much lower probabilities, and no patients with purely psychiatric symptoms tested positive. These findings support a more targeted approach to MOG antibody testing.

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P1055
Post-thymectomy immune dysregulation: Linking myasthenia gravis to neuromyelitis optica spectrum disorder: A case series and literature review

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Introduction: Myasthenia Gravis (MG) and Neuromyelitis Optica Spectrum Disorder (NMOSD) are autoimmune channelopathies driven by complex immune responses, involving Th1, Th17, and T follicular helper cells. These cells activate B cells to produce autoreactive antibodies, leading to complement-mediated tissue damage. Both conditions are associated with certain HLA loci, suggesting a moderate genetic predisposition but strong environmental influences.
Patients with MG are associated with other autoimmune diseases in 5-30% of cases and exhibit a higher incidence of demyelinating diseases compared to the general population. Furthermore, there appears to be an increased risk of NMOSD following thymectomy in these patients.
Objectives/Aims: To describe two adult patients from Bogotá, Colombia, with concurrent MG and NMOSD with anti-Aquaporin-4 (AQP4) antibodies post-thymectomy, and to conduct a literature review.
Methods: We conducted a retrospective literature review using the PubMed and Embase databases for articles published up to October 2024. The search utilized the terms "Neuromyelitis," "Thymectomy," "Myasthenia Gravis," and "Aquaporin 4." We included studies in English and Spanish that reported cases of MG and NMOSD, regardless of thymectomy history.
Exclusion criteria included studies lacking sufficient clinical data, failing to clearly differentiate MG from other neurological conditions, or presenting duplicate reports. We included two case reports of adult patients from Bogotá, Colombia, who developed NMOSD following thymectomy for MG.
Results: We present two adult patients, one male and one female, from Bogotá, Colombia, who were diagnosed with MG and subsequently developed symptoms of NMOSD following thymectomy. 26 studies were included in our review, encompassing 60 patients. The majority of these patients were female, and 83% had MG prior to the onset of NMOSD. Among those with MG, approximately 74% underwent thymectomy before NMOSD symptoms appeared; however, some patients developed NMOSD without a history of thymectomy. In 41 patients, acetylcholine antibodies were positive, and thymic hyperplasia was the most commonly observed pathology.
Conclusion: In most cases, MG presented first, while NMOSD appeared to be preceded by thymectomy, as observed in both patients from our case series. This procedure may disrupt immune regulation by eliminating thymic suppressor T cells, increasing CD4+/CD8+ T cells and reducing regulatory T cells. This immune dysregulation can trigger autoimmune diseases, including NMOSD and systemic lupus erythematosus. In MG patients with thymoma, AQP4 antibodies may represent a paraneoplastic phenomenon, although this theory couldn't be confirmed in our cases due to the lack of pathology results.
The coexistence of MG and NMOSD in our region remains unknown, with no other reports from Colombia to date. More studies are needed to improve clinical understanding and patient care.

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P1056
MOGAD Beyond the First Fire: Treatment Outcomes and Relapses in FLAMES Phenotype

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Introduction: FLAMES (FLAIR-hyperintense Lesions in Anti-MOG-associated Encephalitis with Seizures) is a recently recognized phenotype of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), characterized by unilateral cortical T2/FLAIR hyperintensities and seizures. Relapse patterns and treatment outcomes remain poorly understood.
Objectives/Aims: To evaluate relapse patterns and treatment response in patients with MOGAD presenting as FLAMES.
Methods: This study was conducted at a tertiary referral center for demyelinating disorders. Patients diagnosed with FLAMES based on 3T MRI and standard cell-based MOG antibody assay were included. A systematic literature review (2017–present) was also performed, focusing on relapses and outcomes. Descriptive statistics were analyzed using MS Excel.
Results: Over two years, we identified 3 FLAMES cases at our center and 37 previously reported, yielding 40 cases. Median age was 29 years (range 4–52), with slight male predominance (55%). Median follow-up was 7 months (IQR 4.5–23.5). FLAMES was the initial demyelinating event in 85%, with 15% having concurrent optic neuritis. Seizures were most common (65%), followed by headache (55%), fever (45%), aphasia (22.5%), and hemiparesis (17.5%). Intravenous methylprednisolone (median 1 g/day for 5 days) led to full recovery in 91%; two required additional immunotherapy. Mean steroid duration was 11 $\pm$ 8 months. 60% patients relapsed (median time 22 days). Among 36 relapse episodes in 20 patients: 44.4% were optic neuritis, 38.9% FLAMES recurrences, 8.3% brainstem, 5.6% myelitis, and 2.8% ADEM-like. IV steroids achieved

complete recovery in 75%. At last follow-up, 4 patients were on long-term immunosuppression; one with recurrent optic neuritis stabilized on IVIg.
Conclusion: FLAMES may represent a distinct, steroid-responsive yet relapsing MOGAD phenotype, with optic neuritis being the most common subsequent event. The overlap in meningeal involvement, excellent response to corticosteroids, and overall favourable recovery suggests a shared pathophysiology. Further research exploring these distinct subtypes of MOGAD may aid in the development of tailored treatment protocols.

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P1057
Myelin Oligodendrocyte Glycoprotein (MOG) IgA and IgG3 antibodies in patients with Central Nervous System (CNS) Demyelinating Syndromes: a Retrospective Study Analysis

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Introduction: Antibodies against Myelin-Oligodendrocyte-Glycoprotein (MOG), usually IgG1 subclass, have been linked to MOG-antibody-associated-disease (MOGAD), whereas recently a possible role of MOG-IgA and MOG-IgG3 has also been suggested in CNS demyelination.
Objectives/Aims: This study aims to present data on different Ig classes and subclasses against MOG in patients with CNS inflammation.
Methods: Data from adult patients with ⩾ 1 clinical attack associated with brain, and/or optic nerve and/or spinal cord involvement and from 32 healthy-controls were collected retrospectively by two Academic Neurological Centers in Greece and Turkey. We screened sera from 195 patients with Multiple Sclerosis (MS), MOGAD, aquaporin-4-IgG seropositive or seronegative Neuromyelitis-Optica-Spectrum-Disorder (NMOSD-AQP4+ & NMOSD-AQP4-) and "other CNS demyelinating disorders" (OCNSDD) including monophasic or relapsing optic neuritis (RON) and/or myelitis. MOG-Ig isotypes and subtypes (IgG1, 3 and IgA) were examined by a live cell-based assay (CBA) using MOG–transfected HEK293 cells. The cut-off titer for seropositivity (+) for MOG-IgG1 and IgG3 was defined at 1:20 and for MOG-IgA at 1:250. Retrospective MRI and oligoclonal-bands (OCBs) data analysis was also performed.
Results: CBA showed that patients from clinical groups (RRMS) (n=2/55) and OCNSDD (n=1/30) were MOG-IgA+ with end-titer at 1/320; MRI showed short-segment myelitis in 2/3 and brain supratentorial/subtentorial lesions in 3/3; cerebrospinal-fluid (CSF) specific OCBs were reported in 2/3. Patients with RRMS (n=1/55) and RON (n=1/15) were MOG-IgG3+, short myelitis and supratentorial lesions along with CSF specific OCBs were identified in 1/2. Groups of NMOSD-AQP4- (n=1/29) and RRMS (n=1/55) CBA showed double seropositivity for MOG-IgA and MOG-IgG3 antibodies; MRI showed short myelitis (n=2), longitudinally extensive transverse myelitis (n=1), brain supratentorial/subtentorial lesions (n=1); CSF-specific OCBs (n=1). The control-group (n=32) tested seronegative for MOG-IgG1, -IgG3, and -IgA.
Conclusion: Our study emphasizes on the diversity of anti-MOG antibodies in CNS demyelination and warrants the necessity for anti-MOG-IgA and -IgG3 screening when MOG-IgG1s are negative.

Disclosure of interest: The authors have nothing to disclose.

P1058
Clinical and Radiological Outcomes in People with Aquaporin-4 Antibody Positive Neuromyelitis Optica Spectrum Disorder Following Ravulizumab Treatment (AMAZE)

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune condition of the central nervous system with aggressive involvement of the optic nerves and spinal cord caused by injury to aquaporin-4 (AQP4) water channels. Exacerbations are unpredictable and result in the accumulation of permanent disability. A comprehensive understanding of ideal treatment practices and disease surveillance is needed to improve clinical outcomes. All pivotal trials involving FDA-approved treatments lacked comprehensive neuroimaging outcomes associated with use. In addition, the presence of neuroinflammatory/neurodegenerative activity below the resolution of conventional techniques remains unknown. Effectiveness of ravulizumab on conventional/non-conventional neuroimaging outcomes also remains underexplored.

Objectives/Aims: To prospectively study the clinical performance of ravulizumab, enhance knowledge on conventional MRI outcomes, assess for occult disease activity via quantitative imaging metrics, identify serum biomarkers related to disease progression, and explore contemporary social factors that may impact neurological outcomes in people with AQP4 antibody positive (AQP4-Ab+) NMOSD.
Methods: This single-center, observational, 78-week trial will include 35 individuals fulfilling the 2015 International Panel Criteria for AQP4-Ab+ NMOSD. General physical examinations, Expanded Disability Status Scale assessments, conventional/quantitative MRI sequences, and the collection of biological samples for biomarker analysis will be performed at baseline and at 13-, 26-, 52-, and 78-weeks post-initiation of ravulizumab treatment. Innovative social and environmental factors influencing health outcomes from participant-reported data and external digital resources will be analyzed throughout the study.
Results: Enrollment currently consists of 17 subjects (14 female; 8 White; 12 Non-Hispanic; median age at study start=48 years (y) (range=22-65y); median disease duration from time of diagnosis=5.84y (1.34-19.01y). Up-to-date clinical and MRI outcomes and acquired safety data will be provided at the time of presentation.
Conclusion: Upon study completion, the biological effects of ravulizumab on clinical, serological, and radiological measures of disease, in addition to the impact of social determinants of health on access to care and treatment outcomes, will be better understood. Collectively, these data may guide clinicians towards optimized and equitable healthcare practices for those affected by AQP4-Ab+ NMOSD.

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P1059
Recurrence in Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD): Experience from a Single Center in Argentina

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a demyelinating disorder of the central nervous system that may follow a monophasic or relapsing course. Factors associated with relapse and clinical progression remain poorly understood.
Objectives/Aims: To describe the demographic, clinical, laboratory, MRI and treatment characteristics in a cohort of MOGAD patients.
Methods: This was a retrospective, cross-sectional study conducted at a single reference center in Buenos Aires, Argentina. Twenty consecutive patients evaluated between 2018 and 2024 were included. All patients tested positive for anti-MOG antibodies by either a fixed cell-based assay (Eurimmune CBA®) or a live cell-based assay with a titer >1:100, and had at least 12 months of clinical follow-up. Demographic data, clinical manifestations, MRI findings, and CSF features were recorded. Relapse was defined as the appearance of new inflammatory symptoms at least 31 days after recovery from a prior episode.
Results: Nine out of twenty patients (45%) had a relapsing disease course. No sex differences were observed between monophasic and relapsing groups. The age at disease onset was significantly lower in the relapsing group: median 24 years (IQR 12–34) vs. 38 years (IQR 29–57) in the monophasic group ($p = 0.05$). The median time to first relapse was 2 months (range 1–24) in patients treated with corticosteroids only (7/9). Three patients received immunosuppressive therapy after the first attack; two of them relapsed after 4 and 8 years, respectively.
At disease onset, 71.4% (15/20) presented with optic neuritis (ON), 15% (3/20) with transverse myelitis (TM), 10% (2/20) with brainstem syndrome (BS), and 5% (1/20) with encephalitis. During relapses, TM and BS were more frequent (44% each) than at initial presentation.
CSF protein levels were higher in the relapsing group: 58 mg/dL (IQR: 35–66) vs. 33 mg/dL (IQR: 25–45) in the monophasic group ($p = 0.049$). Although CSF cell count was higher in the relapsing group (median 6.0 vs. 2.0 cells/mm^3), this trend did not reach statistical significance. All patients with relapsing disease had type I OCBs; in the monophasic group, 15% had type IV OCBs. No patients had type II OCBs.

There was a non-significant trend toward higher MOG antibody titers at onset in the relapsing group (median 1:210 vs. 1:100). Five of nine relapsing patients were treated with azathioprine, and three of them experienced new relapses. Four patients were initially treated with rituximab, all of whom responded well.
Conclusion: In this Argentine MOGAD series, relapse was associated with earlier disease onset, elevated CSF protein levels, and trends toward higher CSF cell count and initial MOG antibody titers. Further prospective studies are needed in our region to identify reliable risk markers for recurrence.

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P1060
AQP4-Positive NMOSD Versus MOGAD: Distinct Myelitis Phenotypes

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Introduction: Aquaporin-4 antibody positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are inflammatory diseases that share common features, particularly myelitis. Although it is usually severe and extensive in both conditions, certain clinical, radiological and prognostic characteristics can help distinguish them.
Objectives/Aims: Our study aims to compare myelitis features in AQP4+ NMOSD and MOGAD to facilitate earlier diagnosis and management.
Methods: We retrospectively collected data of patients diagnosed with AQP4+ NMOSD according to 2015 Wingerchuck diagnostic criteria (52 patients) and those having MOGAD according to 2023 international MOGAD panel proposed criteria (27 patients). Among them, we selected those presenting with myelitis as an initial manifestation or during follow-up. Clinical, MRI data and follow-up outcome were analyzed and compared between the two groups.
Results: Myelitis occurred in 36 AQP4+ NMOSD patients (69,2%) and 11 MOG patients (40,7%) during their disease course. Compared to MOGAD, myelitis was significantly more frequent as an initial manifestation in AQP4+ NMOSD patients (57.7% vs 25.9%; p=0.024).
Gait disturbances were common in both groups without a significant difference (53.8% in AQP4+ vs. 44.4% in MOGAD; $p = 0.428$), whereas sensory symptoms and bladder sphincter dysfunction were more frequent in the AQP4+ group (51.9% vs. 22.2%; $p = 0.011$ and 34.6% vs. 18.5%; p=0.135 respectively). Lhermitte's sign and area postrema syndrome were also more frequent in AQP4+ patients with no statistical significance (p=0,41 and p=0,29 respectively). Pruritus (7.4% vs. 0%, $p = 0.114$) and tonic spasms (8.3% vs. 0%, $p = 0.13$) were exclusively noted in the the AQP4+ group.
On imaging, longitudinally extensive spinal cord lesions were significantly more frequent in the AQP4+ patients (42.3% vs. 18.5%; $p = 0.034$), whereas short myelitis was observed comparably in both groups (18,5% vs.15,5%, p=0,75). Terminal cone involvement occurred only in MOGAD patients (7.4% vs. 0%; $p = 0.114$).
At follow-up, myelitis represented approximatively one-third of all relapses in both groups (36.5% vs 34.2%; p=0.07), with a correlation between the presence of myelitis at onset and a higher EDSS at last visit in both AQP4+ NMOSD and MOGAD (p=0,01 and p=0,02 respectively).
Conclusion: Our study emphasizes the importance of identifying specific clinical and radiological patterns of myelitis to better distinguish AQP4+ NMOSD and MOGAD. Integrating MRI analysis with early antibody testing and repeated clinical evaluation can reduce diagnostic and management delays.

Disclosure of interest: Rania Zouari: nothing to disclose.

P1061
Long-term treatment with Interleukin-6 Receptor Inhibitor Tocilizumab in Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease

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Introduction: Data about efficacy and safety of disease-modifying therapeutic options in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are scarce. Interleukin-6 signaling has been suggested to be involved in the pathogenesis of MOGAD.
Objectives/Aims: In this study, we evaluated effectiveness and safety of the interleukin-6 receptor inhibitor tocilizumab in MOGAD.
Methods: In this monocentric, longitudinal, retrospective study, the annualized relapse rate (ARR), the Expanded Disability Status Scale (EDSS), imaging findings, MOG-autoantibody titers and adverse events were evaluated before and after tocilizumab initiation in patients with MOGAD. Possible side effects such as dyslipidemia, impaired liver function, and infections were assessed based on clinical history, physical examinations, and laboratory data.
Results: Sixteen patients with confirmed MOGAD treated with tocilizumab for more than 6 months were included. The median follow-up on tocilizumab treatment was 2.46 years (range 0.5 – 10). The median ARR significantly decreased from 0.75 (IQR 0.5-1.0) 24 months before to 0 (IQR 0-0) at 12 months after tocilizumab initiation ($p = 0.005$). Likewise, the EDSS score improved from 2.75 (IQR 2.0-3.5) at baseline to 2.25 (IQR 1.1-3.0) 12 months after starting tocilizumab ($p = 0.046$). In the first year after starting tocilizumab treatment, MOG-IgG titers

decreased in 10 of 13 patients (76.9%). No patient showed radiological progression under tocilizumab. Infectious adverse events requiring medical treatment occurred in 4/16 patients (25%), including three hospitalizations. Side effects such as dyslipidemia and impaired liver function were prevalent, but rarely required the interruption of tocilizumab. In 5 patients (31.3%), the route of administration of tocilizumab was switched to subcutaneous injections over the disease course. All of these patients have remained relapse-free so far.
Conclusion: Long-term tocilizumab treatment appears effective in patients with MOGAD and severe complications are rare. Subcutaneous tocilizumab administration may improve therapy adherence.

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P1062
Prevalence and Phenotypic Variability of Headache in Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

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Introduction: Pain is gaining increasing recognition as a relevant symptom in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). Although associations with headache and optic neuritis have been documented, specific studies on headache prevalence and clinical features in MOGAD are lacking.
Objectives/Aims: This study aims to assess the prevalence and describe the clinical features of headache in both the acute phase and chronic course of the disease in MOGAD patients.
Methods: We selected 21 patients diagnosed with MOGAD according to the criteria proposed by the International MOGAD Panel. We analyzed clinical, radiological, and laboratory findings throughout the disease course, as well as responses to both acute and chronic treatments. Through a structured interview, we evaluated the presence of onset-related headache and its characteristics (including severity, location, quality of pain, accompanying symptoms, and response to medications). We also retrospectively collected data on the history of preexisting primary headache disorders and prospectively assessed changes in their clinical course following MOGAD onset, along with newly diagnosed headache disorders. Other regional pain symptoms were also investigated.
Results: Twelve patients (57.1%) experienced headache preceding or accompanying the onset of other neurological manifestations. Headache duration ranged from 24 hours to 10 days, and qualitative characteristics varied widely without a consistent pattern. Twelve patients (68.7%) had a history of primary headache disorders; all reported differences in severity, location, and medication response compared to their usual headaches. Four patients experienced newly-onset headaches: three had no recurrence, while the other two currently suffer from episodic migraine. In total, six patients reported improvement in headache severity and frequency following treatment.
Conclusion: The majority of our patients experienced headache at disease onset. Headache is an often under-recognized symptom, and its careful evaluation during the diagnostic work-up of Central Nervous System inflammatory disorders may aid in early disease recognition and potentially in predicting relapses in predisposed individuals. Larger patient cohorts and longer follow-up periods are needed to validate these findings.

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P1063
Characterizing Pain in Neuromyelitis Optica Spectrum Disorder: Prevalence and Clinical Features

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Introduction: Chronic pain is a common symptom that impairs activities of daily living in persons with Neuromyelitis Optica Spectrum Disorder (NMOSD, pwNMOSD). The higher the intensity of pain in pwNMOSD, the worse the physical and emotional quality of life is affected.

Objectives/Aims: To determine the prevalence and characteristics of pain in pwNMOSD.
Methods: This cross-sectional study involved a total of 62 pwNMOSD. The Nordic Musculoskeletal Questionnaire (NMQ) was used to determine the participants' pain levels and pain localization. The PainDETECT Questionnaire (PD-Q) was used to differentiate between nociceptive and neuropathic pain. The scores ⩽ 12 were considered as presence of musculoskeletal pain and >12 as neuropathic pain. The Preference-Based Multiple Sclerosis Index (PBMSI) was used to measure health-related quality of life. Information such as Expanded Disability Status Scale (EDSS), disease duration and age of the participants were also recorded.
Results: The 62 participants included in the study were divided into 3 groups: 14 without pain, 17 with Musculoskeletal Pain (MSP) and 31 with Neuropathic Pain (NP). There was no difference between the groups in terms of age, disease duration and EDSS scores ($p>0.05$). When the pain distribution was analyzed, the regions with the most pain complaints in the last 12 months were neck (n=22, 34.9%), foot-ankle (n=16, 25.4%) and back (n=15, 25.8%), respectively. The frequency of pain sites that prevented work in the last 12 months were neck (n=9, 14.3%), back (n=7, 11.1%) and foot-ankle (n=7, 11.1%). The most common areas of pain in the last 7 days were neck (n=19, 30.2%), foot-ankle (n=16, 25.4%) and back (n=14, 22.2%). When the quality of life of the three groups were compared, there was a difference between PBMSI-Walk, PBMSI-Fatigue and total score. As a result of post-hoc analysis, there was a difference between MSP (0.08 ± 0.23) and NP (0.38 ± 0.40) for PBMSI-Walking. For PBMSI-Fatigue, there was a difference between MSP (0.19 ± 0.28) and NP (0.56 ± 0.35), NP (0.56 ± 0.35) and no pain (0.23 ± 0.39) groups. For the total score, there was a difference between MSP (0.90 ± 0.14) and NP (0.65 ± 0.25), NP (0.65 ± 0.25) and no pain (0.85 ± 0.27) groups.
Conclusion: The results of this study showed that the neck, back, and foot-ankle were the most common and most disabling pain areas in pwNMOSD, regardless of the age, disease duration, and EDSS score of the participant. However, there was a difference between the groups in the parameters related to gait, fatigue and total quality of life against neuropathic pain.

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P1064
The Patient Experience of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease Post-Diagnosis: Results from an International Survey

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Introduction: Data on the post-diagnosis experience of individuals with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) or their caregivers are limited.
Objectives/Aims: Explore post-diagnosis treatment experience and satisfaction with care in individuals with MOGAD and the burden on their caregivers.
Methods: A 57-question survey (multiple-choice, multiple-response and free-text questions; no questions were compulsory) was distributed to individuals with MOGAD between Oct–Dec 2024 via the online platforms of The MOG Project and the Siegel Rare Neuroimmune Association. Respondents were individuals with MOGAD aged ⩾16 years old ('adults'), caregivers of adults with MOGAD, or caregivers of individuals with MOGAD aged ⩽15 years ('children'). Caregivers of children and adults were asked to answer a question about what aspects of their lives have been impacted by being a caregiver.
Results: There were 261 survey responses (adults, 219; children, 42 [41 parents, 1 non-parent]) across 26 countries. Of those previously prescribed a preventative treatment, 43% of adults (71/167) and 42% of children (13/31) reported stopping treatment. Common reasons for stopping most recent treatment were side effects (adults, 39% [26/67]; children, 8% [1/12]), lack of efficacy (adults, 28% [19/67]; children, 25% [3/12]) and other non-specified reasons (adults, 49% [33/67]; children, 75% [9/12]). Most adults (73%, 159/219) and children (64%, 27/42) reported difficulties accessing or trying to access MOGAD treatment and care. Respondents were asked about satisfaction with different types of care. Among respondents on financial support, 36% (57/158) of adults and 38% (12/32) of children were dissatisfied. Other care types with substantial dissatisfaction were chronic symptom management for adults (35%, 71/202) and psychological/emotional support for children (31%, 11/36). Satisfaction with care appeared similar regardless of diagnosis pre- or post-publication of the 2023 diagnostic criteria. Compared to individuals with MOGAD (N=261), caregivers (of adults, n=61; of children, n=42) were significantly more likely to report mental health impacts (26% vs 92%, $p<0.001$).
Conclusion: Multiple unmet care and support needs persist. Individuals have difficulty accessing treatment and care, and treatments are often stopped or changed, highlighting the need for more efficacious and tolerable therapies. Caregivers, both parents and caregivers of adult patients, experience significant mental health impacts and improved support is needed.

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and Co-Founder of The MOG Project and a Consultant for UCB. Panayotes Demakakos and Danielle Hartigh are employees of UCB, the funder of this research. Magali Periquet is an employee of and shareholder in UCB, the funder of this research. Khaleda Ahmadyar and Zara Morrison are employees of OPEN Health Communications, who were commissioned by UCB to conduct the research. Jacqueline Palace has received support for scientific meetings and honoraria for advisory work from Merck Serono, Novartis, Chugai, Alexion, Roche, MedImmune, Argenx, Sanofi, UCB, Mitsubishi, Amplo Biotechnology, and Janssen; has received grants from Alexion, Roche, Medimmune and Amplo Biotechnology; holds patent ref. P37347WO and licence agreement with numares multimarker MS diagnostics; has shares in AstraZeneca; and acknowledges partial funding by highly specialised services NHS England. Funding for this study was provided by UCB. Medical writing support in the preparation of this abstract was provided by Niall Harrison and Reece Bracewell of Mimas, a division of OPEN Health Communications, and was funded by UCB in accordance with Good Publication Practice (GPP) guidelines (www.ismpp.org/gpp-2022).

P1065
Inebilizumab for treatment of NMOSD in a Real-World Cohort: Analysis from the SPHERES Registry

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune disorder of the central nervous system (CNS) that affects the optic nerves and spinal cord. Early initiation of maintenance therapy is recommended to reduce NMOSD relapses and prevent disability. Inebilizumab targets CD19+ B cells to reduce the risk of NMOSD relapses.
Objectives/Aims: This study aimed to describe demographics, disease characteristics, and treatment patterns among patients receiving inebilizumab in a real-world setting.
Methods: Patients with NMOSD from the US-based SPHERES (Synergy of Prospective Health & Experimental Research for Emerging Solutions) Registry who enrolled from June 2, 2021, to February 28, 2025, and had ever received inebilizumab were included (adults age ⩾18 years who were diagnosed with NMOSD according to the 2015 IPND consensus diagnostic criteria). The index visit was defined as the enrollment visit for patients with inebilizumab use prior to SPHERES enrollment, or the registry visit coinciding with inebilizumab initiation for patients who initiated inebilizumab at or after enrollment.
Results: There was a total of 68 inebilizumab users of which 63 (93%) were aquaporin-4 antibody positive (AQP4-IgG+). The mean age was 50 years, 93% were female, 38% were White, and 46% were Black/African American. The mean time from diagnosis to index visit was 6 years, but 19% of users were newly diagnosed (within one year of the index visit). Prior to the index visit, 32%, 19%, and 49% of subjects had one, two, or three or more relapses, respectively; the mean number ± SD of relapses was 3.2 ± 2.6. Of patients on A-BIOs, inebilizumab was initiated as first-, second-, or third-line therapy in 34% (30/89), 31% (21/67), and 24% (9/37) patients, respectively.
Conclusion: This descriptive analysis of real-world NMOSD patients who newly initiated or used inebilizumab provides valuable insights into patient demographic, clinical characteristics, and treatment patterns. While patients were commonly switched to inebilizumab, further analysis is needed to understand long-term real-world outcomes.

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P1066
Considering The Paraneoplastic Neuromyelitis Optica Spectrum Disease Patients: We Need to Explain This Entitiy

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Introduction: An association has been reported especially between breast, lung and gastrointestinal cancers and neuromyelitis optica spectrum disorder (NMOSD). In paraneoplastic NMOSD (P-NMOSD) cases, it is thought that tumors may

express aquaporin-4 (AQP4) and this may be an immunological trigger.
Objectives/Aims: In this study, the frequency and characteristics of AQP4 positive PNMOSD in the NMOSD group were investigated.
Methods: When a group of 375 seropositive NMOSD diagnosed patients was retrospectively screened, 12 (3.2%) patients were evaluated as P-NMOSD.
Results: The mean age of the P-NMOSD group was 61.50 ± 11.42 (44-75) and the number of females was 3 times more than males (F:M; 3/1). When the cancer types of the study group were examined; there were 3 breast cancers, 2 testicular cancers, 2 thymomas, 2 cervical cancers, 1 ovarian cancer, 1 squamous cell lung cancer, and 1 squamous cell skin cancer. 10 patients were diagnosed with cancer after NMOSD (83.3%). It was observed that the male ratio was higher compared to NMOSD (9:1 vs 3:1). At the end of the study period, where the mean follow-up period was 142 months, 4 patients died (33.3%). When the patients who died were evaluated in terms of the attack treatment or maintenance treatments received, no significant difference was observed between the patients who survived and the patients who died.
Conclusion: In the presence of atypical onset NMOSD, such as male gender and older, it was thought that evaluation for malignancy was important both in disease management and in predicting survival. When it was seen that diagnosis was frequent after NMOSD in our series, the importance of malignancy screening in atypical cases also draws attention.

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P1067
Sex Hormonal Influences Across the Lifespan in Women with NMOSD: A Patient-Reported Study

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) predominantly affects women, yet the influence of sex hormonal factors across reproductive stages remains poorly understood worldwide, including the Latin American population.
Objectives/Aims: We aimed to explore whether hormonal milestones and exposures, such as menarche, hormonal contraception, pregnancy, and menopause, are associated with age at NMOSD diagnosis and disease activity.
Methods: We analyzed data from 103 women diagnosed with NMOSD who completed a detailed self-administered questionnaire addressing menstrual history, hormonal therapies, pregnancies, and disease related features. Statistical tests included Spearman correlation, linear regression, ANOVA and Mann–Whitney U.
Results: Older age at menarche was significantly associated with later age at diagnosis (Spearman's rho = 0.51, $p = 0.003$), although this was not confirmed by linear regression. Hormonal contraceptive use and its duration were not associated with age at diagnosis (all $p > 0.1$). In contrast, a higher number of pregnancies was significantly associated with older age at diagnosis (rho = 0.50, $p < 0.001$). Regarding symptom patterns, 26% reported worsening residual symptoms and 44% increased fatigue during menstruation. Relapses were reported during menstruation (18.5% of participants), pregnancy (5.6%), and the postpartum period (7.4%).
Conclusion: In this patient-reported cohort of women with NMOSD, later menarche and higher number of pregnancies were associated with a later age at diagnosis. Moreover, the occurrence of relapses and symptom worsening during menstruation and the postpartum period, highlight a potential role of sex hormonal dynamics in disease expression, warranting further investigation.

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P1068
NMOSD Treatment Patterns in the Era of Approved Biologics: An Analysis from the SPHERES Registry

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune disorder of the Central Nervous System (CNS) that affects the optic nerves and spinal cord, leading to permanent disability and reduced quality of life.
Objectives/Aims: Since 2019, four biologic therapies have been approved to prevent relapses in patients with NMOSD and aquaporin-4 antibodies (AQP4-IgG+): eculizumab, inebilizumab, ravulizumab, and satralizumab (A-BIOs). It is unclear how these newer therapies are utilized in real-world practice.
Methods: Patients with NMOSD from the US-based SPHERES (Synergy of Prospective Health & Experimental Research for Emerging Solutions) Registry enrolled from 6/2/2021 to 2/28/2025 were included (adults age ⩾18 years who were diagnosed with NMOSD according to the 2015 IPND consensus diagnostic criteria). The study sequenced therapies prescribed for NMOSD by tabulating all prior medication history reported up to the current therapy at the time of analysis. Demographics, lifestyle characteristics, history of comorbidities, NMOSD and clinical characteristics were summarized.
Results: This study included 422 patients, of which 294 (70%) were AQP4-IgG+, 58 (14%) were myelin oligodendrocyte glycoprotein immunoglobulin G (MOG) seropositive, and 37 (9%) were seronegative. The mean age of subjects was 51 years, 84% were female, 58% were White, and 33% were Black/African American. Further, 200 (47%) required second line therapy, 96 (23%) required third line therapy.
For monotherapies, rituximab (43%) was the most prescribed first-line therapy, followed by A-BIOs (21%) and IST (20%). Among the patients that required second- or third-line monotherapy, A-BIOs were most commonly prescribed (34% and 39%, respectively). Eculizumab and inebilizumab were the most common first line A-BIOs. Inebilizumab and satralizumab were the most common second-line A-BIOs. Satralizumab was the most common third-line A-BIO.
Conclusion: This study showed a predominant first line use of rituximab followed by A-BIOs. However, nearly half of participants needed a second line therapy or higher. We showed a preponderance of rituximab use in earlier lines of therapy, while A-BIOs, specifically inebilizumab, satralizumab, and eculizumab, were used more often as second or higher lines of therapy. Given the accrual of disability with subsequent attacks, this study underscores the need for consideration of earlier use of the approved biologics to help prevent attacks.

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P1069
Health Literacy in Neuromyelitis Optica Spectrum Disorder: Results from a Global Online Survey

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune disease affecting the optic nerves and spinal cord, often leading to severe disability. Specialized nursing support is essential for patient navigation, communication, and digital health management.
Objectives/Aims: This study assesses the global burden of NMOSD through an online survey, examining healthcare navigation, patient communication, and digital health literacy.
Methods: A cross-sectional online survey was conducted (September 2024–January 2025) via NMOSD patient association channels. Validated questionnaires measured digital health literacy across five domains: HL-DIGI-HI, HL-DIGI-DD, HL-DIGI-INT, HL-NAV, and HL-COM, using the HLS-EU scoring system (0–100). Comparisons focused on the United States and Europe.
Results: The study included 149 participants (85.9% female, mean EDSS: 3.0, SD = 2.11), mostly aged 40–49 (29.5%). NMOSD subtypes included anti-AQP4 (51.7%), anti-MOG (30.9%), and seronegative (17.4%). Rituximab (45.6%) was the most used treatment. Most patients had access to NMOSD-specialized nurses (60.4%) and were satisfied with their care (85.2%). Patients in the USA showed significantly better results than those in Europe, particularly in HL-DIGI-DD ($p=0.003$), HL-NAV ($p=0.049$), and HL-COM ($p=0.050$). A significant correlation was found between digital navigation and communication skills ($r=0.435$, $p<0.001$).
Conclusion: NMOSD impacts healthcare navigation, communication, and digital engagement, with better digital health literacy outcomes in the USA compared to Europe, suggesting disparities in healthcare access and digital literacy. Enhanced

nursing education, digital training, and improved healthcare access could better support NMOSD patients globally.

Disclosure of interest: Author's name: nothing to disclose

P1070
Tailored memory B-cell guided rituximab therapy in AQP4-NMOSD patients

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Introduction: Effective treatment of neuromyelitis optica spectrum disorder with aquaporin-4 antibodies (AQP4-NMOSD) is crucial to prevent relapses, the main drivers of disability accrual. Treatment strategies, include B-cell depletion therapy with rituximab. Optimal dosing and treatment schedule is unknown, and B cell depletion dynamics vary between patients. $CD19^+CD27^+$ memory B cells may be used as surrogate markers for treatment monitoring and re-dosing.
Objectives/Aims: To assess real-world effectivity and safety of a $CD19^+CD27^+$ memory B-cells guided dosing strategy in patients with AQP4-NMOSD.
Methods: Retrospective cohort study, including all adult patients fulfilling the IPND 2015 AQP4-NMOSD criteria referred to the MOGAD-NMO Clinic of our centre, treated with rituximab on a tailored regimen. Data pertaining demographics, disease onset, relapses, rituximab therapy, $CD19^+CD27^+$ levels, and side effects was retrieved and analyzed with descriptive statistics.
Results: Of 67 patients with antibody mediated or seronegative demyelinating syndromes, 16 had AQP4-NMOSD, 15 were on rituximab, and 10 were on a tailored regimen. Median age was 37.5 years (IQR 32-61), with a female:male ratio of 8:2. Most patients (6/10) were treatment naïve before rituximab. Patients had median disease duration and follow-up time of 73.5 (IQR 45-129) and 60 months (IQR 8-120), respectively, with pre-rituximab EDSS of 3.5 (IQR 3-6.5) and crude pre-rituximab annualized relapse rate (ARR) of 0.57. After rituximab initiation, there was only 1 relapse over 39.3 patient-years of treatment exposure (ARR=0.02; 95% relative risk reduction) with a median time to first rituximab re-treatment of 8 (IQR 5.5-9.5) and overall dosing interval of 10.5 (IQR 7-13) months. Regarding safety, 4/10 patients had treatment-related adverse events (1 was serious).
Conclusion: In our cohort, a $CD19^+CD27^+$ memory B-cells guided dosing strategy was an effective and safe option for AQP4-NMOSD patients. Personalized and tailored strategies may be useful in reducing number of treatments with potential cost and safety benefits, without compromising disease control.

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P1071
The effect of Inalizumab treatment on pulmonary nodules in patients with neuromyelitis optica spectrum disorder

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Introduction: There is limited data on whether pulmonary nodule changes should be monitored in NMOSD patients receiving B-cell depletion therapy, and the data regarding pulmonary nodule changes in these patients are scarce.
Objectives/Aims: This study aims to assess the changes in pulmonary nodules in patients with neuromyelitis optica spectrum disorder (NMOSD) undergoing treatment with Inebilizumab, in order to provide a basis for clinical decision-making.
Methods: A total of 49 adult AQP4+ NMOSD patients who started treatment with Inebilizumab for the first time at the Department of Neurology, the First Affiliated Hospital of Kunming Medical University, between March 2023 and March 2025, were included. The observed indicators included the presence or absence of pulmonary nodules and nodule size. The nodule status was compared at baseline (before treatment), the first dose, and the last follow-up visit.
Results: Among the 49 patients treated with Inebilizumab, before treatment, 85.7% (42/49) had pulmonary nodules, and 14.3% (7/49) did not have pulmonary nodules. At the last follow-up visit, 91.8% (45/49) had pulmonary nodules, and 8.2% (4/49) did not have pulmonary nodules. Fifteen patients showed a reduction or disappearance of pulmonary nodules, 16 patients had stable nodule sizes, and 18 patients had newly developed or enlarged pulmonary nodules. After the administration of Inebilizumab, the incidence of pulmonary nodules significantly increased ($P = 0.033 < 0.05$), but no tumor-like lesions were observed. Paired sample Wilcoxon signed-rank test analysis showed that the maximum diameter of pulmonary nodules after treatment was larger than before treatment, but the difference was not statistically significant ($P = 0.060$).
Conclusion: Treatment with Inebilizumab in NMOSD patients increased the incidence of pulmonary nodules, but no tumor-like lesions were observed. Long-term follow-up is required to further clarify the impact of Inebilizumab on pulmonary nodules and assess its long-term efficacy and safety.

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P1072
Beyond the Central Nervous System: Fibrosing Interstitial Lung Disease as an Extraneurological Manifestation of Aquaporin-4 Antibodies?

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Introduction: Neuromyelitis optica (NMO) associated with anti-aquaporin-4 (AQP4) antibodies is a well-characterized autoimmune disease primarily affecting the central nervous system. However, AQP4 channels are also expressed in various non-neural tissues, including the pulmonary epithelium. Although pulmonary involvement is not classically recognized in NMO.
Objectives/Aims: We report a case of AQP4-positive NMO complicated by fibrosing nonspecific interstitial pneumonia (NSIP), raising the question of a potential pathogenic role of anti-AQP4 antibodies in lung tissue.
Methods: A 32-year-old woman with a 4-year history of AQP4-positive neuromyelitis optica (NMO), initially presented with persistent dyspnea that had been gradually worsening over several months, starting after a COVID-19 infection in 2020, and occurring a few months before the diagnosis of NMO. Despite being clinically stable on Ravulizumab treatment for NMO, her respiratory symptoms worsened significantly. Chest CT and pulmonary function tests revealed fibrosing non-specific interstitial pneumonia (NSIP) with a severe restrictive ventilatory defect. Despite oral corticosteroid therapy (20 mg/day), the interstitial lung disease continued to progress, with a further decline in pulmonary function and worsening fibrosis on imaging. A discussion between pulmonologists and neurologists did not conclude a causal link between the two conditions. Given the refractory nature of the pneumopathy, cyclophosphamide therapy was initiated, and lung transplantation is currently being considered.
Results: Associations between anti-AQP4 antibodies and acute lung injury, interstitial pneumonia or lung carcinoma have been reported in the literature; however, no link has yet been established with fibrosing interstitial lung diseases such as non-specific interstitial pneumonia (NSIP). This makes our case particularly atypical and raises the hypothesis of a broader spectrum of anti-AQP4 autoimmunity. The coexistence of AQP4-positive NMO and fibrosing NSIP suggests that anti-AQP4 antibodies may exert direct or indirect pathogenic effects on pulmonary tissue, possibly mediated by AQP4 expression in alveolar epithelial cells. While the association may be coincidental, it highlights the need for further research into potential extraneurological manifestations of AQP4 autoimmunity.
Conclusion: This case suggests a possible pathophysiological link between AQP4 autoimmunity and interstitial lung disease. The progression of pulmonary involvement despite systemic immunosuppression raises important questions about the role of AQP4 antibodies in the pathogenesis of fibrosing NSIP and suggests the need to consider extra-CNS organ involvement in patients with AQP4-positive NMO.

Disclosure of interest: yassine koubci: nothing to disclose

P1073
Predictors of treatment failure in a cohort with neuromyelitis optica spectrum disorder use immunosuppressants

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a relapsing autoimmune demyelinating disease of the central nervous system, often leads to severe disability. Patients with NMOSD develop significant disability over time due to the recurrence of attacks and insufficient recovery from severe attacks.
Objectives/Aims: This study aimed to identify the prognostic predictors of relapses in NMOSD patients using the first-line immunosuppresants (ISTs) regularly.
Methods: In this study, we enrolled patients with NMOSD from Southwest China and performed a long term follow-up. We compared the clinical characteristics and prognosis of aquaporin-4 antibody (AQP4-Ab) positive NMOSD patients with and without relapse using immunosuppressants (mycophenolate mofetil, MMF, and azathioprine, AZA). Logistic regression model was used to explore the prognostic predictors of relapse in NMOSD.
Results: Ultimately, 473 patients were enrolled during 2009 to 2024. The administered ISTs included AZA (n=61, 12.9%), MMF (n=412, 87.1%). Over a median of 7.42 years of ISTs, 55.4% of patients were relapse-free. Patients with relapse exhibited a higher proportion of serum antinuclear positive, higher AQP4 titer, body mass index (BMI) $\geqslant 25 kg/m^2$, severe attack at onset, autoimmune disease than patients without relapse, false discovery rate (FDR) corrected $p < 0.05$. And patients with relapse had a younger age at onset (FDR corrected $p < 0.05$). No significant differences in sex, onset type, Expanded Disability Status Scale at onset were observed between the two groups.The multivariate logistic analyses indicated that age at onset <18 years, severe attack at onset, higher AQP4 titer, BMI$\geqslant 25 kg/m^2$ and serum anti-nuclear (ANA) positive were risk predictors of relapse in NMOSD patients using ISTs ($p < 0.05$).
Conclusion: Our study revealed the potential predictors of relapse in NMOSD patients using immunosuppressive treatments (MMF and AZA). These patients with the predictors may necessitate highly effective immunotherapy as first-line treatment rather than ISTs.

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P1074
Satralizumab in Chinese Patients with NMOSD: Interim analysis from Real-World Data in the SAILOR Study

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Introduction: Satralizumab, an anti-IL-6 receptor monoclonal antibody, holds the distinction of being the first biologic approved in China for aquaporin-4 antibody-positive (AQP4-IgG+) neuromyelitis optica spectrum disorder (NMOSD). The SAILOR study, conducted as part of the China National Registry of Inflammatory Demyelinating Diseases (CNRID, NCT05154370), is designed to assess the real-world effectiveness and safety of satralizumab in Chinese patients with NMOSD.

Objectives/Aims: To assess the real-world effectiveness and safety of satralizumab in Chinese patients with NMOSD.

Methods: SAILOR is a multicenter, retrospective-prospective cohort study (Study Number: ML45235) designed to enroll AQP4-IgG+ NMOSD patients who have received at least one dose of satralizumab. Baseline data, including information on demographics, disease characteristics, treatment history, and comorbidities, were collected as part of the study. Safety data were gathered through standardized follow-up procedures. This interim analysis reports baseline characteristics and safety findings from the first 100 patients enrolled in the study.

Results:

- Demographics: The participants had a mean age of 48.3 years, ranging from 15 to 83 years old, with 84% identified as female.
- Disease Characteristics: The median time from diagnosis to enrollment was 1 year (range: 0–14 years). At baseline, the median Expanded Disability Status Scale (EDSS) score stood at 2.0 (range: 0–9.5). The median serum AQP4-IgG titer was recorded at 1:100 (range: 0.01–1000).
- Relapse History: Over the past two years, 46% of patients experienced no relapses, 29% experienced a single relapse, and 13% experienced two relapses.
- Patient-Reported Outcomes: The average Modified Fatigue Impact Scale (MFIS) score was 27.9, with a range of 0 to 78, while the mean EQ-5D score stood at 64.9, spanning from 10 to 95.
- Comorbidities: Frequently observed comorbidities included hypertension (17%), diabetes (9%), and Sjögren's syndrome (9%).
- Safety: Preliminary data indicated no new safety concerns. Adverse events (AEs) aligned with the established safety profile of satralizumab, and no unexpected serious AEs were observed.

Conclusion: This interim analysis offers a detailed overview of the real-world patient profile and the safety of satralizumab in Chinese patients with NMOSD. The findings indicate that satralizumab is well-tolerated, exhibiting a safety profile aligned with results observed in clinical trials. Continued follow-up will shed light on its long-term effectiveness and safety, aiding in the development of more refined treatment strategies for NMOSD in China.

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P1075
Longitudinal trajectories of disability progression in NMOSD and MOGAD

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Introduction: Disability progression in neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is heterogeneous.
Objectives/Aims: To identify factors associated with reaching EDSS $\geqslant$ 6 and develop a predictive model in AQP4-IgG-positive NMOSD, AQP4-IgG-negative NMOSD, and MOGAD.
Methods: We retrospectively analyzed 613 NMOSD+, 178 NMOSD−, and 147 MOGAD patients from Latin America. Kaplan-Meier survival and Cox proportional hazards models assessed the time to EDSS $\geqslant$ 6. Predictors included diagnosis, age at onset, sex, ethnicity, number of relapses, disease duration, and first-line disease-modifying therapy. Longitudinal EDSS trajectories were assessed using linear mixed models (LMM). K-means clustering identified progression subgroups.
Results: MOGAD had the highest probability of remaining below EDSS $\geqslant$ 6 ($p < 0.001$), with no difference between NMOSD+ and NMOSD− ($p = 0.23$). In Cox models, MOGAD had a lower risk of progression (HR = 0.34, 95% CI: 0.22–0.52), while NMOSD− did not differ from NMOSD+. Higher risk was associated with older age at onset, male sex, mestizo ethnicity, and more relapses ($p < 0.01$). LMM showed worsening trajectories in NMOSD− ($p = 0.031$) and a trend toward improvement in MOGAD ($p = 0.061$). Clustering identified distinct progression patterns within each diagnostic group, revealing intragroup heterogeneity beyond antibody status.
Conclusion: Disability trajectories in NMOSD and MOGAD are variable. Clinical and demographic features contribute to heterogeneity, and clustering highlights subgroups within each diagnosis, supporting personalized management.

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P1076
Cranial neuropathies as an infrequent manifestation of MOG antibody-associated disease: two clinical cases

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is related to central nervous system involvement, primarily affecting the optic nerves and spinal cord.
Objectives/Aims: Although its pathophysiology is not fully understood, the occurrence of cranial neuropathies is a rare but reported manifestation of this entity.
Methods: We present two cases of cranial neuropathies associated with MOGAD.
Results: The first case is a 15-year-old female with no relevant medical history, who presented in October 2024 with acute vertigo and severe hearing loss in the left ear. Initially considered a peripheral acute labyrinthoplegia, she was started on oral corticosteroids and admitted for further evaluation. Brain magnetic resonance (MRI) revealed a T2-FLAIR hyperintense and contrast-enhancing lesion on T1 in the left VIII cranial nerve nucleus extending into the cisternal segment. Audiometry confirmed severe hearing loss. Anti-MOG antibodies were positive in serum and cerebrospinal fluid using a cell-based immunohistochemistry assay (CBA). A comprehensive diagnostic workup ruled out alternative causes. After diagnosis, she received 1 g/day of intravenous methylprednisolone for 5 days followed by an oral prednisone taper over 3 months. Her symptoms resolved completely in the following weeks. At present, she is asymptomatic, off immunosuppressive treatment, with normalized audiometry findings and radiological improvement on follow-up MRI at 3 months. No further relapses have occurred.
The second case is a 64-year-old woman diagnosed with MOGAD in December 2018 after presenting with cortical encephalitis and bilateral optic neuritis, with complete recovery following a prolonged tapering course of corticosteroids and subsequent negativization of anti-MOG antibodies. In September 2024, she developed a right-sided peripheral facial palsy. Anti-MOG antibodies were again positive in serum by CBA. Brain MRI did not reveal new lesions. Electromyography indicated severe axonotmesis of the right facial nerve. She received intravenous methylprednisolone for 5 days followed by an oral taper of prednisone, with partial clinical improvement. The patient declined further immunosuppressive therapy.
Conclusion: These cases illustrate a rare and atypical manifestation of MOG antibody-associated disease. Although cranial nerve involvement is infrequent, it should be considered within the clinical spectrum of this entity. Early recognition and appropriate treatment may contribute to a favorable outcome.

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P1077
Prevalence of neuromyelitis optica spectrum disorder in the Caribbean region of Colombia: Analysis of the official Ministry of Health administrative registry

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease, with prevalence varying by ethnicity: around 1 per 100,000 in White populations, 3.5 in East Asians, and up to 10 in people of African descent. In South America, NMOSD accounts for 11.8% of idiopathic demyelinating diseases, mostly affecting young women of African ancestry. Its prevalence in Colombia is not well documented. However, frequent entries in the national healthcare registry, suggest notable activity along the Caribbean coast.
Objectives/Aims: This study aims to estimate the prevalence of neuromyelitis optica spectrum disorder (NMOSD) in the Caribbean region of Colombia between 2020 and 2024, using the official Ministry of Health administrative database (SISPRO) in adults with a confirmed diagnosis
Methods: This is an observational, retrospective, cross-sectional study that used data from January 2020 to December 2024, obtained from SISPRO, the official administrative database of the Colombian Ministry of Health. The dataset was filtered to include only individuals over 18 years of age with a hospital discharge diagnosis of neuromyelitis optica spectrum disorder (NMOSD). Confirmed cases reported through SISPRO during the study period were analysed. To estimate prevalence, population projections for the year 2025 from the National Administrative Department of Statistics (DANE) were used, applying direct age standardisation based on the international reference population proposed by the World Health Organization (WHO).
Results: The age-standardised prevalence for the entire Colombian Caribbean region was 20.14 cases per 100,000 inhabitants. The department-specific prevalences were as follows: Atlántico (8.55 cases), Bolívar (5.10 cases), Córdoba (7.22 cases) and Sucre (10.50 cases), indicating considerable differences in the epidemiological burden of the disorder among these territories.
Conclusion: This study offers new insights into the prevalence of NMOSD in the Colombian Caribbean region. The findings highlight the value of regional data for understanding disease distribution and guiding public health efforts.

Disclosure of interest: JUAN MIRANDA: nothing to disclose

P1078
Impact of Plasma Exchange on Satralizumab Exposure in Neuromyelitis Optica Spectrum Disorder Patients

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory autoimmune disease of the central nervous system characterized by acute optic neuritis and transverse myelitis. Satralizumab, a humanized anti-IL-6 receptor inhibitor, has been approved for the treatment of NMOSD as it has demonstrated efficacy by significantly reducing the risk of relapse. Pharmacokinetic (PK) simulation of various timing of therapeutic plasma exchange (TPE) is useful to consider the satralizumab dosing timing after TPE.
Objectives/Aims: The impact of TPE on satralizumab exposure in acute NMOSD patients using PK modeling approach.
Methods: Three acute NMOSD patients received intravenous infusion of satralizumab at a dose of 120mg (JP44470 study). TPE was permitted after day 3 of satralizumab administration. Serum satralizumab concentrations were measured by ELISA and analyzed using a non-linear mixed effect model. The model was developed from Phase1 and two Phase 3 trial data, and suggested individual PK time courses.
Results: Patient (Pt) #1 underwent PK monitoring after the first, second, and third TPE sessions. Pt #2 underwent PK monitoring after the third TPE session, while Pt #3 underwent PK monitoring after the second TPE. Following a single TPE in Pt #1, satralizumab concentration exhibited a 53% reduction compared to model-predicted values without TPE. Based on this model, calculations predicted that two sequential TPE procedures would achieve a 78% reduction, and three sequential TPE procedures would achieve an 89% reduction. Observed values showed >90% reduction in blood concentration compared to without TPE after the second plasma exchange in Pt #1, 88% reduction after the third plasma exchange in Pt #2, and 85% reduction after

the second plasma exchange in patient #3. Comparative analysis of post-TPE measurements revealed that satralizumab concentrations on day 8 after one and two plasma exchanges were equivalent to those predicted at days 26 and 41, respectively, without TPE. These findings demonstrate that TPE significantly modifies the PK profile, resulting in substantially reduced drug exposure and providing critical insights into therapeutic drug elimination in clinical scenarios requiring rapid clearance.
Conclusion: Multiple plasma exchanges significantly impact satralizumab exposure in acute NMOSD patients, potentially affecting treatment efficacy. These findings have important implications for optimizing timing of satralizumab dosing in patients undergoing plasma exchange.

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P1079
Demographic Survey of MOGAD in an Adult Hispanic Population of South Texas

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune disorder of the central nervous system that can result in demyelination of the brain, optic nerves, and spinal cord. While it shares clinical features with multiple sclerosis and neuromyelitis optica spectrum disorder, MOGAD is diagnosed using cell-based assay to detect antibodies directed against MOG IgG. As a recently discovered clinical entity, little is known about the epidemiology of MOGAD and how it differentially effects patients of various ethnic backgrounds
Objectives/Aims: Our objective is to evaluate the presentation and disease course of MOGAD in an adult Hispanic population within South Texas.
Methods: An ongoing retrospective chart review identifying patients with MOGAD at the University of Texas San Antonio in the last 5 years. Baseline demographics, clinical presentation, and patient outcomes are recorded for each patient.
Results: At present, a total of 37 adult Hispanic patients with MOGAD have been identified through chart review (70% of our cohort). In the Hispanic population, we observed a female-to-male ratio of 2.36:1 (26 females and 11 males). The mean age of onset was 38 years old, with a range of 7-74 years. A total of 78% (n=29) presented with optic neuritis. Of those, 62% presented with unilateral optic neuritis and 38% with bilateral optic neuritis. Five patients presented with transverse myelitis (80% male) and 3 patients presented with other symptoms (33% male). The overall relapse rate was 62% with similar rates in males versus females (64% and 62%, respectively). Mean follow up was 51 months. Those presenting with unilateral optic neuritis had a relapse rate of 61% (11/18), bilateral optic neuritis with 55% (6/11), transverse myelitis 80% (4/5) and other symptoms 66% (2/3). Of those tested, oligoclonal bands were present in 6/29 (20.7%). Identified MOG titers were at least 1:100 in 22/34 patients (65%; 16 females and 6 males).
Conclusion: Here we provide valuable epidemiological data for adult Hispanic patients with MOGAD in South Texas. Data on MOGAD has historically been obtained from predominantly Caucasian patients. This study provides valuable demographic data for an underrepresented population that may be used to help guide prognosis and treatment decisions.

Disclosure of interest: Nothing to disclose

P1080
Antibody Awareness and Diagnosis Recognition in Neuromyelitis Optica Spectrum Disorder and MOG-Associated Disease: A Cross-Sectional Study

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) and MOG-associated disease (MOGAD) present high risk of disability. Testing for anti-aquaporin-4 (anti-AQP4) antibodies and anti-myelin oligodendrocyte (anti-MOG) antibodies is essential for early diagnosis, associated with a better prognosis. However, awareness regarding these antibodies remains limited, and there is inadequate information about patients' understanding of their condition.
Objectives/Aims: To report the frequency of antibody serostatus and diagnosis awareness between patients with NMOSD/MOGAD in an outpatient tertiary clinic.
Methods: This cross-sectional study was conducted between March 2023 and October 2024. We administered questionnaires to patients diagnosed with NMOSD anti-AQP4 positive, MOGAD, and those with seronegative optic neuritis or longitudinally extensive transverse myelitis to assess their comprehension of their condition. Data were recorded by clinical chart. Descriptive analyses were performed. Mann-Whitney and Chi-Squared Test were performed to identify variables associated with diagnosis awareness.
Results: We interviewed 108 patients. 87 (80%) were female. Self-reported racial backgrounds were black or brown in 69 patients (64%), white in 34 (31%), and yellow in 5 (4%). The median years of education were 12 years (IQR 8-13.5). 56/63 patients with NMOSD AQP4 positive (88%) recognized their diagnosis, but only 38 (59%) were aware of their AQP4-antibody positivity. 13/19 patients with MOGAD (68%) correctly reported their diagnosis, and 12 (63%) were aware of antibody positivity. Among 22 double seronegative patients, only 8 (36%) were aware of being negative for both antibodies. We compared

patients with less than 12 years of education to those with more than 12 years of education (completed secondary education) and found no significant association between the number of years of education and awareness of the diagnosis (p-value = 0.07).
Conclusion: The knowledge about antibody serostatus was missing in almost half of patients. Education may play a role in diagnosis recognition, which should be better analysed in larger samples. Awareness about their disease and necessary exams enable patients to effectively advocate for their care, improved communication with healthcare providers, ultimately enhancing health outcomes. Questions about how determinants social of health may impact in aptitude to hunt for proper and early diagnosis and treatment need to be more evaluated in NMOSD/MOGAD scenario.

Disclosure of interest: No author has anything to disclose regarding this abstract

P1081
Device bridging study demonstrates bioequivalence for 180 mg satralizumab given subcutaneously using prefilled syringe and autoinjector

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Introduction: Satralizumab is a humanised IL-6 receptor monoclonal antibody currently approved for subcutaneous (SC) administration via a prefilled syringe (PFS). An autoinjector (AI) device will facilitate SC administration which may enhance patient adherence.
Objectives/Aims: This Phase I study evaluated the bioequivalence, safety and tolerability of satralizumab administered via the AI vs the PFS in healthy participants.
Methods: Healthy male and female participants, aged 18–55 with a body weight between 55–110 kg, received a single SC dose of 180 mg of satralizumab administered as an injection to the abdomen or thigh using either an AI (1 injection) or PFS (2 injections at least 5 cm apart). Serial blood samples were collected for pharmacokinetic (PK) assessment from Day 1 to the follow-up visit on Day 90. PK parameters were estimated using standard non-compartmental methods: C_{max}, t_{max}, $AUC_{0\text{-inf}}$, $AUC_{0\text{-last}}$, CL/F, V_z/F, and $t_{1/2}$. Safety was assessed in all participants.
Results: 188 participants were randomised to four groups (n=47 in each), according to device and site of injection: AI abdomen, AI thigh, PFS abdomen and PFS thigh. Following a single SC dose of 180 mg satralizumab, the 90% confidence intervals of the geometric least-squares mean ratios (AI vs PFS) of satralizumab for C_{max}, $AUC_{0\text{-last}}$ and $AUC_{0\text{-inf}}$ were entirely contained within the standard bioequivalence margins of 80% to 125% as follows: 100.3% (92.9–108.3%), 103.2% (95.3–111.7%) and 104.9% (97.2–113.3%) for C_{max}, $AUC_{0\text{-last}}$ and $AUC_{0\text{-inf}}$ respectively, demonstrating bioequivalence.
Overall, 200 treatment-emergent adverse events (TEAE) were reported by 105 participants (56%): 122 TEAEs in the AI group (n=58, 62%) vs 78 TEAEs in the PFS group (n=47, 50%). All TEAEs were mild or moderate in severity. A higher incidence of injection site reactions (ISR) was reported in the AI group (79 ISRs, n=47, 50%) vs the PFS group (41 ISRs, n=28, 30%). Reported ISRs were Grade 1 (mild) or Grade 2 (moderate) severity. Notably, almost all ISRs were resolved within 24 hours. Incidence of anti-satralizumab antibodies was similar for both treatment groups at baseline and post-treatment. There were no unexpected safety concerns suggestive of immunogenic response to satralizumab in either group.
Conclusion: Comparison of AI and PFS demonstrated bioequivalence for 180 mg satralizumab administered SC; both devices were found to be safe and generally well tolerated. These data suggest the AI device can be used to facilitate self-administration of satralizumab.

Disclosure of interest: Lottie Rayburn is a full-time employee of Roche Products Limited, UK. Subramanian Ganesasundararajan is a clinical pharmacology consultant for Roche Products Limited, UK. Muna El-Khairi is a full-time employee of Roche Products Limited, UK. Hanna Silber Bauman is a full-time employee of F. Hoffmann La-Roche Ltd. Jean-Christophe Genin is a full-time employee of F. Hoffmann La-Roche Ltd. Alexander Burdeska is a full-time employee of F. Hoffmann La-Roche Ltd. Hayley Bostock is a full-time employee of Roche Products Limited, UK. Ivana Vodopivec is a full-time employee of F. Hoffmann La-Roche Ltd. Sian Lennon-Chrimes is a full-time employee of Roche Products Limited, UK.

P1082
Seasonal and monthly variation of relapses in MOG-IgG associated disease (MOGAD): a retrospective analysis from Latin America

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Introduction: Seasonality and monthly frequency of MOG-IgG-associated disease (MOGAD) relapses have not been reported in Latin America (LATAM), and limited data have been published worldwide.
Objectives/Aims: We aimed to investigate the seasonal and monthly distribution of MOGAD relapses in LATAM, evaluating potential temporal patterns and differences between first and subsequent relapses.
Methods: This retrospective observational study analyzed relapse data from LATAM MOGAD patients (Chile: 40, Peru: 30, Brazil: 22, Argentina: 14, Colombia: 8, and Ecuador: 3). All patients met the 2023 MOGAD criteria. The dataset included number of relapses, month of occurrence, and classification as first or subsequent relapse. Additional demographic and clinical characteristics were recorded. We applied Edward's and Rayleigh's tests for seasonality and Poisson regression analysis to calculate incidence rate ratios (IRRs) with 95% confidence intervals (CIs) for relapses occurring in different months and seasons.
Results: A total of 117 MOGAD patients experiencing 168 attacks (117 first attacks and 51 relapses) were included. Fewer relapses were observed in autumn (N=21, 17%; IRR 0.17, 95% CI 0.11–0.25, p=0.001), but no differences were found across the months when evaluating first attacks. A peak in relapse frequency was observed in November (N = 38, 23%; IRR 0.13, 95% CI 0.08–0.19, p = 0.01), but no significant differences were observed across the seasons when evaluating all relapses. Based on Edward's and Rayleigh's tests, neither first attacks nor subsequent relapses showed a statistically significant monthly or seasonal pattern.
Conclusion: This study suggests that MOGAD relapses are not significantly influenced by seasonal or monthly variation in LATAM. These findings contribute to understanding disease activity and will guide future research into external factors influencing relapses.

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P1083
Tracking MOGAD in Algeria: The Tizi Ouzou Neurology Department's Experience

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) has emerged as a distinct rare inflammatory disorder of the central nervous system, now clearly separated from both multiple sclerosis and neuromyelitis optica spectrum disorder through identification of pathogenic antibodies and clinical-radiological features. Despite 2023 diagnostic criteria, no North African data exist on its characteristics.
Objectives/Aims: To characterize Algerian MOGAD patients aiming to create a regional registry, identify particular features, and benchmark findings against literature.
Methods: We analyzed 27 MOGAD patients from the neurology department of Tizi-Ouzou,Algeria diagnosed using 2023 criteria (clinical/MRI/CBA-positive).
Excluded: atypical cases with transient low-titer MOG-IgG and negative CSF.
Parameters included: demographics, clinical & Radiological phenotypes, immunological profiles, treatment responses and outcomes.
Results: This Algerian MOGAD cohort (27 patients, 2M:3F ratio) included pediatric (n=5, median 7 years), adult (n=21, median 34 years), and one geriatric case, with 50% of attacks occurring in winter (January-February) suggesting viral triggers.
Clinically, optic neuritis (ON) was the most common initial presentation 59%, predominantly unilateral (left eye affected more frequently), with all cases reporting prodromal periorbital pain at a higher rate than previously documented and presence of papillary edema in 60%. MRI findings in ON included retrobulbar involvement (80–90%), T2 hyperintensity (100%), and contrast enhancement (85–95%). 60% achieved complete visual recovery.
Myelitis 25% often manifested as longitudinally extensive transverse myelitis (LETM; 37.5%), with severe motor deficits and poor recovery 62.5%, particularly in delayed consultations. Other rare phenotypes included gait ataxia 4% and cortical encephalitis 4%.
Immunological profiling revealed high-titer MOG-IgG (⩾1:100) in (54%), persistent low titers in (47%), two CSF-positive/seronegative cases, and rare OCBs (11%). Acute management high-dose IV steroids with complementary plasmapheresis (31%).
While (50%) had monophasic courses (62%) receiving prophylaxis), relapsing patients (50%) demonstrated median 6-month-to-2-year recurrence intervals (85% optic neuritis), all maintained on IVIG, azathioprine, rituximab or tocilizumab.
Conclusion: This Algerian cohort exhibited aggressive MOGAD (severe myelitis, high relapse rates vs. global data), underscoring the need for prompt diagnosis, aggressive acute therapy, and sustained immunosuppression to optimize outcomes.

Disclosure of interest: Roumaissa Rekia Adjmi: nothing to disclose

P1084
IL-1β Contributes to Neurological Disability in NMOSD AQP4+ Patients

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a central nervous system inflammatory disease that causes severe disability. Differently from relapsing-remitting multiple sclerosis (RRMS) a group of patients present aquaporin-4 (AQP4) antibodies in the serum. Although its pathogenesis is unclear, cytokine profiles may impact disease activity and severity.
Objectives/Aims: To analyze cerebrospinal fluid (CSF) cytokine levels in NMOSD AQP4+ and their relationship with neurological disability, comparing findings with RRMS patients and non-inflammatory controls (NIC).
Methods: Sixty-four participants were recruited: 11 NMOSD AQP4+, 29 RRMS, and 24 NIC. CSF cytokine levels were measured using a multiplex assay. Group comparisons were performed with Kruskal-Wallis and Mann-Whitney U tests, while linear regression models evaluated the association between cytokine levels and Expanded Disability Status Scale (EDSS) scores.
Results: NMOSD AQP4+ patients displayed significantly higher CSF levels of IL-1β ($p = 0.040$), TNF-α ($p < 0.001$), G-CSF ($p = 0.003$), Eotaxin ($p = 0.008$), and MIP-1α ($p = 0.005$) compared to RRMS and NIC. Moreover, IL-1β CSF levels were positively associated with disability at the time of lumbar puncture ($\beta = 22.24$, $SE = 7.73$, $p = 0.018$), a relationship that remained significant after adjusting for age ($\beta = 18.96$, $SE = 6.33$, $p = 0.040$).
Conclusion: Expression of proinflammatory cytokines may differ between NMOSD and RRMS. Elevated IL-1β levels in NMOSD AQP4+ patients are linked to neurological disability, highlighting a potential role for IL-1β in driving disability. Further studies are needed to confirm these findings and evaluate the therapeutic potential of targeting IL-1β in NMOSD.

Disclosure of interest: Borrelli Angela: nothing to disclose

P1085
Atypical phenotypes in Myelin Oligodendrocyte glycoprotein-associated disease (MOGAD)

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an immune-mediated disorder with six well-described core demyelinating syndromes. However, less common phenotypes have been reported, making their identification and characterization essential for early diagnosis and effective management.
Objectives/Aims: To identify and characterize atypical clinical phenotypes of MOGAD beyond the six established core syndromes, assessing their clinical, paraclinical and treatment approaches.
Methods: A multicenter longitudinal retrospective and prospective study including commercial fixed CBA anti MOG IgG positive patients from 3 hospitals in Chile. We reviewed medical records between March 2021 and March 2025, characterizing phenotypes outside the six core syndromes.
Results: Among 95 seropositive patients, 7 (7%) presented with atypical phenotypes, with a median age of 27 years (7-50), 4/7 males, and 5/7 had a polyfocal presentation. Uncommon phenotypes included: 1 case of intracranial hypertension syndrome (IHS) with an opening CSF pressure of 24-28 mmH_2O, 1 case of sclerouveitis (SU), 3 cases of concomitant anti-NMDAR AE, 1 case of a movement disorder, and 1 case presenting with multiple cranial neuropathies. Anti-MOG-IgG were reported without titer in 4/7 patients (57%), low titer 1/7 (14%) and 2/7 with clear positive titer (29%). Six patients fulfilled the 2023 MOGAD diagnostic criteria; the exception was a patient with SU (antibody titer: 1:100).
MRI findings were consistent with the clinical phenotype, with gadolinium enhancement in 6/7. The median CSF pleocytosis was 48 cells/μL (9–1140), and OCB were positive in 71%. Six patients required hospitalization (median stay: 20 days), and the median EDSS at nadir was 4. Two patients required additional first-line therapies (MP+PLEX/IVIG) and 6/7 received chronic immunosuppression (IS), of whom some required combined IS. At the last follow-up (median: 24 months), the median EDSS was 1 (range 0-4).
Conclusion: This multicenter study highlights the presence of atypical clinical phenotypes characterized by aggressive onset, marked CSF and MRI inflammation, prolonged hospitalizations, and the need for combined immunotherapy.

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P1086
Clinical Presentation and Long-Term Outcomes in Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease: A Multicenter Retrospective Study in Greece

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an inflammatory demyelinating disorder of the central nervous system. Despite emerging recognition of its characteristics, long-term outcomes and relapse predictors remain unclear.

Objectives/Aims: To describe the clinical, laboratory, and therapeutic features of MOGAD patients in Greece.

Methods: We retrospectively analyzed data from seropositive MOGAD patients diagnosed according to the 2023 international proposed criteria and followed between 2013 and 2025 across 10 Neurology Departments.

Results: Thirty-six patients were included (58% female). The mean age at onset was 38.1 ± 12.1 years; mean disease duration was 6.2 ± 4.6 years. Mean time to diagnosis was 14 ± 32 months. Initial presentations included optic neuritis (ON) in 53% (n=19), myelitis in 37% (n=13), cerebral monofocal symptoms in 3, and acute disseminated encephalomyelitis in 1. Interestingly, 2 patients had peripheral nervous system involvement suggestive of chronic inflammatory demyelinating polyradiculoneuropathy. CSF oligoclonal bands were detected in 31%. ON occurred in 55.6% (10 bilateral), and myelitis in 47.2%. The median Expanded Disability Status Scale score at last follow-up was 1.0 (IQR: 0–1.5), with 8.3% of patients having a score ⩾3. All patients received intravenously high-dose methylprednisolone during attacks, resulting in complete recovery in 26 and partial improvement in 10. Three patients also received intravenous immunoglobulin with clinical benefit. Relapses occurred in 50% (n=18), with a median time to first relapse of 12 months (IQR=9-66). Five patients relapsed while on maintenance therapy. At data collection, immunosuppressive prophylaxis included azathioprine (n=5), mycophenolate mofetil (n=3), rituximab (n=6), ofatumumab (n=1), and low-dose prednisolone (n=5). Sixteen patients (44%) were not receiving any long-term immunosuppressive treatment, either due to monophasic disease course or clinical decision-making. Among treated patients, anti-CD20 agents were associated with a lower annualized relapse rate (0.07 vs. 0.47) compared to other treatments, though not statistically significant (p=0.33).

Conclusion: This cohort highlights the clinical variability of MOGAD. Despite favorable clinical outcomes to the acute treatment regimen, relapses were common, supporting the need for individualized long-term management strategies.

Disclosure of interest: Alexandra Akrivaki, Dimitrios Tzanetakos, Viktor Gkotzamanis, Anthi Tsogka, Evangelia Makrina Dimitriadou, Aikaterini Theodorou, Vasiliki Skarlatou, Dimitrios Kitsos, Stella Marousi, Fotios Roussos, Efstratia-Maria Georgopoulou, Anastasia Kaliontzoglou, Stavroula Xylogiannopoulou, Ioannis Markakis, Polyxeni Stasinaki, Michail Papantoniou, George Tagaris, Maria Gryllia, Panagiotis Angelidakis, Triantafyllos Doskas, John Ellul, Elisabeth Chroni, Kleopas A. Kleopa, Nikolaos Fakas, Konstantinos Voumvourakis, Sotirios Giannopoulos, Georgios Tsivgoulis, John Tzartos: nothing to sisclose

P1087
Female patients with late and velry late onset AQP4 positive Neurolyelitis Optica Spectrum Disorder under ravulizumab: Experience of a center of Expertise for Rare Demyelinating and Autoimmune Diseases of CNS

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare, disabling disease, affecting mostly women with an average age of onset of 30-40 years. Recently, immunotherapies targeting the complement pathway have been introduced, changing the disease course. Here, we present four female patients diagnosed with severe AQP4 NMOSD that were

treated with ravulizumab, after appropriate vaccinations, with impressive therapeutic response, within the last one and half year. Two of the patients were overaged, making therapeutic challenges even bigger.
Objectives/Aims: Description of four cases with AQP4 NMOSD and their response to treatment with ravulizumab.
Methods: Case presentation
Results: Case 1: A 53-year-old with right hemiparesis and spinal cord longitudinal extensive transverse myelitis (LETM) from the medulla to T2, with gadolinium enhancement (Gd+). She responded well to intravenous (IV) methylprednisolone (MP) and plasma exchange (PLEX) and was on rituximab for three years. Due to a clinical relapse with left foot weakness, ravulizumab was initiated and she remains improved with no exacerbations or adverse events.
Case 2: A 51-year-old with two episodes of right leg paresis, numbness and urinary urgency. Due to LETM from T5-T9, she received 7gr of IV-MP with good response and was afterwards started on ravulizumab. She remains clinically stable and the length of the lesion is reduced.
Case 3: A 89-year-old (the oldest reported patient with AQP4 NMOSD to date) with right hemiplegia and blindness that occurred three days later and LETM in cervical and thoracic spinal cord with GD+ and hyperintense signal in both optic nerves. She received 6gr of IV-MP with no improvement and 6 PLEX sessions with poor recovery. After initiation of ravulizumab she showed significant clinical improvement starting from the third infusion.
Case 4: A 71-year-old with paraparesis and paresthesia, LETM from T4-T8 level, with Gd+, and clinical improvement after 5 PLEX sessions. She received two infusions of ravulizumab showing remarkable improvement.
Conclusion: Ravulizumab is a recently introduced immunotherapy for AQP4 NMOSD, targeting the C5 complement component. Our experience shows impressive outcomes with a fast onset of action and no adverse events so far, although close monitoring is always required.

Disclosure of interest: Anagnostouli Maria: nothing to disclosure

P1088
Characterization of Cellular Composition and Signaling Networks in Neuromyelitis Optica Spectrum Disorder Using Single-Cell Transcriptomics of Cerebrospinal Fluid

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory autoimmune disease of the central nervous system characterized by acute optic neuritis and transverse myelitis. Elevated blood IL-6 levels are well-documented in NMOSD patients, with excessive IL-6 production reportedly contributing to pathogenesis through mechanisms including blood-brain barrier disruption, plasmablast differentiation, and Th17 cell polarization. However, the specific role of IL-6 within the central nervous system remains inadequately characterized.
Objectives/Aims: This study employs single-cell RNA sequencing to elucidate cellular accumulation patterns and intercellular networks, including IL-6 signaling, among immune cells present in the cerebrospinal fluid (CSF) of NMOSD patients.
Methods: CSF samples were obtained from three patients (two patients are newly diagnosed, one patient is experiencing a relapse, no previous treatment with immunotherapy within 6 months) during NMOSD attacks prior to treatment initiation (JP44470 study). Single-cell RNA sequencing was performed on recovered cell fractions using BD Rhapsody™. All three patients' data were integrated, dimensionally reduced, and subjected to cell annotation. Analyses were conducted to assess inter-patient differences in cell population ratios. Subsequently, second-round annotation was performed on each subpopulation, followed by analysis of gene expression variations among patients.
Results: The IL-6 concentration in CSF was 1.21, 332, and 17.9 pg/mL in patient 1, 2, and 3, respectively. Patients exhibiting high CSF IL-6 concentrations (>normal range; patient 2 and 3) demonstrated accumulation of multiple immune cell populations in the CSF, including monocytes, macrophages, pDCs, and neutrophils. Signal analysis indicated strong IL-6 signaling in myeloid cells. Further examination of myeloid populations revealed an accumulation of monocyte-derived macrophages (moMACs) in patients with elevated IL-6 levels. Cell-cell interaction analysis suggested that accumulated moMACs strongly expressed MCP-1, potentially promoting further monocyte and moMAC infiltration. Additionally, resident epiplexus cells were predicted to receive robust IL-6 signals and express inflammatory cytokines.
Conclusion: In acute NMOSD, enhanced IL-6 signaling in immune cells correlates with increased CSF IL-6 concentrations. This may induce accumulation of monocytes and moMACs, as well as inflammatory cytokine production by myeloid cells, potentially contributing to disease pathogenesis.

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P1089
Anti-NMDAR in AQP4-positive NMOSD: Incidental Finding or Clinically Relevant Marker?

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) associated with aquaporin-4 (AQP4) antibodies is a well-defined autoimmune disorder of the central nervous system. However, the concomitant presence of antibodies against the N-methyl-D-aspartate receptor (anti-NMDAR), typically linked to autoimmune encephalitis, raises questions when found in patients without encephalitic symptoms. The clinical relevance of this incidental finding remains unclear. This study analyses a cohort of AQP4-positive NMOSD patients, comparing cognitive, functional, and quality of life parameters between those with and without anti-NMDAR positivity.
Objectives/Aims: To evaluate anti-NMDAR antibodies in AQP4-positive NMOSD patients and compare cognitive function, functional status, and perceived health between antibody-positive and -negative subgroups, assessing its clinical impact in the absence of encephalitis.
Methods: We included 22 patients with confirmed NMOSD and positive AQP4 serology, from a public hospital in Argentina. Antibodies were detected using indirect immunofluorescence on transfected cells (Cell-Based Assay, CBA). Seven patients tested positive for anti-NMDAR antibodies: five in serum only, and two in both serum and cerebrospinal fluid (CSF). Cognitive function was assessed with the Montreal Cognitive Assessment (MoCA) and the Rey Auditory Verbal Learning Test (RAVLT). Functional status was measured using the modified Rankin Scale and Clinical Assessment Scale in Autoimmune Encephalitis (CASE). Quality of life was assessed using the EuroQol 5-Dimension 5-Level (EQ-5D-5L) and the EuroQol Visual Analogue Scale (EQ-VAS). Statistical analysis was performed using the Mann–Whitney U test.
Results: No statistically significant differences were observed between anti-NMDAR-positive and -negative patients in MoCA, RAVLT, Rankin, CASE, or EQ-5D-5L. A trend toward lower EQ-VAS scores in the anti-NMDAR group was noted ($p=0.073$), suggesting possible subtle impact on perceived health. In a subgroup analysis, the patient with anti-NMDAR detected in both serum and CSF did not exhibit greater clinical or cognitive impairment compared to those with serum-only positivity. Additionally, an exploratory analysis of MoCA subdomains revealed no significant differences between groups; however, a non-significant trend toward lower visuospatial/executive scores was observed in the anti-NMDAR group.
Conclusion: In this AQP4-positive NMOSD cohort, anti-NMDAR positivity without encephalitic symptoms was not associated with significant clinical or functional impairment. Nonetheless, the observed trends in self-perceived health and visuospatial/executive function highlight the need for further studies to explore the clinical significance of anti-NMDAR antibodies in this population.

Disclosure of interest: Carla Seimandi: nothing to disclose, Diego Alarcon: nothing to disclose, Andres Villa: nothing to disclose, Analisa Manin: nothing to disclose

P1090
A View of Neuromyelitis Optica Spectrum Disorder from Genetic Perspective: A Pilot Study

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Introduction: Clarification the genetic basis of Neuromyelitis Optica Spectrum Disorder (NMOSD) has the potential to be important in terms of elucidating pathogenesis and individualizing treatment.
Objectives/Aims: This study aimed to elucidate the genetic characteristics and immunological basis in seropositive NMOSD.
Methods: Demographic, radiological and clinical characteristics of the NMOSD group were recorded. Subtypes of the HLA-A, HLA-B, HLA-C, HLA-DQB1, HLA-DRB1 and HLA-DPB1 gene loci were studied and compared in the patient and control groups.
Results: The study included 22 patients diagnosed with NMOSD with a mean age of 45.95 ± 12.95 years. As a control group, 31 healthy individuals was included in the study. In the distribution of subtypes of the HLA-A gene locus, A*24:02:01:01 A*02:01:01:01 subtypes were detected at a significantly higher rate in the NMOSD group (respectively; $p<0.001$, $p=0.025$). In the HLA-B allele region, the highest proportional difference between the two groups was detected in the B*08 allele (15% vs 0%; $p<0.001$). B*08:01:01:01 subtype was detected at a significantly higher rate in patient group ($p<0.001$). In the HLA-C gene locus of the patient group, the C*04:01:01:01 subtype was detected at a higher rate (13% vs 3%; $p=0.009$). The DQB1*02:01:01:01 subtype was detected at a high rate in the patient group (32% vs 9%; $p=0.001$). In addition, the presence of DRB1*03:01:01:01 and DPB1*04:01:01:01 genes locus subtypes was detected at a significantly higher rate in the NMOSD group (respectively; $p<0.001$, $p<0.001$). As a result of the analysis, no significant difference was found in the distribution of subtypes of HLA-A, HLA-B, HLA-C, HLA-DQB1, HLA-DRB1 and HLA-DPB1 gene loci in terms of disease severity ($p>0.05$).
Conclusion: In our study, in addition to some gene loci seen only in NMOSD, the detection of some gene loci at a significantly

higher rate in NMOSD suggests that studies aimed at elucidating NMOSD and its genetic basis should be increased.

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P1091
Headache in myelin oligodendrocyte glycoprotein antibody-associated disease

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Introduction: Headache is reported more often in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), compared to multiple sclerosis and neuromyelitis optica spectrum disorder.
Objectives/Aims: Our study is aim to describe the characteristics of headache in MOGAD.
Methods: We retrospectively reviewed patients diagnosed as MOGAD in Capital Medical University Xuanwu Hospital between January 2017 to June 2022, and followed them up until December 2023. Demographic information, clinical investigations, MRI tests and treatments were collected and compared between patients with and without headache. $P < 0.05$ was considered statistically significant.
Results: 96 MOGAD patients were included, including 57 (59.4%) females in total, 18/31 (58.1%) females in patients with headache and 39/65 (60%) without headache. The mean (standard deviation, SD) age of the cohort was 33.7 (13.98) years old and no difference in age was determined between the two groups. Compared with patients without headache, more patients with headache presented recurrent disease course ($p = 0.043$), had optic neuritis ($p = 0.014$), higher intracranial pressure ($p = 0.032$) and higher cerebral spinal fluid (CSF) white blood cell (WBC; $p = 0.033$). Statistically significant difference was found in CSF MOG-IgG between the two groups ($p = 0.046$) and more positive CSF MOG-IgG was identified in patients with headache. More cortical/juxtacortical ($p = 0.002$) and optic nerves (0.010) lesions were shown in patients with headache.
Conclusion: We described the headache in MOGAD and found out more relapse, more optic neuritis, higher intracranial pressure and CSF WBC count in patients with headache. The patient with headache could have positive CSF MOG-IgG more frequently and get more lesions in cortical/juxtacortical and optic nerves.

Disclosure of interest: Xixi Yang, Mengyao Zhang, Zhandong Qiu, Huiqing Dong, Junwei Hao, Zheng Liu: nothing to disclose.

P1092
MRI features in myelin oligodendrocyte glycoprotein antibody-associated disease: a cohort study of adult patients

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare demyelinating disorder of the central nervous system that remains underdiagnosed among sero-negative neuromyelitis optica spectrum disorder (NMOSD) patients. This condition may present with imaging patterns distinct from AQP4+ seropositive NMOSD. While optic neuritis, extensive myelitis and brainstem involvement are commonly observed, recent data suggest a broader spectrum of radiological presentations.
Objectives/Aims: This study aims to describe imaging features of MOGAD in a cohort of adult patients, analyzing lesion patterns and evolution in order to improve early recognition and accurate diagnosis.
Methods: In this retrospective study, we reviewed brain and spinal cord MRI findings of adult patients diagnosed with MOGAD according to the 2023 international MOGAD panel proposed criteria. Lesion distribution was evaluated at initial imaging and during follow-up.
Results: We enrolled 26 MOGAD patients (M/F=0,42) with mean age at onset of 37±12,6 years.
Initial brain and spinal cord MRI was normal in 2 patients (7.4%).
The most frequent supratentorial brain MRI findings included unilateral optic nerve lesions (33.3%) with gadolinium enhancement in 40% and optic nerve sheath infiltration in 2 of these cases (22%). Other frequent lesions were periventricular lesions (22.2%), corpus callosum lesions (11.1%), and juxtacortical frontal and parietal lesions (7.4% each).
Bilateral optic neuritis, involvement of the optic chiasm and optic tract were rare, each observed in a single patient. No patient had basal ganglia involvement. One patient had ADEM pattern.
Infratentorial involvement was noted in 22,2% of cases, in the cerebellum (14.8%) and the midbrain (11.1%). Single cases of area postrema lesion and leptomeningeal enhancement were observed.
Spinal MRI revealed longitudinally extensive trasnverse myelitis (LETM) in 18.5% of cases and short myelitis in another 18.5%. Terminal cone involvement was identified in 7.4% of patients.
Gadolinium enhacnement occured with 6 patients having myelitis, 4 patients with optic neuritis and single cases in corpus callosum, cerebrum and terminal cone.
At the follow-up, among the 7 patients explored, one patient had stable MRI lesions. Other patients developed periventricular, corpus callosum lesions and LETM. One patient developed

supratentorial black holes. Spinal cord and cortical atrophy was newly detected in one patient.
Conclusion: Our study highlights specific MRI patterns of MOGAD that can help distinguishing MOGAD from other demyelinating diseases to impacting therapeutic decisions and improve prognosis.

Disclosure of interest: Rania Zouari: nothing to disclose.

P1093
AI-Assisted Management of NMOSD for Neurologists: A Comparative Study of Large Language Model Performance

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Introduction: Patients with neuromyelitis optica spectrum disorders (NMOSD) often present with complex clinical manifestations that can be challenging for general neurologists to evaluate. Those living in underserved or remote areas face additional barriers due to limited access to specialized neuroimmunologists. Large Language Models (LLMs) may serve as valuable support tools, bridging the gap in care and guiding general neurologists in NMOSD management.
Objectives/Aims: To assess the safety, completeness, quality, and comparative performance of multiple LLMs as clinical support tools for general neurologists managing NMOSD.
Methods: A real clinical case was adapted, and nine questions were formulated covering key areas such as differential diagnosis, laboratory work-up, MRI interpretation, acute and chronic treatment and pregnancy management. Three LLMs were evaluated: ChatGPT-4o (flagship model), and open-source models LLaMA 3.1 40B and LLaMA 3.1 8B. Responses were independently rated by seven neuroimmunologists across diverse healthcare systems using five criteria: (1) omission of critical information, (2) factual inaccuracy, (3) potential for patient harm, (4) overall quality, and (5) comparative ranking.
Results: In terms of safety and accuracy (composite score: 1 = safest, 10 = most dangerous), ChatGPT-4o was rated highest (1.38 $\pm$1.24), outperforming LLaMA 8B (2.29 $\pm$2.05) and LLaMA 40B (1.98 $\pm$1.24; $p < 0.001$). ChatGPT-4o also received the highest quality score (9.20), followed by LLaMA 8B (7.90) and LLaMA 40B (7.22; $p < 0.001$). In overall ranking, ChatGPT-4o led with a mean rank of 1.22 (out of 3), versus 2.07 (LLaMA 40B) and 2.66 (LLaMA 8B).
Conclusion: ChatGPT-4o demonstrated superior performance across all metrics, suggesting that well-trained LLMs may be effective tools to support general neurologists, especially in settings lacking neuroimmunology expertise, to deliver safer and more accurate NMOSD care.

Disclosure of interest: Authors have nothing to disclose

P1094
"Risk factors associated with disability and recurrence of outbreaks in patients with optical neuromyelitis spectrum disorder (onmsd) attended in a neuroimmunology unit of a thertiary health care center at the dominican republic"

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Introduction: Neuromyelitis optica (NMO) is a central nervous system's disease with high morbidity and mortality and a good response to immunosuppressive treatment. Its morbidity and mortality are highly severe and recurrent. Therefore, prompt diagnosis of this disorder is mandatory due to its relapsing course, which can cause permanent disability.
Objectives/Aims: To evaluate the risk factors associated with disability and the appearance of flares in patients with Neuromyelitis Optica Spectrum Disorders (NMOSD) attended in a Neuroinmunology Unit of a therthiary health care center at the Dominican Republic.
Methods: A retropesctive, descriptive based study.
Results: A total of 27 patients where included, being the majority female. The mean age was 43.33 years. Hypertension was the most prevalent comorbidity and a single case, presented Systemic Lupus Erythematosus. The diagnostic time most frequently recorded was 1 to 6 years, in 63% of cases, and the time relapsed between diagnosis and the first flare was 0 to 5 months (66.67%). Patients had at least 3 flares or more in one year, with a mean of 1.89. Almost all patients, that is, 66.67%, belonged to the AQP4 positive variant. The most frequent presenting symptom was optic neuritis, with 37% and the most common flare was myelitis, in 74.11%. A moderate degree of disability between 2-3 and 3.5-4.5 was the highest recorded (51.80%). 88.90% of patients already established treatment. A relationship between sex and the number of relapses, age and the number of relapses was identified. Only type 2 diabetes mellitus was

related as a comorbidity with the number of flare-ups. There was a relationship between AQP4+, both with the number of flare-ups and with the degree of disability.
Conclusion: There is an important relationship between risk factors, disability and number of relapses in patients with NMOSD, which is therefore an important predictor of worsening and progression.

Disclosure of interest: Michelle Jimenez: nothing to disclose

Clinical Aspects of MS & Related Diseases – Symptoms (Cognition, Fatigue & Co.)

P1095
Predictors of Sustained Fatigue Development in Multiple Sclerosis: A Survival Analysis of a Real-World Cohort

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Introduction: Fatigue is a common and disabling symptom of multiple sclerosis (MS), also various factors may contribute to fatigue experience in patients with MS. Currently, no studies have followed multiple sclerosis (MS) patients to explore the factors influencing the development of fatigue.
Objectives/Aims: We designed this study to investigate the factors that contribute to the experience of fatigue over time in patients with MS.
Methods: We evaluated data of patients from a large, real-world cohort of people with MS (the Multiple Sclerosis Partners Advancing Technology and Health Solutions; MS PATHS) from 10 healthcare associations. We applied recommended Neuro-QoL suggested T-score cut-points to categorize participants' fatigue at the first visit as no fatigue (T-score≤ (mean+0.5 SD), and fatigued (T score >mean+0.5 SD). Time to event analysis (survival analysis) was conducted to determine factors that affect fatigue experience over time.
Results: Based on inclusion criteria, 6436 patients included. The cox-proportional hazard function showed that baseline characteristics such as physical disability (PDDS), depression T-score, cognition-T score, and sleep-T score were significant predictors of fatigue experience. Median time to experience fatigue in patients with PDDS =<5 was 63.2 months (62.1-64.6), and for individuals with PDDS>5 was 58 months (54.7-60.1) ($p<0.001$). Based on the mean and SD of the depression T score at the first visit, we categorized patients into two groups (T-score ≤51.3 (not-depressed), and T score> 51.3 (depressed)).
Kaplan-Meier log-rank test showed that median time to experience fatigue was significantly lower in non-depressed group than depressed group ($p<0.001$).
Conclusion: The results of this study show that physical disability, depression, cognition, and sleep problems play significant role in experiencing fatigue in patients with MS.

Disclosure of interest: Mahsa Ghajarzdaeh: nothing to disclose

P1096
The Role of Personality Traits in Disease Course, Cognition, and Mental Health in Multiple Sclerosis

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Introduction: Personality plays a crucial role in explaining individual differences in disease acceptance, coping strategies, and psychological well-being. It also influences the functional outcomes of brain diseases. Personality is commonly defined as a stable set of thoughts, feelings, and behaviors that differentiate individuals and persist over time and across situations. The term "personality trait" refers to enduring personal characteristics that predict behavior. Many studies have used personality traits to understand patients' responses to illness-related challenges. Since personality changes and personality disorders are frequently observed in multiple sclerosis (MS), personality may play a role in disease progression and outcomes.
Objectives/Aims: The aim of this study is to investigate the relationship between personality traits, disease characteristics, and their effects on cognitive, physical, and psychosocial factors in people with MS (pwMS).
Methods: One hundred two pwMS were enrolled in this study. Demographic and clinical characteristics were recorded. The Revised Eysenck Personality Questionnaire-Abbreviated Form (EPQR-A) was used to measure personality dimensions, including four subscales: extraversion, neuroticism, psychoticism, and the lie scale. Anxiety and depression levels, quality of life, and neuropsychological symptoms were measured using the Hospital Anxiety and Depression Scale (HADS), the EuroQol-5D Quality of Life Scale (EQ-5D), and the Multiple Sclerosis Neuropsychological Questionnaire (MSNQ), respectively.
Results: There was no significant correlation between the extraversion, psychoticism, and lie subscales of the EPQR-A and EDSS, number of relapses, disease duration, HADS, EQ-5D, and MSNQ ($p>0.05$). While there was no relationship between the neuroticism subscale of the EPQR-A and disease-related measures such as EDSS, disease duration, and number of relapses, neuroticism was found to be associated with EQ-5D mobility ($r=-.273$, $p=0.007$), usual activity ($r=-.286$, $p=0.005$), pain ($r=-.556$, $p<0.001$) and health subscales ($r=-.287$, $p=0.005$), MSNQ ($r=.478$, $p<0.001$), HADS-anxiety ($r=-.577$, $p<0.001$), and HADS-depression ($r=.414$, $p<0.001$).
Conclusion: This study highlights the significant relationship between personality traits, particularly neuroticism, and various aspects of disease impact in pwMS. While no strong associations were found between extraversion, psychoticism, and lie subscales and clinical and psychological factors, neuroticism

showed a clear connection with reduced quality of life, increased neuropsychological symptoms, and higher anxiety and depression levels. These findings emphasize the role of personality traits in shaping the experiences and outcomes of individuals with MS, suggesting that psychological interventions targeting neuroticism-related vulnerabilities may improve overall well-being and disease management.

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P1097
Analysis of the earliest atypical manifestation in patients with multiple sclerosis from southwestern Colombia

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Introduction: Multiple sclerosis (MS) has infrequent manifestations that include headache, epilepsy, movement disorders, sleep disorders, and paroxysmal symptoms, amongst others. In Colombia, the type and frequency of the first clinical manifestation of MS in patients and its relationship with the Expanded Disability Status Scale (EDSS) are unknown.
Objectives/Aims: To establish the frequency of the first atypical symptom and its relationship with the EDSS of patients diagnosed with multiple sclerosis, between their first and last consult with the neuroimmunology service.
Methods: This observational, descriptive, cross-sectional study examined patients diagnosed with Multiple Sclerosis (MS) attending a neuroimmunology unit at a tertiary care hospital from 2012 to 2024. Patients with unclear or indeterminate diagnoses were excluded. Data was categorized into demographic, clinical, diagnostic tests, prognosis, and treatment variables. A bivariate analysis compared patients with typical and atypical manifestations. The Student's t-test was used for parametric variables, and the Mann-Whitney U test for nonparametric variables. Pearson's Chi-square or Fisher's exact test was used for categorical variables. The magnitude of the mean difference was assessed using Cohen's delta or Cramer's V for significant variables.
Results: A total of 201 patients were included. 71.6% were female, with a mean age of 31.67 years ± 11.23. The average age at the time of the first manifestation was 31.57 years. The most common phenotype observed was relapse-remission (85.5%). About 83.08% of patients presented typical manifestations, with sensory symptoms (39.52%), unilateral optic neuritis (20.35%), and motor symptoms (14.37%) being the most frequent. On the other hand, 16.91% presented atypical manifestations, such as de novo headache (29.41%), paroxysmal symptoms (23.52%), and movement disorders (14.70%). Patients with typical manifestations began treatment at approximately 26.5 months, while those with atypical manifestations started at 12 months. No significant differences in EDSS scores were found between typical and atypical manifestation groups ($p= 0.086$).
Conclusion: In this cohort, atypical MS manifestations accounted for a quarter of cases. De novo headaches were the most frequent. No association with worse EDSS was observed.

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P1099
Language Skills and Cognitive Perspective in Multiple Sclerosis

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Introduction: Cognitive impairments can be seen in MS long before the onset of physical disability. Language impairments may affect cognitive evaluations.
Objectives/Aims: In this study, we aimed to investigate the effect of language skills on cognitive functions in MS patients and to reveal the relationship with regional brain volumes.
Methods: 50 MS patients and 30 healthy controls were included. Expanded Disability Status Scale (EDSS), Boston Naming test(BNT),Gulhane Aphasia Test(GAT), detailed cognitive tests were applied. Volumetric MRI analyses were performed in selected regions.
Results: BNT and GAT were significantly associated with cognitive tests. One unit increase in GAT scores increases SDMT,BVMT-R,CVLT-II,MMT,MoCA consecutively by 4.538,0.647,3.120,1.182 and 2.074 units.One unit increase in BNT increases SDMT, BVMT-R, CVLT-II,MMT,MoCA consecutively by 2.392, 0.295, 1.741,0.643, 1.158 units. There was a same directional correlation between SDMT, BVMT-R and total volume of the medial segment of the presantral gyrus. An inverse correlation was obtained between CVLT-II and left thalamic volume. One unit increase in total volume of the medial segment of the precentral gyrus in patients increases the SDMT value by 0.008 units.
Conclusion: Aphasia tests have the same directional correlation with all cognitive parameters and the same relationship was observed in patients with low disability. Total volume of the medial segment of the precentral gyrus had a positive effect on information processing speed. The findings show the significant effect of language skills on cognitive assessments in MS patients and emphasize the importance of these tests in clinical terms.

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P1100
From executive functions to everyday challenges: cognitive flexibility and its relationship with quality of life and employment in People with MS from Argentina

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Introduction: Cognitive flexibility is a critical executive function for adapting to daily challenges and demands.
Objectives/Aims: 1) To compare cognitive flexibility performance between people with MS (PwMS) and healthy controls (HCs); 2) to examine the relationship between cognitive flexibility and demographic, clinical and cognitive variables in PwMS; and 3) to analyse its association with depression, fatigue, health-related quality of life (HRQol), and work status in PwMS.
Methods: A case-control, cross-sectional study including two samples: 80 individuals with relapsing-remitting MS (RRMS) matched with 80 HCs, and an additional group of 140 individuals with RRMS (disease duration: 9.71 ± 7.08 years). Cognitive assessment included the BICAMS battery (CVLT-I, BVMT-R and SDMT), PASAT-3', verbal fluency and the Brixton Spatial Anticipation Test. Total errors on the Brixton test were used to assess cognitive flexibility. Both PwMS and HCs completed the cognitive battery and the Beck Depression Inventory-II (BDI-II). To assess functionality, PwMS completed the Fatigue Severity Scale (FSS), the MS International Quality of Life Questionnaire (MusiQoL) and the Buffalo Vocational Monitoring Survey (BVMS). Work status was classified as work-stable, work-challenged or work-loss. A significance level of $p<0.05$ was accepted.
Results: PwMS and HCs were matched on demographics. A higher proportion of PwMS showed impairment on the Brixton test compared to HCs (PwMS: 22.5% vs. HCs: 7.5%; $p<0.01$). In PwMS, Brixton performance was associated with disease duration ($r=-0.20$; $p<0.01$) and years of education ($r=-0.22$; $p<0.01$). Brixton errors were significantly correlated with BICAMS scores (CVLT-I: $r=-0.35$; $p<0.001$, BVMT-R: $r=-0.45$; $p<0.001$ and SDMT: $r=-0.42$; $p<0.001$), PASAT-3' ($r=-0.43$; $p<0.001$) and verbal fluency ($r=-0.30$; $p<0.001$). No significant associations were found with depression ($p=0.07$) and fatigue ($p=0.138$). Regarding HRQoL, Brixton errors were associated with difficulties in activities of daily living ($r=-0.20$; $p<0.05$), more severe disease symptoms ($r=0.32$; $p<0.001$),

lower satisfaction with sentimental and sexual life (r=-0.22; p<0.01) and a lower total HRQoL index (r=-0.22; p<0.01). In terms of employment, the ANOVA and post hoc analysis showed that work-stable PwMS had better cognitive flexibility than both the work-challenged group (p<0.05) and the work-loss group (p<0.001).
Conclusion: PwMS exhibit greater cognitive flexibility impairment than HCs. Better performance is associated with higher education and shorter disease duration, while poorer flexibility relates to lower HRQoL and employment challenges. Assessing and treating this domain is essential for improving overall functioning.

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P1101
The correlation of MIND diet adherence with physical and cognitive function in patients with multiple sclerosis

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Introduction: The MIND diet is a combination of the Mediterranean and DASH (Dietary Approaches to Stop Hypertension) dietary patterns, which focuses on brain health, protection against cognitive dysfunction, and dementia, and appears to have neuroprotective effects. Recently, a study has reported the effects of MIND diet adherence on the reduced risk of MS.
Objectives/Aims: We assessed the correlation between adherence to the MIND diet and cognitive function, and also physical disability in MS patients.
Methods: We conducted a cross-sectional study among 80 definite MS patients in Sina hospital, Tehran, Iran. MS diagnosis was performed based on the revised 2017 McDonald criteria. Dietary patterns of participants during last year of attendance to the study were evaluated using a validated 168-items food frequency questionnaire and MIND diet score were calculated accordingly. Physical disability was examined by an expert neurologist and reported according to the Expanded Disability Status Scale (EDSS). Brief International Cognitive Assessment for MS (BICAMS) battery was applied to assess cognitive function. Normality test was done and Spearman correlation test were used for analysis.
Results: The mean ± SD age of participants was 38.65±8.89 years old and 75% (n: 60) of them were women. RRMS was the most frequent type of MS among participants (65.0% (n:52)). The mean EDSS was 2.91±1.67 with the mean disease duration of 10.92±5.93 years. 63.7% of patients were receiving Ocrelizumab, 30.0 % Natalizumab, and 3.8% Fingolimod. Higher adherence to the MIND diet was significantly correlated with higher scores in the SDMT (P: 0.04; r:0.22) and CVLT-II-Delayed (P: 0.05; r: 0.22) subtests of BICAMS. In addition, MIND diet score was inversely correlated with EDSS (P: 0.04; r: -0.22).
Conclusion: Our results suggest that a higher adherence to mind diet which consists of brain-healthy food groups including green leafy vegetables, beans, nuts, whole grains, olive oil, berries, fish and poultry could be correlated with better cognitive and physical function in patients with MS.

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P1102
Correlation of serum glial biomarkers with physical disability in Multiple Sclerosis patients

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Introduction: Microglia and astrocytes play crucial homeostatic roles, including promoting neuronal activity, development, and survival. In multiple sclerosis (MS), proinflammatory microglia and astrocytes contribute to neurodegenerative pathways, leading to the progression of disability. Two indicators of astroglial and microglial activation are the soluble triggering receptor expressed on myeloid cells 2 (sTREM2) and glial fibrillary acidic protein (GFAP). The levels of these biomarkers can aid in assessing neuroinflammation and disease activity.
Objectives/Aims: We aim to evaluate the association between serum levels of GFAP and sTREM2 and the Expanded Disability Status Scale (EDSS) as a measure of disability in MS patients.
Methods: This cross-sectional study was conducted at Sina Hospital in Tehran, Iran, on 120 patients with MS diagnosed according to the revised 2017 McDonald criteria. During face-to-face interviews, demographic data were collected, and EDSS was assessed by an expert neurologist. Blood samples were obtained from the patients, and serum levels of GFAP and sTREM2 were measured using the enzyme-linked immunosorbent assay (ELISA) method. The correlation between serum levels of GFAP and sTREM2 and EDSS was evaluated using Spearman's rho test. The significance level was set at $p < 0.05$.
Results: The mean ± standard deviation (SD) age of participants was 38.97 ± 9.80 years. The majority were female, comprising 79.2% of the sample (95 out of 120). Participants included 79.2% with relapsing-remitting MS (RRMS), 17.5% with secondary progressive MS (SPMS), and 3.3% with primary progressive MS (PPMS). The average EDSS score was 2.75 ± 1.77. The average serum levels of GFAP and sTREM2 were 1.10 ± 0.45 ng/ml and 0.62 ± 0.29 ng/ml, respectively. A significant positive correlation was observed between EDSS and

both GFAP ($p = 0.002$, $r = 0.279$) and sTREM2 ($p = 0.030$, $r = 0.199$).
Conclusion: Our findings indicate a significant association between EDSS and serum levels of sTREM2 and GFAP. This suggests that these biomarkers may serve as useful tools for monitoring disability and may contribute to a better understanding of MS pathogenesis.

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P1103
MS-related fatigue is strongly and consistently predicted by greater inhibition of the corticospinal tract, anxiety, poor sleep and neurotransmitter-modifying medications

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Introduction: Decades of research examining fatigue in MS supports that there is a very long list of primary and secondary contributors making it difficult to treat.
Objectives/Aims: We present comprehensive data from a large group of persons with MS to elucidate the collective contributions of fatigue's likely players.
Methods: We recruited 80 females and 30 males (disease duration 13.9±8.4 years; Expanded Disability Status Scale (EDSS) 2.4 ±2; Age 48.4±10.5 years from a MS Neurology clinic. During one laboratory visit, participants rated their current fatigue level (State Fatigue) using a 100mm visual analogue scale and their typical fatigue over the previous 2 weeks (Trait Fatigue) using question #23 from the MS Impact Scale; 1 (not at all) to 5 (extremely). They underwent comprehensive physical and cognitive phenotyping. We used 3-step regression modelling to predict State and Trait Fatigue with variables initially assigned to 5 subgroups; patient/disease demographics, corticospinal tract function using Transcranial Magnetic Stimulation (TMS), mood, prescription medications, and cardiopulmonary fitness. In the concluding step, significant predictors were entered into a final model from most to least predictive.
Results: Predictors differed between State and Trait Fatigue. 54% of the variability in State Fatigue was predicted by, from greatest to least, TMS variables indicating hemispheric asymmetry and greater inhibition of the corticospinal tract, poor sleep, anxiety, prescribed medications (benzodiazepines, dopamine agonists/antagonists, modafinil), and lower fitness ($R=0.74$, $R^2=0.54$). 72% of variability in Trait Fatigue was predicted by, from greatest to least, disease duration, greater inhibition of the corticospinal tract, grip strength, body mass index, depression, anxiety, poor sleep and the medications, benzodiazepines and GABA-analogues ($R=0.85$, $R^2=0.72$).
Conclusion: Predictors of fatigue depended on whether you asked the patient to rate their fatigue at present or in the previous weeks. Consistent and strong predictors of both State and Trait Fatigue included TMS-derived measurement of greater corticospinal inhibition, anxiety, poor sleep, and prescription of neurotransmitter-modifying medications.

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P1104
Serum Neurofilament Light Chain as a Biomarker in Therapeutic Decision-Making for Relapsing Multiple Sclerosis

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Introduction: Neurofilament light chain serum concentration (sNfL) has been established as a biomarker for neuroaxonal damage and subclinical disease activity in multiple sclerosis (MS). However, its role and significance in therapeutic decisions remains to be further elucidated.
Objectives/Aims:
Here, we investigated whether sNfL levels are associated with key clinical parameters that are often considered when initiating high-efficacy treatment (HET), including the degree of physical impairment, cognitive performance and presence of disease activity.
Methods: We measured sNfL in a cohort of patients with relapsing multiple sclerosis (RMS) who were either treatment-free or receiving a low-efficacy treatment (LET) and scheduled for initiation of HET. Neuropsychological assessment was performed using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS).
Pearson correlations were used to assess associations between sNfL and clinical variables. One-way ANOVA was employed to examine the effects of current and previous disease-modifying therapies (DMTs).
Results: Data from 54 RMS patients were analyzed (mean age: 35.0 years ± 10.7, mean expanded disability status scale [EDSS]: 1.8 ± 1.3, mean annual relapse rate [ARR]: 0.8 ± 0.9). A total of 32 patients (59.3%) were treatment-naïve.
sNfL levels showed significant correlations with EDSS (Pearsons's $r = 0.43$, $p = 0.002$) and information processing speed (Pearson's $r = -0.348$, $p = 0.015$), but not with ARR, fatigue, or depressive symptoms. The presence of gadolinium-enhancing lesions (GEL) on MRI was associated with elevated sNfL levels. These correlations remained significant after correcting for age, BMI and renal function. Notably, sNfL concentrations did not differ between patients on LET and those receiving no treatment.

Conclusion: When considering the change to or initiation of HET, sNfL might be of important diagnostic value since it is closely associated not only with the degree of physical impairment and MRI signs of disease activity but also with current level of cognitive deficits. Therefore, sNfL should be incorporated firmly in the therapeutic decision. Interestingly, in our cohort patients on LET had the same sNfL levels as patients on no DMT suggesting that LET may be insufficient in reducing neuroaxonal injury and subclinical disease activity, highlighting the potential benefit of early escalation to HET in selected patients.

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P1105
The role of corpus callosum atrophy in cognitive impairment, fatigue, and depression in a Tunisian cohort of patients with multiple sclerosis

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Introduction: Cognitive impairment, fatigue, and depression are common symptoms of relapsing-remitting multiple sclerosis (RRMS). They are often unrecognized and underdiagnosed, presenting as silent markers of progression. The corpus callosum (CC), essential for cognitive tasks requiring connectivity, is particularly affected in multiple sclerosis (MS).
Objectives/Aims: The aim of our study is to develop an objective radiological biomarker for assessment of fatigue, cognitive impairment and depression in MS patients.
Methods: A cross-sectional study in the neurology department at Monastir including 70 Tunisian patients with definite RRMS and 30 healthy controls. All patients underwent brain magnetic resonance imaging, standardised neurological assessment and testing via the BCcogSEP battery, including assessments of fatigue via the Fatigue Impact Scale (FIS) and depression via the Beck Depression Inventory. Total and regional CC atrophy was assessed using the corpus callosum index (CCI).
Results: The mean age was 31± 11 years, 49/70 females, the mean disease duration was 5 ± 4 years, the mean Expanded Disability Status Scale (EDSS) score was 2.4 ± 1,7. The frequency of Cl was 70%, fatigue 85.4% and depression 56%. The CCI was highly correlated with the Paced Auditory Serial Addition Test (PASAT), Verbal Fluency Test (VFT) and Verbal Memory Test (VMT). As well, it was highly correlated with the fatigue score ($p = 0.0001$). Posterior CC segment atrophy was significantly associated with a poor PASAT result. However, anterior CC segment atrophy was significantly associated with depression (0.02) and a poor VMT results in our study.
Conclusion: Corpus callosum atrophy is associated with CI, fatigue and depression in MS. This relationship supports its potential as an objective surrogate marker for screening disease progression even in early stages of MS.

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P1106
Motor Fatigue in Multiple Sclerosis: The Distinct Role of Motor and Psychological Factors

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Introduction: Motor fatigue hampers daily functioning and quality of life in people with multiple sclerosis (pwMS).
Objectives/Aims: While both motor and psychological factors have been linked to motor fatigue, their distinct contributions require further investigation.
Methods: We analysed a longitudinal cohort of 110 pwMS (60% female; mean age: 37.8±9.7 years; Median EDSS (expanded disability status scale)=1, IQR=2) who underwent clinical and neuropsychological assessments at baseline (BL) and follow-up (FU) after 1.5 years. Disability and motor function were assessed via EDSS and Timed 25-Foot Walk (T25FW); psychological factors included depression and anxiety (Hospital Anxiety and Depression Scale), resilience ("Resilience-Scale-13"), and motor fatigue (Fatigue Scale for Motor and Cognitive Functions). At BL, we performed cross-sectional hierarchical linear regression models on motor fatigue, with demographic and clinical variables (age, sex, relapse number) in block1, disability and motor function (EDSS, T25FW-speed) in block2, and psychological variables (resilience, anxiety, depression) in block3. Predictors of FU motor fatigue were examined

using two models: one with BL variables as stated above, and one with BL motor fatigue (block 1), changes in motor function/disability (block 2), and changes in psychological factors (block 3).
Results: Mean BL motor fatigue was 26.4±10, with 49% of pwMS reporting moderate or severe fatigue. At BL, the final model explained 58% of variance in motor fatigue (adj.R^2), with disability and motor function explaining an additional 28% of variance (R^2 change) beyond demographics, and psychological factors contributing a further 23%. Significant predictors in the final model were EDSS (β=0.37, p<0.001), anxiety (β=0.21, p=0.021), and depression (β=0.38, p<0.001). In FU-analyses, BL EDSS (β=0.27, p=0.002) and depression (β=0.32, p=0.003) predicted motor fatigue at FU (total adj.R^2=47%). In the model including changes, BL motor fatigue explained 65% of variance in FU motor fatigue (total adj.R^2=71%). Changes in psychological factors explained additional 6% of variance (change in resilience: β=-0.17, p=0.003), whereas changes in disability or motor function did not explain a significant proportion of variance.
Conclusion: Disability, motor function, and psychological factors independently contribute to motor fatigue in pwMS. Over 1.5 years of FU, especially changes in psychological variables appear to be crucial predictors, highlighting their relevance in motor fatigue management.

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P1107
Assessing the effects of induced fatigability on motor and cognitive performance in Multiple Sclerosis: a multicenter cross-sectional study

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Introduction: Fatigability is one of the most disabling symptoms in People with MS (PwMS) that contributes to reduce walking, balance, and cognitive capacity. These changes in performances seem to affect and quality of life. However, the impact of fatigability on walking, balance, and cognitive functions has not yet been studied.
Objectives/Aims: This study investigates the acute effects of induced fatigability on gait, balance, and cognition.
Methods: So far, 96 PwMS (age: 54.1±10.2 years, EDSS: 3.1±1.2 points,52% women) and 22 age- and sex-matched Healthy Subjects (HS) were assessed. Participants completed 30-minute or until exhaustion (Rate of Perceived Exertion (RPE) >17 points) Fatiguing Walking Test (FWT), followed by balance tests with three Inertial Measurement Units and cognitive assessment using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) at Pre (before), Post (after), and Rest (after 30-min). Between-group differences were calculated using non-parametric ANOVA (Kruskal-Wallis test) and Wilcoxon tests.
Results: Healthy Subjects completed FWT (RPE:10.5±2.6 points), 49% of PwMS completed FWT (RPE:14.5±3.7 points), and 51% of PwMS walked for 15.6±6.3 minutes (RPE:19.1±1.1 points, p Time*Group<0.001).
Static balance tests showed significant Time*Group interactions for trunk Medio-Lateral (ML) sway amplitude (p=0.011), and sample entropy (p=0.043). No changes were observed in cognition measured by BICAMS (p>0.05). Dynamic balance showed increased ML instability in PwMS versus a decrease in HS (p=0.007).
Conclusion: Preliminary data show an acute effect of motor fatigability on balance in PwMS, but no effect on cognitive functions.

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P1108
Sensitivity of the cortical excitability in patients with Multiple Sclerosis and clinical Fatigue

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Introduction: Fatigue is a common and disabling symptom in patients with multiple sclerosis (MS). It may influence disease progression and quality of life by altering cortical excitability. Paired transcranial magnetic stimulation (pTMS) is a neurophysiological method used to evaluate intracortical inhibition (ICI) and facilitation (ICF) in MS patients.
Objectives/Aims: To assess differences in short intracortical inhibition (SICI) and facilitation (SICF) in patients with MS depending on fatigue severity.
Methods: Ninety-six MS patients were assessed using the Fatigue Assessment Scale (FAS) and divided into four subgroups: Group I (<22 points, n=25), Group II (22–30, n=28), Group III (31–36, n=27), Group IV (>36, n=16). pTMS was performed using a 90-mm circular coil connected to a MagPro R30 stimulator. Electromyographic signals were recorded from the abductor pollicis brevis of the dominant hand. Parameters evaluated included: resting motor threshold (MT), motor evoked potential amplitude (AMEP), SICI1 and SICI2 (2 and 3 ms), SICF1 and SICF2 (12 and 15 ms). Differences were analyzed using variance analysis.
Results: Mean values: MT – 50.65±12.36%; AMEP – 1.38±1.05 mV; SICI1 – 46.52±34.21%; SICI2 – 62.27±36.55%; SICF1 – 153.63±60.70%; SICF2 – 146.1±180.43%. A statistically significant effect of fatigue severity was observed (p=0.02): patients with lower fatigue (Groups I–II) demonstrated higher cortical facilitation than those with greater fatigue (Groups III–IV).
Conclusion: Fatigue in MS negatively affects cortical excitability and is associated with reduced facilitation patterns. This may contribute to impaired motor performance and functional decline.

Disclosure of interest: Mariana Andriievska: nothing to disclose

P1109
Increase in disability is associated with increase in fatigue and depression

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Introduction: Fatigue is a prevalent symptom in patients with multiple sclerosis (MS), closely related to depression and physical disability, and has a significant impact on quality of life. However, data on its longitudinal evolution remain scarce
Objectives/Aims: We aimed to analyze changes in fatigue, depression, and disability over a 7-year period.
Methods: Prospective, observational study including MS patients evaluated at two time points over 7 years. Fatigue was assessed using the Modified Fatigue Impact Scale (MFIS) and a Visual Analogue Scale (VAS); depression using the Patient Health Questionnaire-9 (PHQ-9). The first assessment occurred between June 2016 and February 2017, and the second between April 2023 and March 2025. Additional variables collected included age, sex, Expanded Disability Status Scale (EDSS) score, and MS treatment. Correlations between changes in MFIS, PHQ-9, and EDSS were analyzed. A subgroup analysis was conducted based on EDSS progression: stable, increase of 0.5–1.0 points, and increase of ⩾1.5 points.
Results: A total of 276 patients were included in the baseline evaluation (68.8% women, mean age 43.7 ± 9.7 years, median EDSS 2.0 [IQR 1.5–2.5]); 32.6% were receiving high-efficacy treatment. Median baseline scores were: MFIS 36 [IQR 16.2–51.7], VAS 6 [IQR 2.8–7.5], and PHQ-9 6 [IQR 3–11].
At follow-up (7.5 ± 0.5 years later), 237 patients were reassessed (mean age 50.8 ± 9.1 years, median EDSS 2.0 [IQR 1.5–3.5], 50.6% on high-efficacy treatment. Median scores were: MFIS 42 [IQR 22.5–59], VAS 6 [IQR 3.4–7.8], and PHQ-9 7 [IQR 4–15].
Increases in EDSS correlated with changes in MFIS ($r = 0.23$, $p < 0.001$) and PHQ-9 ($r = 0.20$, $p = 0.02$). Patients with stable EDSS showed no worsening in fatigue or depression, whereas those with EDSS increase ⩾1.5 points showed significant deterioration.
Conclusion: Increased fatigue and depression over time correlate with greater disability progression in MS. Patients with substantial EDSS worsening (⩾1.5 points) experienced the most pronounced increases, highlighting the interrelation of these clinical domains.

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P1110
Facial Emotion Recognition in Multiple Sclerosis: Evaluation through Genuineness-Based Dynamic Stimuli

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Introduction: Facial emotion recognition is a fundamental component of social cognition, which encompasses the ability to perceive, interpret, and respond to social and emotional cues. In MS social cognition is increasingly recognized as a domain frequently affected, with potential consequences on interpersonal functioning and quality of life.
Objectives/Aims: We used the Emotion Authenticity Recognition (EAR) test—featuring both genuine and posed dynamic expressions—to assess facial recognition in MS patients.
Methods: Fifty-four MS patients (36F; age=41.4±11 years, education=15.2±3) completed the EAR test, which provides two indices: Emotion Recognition (ER) and Emotion Authenticity (EA). Associations were explored with clinical, neuropsychological, self-report, and MRI data. Structural MRI was analyzed using Voxel-Based Morphometry (VBM) for regional gray matter volume and FreeSurfer for cortical thickness and volumetric surface-based morphometry. A Bayesian comparison with 54 matched for age, sex, and education healthy controls (HCs) was also performed (36F; age=41.0±11 years, education=14.7±3).
Results: Mean±SD scores in MS were 50.9±4.7 (ER) and 52.1±4.9 (EA). ER correlated negatively with age and disease duration, and positively with education. ER was also linked to semantic verbal fluency, memory, attention/processing speed, executive functions, and global cognitive functioning. EA was lower in patients with severe cognitive impairment and associated with self-reported empathy and distress.
VBM data showed that ER was associated with bilateral temporal and frontal regions; EA was associated with prefrontal, hippocampal, and fusiform areas. FreeSurfer data confirmed widespread cortical thinning, white matter abnormalities, and subcortical atrophy associated with facial recognition performance.
T-test comparison for ER and EA showed no significant differences between MS and HCs. To determine whether the absence of a significant group effect could be interpreted as evidence favouring the null effect of the group, Bayesian independent t-tests were performed; the t-test revealed moderate evidence for no group difference in ER (BF_{10} = 0.210, %error= 0.029) and anecdotal evidence in favor of the null hypothesis for EA (BF_{10} = 0.658, %error = 0.017).
Conclusion: MS patients showed comparable facial emotion recognition performance compared to HCs. However, facial recognition in MS was associated with cognitive status and brain damage. The EAR test captures subtle alterations in social cognition, underscoring the value of dynamic, genuineness-based measures in MS assessment.

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P1111
Impact of Autologous Hematopoietic Stem Cell Transplantation (aHSCT) on Cognitive Functions, Mood, and Fatigue in Multiple Sclerosis

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Introduction: Autologous hematopoietic stem cell transplantation (aHSCT) is highly effective in suppressing clinical relapses and MRI activity in aggressive multiple sclerosis (MS). However, the short and long-term effects of aHSCT on cognition, mood, and fatigue remain poorly studied.
Objectives/Aims: This study aimed to describe cognitive outcomes, as well as changes in depression, anxiety, fatigue and apathy in patients with MS treated with aHSCT.
Methods: Patients were tested with the Brief International Cognitive Assessment for MS (BICAMS) which includes the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test 2nd ed (CVLT-II) and the Brief Visuospatial Memory Test Revised (BVMT-R). Changes over time in cognition were assessed using the 90% confidence interval regression-based change index (RB-CI), which identify cognitive meaningful changes over follow-up by using regression methods, estimating expected changes in cognitive tests, accounting for baseline score, age, sex and education. Seven patients additionally underwent assessments of mood, fatigue, and apathy using the Hospital Anxiety and Depression Scale (HADS), the Modified Fatigue Impact Scale (MFIS), and the self-administered version of the Apathy Evaluation Scale (AES-S). Differences in mean scores between baseline and follow-up were evaluated using paired Student's t test or Wilcoxon Ranks.
Results: 14 MS patients, 11 with Relapsing-Remitting MS (RRMS) and 3 with Secondary Progressive MS (SPMS), were included in the analysis. After a mean time of 1.57 year (SD=0.727), 1 SPMS patient had significant worsening on the SDMT and 1 RRMS patient had worsening on the CVLT-II, while none worsened on BVMT-R. Overall, 5 RRMS patients had improvements at BICAMS (1 at SDMT, 3 at CVLT-II and 2 at BVMT-R). The remaining 9 patients had stable BICAMS score. No significant differences in mean scores were found in HADS (12.40 vs 11.10), MFIS (34.40 vs 31.10), and AES-S

(30.90 vs 29.70) total scores from baseline to follow-up, despite a trend indicating a reduction of symptoms across all domains considered.
Conclusion: Cognitive functions remain stable or improve in most patients treated with AHSCT. A trend
towards a reduction in depression, anxiety, fatigue and apathy was observed.

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P1112
Investigating the Interplay of Psychological, Cognitive, and Physical Comorbidities in Sexual Function Among Women with Multiple Sclerosis: A Cross-Sectional Study in Iran

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Introduction: Multiple sclerosis (MS) is an inflammatory disease affecting the central nervous system, with significant impacts on various aspects of life, including sexual function. Sexual dysfunction is a prevalent issue among women with MS, affecting their quality of life. It is crucial to assess and address sexual function as it often correlates with psychological factors such as depression and anxiety, cognitive impairment, and other MS-related symptoms like urinary disorders.
Objectives/Aims: To explore the relationship between sexual function and these associated factors in an Iranian population of women with MS, providing insights for improved management and care.
Methods: A cross-sectional study was conducted on women with MS attending the MS clinic at Sina Hospital, Tehran, Iran, between April 2024 and September 2024. Demographic and clinical data such as disease duration, Expanded Disability Status Scale (EDSS) score and disease modifying therapies were collected; and sexual function, fatigue, anxiety, depression, and urinary dysfunction were assessed using validated Persian versions of the Female Sexual Function Index (FSFI), Fatigue Severity Scale (FSS), Beck Anxiety Inventory (BAI), Beck Depression Inventory-II (BDI-II), and Actionable Bladder Symptoms Screening Tool (ABSST) questionnaires, respectively. Moreover, cognitive assessments were completed using The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery. The correlation between FSFI scores and demographic/clinical variables, cognitive function, depression, anxiety, and fatigue was analyzed using linear regression. Statistical analyses were performed in SPSS software (v24), with significance set at $p \leqslant 0.05$.
Results: The study included 39 patients (median age: 38.9 years, IQR=11.4; disease duration: 11.21 years, IQR=5.29; EDSS score: 2.7, IQR=1.4). The Majority of patients had relapsing-remitting MS (RRMS, n=28, 71.8%) and were treated with Ocrelizumab (n=23, 59%) or Natalizumab (n=14, 35.9%). No significant crude correlation emerged between FSFI scores and psychological disorders or cognitive function. However, FSFI scores inversely correlated with bladder dysfunction (ABSST: $r = -0.32$, $p = 0.04$) and age ($r = -0.39$, $p = 0.01$), the latter retained as a confounder in regression analysis. Adjusted pairwise comparisons revealed significant negative associations between sexual function and depression ($\beta = -0.50$, $p < 0.01$) and a negative association with delayed visuospatial memory (BVMT-delay: $\beta = -0.39$, $p = 0.03$). No other adjusted correlations with comorbidities, cognitive domains, or physical symptoms (including aforementioned ABSST) were observed.
Conclusion: Sexual function in women with MS is influenced by multiple factors, emphasizing the need for a multidisciplinary approach to address sexual health in MS management, considering psychological, cognitive, and physical aspects to enhance patient care and quality of life.

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P1113
Late-Onset Multiple Sclerosis: Cognitive Profile and Associated Variables in an Understudied Population

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Introduction: Multiple sclerosis (MS) mainly affects young adults, but it can occur at any age. Late-onset MS (LOMS), defined by symptom onset after age 50, presents unique clinical and radiological characteristics. While cognitive impairment

(CI) is common in MS, its manifestation in LOMS remains poorly understood.
Objectives/Aims: a) Analyse demographic and clinical features in LOMS versus adult-onset MS (AOMS); b) Compare CI prevalence in both groups; c) Compare neuropsychological performance.
Methods: Cross-sectional study in MS patients from two referral centres in Buenos Aires. Assessments included EDSS, Fatigue Severity Scale, Beck Depression Inventory-II, BICAMS, PASAT, semantic/phonemic fluency, and 7/24 visuospatial memory test. CI was defined as impairment in ⩾2 cognitive domains. Descriptive and inferential statistics were applied ($p<0.05$).
Results: 458 MS patients were included (64.4% women), 37 LOMS and 421 AOMS. Groups differed in age ($z = -8.745$, $p < .001$), but not in gender ($\chi^2 = 0.089$, $p = .858$) or education ($z = 0.990$, $p = .322$). Progressive phenotypes were more frequent in LOMS ($p < .001$). No differences were found in EDSS ($z = -0.719$, $p = .272$), fatigue ($z = -0.581$, $p = .561$), disease duration ($z = -1.768$, $p = .077$), depression ($z = -0.447$, $p = .655$), or anxiety ($z = -1.037$, $p = .300$). CI was more prevalent in LOMS (62%) than in AOMS (40%; $\chi^2 = 6.618$, $p = .016$). LOMS patients performed worse in attention, processing speed, verbal and visual memory ($p < .001$), and semantic fluency ($p = .004$). However, a multiple linear regression model using CI as the dependent variable and disease onset type as predictor—adjusted for age, gender, education, EDSS, and clinical form—was not significant ($p > 0.05$).
Conclusion: Despite similar disability, fatigue, mood, and disease duration, LOMS patients showed more CI and worse cognitive performance. However, disease onset type was not independently associated with CI after adjusting for confounders.

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P1114
Differentiating cognitive impairment in multiple sclerosis and Alzheimer's disease: insights from the MoCA

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Introduction: Cognitive deficits, especially in language and memory, are common among older adults with multiple sclerosis (MS), complicating the distinction between MS-related cognitive decline and early signs of Alzheimer's disease (AD). The Montreal Cognitive Assessment (MoCA) is widely used to screen for cognitive impairment in neurological populations, including MS. This study examines MoCA performance in older adults with MS and AD to identify features that may support differential diagnosis and reduce misdiagnosis risk.
Objectives/Aims: This study examines MoCA performance in older adults with MS to identify items that distinguish MS-related cognitive impairment from AD, improving diagnostic accuracy and understanding of these distinct cognitive profiles.
Methods: We conducted a retrospective, cross-sectional study of MS patients over 60 years old who completed cognitive screening with the MoCA as part of routine clinical care. We utilized publicly available normative data for adults with AD as a comparison group. Group differences between MS and AD were analyzed using Mann-Whitney U tests; effect size was calculated using rank biserial correlation (r_{rb}). Stepwise binary logistic regression was used to identify MoCA items that best predicted group membership, controlling for age. Sensitivity and specificity were calculated for the final model.
Results: The MS cohort included 100 patients (72% women; mean age: 68.2 years, SD = 6.2; range: 60–88 years); most with relapsing-remitting (n = 43) or secondary progressive (n = 31) phenotypes. The AD cohort had 81 individuals, with a mean age of 76.7 years, SD = 8.3; range: 59–94. Analysis of the MoCA Total Score (max score 30) showed a mean of 23.7 for MS and 15.3 for AD. Groupwise comparison found Orientation ($r_{rb} = 0.64$), Recall ($r_{rb} = 0.54$), and Naming ($r_{rb} = 0.50$) best discriminated between MS and AD. Notably, 82% of the MS cohort scored 6/6 on Orientation, whereas only 21% of AD individuals scored similarly. In the best-fitting logistic regression model—controlling for age—Orientation, Naming, and Fluency were the strongest predictors of group membership, with lower scores increasing the likelihood of AD classification over MS. This model showed 88.2% sensitivity to correctly identify MS and 83.5% specificity to correctly identify AD.
Conclusion: Among older adults with MS, Orientation, Recall, and Naming emerged as key MoCA items that distinguish MS-related cognitive changes from those associated with AD. These findings suggest distinct pathophysiological mechanisms underlying cognitive impairment in MS compared to AD. With newly available anti-amyloid therapies for AD, accurate differentiation is critical to avoid unnecessary work-up and treatment in MS patients. Moreover, our results align with emerging literature suggesting that MS may confer a protective effect against AD, potentially reducing the likelihood of co-occurrence between the two conditions.

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P1115
Memory Rehabilitation in Multiple Sclerosis: Who Benefits Most?

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Introduction: Cognitive dysfunction, specifically memory impairment, is prevalent in individuals with multiple sclerosis (MS), affecting 40-65% of patients. Cognitive rehabilitation (CR) has shown promise in improving outcomes for persons with MS (pwMS). However, heterogeneity in treatment response is observed, with not all patients demonstrating equivalent benefits from CR. Reliable predictors of success in CR have yet to be identified.
Objectives/Aims: To evaluate predictors of memory gains in pwMS after participation in a CR program
Methods: Twenty-three pwMS who reported cognitive difficulties took part in a 9-week computerized CR program ('Rehacom', 2x/week for 45 min). A neuropsychological battery of performance tests comprising the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS) and self-report instruments (demographics, mood, perceived cognitive deficits) were completed at baseline. The Brief International Cognitive Assessment for MS (BICAMS), including tests of verbal memory, spatial memory, and processing speed, was completed at 10 weeks. Binary logistic regressions were used to identify factors predicting whether an individual would benefit from CR or not.
Results: For verbal memory, the final model, $\chi^2(1) = 5.79$, $p = .016$, included a single predictor: baseline cognitive performance. A higher number of failed tests on the MACFIMS was associated with lower odds of improvement in verbal memory ($\beta = -.723$, $p = .053$). While the effect just fell short of the conventional significance threshold, an effect size of 0.19 (standardized Odds Ratio, sOR) was noted, indicating a small relationship between predictor and outcome. For spatial memory, the final model included the number of failed MACFIMS tests, baseline scores at the Symbol Digits Modalities Test (SDMT), and age, $\chi^2(3) = 8.56$, $p = .036$. The model correctly classified 81% of participants as having improved or not. The odds of improvement decreased as the number of MACFIMS tests failed increased ($\beta = -1.02$, $p = 0.03$, sOR=.10). Age and SDMT scores were not significantly associated with response to CR.
Conclusion: Initial baseline performance was identified as the primary factor associated with an increased likelihood of memory gains following CR in pwMS. The chances of improvement decrease as the number of failed tests increases. These findings may inform allocation of scarce neuropsychological resources in clinical practice by prioritizing CR for pwMS with the highest potential for positive outcomes.

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P1116
What Drives Change in Cognitive Speed? Predictors of One-Year Symbol Digit Modalities Test Performance in Multiple Sclerosis

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Introduction: The Symbol Digit Modalities Test (SDMT) is a sensitive measure of information processing speed and attention, widely used in the cognitive assessment of people with multiple sclerosis (pwMS). Longitudinal tracking of SDMT performance can help uncover the clinical and behavioral factors that contribute to cognitive decline or improvement over time.
Objectives/Aims: To identify the clinical, cognitive, and behavioral predictors of one-year changes in SDMT performance in pwMS.
Methods: This retrospective analysis examined one-year changes in SDMT scores as the primary outcome. Predictor variables included changes in California Verbal Learning Test–II (CVLT-II), Brief Visuospatial Memory Test–Revised (BVMT-R), Timed 25-Foot Walk (T25-FW), and 9-Hole Peg Test (9-HPT), as well as baseline and follow-up EDSS scores, annual relapse count, and lifestyle behaviors (smoking and alcohol use). Statistical analyses involved Pearson correlations, ANOVA, and multiple linear regression. For group comparisons, participants were categorized into three subgroups based on the percentage change in SDMT performance over one year: ⩾20% improvement, ⩾20% worsening, and stable performance. Age and disease duration were matched across groups.
Results: The analysis included 399 pwMS. Among them, 95 showed ⩾20% improvement in SDMT scores, 43 experienced

⩾20% worsening, and 261 remained stable. The three groups were matched for age and disease duration.
The mean SDMT change over one year was 1.07 (SD = 0.22). SDMT improvement was positively correlated with changes in CVLT-II ($r = 0.294$, $p < 0.01$), BVMT-R ($r = 0.218$, $p < 0.01$), and 9-HPT ($r = 0.141$, $p < 0.01$), and negatively correlated with changes in T25-FW ($r = -0.168$, $p < 0.01$) and EDSS at follow-up ($r = -0.080$, $p < 0.05$).
ANOVA indicated significant group differences based on EDSS scores ($F(2, 396) = 4.804$, $p = 0.009$) and relapse count at follow-up ($F(2, 396) = 3.944$, $p = 0.020$), but no differences in other clinical variables.
Multiple linear regression showed a statistically significant model ($F(14, 323) = 4.132$, $p < 0.001$), explaining 15.2% of the variance in SDMT change ($R^2 = 0.152$). The most significant predictors were change in CVLT-II ($\beta = 0.319$, $p < 0.001$) and change in T25-FW ($\beta = -0.121$, $p = 0.023$).
Conclusion: One-year changes in information processing speed, as measured by the SDMT, are shaped by both cognitive and motor performance. Improvements in verbal learning strongly align with gains in SDMT, whereas deteriorations in gait function are associated with slower cognitive speed. These findings underscore the need to monitor both cognitive and physical domains when evaluating cognitive trajectories in MS. A multidimensional follow-up approach may improve the early detection of decline and guide targeted interventions to preserve cognitive health.

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P1117
Factors Contributing to Fatigue in People with Multiple Sclerosis: A Cross-Sectional Analysis

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Introduction: Fatigue is a common and disabling symptom in multiple sclerosis (MS), often influenced by both primary disease mechanisms and secondary factors. Physical problems such as muscle weakness, mobility limitations, and balance problems can contribute to secondary fatigue by increasing energy demands and reducing functional capacity.
Objectives/Aims: The aim of this study was to identify the factors associated with fatigue in people with MS (PwMS).
Methods: A total of 60 participants with an Expanded Disability Status Scale (EDSS) score of ⩽ 5.5 were included in the study. Fatigue levels in PwMS were assessed using the Fatigue Severity Scale (FSS). To identify factors associated with fatigue, participants underwent a comprehensive evaluation that included the Two-Minute Walk Test (2MWT) for functional mobility, isokinetic muscle strength assessment of the knee flexor and extensor muscle groups at an angular velocity of 90º/s, trunk strength (curl-up test), endurance tests (plank and lateral bridge), and postural sway analysis using the Postural Stability Test (PST).
Results: A strong negative correlation was observed between the FSS and the 2MWT ($r=-0.651$, $p<0.001$). Knee flexor and extensor muscle strength on the affected side were found to be associated with FSS ($r=-0.331$, $p=0.019$; $r=-0.327$, $p=0.020$, respectively), while muscle strength on the less affected side showed no significant correlation. A significant relationship was also found between the FSS and the lateral bridge test on both the affected and unaffected sides, as well as with the plank and curl-up tests ($r=-436$, $p=0.002$; $r=-0.410$, $p=0.003$; $r=-524$, $p<0.001$; $r=-0.370$, $p=0.008$, respectively). FSS also had a positive correlation with the PST sway index ($r=0.686$, $p<0.001$).
Conclusion: Reduced walking distance, diminished muscle strength in the affected leg, decreased trunk strength and endurance, and increased postural sway are associated with higher levels of fatigue. These findings highlight the importance of targeting physical function, including walking distance, muscle strength, trunk endurance, and postural control, in interventions aimed at managing fatigue in individuals with MS. A comprehensive approach focusing on physical rehabilitation and tailored exercise programs may help mitigate the impact of fatigue.

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P1118
Emotional Response Inhibition in Multiple Sclerosis: Behavioral and Neuroimaging Correlates from an Emotional Stop Signal Task

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Introduction: Cognitive and emotional dysfunctions are key features in MS, but their interaction remains underexplored. The Emotional Stop Signal Task (eSST) assesses inhibitory control in emotionally salient contexts. Emerging evidence suggests that emotional stimuli can modulate inhibitory processes, highlighting the importance of investigating how emotional reactivity may impact cognitive control in MS.
Objectives/Aims: To examine emotional modulation of inhibition in MS using the eSST and explore behavioral, neuropsychological, and neuroanatomical correlates.
Methods: Twenty-seven MS patients (years: 36.9±10.4) and 26 healthy controls (HCs; years: 26.5±4.6) completed an eSST

involving emotional (fearful) and neutral facial stimuli. The primary outcome was the differential Stop Signal Reaction Time (ΔSSRT=emotional – neutral). Due to age mismatch, an ANCOVA with age as covariate was used. For MS, correlations were examined with clinical variables, cognitive status, and MRI data. Structural MRI was analyzed using Voxel-Based Morphometry (VBM) for regional gray matter volume and FreeSurfer for cortical thickness and volumetric surface-based morphometry.

Results: ΔSSRT was near zero in MS (0.9±26.9 ms), suggesting no facilitation of inhibitory control by emotional stimuli, unlike HCs (HCs =-2.4±11.798). The effect of group in the ANCOVA showed a trend toward significance ($F_{(1,51)} = 3.288$, $p = 0.076$), pointing to a possible difference in emotional modulation of inhibition. In MS, higher ΔSSRT was associated with preserved executive function (p=0.008). Age inversely correlated with ΔSSRT ($r = 0.41$, $p = 0.036$), suggesting reduced emotional sensitivity in younger patients. Uncorrected neuroimaging analyses showed significant associations between ΔSSRT and regions involved in motor inhibition and social cognition, as the cingulate cortex, cerebellum, fusiform gyrus, inferior frontal gyrus, precuneus, and supramarginal gyrus.

Conclusion: Emotional modulation of inhibitory control in MS shows significant individual variability, linked to executive functions and age. Imaging results suggest involvement of regions related to motor inhibition and social cognition. These findings underscore the importance of cognitive resources in emotional response regulation and warrant further investigation into emotion–cognition interactions in MS.

Disclosure of interest: Rachele Pezzetta: nothing to disclose.

P1119
Applying the International Classification of Cognitive Disorders in Multiple Sclerosis (IC-CoDiMS) at Diagnosis: Insights from a Single-Centre Cohort

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Introduction: Cognitive impairment (CI) affects up to 70% of people with multiple sclerosis (PwMS). A recent study adapted the International Classification of Cognitive Disorders in Epilepsy (IC-CoDE) to define cognitive phenotypes in MS (IC-CoDiMS) using a large, multinational cohort. However, CI can appear from the disease onset, and studies exploring early cognitive changes, as well as the influence of fatigue and neuropsychiatric symptoms, remain limited.

Objectives/Aims: This study aimed to investigate these aspects in a single-center cohort at MS diagnosis.

Methods: At diagnostic work-up, PwMS underwent neurological and neuropsychological evaluation (Rao Brief Repeatable Battery, Stroop Test), fatigue assessment (Fatigue Severity Scale, Modified Fatigue Impact Scale), and mood evaluation (Beck Depression Inventory, State-Trait Anxiety Inventory). An established algorithm defined domain impairment when two tests in a domain scored below −1.5 SD from the mean.

Results: 216 PwMS (mean age 39.6±11; 70% women; median EDSS 2.0) were included. At the −1.5 SD threshold, 58.9% were cognitively intact, 25.7% had single-domain, 14.5% bi-domain, and 4.3% multi-domain impairment. Language (44.5%) and memory (37%) were the most affected domains. Older age increased risk for multi-domain impairment (p=0.04). No associations were found with EDSS or education. Even without CI, PwMS frequently showed fatigue (FSS: 28.2%; MFIS: 22.1%), depression (40.3%), and anxiety (state: 28.3%; trait: 13.8%).

Conclusion: IC-CoDiMS appears suitable for identifying cognitive phenotypes from early MS stages. Including fatigue and mood symptoms may enhance its clinical and research applicability, especially in selecting candidates for cognitive rehabilitation.

Disclosure of interest: Nothing to disclose

P1121
An Integrated Regional Approach to the Management of Multiple Sclerosis

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Introduction: More than 120,000 people in England live with multiple sclerosis (MS). Secondary and Tertiary specialist care have developed efficient pathways to address a new diagnosis, the initiation and monitoring involved with treatment, relapse management and rehabilitation within the hospital care setting, however, most of the life of a person with MS is spent in the community. In North Central London there is considerable variation in community provision from one borough to the next. Clinicians (Primary Care, Community therapy and nursing) need equitable, timely access to specialist support, and patients benefit from care closer to home by services who interface with their specialist MS services when needed.

Objectives/Aims: To support and complement the existing services in our sector, we developed a model to support the management of multiple sclerosis as part of a regional integrated neuroscience model. This innovative approach provides timely access and promotes collaborative care across community, primary, secondary and tertiary care for the benefit of patients and the system.

Methods: Specialist input works across primary, secondary and community care to support teams look after their patients with multiple sclerosis, interfacing with hospital services when needed. Pivotal to our pathway is the collaborative weekly virtual multidisciplinary discussion where referrals are invited from clinicians of any discipline. The core clinical team has hospital neurology and community representation and support the clinicians care for their patient. We have developed pathways from the emergency department and streamlined pathways to the appropriate sub-specialist services where needed.
Results: 35 patients with MS (46% relapsing remitting MS, 14% primary progressive MS, 34% secondary progressive MS and 6% obtaining new diagnosis) have been supported through this model to date. Involvement has included initiating the diagnostic investigations, education, spasticity and pain management, responding to acute concerns and supporting holistic care in the community, thus complementing the existing services. Our multidisciplinary team (MDT) have also participated in patient consultations alongside the patient's clinicians in the community (GPs, community therapists, nurses and other healthcare professionals) in patient homes (virtually) and in virtual and face to face consultations within the primary care, community hospitals and acute hospital settings to support and streamline the patient pathway.
Conclusion: We have developed and implemented a model which enhances the quality of existing services for MS by developing relationships between primary, secondary, tertiary and community care. Collaboration with the clinicians in the community means the right care can be delivered closer to the patient home.

Disclosure of interest: Nothing to disclose

P1122
Relationship Between Demographic, Clinical, and Radiological Factors with cognitive function evaluating by Symbol Digit Modalities Test in Multiple Sclerosis Patients

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Introduction: The Symbol Digit Modalities Test(SDMT) is widely used to assess processing speed in patients with MS. Several factors can influence the results.
Objectives/Aims: To evaluate the association between demographic, clinical, and radiological variables in MS patients and SDMT.
Methods: 219 MS patients who started a disease-modifying treatment(DMT) between 2019 and 2024 were included. Participants underwent baseline MRI, fatigue and depression assessments using the Modified Fatigue Impact Scale(M-FIS) and Beck Depression Inventory-Fast Screen(BDI FS) scales respectively, and cognitive screening using the Brief International Cognitive Assessment for MS(BICAMS).
Results: The study included 169(73.1%) women, with a median age at onset of 33(IQR 26-40) years, disease duration of 27 months, and an EDSS score of 2(IQR 1.5-2.5). The median number of lesions in T1 and T2 was 8(IQR 3-16) and 15(IQR 9-33%), respectively. 26% of patients had gadolinium-enhancing lesions. The mean SDMT score was 52.35. Higher SDMT scores were found in those with higher education levels($p<0.001$). A negative correlation was observed between SDMT and age at MS onset($r=-0.359$, $p<0.001$), age at DMT initiation($r=-0.356$, $p<0.001$), EDSS score($rho=-0.283$, $p<0.001$), number of T2 lesions($rho=-0.231$, $p<0.001$), and a trend toward a negative relationship with T1 lesions($rho=-0.125$, $p=0.065$). Fatigue($rho=-0.334$, $p<0.001$), depression($rho=-0.251$, $p<0.001$), and psychotropic drugs use ($p=0.026$) were also negatively associated. Positive correlations were found with the other BICAMS subtests. No differences were found based on sex, previous relapses number, or gadolinium-enhancing lesions.
Conclusion: In MS patients, older age at disease onset and at DMT initiation, higher disability, and greater lesion load on MRI were associated with lower SDMT scores. Fatigue, depression and psychotropic drugs use also showed a negative association. On the contrary, higher education levels were associated with higher scores.

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P1123
Impact of urinary disorders on the quality of life of patients withmultiple sclerosis

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Introduction: Multiple sclerosis (MS) is an autoimmune, degenerative, and disabling disease of the central nervous system. Sixty-eight percent of patients present with urinary disorders, such as urinary incontinence.
Objectives/Aims: To describe urinary tract disorders (UTD) in patients with MS, their clinical characteristics, frequency, duration of onset, and impact on quality of life
Methods: This was a cross-sectional, descriptive, observational study conducted using a questionnaire that discriminated between symptoms of detrusor overactivity (DOO), bladder emptying disorder (BID), and urinary incontinence (UI). The latter was classified as overflow (URI), urge urinary incontinence (UUI), or associated with a prior mobility and gait disorder (MGI). The degree on how these symptoms affected the patient's quality of life was investigated.

Results: The questionnaire was administered to 67 patients with MS. Sixteen were excluded due to previous UT or use of tricyclic antidepressants.38 (73.1%) from 52 patients with MS, presented UT. Incontinence (52%), with urinary urgency being the most common (45%). Those with impaired bladder emptying also presented at least one symptom of detrusor overactivity, with urinary frequency being more prevalent than incontinence in 65.8% of the study sample.
Rectal continence disorders (70.6%) were more common than sexual dysfunction, although the latter was found more present in patients without urinary incontinence Surprisingly, only 25% of patients with mobility and gait disorders presented MUI.
The patients in the study presented very low levels of impairment and impact on quality of life. However, in patients with UUI we found a mild degree of affectation, over the rest of the sample, with a statistical significance of 0.01.
Conclusion: UUI is the most common type of urinary incontinence. Patients who suffer from it report a greater degree of impairment in quality of life compared to other urinary symptoms. Furthermore, it is important to recognize other symptoms, such as pollakiuria as the most common entity, other SHDs, and associated disorders such as sexual dysfunction, which can occur without urinary incontinence

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P1124
Clinical Significance Of The Hidden Symptoms In Patients With Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is accompanied by hidden symptoms that often remain unnoticed by both patients and clinicians, despite their significant impact on the quality of life.
Objectives/Aims: The aim of the study was to assess the relationship between hidden symptoms (depression, anxiety, cognitive impairment, and sexual dysfunction) and disease duration and disability level in patients with MS.
Methods: The study involved 116 patients with MS (43 men and 73 women), aged 18 to 67 years (mean age 39.6 ±). The following tools were used to assess hidden symptoms: the Beck Depression Inventory, the Hamilton Anxiety Rating Scale, the Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ-19), and the Symbol Digit Modalities Test (SDMT). Disability level was assessed using the Expanded Disability Status Scale (EDSS).
Results: The prevalence of hidden symptoms among the patients was as follows: cognitive impairments – 61.2%, depression – 33.6%, anxiety – 58.6%, sexual dysfunction – 54.3%. All the symptoms were present simultaneously in 15.5% of patients. Patients with disease duration $\geqslant$ 4 years more often had 3–4 symptoms, while patients with disease duration $<$ 4 years mostly had 1or 2 symptoms ($p = 0.031$). The frequency of depression ($p = 0.0347$) and anxiety ($p = 0.0251$) was remarkably higher in those patients with longer disease duration. A statistically significant negative correlation was found between disease duration and the SDMT score ($r = -0.277$; $p = 0.019$). Patient`s age also negatively correlated with SDMT score ($r = -0.320$; $p = 0.006$). A negative correlation was found between the EDSS score and the SDMT score ($r = -0.6187$; $p < 0.0001$), while a positive correlation was found between sexual dysfunction severity according to MSISQ -19 and EDSS score ($r = 0.5139$; $p = 0.0004$). An association was found between the duration of the disease and levels of anxiety, depression, and cognitive impairment in patients with MS. Patients' age also had a significant impact on the development of cognitive impairment in MS. In addition, a moderately strong relationship was found between the level of disability and the development of sexual and cognitive impairment in patients with MS.
Conclusion: Our findings confirmed association between disease duration and the number of hidden symptoms in patients with multiple sclerosis, including depression, anxiety, cognitive impairments, and sexual dysfunction. These results emphasize the importance of timely detection and monitoring of hidden symptoms, that can improve therapeutic approaches in patients with MS.

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P1125
Cognitive and Motor Trajectories in Multiple Sclerosis Phenotypes

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Introduction: Multiple sclerosis (MS) leads to motor disability, with 40–70% of patients also experiencing cognitive dysfunction.
Objectives/Aims: This study investigates motor and cognitive characteristics across MS phenotypes (relapsing-remitting [RR], primary progressive [PP], and secondary progressive [SP]), evaluating changes from baseline to follow-up.
Methods: We retrospectively analyzed 68 MS patients. We collected neuroimaging and clinical data. Cognitive function was assessed using the RAO battery, with a composite Cognitive Impairment Index (CII) measuring memory, executive, and overall cognitive function.
Results: Patients were categorized into RR, SP, and PP groups. The PP group was significantly older ($p<0.03$) and had a higher prevalence of spinal lesions ($p=0.01$). SP patients exhibited the highest EDSS scores ($p<0.001$). No significant differences

were observed in sex distribution, site of onset, brain lesion burden, or follow-up duration. Motor deterioration occurred in 50% of patients, with 32.3% of those initially classified as RR converting to SP. This subgroup also demonstrated the greatest progression in EDSS (ΔEDSS 1.91±1.16), followed by the PP group (ΔEDSS 0.75±0.61). At baseline, cognitive impairment was present in 52.9% of patients, rising to 57.4% at follow-up. Memory impairment significantly worsened in RR (p=0.013) and SP (p=0.02) patients, whereas no significant changes were observed in the PP group. Executive functions remained stable across all three groups overall; however, at follow-up, SP patients showed significantly worse executive performance compared to RR patients (p<0.01). Additionally, SP patients experienced a significant global cognitive decline over time (p=0.044).

Conclusion: These findings highlight the heterogeneous progression of motor and cognitive impairment across MS phenotypes. SP patients exhibited the most significant deterioration, with marked worsening in both motor function and cognition, particularly in memory and executive domains. RR patients experienced milder progression, primarily involving memory decline, while executive functions remained largely preserved. However, the transition to SP in one-third of these patients, accompanied by increasing EDSS scores, indicates a shift toward more rapid deterioration. In contrast, PP patients, despite being older and having a higher burden of spinal lesions, showed stable cognitive function over time, suggesting a more motor-predominant and less cognitively aggressive disease course. These results underscore the importance of early identification of patients at risk of progression, especially those transitioning from RR to SP, to enable timely, targeted interventions aimed at slowing both motor and cognitive decline.

Disclosure of interest: Nothing to disclose

P1126
Subjective experience in multiple sclerosis: the role of self-determination and clinical correlates

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Introduction: In chronic conditions such as multiple sclerosis (MS), which primarily affects young adults, identifying the factors that impact functioning and quality of life is essential. Self-determination—defined as the perception of autonomy and personal competence—plays a key role in well-being, motivation, and overall life satisfaction, making its study highly relevant.

Objectives/Aims: To explore clinical and cognitive predictors of self-determination in people with MS (PwMS).

Methods: A total of 88 PwMS participated (78% women; mean age: 44.81±9.64 years; education: 14.75±2.98 years; disease duration: 11.13±8.42 years). Clinical phenotype distribution was: 77 relapsing-remitting (88%), 6 secondary progressive (7%), and 5 primary progressive (5%). The following patient-reported outcome measures were administered: the Personal Self-Determination Scale, Fatigue Severity Scale (FSS), Beck Depression Inventory-II (BDI-II), and the Multiple Sclerosis Neuropsychological Questionnaire–Patient version (MSNQ-P). Objective cognitive performance was assessed using the Brief International Cognitive Assessment for MS (BICAMS), including the California Verbal Learning Test-I (CVLT-I), Brief Visuospatial Memory Test–Revised (BVMT-R), and Symbol Digit Modalities Test (SDMT).

Statistical analysis: A stepwise linear regression was performed to identify predictors of self-determination, including fatigue, depression, self-perceived cognitive difficulties, disease duration, and cognitive test scores: proccessing speed, verbal memory and visual memory.

Results: Mean scores were: BDI-II = 15.31±9.08, FSS = 4.34±3.39; CVLT-I = 48.18±11.16, BVMT-R = 21.94±7.24, SDMT = 46.19±13.39. Fatigue, depression, and self-reported cognitive difficulties significantly predicted self-determination (F=21.13, p<.001), explaining 43.4% of its variance (adj. R^2 = .434). Objective cognitive variables were excluded due to lack of statistical significance.

Conclusion: Self-determination in PwMS is better predicted by subjective factors—namely self-perceived cognitive difficulties, fatigue, depressive symptoms, and—than by objective cognitive performance. These findings underscore the importance of considering patients' subjective experience for comprehensive MS care.

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P1127
Frailty Predicts Cognitive and Psychiatric Impairment in Multiple Sclerosis: A Cross-Sectional Study

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Introduction: Cognitive impairment (CI) is a common and disabling feature of multiple sclerosis (MS), affecting daily functioning and quality of life. It affects approximately 45% of patients, often from early disease stages. While variable, CI in MS typically involves deficits in processing speed, learning, and memory. Early identification of individuals at risk remains an unmet clinical need to enable timely, personalized interventions.
Frailty is an age-related, multidimensional condition reflecting reduced physiological reserve and vulnerability to stressors, due to the accumulation of health deficits. In MS, frailty—measured by the Frailty Index (FI)—has been associated with disease duration, disability, phenotype, and fatigue. Recent studies suggest shared mechanisms between frailty and CI, including inflammation, neurodegeneration, and impaired neuroplasticity, but their relationship in MS is still poorly understood
Objectives/Aims: To investigate the association between frailty and cognitive impairment in people with MS (pwMS), and assess whether frailty predicts cognitive decline.
Methods: A total of 113 pwMS (mean age 45.6 ± 11.8 years; 72% women) were included. Clinical assessments covered disability, fatigue, and psychiatric symptoms. MS phenotype was recorded. Frailty was measured using a 42-item FI. Cognitive function was assessed using the Brief Repeatable Battery of Neuropsychological Tests. Correlation and regression analyses explored associations between FI, clinical-demographic variables, and cognition.
Results: The mean FI was 0.17 (SD = 0.11); 27% of participants were classified as frail (FI ⩾ 0.25). FI scores were higher in progressive vs. relapsing MS and correlated with age, disease duration, EDSS, and lower education (all $p < 0.001$). Higher FI predicted fatigue, depression, anxiety, and executive dysfunction (all $p < 0.001$).
Conclusion: Frailty is a strong predictor of cognitive and psychiatric symptoms in MS. Incorporating frailty assessment into routine care may help identify patients at risk of CI and guide early, multidimensional interventions

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P1128
Neurogenic Bowel Dysfunction in Multiple Sclerosis: Patterns and Clinical Impact

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Introduction: Neurogenic intestinal dysfunction constitutes a significant but frequently overlooked aspect of multiple sclerosis (MS), contributing to disability accrual.
Objectives/Aims: To analyze the presentation and clinical characterization of neurogenic bowel dysfunction in a MS real world cohort, emphasizing bowel and pelvic floor involvement and correlating these findings with other clinical variables of the disease.
Methods: A retrospective cohort study was conducted in patients followed at the Multiple Sclerosis Center and Rehabilitation Medicine Unit of the University Hospital Policlinico of Bari. Variables included data from patient history and pelvic physical examination with Neurogenic Bowel Dysfunction (NBD) score evaluations. Comparisons between groups of interest were formally conducted with Student's T test or the chi-square test.
Results: We retrieved a cohort of 79 MS patients, of whom 58 (73.4%) were female, 55 were diagnosed with RRMS, 8 with PPMS, and 16 with SPMS. The median (IQR) age at onset was 27.71 (22.17-37.87), and the mean (SD) follow-up was 15.01 (8.94) years. Pelvic floor dysfunction was categorized as underactive in 51 (64.6%) and hyperactive in 23 (29.1%) subjects. 42 patients (52.1%) showed a moderate-severe bowel dysfunction (NBD⩾10). This sub-cohort had a higher prevalence of patients with a progressive course (35.7% vs 24.3% in patients with lower scores), an irreversible EDSS ⩾4 (64.3% vs 36.5%) and a longer mean disease duration (19 years vs 15.47 years). The majority of patients (88.6%) presented brain and spinal lesions. 33 patients (41.8%) reported symptoms of obstructed defecation syndrome, 33 patients (41.8%) primarily experienced constipation with fecal urgency, while 9 (11.4%) had abdominal bloating and fecal incontinence associated with constipation and 4 (5.1%) reported exclusive fecal incontinence. Fecal calprotectin was measured in a sub-cohort of patients with mixed or atypical symptoms (e.g., abdominal bloating) and was positive in only 2.4% of cases. Lactose intolerance was diagnosed in 27 patients (34.2%).
Conclusion: Neurogenic bowel dysfunction in MS occurs in different patterns, worsens in progressive forms, and correlates with greater disability. MS-related bowel symptoms must be identified and not mistaken for distinct gastrointestinal conditions.

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P1129
Clinical characteristics and urodynamic analysis of urinary dysfunction in multiple sclerosis: a single center study

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Introduction: Neurogenic urinary dysfunctions are frequent and debilitating manifestations of multiple sclerosis (MS).
Objectives/Aims: To characterize the urodynamic patterns in patients with multiple sclerosis and to evaluate their association with clinical phenotype, lesion distribution, disability, and therapeutic approaches.
Methods: A retrospective cohort study was conducted in patients followed at the MS Center and Rehabilitation Unit of the University Hospital Policlinico of Bari. Urodynamic study (UDS) patterns were evaluated. MS lesion sites were determined by combining neurological examination and magnetic resonance imaging (MRI) during the follow-up. Comparisons between groups of interest were conducted with Student's *T* test or the chi-square test.
Results: The cohort included 287 patients, of whom 189 (65.9%) were female, 187 were diagnosed with RRMS, 28 with PPMS, and 72 with SPMS. The mean (SD) follow-up was 13.59 (8.88) years. 260 (90.6%) subjects presented brain and spinal cord MS lesions, 9.4% only brain lesions; no significant correlation was found between MRI topography and occurrence of urinary dysfunctions. A total of 152 patients (52.9%) presented with detrusor overactivity: 47 with high pressure (30.9% of 152), 44 (28.9%) with medium pressure, 35 (23.0%) with low pressure, and 26 (17.1%) with terminal pressure. Among them, 122 (80.3%) had reduced compliance and 124 (81.6%) had decreased cystometric capacity. Detrusor hypocontractility was observed in 69 patients (24.0%), including 12 (17.4%) with absent bladder sensation and 17 (24.6%) with increased bladder compliance. Three patients (1.0%) had coexistent overactive-underactive bladder. Detrusor sphincter dyssynergia was present in 92 patients (32.1%) and, compared to RR, SPMS patients presented it more frequently (34.7% vs 32%). Intermittent catheterization (IC) was indicated in 102 patients (35.5%), corresponding to 29.6% of those with detrusor overactivity and 75.4% of those with hypocontractility. The IC group presented a significative longer median disease duration at treatment start compared to other therapies (11.96 vs 7.15 years, $p<0.005$). Urinary dysfunction was evident at MS onset in 27 (9.4%) patients, which presented irreversible severe disability scores during the follow-up.
Conclusion: Urinary dysfunctions in MS can present in various forms and require careful evaluation. Early diagnosis is crucial to help patients access effective therapies and improve their quality of life.

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P1130
Is vision loss always due to optic neuritis? Challenges for vision loss diagnosis

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Introduction: Acute onset vision loss etiologies include optic neuritis (ON) and MOGAD, NMO and NMOSDs and also infectious, toxic, hereditary and compressive etiologies.
Objectives/Aims: In this case series, we aimed to describe the clinical features of atypical presentation of vision loss and discuss management strategies.
Methods: We described the clinical laboratory and MR findings of our 10 patients who were diagnosed with infectious etiologies including COVID-19, syphilis and bartonella infections and compared the clinical features and prognosis with typical demyelinating optic neuritis.
Results: Study included 10 patients, 3 patients covid-19 infection related (2 females), 1 male patient had syphilis and 6 patients had Bartonella infection (4 females). Bartonella and syphilis patients were treated with antibiotics and Covid patients had IVMP. When compared to ON, the clinical course and prognosis was worse in the infection group. Covid patients had MR with hyper intense lesions, the other patients had normal MRI. CSF was within normal limits with (-)OCB.
Conclusion: With the new diagnostic criteria differential diagnosis for vision loss and optic neuritis carries more importance. Does the differential diagnosis should be carried with care and management strategies for vision loss should be carefully selected.

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P1131
Anxiety and Self-Efficacy Predict Subjective Cognitive Fatigue in Multiple Sclerosis

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Introduction: Cognitive fatigue (CF)—a decrease in cognitive performance with sustained activity—is a common but underexplored symptom in people with multiple sclerosis (PwMS). Understanding predictors of CF could facilitate developing targeted interventions to address this debilitating issue.
Objectives/Aims: This study examined whether depression, anxiety, sleep quality, and self-efficacy predict subjective and objective CF in PwMS.

Methods: PwMS were recruited mostly via the MS Society of Canada. Objective CF was measured using the Paced Auditory Serial Addition Test (PASAT). Subjective CF was assessed through the cognitive component of the Modified Fatigue Impact Scale (MFIS). Depression, anxiety, sleep quality, and self-efficacy were evaluated using the Patient Health Questionnaire (PHQ-9), Hospital Anxiety and Depression Scale (HADS), Pittsburgh Sleep Quality Index (PSQI), and General Self-efficacy Scale (GSE), respectively. Pearson's r and linear regression were used to analyze associations and predictions.
Results: The sample included 41 participants, primarily female (87.8%) with a mean age of 47.2 years; most (88.5%) had relapsing MS. Objective and subjective CF were not significantly correlated ($r = -0.09$), and no variables predicted objective CF. However, subjective CF was significantly related to anxiety ($r = 0.45$, $p < .001$) and self-efficacy ($r = -0.41$, $p < .001$), with anxiety significantly predicting subjective CF when controlling for other factors ($R2adj = 0.213$, $F(5, 38) = 3.058$, $p = .022$).
Conclusion: Subjective CF is significantly predicted by anxiety and influenced by self-efficacy and depression. Addressing affective factors such as anxiety and depression may help reduce subjective CF in PwMS, improving their quality of life.

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P1132
Don't dream its over: Impact of Sleep and MS, a UK MS Register Study

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Introduction: Quality sleep is important for mental and physical health and wellbeing, there is evidence that genes expressed during sleep can effect oligodendrocytes, potentially impactful in Multiple Sclerosis. The UK Multiple Sclerosis Register (UKMSR) deployed the Pittsburgh Sleep Quality Index (PSQI) a 19 question Patient Reported Outcome (PRO) designed to assess sleep quality over a 1-month interval.
Objectives/Aims: To assess the impacts of poor sleep in the UKMSR population.
Methods: We deployed the PSQI for 1 month in December 2024, calculating an overall PSQI (0-21), and grouped respondents into; Good Sleepers (GS), PSQI $\leqslant 5$, and Poor Sleepers (PS), PSQI >5. PSQI data were linked to pre-existing UKMSR data including demography, disease milestones, and data from most recent submissions for Hospital Anxiety and Depression Scale (HADS), Multiple Sclerosis Impact Scale (MSIS-29) and Fatigue Severity Scale (FSS).
Results: 2758 (72.3% female) participants with sufficient data completed the PSQI, GS=667 (24.2%), PS=2091 (75.8%). Mean population age 58, mean age at onset 41. 40.7% were progressive MS, 54.2% relapsing MS, 5.1% benign/other. 2.5% of the population were not Caucasian. We found significant differences in physical disability, fatigue, anxiety and depression, with bad sleepers all scoring highly across domains. MSIS, HADS (anxiety and depression) and FSS scores between GS and BS were all significant ($p<0.001$). There was higher incidence of tobacco usage (GS=39.1%, BS=43.5%, p=0.046) and BS were less likely to be in employment (GS=43.5%, BS=36.5%, p=0.001).
Age, age at onset and ethnicity were not found to be significant.
Conclusion: There are multiple significant factors that contribute to poor sleep and pwMS report poor sleep at higher levels than in other general population studies. Poor sleep is associated with increased disability, lower mood and lower sustained employment. More work is needed to disentangle whether poor sleep is caused by or is a result of increasing MS impact.

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P1133
Relapse characteristics in the new high efficacy era Single-center relapse registry.

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Introduction: Relapse-associated worsening (RAW) accounts for 30% of disability in relapsing-remitting MS (RRMS) and 15% in secondary progressive MS (SPMS) and relapses are associated with worse prognosis.
Objectives/Aims: To describe people with MS (pwMS) experiencing a relapse between September 2024-2025 in an MS unit ($\approx$1,200 patients). We present 6-month data.
Methods: We included pwMS who reported symptoms onset within $\leqslant$14 days. Visits are scheduled at onset, five weeks, and three months. Demographic, disease, and relapse-related data is collected. RAW is assessed at three months.
Results: Results are expressed as median [Min., Max.]. We included 20 confirmed relapses. Relapse rate was 2.5 events per 1,000 patients/month. Female:male ratio 1.85:1, age 42y [30, 70], 85% RRMS, 15% SPMS, disease duration 11y [1, 26], baseline EDSS 2.25 [0, 6.5], prior Annual Relapse Rate last 2 years was 0 [0, 2]. MRI Lesion load was $>$20 in 70%, 10-19 in 30%. MRI activity since last Disease Modifying Treatment

(DMT) was detected in 35% (last 5y). Spinal cord lesion load was 6.5 [0, uncountable] (5 missing). DMTs were 6 (8.1%) dimethyl fumarate, 4 (3.4%) ocrelizumab, 2 naïve, 2 (4.3%) interferon beta-1a, 1 (3.3%) glatiramer acetate, 1 (3.4%) alemtuzumab, 1 (1%) cladribine, 1 (1.5%) ofatumumab, 1 (1.5%) rituximab, 1 untreated (% correspond to pwMS under that DMT; treatment duration: 4.16y [0.16, 14.39]).
Possible triggers were identified in 30%, mainly infections. Relapses were mainly sensitive (70%) and monosymptomatic (70%). Suspected location was spinal cord in 50%, optic nerve 10%, brainstem 5%, multifocal 5%, undetermined 30%. EDSS worsened in 70% (+1 point [0, 3.5]). 45% received methylprednisolone, 1 required plasma exchange.
At five weeks, 75% improved; and at three months, 80% (EDSS +0.25 [0, 2.5] and +0.5 [0, 3]). RAW was confirmed in 8/10 patients at three months.
Conclusion: Relapses were infrequent in our series and, although improving with or without treatment, most patients experienced RAW.

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P1134
Beyond Recognition: Uncovering automatic aversion to negative stimuli in MS

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Introduction: Emerging evidence suggests dissociations in emotion recognition between preserved positive and impaired negative emotion processing in multiple sclerosis (MS) patients, potentially linked to a "positivity effect" driven by altered time perception.
Objectives/Aims: This study investigated whether MS patients demonstrate an attentional preference for positive stimuli, potentially reflecting compensatory adaptation to reduced future time perspectives. We further examined whether such preferential attention might enhance recognition accuracy for positive facial emotions compared to negative ones.
Methods: We assessed emotion recognition, attentional bias, and time perception in 50 MS patients and 50 matched healthy controls. Participants completed standardized tasks measuring dynamic facial emotion recognition through complex emotions and attentional preference for valenced stimuli, alongside self-reported measures of future time perspective.
Results: Contrary to initial hypotheses, no significant group differences emerged in recognition accuracy for negative or positive emotions, despite MS patients reporting significantly shorter perceived future timelines ($p < 0.045$). While no group differences emerged in attentional preference for positive information, MS patients showed significantly longer reaction times specifically during congruent trials featuring negative stimuli compared to other valence conditions ($p < 0.01$).
Conclusion: We suggest that this pattern could indicate an automatic disengagement from negative information without systematic consequences on emotion recognition. These results challenge assumptions of valence-specific recognition deficits in MS and indicate that shortened future time perspectives might not directly drive emotional processing biases. The reaction time asymmetry reveals nuanced alterations in emotional attention not captured by traditional bias scores, potentially reflecting either avoidance strategies or impaired attentional control mechanisms.

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P1135
The Effects of Fatigue on Physical and Cognitive Performance in People with Multiple Sclerosis at Similar Disability Levels

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Introduction: Fatigue is a prevalent and debilitating symptom in people with multiple sclerosis (PwMS), resulting in considerable functional impairments. This multifaceted and subjective experience encompasses physical, cognitive, and emotional dimensions. A comprehensive understanding of the effects of fatigue on both physical and cognitive performance is essential for effective symptom management, as it plays a critical role in the perceived functional limitations.
Objectives/Aims: This study aimed to compare physical, cognitive, and activities of daily living (ADL) performance between fatigued and non-fatigued PwMS who were similar in terms of Expanded Disability Status Scale (EDSS) scores, disease duration, and number of relapses.
Methods: Participants with EDSS ⩽ 4.5 were administered the Modified Fatigue Impact Scale (MFIS), 6-Minute Walk Test (6MWT), Click Speed Test (CST), Four-Step Square Test (FSST), Symptom Screen scale, and Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS), which includes the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test–Second Edition (CVLT-II), and the Brief Visuospatial Memory Test–Revised (BVMT-R).
Results: Fifty-nine PwMS were enrolled and divided into two groups as fatigued (n=21) and non-fatigued (n=38) based on the MFIS cutoff value (>38). Two groups were similar in terms of EDSS (p=0.193), disease duration (p=0.116), the number of relapses (p=0.263), BICAMS subscales (p=0.126 for SDMT,

p=0.974 for CVLT-II and p=0.543 for BVMT-R), and CST performance for the right and left hands (p=0.214 and p=0.064, respectively). 6MWT and FSST were significantly different in favor of the non-fatigued group (p=0.011 and p=0.008, respectively). There was a significant between-group difference in the reflection of symptom severity on ADL according to Symptom Screen scale, with non-fatigued participants exhibiting lower levels of impairment ($p<0.001$).

Conclusion: Although PwMS present with similar levels of disability, those experiencing fatigue demonstrate reduced endurance and slower reaction times compared to their non-fatigued counterparts. MS symptoms appear to have a more detrimental impact on ADL performance in the fatigued group. Effective fatigue management is crucial for enhancing physical performance and minimizing the deterioration of ADL due to symptom severity.

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P1136
Analytical artificial intelligence in the study of cognitive impairment in multiple sclerosis: a scoping review of existing gaps and future directions

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Introduction: Cognitive impairment is a common, disabling and highly heterogenous symptom among people with multiple sclerosis. Analytical artificial intelligence (AI) techniques have emerged as a powerful set of tools for identifying hidden patterns and improving assessment methods, offering potential for advancing the understanding of cognitive profiles in MS.

Objectives/Aims: The overarching goal of this scoping review is to examine analytical AI applications in the study of cognitive impairment in people with multiple sclerosis (pwMS). Specific aims include characterizing the existing uses of methodological models in literature and their limitations, identifying the new practical insights these novel methods have provided and the remaining gaps in this niche field.

Methods: This study was designed as a scoping review and conducted in accordance with PRISMA guidelines. A systematic search of PubMed and Web of Science was conducted for articles satisfying the Boolean search "Multiple Sclerosis" AND ("Artificial Intelligence" OR "Machine Learning") AND ("Cognitive" OR "Cognition"). Reviews and non-English papers were excluded.

Results: Of the total of 223 studies identified on the initial search, 31 met the inclusion and exclusion criteria. These studies represented 6,778 individuals with multiple sclerosis (4,696 females). MRI-derived features were utilized in 21 of 31 studies, with subsets incorporating clinical (6/31) and demographic (4/31) data for model training. Several studies explored unique predictive features including microRNA profiles and smartphone keyboard interactions. The Symbol Digit Modalities Test (SDMT) was the most frequently used cognitive impairment metric (21/31, 68%), followed by the Brief Visuospatial Memory Test–Revised (5/31, 16%). Prediction of cognitive impairment was the most common outcome measure (18/31, 58%), with cognitive assessment test quality (4/31, 13%) and hidden pattern identification (2/31, 6%) also observed among outcomes of AI utilization. Sample sizes ranged from >500 (7/31, 23%) to <100 (3/31, 26%), with 4 studies (13%) including fewer than 50 participants.

Conclusion: While artificial intelligence methodologies have been used widely to predict cognitive impairment in MS, its implementation remains especially limited in domains of hidden pattern identification using non-MRI data. Furthermore, existing studies are commonly limited by small sample sizes and inconsistencies in statistical reporting, highlighting the need for larger scale studies with greater standardization and validation.

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P1137
Cognitive and Neuroimaging Assessment in Patients with Benign and Relapsing-Remitting Multiple Sclerosis

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Introduction: Benign Multiple Sclerosis (BMS) is traditionally defined by an EDSS score $\leqslant 3$ after at least 10 years of disease clinical onset. However, this classification overlooks non-motor aspects such as cognitive impairment, mood disorders, and fatigue. While some studies compare BMS and Relapsing-Remitting MS (RRMS) regarding non-motor aspects, only a few systematically addressed cognition and neuroimaging. Moreover, the presence of non-motor deficits in BMS patients raises questions about the accuracy of this criterion.

Objectives/Aims: To assess brain atrophy and cognitive domains in BMS and RRMS patients.

Methods: Brain volumes and cortical thickness were analyzed using the FreeSurfer software; cognitive function was tested using the Brief Repeatable Battery of Neuropsychological Tests (BRB-N); questionnaires for fatigue and depression assessments were also employed.

Results: Twenty-seven female patients were evaluated, including 13 with RRMS and 14 with BMS, classified by EDSS score and disease duration. No significant differences were found in the frequency of deficits on cognitive domains (verbal memory, visual memory, processing speed, and verbal fluency; $p > 0.2$). The frequency of fatigue and depression was also comparable ($p > 0.4$). Brain volumetric analysis, adjusted for age and intracranial volume, revealed no significant differences in the cerebellum, thalamus, striatum, hippocampus, corpus callosum, or

cortical thickness ($p > 0.4$). As expected, RRMS patients performed worse on physical disability tests (T25FW, $p = 0.011$; EDSS, $p = 0.002$).
Conclusion: Cognitive impairment is common in MS. Our results showed similar cognitive and volumetric profiles in BMS and RRMS, aligning with Hegedüs et al. and Niiranen et al. In line with Tallantyre et al., we suggest that relying solely on EDSS may underestimate mood disorders, cognitive decline, and brain atrophy.

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P1138
Cognitive Components Predicting SDMT Performance in Multiple Sclerosis

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Introduction: The Symbol Digit Modalities Test (SDMT) is widely used to screen for cognitive dysfunction in MS. Although it is typically considered a measure of information processing speed, SDMT performance may also be influenced by other disease-related or individual factors. In this study, we examined which specific cognitive components contribute to SDMT performance in people with MS. We used Cogstate, a validated, computer-based cognitive testing platform designed to assess key domains with high sensitivity and minimal practice effects. Its Brief Battery includes measures of simple and choice reaction time, as well as working memory speed and accuracy, making it well-suited for evaluating components of information processing relevant to MS-related cognitive dysfunction.
Objectives/Aims: To evaluate whether computer-based measures of information processing predict SDMT performance in a large, representative sample of people with MS.
Methods: A total of $n = 103$ participants with any MS subtype (64% RRMS, 28% SPMS, 8% PPMS) and significant fatigue, enrolled in a fatigue treatment study, completed the baseline cognitive evaluation. Participants had a mean age of 48.5 ± 12 years, a median EDSS of 3.0 (range 0–7.5), and were 82% female, 75.5% White, 20.5% Black, and 4% Asian. All participants were screened for depression (BDI-FS < 10), neurological impairment (EDSS $\leqslant 7.5$), and severe cognitive impairment (SDMT z-score > -3.0).
Results: Among the individual Cogstate measures, working memory speed was the strongest predictor of SDMT performance ($R^2 = 0.2291$; $\beta = 0.3878$, $p = 0.007$), followed by choice reaction time ($R^2 = 0.2061$; $\beta = 0.3049$, $p = 0.028$), and simple reaction time ($R^2 = 0.1036$). Working memory accuracy contributed minimally ($R^2 = 0.0338$). When all four variables were entered into a combined model, they accounted for 28.7% of the variance in SDMT scores ($R^2 = 0.2868$), suggesting that factors beyond processing speed and accuracy also influence SDMT performance.
Conclusion: Although the SDMT is a sensitive and efficient tool for detecting processing speed deficits in multiple sclerosis, its performance is shaped by a broader range of cognitive functions. By using Cogstate to isolate these components, our findings show that working memory speed and attentional control, reflected in reaction time, are key contributors to SDMT performance. These results clarify the cognitive processes underlying the SDMT, advance our understanding of its functional mechanisms, and underscore the need for additional targeted, process-based assessments to enhance cognitive screening in MS.

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P1139
Digital version of Fitts' Tapping Test as a new test for psychomotor performance and cognitive decline: preliminary validation in young healthy controls

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Introduction: Screening for early psychomotor impairment in many neurological diseases requires development of very sensitive, easy to perform and time-sensitive tests that integrate both cognitive and motor inputs. In previous work, we demonstrated that Fitts' Tapping Task (FTT) can detect early and subclinical impairments in people with multiple sclerosis (pwMS).
Objectives/Aims: To perform test validity and determine the construct validity of FTT in healthy individuals when compared to currently gold standards for testing of cognitive processing speed and hand dexterity.
Methods: Total of 80 young healthy participants were enrolled in the study. Participants performed both the analog and digital version of the FTT (aFTT and dFTT, respectively) during the same testing day, together with Symbol Digit Modalities Test (SDMT; as current gold standard for testing of cognitive processing speed; CPS), 9-hole peg test (9HPT; as current gold standard for testing manual dexterity) and timed 25-foot walk test (T25FWT; as gold standard for walking disability). The FTT test consists of 6 difficulty levels and participants performed the trials in randomized fashion, limiting practice effect.

Results: Healthy young population with mean age of 21.4 years old (SD=1.6), majority female (n=72, 90%) was tested. The average aFTT time was 19.9s (SD=2.2) versus dFTT of 28.9s (SD=3.9) and significant performance correlation between them (r=0.581, p<0.001). Average SDMT score of 54 (SD=7.4) and average 9HPT of 17.3s (SD=2.2). The dFTT demonstrated more consistent pattern of correlations with SDMT, for difficulty 1 (r=-0.261, p=0.019), 2 (r=-0.233, p=0.037) and 3 (r=-0.276, p=0.013). Contrarily, only better performance on difficulty 3 of the aFTT was correlated with better SDMT (r=-0.304, p=0.004). Similar congruent findings were seen in terms of correlations between aFTT/dFTT and 9HPT.
Conclusion: Performance on the early difficulties from the digital version of the FTT are associated with CPS as measured by SDMT. The later FTT difficulties most likely utilize greater number of cognitive domains, superseding the CPS needed in the easier trials. Manual dexterity is associated with performance in the first and cognitively-easy FTT trials.

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P1140
Cognitive performance, sleep disturbances and fatigue in Multiple Sclerosis: Preliminary findings from a prospective polysomnography study in Germany

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Introduction: Fatigue is among the most disabling symptoms in multiple sclerosis (MS), significantly impairing quality of life and occupational functioning. Although sleep disturbances are suspected to contribute to fatigue, studies employing objective assessments such as polysomnography (PSG) in specialized sleep clinics are scarce. Moreover, the interplay between fatigue, sleep disturbances, and cognitive impairment is not yet fully understood.
Objectives/Aims: This study aims to investigate the associations between objective and subjective sleep parameters, cognitive performance, and fatigue in individuals with MS and fatigue compared to non-MS controls referred to our sleep clinic.
Methods: In this ongoing cross-sectional, non-interventional study, individuals with MS and clinically relevant fatigue are compared to age-, sex-, and education-matched non-MS controls referred to our sleep clinic. All participants undergo two consecutive nights of PSG, neuropsychological testing (Symbol Digit Modalities Test, Brief Visuospatial Test – Revised, and German version of the Rey Auditory Verbal Learning Test), the Pupillographic Sleepiness Test (PST), and complete validated questionnaires assessing fatigue, sleep quality, daytime sleepiness, anxiety and depression. Statistical analyses of preliminary data included Mann-Whitney-U-test and Spearman's Rank correlation.
Results: Preliminary data from nine individuals with MS (median age: 37 years; 67% female; 78% relapsing-remitting MS, median Expanded Disability Status Scale: 2) and nine matched non-MS controls indicated significantly higher self-reported fatigue in the MS group (p=.001). All participants met criteria for a clinically relevant sleep disorder per American Academy of Sleep Medicine guidelines. No significant group differences were found in subjective sleepiness, subjective sleep quality, or PST-based sleepiness. In the MS group, fatigue severity did not correlate with subjective or objective sleepiness, sleep quality, depression, anxiety or cognitive performance.
Conclusion: Preliminary findings suggest a high prevalence of sleep disorders among fatigued individuals with MS, underscoring the importance of routine sleep assessment in this population. Ongoing data collection will allow for robust statistical analyses and may help clarify the relationship between subjective sleep complaints, fatigue severity, and cognitive performance in MS. Data from approximately n=30 per group will be presented at the conference.

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P1141
Physical capacities and psychological status in fatigued people with multiple sclerosis: recently vs longer-standing diagnosis

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Introduction: MS-related fatigue is multifactorial, involving performance fatigability, depression, and reduced quality of life (QoL), all of which contribute to the overall severity of fatigue. Although people with MS (PwMS) experience fatigue from the early stages of MS, disease duration has been little considered in the exploration of fatigue and its associated factors.
Objectives/Aims: To characterise and compare physical capacities and psychological status in fatigue PwMS with a recent (R-MS) and longer-standing (LS-MS) diagnosis.
Methods: Twenty-eight (23 women, 5 men) R-MS (diagnosis $<$ 2 years and/or first symptoms $<$ 5 years) and 30 (25 women, 5 men) LS-MS relapsing-remitting PwMS (diagnosis $>$ 2 years and first symptoms $>$ 5 years) were recruited. All the participants were considered fatigued (Fatigue Severity Scale [FSS] $\geqslant$ 4) with a relatively low level of disability (Expanded Disability Status Scale $<$ 4). They completed questionnaires assessing QoL (SEP-59), anxiety and depression (Hospital Anxiety and Depression scale, and physical activity level (International Physical Activity Questionnaire). They also performed physical tests, including cardiopulmonary exercise testing to assess maximal oxygen uptake (VO_2max) and maximal aerobic power (MAP), fatiguing test (performance fatigability and voluntary activation [VA]) and strength measurements (leg extension and handgrip) and flexibility test.
Results: R-MS group was younger than LS-MS group (37.2 vs. 44.6 years; $p < 0.001$), and the Body Mass Index was similar. The two populations have similar subjective parameters (FSS, QoL, physical activity level and anxiety), except for the depression score, which was higher in the R-MS group (7.2 vs 5.5; $p = 0.046$). The objective parameters measured were generally similar between the two groups (VO_2max, leg extension, handgrip, flexibility and VA), but the MAP was higher in the R-MS group (129.5 vs 111.3; $p = 0.047$). The R-MS group also has less fatiguability (-8% vs -14%; $p = 0.022$). Fatigue severity (FSS) in LS-MS was negatively correlated to VA ($r = 0.43$, $p = 0.026$) and with 4 items from the QoL questionnaire ($r = 0.44$, $p = 0.015$). Fatigue severity in R-MS was negatively correlated to depression score ($r = 0.463$, $p = 0.013$) and 8 items from the QoL questionnaire ($r = 0.637$, $p < 0.001$).
Conclusion: R-MS and LS-MS exhibit quite similar physical and psychological characteristics. However, depressive symptoms are more important in R-MS group and are a factor of the MS-related fatigue. It might be due to the traumatism linked to a more recent diagnosis. Impaired physical capacities (MAP and performance fatigability) had been observed in LS-MS, and VA failure is an associated factor of MS-related fatigue. It might cause a progressive degradation of neuromuscular function due to ageing, disease progress and/or sedentary lifestyle observed in PwMS.

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P1142
Gender Differences in Cognitive Fatigue and Motor Dexterity in MS: Analysis of PROMs and Objective Measures

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Introduction: Gender differences in MS including cognitive fatigue and patient-reported outcomes such as motor functions, have been less explored than objective measures. While previous studies suggest women experience more fatigue, data on objective motor and cognitive differences and their clinical implications are conflicting, limiting personalized care strategies
Objectives/Aims: To assess gender differences in Patient-Reported Outcome Measures (PROMs) and objective assessments in MS
Methods: Cross-sectional study of 76 age- and disease-modifying therapy (DMT)-matched people with MS (pwMS; 38 women, 38 men). We analyzed demographics, clinical characteristics,

falls, objective functional tests (Expanded Disability Status Scale [EDSS], 9-Hole Peg Test [9-HPT; dominant/non-dominant hands], Timed 25-Foot Walk [T25FW], Symbol Digit Modalities Test [SDMT]) and PROMs (Modified Fatigue Impact Scale [MFIS; physical/cognitive/psychosocial/global fatigue], Beck Depression/Anxiety Inventory [BDI/BAI], Multiple Sclerosis Walking Scale-12 [MSWS-12; walking impact], Multiple Sclerosis Impact Scale-29 [MSIS-29; disease impact], and Short Falls Efficacy Scale-International [Short FES-I; fear of falling]). Non-parametric (Mann-Whitney U, Fisher's exact) and parametric tests (unpaired t-test) were applied (α=0.05)

Results: No significant differences were observed in employment (women 66% vs men 71%), Relapsing-Remitting MS prevalence (women 84% vs men 71%), falls in the last six months (women 29% vs men 34%), EDSS (median: women 1.75 vs men 2.0), non-dominant 9-HPT, T25FW, physical/psychological impact (MSIS-29), anxiety (BAI), or fear of falling (Short FES-I). A trend was observed in women experiencing more depression than men (p=0.057). Significant differences included: Dominant 9-HPT (men 9-HPT median: 20.05s vs. women 18.05s; $p<0.001$), SDMT (men mean z-score=-0.403 vs. women=0.298; p=0.008), cognitive fatigue (MFIS-cognitive median: women 15.0 vs. men 3.50; p=0.002), and global fatigue (MFIS-global median: women 29.0 vs. men 11.0; p=0.017).

Conclusion: Gender-specific differences in MS reveal worse objective hand dexterity and processing speed in men, while women report significantly greater levels of cognitive/global fatigue and a trend toward depression. These findings highlight the relevance of PROMS in guiding symptomatic management and rehabilitation strategies tailored to each gender, addressing motor training and fatigue management, while acknowledging MS complexity

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P1143
Serum biomarkers GFAP and sTREM2: Indicators of cognitive impairment in Multiple Sclerosis patients

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Introduction: Cognitive impairment (CI) is one of the most disabling symptoms in multiple sclerosis (MS) patients, significantly affecting their quality of life. Glial fibrillary acidic protein (GFAP) and soluble triggering receptor expressed on myeloid cells 2 (sTREM2) are two potential biomarkers related to neurodegeneration and neuroinflammation. There are findings regarding the role of these biomarkers in predicting CI in other neurological diseases. However, to the best of our knowledge, this association has not been well studied in MS patients.

Objectives/Aims: We aim to evaluate relation of serum GFAP and sTREM2 with cognitive function in MS patients.

Methods: This cross-sectional study was conducted at Sina Hospital in Tehran, Iran, on 59 MS patients diagnosed according to the revised 2017 McDonald criteria. After obtaining informed consent, blood samples were collected from the patients, and GFAP and sTREM2 levels were measured using the enzyme-linked immunosorbent assay (ELISA) method. Demographic and clinical data were obtained through face-to-face interviews. Cognitive function was assessed using the Persian version of the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS) by a physician. The Shapiro-Wilk test was used to assess normality and indicated that the data were not normally distributed. Therefore, the correlation between serum levels of GFAP and sTREM2 and the MACFIMS subtests was evaluated using Spearman's rho test. The significance level was considered at $p < 0.05$.

Results: The mean $\pm$ standard deviation (SD) age of participants was 38.54 $\pm$ 8.32 years. The majority were female (89.8%, 53/59), and 98.3% (58/59) were diagnosed with relapsing-remitting multiple sclerosis (RRMS). The average serum levels of GFAP and sTREM2 were 1.14 $\pm$ 0.43 ng/ml and 0.75 $\pm$ 0.29 ng/ml, respectively. A significant inverse association was observed between GFAP and the California Verbal Learning Test (CVLT) ($p = 0.019$, $r = -0.304$), as well as CVLT delayed recall ($p = 0.022$, $r = -0.299$). Similarly, sTREM2 showed a significant inverse association with CVLT ($p = 0.031$, $r = -0.282$) and CVLT delayed recall ($p = 0.024$, $r = -0.294$). However, no significant associations were found between these two biomarkers and other subtests of the MACFIMS.

Conclusion: Our results indicate that higher levels of sTREM2 and GFAP are correlated with poorer performance in episodic verbal memory and retrieval of verbal information in MS patients, highlighting the potential role of these biomarkers in predicting CI in this population.

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P1144
Unravelling Social Cognitive Deficits in Multiple Sclerosis

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Introduction: In addition to cognitive impairment, recent studies suggest that deficits in social cognition may be present in patients with MS, particularly in Theory of Mind (ToM), referring to the ability to infer the mental state and content of another person. Deficits in this domain have a long-term negative impact on social functioning and quality of life. The Reading the Mind in the Eyes Test (RMET) and Ekman's Faces Test (EFT) allow to assess ToM.
Objectives/Aims: We aimed to explore the potential impact of sociodemographic, clinical, and neuropsychological variables in social cognition, specifically in ToM.
Methods: 94 patients with MS were included (71 females, mean age 41,65 years), all of which were assessed with the Brief International Cognitive Assessment for MS (BICAMS, composed by the Symbol Digit Modalities Test – SDMT, Brief Visual Memory Test-Revised – BVMT-R, and California Verbal Learning Test-II – CVLT-II). RMET, and EFT. Disability was assessed with the Expanded Disability Status Scale (EDSS), fatigue with the Modified Fatigue Impact Scale (MFIS), and depression with the Beck Depression Inventory (BDI).
Results: Both social cognitive tests showed significant negative correlations with age (RMET: s=-.367, p=.000; EFT: s=-.283, p=.006) and EDSS (RMET: s=-.280, p=.007; EFT: s=-.32, p=.002), and a significant positive correlation with years of education (RMET: s=.284, p=.005; EFT: s=.221, p=.033). RMET additionally showed a significant negative correlation with fatigue (s=-.239, p=.018), and EFT showed a significant positive correlation with CVLT-II (s=.311, p=.002). None of the tests correlated with BDI (RMET: s=-.099, p=.344; EFT: s=-.033, p=.752).
Conclusion: These results suggest that age, disease progression, and fatigue can negatively affect the social-cognitive performance of MS patients and, therefore, must be taken into consideration during the neuropsychological assessment (NP). RMET should be administered at the beginning of the NP, to avoid the effect of fatigue. Nonetheless, higher cognitive reserve may help mitigate some of these effects, enabling a better understanding of tasks and emotions. Furthermore, improving verbal memory could enhance performance on certain social cognitive tests, highlighting the importance of cognitive training or interventions for MS patients.

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P1145
Environmental Heat Stress and Symptomatology in Individuals with Multiple Sclerosis

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Introduction: Climate change has resulted in more frequent and intense heat waves, especially in Mediterranean countries like Greece, where summer temperatures often reach extreme levels. These conditions pose particular challenges for individuals with multiple sclerosis (MS), who are well known to experience thermoregulatory dysfunction and neurological symptom exacerbation in response to heat exposure. Understanding how environmental heat affects this population is crucial for improving symptom management and quality of life.
Objectives/Aims: This cross-sectional study aimed to evaluate the impact of high environmental temperatures on symptom severity in individuals with MS during the summer of 2024 in Greece.
Methods: Seventy individuals diagnosed with MS and a mean age of 42 $\pm$10.3 years participated in this study. Participants were recruited online and completed the 68-item Environmental Symptoms Questionnaire (ESQ-IV) at the end of the summer of 2024. The questionnaire was administered electronically, and demographic and clinical information, including age, sex, and MS subtype, were collected.
Results: The summer of 2024 was the warmest on record in Greece. The majority of participants reported high sensitivity to heat, as 88.5% reported that they felt "very" or "extremely hot". Fatigue was among the most prevalent symptoms, with over 70% reporting moderate to extreme fatigue and 66% experiencing concentration difficulties. Furthermore, muscle pain and muscle cramps were reported by 45.7% and 41.4% of participants, respectively. Finally, over 60% of the respondents experienced increased irritability, and nearly 50% reported feelings of psychological discomfort or unease when exposed to high environmental temperatures.
Conclusion: These findings highlight the significant impact of summer heat on symptom burden in people with MS and underscore the importance of developing heat-adaptive strategies and personalized interventions.

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P1146
The Relationship Between Stigma Level and Depression, Anxiety and Quality of Life in People with Multiple Sclerosis

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Introduction: Stigma in MS refers to the negative attitudes, beliefs, and behaviors that patients may encounter because of their diagnosis. Patients who hold stigmatizing beliefs are more

prone to experiencing anxiety and depression, social isolation, and poor treatment adherence.
Objectives/Aims: This study aimed to investigate the relationship between the stigma and anxiety, depression and quality of life (QoL) of people with MS (PwMS).
Methods: One hundred and forty PwMS were enrolled in the study. 12-item Multiple Sclerosis Stigma Scale (MSSS12) were used to assess stigma level. Hospital Anxiety and Depression Scale-Anxiety and Depression subscales (HADS-A, HADS-D) and Euro Quality of Life – Five Dimension - Three Level (EQ-5D-3L) were used to evaluate the level of anxiety, depression and QoL, respectively.
Results: Sixty-seven percent of the participants were female and 49% were university graduates. The mean age of the PwMS was 38.25±10.53 years, the mean EDSS score was 1.98±1.46, and the mean time to diagnosis was 9.54±6.73 years. Fifty percent of PwMS were found to exhibit varying levels of anxiety (23.6% mild, 13.6% moderate, and 12.9% severe) and 34.3% of PwMS were found to have varying levels of depression (20% mild, 10% moderate, and 4.3% severe). There was a moderate correlation between 12-item MSSS and both HADS-A and HADS-D score ($r=0.464$; $r=0.555$, $p<0.001$ for all). A moderate and statistically significant correlation was found between the 12-item MSSS and the EQ-5D-3L ($r=0.501$, $p<0.001$). The correlation between two subscales of the 12-item MSSS (discrimination and disclosure) and HADS-A, HADS-D and EQ-5D-3L also were statistically significant.
Conclusion: Even in the early stages of the disease, PwMS experience significant levels of stigma, anxiety, and depression. As stigma levels increase, anxiety and depression tend to rise, while quality of life declines. For successful treatment outcomes, it is essential not to overlook invisible symptoms such as stigma.

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P1147
Depression and Cognition in MS: Unraveling the Impact on verbal Short-term Memory

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Introduction: Depression is common in MS patients, with prevalence ranging from 20% to 50%. It significantly affects quality of life and may interfere with cognitive function like attention and working memory. However, its impact on other cognitive domains remains unknown.
Objectives/Aims: This study explores its relationship with short-term memory, episodic memory, and executive function, while considering its known link to attention and working memory.
Methods: A total of 80 MS patients from the Department of Neurology, Ulm University, were assessed for verbal and nonverbal memory, cognitive processing speed, attentional function, verbal fluency, and executive function. Depression was measured using the Patient Health Questionnaire-9 (PHQ-9). A linear regression analysis determined the predictive value of depression on cognitive function domains.
Results: Depression was a significant predictor of verbal short-term memory ($\beta=-.12$, $t(78)=-3.75$, $p<.001$), accounting for 14.2% of variance, and the effect remained significant after adjusting for age, education, and gender. It also significantly predicted nonverbal short-term memory, cognitive processing speed, and attentional function, although depression explained less than 10% of variance in these cognitive domains. No significant associations were found with episodic memory or executive function.
Conclusion: This study provides evidence that depression has a notable impact on verbal short-term memory in MS patients, explaining 14% of its variance, independent of demographic factors. The findings underscore the importance of addressing depressive symptoms to manage cognitive impairment in MS, as depression may exacerbate cognitive deficits, particularly in the context of adjustment disorder following the diagnosis of a severe neurological disease.

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P1148
Fatigue and cognition differences in their relationship with social and biological markers of stress in Black and White patients with Multiple Sclerosis

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Introduction: Racial differences in MS etiology and fatigue may be influenced by cortisol dysregulation and HPA-axis

dysfunction, yet the interplay between race, cumulative stress, and fatigue in MS remains limited.
Objectives/Aims: To examine the relationship of race, perceived stress, cumulative cortisol, and depression with reported fatigue and cognition (Symbol Digit Modality Test- SDMT).
Methods: Eighty-three MS patients (77% female; 49% Black) and 43 controls (72% female; 26% Black) underwent self-reported assessments, tests of cognition, and hair cortisol collection in a study on novel cognitive evaluation methods.
Results: Participants with MS report higher total, psychological and physiological fatigue than controls. All regression models controlled for age, education and residualized depression. Higher levels of total fatigue were associated with perceived stress and MS while higher cognitive fatigue was only associated with higher reported perceived stress but not MS. Lower SDMT was associated with higher LnCort ($B = -2.00$, $p = .016$), MS ($B = -8.72$, $p = .003$), and being Black ($B = -7.33$, $p = .007$). Higher total fatigue ($R^2 = .46$, $p < .001$) associated with higher reported stress ($B = 0.79$, $p < .001$) and depression ($B = 6.96$, $p < .001$). Cognitive fatigue associated with higher reported stress ($B = 0.44$, $p < .001$) and depression ($B = 4.16$, $p < .001$), but not MS.
Conclusion: Self-reported perceived stress captured reports of fatigue in both MS and control groups. Higher cortisol, having MS, and being Black were associated with worse cognitive performance, whereas self-reported measures did not.

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P1149
Gut Microbiome Modulation Through Diet: A Novel Approach to alleviate Fatigue, Anxiety and Depression Symptoms in People with MS

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Introduction: Recent research has increasingly highlighted gut microbiota's role in autoimmunity and neurodegenerative diseases. Studies suggest that individuals with multiple sclerosis (MS) exhibit an altered gut microbiota, potentially contributing to disease pathogenesis and progression. Among the key factors influencing microbiota composition, diet stands out as one of the most influential.
Despite the growing interest in diet among individuals with MS, there are currently no specific nutritional guidelines tailored to this population. This study investigates the effects of a six-month nutritional-culinary intervention, based on a modified Mediterranean diet, in individuals with relapsing-remitting MS.
Objectives/Aims: The key aim of the intervention is to evaluate its capacity to modulate intestinal microbiota and alleviate "invisible" symptoms, such as fatigue and depression, which significantly impact the quality of life of individuals with MS.
Methods: Throughout the 6 months of the intervention, participants were asked to watch one nutrition education video per month and were provided with a nutritional guide outlining dietary recommendations. Stool samples were collected at baseline and after six months to analyze changes in gut microbiota composition. Additionally, participants completed the Fatigue Scale for Motor and Cognitive Functions (FSMC) and the Hospital Anxiety and Depression Scale (HADS) at both time points.
Results: Fatigue and anxiety scores correlated with specific gut bacterial populations previously linked to MS. Notably, *Butyricimonas, Parabacteroides, Fusobacterium*, and *Sutterella* exhibited positive correlations with fatigue, while *Anaerostipes* was associated with both fatigue and anxiety.
At the end of the intervention, participants reported Improvements in physical fatigue, depression and anxiety symptoms. Gut microbiota analysis revealed an increase in both Shannon diversity index and species richness. Furthermore, taxonomic shifts were observed at the phylum level, with a significant reduction in *Proteobacteria* across all samples.
Conclusion: Preliminary findings suggest that this dietary intervention could enhance the quality of life of individuals with MS. These improvements are reflected not only in self-reported outcomes but also by changes in microbiota composition, reinforcing the potential role of diet, as a complementary strategy, in MS management.

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P1150
Fatigue in Colombian Multiple Sclerosis Patients Exploring association with aging, functional independence and disability. A single-center study

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Introduction: Fatigue is a prevalent and disabling symptom of multiple sclerosis (MS) with multifactorial causes, involving aging, demyelination, inflammation, disease-modifying therapies (DMTs), and phenotype.
Objectives/Aims: This study aimed to explore the association between these factors and the severity of fatigue.
Methods: A cross-sectional, register-based study was conducted in 2024 at the Cayre Multiple Sclerosis Center in Bogotá, Colombia. Data on demographics, including age, gender, disease duration, Expanded Disability Status Scale (EDSS), disease-modifying therapies (DMTs), MS phenotypes, and Barthel index were collected. The normality of the data was assessed using the Shapiro-Wilk test. Fatigue severity was assessed using the Fatigue Severity Scale (FSS). Non-parametric tests were applied to analyze the associations among the variables.
Results: 255 patients (median age 36 years [20-85], of which 179 were female (79.5), and the median disease duration was 9.1 years [1-45]. Median EDSS 2.0 IQR [3.0]. 76.9 % of the patients had relapsing-remission (RRMS) phenotypes. Median FSS was 2.6 [IQR 3.9]. The results revealed no statistically significant difference in fatigue levels between males and females ($W = 5899.5$, $p = 0.09351$), or age ($\rho = 0.099$), though a weak positive trend was observed. Kruskal-Wallis rank sum test was performed to examine FSS between MS phenotypes. We found a significant difference in fatigue levels when comparing relapsing-remitting phenotype (RRMS) and progressive forms (PMS) ($Z = -2.5959$, $p = 0.0047$). No significant differences were observed in FSS across DMTs. A Spearman's rank correlation test revealed a positive association when comparing EDSS and FSS (Spearman's rho $= 0.38$, $p < 0.001$). A significant negative correlation was found between fatigue severity (Spearman's rho $= -0.43$, $p < 0.001$) and Barthel index.
Conclusion: These findings underscore the association between disability, functional independence, MS phenotype, and fatigue. Although the association with age was weaker, its potential interaction with disease progression warrants further investigation in longitudinal studies. Collectively, these results highlight the importance of implementing individualized, targeted interventions to address fatigue, particularly in patients with higher disability and reduced independence in daily activities.

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P1151
The impact of Cognitive reserve on Cognitive function in Multiple Sclerosis

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Introduction: Cognitive reserve (CR) represents the ability of the brain to adapt cognitive processes in response to brain atrophy. It is proposed as a factor that can explain some of the discrepancies between brain atrophy and cognitive functioning in multiple sclerosis (MS).
Objectives/Aims: The aim of the study is to evaluate the role of different CR dimensions in MS patients, including the level of education, work activity and participation in cognitively demanding activities in leisure time.
Methods: This study included 60 MS patients, treated at the Department of Neurology, Clinical Centre University of Sarajevo. For evaluation of cognitive functions, the Montreal Cognitive Assessment (MoCa) screening test was used. CR was measured by the cognitive reserve index questionnaire (CRIq) which is a semi-structured interview to quantify a person's CR considering their education (CRI-Education), working activity (CRI-Working Activity) and leisure time activities (CRI-Leisure Time) carried out during adulthood.
Results: 47 (78.3%) participants were women. The average age was 42.9+/-11.7 years. 38 (63,3%) of patients had cognitive impairment. The most of patients 48 (80.0%) subjects belonged to the category of moderate, 7 (11.7%) of medium-low, 3 (5.0%) of high, and 2 (3.3%) of medium-high CRi. The median value of CRIq score was in moderate range 96 (91.0-103.0), with highest median value in CRI Leisure time category 97 (91,0-110). The highest median values of MoCA test results were among patients with moderate-high and high range of CRIq scores. MoCA scores exhibits a statistically significant positive correlation with the CRIq ($r = 0.496$; $p < 0.001$), CRI Education ($r = 0.327$; $p < 0.015$, CRI Working Activity ($r = 0.370$; $p < 0.005$), CRI Leisure Time ($r = 0.484$; $p < 0.001$ and monthly income ($r = 0.275$; $p < 0.042$), while controlling for age, EDSS, disease duration, gender and disease form.
Conclusion: Cognitive reserve level significantly impacts cognitive function in MS patients. Cognitively demanding leisure time activities exhibited the strongest impact which signifies the importance of patient encouragement in forming cognitively demanding habits in their free time. Early cognitive decline detection and more intensive focus on cognitive rehabilitations

including the need for patients' education, more efficient integration into society, and regular periodic cognitive testing should be applied in regular treatment and management procedures of MS patients.

Disclosure of interest: Nothing to disclose

P1152
Preliminary results of validation of the brief international cognitive assessment for multiple sclerosis (BICAMS) tool and potential predictors of BICAMS test in an Ecuadorian population with multiple sclerosis

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Introduction: The BICAMS battery has been validated in Argentina, Mexico, and Colombia. However, cultural and economic differences influence neuropsychological test performance among native Spanish speakers. Therefore, validating the BICAMS battery in Ecuador will enable a more accurate diagnosis of cognitive impairment. In addition, data regarding how patient characteristics might predict low cognitive performance and therefore require particularly close monitoring is, however, limited so far.
Objectives/Aims: To validate the BICAMS battery in Ecuador and obtain regression-based normative data. (II) To determine the test-retest reliability of the BICAMS battery in Ecuador. (III) To calculate the percentage of patients with cognitive impairment and (IV) to analyze which demographics parameters are associated with cognitive performance.
Methods: The BICAMS battery was administered to 50 patients diagnosed with multiple sclerosis and 86 controls matched for age, sex, and education. The Ecuadorian validation of BICAMS comprises the SDMT, BVMT-R, and the Free Recall and Learning Test (PAMCL for its acronym in Spanish). Regression-based norms were established, and construct validity was assessed using Cohen's d. To evaluate test-retest reliability, 50 patients completed the battery with a 15-day interval. The percentage of patients with cognitive impairment was calculated by transforming raw scores into Z-scores and determining the percentage of patients scoring below the 5th percentile on one or more tests.
Results: The patient group performed significantly worse than the control group on the SDMT ($t(134) = 2.02$, $p = .046$, $d = 0.35$), PAMCL ($t(134) =$, $p = .003$, $d = 0.54$), and BVMT-R ($U = 1152$, $p < .001$, $r = 0.46$). Significant test-retest correlations were observed for all three tests: SDMT ($r = .95$, $p < .001$), PAMCL ($r = .74$, $p < .001$), BVMT-R ($rs = .69$, $p < .001$).
Stepwise-backward regressions showed a significant inverse relationship between age (β SDMT = -0.121; β PAMCL = -0.09) and educational level (β SDMT = 0.321; β PAMCL = 0.211) with performance on the SDMT and PAMCL. Additionally, female gender was associated with better performance on the CVLT (β = -1.480). For the BVMT-R, older age (β = -0.090) and lower education levels (β = -0.205) were related to better performance.
According to regression-based norms, 52% of the evaluated patients showed cognitive impairment.
Conclusion: The Ecuadorian validation of the BICAMS tests demonstrates adequate construct validity and test-retest reliability. The cognitive impairment rate in Ecuador is similar to that reported in other countries in the region. There were relationships between age, education level and gender and performance off the SDMT, CVLT-1 and BVMT-R.

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P1153
Current versus chronic fatigue in people with multiple sclerosis and healthy controls – impact of cognition, sleep, anxiety and depression

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Introduction: Fatigue is a highly prevalent and persistent symptom in people with MS (pwMS), but levels of severity vary throughout the disease. While chronic fatigue is commonly not associated to objective cognitive function, it has been related to quality of sleep, anxiety and depression. The (distinct) impact of these measures on current fatigue severity is rarely explored.

Objectives/Aims: We aimed to assess if and how cognition, quality of sleep, anxiety and depression influence current versus chronic fatigue.
Methods: We assessed chronic fatigue using the "Fatigue Scale for Motor and Cognitive function (FSMC)" and current fatigue on a visual analogue scale (0-100). We assessed cognition using the Brief International Cognitive Assessment for MS (BICAMS), sleep quality using the Pittsburgh Sleep Quality Index (PSQI) and anxiety and depression by the Hospital Anxiety and Depression Scale (HADS). We performed regression models including demographics (age, sex, education), clinical variables (EDSS, disease duration) and neuropsychological variables (cognition, sleep, anxiety, depression), to identify predictors of current or chronic fatigue.
Results: 96 pwMS (mean age 41 years, 56% female, median EDSS=1.5) and 138 healthy controls (mean age 36 years, 59% female) participated in our study. According to the FSMC, more pwMS suffered from fatigue (64.6%; 34.4% severe, median score=52.50 [37.00,69.75]) compared to HC (50%; 12% severe; median score=42.00 [32.75,52.00]). Median current fatigue was higher in pwMS (24.5 [4.25,54.25]) compared to (HC 13.0 [1.00,37.00]). Current and chronic fatigue correlated in pwMS (r=.555) and HC (r=.545). In pwMS, current fatigue was predicted by quality of sleep and anxiety (adjusted R^2 (adjR^2)=27.2%). Chronic fatigue was predicted by sleep and severity of depression (adjR^2=33.4%). Cognition was not related to current or chronic fatigue. In HC, current fatigue was predicted by anxiety (adjR^2=26.3%) and chronic fatigue was influenced by sleep and depression (adjR^2=21%).
Conclusion: Although current and chronic fatigue are associated with sleep quality in pwMS, anxiety and depression contribute distinctly to current versus chronic fatigue, highlighting the need for a comprehensive neuropsychological assessment.

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P1154
Early detection of cognitive deficits using the CogState Computerized Battery in Multiple Sclerosis: Argentine Multicentre Study

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Introduction: The Argentine Multicentre Study was formed with 8 provinces to incorporate a new digital tool for assessing cognitive deficits in people with Multiple Sclerosis (PwMS). The digital CogState Brief Battery (CogState) facilitates the identification of prodromal response deficits, such as changes in accuracy across a task, changes in reaction time and measures of vigilance detection, which cannot be recognised by conventional tests.
Objectives/Aims: To compare the detection of cognitive deficits in digital tests in relation to traditional tests in PwMS in Argentina.
Methods: 56 PwMS with less than 5 years of disease evolution were enrolled. Assessment instruments: Cognitive variables: CogState Battery: Stimulus Detection Tests (DET), Identification (IDN) and One Back Test (OBN). Brief International Cognitive Assessment for MS (BICAMS): California Verbal Learning Test-I (CVLT-I), Brief Visual Memory Test-Revised (BVMT-R) and Symbols and Digits Test (SDMT). Clinical variables: EDSS,

Fatigue Severity Scale (FSS) and Beck Depression Inventory-II (BDI-II). Statistical analysis: Performance was compared between CogState and BICAMS. A generalised linear mixed model (GLMM; binomial distribution, logit link) was used to assess the relationship between the presence of a deficit and the cognitive battery (BICAMS vs. CogState), including the participant variable as a random factor, as well as its interaction with time from baseline (months). In addition, the rate of impairment was estimated for each task.
Results: Demographics data: Age: M = 34.9 ± 10.2, Education: M = 14.4 ± 2.5, gender: 63% female, EDSS: mdn = 1 (range 0 - 6), fatigue (FSS): M = 3.4 ± 1.5, depression (BDI II): M = 14.9 ± 9.5, evolution (years): M= 2.3 ± 1.5. There was no significant difference in the proportion of deficits between the batteries, with 22.6% for CogState and 22% for BICAMS (BICAMS/CogState: OR = 0.89, 95% CI [0.50, 1.57], z = -0.40, p = .686). Proportion for individual tasks: 14% BVMTR, 30% CVLT, 22% SDMT, 30.8% DET, 34.6% IDN, 13.5% OBN, 11.5% one card learning. No significant interaction with disease progression (months) was found (B = 0.02, p = .243).
Conclusion: Early detection of decreased reaction times and processing speed in tasks that can only be implemented in computerised form is highlighted. Digital cognitive measures detect a similar proportion of cognitive impairment at earlier stages of the disease than traditional tests. These results are promising for considering the use of the CogState Battery in routine clinical practice.

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P1155
The Effect of Sexual Counselling with the PLISSIT Model on Sexual Function and Sexual Quality of Life in Women with Multiple Sclerosis: A Randomized Controlled Trial

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Introduction: Sexual dysfunction is a common but often overlooked issue in women with multiple sclerosis (MS), significantly impacting their quality of life. The PLISSIT model offers a structured approach to sexual counselling, yet most studies focus on short-term outcomes, with limited data on its long-term effects.
Objectives/Aims: This study aimed to evaluate the 12-month effects of PLISSIT-based sexual counselling on sexual function and sexual quality of life among women with MS.
Methods: This single-blind, randomized controlled trial was conducted in an MS outpatient clinic. Women aged 18–45 years with an Expanded Disability Status Scale score ⩽5.5 were randomly assigned to either the sexual counselling group (n = 31) or the control group (n = 32). The intervention included four structured counselling sessions based on the PLISSIT model, delivered over four weeks via face-to-face and telephone interactions. Assessments were conducted at baseline, 3rd, 6th, and 12th months using the MS Intimacy and Sexuality Questionnaire-15 (MSISQ-15) and the Sexual Quality of Life-Female (SQOL-F) scale.
Results: While within-group comparisons revealed significant improvements in sexual function in the intervention group over time (F = 3.198, P = 0.027), between-group differences were not statistically significant. SQOL-F scores significantly increased at the 6th (P = 0.022) and 12th months (P = 0.032) in the intervention group, while no significant changes were observed in the control group. The frequency of weekly sexual intercourse increased significantly in the counselling group from baseline to the 6th month (P < 0.001), and this improvement was sustained at the 12th month (P= 0.006).
Conclusion: The findings indicate that PLISSIT-based sexual counselling may contribute to long-term improvements in sexual quality of life and activity frequency among women with multiple sclerosis. Although no significant differences were found between groups, the within-group improvements support the potential value of structured and sustained sexual counselling. These results highlight the need for comprehensive, long-term interventions in managing MS-related sexual dysfunction and warrant further investigation with larger, multi-centered samples and partner inclusion.

Disclosure of interest: nothing to disclose

P1156
MRI predictors of long-term cognitive changes in Multiple Sclerosis: a longitudinal multicenter study

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Introduction: Cognitive decline in Multiple Sclerosis (MS) can occur over time, with some individuals transitioning from a cognitively preserved (CP) to a cognitively impaired (CI) status. Identifying MRI-derived structural markers associated with cognitive decline may be crucial for early intervention.
Objectives/Aims: To identify MRI-derived structural correlates of CI at follow-up in people with MS (pwMS).
Methods: 388 pwMS from four Italian MS Centers participating to the Italian Neuroimaging Network Initiative (INNI) consortium underwent neuropsychological assessment with the Brief Repeatable Battery of Neuropsychological Tests (BRB-N) at baseline and follow-up (⩾4 years later). CI was defined by adjusted Z scores ⩽-1.5 SD below normative values in ⩾2 cognitive domains (verbal memory, visual memory, attention, verbal fluency). An additional classification was performed by combining BRB-N domains into two cognitive macrodomains—memory and executive functions. Baseline 3T MRI-derived measures - including subcortical volumes and cortical thickness (CTh) extracted with FreeSurfer - were used to predict follow-up cognitive scores via multiple linear regression, adjusting for age, sex, education, disease duration, phenotype, site, and, for CTh measures, global CTh. The results were Bonferroni corrected ($p < .05$).
Results: At baseline, 104 pwMS (26.8%) were classified as CI, while 111 CP (28.6%) showed impairment in a single domain. 28 CP converted to CI at follow-up, while among pwMS with impairment in a single domain, those with executive dysfunction were being more likely to transition to CI than those with memory impairment ($\chi^2 = 3.88$, $p = .0486$). Among different subcortical volumes associated with follow-up cognitive performance, thalamus emerged as the strongest predictor of Symbol Digit Modalities Test (SDMT) ($\beta = 0.25$, $p = .006$) and Word List Generation (WLG) ($\beta = 0.27$, $p = .001$) scores. SDMT scores were inversely associated with the CTh of the rostral anterior cingulate cortex (rACC; $\beta = -0.22$, $p = .041$).
Conclusion: PwMS with subtle executive deficits are at higher risk of cognitive decline. Reduced thalamic volume was a robust predictor of poorer long-term attention and executive performance, while thicker rACC was inversely related to processing speed, possibly reflecting maladaptive or inefficient compensatory mechanisms. Baseline MRI-based measures may support early interventions to preserve cognitive functioning in MS.

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P1157
Health care professional feedback on implementation of MS bladder check tool in clinical practice

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Introduction: Symptoms of lower urinary tract dysfunction (LUTD) occur frequently in people with MS, significantly impacting their quality of life. Despite this, there is a lack of awareness among both patients and health care professionals, which can lead to bladder problems not being treated in a timely manner. The MS bladder check awareness tool was developed to help ensure timely treatment.
Objectives/Aims: To investigate how health care professionals perceive that the MS bladder check patient awareness tool supports both patients and health care professionals in identifying and discussing MS-related bladder problems.
Methods: In order to assess the effectiveness of the MS bladder check tool in clinical practice, we engaged health care professionals from various specialties and countries. These professionals were asked to share the MS bladder check with a minimum of 10 patients prior to their consultation. Subsequently, they were requested to evaluate whether they believe the MS bladder check would increase awareness of bladder problems in MS patients and if the tool supports health care professionals in their daily work. Data were collected using an assessment questionnaire with 12 multiple-choice questions and one free text question
Results: A total of 32 out of 45 health care professionals from Italy (n = 10), France (n = 10), Netherlands (n = 6), UK (n = 5) and Norway (n = 1) responded to the survey. The healthcare professionals cover a wide range of specialties and when asked how they think the MS bladder check supports their patients, 94% agree/highly agree that the MS bladder check makes their patients more aware of the impact MS can have on their bladder function. There were 81% health care professionals who agree that the tool makes it easier for their patients to talk about bladder symptoms, and further 80% agree that it helps their patients identify MS-related bladder problems earlier. Additionally, 83% of the health care professionals agree/highly agree that the MS bladder check supports them in their daily work, and 93% would recommend the MS bladder check to others.
Conclusion: The results support MS bladder check as an easy-to-use tool to enhance awareness of MS, and it can help health care professionals to ensure a more timely bladder assessment in people living with MS.

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P1158
Prediction of individual fatigue levels in multiple sclerosis from clinical, metacognitive and neuroimaging data

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Introduction: Fatigue is one of the most frequent and disabling symptoms in multiple sclerosis (MS) and likely caused by diverse pathophysiological mechanisms. So far, diagnostic tests are lacking that detect patient-specific disease mechanisms and could guide individual treatment.
Objectives/Aims: This observational study with a pre-registered analysis plan investigated potential mechanisms contributing to fatigue in MS by integrating clinical assessments, questionnaire data, physiological measures, sleep data, as well as quantitative and functional magnetic resonance imaging (MRI) from 75 individuals with MS.
Methods: Using machine learning (elastic net regression, nested cross-validation and late fusion), we examined the utility of individual and combined feature sets for predicting subject-level fatigue scores (Fatigue Severity Scale [FSS] and Fatigue Scale for Motor and Cognitive Functions [FSMC]) out-of-sample. Furthermore, we assessed the feature importance of individual predictors.
Results: Our results show statistically significant performance for models based on sleep-related and clinical information, as well as those incorporating information from all data modalities combined. Higher scores on sleep questionnaires, along with increased disability, urinary urgency, and depressive symptoms, were positively associated with increased fatigue scores. Notably, sleep-related features consistently emerged as the most predictive, including in the combined model. Cognitive measures related to self-efficacy, interoceptive awareness and metacognition of control also demonstrated significant associations with fatigue, consistent with the Allostatic Self-Efficacy (ASE) theory of fatigue. However, models incorporating these cognitive features failed to consistently generalize well to unseen data.
Conclusion: Our work highlights the role of sleep disturbances, clinical factors, and interoceptive and metacognitive processes in MS-related fatigue. Overall, our work demonstrates the feasibility of predicting fatigue severity from simple, easily accessible measures. Provided our findings can be confirmed in larger, independent samples, they might provide

the basis for establishing more objective clinical tests of fatigue that go beyond pure self-report.

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P1159
Fine Motor Impairment in Early-Phase Multiple Sclerosis Without Disability: A Comparison with Matched Healthy Controls

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Introduction: Early detection of functional impairments in multiple sclerosis (MS) is essential for timely intervention. While previous research has identified significant physical, cognitive, and patient-reported deficits in early-phase MS, the extent of upper limb dysfunction in patients with no measurable disability [Expanded Disability Status Scale (EDSS) 0] remains unclear.
Objectives/Aims: This study aimed to assess upper limb function in people with early-phase MS (⩽2 years from diagnosis) with no disability (EDSS = 0) compared to age- and sex-matched healthy controls (HC).
Methods: A cross-sectional study was conducted with 50 persons with MS and 50 HC. Upper limb function was evaluated using the Nine-Hole Peg Test (9HPT) for both dominant and non-dominant hands and handgrip strength using a Jamar dynamometer. The Mann-Whitney U test with rank biserial correlation was used to assess group differences.
Results: Persons with MS exhibited significantly slower performance on the dominant-hand 9HPT compared to HC, with people with MS being approximately 8% slower ($p = 0.019$, rank biserial correlation = 0.2736). No significant differences were observed in non-dominant 9HPT, total 9HPT time, or grip strength measurements ($p > 0.05$).
Conclusion: Despite the absence of measurable disability, individuals with early-phase MS show subtle fine motor impairments in the dominant hand. These findings underscore the need for sensitive functional assessments in early MS, as upper limb dysfunction may develop before overt disability emerges.

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P1160
Acute Paroxysmal Dystonia as a Manifestation of Multiple Sclerosis Relapse due to Demyelinating Lesion in Basal Ganglia: A Case Report and Pathophysiological Insights

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Introduction: Cognitive impairment can occur early in the disease course of relapsing multiple sclerosis (RMS) and may be influenced by education level and sex. The primary endpoint of the open-label ozanimod ENLIGHTEN study was to determine the proportion of patients with improved Symbol Digit Modalities Test (SDMT) scores, defined as an increase of ⩾ 4 points or 10% from baseline; however, an 8-point improvement may better represent individual-level cognitive processing speed changes.
Objectives/Aims: To explore the effects of baseline SDMT score, education level, and sex on 8-point SDMT improvement after 1 year of ozanimod treatment.
Methods: ENLIGHTEN (NCT04140305) is a multicenter, phase 3b, open-label study of ozanimod 0.92 mg in adults with early RMS (⩽1 disease-modifying therapy; Expanded Disability Status Scale score ⩽3.5; ⩽5 years since diagnosis; ⩽10 gadolinium-enhancing lesions). Improved or worsened SDMT scores were considered an increase or decrease of ⩾8 points from ENLIGHTEN baseline, respectively, while stable was a change <8 points. A multivariable logistic regression model assessed baseline SDMT scores, education level (college degree or higher vs no college degree), and sex (male vs female patients) as predictors of improved 8-point SDMT scores after 1 year of ozanimod treatment (data cutoff: 7 Feb 2024).
Results: For the 168 patients with baseline and year 1 SDMT data, baseline mean (SD) age was 39.9 (10.7), mean (SD) SDMT score was 53.2 (11.6), 101 (60.1) had a college degree or higher, and 132 (78.6%) were female patients. After 1 year of ozanimod treatment, 48 (28.6%), 106 (63.1%), and 14 (8.3%) patients had improved, stable, or worsened SDMT scores, respectively. Lower baseline SDMT scores were associated with increased 8-point improvement after 1 year of ozanimod treatment (odds ratio [95% CI] per 1-point SDMT score increase at baseline 0.96 [0.94–0.99]; $P = 0.008$). Education level and sex did not significantly affect the odds of 8-point improvement (odds ratio [95% CI] 0.67 [0.34–1.32]; $P = 0.243$, and 1.04 [0.47–2.29] $P = 0.925$, respectively).
Conclusion: After 1 year of ozanimod in ENLIGHTEN, most patients had improved or stable SDMT scores, with lower baseline SDMT scores, but not education level or sex, being associated with 8-point improvement on the SDMT. These interim findings support the use of ozanimod early in the treatment of patients with RMS.

Disclosure of interest: Author's Adelaida Cuenca Relinque: nothing to disclose.

P1161
Perceptual Sensitivity to Changes in Self-Paced Maximal Walking Speed During the Six-Minute Walk Test in Individuals With Multiple Sclerosis and Healthy Controls: Preliminary Results

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Introduction: People with multiple sclerosis (PwMS) walk slower than their healthy peers and report more negative experiences associated with walking. Perception of walking performance integrates sensory inputs about performance and body-homeostasis, but is inferential: prior beliefs are confronted with sensory inputs to compute precision-weighted updates and lower prediction errors over time. In PwMS, imprecise inputs may lower perceptive sensitivity during motor tasks with the risk of maladaptive behaviors such as slow walking speed and dysfunctional gait patterns. Tests like the 6-minute walking test (6MWT) assess motor capacity, and objective parameters such as gait speed variability may reflect movement quality. In addition, task-specific perceptual abilities that could help inform rehabilitation strategies remain unknown.
Objectives/Aims: The aim of the study was to examine perceptive sensitivity for performance variations in PwMS and healthy controls (HC), with a focus on the perception of gait speed during the 6MWT.
Methods: Eight mildly-disabled PwMS (median age: 39 IQR: 34-44,5 ; median EDSS: 3) and 8 HC (median age: 31 IQR: 28-31) were included. They performed an instrumented (6 wearable inertial measurement units) 6MWT at maximal speed in silence, carrying a handheld sensor to save perceptive reports. They were all instructed to squeeze it when perceiving gait speed variations in the straight parts of a 30-meter track, regardless of them being perceived accelerations or decelerations. Detection rates were calculated as the ratio between report quantity and speed variability (CV), and compared with subjective confidence ratings about the accuracy of their given reports (Visual analog scale, expressed in %).
Results: Lower walking speed was measured in PwMS compared to HC's [median: 1,529 m/s Vs 1,891 m/s). Despite similar walking speed variability [median: 0,029 vs 0,030], detection rates were higher in HC [median:4,67 IQR: 3,01-8,35] than in PwMS [median: 1,19 IQR: 0,30-1,76]. In contrast, controls reported lower subjective confidence ratings [median: 62,5% IQR: 60-75%] than PwMS [median: 80% IQR: 62,5-92,5%].
Conclusion: These findings may indicate a reduced sensitivity in PwMS to perceive ongoing variations in their walking performance. This could be related to overconfidence in their perceptual abilities or underlying perceptual impairments

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P1162
Perceived sleep quality and disorders of sleep in patients with multiple sclerosis

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Introduction: The motor symptoms of multiple sclerosis (MS) are well recognized, however, non-motor symptoms are often overlooked.Sleep disorders occur in almost 50% of all persons living with MS (PwMS).
Objectives/Aims: The aims of this study were to determine the frequency of sleep disorders and the impact of anxiety, depression and fatigue on sleep quality in PwMS.
Methods: This study was conducted at the Clinic of Neurology, University Clinical Center of Serbia (UCCS), from November 2024 to March 2025. For the purposes of the study, a questionnaire was designed to collect socio-demographic characteristics and several scales were used: Pittsburgh sleep quality index (PSQI), Epworth sleepiness scale (ESS), Restlessleg syndrome rating scale, Hospital Anxiety and Depression Scale (HADS), and Fatigue Impact Scale (FIS).
Results: The study included 103 PwMS, out of which 19 (81.6%) were male and 84 (18.4%) were female. Mean age was 41.9±12.7 years. Mean EDSS was 2.9 (±0.2).The minority of respondents worked a manual labour, in shifts, longer than 8 hours (7.8% vs. 27.2% vs. 12.6%, respectively). More than a half of PwMS in our study had poor sleep quality (54.4%), and nearly a quarter had excessive daytime sleepiness (22.3%). Twenty three patients (22.3%) fulfilled the criteria for restless leg syndrome. Eleven patients had anxiety, while 9 patients had depression (10.7% vs. 8.7%, respectively). We found a statistically significant positive correlation between poor sleep quality- and anxiety ($p=0.001$, $\rho=0.310$), depression ($p<0.001$, $\rho<0.01$), ESS ($p=0.02$, $\rho=0.02$), and FIS scores ($p<0.01$, $\rho=0.338$).
Conclusion: Fatigue and poor sleep quality persisted despite a lack of physically demanding work. The connection between poor sleep quality and anxiety, depression, daytime sleepiness and fatigue is mutual, one worsens the other, and vice versa.It is important to recognize and initiate timely treatment of poor sleep quality.

Disclosure of interest: Olivera Tamas: nothing to disclose.

P1163
Evaluating Cognitive Function in Relapsing-Remitting Multiple Sclerosis Following Escalation from First-Line Disease-Modifying Therapies to Ocrelizumab (Xarcel®): A Cohort Study in Iran

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Introduction: The central nervous system (CNS) is affected by multiple sclerosis (MS), a neuro-inflammatory disease characterized by the destruction of myelinated axons. Relapsing-remitting multiple sclerosis (RRMS), the most common form of the disease, often presents with distinct symptoms and potential disability, including cognitive impairment even in the absence of physical impairments. The effects of Disease-Modifying Therapies (DMTs) on cognitive function in individuals with RRMS are not well understood due to a scarcity of comprehensive research.
Objectives/Aims: To evaluate the cognitive functions of RRMS patients whose treatment was escalated from first line DMTs to Ocrelizumab (Xarcel®).
Methods: We conducted a prospective cohort study from May 2023 to September 2024 in Tehran, Iran, enrolling RRMS patients who were escalating from first-line DMTs to Ocrelizumab. Cognitive assessments using the Minimal Assessment of Cognitive Function in MS (MACFIMS) battery were completed at baseline, 6 months, and 12 months. The MS Quality of Life-54 (MSQOL-54) questionnaire was administered at each time point to assess quality of life (QoL) addressing it as a possible confounding. Statistical analyses were performed using R software with a significance level of $p \leqslant 0.05$.
Results: Twenty-seven patients (median age: 35 years, IQR = 12.5) were enrolled, predominantly females (n = 22, 81.5%) with a bachelor's degree (n = 11, 40.7%). The median Expanded Disability Status Scale (EDSS) score decreased from 2 (IQR=1.5) to 1 (IQR=1.0) through the end. Cognitive function improved significantly in six of ten MACFIMS domains: California Verbal Learning Test (CVLT), CVLT- delay, Paced Auditory Serial Addition Test (PASAT), Controlled Oral Word Association Test (COWAT) (all with $p < 0.001$), Delis-Kaplan Executive Function System (D-KEFS) (total group) ($p = 0.038$), and Judgment of Line Orientation (JLO) ($p = 0.015$). Additional pairwise comparisons with p-value adjustments indicated a statistical significance across all three CVLT assessments. For the CVLT- delay, the difference was meaningful between the first and third ($p<0.001$) and between the second and third assessments ($p = 0.022$); whereas for PASAT, the significant difference existed between the first and second as well as the first and third assessments (both $p<0.001$). Other distinctions were between COWAT's first and third ($p = 0.002$) and JLO's first and third evaluations ($p = 0.006$). Although there were differences in the D-KEFS group raw scores, none of the adjusted values showed statistically significant results. Moreover, No significant changes were observed in QoL scores over time.
Conclusion: This cohort study revealed that switching from first-line DMTs to Ocrelizumab was associated with an improvement in cognitive function among patients with RRMS. QoL scores for physical and mental health remained stable across the assessed time points.

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P1164
Cognitive assessment in patients with concentric balo sclerosis: analysis of a series of nine cases from rio de janeiro/brazil

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Introduction: Baló's Concentric Sclerosis (BCS) is a rare inflammatory demyelinating disease of the central nervous system, usually of acute onset and heterogeneous clinical manifestations. Common symptoms include hemiparesis, ataxia, hypoesthesia, diplopia, headaches, seizures, urinary incontinence, behavioral changes, aphasia, memory deficits, and attentional dysfunction. Trough Magnetic Resonance Imaging (MRI) is identified the concentric layers of preserved myelin alternating with demyelinated zones, forming an "onion-ring" pattern. Despite the increasing number of case studies on this disease, researchers lacked studies on cognitive functioning profiles in this population, and no standardized protocols for neuropsychological assessments have been established.
Objectives/Aims: To evaluate neuropsychological impairments—memory, verbal fluency, executive dysfunction, and depressive symptoms—in a series of nine patients diagnosed with BCS via MRI.
Methods: The cognitive performance was measured using the Rey Auditory Verbal Learning Test and verbal fluency task. The occurrence of dysexecutive symptoms and depressed mood was investigated using the Barkley Executive Dysfunction Rating Scale and Beck Depression Inventory II. In this series, six were

women and three were man. The mean current ages were 35.66 (17-48 years) and the mean duration of the disease was 7.44 years (4-15 years). All had acute onset, one was monophasic and eight had recurrence. At the time all were undergoing preventive treatment with corticosteroids.
Results: In the neuropsychological assessment, no patient presented episodic memory deficit, four (44.4%) presented verbal fluency deficit, three (33.3%) reported symptoms of executive dysfunction and five (55.6%) had depressed mood.
Conclusion: While episodic memory remains preserved, deficits in verbal fluency (44.4%), executive dysfunction (33.3%), and depressive symptoms (55.6%) are frequent. Our findings suggest that cognitive symptoms may persist in patients undergoing corticosteroid treatment and the prevalence of depressive symptoms indicate a need for multidisciplinary management.

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P1165
Body Composition Affects Sexual Function and Disability in Multiple Sclerosis

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Introduction: Sexual dysfunction is a frequent and complex symptom in MS, resulting from both neurological damage and psychological or physical factors. Nutritional status, particularly obesity and changes in body composition, has been shown to influence the degree of neurological disability in patients with MS
Objectives/Aims: The aim of this study was to assess the relationship between nutritional status and both neurological impairment and sexual dysfunction in individuals with MS.
Methods: A total of 242 pwMS (175 females) with a mean age of 40.07 ± 10.97 years were included in the study. The Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ-19) was used to assess sexual dysfunction (SD). Anthropometric measurements included body mass index (BMI), waist-to-height ratio (W/HtR), and waist-to-hip ratio (WHR). Body composition was evaluated using bioelectrical impedance analysis (BIA), with fat mass (FAT%) and skeletal muscle mass (SMM%) expressed as percentages of total body mass. The median Expanded Disability Status Scale (EDSS) score was 2.26 (range: 1.0–6.5).
Results: FAT% was significantly correlated with the MSISQ-19 total score and with the total score for primary SD (all $p < 0.05$). FAT% also showed significant correlations with the following MSISQ-19 items: Primary: Items 16, 17, 18; Secondary: Items 1, 3; Tertiary: Items 7, 14. SMM% was significantly associated with item 13 (tertiary), WHR showed a significant correlation with item 2 (secondary) (all $p < 0.05$). An MSISQ-19 score greater than 30 was used as a cutoff point to classify patients into two groups. A significant difference in FAT% was found between these two groups ($p < 0.05$). BMI effectively differentiated nutritional status within the cohort. Patients with obesity exhibited significantly higher mean MSISQ-19 total scores and higher scores across all SD domains (primary, secondary, tertiary) (all $p < 0.05$). Finally, EDSS scores were negatively correlated with SMM% and positively correlated with W/HtR ($p < 0.05$).
Conclusion: Nutritional status, specifically excess fat mass, obesity, and reduced muscle mass, is associated with greater neurological disability and more severe sexual dysfunction in patients with MS. Obesity seems to be an additional therapeutic target to improve sexual functioning in the MS patients.

Disclosure of interest: Edyta Matusik: nothing to disclose.

P1166
A Study on Spectrum of Autonomic Dysfunction in Demyelinating Disorders in a Tertiary Care Centre from Eastern India

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Introduction: Primary demyelination comprises of diseases like Multiple sclerosis (MS), neuromyelitis optical spectrum disorder (NMOSD), Myelin Oligodendrocyte Glycoprotein antibody associated diseases (MOGAD), with their exclusiveness in affecting several parts of Central nervous system. Direct Autonomic Nervous System (ANS) affection by brainstem and Spinal cord involvement has been documented and experienced by clinicians. Magnitude of problem apparently visible is only a tip of iceberg.
Objectives/Aims:

- Explore the spectrum and incidence of autonomic dysfunction in patients with primary demyelination
- Relationship if any between specific autonomic dysfunction domain and radiological involvement.
- To assess any correlation of primary demyelination etiology (MS/NMOSD/MOGAD) with the autonomic burden of patients.

Methods: In this cross-sectional observational study, all adult primary demyelination cases attending indoor and 'Neuroimmunology clinic'. Autonomic function was assessed by clinical bedside tests, Autonomic dysfunction by Composite autonomic symptom score (COMPASS 31) questionnaire, Male sexual dysfunction by International Index for erectile function (IIEF), Female sexual dysfunction by Female Sexual Function Index (FSFI) and Disease burden by expanded disability severity scale (EDSS).

Results: Out of 90 cases 54.4% (49/90) female and 45.6%(41/90) were male. LETM patients had higher mean COMPASS31 score (14.6) with more ANS affection in individual COMPASS domains. In our study population Sexual dysfunction in Males in our population was more prevalent in MS group followed by NMOSD, MOGAD and NMO group followed by MS and MOGAD for females. Radiological involvements like supratentorial, brainstem, long/short segment spinal cord involvement with respect to abnormal COMPASS scores, was statistically insignificant. Autonomic dysfunction (COMPASS) correlated positively with depression (HDRS) and anxiety (HAM-A). IIEF scores correlated significantly with HDRS.
Conclusion: Personal and social consequences can be immense due to autonomic dysfunction which is often underrepresented in literature. Future longitudinal follow up studies will be required to address the long-term consequences

Disclosure of interest: Nothing to disclose

P1167
Features of anxiety-depressive and asthenic syndromes in the structure of early clinical manifestations of multiple sclerosis

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Introduction: The early clinical manifestations of multiple sclerosis (MS) can be quite diverse. Anxiety-depressive and asthenic disorders can be the first and, most often, the only symptoms of the onset of MS.
Objectives/Aims: The aim of the study was to determine the severity of anxiety-depressive and asthenic syndromes in patients with early and pronounced clinical manifestations of multiple sclerosis.
Methods: Forty patients with multiple sclerosis, meeting the 2017 McDonald criteria and the Magnetic Resonance Imaging in Multiple Sclerosis (MAGNIMS) criteria, were examined using the Modified Fatigue Impact Scale (MFIS) and the Hospital Anxiety and Depression Scale (HADS). The first group consisted of 20 patients with early clinical manifestations (mean Expanded Disability Status Scale (EDSS) score = 4.09±0.45, disease duration = 2.88±0.40 years), while the second group included 20 patients with pronounced clinical symptoms (mean EDSS score = 4.79±0.40, disease duration = 12.29±1.34 years).
Results: According to the MFIS scale, in the first group, more than half of the patients (53%) showed a moderate impact of fatigue, while in the second group, this figure was 35%. In the second group, two out of three patients (65%) experienced a severe impact of fatigue, which was twice as high as in the first group (35%).
On the HADS scale, 41% of patients in the first group had mild symptoms of depression, and the remaining 59% had clinically significant depression. In the second group, the percentage of clinically significant depression was almost twice as high, at 88%. Regarding the anxiety subscale (HADS), the first group had 5% fewer patients with mild symptoms of anxiety compared to the second group, with 30% in the first group and 35% in the second. The percentage of clinically significant depression was almost identical in both groups, at 29% and 30%, respectively.
Conclusion: The study showed that patients with early manifestations of multiple sclerosis exhibit moderate symptoms of asthenia, depression and anxiety. As the disease progresses, these symptoms become more pronounced, especially depression and fatigue, which emphasizes the need for early diagnosis and a comprehensive approach to treatment, including psychoemotional support.

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P1168
Proportion of patients with multiple sclerosis and cognitiveimpairment at Hospital Escuela from February to July 2024

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Introduction: Multiple sclerosis affects 2.8 million people worldwide, mainly young adults, generating both motor and cognitive disability and compromising their quality of life. Cognitive impairment is present in about 43 to 70% of patients at any given time during the disease and its finding at the time of diagnosis leads to a poor prognosis. The Extended Disability Status Scale does not allow for adequate cognitive assessment by domains, therefore specific tests are required.
Objectives/Aims: The purpose of this study was to determine the proportion of patients with multiple sclerosis and cognitive impairment through the application of standardized cognitive batteries in Honduras, becoming the first study of its kind.
Methods: This was a descriptive, cross-sectional, observational study. A total of 37 patients with multiple sclerosis were included, to whom a form was applied, and of these, 28 were eligible for neuropsychological tests (BICAMS and BRB-N).

Results: According to the demographic profile, the mean age was 32 years, 75.7% were female, 48.6% had higher education, 64.9% had recurrent remitting clinical subtype, 89.2% were receiving disease-modifying therapy, and 67.6% were treated with interferons. 73% had never undergone a cognitive evaluation while 92.8% of the evaluated patients showed impairment in at least one cognitive domain and 57.1% was diagnosed with depression as comorbid state.
Conclusion: Visual memory encoding, information processing speed, visuospatial memory, working memory, auditory information processing speed, and verbal fluency were the predominantly affected domains. Considering these results, we recommend early cognitive rehabilitation therapy and active assessment of depression through equally standardized testing.

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P1169
Neuropsychological disorders in multiple sclerosis: dynamics, correlations, and approaches to correction

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Introduction: Multiple sclerosis (MS) is a chronic central nervous system disorder causing motor, cognitive, and emotional impairments. Cognitive dysfunction and emotional disturbances, including anxiety and depression, are common and significantly affect daily functioning. This thesis explores the nature and progression of these neuropsychological disturbances in MS, aiming to improve patient assessment and rehabilitation approaches.
Objectives/Aims: To study the dynamics of neuropsychological disorders in multiple sclerosis (MS) and develop a correction algorithm.
Methods: 25 MS patients were examined at Tashkent Medical Academy and City Clinical Hospital No. 7 in 2023–2024. Clinical and neurological assessments, Montreal Cognitive Assessment (MoCA), Hospital Anxiety and Depression Scale (HADS), and brain MRI were used.
Results: The cerebrospinal form predominated (80%). Cognitive function assessment (MoCA) in younger patients (18–44 years) showed 63.2% had scores below 26. In older patients (45–59 years), 73% scored 21–25 points. A significant decline in MoCA was found in older patients ($p \leqslant 0.041$). Anxiety and depression were observed in 24% (subclinical) and 12% (clinical) for anxiety, and 23% (subclinical) and 15% (severe) for depression. Significant correlations were found between cognitive function (MoCA) and anxiety ($r = -0.51$, $p \leqslant 0.05$), and depression ($r = -0.48$, $p \leqslant 0.05$). A positive correlation was observed between neuropsychological impairments and MRI-detected demyelinating changes ($r = 0.57$, $p \leqslant 0.032$).
Conclusion: Neuropsychological disorders in MS progress with cognitive decline, anxiety, and depression correlating with MRI-detected demyelination. Comprehensive neuropsychological monitoring and individualized correction strategies are necessary.

Disclosure of interest: Madinabonu: nothing to disclose

Clinical Aspects of MS & Related Diseases – Paediatric MS

P1170
Implementation of the first adolescence-to-adulthood transition programme for MultipleSclerosis in Latin America

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Introduction: Hospital-based transition programmes to adult care for paediatric patients with chronic diseases have proven effective in improving both quality of life and patient autonomy. However, there are few reports concerning Multiple Sclerosis (MS), and none to date from Latin America.
Objectives/Aims: To evaluate the implementation of an adolescence-to-adulthood transition programme for patients with paediatric-onset MS (pwPOMS), focusing on current quality of life and independence in disease management.
Methods: A prospective study was conducted involving patients aged 18 to 24 years with MS onset before the age of 18, currently followed at an MS centre in Buenos Aires, Argentina. The following validated Spanish-language scales were administered: the European Quality of Life – 5 Dimensions (EQ-5D), the MS International Quality of Life Questionnaire (MusiQoL), and the Transition Readiness Assessment Questionnaire 5 (TRAQ-5) to assess readiness and autonomy longitudinally. Clinical and demographic data were also collected.
Results: Thirty-three patients were included; 54.5% (n=18) were female, with a mean age of 21.3 ± 2.04 years and mean disease duration of 6.6 ± 2.05 years. A total of 57.6% (n=19) were on monoclonal antibody therapy, most commonly natalizumab (n=14), and 60.6% (n=20) had previously received at least one disease-modifying therapy. Regarding transition, 36.4% (n=12) enrolled in the hospital transition programme, which began at age 18 and lasted an average of 13.9 ± 1.7 months. Significant differences were observed in current TRAQ-5 and MusiQoL scores between those who had and had not participated in the transition programme ($p < 0.0001$ and $p = 0.0002$, respectively), with a positive correlation between both scales ($r = 0.71$, 95% CI = 0.4–0.8, $p < 0.0001$). Additionally, differences in EQ-5D domains were observed in anxiety ($p = 0.007$) and daily activity ($p = 0.003$). Access to the transition programme was also associated with higher educational attainment ($\chi^2 = 22$, $p = 0.001$). Longitudinally, TRAQ-5 scores increased significantly from baseline to the end of the transition (initial $= 61.7 \pm 11.07$ vs. final $= 94.2 \pm 6.2$, $p = 0.0005$). In multiple linear regression, participation in the transition programme was significantly associated with higher MusiQoL scores ($B = 13.84$, $p = 0.024$; adjusted $R^2 = 0.331$).

Conclusion: The implementation of a structured transition programme from paediatric to adult care for patients with MS is associated with improved quality of life, increased autonomy, and better disease self-management in early adulthood.

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P1171
Defining prognostic factors in Pediatric Onset Multiple Sclerosis: a systematic literature review

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Introduction: Pediatric Onset Multiple Sclerosis (POMS) is a rare disease, accounting for 3-5% of all MS cases; despite being regarded as in a continuum with its adult counterpart, POMS has its own distinct features, differing greatly from Adult Onset Multiple Sclerosis (AOMS) in its clinical trajectories and prognostic factors.
Objectives/Aims: To provide a comprehensive review of the prognostic significance of clinical, radiological, laboratory and environmental features in POMS. This study falls within the framework of the PROMISING study (Enhancement and Strengthening of Biomedical Research in the NHS - PNRR-MAD-2022-12376868), which aims to predict MS disease progression through the development of a prognostic score.
Methods: A systematic literature search was conducted using PubMed, applying strict inclusion criteria.
A total of 30 relevant articles were selected, published between 2002 and 2023.
We included data pertaining to demographic characteristics, clinical presentation, magnetic resonance imaging (MRI) findings, environmental factors, and biomarker profiles, and their impact on key clinical and radiological outcomes.
Results: Clinical factors such as higher baseline EDSS score (HR: 2.26, CI: 1.25– 4.06), shorter time to second attack (HR: 1.56, CI: 1.07–2.28), and primary progressive course (2.93, 1.37–6.26) were associated with increased risk of long-term disability accrual.
MRI features at baseline, such as MS diagnostic criteria fulfilled at first MRI (HR: 1.89, CI: 1.26–2.85) and optic nerve lesions (HR: 2.10, CI: 1.12–3.91), were associated with higher relapse frequency.
Biomarkers, especially high sNfl levels, were strongly linked both with clinical (HR 0.029 to 1.040) and radiological (HR: 0.112 to 1.404) disease progression.
Early exposure to High Efficacy Treatments (HETs) was protective towards disability accrual; delay in treatment initiation, on the other hand, increased likelihood of reaching EDSS 4.0 (HR: 0.39, CI: 0.26 – 0.59).
Environmental factors that impacted the most were, as expected, lower vitamin D levels (OR: 0.72; CI: 0.55, 0.94) and higher BMI (OR 1.17; CI 1.05, 1.30).
Conclusion: Several factors can help predict disease course in POMS. According to our findings, a more aggressive disease presentation at onset and treatment exposure can help stratify risk of disease progression.
The development of individualized prognostic scores may facilitate early intervention strategies, optimize treatment selection, and ultimately improve long-term patient outcomes.

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P1172
Baseline Characteristics of Paediatric Patients with Multiple Sclerosis in the Phase 3 NEOS Study of Ofatumumab and Siponimod Versus Fingolimod

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Introduction: Paediatric multiple sclerosis patients (PedMS pts) have higher levels of inflammation than adult MS pts and, if untreated, show early progressive loss of brain volume and develop disability at a young age. New options of Disease

Modifying Therapies (DMTs) with well-characterised efficacy and safety based on controlled clinical studies are a major unmet need, as fingolimod is the only globally approved DMT in PedMS. The NEOS study (NCT04926818) has an innovative Bayesian noninferiority (NI) design and evaluates the efficacy and safety of two new potential treatment options, siponimod and ofatumumab, with fingolimod as the comparator. NEOS, providing PedMS pts with 1 of 3 highly effective DMTs for up to 7 years, has recently completed enrolment.

Objectives/Aims: To present the baseline characteristics of PedMS pts enrolled in the ongoing phase 3 NEOS study.

Methods: NEOS is a 2-year, randomised, 3-arm, double-blind, parallel-group, multicentre study comparing ofatumumab and siponimod vs fingolimod during the core phase, followed by 2–5 years of an open-label extension phase. The primary objective is to show NI of ofatumumab and siponimod vs fingolimod, assessed by ARR ⩽2 years. Randomisation of ~120 pts (~40/arm) will provide >80% power for the demonstration of NI. Key baseline demographic and MS disease characteristics are presented (cut-off: 7-Mar-2025), including age, sex, race/ethnicity, height, body weight, body mass index (BMI), pubertal status, EDSS, duration since MS diagnosis and first symptoms, number of relapses in the last 12 months prior to screening and in the last 24 months, time since onset of most recent relapse, naive vs pre-treated subjects and T2 lesion volume.

Results: 129 PedMS participants were enrolled with mean age of 15±1.7 years, with a mean BMI of 23.8±6.3 kg/m^2, and 122 participants (95%) weighed >40 kg. A majority of participants were treatment naive (74%), female (60%) and had reached puberty (Tanner status ⩾2; 87%). The average time since MS diagnosis was 0.71±0.8 years and the mean duration since first symptoms was 1.25±1.6 years. Mean baseline EDSS score was 1.6±1.2, the average number of relapses in the last 12 months prior to screening was 1.3±0.73 and the mean time since the most recent relapse onset was 6.4±6.1 months among participants providing these data (n=127, 124 and 121 respectively).

Conclusion: Participants included in the NEOS study are representative of typical PedMS pts and comparable to pts included in the pivotal study of fingolimod in PedMS (PARADIGMS: NCT01892722).

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P1173
Therapeutic Challenges in Pediatric-Onset Multiple Sclerosis: A Real-World Cohort Study

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Introduction: Pediatric-onset multiple sclerosis (POMS) presents unique therapeutic challenges due to its potentially aggressive course contrasting with a limited availability of approved treatments for children. Off-label use of high-efficacy disease-modifying therapies (DMTs) has increased, but real-world data remain scarce.

Objectives/Aims: This study aimed to describe the management strategies and treatment outcomes in a real-life POMS cohort.

Methods: We retrospectively analyzed demographic, clinical and therapeutic data of patients diagnosed with MS before the age of 18, according to the 2017 McDonald criteria, at the Pediatric Neurology department of the National Institute Mongi Ben Hmida of Neurology of Tunis. Patients with a minimal follow-up duration of 12 months after DMT initiation were included. Outcomes included the Expanded Disability Status Scale (EDSS), Progression Index (PI), Annualized Relapse Rate (ARR), and No Evidence of Disease Activity-4 (NEDA-4).

Results: A total of 52 patients were included (female-to-male ratio: 0.37). The median age at onset was 14 years [range: 4–17.5], with 75% presenting post-pubertally. Relapsing-remitting MS accounted for 98% of cases. Median EDSS at diagnosis was 1.0 [0,6].

All patients received DMTs: 73% (n=37) were on first-line therapies at the time of study, 12% (n=6) on second-line therapies, 12% (n=6) on off-label high-efficacy therapies (HET), and 3% had discontinued their treatment (n=2). Rituximab was initiated in seven patients before the age of 18, with a mean delay of 14 months [range: 2–34]. One patient underwent successful de-escalation after maintaining NEDA-4 for two years.

Mean PI on different DMTs was 0.4 ± 0.5 and median ARR was 0,73 [0-3]. Overall, 50% (n=26) of patients achieved NEDA-4, with the following treatments: interferon beta (n=12), glatiramer acetate (n=4), dimethyl fumarate (n=2), rituximab (n=5), fingolimod (n=1), and ocrelizumab (n=1). Patients on HET had significantly lower EDSS on follow-up (p=0,045).

Conclusion: This study underscores the complexity of treating POMS and highlights the real-world use of off-label high-efficacy therapies. Early intervention may improve long-term

outcomes, and the growing evidence should prompt a shift toward a consensus on early aggressive management strategies in pediatric MS.

Disclosure of interest: Maha Jamoussi: nothing to disclose

P1174
Utilization of Electronic Medical Record for Performance of Large Dataset Analysis in Paediatric Onset MS

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Introduction: The digitization of healthcare has transformed clinical research capabilities. In paediatric-onset multiple sclerosis (POMS), where longitudinal data has historically been limited, the adoption of the electronic health record (EHR) has enabled large-scale, retrospective analyses. For the first time, it is now possible to examine long-term disease trajectories, treatment responses, and real-world healthcare utilization patterns in this population.
Objectives/Aims: To establish a robust, longitudinal cohort of POMS patients using structured EHR data, and to characterize patterns of healthcare utilization, disease monitoring, treatment response, and the impact of socioeconomic and geographic factors.
Methods: We retrospectively reviewed patients with POMS at Texas Children's Hospital between 2015 and 2024. Structured clinical and administrative data were extracted using SQL queries from the institutional enterprise data warehouse and visualized using QlikView dashboards. Data sources included inpatient, outpatient, emergency, therapy, and infusion encounters. Key variables included functional scores (EDSS), imaging, laboratory results, medications, procedures, payor information, and geographic indicators.
Results: A total of 189 patients were identified (66% female, 34% male; aged 5 to 26 years), accounting for 7,266 total encounters: 1,620 outpatient neurology visits, 1,970 subspecialty visits, 669 therapy visits (physical, occupational, and speech), 58 emergency visits, and 454 hospital admissions. Patients received 739 disease-modifying infusions. Disease monitoring was comprehensive, with 535 EDSS scores tracked, over 18,000 laboratory tests obtained during infusions, and over 12,000 tests performed at outpatient visits. Hospitalizations generated nearly 30,000 lab results and over 900 discharge medications. Socioeconomic analysis showed that 36% were Medicaid-insured, 34% had private insurance, and 29% had no documented payor. Only 20% of patients lived within 30 kilometers of the hospital.
Conclusion: This large-scale, clinically rich dataset offers unprecedented opportunities for retrospective analysis and predictive modeling in paediatric neuroimmunology. By applying machine learning and artificial intelligence, we aim to uncover longitudinal disease patterns, identify relapse and treatment response predictors, and develop precision strategies that support personalized and equitable care for children with multiple sclerosis.

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Clinical Aspects of MS & Related Diseases - Progression

P1175
Observed associations between educational attainment and disability accumulation in multiple sclerosis are explained by lifestyle-related factors and treatment choices

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Introduction: The impact of socioeconomic factors, including educational attainment, on multiple sclerosis (MS) progression remains uncertain.
Objectives/Aims: We aimed to investigate the association between educational level and MS outcomes, considering the potential confounding/mediating effects of lifestyle factors and treatment choices.
Methods: We analyzed data from the cases in two large, population-based case-control studies in Sweden. Cases with relapsing-onset MS, with an age at disease onset of at least 25 years, and with disease onset after 1995 were included (n=3695). Participants were classified by educational attainment (pre-secondary, secondary, or post-secondary). Clinical outcomes were assessed using the Expanded Disability Status Scale (EDSS), MS Impact Scale (MSIS-29), and Symbol Digit Modalities Test (SDMT). Cox proportional hazards models and linear progression were used to evaluate associations between educational level and disability progression, adjusted for lifestyle factors and treatment.
Results: Participants with lower educational attainment were older at disease onset, had worse clinical status at baseline, and were less frequently treated with high-efficacy therapies. In the unadjusted analysis, lower education was associated with faster disability progression (β 0.026, 95% confidence interval (CI) 0.008 to 0.044), but the association disappeared after adjustment (β 0.001, 95% CI -0.017 to 0.019). Similarly, after adjusting for lifestyle factors and treatment exposure, no significant associations were found between educational attainment and changes in EDSS (confirmed disability worsening hazards ratio (HR) 1.14, 95% CI 0.97-1.33), MSIS-29 scores (HR 1.14, 95% CI 0.90-1.44, for MSIS-physical component and HR 1.00, 95% CI 0.79-1.26 for MSIS-psychological component) or SDMT performance over the 15-year follow-up (HR 1.05, 95% CI 0.76-1.46). Mediation analysis revealed that treatment choices and lifestyle factors together explained approximately 80% of the observed association between educational attainment and disability progression.

Conclusion: Our findings indicate that the observed associations between educational attainment and MS outcomes are primarily explained by differences in lifestyle factors and treatment choices. Educational attainment, per se, does not appear to directly influence MS progression when these factors are accounted for.

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P1176
Predicting risk of progression in MS: Validation of the CLIMB 10-year model

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Introduction: Multiple sclerosis (MS) is a complex disease of uncertain clinical course where patient outcomes range from relatively benign to a more aggressive course and certain patients develop a secondary-progressive (SP) phenotype. Several clinical, imaging and laboratory biomarkers combine to inform on long-term outcomes, however individually, they are insufficient to predict prognosis. Though early use of higher efficacy treatments improves overall outcomes, risk-stratifying patients using comprehensive multivariable models may be useful to develop a more personalized approach to treatment selection and encourage adherence. A predictive model developed from the Comprehensive Longitudinal Investigation of MS at the Brigham and Women's Hospital (CLIMB) cohort identified routinely measured clinical variables that reliably predicted 10-year outcomes but has not been validated in an external cohort.
Objectives/Aims: To validate the CLIMB predictive model in The Ottawa Hospital (TOH) MS patient cohort.
Methods: Patients with relapsing MS at TOH MS Clinic were enrolled in the study if assessed within 3 years of symptom onset. Ten predictor variables were measured at onset and applied to the same least absolute shrinkage and selection operator (LASSO) model identified from CLIMB. The 10-year outcomes assessed for predictive accuracy were retaining benign MS (Expanded Disability Status Scale (EDSS) $\leqslant$2), developing aggressive MS (EDSS $\geqslant$6), and developing SPMS by physician designation.
Results: A total of 151 patients were included with similar characteristics as CLIMB: 71% were female, the mean ($\pm$standard deviation) age was 34.3$\pm$10.0 years, and the mean initial EDSS was 1.9$\pm$1.3. At 10 years, 117 (77.5%) patients retained a benign MS status, 31 (20.5%) patients developed SPMS, and 12 (8.0%) patients developed aggressive MS. The model had limited accuracy in benign MS, predicting the correct diagnosis in 47.2% of those cases, while it performed better at predicting SPMS and aggressive MS, correctly identifying 74.8% and 76.9%, respectively. With a cut-off value of $>$50% probability, the sensitivity of the model was 47.0%, 74.2%, and 83.3% for benign MS, SPMS, and aggressive MS, respectively. The specificity of this model for developing SPMS and aggressive MS is 53.3% and 41.7%, respectively.
Conclusion: The CLIMB model was sensitive at predicting SPMS and aggressive MS in the TOH MS Clinic cohort. It was less capable of predicting benign disease. This model may be useful as a screening tool for identifying at-risk patients.

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P1177
Defining composite markers to predict EDSS progression in SPMS by artificial intelligence

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Introduction: We hypothesized that 1) composite markers predict progression better than single features and 2) definition of composites depends on disability.
Objectives/Aims: By using artificial intelligence (AI) and combining clinical measures, serum biomarkers, cognition, MRI features, and patients' own perception in differentially disabled SPMS patients, we aimed to identify clinically useful composites that predict EDSS progression.
Methods: 61 patients with SPMS were classified as stable or with EDSS worsening over 24 months. To predict progression, 29 features were evaluated by two AI models: incremental feature analysis using Random Forest and logistic regression with balanced class weights. Cross-validation (50×5-fold) was used for robust performance estimation. Features included upper/lower limb function (T25FWT, 9HPT, 6SST), cognition (SDMT, BVMT), serum biomarkers (NFL, GFAP), MRI metrics (volumetry, WM integrity), and PROs (fatigue, quality of life, daily function, working ability).
Results: In patients with moderate disability (EDSS 3.5-4.5, n=26), AI achieved up to 67% accuracy with ⩽3 features. Cognitive processing speed and mental fatigue were the most important with GFAP, NFL, and hand function as top five features in the predicting composites.
In patients with advanced disability (EDSS⩾5.0, n=35), both AI models achieved 80% accuracy with 2-5 features. PROs measuring health and quality of life emerged as major predictors in composites with cognition and walking ability as top five features.
When volumetric/WM integrity MRI metrics were added, hippocampus and T1 black hole volume were strong predictors in the moderate disability group while top features still included cognition and hand function. For patients with advanced disability, walking ability and PROs still remained top features, while hippocampus and corpus callosum volume, cognitive function and GFAP were part of the predicting composites.
Conclusion: Simple composites defined by AI predicted EDSS progression in SPMS over 24 months better than single features and with robust performance. Cognitive processing speed, hand function, and biomarkers were important for moderate disability, while PROs measuring fatigue, walking ability, and cognition were key predictors in more disabled patients. Volumetric MRI features provided substantial additional value, particularly for patients with moderate disability. In summary, while simple composites can be effective in predicting SPMS progression, it is important to consider the level of disability.
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P1178
Integrating multicentre data to explore rwPIRA: Results from the INTONATE-MS consortium

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Introduction: With the wide use of high-efficacy therapy (HET) in people with multiple sclerosis (pwMS), chronic inflammation and degeneration rather than acute inflammation are thought to be key contributors to ongoing neurological deterioration. The challenges and heterogeneity with detecting and measuring progressive symptomatology in clinical settings have limited a deeper understanding of meaningful features that contribute to progression independent of relapse activity in the real world (rwPIRA).
Objectives/Aims: To evaluate real-world measures of "lack of disease stability" (LDS) and define rwPIRA by leveraging a federated infrastructure integrating clinical trial and real-world data.
Methods: Study cohorts from the INTONATE-MS consortium included pwMS on HET (alemtuzumab, natalizumab, ocrelizumab and ofatumumab) from 2015–2022 with at least two longitudinal assessments. Data were collected retrospectively, harmonised and made available for federated analyses. Descriptive statistics assessed for differences in population characteristics across cohorts. Clinical relapses, MRI activity and available clinical outcome measures (e.g. Expanded Disability Status Scale [EDSS], Timed 25-Foot Walk Test [T25FW], Symbol Digit Modalities Test and clinician-assessed Clinical Global Impression [CGI], defined as disease stability or disease worsening) were analysed to assess LDS at each site.
Results: In the current analysis, we assessed 1,995 pwMS on HET across four clinical sites (Uniklinik Münster, Unity Health Toronto, Erasmus Medical Center and University of Pennsylvania). In the combined cohort, the annual rate of relapses was 7.66%, with 4.7% showing MRI activity (new/enlarging T2-weighted lesions or gadolinium enhancement). EDSS was the most frequently assessed outcome with 69.47%

of pwMS having two or more measures, followed by CGI 16.58% and T25FW 8.81%.
Conclusion: After expanding the INTONATE-MS consortium to five sites, we explored the concept of LDS using heterogeneous clinical measures acquired during routine clinical visits. We found great variability in frequency and consistency of outcome measures captured across medical practices. This initial step will enable us to understand how heterogeneous measures could contribute to an operational definition of rwPIRA. This work will allow implementation of more uniform measures of disease progression to optimise treatment strategies and investigate biological mechanisms underlying MS disease progression.

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P1179
Disability profiles in progressive multiple sclerosis reflect the distribution of brain pathology

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Introduction: Progressive multiple sclerosis (MS) presents with heterogeneous cognitive and neurological impairments.
Objectives/Aims: To identify clinical subgroups based on neurological and cognitive features, explore their relationships with conventional MS phenotypes (primary and secondary progressive MS), and associations with the distribution of brain pathology.
Methods: Baseline data from 580 participants in the CONSONANCE (NCT03523858) trial were analysed. Latent profile analysis (LPA) was used to identify clinical subgroups based on expanded disability status scale, 9-hole-peg-test, 25-feet walking test, symbol digit modalities test and brief visuospatial memory test revised scores. Brain lesions, disconnection, and grey matter volumes were quantified from 1.5/3T MRI data. We assessed associations at the macroscale (global measures), microscale (regional features), and mesoscale (independent component analysis, ICA)—to examine structural correlates of disability profiles. SHapley Additive exPlanations (SHAP) analysis identified the most important features contributing to each profile.
Results: LPA revealed three disability profiles: "non-focal" (n=138), "cognitive prominent" (n=181), and "neurological prominent" (n=261). These profiles were independent of age, sex, and MS clinical phenotype ($\chi^2 = 0.675$ after propensity matching for clinical disability and disease duration). SHAP analysis showed that regional MRI features were the most relevant for distinguishing profiles. The "cognitive prominent" profile was associated with independent components reflecting disconnection in the default mode network (DMN), lower grey matter volumes in the posterior cingulate, anterior insula, and prefrontal regions, and lower volumes and disconnection incerebellar vermal lobules, temporal pole, posterior cingulate gyrus, and parietal operculum. The neurological prominent profile was associated with widespread grey matter atrophy and disconnection within default mode network and frontoparietal-motor network, along with lower volumes in the superior frontal gyrus, cerebellum, and globus pallidum.
Conclusion: People with progressive MS exhibit distinct disability profiles that are not captured by conventional clinical phenotypes and reflect the regional rather than global distribution of brain pathology.

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P1180
Depression and Anxiety as Biomarkers of Disability Progression in Primary Progressive MS

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Introduction: Depression and anxiety are highly prevalent and impactful complaints in multiple sclerosis (MS). Beyond their immediate burden, their potential link to disease progression is unclear. We hypothesize that depression and anxiety could be symptoms of progressive disease. As such these symptoms could be useful in identifying people with MS at risk for disability progression.
Objectives/Aims: This study aims to investigate the association between depressive and anxiety symptoms, and neurological disability progression in people with (pw) primary progressive MS (PPMS).
Methods: In our prospective observational cohort study of pwPPMS, depressive and anxiety symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS). Early neurological disability progression was determined by Expanded Disability Status Scale (EDSS) scores at one-year follow-up and sustained disability progression in subsequent years. Secondary outcomes included changes in cognitive function (Symbol Digit Modalities Test, SDMT), walking ability (Timed 25 Foot Walk, T25FW and Patient Determined Disease Steps, PDDS) and arm function (Arm function in Multiple Sclerosis Questionnaire, AMSQ). Multivariable models were used to adjust for potential confounders including baseline EDSS, age, sex, immune-modulating treatment and fatigue severity (Fatigue Severity Scale, FSS).
Results: Among 109 pwPPMS (at time of HADS assessment median age 61 years, interquartile range (IQR) [54-66]; median EDSS 5.5 IQR [4.0-6.5]; 52% female), 16 experienced EDSS progression at the subsequent year. Total HADS scores showed a higher trend in the group with subsequent EDSS progression (median 11, IQR [8-15] versus 7 IQR [5-13], respectively, p=0.077), as did HADS anxiety scores (median 5.0, IQR [2.0-8.0] versus 3.0 IQR [1.0-7.0], p=0.2) and HADS depression scores (median 6.0, IQR [4.0-8.5] versus 4.0, IQR [3.0-7.0], p=0.2). In the group with EDSS progression at the subsequent year, all participants who already had a follow-up visit in the year thereafter, also demonstrated confirmed EDSS progression. Further multivariable analyses and analyses on (other) secondary outcomes are ongoing.
Conclusion: Preliminary findings suggest that pwPPMS with more anxiety and depressive symptoms and higher total scores on the HADS might be at higher risk for early disability worsening. If confirmed in analyses currently underway, symptoms of anxiety and depression could potentially serve as biomarkers for predicting disease progression.

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P1181
Progressive Motor Impairment from Intracerebral Critical Demyelinating Lesions

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Introduction: Critical demyelinating lesions anatomically associated with progressive motor impairment are described in typical progressive MS and those with highly restricted demyelinating lesion burden (e.g., progressive solitary sclerosis). The commonest critical lesion locations are within the spinal cord

lateral column followed by the ventral cervicomedullary junction (CMJ).
Objectives/Aims: Describe people with critical demyelinating lesions of the intracerebral corticospinal tracts.
Methods: Retrospective review of people seen at Mayo MS Clinic from 2000 - 2025, with progressive (⩾1year) upper motor neuron weakness, anatomically associated with a demyelinating corticospinal tract lesion of the: cerebral white matter, internal capsule, or upper brainstem without alternative critical lesion within the lateral spinal cord or cervicomedullary junction. We recorded demographics, demyelinating disease clinical course, Expanded Disability Status Scale (EDSS) at evaluation, MS disease modifying therapies (DMT) and reviewed all magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) studies and neuropathology where performed.
Results: Eighteen people were found to have intracerebral critical demyelinating lesions involving the corticospinal tracts of the: cerebral white matter 12 (67%), internal capsule 3 (17%) and brainstem above the CMJ 3 (17%). Ten were female (56%),17 (94%) were white, median and interquartile range (IQR) for the age of onset of progressive motor impairment was 45.5 (38-52) years. Median and IQR for EDSS at last evaluation was 5.5 (4.0-5.5). Clinically,15 (83%) had progressive spastic hemiparesis, 2 (11%) monoparesis and 1 (6%) quadriparesis and seizures occurred in 3/12 (25%) with cerebral white matter critical lesion. CSF abnormalities consistent with MS were found in 11/16 (69%) where performed. Neuropathology in 7 people showed demyelinating disease in all 5 (biopsy 4, autopsy 1) where conclusive and was inconclusive in 2 biopsies. Seven (39%) received MS DMT.
Conclusion: Intracerebral critical demyelinating lesions along corticospinal tracts associated with progressive motor impairment occur but are comparatively very rare.

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P1182
Predicting EDSS scores using patient-reported outcomes and baseline clinical data in multiple sclerosis: a machine learning approach

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Introduction: The Expanded Disability Status Scale (EDSS) remains the gold standard for assessing disability in multiple sclerosis (MS), but its in-person administration limits its use in telemedicine. Patient-reported outcome measures (PROMs) combined with routinely collected clinical data could support remote EDSS inference, yet their predictive value remains underexplored.
Objectives/Aims: To assess whether PROMs collected in the 6 months preceding outpatient consultations, combined with baseline clinical data, can reliably predict EDSS levels using machine learning (ML) models.
Methods: We analyzed data from 240 MS patients from a second-level hospital in Spain, followed prospectively over 18 months. PROMs included MSIS-29, FSS, HAQ, and Neuro-QoL (cognition, depression). These were combined with baseline variables such as disease duration, age, gender, and evolution form. We trained several regression models (Ridge, Random Forest, Gradient Boosting, and Stacking), treating EDSS as a continuous variable. Due to imbalanced EDSS distribution, manual oversampling was applied to underrepresented categories. Model performance was evaluated using mean squared error (MSE) and R^2.
Results: The Random Forest model trained with PROMs and baseline data achieved an MSE of 0.42 and R^2 of 0.89. Top predictors included disease evolution form (importance: 0.56), HAQ (0.18), weeks since symptom onset (0.09), FSS (0.04), and MSIS-29 (0.02). The model provided clinically acceptable predictions (absolute error ⩽1 EDSS point) in 90% of cases. A tendency to underestimate EDSS was observed, likely due to the overrepresentation of lower scores in the dataset.
Conclusion: PROMs, when combined with basic clinical data, can accurately estimate EDSS levels using ML techniques. These findings support the integration of PROMs into

telemedicine workflows, offering a scalable and reliable alternative to in-person EDSS evaluation.

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P1183
Investigation of correlation between length of Telomeres and clinical severity in Multiple Sclerosis patients

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Introduction: In the last years genomic research led to great increase on our knowledge about the genetic loci involved with genetic susceptibility to MS and its pathogenetic mechanisms, however, the genetic ad epigenetic mechanisms withstanding the different clinical phenotypes, and disease severity still escape our knowledge. Among epigenetic modifications, shortening of telomeres is an important senescence-related changes in the immune system that may impact MS phenotypes, such as disability and progression. So far, the few studies conducted reveal interesting results, as the association of shorter telomeres with disability (EDSS and brain volume) independently of clinical age (Krysko 2019).
Objectives/Aims: We aimed to investigate the association between the length of telomeres and several clinical outcomes (MSSS, EDSS, age at onset).
Methods: We analyzed telomere length in 584 persons with MS (pwMS) (2.07 female:male ratio, 7.3% PP, 3.52 mean MSSS at blood sampling, age: 43.4+/-11.1). Telomere length was evaluated from whole blood DNA with a multiplex real-time PCR, as normalized T/S (telomere/single copy gene) ratio. After QC, we retrieved a sample set of 320 samples. The mean T/S value was 0.71 +/- 0.02, extreme values: 0.66 - 0.82.
Results: As expected, the TS ratio correlated positively with age at blood sampling (R=0.17).
We observed a weak positive correlation between T/S ratio and MSSS (R=0.11), EDSS (R=0.13) and age at onset (R=0.12). Furthermore, we compared MSSS in the extreme categories in telomere length (below the 25th percentile or above the 25th percentile), stratifying our analysis by age at blood sampling (below or above 43, the median age of the samples). In "elder" patients, we observe higher MSSS in pwMS with short telomere (4.31) compared to pwMS with short telomere (3.36), although the difference is not statistically significant (p=0.14) probably due to the small sample size of the subset (32 vs. 25).
Conclusion: Our results suggest that telomere length may contribute to clinical variability in MS. Additional efforts are ongoing to replicate the finding in an independent large cohort of Italian MS patients.
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P1184
Cognitive stability among persons with MS in the modern treatment era

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Introduction: Recent articles suggest prevalent cognitive worsening over time among persons with MS (⩾8 point decrease on Symbol Digit Modalities Test, SDMT). Importantly, mean SDMT change and percent of patients with improvement were not reported in these articles; and one article was based on data from 2001-2017 before the current era of high efficacy therapies.
Objectives/Aims: Characterize cognitive change with the SDMT, including mean change, decline, and improvement, among current patients with MS evaluated within the modern treatment era.
Methods: Persons with MS (n=400; age mean [sd] 40.4 [11.0]; female n=276; 50 progressive) were evaluated in 2016 or later with the oral SDMT once and then for a second time 1.5 to 5.5 years later (mean [sd] 2.7 [0.8] yrs) as part of a research study (n=172) or for clinical monitoring (n=228). Dependent t-test (two-tailed) assessed for performance change. Employing the current approach to meaningful change, decline was operationalized as an ⩾8-point decline; we also classified patients as improved if performance increased ⩾8 points.

Results: SDMT (mean [95%CI]) was 53.3 [52.1, 54.5] and 54.0 [52.7, 55.4] at the first and second evaluations, respectively (normatively at 25th%ile). There was a very small increase in performance (mean change [95%CI], 0.74 [0.05, 1.45]; t[399]=2.09, p=0.037; d=0.10 [0.01, 0.20]). Notably, SDMT change scores closely approximated a normal distribution (skewness: 0.200; kurtosis: 0.732; median [IQR] 0.5 [-4.0, 5.0]). SDMT change was more negative in progressive vs relapsing disease (mean difference [95%CI]: -2.54 [-4.21, -0.91]). Although 10.8% (n=43) of patients met the 8-point threshold for decline, another 13.8% (n=55) improved. Findings were the same when limiting the sample to patients with ⩾2.0 years between assessments (mean change [95%CI], 0.52 [-0.31, 1.36]; t[296]=1.23, p=0.219; d=0.07 [-0.04, 0.19], with decline and improvement in 12.8% (n=38) and 13.5% (n=40) of patients, respectively.
Conclusion: Cognitive difficulties in MS are prevalent and impactful, but recent work on cognitive change reported high percentages of decline without reporting mean change or percent improvement, and data were collected before the current era of high efficacy therapies. Among current patients, SDMT was below expectations when first tested, but with stability thereafter. This may better reflect the cognitive experience of most patients in the modern treatment era.

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P1185
Cognitive Decline in Multiple Sclerosis: Clinical Predictors from a Longitudinal BICAMS-Based Study

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Introduction: Cognitive decline is a frequent and disabling manifestation in people with multiple sclerosis (PwMS), impacting autonomy and overall quality of life. The Brief International Cognitive Assessment for MS (BICAMS) is a validated and widely used tool for detecting early cognitive changes in clinical practice. However, the clinical factors associated with poorer cognitive performance on this battery in specific MS populations remain insufficiently understood.
Objectives/Aims: To assess the prevalence of cognitive decline and identify clinical factors associated with reduced cognitive performance in an Argentinian MS cohort.
Methods: This retrospective cohort study included 150 PwMS evaluated longitudinally. Cognitive decline was defined as a clinically meaningful reduction in at least one BICAMS test: SDMT (>8-point decrease), CVLT-II total learning score (>11-point decrease), or BVMT-R total recall (>7-point decrease). Linear mixed-effects models were used to examine associations between clinical variables and cognitive performance. Logistic regression was conducted to identify predictors of cognitive decline.
Results: The mean age of participants was 39.95 years (SD = 13.27), with a mean education level of 13.36 years (SD = 3.59). Cognitive decline was observed in 39 patients (26%). Specifically, 8 patients (5.3%) declined in CVLT-II, 5 patients (3.3%) in BVMT-R, and 19 patients (12.7%) in SDMT. In the linear mixed-effects model for SDMT, both age and Expanded Disability Status Scale (EDSS) were significant negative predictors of cognitive performance ($p < 0.05$).
Conclusion: Over one-quarter of PwMS experienced cognitive decline, with SDMT being the most sensitive test. Age and EDSS were associated with poorer cognitive performance. These findings support routine cognitive screening in MS using BICAMS and highlight the need for early cognitive monitoring and intervention.

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P1187
Multiple Sclerosis from onset to secondary progression: a 30-years Italian register study

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Introduction: Three decades have passed since the initial approval of disease modifying therapies (DMTs). Ongoing discussion is focused on fundamental aspects of the disease, highlighting a growing division between successes in managing relapsing Multiple Sclerosis (MS) and the persistent challenges posed by disease progression.
Objectives/Aims: The primary outcome was to describe the MS disease course from onset to secondary progression (SP) defined according to a data driven algorithm over 30-years follow up and according to five different eras of disease onset.
Methods: A cohort study on prospectively acquired data from the Italian MS register extracted in November 2023. At the time of data extraction, longitudinal data of 85.992 patients from 137 were available.
The main outcomes included the overall and 10-years incidence rates (IR) for SP conversion. IRs were estimates also within each era. Kaplan-Meier curves for time to SP conversion were represented. Univariable and multivariable proportional hazards Cox regression models.
Results: A total cohort of 9,958 patients was analyzed; 1,364 converted to SP after a mean of 8·5 (SD 5·5) years. A higher rate of patients converting to SP had never been exposed to DMTs (135, 9·9% vs 424,5·2%) than non-converting ones. The treatment coverage was also lower in patients converting to SP than non-converting ones 58·4 (SD 31·5) vs 73·6 (SD 27·6). The 10-years SP incidence rate was 1·26 (1·19·1·32) overall. The rates showed a downward trend among the different era: from 1st era 1·98 (1·73-2-27) to 5th era 1·15 (0·97-1·35). In the multivariable Cox model 10% increase of treatment coverage was associated to 19%lower risk to convert to SP (10% HR=0·89, 95%CI=0·87-0·90).
Conclusion: Further research is needed to explore the roles of inflammation and neurodegeneration in MS progression. These findings could inform clinical practice and health policy, emphasizing the need for continued therapeutic advancements.

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P1188
Multiple sclerosis at Tertiary Hospitals in Johannesburg, South Africa: Clinical features, outcomes and barriers to care

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Introduction: Multiple sclerosis (MS) prevalence, clinical features, and disease progression vary significantly among ethnic groups, yet data from African populations remain limited.
Objectives/Aims: This study addresses this gap by describing the clinical presentation, disease outcomes, and barriers to care for MS patients treated at tertiary hospitals in Johannesburg, South Africa.
Methods: A retrospective cross-sectional review was conducted using patient records from three tertiary hospitals in Johannesburg, South Africa from April 2024 to December 2024. The data included demographics, clinical presentation, Expanded Disability Status Scale (EDSS) scores, time to diagnosis, and treatment status. Data from patients who were first diagnosed in the private healthcare sector was compared to those who have been exclusively seen in the public healthcare sector.
Results: Interim analysis of 55 patients revealed a mean age of 44.04 ± 12.7 years. Most were female (58.2%). Race distribution included African (32.7%), European (27.3%), Mixed Race (14.5%) and Indian (12.7%) participants. Of the 55 patients, 49 had a clearly documented sector of diagnosis with 27 (55.1%) diagnosed in the public sector and 18 (36.7%) in the private sector. RRMS was the most common phenotype (70.91%). Optic nerve involvement was the first area affected among Africans (23.08%) and Indians (42.86%), whereas motor symptoms were more frequent in Europeans (33.33%). The mean delay to diagnosis was significantly longer in the public sector (527.2 days) compared to the private sector (108.7days, p=0.1393). This correlated with higher EDSS scores at diagnosis in the state sector (r=0.82, 95%CI 0.47-0.95). EDSS progression showed no significant difference between racial groups (p=0.8004). Treatment status analysis revealed only 46.15% of patients were currently on therapy, with affordability cited as the major barrier
Conclusion: Our interim findings highlight substantial delays in MS diagnosis and disparities in healthcare access between the public and private healthcare sectors, with resultant greater disease severity at diagnosis in the public sector. Further research with larger sample sizes is necessary to elucidate these findings comprehensively and address barriers impacting patient outcomes.

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P1189
Multiple Sclerosis Disease Activity in Patients with Concomitant Human Immunodeficiency Virus Infection: A Case Series Analysis from Portugal

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Introduction: The most recent research indicates that people living with Human Immunodeficiency Virus (HIV) infection may have a lower incidence and possibly slower progression of multiple sclerosis (MS). This raises interest in the potential role of HIV-related immunosuppression and anti-retroviral treatment (TARV) in modulating MS risk and activity.
Objectives/Aims: This study aims to investigate the clinical and radiological progression of MS in patients with coexisting HIV infection, and to assess the association between specific HIV-related factors (CD4 counts, viral load) and MS disease activity.
Methods: We conducted a national multicenter cross-sectional study of adults with a confirmed diagnosis of MS and HIV from neurology outpatient clinics of the collaborating hospitals. Clinical and demographic data were collected and analyzed using descriptive statistics and Pearson correlation.
Results: A total of 10 patients with MS and HIV were identified (60% male; median age 48.5 ± 8.0 years). The majority had relapsing-remitting MS (90%) and was infected with HIV-1 (90%). All were receiving TARV and had been treated with disease-modifying therapies, including interferon beta, glatiramer acetate, natalizumab, fingolimod, ocrelizumab, cladribine and dimethyl fumarate. In 9 cases, MS occurred prior to HIV infection at a mean interval of 7.7 (± 7.4) years. Patients were followed for a mean of 14.7(± 8.8) years after MS diagnosis. After HIV infection: MS median relapse rate dropped from 2.5 to 0.5, 70% of the patients had no magnetic resonance imaging (MRI) activity and mean disability increased modestly from 1.78 at diagnosis to 2.7 over follow-up on the Expanded Disability Status Scale (EDSS). A moderate positive correlation was observed between CD4+ count and post-HIV relapse frequency ($r = 0.58$, $p = 0.133$), and between viral load and EDSS ($r = 0.41$, $p = 0.314$), though neither reached statistical significance. Notably, only one relapse occurred after starting TARV.
Conclusion: The combination of reduced relapse rate, minimal radiological activity, and modest disability progression suggests a trend towards reduced disease activity in patients with MS with concomitant treated HIV infection. The timing of relapses, mostly occurring before TARV initiation, suggests a stabilizing role of treatment. Although limited by sample size, these results align with previous observations that immune status and treatment timing may modulate MS progression in people with HIV infection.

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P1190
Neurofilament Light Chain Predict Disease Activity and Disability Progression in Korean Patients with MS

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Introduction: Serum neurofilament light chain (sNfL) has been identified as a useful biomarker for disease activity, prognosis, and treatment response in patients with multiple sclerosis (pwMS). However, its utility in Asian pwMS remains underexplored.
Objectives/Aims: This study investigates the predictive value of sNfL for disease activity and long-term disability as well as the applicability of Western-derived z-scores in Korean MS patients.
Methods: We analyzed 169 blood samples from 117 Korean pwMS across three referral hospitals. Baseline samples were obtained within one year of disease onset, with follow-up samples at least three months later. Age- and BMI-adjusted z-scores of baseline sNfL were analyzed for correlations with disease activity and prognosis, while delta z-scores —calculated as the difference between baseline and follow-up z-scores— were used to evaluate disease progression.
Results: Higher baseline sNfL level and z-scores were significantly associated with greater radiological disease activity, including T2 lesion burden and gadolinium-enhancing lesions. Patients with a baseline sNfL z-score >2.86 had a 2.34-fold higher relapse risk within two years. Additionally, a delta z-score <1, reflecting persistently elevated sNfL levels despite disease-modifying treatment, was strongly associated with an increased risk of reaching confirmed EDSS 3 (HR 15.56, 95% CI 1.49–398.1).
Conclusion: These findings support sNfL as a useful biomarker for predicting disease activity and long-term outcomes in Korean pwMS. Elevated baseline sNfL levels reflect active disease and a higher risk of relapse, while persistently elevated sNfL following treatment initiation is associated with worse long-term disability outcomes.

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P1191
Low Sun Exposure, Comorbidities and Smoking Aggravates the Disease Progression in Patient with Multiple Sclerosis – A Four-Year Prospective Observational Cohort Study

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Introduction: MS is a multifaceted disease resulting from both genetic and environmental factors leading to central nervous system (CNS) inflammation and degeneration. Currently, available disease-modifying therapies (DMTs) substantially reduce disease activity, but MS remains uncurable.
Objectives/Aims: Identifying modifiable clinical and environmental risk factors of disease progression is essential to enhance disease outcomes.
Methods: 132 individuals (74.2% women) with relapsing-remitting MS (RRMS) treated with different DMTs were enrolled in the study. The mean age was 45.9 years (± 10.9) and the median Expanded Disability Status Scale (EDSS) score was 2.0 (lower/upper quartile 1.5 – 6.0). The participants were prospectively observed for 48 months. At baseline and every 12-months, a thorough evaluation of the number of relapses, EDSS score, and radiological outcomes including new/enlarged T2-weighted lesions, gadolinium-enhancing lesions (GELs), and atrophy assessment with multiple 2D measurements in magnetic resonance imaging (MRI), as well as detailed medical history, assessment of clinical and environmental factors, sun exposure, smoking and 25-hydroxyvitamin D (25(OH)D) serum level were performed.
Results: Subjects with comorbidities were more likely to have a relapse during the whole follow-up (39.4% (95% of confidence interval (CI): 30.2 – 49.3%) vs 27.5% (95% CI: 23.9 – 31.4%); $p < 0.05$) and had increasing probability of GELs through the follow-up (30.0%, 20.0%, 25.0%, 24.9%, 56.8% vs 16.0%, 21.8%. 15.2%, 22.2%, 29.5%). Smoking was also associated with increased probability of GELs (29.5% (95% CI: 22.1 – 38.2%) vs 20.9% (95% CI: 17.6 – 24.6%); $p < 0.05$). Additionally, subjects with adequate sun exposure had significantly ($p < 0.001$) lower EDSS at every time point of observation. The gender, obesity and serum level of 25(OH)D did not influence the disease progression.
Conclusion: Comorbidities and smoking enhanced the clinical and radiological disease activity whereas sun exposure but not 25(OH)D serum level reduced the disability progression in MS.

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P1192
Association of disability progression with Patient Reported Outcome measures in the OFSEP-HD cohort

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Introduction: Disability progression remains a major challenge in MS patients care and we need fine outcomes to detect subtle effects of potential remyelinating drugs in future clinical trials. The assessment of different progression definitions and their association with Patient Reported Outcomes (PRO) could provide a better understanding of which progression definition is better correlated to quality of life.

Objectives/Aims: Our main objective is to assess the risk of disability progression at 2 years in the High Definition French Registry database (OFSEP-HD), using different definitions of progression. We will also assess the associations between PRO evolution and risk of progression, based on the different definitions.
Methods: All MS patients with at least 2 visits (baseline and 2-year follow-up) were included. Disability Accumulation (DA) was defined (i) using EDSS increase only or (ii) using a composite score based on EDSS increase and/or increase of at least 20% in the Timed-25 Foot Walk (T25W), and/or increase of at least 20% in the 9-Hole Peg Test (9HPT) on one hand and/or decrease below the 5th percentile of the Computerized Speed Cognitive Test (CSCT). DA was classified as relapse-associated worsening (RAW) if one or more clinical relapses had been reported in the interval between the CDA event and the reference EDSS measurement, and as progression independent of relapse-activity (PIRA) otherwise. The Multiple Sclerosis International Quality of Life questionnaire (MusiQoL), the SF-12 and EQ-5D were collected at baseline and Y2. First, we measured proportions of patients having a progression event according to the different definitions, overall and according to MS form. Then, we compared PRO changes between progressors and non-progressors.
Results: 1618 MS patients were included (1294 with a relapsing form (RMS), 324 with a primary/secondary progressive form (PMS)). Mean age at baseline was 42±11 years old, median disease duration was 9 years, and 84% of patients were treated at baseline (89% RMS, 65% PMS). Overall, 17% of patients (13% RMS, 36% PMS) presented EDSS-based DA at Y2, and 39% (32% RMS, 67% PMS) based on the composite score. Progressors had a significantly impaired quality of life at baseline compared to non-progressors and the impairment significantly (except for MUSIQOL) increased at Y2 (while it was stable for non-progressors).
Conclusion: Preliminary results confirmed that disability progression based upon different definitions has an impact on PRO.

Disclosure of interest: The authors have no disclosures

P1194
Age-MicroRNA correlation is different in people with MS vs Healthy controls

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Introduction: Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease in which immune dysregulation is a key factor. Regulation of the Immune transcriptome in the disease has been shown as key to understand the disease. MicroRNA are small non-coding RNA(sncRNA) that regulate the transcriptome in MS. Immunosenescence is an important player in MS.
Objectives/Aims: We study the sncRNA expression in 150 PBMS samples (75 Health and 75 persons with MS(pwMS)) with an age range of 20-80 years old.
Methods: Blood samples were collected from pwMS (75) and healthy controls (HCs, 75) after informed consent. RNA was extracted from the PBMC and after a quality control of the RNA by Bionalalyzer, a library for small RNA was produced and sequenced by Illumina equipment. Analysis has been done through Nf-Core using the scrnaseq pipeline and a linear regression analysis between microRNA and age was done with own python scripts.
Results: From the 2332 trasncripts analyzed, 199 sncRNA correlate with a significant p-value (<0.05) in the HC group, while 81 were significant in the MS group. 6 of them are coincident in both groups, and from these 3 (miR-153-p, 1271-5p and 21-5p) show different slope directions between MS and HC, although the R values show a modest effect. 196 and 75 sncRNA correlate with the age exclusively in each group.
Conclusion: Our findings reveal age-related microRNA expression showing a different firm between pwMS and HC. 3 of the studied sncRNA show opposite significant correlation between the groups, while each group shows its unique correlation pattern. The influence of age in the transcription regulation is clear and dependent of the disease status.

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P1196
Metformin for multiple sclerosis: a living systematic review

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Introduction: Disease-modifying therapies are used to reduce immune response in MS, with the most effective ones nearly suppressing acute disease activity and preventing relapse-related symptoms. However, most have failed to prevent the gradual disability progression. Researchers are now investigating medications originally used for other conditions, like metformin (used for type 2 diabetes), as potential neuroprotective treatment in MS slowing down disability worsening.
Objectives/Aims: To continually monitor and assess the related evidence, we initiated a living systematic review on the effectiveness of metformin treatment in MS.
Methods: We include any randomised trial assessing metformin on any clinical outcome, patient-reported outcome, and fluid, imaging or digital biomarker in adults with any type of MS (for detailed methods see: PROSPERO CRD42024607356). Twice a year (January and July), we search MEDLINE, Embase, CENTRAL, Clinicaltrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP), and cited and citing articles of any eligible trial report. The search results are continually and publicly accessible on Open Science Framework (OSF; https://osf.io/gyu8c/). Risk of bias and the certainty of evidence are assessed once a meaningful number of trial results is available.

Results: Our first search cycle in January 2025 retrieved 12 reports on 6 trials (ISRCTN14048364/OCTOPUS; NCT05131828/CCMR Two; NCT05893225/MACSiMiSE-BRAIN; NCT05298670/MSMet; NCT05349474; NCT06463743) from Belgium, Egypt, the United Kingdom, and the United States that were initiated between 2022 and 2024 and planned to observe a median of 75 persons with MS (total 1544) for a median follow-up of 12 months (6-60 months). We identified for one trial (NCT05298670) final results and for another trial (NCT05131828) preliminary results. They suggest no clear effect on immunological, imaging, and clinical outcomes (NCT05298670) but positive effects on neurofilament light chain levels (NCT05131828).
Conclusion: Currently, there is no conclusive trial evidence on health-related benefits and harms of using metformin in treating MS. At the conference, we will provide an integrated overview of the evidence with added results retrieved by the updated search in July 2025.

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P1197
Evaluation of Fatigue, Depression, Sleep Quality, and Quality of Life in Multiple Sclerosis Patients: A 5-Year Follow-Up Study

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Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative disease that significantly impacts patients' physical and mental well-being, making it essential to evaluate long-term changes in fatigue, depression, sleep quality, and quality of life over a 5-year follow-up period to better understand disease progression and improve patient care.
Objectives/Aims: This study aims to evaluate 5-year changes in fatigue, depression, sleep quality, and quality of life in MS patients to better understand disease progression.
Methods: This descriptive longitudinal study was conducted with 62 multiple sclerosis (MS) patients followed at a university hospital neurology outpatient clinic. The Fatigue Severity Scale (FSS), Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Index (PSQI), and Multiple Sclerosis Quality of Life-54 (MSQoL-54) questionnaires, which were initially administered in 2019, were readministered in 2024 to the same patient cohort to assess longitudinal changes. From an original cohort of 178 patients enrolled in 2019, follow-up data were obtained from 62 participants (34.8% retention rate) who completed the five-year assessment. All statistical tests were conducted with a 95% confidence interval, and significance was set at $p<0.05$.
Results: This longitudinal study evaluated 62 MS patients (mean age 38.8±9.8 years; 56.5% female) over a 5-year period. Comparative analysis revealed no significant changes in fatigue severity (FSS: 4.8±1.5 to 4.6±1.8; p=0.261) or depression scores (BDI: 13.9±11.1 to 12.3±8.4; p=0.217). However, sleep quality significantly deteriorated (PSQI: 6.8±2.6 to 8.0±4.4; p=0.011), and mental health-related quality of life declined markedly (MSQoL-54 mental: 52.7±16.4 to 44.5±20.1; p=0.003). Physical health-related quality of life showed a non-significant reduction (55.1±20.4 to 50.9±21.1; p=0.090).
Conclusion: This longitudinal study demonstrates significant declines in sleep quality and mental health-related quality of life among MS patients, while physical health and symptom burden (fatigue and depression) remained stable. The findings highlight the progressive nature of sleep and psychosocial impairments in MS, independent of physical disability progression. These results underscore the need for regular monitoring of sleep and mental health in MS clinical practice, with particular attention to long-term psychological well-being.

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P1198
Assessing Clinical, Radiological, and Biochemical Predictors of PIRA in Rituximab-Treated Cohort of Multiple Sclerosis Patients: A Real-World Study from India

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Introduction: Progression independent of relapse activity (PIRA) significantly contributes to disability in MS, even among patients on high-efficacy therapies like rituximab.
Objectives/Aims: To evaluate PIRA-related disability in rituximab-treated MS patients and identify clinical, radiological, and biochemical predictors.
Methods: MS patients on rituximab ⩾2 years were included. Confirmed disability accumulation (CDA) was defined as a ⩾12-week sustained EDSS increase of ⩾1.0 (baseline EDSS ⩽5.5) or ⩾0.5 (>5.5). PIRA was CDA without relapse in the prior 90 days. Pre-treatment MRIs were assessed for lesion topography: perivenular (central vein sign/anatomical location) or meningeal (subpial, cortical/juxtacortical). Spinal lesions were central (all quadrants) or segmental (⩽2 quadrants). Brain volumes were compared with age-matched healthy Indian controls. Serum neurofilament light chain (NfL) was measured via ELISA in patients with no relapses in the previous 3 months. Statistical tests included Chi-square, ANOVA, Kruskal-Wallis, Bonferroni correction, and Mann-Whitney U.

Results: Ninety-one patients (76% female, median age 35 [IQR 33–37], median follow-up 6 years) were included. PIRA occurred in 39 patients (43%). Mean EDSS rose from 2.2 ± 1.7 to 3.7 ± 1.8. ARR significantly decreased post-rituximab (0.45 to 0.03, p = 0.002). Clinical predictors of PIRA were older age(38.8 vs 32.2 years, p = 0.006) and motor onset (25.6% vs 4.4%,p = 0.022). Radiological predictors included higher lesion volume (16.8 vs 6.8 cm3, p = 0.01), mixed lesion topography—i.e., involvement of both meningeal and perivenular regions (meningeal-to-perivenular ratio 0.5–1.0, p = 0.01), central-to-segmental spinal lesion ratio ⩾1 (p = 0.01), paramagnetic rim lesions (4.05 vs 1.13, p = 0.01), and reduced volumes of the caudate, putamen, and thalamus (all p ⩽ 0.02). Elevated NfL (1.77 vs 0.41 ng/ml, p = 0.01) also correlated with PIRA.
Conclusion: PIRA was the main driver of disability despite rituximab. Older age, motor onset, mixed lesion topography involving both meningeal and perivenular regions, central spinal lesions, deep grey matter atrophy, and elevated NfL may help predict progression.

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Clinical aspects of MS & Related Diseases - Epidemiology

P1199
10-Year Trend Analysis of Medicare Payment in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder Inpatient Hospital Admission

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Introduction: In 2019, direct medical costs associated with multiple sclerosis (MS) in the United States were estimated at $63.3 billion. Although comparable large-scale economic evaluations are lacking for neuromyelitis optica spectrum disorder (NMOSD), a 2019 analysis estimated the average annual all-cause healthcare cost per individual with NMOSD to be $60,599. However, the specific costs associated with inpatient care for both MS and NMOSD remain largely unknown. Furthermore, given that the Centers for Medicare & Medicaid Services (CMS) shoulder a substantial portion of federal healthcare expenditures, the total federal costs related to inpatient care for MS and NMOSD have not been thoroughly investigated.
Objectives/Aims: Describe the 10-year trend in Hospital and Medicare Payments for MS and NMOSD from 2013 to 2022 at the national level.
Methods: This is a retrospective analysis of the 2013 to 2022 Medicare Inpatient Hospitals - by Provider and Service Data that provides inpatient hospital charges by Medicare Severity Diagnosis Related Group (DRG) in MS and NMOSD admission (DRG: 58-60). Percentage change in MS and NMOSD admission cost adjusted for healthcare inflation between 2013-14 to 2021-22 weighted for the number in each MS and NMOSD related-DRG was included in the analysis.
Results: Between 2013 and 2022, nationwide, there were 1,554,280 unique MS and NMOSD-related inpatient hospital claims, resulting in Medicare payments totaling $14.7 billion from Medicare Services. In 2013, the mean Medicare payment, weighted per DRG for each MS and NMOSD admission, was $7,667.50 (95% CI: $7,628.23-$7,706.76), while the mean hospital-covered charges per admission were $37,605.59 (95% CI: $37,364.96-$37,846.23). By 2022, after adjusting for healthcare inflation, the mean Medicare payment, weighted per MS and NMOSD DRG, decreased to $7,603.79 (95% CI: $7,524.31-$7,683.27), but the mean hospital-covered charges per admission were increased to $48,607.76 (95% CI: $48,012.17-$49,203.34).
Conclusion: Nationwide, inflation-adjusted inpatient hospital charges for MS and NMOSD admissions have increased by 29.3% over the past decade. In contrast, inflation-adjusted Medicare reimbursements are comparable and slightly declined by 8.4% during the same period. Moreover, the proportion of inpatient hospital expenditures covered by Medicare decreased from 20.4% in 2013 to 15.6% in 2022, placing an increasing financial burden on the healthcare system.

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P1200
Turning Data into Action: How the ReMuS Registry's Benchmarking Framework Drives MS Care Improvement in the Czech Republic

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Introduction: The ReMuS registry is a comprehensive nationwide database collecting longitudinal clinical data on patients with multiple sclerosis (MS) across all 15 specialised centres in the Czech Republic. As of 31 December 2024, ReMuS includes 23,398 MS patients and 542,590 clinical visits, making it one of the largest and most detailed MS datasets in Europe. Since 2020, benchmarking has supported quality assurance across the registry.

Objectives/Aims: This analysis evaluates the impact of benchmarking on data collection, clinical practices, and its broader utilisation.

Methods: Benchmarking reports are generated every six months for each MS site and are structured into six domains: (1) patient characteristics, (2) visit completeness, (3) relapse characteristics, (4) DMT patterns, (5) adverse events, and (6) pregnancies. Each report includes over 60 indicators, 40–50 pages of site-specific and comparative data, and five-year longitudinal trends. Visualisations use confidence bands (±1.5 standard deviations from the registry mean). Each centre sees its own data unblinded, while others are presented by indicator-specific ranking only. Year-on-year comparisons enable trend evaluation. The present analysis compares indicators extracted as of 31 December 2020 and 31 December 2024.

Results: Between 2020 and 2024, centres improved data completeness and reporting consistency. EDSS missingness decreased from 0.03% to 0.02%, and FSS from 5.97% to 3.12%; in total, 525,672 visits now include both EDSS and FSS records. Over the same period, the pregnancy capture rate among women of childbearing age increased by more than 15%, reflecting improved data quality. In total, 8,062 pregnancies have been recorded across all MS patients included in the registry. The proportion of relapses managed during hospitalisation decreased from 14.35% to 12.20%—a relative reduction of 14.9%—indicating a gradual shift towards outpatient care. Centres have used the results not only for internal audits, but also for budget reallocations or external negotiations—for example, to secure staffing support, expand MRI services, or improve DMT reimbursement. The share of high-efficacy DMTs among treated patients rose from 32.2% to 60.6%.

Conclusion: Benchmarking within ReMuS measurably improves data quality and alignment with care standards. It enables inter-centre comparisons, supports local decision-making, and offers a scalable model for registry-driven quality assurance. The concept is transferable to other national or regional registry settings.

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P1201
Causal association of sleep-related traits with multiple sclerosis risk and severity: Mendelian randomisation studies

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Introduction: Sleep disorders are elevated in multiple sclerosis (MS), but whether such associations reflect causal relationships with MS risk and/or severity are unknown.
Objectives/Aims: To investigate if sleep-related traits are causally associated with MS risk and/or severity.
Methods: Mendelian randomisation (MR) studies were conducted using summary statistics from the UK Biobank and the International MS Genetic Consortium genome-wide association studies (GWAS) on European populations. GWAS exposure traits (from UKB category 100057, N>433,000) were: (i) sleep duration; (ii) insomnia; (iii) chronotype (morningness); (iv) narcolepsy; and (v) nap during day. Single nucleotide polymorphisms (SNPs) associated with exposure traits ($p<5e-8$, and linkage disequilibrium clumping with r2=0.05, distance=100 kbps) constituted genetic instrumental variables of those traits. Strength of instruments was confirmed with F-statistics. Outcomes were (i) MS diagnosis (47,429 cases, 68,374 controls) and (ii) age-related MS severity score (12,584 cases). Various MR methods (e.g., inverse-variance weighted [IVW], MR-Egger, weighted median, MR-PRESSO) were explored. Directionality, heterogeneity, outlier influence, and horizontal pleiotropy (HP) were investigated with respective methods (e.g., Steiger test, Cochrane's Q, MR-Egger intercept, leave-one-out, MR-PRESSO).
Results: Daytime napping was causally associated with increased MS risk (MR-IVW β [SE]: 0.80 [0.18], $p<0.0001$), but Q, MR-Egger intercept, and MR-PRESSO indicated presence of significant heterogeneity and HP ($p<0.05$). Still, significance persisted with MR-weighted median, MR-Egger, and MR-PRESSO—HP-robust methods. Longer sleep duration (MR-IVW β [SE]: 0.30 [0.09], $p<0.001$), and being more of a morning person (MR-IVW β [SE]: 0.12 [0.04], $p=0.005$) were causally associated with more severe MS. Results, although not statistically-significant, also suggested that daytime napping may be associated with MS severity (MR-IVW β [SE]: 0.18 [0.10], $p=0.057$). Regarding daytime napping, Q and MR-Egger intercept (but not MR-PRESSO) indicated presence of heterogeneity and HP; results turned significant ($p<0.05$) with MR-weighted median and MR-Egger methods, but not with MR-PRESSO.
Conclusion: This is the first study to provide evidence that specific sleep-related traits causally confer increased MS risk and greater MS severity. Underlying mechanism(s) remain to be elucidated. Meanwhile, findings emphasise the need to address sleep improvement in persons at risk of, and living with MS.

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P1202
Refining clinical prognostic factors in adult-onset multiple sclerosis: a systematic literature review

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Introduction: Predicting the heterogeneous clinical course of multiple sclerosis (MS) has proven to be challenging. Thus, in clinical practice, prognostic factor evaluation becomes essential.

Objectives/Aims: To provide a comprehensive and up-to-date review of clinical and radiological prognostic factors in adult-onset MS. This study falls within the framework of the PROMISING study (Enhancement and Strengthening of Biomedical Research in the NHS–PNRR-MAD-2022-12376868), which aims to predict MS disease progression through the development of a prognostic score.
Methods: A systemic search was conducted in the two primary academic databases, PubMed and Google Scholar. The time frame considered was 2015–2024 and stringent inclusion criteria were applied to guarantee applicability of this review, thus retrieving 72 articles including real-world data of large MS cohorts. The analysis focused on the association of demographic, clinical and magnetic resonance (MRI) data with outcomes of disease activity and progression. For each prognostic factor identified, the following variables were analyzed: study designs, population sizes, effect measures, prognostic validity and strength of evidence.
Results: Age consistently emerges as a strong determinant, with older patients exhibiting increased global disability and a heightened risk (HR 2.98, 95% CI 2.60-3.41; $p < 0.001$) of progression independent of relapse activity (PIRA), while younger patients show greater responsiveness to disease modifying treatment (DMTs) and improved outcomes. Delayed DMT initiation is associated with higher risk (HR 1.75, 95% CI 1.28-2.39; $p < 0.001$) of disability, dependent and independent of neuroinflammation. MRI parameters, particularly the burden and location of T2 lesions and spinal cord involvement, have been associated with long-term disability accumulation, often independently of relapse activity, and drove treatment changes. Secondary progressive conversion risk is higher in patients with multifocal symptoms, higher Expanded Disability Status Scale scores at onset, and with elevated relapse rates ($p < 0.0001$). Fluid biomarkers are linked to immune-related pathways, predict future impairment and correlate with clinical and imaging outcomes of MS severity.
Conclusion: Several biomarkers have crucial prognostic relevance in guiding MS clinical management. A systematic prognostic assessment could assist in stratifying the risk of disability accumulation and identifying strategies to improve outcomes.

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P1203
High prevalence of individuals with MS who want help for their limiting bladder problems

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Introduction: Individuals with multiple sclerosis (MS) who experience bladder problems have shown to report significantly lower well-being. This highlights the importance of clarifying the extent of unmet bladder needs among individuals with MS who require professional healthcare.
Objectives/Aims: In this cross-sectional study, the aim is to explore the unmet need of wanting help for one's unresolved bladder problems among individuals with MS.
Methods: An online survey was disseminated targeting individuals with MS via social media channels, healthcare professionals, and Coloplast user databases in France, Germany, Italy, and UK. Descriptive data were analysed and obtained from individuals reporting about their lives with MS, treatment of MS, and bladder awareness and problems, incl. assessment of overactive bladder using the validated Actionable Bladder Symptom Screening Tool (ABSST).
Results: Among 1410 individuals with MS who consider themselves as having bladder problems, 37% want help for their bladder problems despite not having sufficient symptoms to be defined as needing treatment for overactive bladder based on ABSST. Of those who feel embarrassed because of their bladder problems, 54% want help, while 54% of those who feel that activities with friends and family have been limited want help, and 55% want help among those feeling that their ability to work outside their home has been limited. Among individuals who are self-managing their bladder problems without professional healthcare, 44% want help, and 57% of those with unresolved bladder problems want help. There are 52% of those diagnosed with MS 0-4 years ago who want help, 52% want help among those diagnosed 5-10 years ago, 47% want help among those diagnosed 11-15 years ago, and 49% of those diagnosed more than 15 years ago want help.
Conclusion: The findings show that there is a high prevalence of individuals with MS who want help for their bladder problems which they feel are limiting their daily lives, and many are self-managing their bladder problems without help from healthcare professionals. Despite how long individuals lived with their MS diagnosis, many report wanting help, indicating that there may still be unmet needs to be considered in terms of unresolved bladder problems that are yet to be identified and managed with help from healthcare professionals.

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P1204
The frequency and characteristics of multiple sclerosis misdiagnosis referrals to a tertiary center in Saudi Arabia

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Introduction: Accurate diagnosis of multiple sclerosis (MS) remains a clinical challenge, particularly in tertiary care settings

where referrals often include cases with atypical presentations. MS Misdiagnosis can lead to unnecessary treatment and delay appropriate care.
Objectives/Aims: This study aims to evaluate the frequency and patterns of MS misdiagnosis among patients referred to a specialized MS center in Saudi Arabia and investigate the financial burden due to MS misdiagnosis.
Methods: We retrospectively reviewed 416 new referrals to the MS clinic at King Fahad Medical City in Saudi Arabia, from 2018 to 2024. Eleven patients were excluded due to unavailable MRI or clinical data. New referrals were categorized as: confirmed MS diagnosis (n=255), possible MS for further evaluation (n=137), clinically isolated syndrome (CIS; n=6), radiologically isolated syndrome (RIS; n=5), and two cases lacking data from the referring physician. Final diagnoses were determined through careful review of clinical, radiologic, and laboratory findings by 3 expert neuroimmunologists.
Results: Of the 255 patients referred with a confirmed MS diagnosis, 16 (6.3%) patients were found to have been misdiagnosed with MS. The most common alternative diagnosis found was migraine and non-specific white matter changes. Direct medication cost for this group of misdiagnosed patients were 225638 USD. Among the 137 patients referred for suspected MS, 34 (24.8%) were diagnosed with alternative conditions. Common alternative diagnoses included migraine, nonspecific white matter lesions, small vessel disease, neuromyelitis optica spectrum disorder (NMOSD), and genetic leukoencephalopathies.
Conclusion: Misdiagnosis of MS was identified in about 6.3% of new confirmed MS referrals to our tetiary center. These findings highlight the need for rigorous application of MS diagnostic criteria and enhanced training among general neurologists. Improved referral pathways and early specialist input may reduce diagnostic errors and ensure timely, appropriate care for demyelinating disorders and ultimately reducing health care costs.

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P1205
Career trajectories among people with multiple sclerosis in Sweden: a register-based follow-up study

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Introduction: The negative impact of multiple sclerosis (MS) on employment and income among people with MS (PwMS) has been previously reported. However, there is a need for long-term and recent data on changes in career over time among PwMS.
Objectives/Aims: To assess career trajectories among PwMS and to determine sociodemographic and clinical predictors associated with them.
Methods: A longitudinal register-based study of 1842 PwMS diagnosed during the years 2004 to 2007 were analyzed to determine career trajectory over a 13-year period from 3 years before to 10 years after diagnosis. The odds of changes in career over time was calculated using multinomial logistic regression analysis.
Results: In terms of career trajectories, while a majority of the PwMS remained in occupations of comparable qualification or moved into those of higher qualifications, a substantial proportion entered sickness absence and/or disability pension (SADP) or left the work force. Older age was associated with leaving work or SADP, higher education was associated with lower odds of SADP and jobs of higher qualification. In the transition from three years before, to the year of diagnosis, more than half of the PwMS (54.5%) remained in occupations requiring a comparable level of qualification. A proportion of PwMS changed to jobs requiring lower levels of qualification (3.2%), while, 4.7% changed to jobs requiring higher levels of qualification. The trajectory in occupation from diagnosis to the fifth year of follow-up showed that about two-thirds of the PwMS remained in the same qualification level this proportion decreased over the follow-up time.
Conclusion: The present study showed long-term career trajectories among PwMS in Sweden, suggesting most PwMS initially maintain their qualification level, although occupational stability decreases over time as the disease progresses. Baseline characteristics such as education, occupation, SADP days and EDSS score were important predictors of career trajectories over the follow-up.

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P1206
Multiple Sclerosis Disability Progression and Its Predictors Over Five Decades: A Retrospective Cohort Study

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Introduction: Long-term data on disability progression in real-world MS populations remain limited. Understanding these trajectories and their predictors may support more accurate risk stratification and personalized care.

Objectives/Aims: To describe long-term disability outcomes and identify predictors of EDSS milestones and secondary progression (SPMS) in a large relapsing MS (RRMS) cohort.
Methods: This retrospective study included patients from the Montreal University Health Center's MS Clinic registry, diagnosed with RRMS, SPMS, or clinically isolated syndrome (CIS) between 1976 and 2020. Outcomes were time to EDSS 3, 4, 6, 8, and transition to SPMS. Cox proportional hazards models assessed associations with sex, age at onset, period at onset, relapse frequency, treatment exposure, treatment timing, and pregnancy.
Results: A total of 2,769 patients were included (75.8% women), with a median age at onset of 29.8 years and median follow-up of 24.6 years. Median time to EDSS 3, 4, 6, 8, and SPMS was 13.2, 15.1, 16.6, 18.8, and X years*, respectively. Male sex was associated with significantly increased risk of reaching all EDSS milestones and earlier SPMS. Age at onset ⩾30 years predicted faster progression to EDSS 3, 4, 6, and SPMS. Two or more relapses per year was associated to increased risk of progression at all EDSS levels and SPMS. Pregnancy after onset was associated with slower progression to EDSS 4 (HR:0.81), EDSS 6 (HR:0.76), and EDSS 8 (HR:0.70). Patients exposed to both low- and high-efficacy therapies (LET-HET) progressed faster. LET alone showed no significant effect. Early treatment (<2 years) was not associated with delayed progression.
Conclusion: Descriptive analyses illustrate overall disability trajectory, while inferential models highlight male sex, older onset, and number of relapses as key predictors. Pregnancy after onset may be protective. Apparent lack of treatment benefit likely reflects confounding, underscoring the need for cautious interpretation in observational data.

Disclosure of interest: Tennessee Quevillon: Nothing to disclose.

P1207
The Invisible Enemy: Shedding Light on Antibody-Negative Autoimmune Encephalitis

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Introduction: Antibody-negative autoimmune encephalitis (AE-) are frequent forms of non-demyelinating AE cases. Despite diagnostic criteria proposed in 2016, these forms remain diagnostically elusive, often delaying access to effective treatments. While antibody-positive AE (AE+) has been extensively characterized, AE- remains underexplored.
Objectives/Aims: To delineate the clinical, radiological, and biological features that distinguish AE- from AE+.
Methods: We built a multicenter database from the three French AE reference centers (Lyon, Paris, Toulouse), including patients diagnosed between 2016 and 2023, and followed for 2 years. This preliminary analysis includes 139 patients from Paris and Toulouse.
Results: We identified 110 AE+ (79%) and 29 AE- (21%). Mean age (56 years old) and sex-ratio (1:1) were similar. AE- occurred more frequently in a post-infectious context (17% vs 3%, *P*=0.01) and showed less epilepsy (21% vs 43%, *P*=0.03), and a trend to more neuro-ophthalmologic involvement (31% vs 15%, *P*=0.07). Non-limbic presentations were also more frequent in AE- (45% vs 20%, *P*=0.01). Despite these differences, the clinical severity was comparable between AE- and AE+, with similar rates of intensive care unit admissions (30% and 28%, respectively) and clinical scores (median modified Rankin score=3 and CASE=5 in both groups). Nevertheless, the prognostic RAPID score was higher in AE- (3 vs 1, *P*=0.0001). On complementary investigations, we did not show differences in brain MRI features. However, AE- more frequently exhibited basal ganglia hypermetabolism on brain positron-emission tomography (100% vs 39%, *P*=0.0169), and diffuse or focal slowing on electroencephalography (63% vs 36%, *P*=0.02). CSF cell count and proteins were similar, but interleukin-6 levels were higher in AE- (21.5 pg/mL vs 3.4 pg/mL, *P*=0.0265) Interestingly, the absence of antibody led to biopsy (31% vs 12%, *P*=0.0199) more often.
Conclusion: These preliminary findings suggest that AE- follows a distinct clinico-radiological profile. Early identification may help guide more timely and targeted treatment strategies.

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P1208
Predicting multiple sclerosis onset using EBV-related antibodies and machine learning methods in Swedish population

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Introduction: Epstein-Barr virus (EBV) infection has long been implicated in the pathogenesis of multiple sclerosis (MS). Notably, the EBV nuclear antigen 1 (EBNA1) shares structural similarity with several human central nervous system (CNS) proteins, including ANO2, GlialCAM, and CRYAB. This molecular mimicry may trigger the production of cross-reactive antibodies that mistakenly target human antigens and myelin sheaths, contributing to MS development which also may be used for identifying individuals at risk of developing MS.
Objectives/Aims: To assess the diagnostic value of EBV-related antibodies in MS, identify key biomarkers using statistical and machine learning methods, and develop predictive models for early risk detection.
Methods: To explore the diagnostic potential of EBV-related antibodies, serum samples from 650 MS patients and 650 healthy controls were analyzed. IgG reactivity against 33 candidate proteins was measured as median fluorescent intensity (MFI). Predictive models were built using antibody level and logistic regression, LASSO, and random forest with 10-fold cross-validation and bootstrap resampling. Feature selection was performed using significance testing and AIC-based stepwise selection. Model performances were evaluated using accuracy, Cohen's kappa, and area under the receiver operating characteristic curve (AUC).
Results: Initial models using all 33 antibodies achieved an accuracy of 0.65, kappa of 0.30, and AUC of 0.75. LASSO regression selected 21 antibodies and yielded comparable performance (accuracy = 0.65, kappa = 0.31, AUC = 0.74). The random forest model identified 7 stable predictors with slightly improved accuracy (0.66), kappa (0.33), and an AUC of 0.70. Stepwise AIC selection followed by scaling slightly improved the results (accuracy = 0.66, kappa = 0.31, AUC = 0.75). Cross-validation and bootstrap resampling confirmed the stability of these models. These findings suggest that while logistic regression offers some predictive value, complex patterns in antibody reactivity may require more flexible models for improved accuracy.
Conclusion: Antibody-based biomarkers derived from EBV-induced immune responses offer a promising, non-invasive approach for early MS prediction. To enhance model performance, we plan to select independent antibodies based on correlation analysis and explore advanced machine learning methods and deep learning approaches to capture nonlinear patterns. In addition, we aim to define diagnostic cut-off values for antibody titers to support clinical translation. Ultimately, our goal is to integrate antibody-based biomarkers with genetic variants and HLA haplotypes to enhance the predictive accuracy of MS risk models.

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P1209
VIRTUAL-MS randomized controlled trial evaluating longitudinal telemedicine care for multiple sclerosis: Representative enrollment

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Introduction: Telemedicine represents a tool to reduce barriers that People with MS (PwMS) face in accessing specialized, comprehensive care. VIRtual versus UsuAL In-office care for Multiple Sclerosis (VIRTUAL-MS) is a two-site randomized clinical trial evaluating the impact of longitudinally-delivered telemedicine for MS care on patient clinical outcomes (including disability worsening, relapses, MRI activity, quality of life), economic costs, and patient and clinician experience.

Objectives/Aims: To evaluate the representativeness of VIRTUAL-MS participants at trial enrollment.
Methods: Adult PwMS were enrolled in VIRTUAL-MS if they had been diagnosed with MS within 24 months. Participants were randomized 1:1 to standard in-clinic visits or telemedicine care for 24 months. The study was conducted in two MS Centers with heterogeneous patient populations (geography, ancestry, income): University of California San Francisco and Cleveland Clinic. Pragmatic study design factors intended to facilitate representative enrollment included: minimal inclusion/exclusion criteria, limited study visits, and translations of trial materials. Demographic and clinical characteristics at enrollment visit were summarized.
Results: Enrollment opened 3/31/2023. To date, 97 participants are enrolled (80.8% of the target sample size of 120). Mean age is 40 years (range: 21-78); 27.4% identify as non-White (16.8% Black, 2.1% Asian, 8.5% Other), 9.3% as Hispanic, and 67.4% as White and non-Hispanic. Most participants are married/civil union (57.7%), have some degree of post-secondary education (71.2%), and are in paid work (73.2%). Both relapsing remitting (90.5%) and primary progressive (9.5%) subtypes were enrolled. The range of disability as measured by the EDSS is broad, with median EDSS of 2.0 (0: 8.6%, 1-2.5: 61.3%, 3-4.5: 18.3%, 5-6: 9.8%, and ⩾6.5: 2.2%).
Conclusion: Enrollment in the VIRTUAL-MS clinical trial includes a substantial proportion of non-White and/or Hispanic participants (32.6%). Indeed, this enrollment is higher than Phase III clinical trials in MS (median 93.8% White [28 studies], 1.9% Black [14 studies], 0.5% Asian [11 studies]) and similar to the United States MS population estimates (77% White, 10% Black, 7% Hispanic, and 4% other). Including a cohort broadly representative of the population living with MS in the US will facilitate generalizability of the study findings and demonstrates the feasibility of equitable trial enrollment.

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P1210
Metabolomic Profiling Reveals Early Sex-Dependent Hormonal Alterations in Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder

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Introduction: Sex-specific differences in disease susceptibility, progression, and pathogenesis have long been observed in demyelinating diseases such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD). Prior research has shown distinct patterns of sex hormones, including DHEA-S and estrogen/testosterone derivatives, across healthy controls (HC), MS, and NMOSD cases. These differences may underlie the varied clinical presentations seen between sexes.
Objectives/Aims: To compare sex hormone profiles in MS, NMOSD, and HCs occurring within five years of onset.
Methods: We analyzed metabolomic data from non-Hispanic white HC (n=83), relapsing-remitting MS (RRMS, n=61), and AQP4-antibody positive and negative NMOSD cases (NMOSD+, n=10; NMOSD−, n=12). Cases were DMT-naive or free, <5 years from onset, and no recent steroid use (<30 days). Those on hormone therapy or birth control were excluded. Levels of 46 sex hormones were analyzed by fixed-effects linear regression with case status vs HC as the primary predictor and adjusting for likely confounders including menstrual/menopausal/sex status, time of day, fasting duration, BMI, age, smoking history, and statin use. Sex-stratified models were also conducted.
Results: Unique sex hormone signatures emerged across disease states when stratifying by sex. MS females showed no significant differences compared to HC females, whereas MS males had elevated levels of several sex hormones compared to HC males, notably the androgenic and progestin classes. In contrast, NMOSD+ males and females had reduced levels of multiple sex hormones in the pregnenolone class, followed by androgenic and progestin steroids. This reduction was more pronounced in NMSOD+ males who also had elevated lipid hormone precursors (i.e. cholesterol, cholesterol sulfate). Minimal changes in sex hormone expression were observed in both NMSOD- males and females compared to HCs. Similar findings were observed when comparing NMOSD vs RRMS by sex alone.

Conclusion: Collectively, these novel results suggest early sex-specific alterations in hormone metabolism may contribute to differences in disease mechanisms and presentation in MS and NMOSD across genders. These changes may represent differences in neuroendocrinological function or the downstream effect of global lipid dysregulation across disease states. These insights may inform future understanding of sex differences in disease course and guide development of sex-specific biomarkers and tailored therapeutic strategies in demyelinating diseases.

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P1211
Disability, Cognition, and Workplace Functioning in MS: Real-World Insights from the POINT-MS Cohort

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Introduction: Multiple Sclerosis frequently affects individuals during their most active working years, leading to substantial employment challenges and making job retention a key concern for those with the condition. While physical and cognitive impairments contribute to unemployment, less is known about their impact on job quality, or whether workplace accommodations can mitigate these effects.
Objectives/Aims: To examine the relationship between disability, cognitive function, and employment outcomes in people with MS (pwMS), and to evaluate whether workplace modifications mediate or modify these relationships.
Methods: This is a cross-sectional analysis of baseline data from participants who consented to take part in the Predicting Optimal INdividualised Treatment response in MS (POINT-MS) study. Disability was assessed using the Expanded Disability Status Scale (EDSS), while cognitive function was evaluated using the Symbol Digit Modalities Test (SDMT), z-scored according to normative data (Parmeter, et al,2010). Outcome variables were employment status, workplace modifications (yes/no), monthly earnings, and Work Productivity and Activity Impairment (WPAI) subscales. Logistic regression modelled employment status, while linear regressions assessed continuous outcomes. Chi-Square and t-tests compared employed versus unemployed groups and mediation analyses tested indirect effects of workplace modifications.
Results: Data from 534 pwMS (mean age 40.2±10.1 years; 67% female; 95.4% relapsing remitting; disease duration 88.6±83.2 months) was analysed. Median EDSS was 2.0 (range 0-7.5), and the mean SDMT z-score was -0.13±1.11. Among participants, 410 (76.8%) were employed, and 150 (28.1%) reported using workplace modifications. Higher EDSS was significantly associated with lower odds of being employed (B = -0.007, 95%CI [-0.01—0.003], $p<0.001$], but was not related to perceived work impairment (B = -1.10, 95%CI [-4.03-1.84], p = 0.46). SDMT was associated with higher weekly earnings (B = 170, 95%CI [87-253], p = 0.001), but not employment status. Workplace modifications were associated with reduced perceived impairment while working (B = -11.1, 95%CI [-1.42—0.02, p = 0.04), but not employment status (p = 0.66).
Conclusion: Physical disability remains the strongest predictor of employment status in pwMS, while cognitive function relates to individual economic output. Workplace modifications do not significantly influence employment status but is associated with reduced perceived impairment. Future studies could explore the long-term impact of workplace modifications on retention rates, job satisfaction and productivity. Investigating individual factors, such as job role and health status, along with the varying forms of modifications may potentially provide employers valuable insights for tailoring more efficient strategies.

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P1212
Age and sex differences in timing and selection of first disease-modifying therapy in multiple sclerosis

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Introduction: Early initiation of disease-modifying therapies (DMTs) is crucial in managing multiple sclerosis (MS). However, comprehensive analyses integrating both age and sex differences in the timing and selection of the first treatment for multiple sclerosis remain limited.
Objectives/Aims: To evaluate age- and sex-related differences in the time to first DMT initiation and to assess sex-specific patterns in the choice of first-line DMT within the first year after diagnosis.
Methods: We analyzed data from 23,416 individuals newly diagnosed with MS between 2012 and 2022 using Cox proportional hazards regression to estimate the associations of age category and sex with time to first DMT initiation. Logistic regression models, stratified by sex, were applied to evaluate the odds of initiating specific classes of DMT within one year after diagnosis, adjusted for age at diagnosis and year of diagnosis.
Results: Overall, 39% of patients initiated a DMT within the first year following diagnosis. The proportion of treated patients decreased with increasing age and was slightly lower among females compared to males. Younger individuals were more likely to initiate DMTs earlier after diagnosis. This was reflected in significantly lower hazards of DMT initiation with increasing age (e.g. Hazard Ratio (HR) for age 30–40 vs. 9–20: 0.85, p-value < 0.001; HR for age 60–70 vs. 9–20: 0.097, p-value < 0.001). Female patients experienced a modest but statistically significant delay in treatment initiation compared to males (HR $= 0.94$, p-value $= 0.005$). In the first year after diagnosis, male patients had higher odds of initiating S1P receptor modulators (Odd Ratios (OR) $= 1.45$, 95% CI: 1.12–1.86), anti-CD20 therapies (OR $= 1.96$, 95% CI: 1.28–3.00), and teriflunomide (OR $= 1.65$, 95% CI: 1.44–1.88), compared to female patients.
Conclusion: Our findings highlight a significant age-related delay in DMT initiation, with older individuals being substantially less likely to begin treatment shortly after diagnosis. Additionally, modest sex differences were observed in both treatment timing and initial DMT selection. These patterns underscore the need for personalized approaches in MS care and raise important considerations for equitable treatment strategies across demographic subgroups.

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P1213
Epidemiological Profile of Multiple Sclerosis Patients from a Tertiary Hospital in Southern Brazil

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system, often resulting in significant neurological disability. Understanding the epidemiological characteristics of affected individuals is essential for optimizing patient management and healthcare planning.
Objectives/Aims: To describe the demographic and clinical profiles of patients diagnosed with MS, according to the 2017 McDonald criteria, treated at a tertiary hospital in southern Brazil.
Methods: We conducted a retrospective analysis of patients with MS followed at São Lucas Hospital, Brazil. Data were collected on sex, ethnicity, age at disease onset, MS phenotype, topography affected during the first clinical episode, and initiation of disease-modifying therapies (DMTs). Expanded Disability Status Scale (EDSS) scores at baseline and at the most recent follow-up were also analyzed.
Results: A total of 612 patients were included, of whom 68% were female and 32% male. The ethnic distribution was 418 (90%) White, 24 (5.1%) Afro-Brazilian, and 25 (5.3%) of other ethnic backgrounds. The mean age at disease onset was 31.6 years. Regarding MS phenotypes, 445 (74%) had relapsing-remitting MS (RRMS), 63 (10%) secondary progressive MS (SPMS), 51 (8.4%) primary progressive MS (PPMS), and 45 (7.5%) clinically isolated syndrome (CIS) or radiologically isolated syndrome (RIS). Among 424 patients with a documented first clinical episode, the most frequently affected regions were the spinal cord (132; 42%) and the optic nerve (105; 33%). The most common initial DMT was interferon beta, initiated in 180 (36%) patients. At the time of analysis, 319 (52%) patients were

receiving moderately to highly effective therapies, with natalizumab, ocrelizumab, and fingolimod being the most frequently prescribed. The mean baseline EDSS score was 2.5, increasing to 2.7 at the latest follow-up

Conclusion: This study provides an updated epidemiological and clinical characterization of MS patients at a tertiary center in southern Brazil. The results reflect regional disease patterns and treatment practices, contributing valuable data to support clinical decision-making and public health strategies in MS management.

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P1214
Timing of onset of bladder and bowel problems in MS - A cross-sectional study

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Introduction: Bladder and bowel problems are common among people with MS. Understanding the timing and nature of these issues is crucial for assessing the unmet need and ensuring timely treatment.

Objectives/Aims: In this cross-sectional study, the aim is to investigate timing of onset and types of bladder and bowel problems in people with MS. Furthermore, the impact of suffering from both bladder and bowel problems is investigated.

Methods: An online survey targeting individuals with MS was disseminated via social media channels, healthcare professionals, and Coloplast user databases in France, Germany, Italy, and the UK. The survey included questions designed to assess bladder and bowel problems. Bladder problems were defined as having overactive bladder measured by the Actionable Bladder Symptom Screening Tool, or having urinary retention measured as having difficulty passing urine. Bowel problems were defined as having experienced specific symptoms since MS diagnosis, including constipation, diarrhea, or bowel accidents, while also acknowledging the presence of a bowel problem. These issues were recorded in relation to the time since MS diagnosis. Poor well-being was defined as a score below 50% on the WHO-5 scale.

Results: Of 1872 individuals with MS, 1089 reported having both bladder and bowel problems, 316 reported having bladder problems only and 81 reported having bowel problems only. The onset of problems occurred within 1 year of MS diagnosis for 32.6% who experienced either bladder, bowel or both type of problems. Among individuals who had both bladder and bowel problems, there was a 3 times higher risk of having lower well-being compared to not having both type of problems (OR = 3.08; 95% CI: 1.44-6.61).

Conclusion: This study shows that over time, the majority of people with MS suffer from both bladder and bowel problems and that they report significantly lower well-being. This highlights a need for timely diagnosis and treatment of such problems.

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P1215
Leveraging multiple-country data sources for a comparative drug safety study: complexities and rewards in pharmacoepidemiology

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Introduction: In cases of rare drug exposure and rare outcomes, pooling data from various data sources can increase precision in risk estimation. However, heterogeneity may exist in drug exposed populations.

Objectives/Aims: Using a study that compared mortality risk in patients with multiple sclerosis (MS) treated with alemtuzumab vs those on other highly efficacious disease modifying therapies (HE-DMTs), we highlight the opportunities and challenges of multi-country studies. We focused on understanding differences in underlying drug exposed populations and potential biases, before outcome analyses.

Methods: The cohort study included MS patients initiating alemtuzumab or other HE-DMTs after alemtuzumab

reimbursement in each country. The outcome was all-cause mortality. We used routine health care data from 5 countries: UK (chart review data from three academic centres); Denmark, Sweden, Czech Republic(CR) (national MS registries); Germany (administrative claims data). A common data model was used for data management (except Germany). Propensity score (PS) weighting was used to address confounding by MS disease severity within each country. The success of PS weighting was evaluated using standardized mean differences, PS overlap in graphical outputs, percentages of balanced variables and the effective sample size (ESS) of the comparator cohort.

Results: We included 1,183 patients treated with alemtuzumab (56 (Sweden) to 457 (UK) patients) and 27,573 comparator patients treated with HE-DMT (503 (CR) to 10,511 (Sweden)). Considerable heterogeneity in clinical and demographic characteristics was observed across countries for alemtuzumab patients. E.g., in the UK, 94% alemtuzumab patients were naïve to other HE-DMTs, 52.5% had low levels of disability (Expanded Disability Status Scale [EDSS] < 2.25), and mean MS disease duration was 5.3yrs. In contrast, for Denmark, few alemtuzumab patients (19.4%) were naïve to other HE-DMTs, 20% had low levels of disability (EDSS < 2.25), and mean MS disease duration was 12.2yrs. Despite PS weighting, core covariates remained imbalanced in UK and multiple non-core variables were imbalanced in all countries. The ESS of the HE-DMT cohort was 23% of its original size.

Conclusion: Heterogeneity is often viewed as a challenge. However, in this study heterogeneity led to deep understanding of the drug exposed populations in each country, and the influence of local treatment guidelines. Consequently, crude mortality rates in each country could be better contextualised. Such understanding is critical to informing whether a formal comparative analysis should be conducted.

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P1216
Increased Risk of Autoimmune Diseases over Time prior to Multiple Sclerosis and Neuromyelitis Optica Spectrum Disorder Onset: A Nationwide Population Cohort Study in South Korea

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Introduction: Multiple sclerosis (MS) and neuromyelitis optics spectrums disorder (NMOSD) are the autoimmune disease in the central nervous system and frequently reported in patients with other autoimmune diseases. However, the relative risk of autoimmune diseases prior to the onset of MS changes over time has not been well reported.

Objectives/Aims: We aimed to elucidate the temporal association of autoimmune diseases before the diagnosis of MS/NMOSD.

Methods: MS (n=3,019) and NMOSD (n=1,391) cohorts were collected from the Korean National Health Insurance Service between 1 January 2011 and 31 December 2021, using the International Classification of Diseases-10th revision diagnosis codes and information from the Rare Intractable Disease program. Ten age- and sex-matched controls were selected for each MS/NMOSD case. The risk ratios (RR) of autoimmune diseases in MS/NMOSD were calculated compared with controls for 10 years prior to diagnosis. Autoimmune diseases included psoriasis, type I diabetes mellitus, RA, SLE, uveitis, thyroiditis, asthma, and inflammatory bowel disease.

Results: Approximately 39.5% in MS cohort and 28.0% in NMOSD were under the age of 40 and 37.6% in MS and 27.4% in NMOSD were female. The RR of autoimmune diseases in the 10 years prior to diagnosis was 1.79 (95% confidence interval [CI] 1.66−1.92) in MS and 1.39 (95% CI 1.24−1.55) in NMOSD. The autoimmune diseases with the highest RRs are Crohn's disease in MS and SLE in MS. The RR of total autoimmune diseases was higher closer to the index date and was highest in the year before diagnosis. In the year before diagnosis, the autoimmune diseases with the highest RRs are Rheumatoid arthritis in MS and SLE in MS. The autoimmune diseases with the highest RRs are Crohn's disease in MS and SLE in MS.
Conclusion: Autoimmune diseases are more common in patients with MS/NMOSD than in controls before MS/NMOSD diagnosis, especially closer to the onset of MS/NMOSD.

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P1217
Substance and Drug abuse in Iranian Multiple sclerosis patients

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Introduction: Evidence suggests an association between substance and drug abuse with multiple sclerosis (MS), posing a significant burden worldwide. Specific patient characteristics increase the risk of substance abuse, contributing to MS development and progression.
Objectives/Aims: This study evaluates the prevalence of substance and drug abuse in MS patients and examines the relationship between demographic and clinical characteristics and substance abuse.
Methods: A cross-sectional study was conducted on 400 MS patients at the MS Research Center, a referral outpatient clinic in Tehran, Iran (2024). Participants completed a self-reported questionnaire covering socio-demographic characteristics, clinical history, and substance abuse (alcohol, cigarettes, opioids—including natural, semi-synthetic, and synthetic derivatives—and drug abuse). The Chi-Square and T-Test identified qualitative and quantitative factors associated with substance use. Analyses were performed using SPSS, with statistical significance set at $P < 0.05$.
Results: The sample included 55.8% women, with a mean age of 36.91 $\pm$ 8.22 years. Substance abuse prevalence was as follows: smoking (13%), alcohol abuse/dependence (21%), opioid/illicit drug use (5%), and psychiatric drug use (33.3%). Younger patients were more likely to consume alcohol (p=0.006) and psychiatric drugs (p=0.000). Smoking (p=0.000) and opioid abuse (p=0.008) were significantly higher in men. Opioid abuse was more prevalent among unemployed (p=0.022), unmarried individuals (p=0.022), and those with low education (p=0.016). Alcohol use was reported in 21% of Relapsing-remitting MS, 19% of Primary progressive MS, and 15% of Secondary progressive MS patients (p=0.018). Other factors, including MS duration and onset of substance use, showed no significant differences.
Conclusion: These findings highlight the need for policies to screen and counsel MS patients, particularly unmarried, unemployed men with low education levels (for opioid abuse) and younger patients (for alcohol use).

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P1218
Relationship between fatigue and adherence to treatment in patients with multiple sclerosis

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Introduction: Non-adherence to disease-modifying therapies (DMTs) in patients with multiple sclerosis (MS) is associated with poor prognosis, increased risk of relapses, disease progression, and higher healthcare costs. Adherence to DMTs is influenced by multiple factors, one of the most significant being fatigue—a common and debilitating symptom in MS.
Objectives/Aims: The aim of this study was to evaluate fatigue in patients with MS and its impact on adherence to treatment.
Methods: A total of 153 patients (95 females, 58 males, mean age 44.44 years) diagnosed with MS, were included in the study. All patients were receiving DMT. Adherence was assessed using the Adherence in Chronic Diseases Scale (ACDS), while fatigue levels were evaluated using the Modified Fatigue Impact Scale (MFIS) and the Fatigue Severity Scale (FSS).
Results: Among the participants, 89% had relapsing-remitting MS (RRMS), while 12% had progressive forms of MS (7% primary progressive MS [PPMS], 4% secondary progressive MS [SPMS]). Mean disease duration was 12.01 years. All patients were treated with DMTs, within the RRMS group - predominantly moderately effective therapy. The symptoms most

reported by the patients were limb weakness (52%), gait disturbances (43%), vision disturbances (29%) and fatigue (27%). The mean MFIS score was 34.72 points, with the highest subscores for physical fatigue, followed by psychosocial and cognitive domains. Clinically significant fatigue, as indicated by the FSS score, was present in 40.0 % of patients (n=61). The mean score in ACDS scale was 24.49 +/- 3.21. According to the ACDS scale, 55% of patients have scores between 21 and 26 points, indicating a moderate level of adherence. A significant correlation was observed between ACDS results and level of fatigue in FSS ($r=-0.14, p<0.05$) and MFIS in physical subscale($r=-18$ $p<0.05$).

Conclusion: Fatigue is a highly prevalent symptom in patients with MS and has a significant impact on adherence to treatment. Addressing fatigue through targeted interventions may improve adherence to DMTs and, consequently, patient outcomes.

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P1219
Validation of Electronic Algorithms for Administrative Case Definition of Multiple Sclerosis

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Introduction: Administrative health data derived from healthcare service utilization sources offers valuable opportunities for conducting population-based research. However, the accurate identification of MS cases within these datasets requires validation of algorithms against clinical diagnosis to ensure reliability and applicability in epidemiological and health services research.

Objectives/Aims: To validate and compare multiple electronic algorithms for identifying MS cases using administrative healthcare data from a single tertiary hospital in Colombia.

Methods: A systematic literature review was conducted across three databases to identify previously published administrative algorithms for MS case identification. Out of 92 initially identified studies, 37 studies were retained after screening, yielding 77 distinct algorithms. Of these, 41 algorithms were successfully operationalized using available data on hospitalizations, outpatient visits, and use of disease-modifying therapies. Each algorithm's diagnostic performance was evaluated using a dataset of 600 clinically confirmed MS cases and a random sample of 9,400 controls. Performance was assessed through sensitivity, specificity, and the area under the Receiver Operating Characteristic curve (AUC).

Results: The algorithm with the best diagnostic performance required at least one hospitalization within a six-year period with MS as the discharge diagnosis, achieving a sensitivity of 100% (95% CI: 98.2–100), specificity of 99.7% (95% CI: 99.0–99.9), and an AUC of 0.99 (95% CI: 0.99–0.999).The second-best performing algorithm, which required ⩾2 hospitalizations or outpatient visits with MS as the main diagnosis over more than three years, demonstrated similarly high diagnostic accuracy. Among the top five performing algorithms, all required a minimum follow-up period of two years, highlighting the importance of longitudinal data for optimal diagnostic precision.

Conclusion: This study provides a comparative validation of administrative algorithms for MS case identification within the Colombian context. Several algorithms demonstrated excellent diagnostic accuracy, supporting their utility for epidemiological surveillance and health services research. The findings underscore the importance of extended follow-up periods (minimum two years) for maximizing performance. Furthermore, the strong performance of these algorithms suggests their potential applicability in broader national datasets or similar healthcare systems.

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P1220
Clinical Characteristics of Multiple Sclerosis in Colombia: A Descriptive Study from a Referral Centre

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Introduction: In Colombia, MS is considered a rare disease, and local data on its clinical profile remain scarce. However, the rising prevalence observed in recent years highlights the need for research to better characterize the disease in this population.

Objectives/Aims: To describe the clinical characteristics of MS patients in Colombia.

Methods: This ambispective study was conducted at the MS Centre of the National University Hospital of Colombia, Bogotá. Data were obtained from electronic health records, including demographics, clinical presentation, relapses, and

disability progression. Outcomes included annualized relapse rate (ARR), measured for pre- and post-follow up periods. Incidence rates were estimated for events of confirmed disability worsening (CDW), confirmed disability improvement (CDI), and progression independent of relapse activity (PIRA) after enrolment. The normalized age-related MS severity score (nARMSS) was calculated to assess disease severity. Median times to clinical milestones (from radiologically isolated syndrome [RIS] to clinical onset, clinically isolated syndrome [CIS] to diagnosis, and from MS onset to death) were recorded. Survival data and age at death were collected for deceased patients during follow-up.

Results: By April 2025, 811 patients had attended the centre, with 686 (84.6%) included in the registry. Mean follow-up was 56.7 months, totaling 3232 patient-years. The dataset included 6042 EDSS scores (mean: 8.8 per patient), 1552 relapses, and 6723 MRIs (including 2974 brain MRIs). Mean age was 44.5 years, with 68.8% women. Mean age at onset was 32.3 years, with 92.5% diagnosed with RRMS. Overall ARR was 0.015 (95% CI: 0.014–0.016); pre-follow up ARR was 0.245 (95% CI: 0.232–0.259), and post-follow up ARR was 0.007 (95% CI: 0.007–0.008). Incidence rates were: CDW, 0.0058 (95% CI: 0.005–0.007); CDI, 0.0009 (95% CI: 0.001–0.001); and PIRA, 0.0049 (95% CI: 0.004–0.006). Mean (SD) nARMSS score was −1.47 (2.46) (range: −4.89 to 4.90). Clinical milestones occurred after a median (IQR) of 48.7 months (65) from RIS to clinical onset; 0.63 years (2.74) from CIS to diagnosis (range: 0–43 years); and 18 years (8.07) from MS onset to death (range: 6.29–22.74 years). Mean age at death was 59.2 years (SD: 10.16; range: 35.3–81.3), in five recorded cases.

Conclusion: This registry-based study provides a comprehensive overview of the clinical profile of MS patients in Colombia.

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P1221
Epidemiologic trends of multiple sclerosis in Puerto Rico (2013–2023)

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Introduction: The Puerto Rico Multiple Sclerosis Foundation (PRMSF) registry, enforced by Law 85, was created in 2013 using data collected from questionnaires completed by a medical healthcare provider. Several studies have shown the importance and utility of having multiple sclerosis (MS) registries. Since the creation of the MS registry, multiple studies have used this data in clinical and research settings and have helped assist physicians and healthcare providers to have access and acquire knowledge on individual patient's data. Furthermore, MS registries are a valuable instrument for epidemiologic trends; thus, enabling a longer follow-up to capture developments of patterns in a population.

Objectives/Aims: Update the epidemiologic trends in MS incidence and prevalence rates for PR from 2021 to 2023 and compare them to prior data from 2017 to 2020.

Methods: The PRMSF registry was used to identify all newly diagnosed MS cases between January 2021 and December 2023 and using the 2020 US census population estimates for PR. Data was evaluated using Strata v.11 and stratified by age and sex. Descriptive statistics such as frequencies, percentages, and calculated means were used to characterize the study sample.

Results: A total of 402 new MS cases were reported 2021 to 2023 using the rates estimates using PR census population was 3.2 million for these years. The number of prevalent cases obtained from 2021 to 2023 were 3211, 3350, and 3476, respectively. The prevalence of MS per 100,000 for each year was 118.1, 124.0, and 128.4. Incident cases were 137, 139, 126, respectively from 2021 to 2023. Also, the incidence of MS per 100,000 was 6.9, 7.0 and 6.1, respectively for each year. Comparison of this new data mas made with the results obtained from the 2017-2020 census of PR MS patients to verify the changes in prevalence and incidence of the disease.

Conclusion: Accurate knowledge of incidence and prevalence of MS is essential for healthcare professionals involved in disease management, resource planning, and research. MS registries serve as critical tools in capturing real-world data, enabling the identification of epidemiological trends, treatment responses, and long-term outcomes across diverse patient demographics such as the PR community. By tracking disease progression and healthcare utilization, these registries support evidence-based clinical decision-making, facilitate early intervention strategies, contribute to the optimization of clinical care pathways, and guide the development of effective healthcare policies.

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P1222
The Global Prevalence of Optic Neuritis: the ON-COLOUR Study

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Introduction: Optic neuritis (ON) is an acute condition characterized by inflammation or degeneration of the optic nerve, often arising from infections or immune-related inflammatory diseases.
Objectives/Aims: Prevalence offers essential insights into the disease's spread and serves as a key indicator in epidemiology and public health. With this study we aimed to perform an in-depth literature review to assess the prevalence of ON worldwide.
Methods: Following PRISMA guidelines, a literature synthesis was conducted, focusing on articles published between January 2010 and March 2025 in English on PubMed. To identify relevant studies, the following keywords sequence was used: ((optic neuritis[Title]) AND (prevalence[Title/Abstract])).
Results: A review of articles from the past 15 years on the prevalence of ON was conducted, yielding 41 results. Of these, 5 full-text articles were assessed, and 3 studies were selected for inclusion. Two of the articles focused on the prevalence of ON in the European adult population, while one study from Asia included both pediatric and adult groups. The prevalence of ON ranged from 7.87 to 114.8 per 100,000 individuals in Europe, while for Asia, estimates were 7.68 among children and 19.01 among adults.
Conclusion: Prevalence estimates of ON at global level are consistent and indicate an increase compared to earlier surveys. Higher prevalence estimates were identified in regions at higher latitudes, as it is seen for multiple sclerosis, the condition most frequently associated with ON. Furthermore, all reported estimates were higher in women than in men across all age groups. However, current knowledge on the prevalence of ON is limited, and the presence of a limited number of recent epidemiological studies makes it difficult to accurately assess the global picture. For a clearer detection and understanding of epidemiological trends following the introduction of new diagnostic criteria for ON and the impact of the COVID-19 pandemic, longitudinal population-based assessments in all geographic regions is claimed
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P1223
The Incidence of Optic Neuritis worldwide: the ON-COLOUR Study

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Introduction: Due to its significant impact on disability, optic neuritis (ON) is most frequently investigated in the context of demyelinating diseases, and especially multiple sclerosis (MS).
Objectives/Aims: We aimed to report the incidence of ON worldwide and beyond occurrence in demyelinating diseases.
Methods: Literature search was performed in accordance with PRISMA guidelines, and included articles published between January 2010 and March 2025, written in English and indexed in PubMed. To identify relevant studies, the following keywords sequence was used: ((optic neuritis[Title]) AND (incidence[Title/Abstract])).
Results: A review of 56 articles on ON incidence identified 10 relevant studies in Europe, Americas and Asia, in both pediatric and adult populations. The highest mean incidence rate of ON is reported for Canada, with 75.9 [95% CI: 72.1–79.1]/100,000 person-years. The U.S. Armed Forces reported 8.1, while Olmsted County, Minnesota, recorded 4.0 [95% CI: 3.2–4.7]; in this study, 9% of ON cases were associated with NMO and MOG antibodies, and 57% with MS. A study from Barcelona reported a rate of 5.36, higher than that in the United Kingdom – 4.5 [95% CI: 4.3–4.6]. In contrast, the lowest rates were recorded in South Korea, ranging between 2.34 [95% CI: 2.20–2.49] and 3.29 [95% CI: 3.28–3.30]. A Danish study reported an incidence of 3.28 [95% CI: 2.44–4.31], with 39% of patients developing MS during the follow-up. In the pediatric population, the lowest incidence was observed in the United Kingdom – 0.77 [95% CI: 0.64–0.90], while Asian countries, such as South Korea and Taiwan, recorded rates of 1.04 [95% CI: 1.01–1.07] and between 1.79 and 2.46, respectively.
Conclusion: The incidence of ON widely varies by world regions, age group, and sex. Rates are higher in women than men the highest peak being in, middle-aged adults, and are lower in children. Western countries report higher incidence rates compared to Asian countries. Several factors, including healthcare access, changes in diagnostic criteria, and environmental conditions are hypothesized to explain these differences. Future research should further explore the ON-MS relationship, and, for more recent times, the potential influence of external factors like the COVID-19 pandemics.
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P1224
Demographic, Clinical, and Radiological Characteristics of Familial Multiple Sclerosis: A Multicenter Retrospective Study from Türkiye

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Introduction: Familial MS (FMS) is defined as the presence of MS in the first, second, third degree or other relatives of patients with proband. The familial MS rate is 10.8%. This entity is of increasing interest since it sheds light on possible epigenetic factors and makes necessary studies FMS in different ethnic groups.
Objectives/Aims: In our study, we aimed to determine the demographic, radiological and clinical characteristics of familial MS patients followed in 11 MS centres in Türkiye.
Methods: A retrospective chart review of familial MS patients collected from 11 MS centres in Turkey between 2015 and 2025 was performed. Demographic, radiological and clinical data were collected.
Results: In our study, data from 4,350 patients with multiple sclerosis (MS) were evaluated, and 311 individuals from 139 families were identified with familial MS (FMS), yielding a prevalence of 7.14%. Among the 240 FMS patients with complete data, 66.95% were female, and 33.05% were male, with a female-to-male ratio of 2.03. The mean age of FMS patients was 37.00 $\pm$ 10.77 years, and the mean age at disease onset was 28.25 $\pm$ 9.73 years, with no statistically significant difference between sexes ($p > 0.05$). The mean body mass index (BMI) was 24.78 $\pm$ 4.24, and the annualized relapse rate was 0.77 $\pm$ 1.09. Regarding familial relationships, 37.08% of FMS patients were first-degree relatives (with the top three being: siblings 25.83%, mother–daughter 5.0%, mother–son 2.5%), while 9.2% were third-degree and 5.9% second-degree relatives. The mean number of siblings was 4.79 $\pm$ 2.14, and the mean birth order was 3.03 $\pm$ 1.74. There was no significant difference in EDSS scores between first-born and last-born patients. The mean EDSS score was 2.12 $\pm$ 1.66. EDSS scores were significantly higher in males, in those with later disease onset, and across different treatment groups ($p < 0.05$). FMS patients were most commonly treated with dimethyl fumarate (24.89%), followed by fingolimod (19.83%) and ocrelizumab (14.77%). Brain MRI findings showed that 40.43% had 0–10 lesions, 33.19% had $\geqslant$20 lesions, and 26.38% had 10–20 lesions. The mean number of spinal MRI lesions was 2.14 $\pm$ 2.62, and the lesion count was significantly higher in first-degree relatives, as well as among different treatment groups and by EDSS scores ($p < 0.05$). Among FMS patients, 93.75% had grown up in the same environment, and 17.08% reported parental consanguinity. The prevalence of comorbid systemic and autoimmune conditions was 18.75%. Cerebrospinal fluid (CSF) analysis was not performed in 42.5% of patients; among those with CSF analysis, 76% were positive for oligoclonal band (OCB) type 2.
Conclusion: Our study provides important insights into the demographic, clinical, and radiological characteristics of patients with familial multiple sclerosis (FMS). Preliminary findings suggest that the mean age and age at disease onset in FMS patients are lower compared to those reported in the general MS population. Additionally, the significantly higher number of spinal lesions observed in first-degree relatives stands out as a noteworthy result.

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P1225
Autoimmune encephalitis in patients on immune checkpoint inhibitor therapy: a multi-center retrospective study

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Introduction: Immune checkpoint inhibitors (ICI) are monoclonal antibodies that cause enhanced T cell-mediated antitumor immunity. While they have dramatically improved outcomes in cancer treatment, a subset of patients experience immune-related adverse events (irAEs) including autoimmune encephalitis (AE).
Objectives/Aims: We retrospectively reviewed 11 patients to evaluate their clinical presentations, treatment response, and overall prognosis to help inform future therapeutics in this rare cohort.
Methods: Using the Stanford Research Repository (STARR) database, we searched patients who received an ICI and had documented diagnosis of AE. Patients were considered to have an AE based on documented diagnosis by the treating neurologist. Patients were excluded who were not evaluated by neurology and did not have the minimum clinical data to assess for AE by consensus criteria.
Results: Eleven patients were identified, with mean age of onset 68.5 years (IQR 18 years). Cancer diagnosis included: melanoma (45%), sarcoma (27%), NSCLC (18%), small cell lung cancer (9%). ICIs received included pembrolizumab, ipilimumab/nivolumab (alone and in combination), and atezolizumab. 81% of patients had CSF studies demonstrating lymphocytic pleocytosis (WBC 6 – 71). None had typical MRI abnormalities, however some were limited by motion artifact. One patient had positive serum ANNA-1 antibodies in the serum. ICI was discontinued in all patients after developing encephalitis, without re-exposure. All patients received either IV or oral steroids. 27% of patients were treated with IVIG in addition to steroids as first line treatment. One patient was treated with mycophenolate, and one patient was treated with rituximab.
Conclusion: In this cohort of predominantly seronegative patients without history of prior encephalitis, patients were steroid responsive with monophasic course over an average of 1.4 years of follow-up. Most patients in our cohort did not meet criteria for probable seronegative autoimmune encephalitis based on the 2016 Graus criteria, however almost all had a robust steroid response. In initial chart review several patients excluded from our study were diagnosed with autoimmune encephalitis by the treating but had incomplete work-up
including missing MRI and/or missing lumbar punctures or autoantibodies sent. There is an unmet need to identify if there are a subset of patients who are at low risk of encephalitis recurrence, for whom a re-trial of ICI could be considered. Patients would benefit from a more standardized diagnostic approach.

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P1226
Three's a Pattern? Familial Clusters of MS from a Multi-Centre UK Consortium

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Introduction: Familial multiple sclerosis (MS) involving first-degree relatives is uncommon. Triads—families with three affected members—are exceptionally rare and may provide valuable insights into genetic susceptibility and disease variability.
Objectives/Aims: To describe the clinical features of five MS triads identified within a large UK regional MS consortium.
Methods: The South East London, Kent and Medway MS consortium (SELKAMS) comprises six hospitals with a combined MS cohort of 7,760 patients. A retrospective review identified five families, each with three first-degree relatives diagnosed with MS. Demographic and clinical data—including age at symptom onset, MS subtype, and Expanded Disability Status Scale (EDSS) scores—were collected. One family underwent whole genome sequencing (WGS).
Results: The five MS triads comprised:

1. **Three sisters**, including monozygotic twins, mean onset age 17.7 years (range: 17–19).
2. **Two sisters and one brother**, mean onset age 35 years (range: 27–47); one sister progressed to SPMS and died aged 50.
3. **Father, daughter, and son**, mean onset age 32.3 years (range: 16–58); this family underwent WGS.
4. **Son, mother, and maternal aunt**, mean onset age 23 years (range: 17–29); two converted to SPMS.
5. **Mother, daughter, and son**, mean onset age 37 years (range: 31–45); all with RRMS.

All 15 individuals were diagnosed with relapsing-remitting MS (RRMS); three converted to secondary progressive MS (SPMS). Disease onset and presentation showed intra-family similarities, while progression and imaging features varied. The prevalence of MS triads in this cohort is **0.19% (15/7,760)**, reflecting the rarity of such familial clustering.
Conclusion: This case series presents five MS triads from a large regional cohort, representing 0.19% of the study population. These families, spanning both sibling and multigenerational patterns, offer valuable insights into heritable MS risk. Ongoing genetic analysis may uncover shared susceptibility factors and inform future research into MS pathogenesis.

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P1227
Assessing the association between clinical follow-up visits and mortality in Multiple Sclerosis

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Introduction: Existing studies have compared mortality rates between people with Multiple Sclerosis (MS) and the general population, but the association between specialized care utilization and mortality remains unexplored. Exploring potential associations between frequencies of specialist care visits and mortality may offer insights into whether disparities in care access could be linked to differences in health outcomes.
Objectives/Aims: To investigate the association between visits to specialized MS care centers in Denmark and mortality.
Methods: We utilized data from the Danish Multiple Sclerosis Registry and national Danish health registries. The primary outcome was all-cause mortality. Patients were followed from MS diagnosis date until date of death, or end of follow-up December 2020, whichever occurred first. We used a multivariable Cox regression model incorporating cumulative number of visits as a time varying exposure and adjusting for sociodemographic and clinical factors.
Results: In total 9,929 patients with an MS diagnosis between year 2000 and 2020 were included, contributing with 105,115 person-years at risk. During a median follow-up of 10.3 years, 316 patients died. In a model adjusted for demographic, clinical, and comorbidity factors, cumulative visits were not statistically significant associated with mortality (HR: 0.99. 95% CI: 0.98-1.01). Factors significantly associated with reduced mortality were female sex (HR: 0.60. 95% CI: 0.47-0.75), being married or in a partnership (HR:0.60. 95% CI: 0.45-0.79), and higher education (HR: 0.56. 95% CI: 0.40-0.78), independent of visits. Expanded Disability Status Scale score $\geqslant 3$ (HR: 2.87. 95% CI: 1.94-4.24), cerebrovascular diseases (HR: 1.69. 95% CI: 1.19-2.39), and pneumonia (HR: 2.82. 95% CI: 2.09-3.79) at baseline were associated with a statistically significant increase in mortality.
Conclusion: Cumulative visits to MS clinics were not associated with mortality. Disparities in survival by sex, education, and marital status underscore the need to be aware of social determinants alongside clinical care.

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P1228
Conversion Rate of Pediatric Optic Neuritis to Demyelinating Disorders: the ON-COLOUR Study

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Introduction: Optic neuritis (ON) is an acute inflammation of the optic nerve, which frequently leads to damage of the myelin sheath and presents as an early clinical sign of demyelinating disorders, particularly multiple sclerosis (MS).
Objectives/Aims: This study aimed to evaluate the global conversion rate of ON to demyelinating disorders in the pediatric population through a literature review.
Methods: A literature review was conducted in line with PRISMA guidelines, focusing on PubMed articles published in English between 01/2015 and 03/2025, focused on the pediatric population. The search combined "optic neuritis" in the title with terms such as "conversion," "prognostic," "risk," or "epidemiology," and "multiple sclerosis," "NMO," "MOG," or "demyelinating" in the title or abstract.
Results: Out of 41 articles reviewed, 10 were included in the final analysis. Most studies were retrospective, with follow-up periods of 1 to 10 years, and originated from diverse global regions. Conversion rates from ON to demyelinating diseases (MS, NMO, MOG-ON) varied widely. MS conversion was lowest in Asian and US studies (1–14%) and highest in European cohorts (up to 42%). NMO conversion rates ranged from 1.95–5.88% in Europe and up to 11% in Asia and the USA. Recurrence rates were higher in Asia (12–25%) compared to Europe and the USA (up to 7% and 13%, respectively). Visual outcomes were generally favorable, with recovery rates of up to 89% within one year.
Conclusion: An increased risk of MS conversion is linked to age >10 years, female sex, demyelinating brain lesions on Magnetic Resonance Imaging, positive cerebrospinal fluid oligoclonal bands, and unilateral ON. While visual recovery is generally good in isolated ON, outcomes are poorer in cases progressing to MS or NMO. Based on these findings, early diagnostic evaluation is recommended in pediatric ON, including neurological examination, brain MRI, and antibody testing (with serological screening for MOG-IgG and AQP4-IgG antibodies).
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P1229
Rising Prevalence of Multiple Sclerosis in Tehran, Iran (2017–2024): Trends, Epidemiological Insights, and the Impact of the COVID-19 Pandemic

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Introduction: Multiple sclerosis (MS) is a chronic neuroinflammatory disorder with a rising global prevalence. Iran, particularly Tehran, has one of the highest MS prevalence rates in the Eastern Mediterranean Region. Understanding prevalence trends and potential influencing factors, including environmental changes and the COVID-19 pandemic, is essential for healthcare planning.
Objectives/Aims: This study aimed to determine the prevalence, incidence and demographic characteristics of MS in Tehran and evaluate the impact of the COVID-19 pandemic.
Methods: A retrospective population-based study was conducted using data from the Iranian MS Society (IMSS) and the National MS Registry System of Iran (NMSRI). The study analyzed MS prevalence and incidence rates from 2017 to 2024, stratified by age and gender. The annual percent change (APC) was calculated, and the mean age at MS onset before and after the COVID-19 pandemic was compared using an independent t-test.
Results: A total of 29,926 MS cases were identified from 1991 to 2024, with a female-to-male ratio of 3.05:1. The overall prevalence of MS in Tehran increased from 181.34 per 100,000 in 2017 to 207.46 per 100,000 in 2024. The incidence ratio was 5.26 per 100000 in 2024. The mean ± SD age at MS onset was 29.67±9.0 years, with a significant increase in post-pandemic cases (29.44±8.84 years pre-COVID-19 vs. 33.29±9.48 years post-COVID-19, $p < 0.001$). Although MS prevalence continued to rise, APC did not increase by Covid-2019 epidemic.
Conclusion: Conclusion: MS prevalence in Tehran has significantly increased over the past decade, with a slowing APC trend in recent years. The COVID-19 pandemic may have influenced MS diagnosis patterns, potentially delaying case identification. These findings highlight the need for improved healthcare strategies for MS management in high-prevalence regions.

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P1230
Characteristics of Late Onset versus Adult-Onset Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is a chronic immune-mediated disorder of the central nervous system (CNS). Its prevalence in Egypt is approximately 13.7 per 100,000. However, there is a lack of literature on the clinical characteristics of patients with late-onset MS (LOMS) .
Objectives/Aims: The aim of this study is to compare the clinical characteristics, disease course, imaging findings between patients with LOMS and adult-onset MS (AOMS).
Methods: This retrospective cohort study included 54 patients with LOMS (patients with age of onset 48 or above were included) and 111 patients with AOMS (age of onset between 18-40) who were diagnosed according to the revised McDonald criteria 2017. They were recruited from Kasr Alainy Multiple Sclerosis Unit (KAMSU) Cairo University.
Results: The mean age of onset for LOMS was 51.18 ± 2.8, while for AOMS it was 25 ± 6.13. Medical comorbidities were more prevalent in LOMS. A higher prevalence of primary progressive MS (PPMS) was found among LOMS while relapsing-remitting MS (RRMS) was more common in AOMS. Additionally, the LOMS group had a significantly lower total number relapse (median=3) than AOMS (median= 4) ($p=0.01$), LOMS also had a lower annualized relapse rate (ARR) (mean±SD, 0.36±0.28) compared to AOMS (mean±SD,3.5±2.7) ($P<0.0001$). Moreover, LOMS had a higher initial Expanded Disability Status Scale (EDSS) compared to AOMS (median=3.25,2.5 receptively, P= 0.01). Regarding the initial presenting symptoms, motor impairment was more common in LOMS patients 25 (46.3%), while visual and sensory symptoms were more common among AOMS patients (23 (20.7%),17 (15.3%)) respectively, ($P=0.002$). During the disease course visual loss and fatigue were observed significantly more often in AOMS compared to LOMS ($P<0.5$). The initial MRI brain showed a higher percentage of infratentorial lesions in the LOMS group compared to the AOMS group.Furthermore LOMS had a significantly longer duration to treatment.
Conclusion: LOMS had lower ARR yet it is associated with a higher intial EDSS and more infratentorial lesions, PPMS is more common LOMS group

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Clinical Aspects of MS & Related Diseases – Pregnancy and Gender Aspects

P1231
Understanding the experiences of neurologists treating women with MS and their perspectives about family planning with MS in Europe and the United States

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Introduction: While multiple disease-modifying therapies (DMT) have been approved for the treatment of MS, safety data during pregnancy are limited due to the exclusion of pregnant women from pivotal clinical trials. Thus, neurologists face challenges in supporting and ensuring optimal outcomes for women with MS (WwMS) during family planning (FP).
Objectives/Aims: To assess neurologists' experiences and attitudes towards FP in MS and explore differences between neurologists working in specialised and non-specialised MS centres.
Methods: Data were collected via the Adelphi Real World MS Disease Specific Programme, a cross-sectional survey across Europe (EU; France, Germany, Italy, Spain, UK) and the US. Neurologists reported their centre level and experiences and attitudes towards FP.
Results: Overall, 400 neurologists (EU=314, US=86) responded to the survey; 49.3% worked in specialised MS centres. MS specialists managed more WwMS in the context of FP compared with non-MS specialists (mean 20.5 vs 11.7, $P<0.0001$). 86.3% of neurologists said they proactively discuss FP with WwMS of childbearing age and 87.8% proactively discuss postpartum DMT and breastfeeding plans during pregnancy. The main reported considerations when prescribing a DMT in the context of FP were MS disease activity presence (70.3%), possibility of an unplanned pregnancy during a DMT (68.5%), time required to be off a DMT prior to conception (66.8%) and the safety of continuing treatment during pregnancy (65.8%). Most neurologists (69.5%) would counsel to delay FP if disease activity is not well controlled, although MS specialists were less likely to provide such advice (65.0% vs 73.9%, $P=0.0459$). 54.3% of neurologists would delay initiating a DMT if a WwMS is planning to get pregnant, with MS specialists less likely to delay DMT initiation (46.2% vs 62.1%, $P=0.0034$). 57.8% of neurologists would prioritise the safety of a DMT to the unborn over its ability to control maternal disease activity, although 31.0% reported both aspects to be of equal priority.
Conclusion: FP is a key consideration for neurologists caring for WwMS of childbearing age. MS specialists were less likely to delay DMT initiation in WwMS planning to get pregnant and delay FP in the presence of disease activity. This may reflect more confidence in treating pregnant WwMS, commensurate with greater experience with WwMS and familiarity with evidence on safe use of DMTs in the context of pregnancy and breastfeeding.

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P1232
Impact of Cross-Sex Hormone Therapy on Prognosis in Multiple Sclerosis

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Introduction: Individuals who do not identify with their sex-assigned-at-birth constitute 0.5% of persons with MS (PwMS) in North America. While a previous study showed that feminizing-CSHT might increase MS risk, MS disease course in individuals undergoing CSHT remains unexplored.
Objectives/Aims: Evaluate the disease course in individuals who are genetically male on feminizing-CSHT with MS (MtF-MS) and individuals who are genetically female on masculinizing-CSHT with MS (FtM-MS).
Methods: An institutional database search was completed for PwMS not identifying with their sex-assigned-at-birth. After a chart review, 10 PwMS who received CSHT (five MtF-MS, five FtM-MS) were identified. MS outcomes of clinical and radiological disease activity and progressive MS (PMS) onset were investigated.
Results: CSHT was uninterrupted in all PwMS (off-CSHT period ⩽2 months), but CSHT varied in dose, route, and formulation. Mean age (years, range) at last follow-up was older in MtF-MS (54.9, 35.1-66.3) than in FtM-MS (39.3, 29.6-47.3). MtF-MS (31.5, 25.1-39.1) were older at MS onset than FtM-MS (21.0, 15.0-29.8). MtF-MS (43.1, 29.0-56.6) were also older at CSHT initiation than FtM-MS (35.6, 20.3-46.5). New clinical disease activity was observed in three PwMS (one MtF-MS, two FtM-MS) within 10 months after CSHT initiation. In two PwMS (one MtF-MS, one FtM-MS), the disease activity marked the onset of symptomatic MS (one MtF-MS, one FtM-MS). In total, seven PwMS (four MtF-MS, three FtM-MS) experienced at least one clinical/radiological disease activity. The 5-year average annual disease activity slightly increased post-CSHT (0.27) compared to pre-CSHT (0.09). Four PwMS transitioned to PMS (50.5, 38.1-59.1); all were MtF-MS. In three PwMS, PMS onset followed CSHT initiation (1-5 years). In parallel, median EDSS was higher in MtF-MS (4.0, 1.5-7.5) than in FtM-MS (2.0, 0.0-3.5).

Conclusion: Both MtF-MS and FtM-MS exhibited increased disease activity following CSHT administration. Transition to PMS was observed exclusively in MtF-MS, with likely contribution of age and male sex-assigned-at-birth with an additional potential effect of CSHT. Comprehensive CSHT history and close follow-up are warranted in PwMS receiving or considering CSHT, and larger long-term studies are needed to better individualize MS care in these individuals.

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P1233
Assisted Reproduction Therapies as a Safe and Effective Option for Women with Multiple Sclerosis Struggling to Conceive: A Systematic Review

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Introduction: MS typically affects women of childbearing age. However, changes in pregnancy decision-making after an MS diagnosis occur, resulting in fewer children and at an older age. Therefore, Assisted Reproduction Therapies (ART) have emerged as a potential option for women with MS (wMS) who wish to become mothers. Despite this, the evidence surrounding ART use in wMS remains scarce.
Objectives/Aims: To summarize the risk of MS and MS relapses after ART producers as well as their rate of success in wMS.
Methods: Following the PRISMA guidelines, we conducted structured searches in EMBASE, PUBMED, and LILACS from July 6, 2021, to December 20, 2024. Studies were included if they were original articles, published in full text, in English or Spanish, and involving human subjects. No restrictions were placed on epidemiological design, sample size, or publication date. The outcomes assessed were the occurrence of MS and its relapses after ART and the success rate in wMS who used ART. The outcomes assessed were the occurrence of MS and its relapses after ART and the success rate in wMS who used ART. The quality of the studies was evaluated using the ROBINS-I and ROBINS-E tools. We did not perform a meta-analysis.
Results: From 532 titles screened, 12 studies met the inclusion criteria. Regarding the risk of MS, one study suggested a protective effect, and another found no association of ART with MS. Eight studies assessed the risk of relapses and disease activity, suggesting that relapse rates post-ART may not be significantly different from pre-ART rates, and one study found an increased risk of relapses after unsuccessful ART procedures. Three studies showed similar birth rates in women with MS using ART. The risk of bias was serious or critical in ten studies, moderate in one and with some concerns in one study.
Conclusion: ART appears to be an effective and safe alternative for wMS who struggle to conceive spontaneously

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P1234
Clinical and MRI predictors of disease activity in the postpartum of women with multiple sclerosis

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Introduction: Pregnancy in MS reduces risk of relapses due to hormonal changes, followed by an increased relapse risk in the postpartum period. Although relapses occurring before or during pregnancy are associated with postpartum disease activity, the role of MRI activity in this context remains less understood.
Objectives/Aims: Pregnancy in MS reduces risk of relapses due to hormonal changes, followed by an increased relapse risk in the postpartum period. Although relapses occurring before or during pregnancy are associated with postpartum disease activity, the role of MRI activity in this context remains less understood. This study aimed to identify clinical and radiological predictors from the prior year to pregnancy associated with postpartum relapses and radiological disease activity.
Methods: This retrospective observational study included pregnancies occurring between April 2014 and April 2024 in women with multiple sclerosis (MS) followed at our MS unit. The analyzed variables included MS relapses in the year before pregnancy, during pregnancy, and in the first postpartum year, EDSS scores and MRI findings, including new T2 lesions and gadolinium-enhancing lesions before and after pregnancy. Statistical analyses assessed differences in MS activity before and after pregnancy. Multivariable analyses identified predictors of relapses and MRI activity during the first postpartum year.
Results: The cohort included 101 pregnancies in 87 women with MS. The mean age at delivery was 35.5 (SD 4.6) years. The

median EDSS score prior to pregnancy was 1.5 (IQR 1.0) and it remained unchanged after the first postpartum year. In the year before pregnancy, 27.7% of patients had at least 1 relapse, and 37.6% in the postpartum year. Relapses prior to pregnancy were associated with postpartum relapses, 60.7% vs 28.8% (p=0.003). Similarly, relapses during pregnancy were also associated with a higher risk of postpartum relapses, 73.3% vs 31.4% (p=0.002). Among the 91 patients with postpartum MRI, 40.7% showed disease activity, with 22.5% presenting gadolinium-enhancing lesions. In this subgroup, pre-pregnancy relapses were associated with postpartum MRI activity, 60% vs 33.3% ($p<0.05$). In the 60 patients with pre-pregnancy MRI, there was no association between MRI activity and postpartum relapses. Among the 52 patients with both pre- and postpartum MRIs, 26.9% showed activity before pregnancy and 32.7% after delivery, with no significant difference. Multivariable analysis revealed that relapses in the year before pregnancy year were associated with postpartum relapses (OR: 7.43 [95% CI: 1.05–52.51], p=0.044), whereas a higher EDSS score was protective (OR: 0.36 [95% CI: 0.14–0.89], p=0.028) and MRI activity had no significant impact.
Conclusion: Relapses may have a greater impact than MRI activity in predicting postpartum relapses

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P1235
The UK MS Pregnancy Register: Insights into Pregnancy and Postpartum Outcomes in Multiple Sclerosis

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Introduction: MS predominantly affects people of childbearing age with people diagnosed with MS facing complex decisions around pregnancy planning. The UK MS Pregnancy Register is a patient-facing register established in 2021.
Objectives/Aims: To generate evidence around pregnancy and MS to inform clinical practice using real-world data.
Methods: Structured questionnaires were completed by participants at 15- and 24- weeks gestation and 3- and 12- months postpartum. Data until March 2025 is presented.
Results: 321 pregnancies were included with a mean age of 34.4; of these, 45% reported at least 1 prior pregnancy with a mean age of 30.8. Most (90%) participants had previously taken a disease-modifying therapy (DMT); 50% participants continued DMT at least until conception and 30% planned to continue throughout pregnancy. Glatiramer acetate (29%) and natalizumab (44%) were the most common DMTs to be continued. Pregnancy loss was reported by 8 (2%) participants. 14 (4%) reported a relapse, all were mild-moderate; 31% of those during pregnancy and 69% postpartum or following miscarriage. Of those with postpartum data available (n=61), 69% had a vaginal birth, with 38% of these requiring assistance. Around two-thirds of caesarean sections were emergencies and approximately half of the planned caesarean sections were elective at the participant's request. Of those with infant postpartum data available (n=48), average gestational age at birth was 39.5 weeks (36 – 42 weeks) and average birth weight was 3.39kg (2.04 – 4.95kg). Half (52%) of participants were exclusively breastfeeding at 3 months. 15 participants reported that MS had impacted their breastfeeding decision, with DMT use cited by 6. A medical issue at 3 months postpartum occurred in 21% infants, most frequently cow's milk protein allergy. For participants, a delivery-related complication was reported by 30%, most commonly postpartum haemorrhage. Median scores for the Edinburgh Postpartum Depression Scale at 3 and 12 months were 9.5 and

5.0 respectively. All infants with available data (n=20) were meeting all expected milestones at 12 months.
Conclusion: Pregnancy outcomes and developmental trajectories of infants born to people with MS appear similar to the general population, providing important reassurance. DMT use appears an important consideration in postpartum decision making, particularly breastfeeding.

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P1236
The Role of Informational Support and Counseling in Improving Sexual Function in Patients with Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) can affect sexual function both directly and indirectly. Sexual dysfunction (SD) in MS patients can be categorized into primary, secondary, and tertiary.
Objectives/Aims: This study aimed to compare the results of the first and second administrations of the Multiple Sclerosis Intimacy and Sexuality Questionnaire-19 (MSISQ) before and after the intervention, to evaluate the effectiveness of the implemented measures.
Methods: Participants completed the MSISQ questionnaire along with socio-demographic and clinical data on two separate occasions, with an interval of 6–12 months. A total of 164 patients (117 females; mean age 39.6 ± 10.9; mean Expanded Disability Status Scale [EDSS] score 2.17 ± 1.27) participated in the first phase. All received educational brochures on managing SD and personalized counseling sent via mail or email. Eighty-three patients (50.6%) agreed to participate in the second phase. Data from both time points were analysed to assess within-subject differences, including only those who responded to both questionnaires. Data were collected at MS centers in Katowice, Poland, between January 2024 and February 2025.
Results: Only 19 patients (22.9%) reported taking action to improve their sexual health during the study: consultations with a sexologist (2.4%) or psychologist (6%), rehabilitation (3.6%), applying brochure recommendations (10.8%), or other methods (3.6%). Subjectively, 59 participants (71.1%) reported no change in their sexual life, 20 (24%) noted improvement, and 5 (6%) reported worsening. The mean MSISQ total score decreased from 36.2 ± 12.5 at baseline to 34.2 ± 13.6 post-intervention, indicating a statistically significant reduction in SD ($t = 2.33$; $p < 0.05$). Secondary SD scores improved significantly ($t = 3.26$; $p < 0.01$), while primary and tertiary SD showed no change. No gender differences ($p > 0.05$) or correlations between MSISQ improvement and EDSS ($r = 0.033$; $p > 0.05$) were observed.
Conclusion: The combination of informational brochures and personalized counseling may effectively alleviate SD in MS patients, particularly secondary SD. However, the low rate of active help-seeking underscores the need for proactive, integrated sexual health strategies in MS care.

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P1237
Reproductive and Sex Hormonal Factors in Multiple Sclerosis: A Study of Their Impact on Diagnosis and Disease Progression

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Introduction: MS predominantly affects women of reproductive age. Fluctuations in sex hormone levels throughout a woman's life, may influence the course of the disease.
Objectives/Aims: To explore the impact of menarche, menstrual cycles, hormonal contraception, pregnancy history, menopause, and hormone replacement therapy (HRT) on MS onset and progression.
Methods: A cross-sectional survey of 336 women with MS was conducted. Data on reproductive milestones, contraception, and disease progression were analyzed using statistical tests, including correlations and regression models.
Results: No significant correlation was found between age at menarche and age at MS diagnosis ($r = -0.014$, $p = 0.81$), and regression analysis showed no predictive relationship ($\beta = -0.0879$, $p = 0.806$). Regarding menstrual cycles, 23.2% of participants reported worsened MS symptoms during menstruation, particularly fatigue. There was a trend toward lower use of hormonal contraception among patients with SPMS ($p = 0.059$). Pregnancy history revealed that women with more than three pregnancies were diagnosed 12.5 years later than those with no pregnancies ($p < 0.001$), with minimal impact on relapses. No differences were found when evaluating the association between early menopause (<40 years) and age of MS diagnosis and progression to SPMS. Few women (3.3%) using HRT reported symptom improvement, with no significant impact on disease progression.
Conclusion: In this cohort of Argentinean women, a history of multiple pregnancies was associated with a delayed MS diagnosis. Other reproductive and hormonal factors, including menarche, menstrual cycles, and contraception, did not show a significant influence on MS onset or progression. The roles of menopause and HRT warrant further investigation to clarify their potential impact on disease course.

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P1238
Gender and Multiple Sclerosis in the real-world: what remains after matching? A propensity score study from the Italian Multiple Sclerosis and Related Disorders Register

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Introduction: Sex and gender play a relevant role in several diseases at many levels. Greater attention to the actual differences in men's and women's health risks, health status, and access to services is critically important for improving the performance of health systems. Without explicit attention to the different health needs of men and women, equitable goals in terms of access to care and treatment will be difficult to achieve.
Objectives/Aims: To analyse differences between males and females in treatment and clinical outcomes of people with MS (pwMS) registered in the Italian Multiple Sclerosis and Related Disorders Register (RISM).
Methods: Data from 11,208 males and 22,414 females pwMS with an onset after 2000 and complete sociodemographic and clinical information were extracted from the RISM. A 1:1 propensity score matching analysis was conducted, using logistic regression, with the first Expanded Disability Status Scale (EDSS) assessment, age at onset, first disease course, year of first disease modifying treatment (DMT), and follow-up as covariates.
Results: The matching led to 11,208 pairs. The median time from onset to diagnosis was approximately 9 months for both sexes. The median time from diagnosis to the first DMT prescription was 2.5 months for males and 2.8 months for females (p-value <0.0001). Significant differences were found in the DMT administration modalities (injection: 64.9% males vs 67.4% females; oral: and 23.6% males vs 21.4% females), last disease course (relapsing remitting: 84.8% males vs 87.0% females; secondary progressive: 7.8% males vs 5.7% females),

last EDSS (low: 69.0% males vs 71.0% females; high 7.2% males vs 5.8% females) and annualized relapse rate (median AAR: 0.24 in males and 0.27 in females).
Conclusion: After propensity score matching, significant differences with respect to the disease course emerged between males and females in accordance with the existing literature, reporting more pronounced inflammation in females, as confirmed by a higher AAR, and a worse prognosis in males, supported by a higher last EDSS score. Despite a significant difference between times from diagnosis to first DMT (±0.33 months), this datum lacks of clinical relevance. Notably, differences in DMT administration were observed, with males receiving more oral and fewer injection drugs than females. These findings suggest that, within this cohort, gender disparities do not appear to influence the access to or quality of MS care.

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P1239
Response to diphtheria and pertussis vaccination in untreated or anti-CD20 exposed Multiple Sclerosis pregnant women

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Introduction: Vaccination during pregnancy provides active immunity of the mother, but also passive immunity of the neonate thanks to maternal antibodies' transfer. In pregnancy, the tetanus-diphtheria-pertussis (Tdap) vaccine is internationally recommended from gestational weeks 27 through 36. Vaccination is recommended also in women with Multiple Sclerosis (MS), but only few studies investigate their immunological response to immunization, especially in women treated with antiCD20 drugs that are known to target B cells.
Objectives/Aims: Aim of this cohort study was to evaluate the response to diphtheria and pertussis vaccination in MS pregnant women untreated or exposed to anti-CD20 therapy before pregnancy.
Methods: Between 2020 and 2024, 37 pregnant women with diagnosis of relapsing-remitting MS were enrolled at the SMamma pregnancy service of the MS Center of Tor Vergata University, Rome, Italy. Serum samples were obtained before Tdap vaccination during II trimester of pregnancy (T0), after immunization at T1 (within 2 weeks *post partum*) and at T2 (within 3 months *post partum*). Anti-diphteria toxin (DT) IgG antibodies and anti-pertussis toxin (PT) IgG were measured on serum samples using Euroimmune and Diasorin ELISA Kits, respectively. Descriptive statistics were performed.
Results: Preliminary results of this study suggest that both untreated and anti-CD20 exposed MS pregnant women can mount an adequate immune response to Tdap vaccination. Further investigation and analyses are needed to draw final conclusions.In our sample, 29 (78.4%) women got the Tdap vaccine during pregnancy and of these 4 (13.8%) had been treated with anti-CD20 therapies before pregnancy.
At baseline (69 median days (63-88.75) pre-immunization), only 8/37 women (22.2%) of the whole sample were not protected for diphtheria, while most of the women had no protection for pertussis (25/37- 71.5% for PT IgG).
Preliminary data showed that after immunization, the whole vaccinated sample had an increase of the levels of both DT and PT IgG antibodies reaching a protection rate for diphteria in untreated MS women of 75% (18/24) and for pertussis of 66,6% (16/24). In anti-CD20 exposed women protection was 75% (3/4) and 50% (2/4) for diphteria and pertussis, respectively.
Conclusion: Preliminary results of this study suggest that both untreated and anti-CD20 exposed MS pregnant women can mount an adequate immune response to Tdap vaccination. Further investigation and analyses are needed to draw final conclusions.

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P1240
Sex differences in multiple sclerosis treatment with disease modifying drugs: a step towards gender neurology

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Introduction: Multiple sclerosis (MS) is an autoimmune demyelinating disorder of the central nervous system. Relevant differences between men and women are known in MS epidemiology, disease course, clinical manifestations and instrumental findings. However, differences in response to disease-modifying treatments (DMTs) have been rarely assessed.
Objectives/Aims: To compare efficacy and safety of DMTs between men and women.
Methods: We performed a registry-based study on patients of our reference center in Palermo, Italy. Only patients with relapsing-remitting course or clinically isolated syndrome were included. Efficacy endpoints we considered were confirmed disease progression risk, relapse risk and magnetic resonance imaging active lesion risk during treatment with each DMT. For safety analysis, withdrawal due to adverse events was considered. Cox multivariable survival analysis was performed to assess the impact of sex on each endpoint.
Results: 1805 records were retrieved. However, due to limited sample size, only data regarding 3 drugs (dimethylfumarate, glatiramer acetate and interferon) were analyzed. No significant differences between the two sexes were found for efficacy endpoints. Men showed a significantly lower risk of withdrawal from glatiramer acetate due to adverse events than women (p=0.002, HR=0.32, 95%CI=0.16-0.65); dyspnea was the most frequent cause of interruption in both sexes.
Conclusion: Our results show few differences in response to DMTs between men and women. Interpretation of these findings is challenging due to scarce evidence available about this topic and to sexual dysmorphism involving many aspects of the disease. Small sample size, preventing from analysis of other DMTs and disease courses, is the main limit of this study. Further evidence will be needed in the future.

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P1241
Pregnancy and Multiple Sclerosis: Outcomes from a Portuguese Terciary Center

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Introduction: The relationship between pregnancy and multiple sclerosis (MS) remains complex, with ongoing debate about their mutual influence. As MS is predominantly diagnosed in women of reproductive age, understanding this interaction is essential for informed clinical decision-making.
Objectives/Aims: To characterize a Portuguese population of pregnant women with MS, describe maternal and fetal outcomes, and evaluate pregnancy's impact on the disease course.
Methods: A retrospective, and observational study was conducted at a tertiary care center in Portugal between January 2017 and December 2024. Pregnant women with a confirmed diagnosis of MS were included. Cases involving multiple gestations or voluntary pregnancy termination were excluded. Data from medical records were analysed using descriptive statistics (frequencies, percentages, mean±SD, median [IQR]).
Results: A total of 49 patients were included, all with relapsing-remitting MS, with a mean age at diagnosis of 26.1±5.4 years. 51.0% were nulliparous. Only 6.1% experienced a relapse during pregnancy, with 66.6% of those managed with corticosteroid therapy. Most patients (77.6%) were not under disease-modifying treatment during pregnancy. 10.2% received natalizumab, 10.2% glatiramer acetate, and 2.0% interferon-beta. The median EDSS score remained stable before and after pregnancy (1.5; 1.0-1.5). The annualized relapse rate was 0.7 in the year preceding pregnancy and 0.6 in the year following delivery. The mean maternal age at delivery was 33.6±4.2 years. Preterm birth occurred in 10.4% of cases, with a median gestational age at delivery of 38.0 (38.1–40.0) weeks. Spontaneous labor occurred in 54.2% of pregnancies. Instrumental assistance was required in 34.6% of cases, while cesarean section was performed in 24.5%, most frequently due to fetal distress (40.0% of cesareans). The median birth weight was 3220 grams (2837.5–3557.0). A 1st-minute Apgar score below 7 was observed in 6.3% of newborns, and neonatal intensive care unit admissions occurred in 6.1% of cases. The average length of maternal hospital stay was 3.0 (2.0-3.5) days. Breastfeeding was achieved by 56.4% of mothers.
Conclusion: In this Portuguese cohort, pregnancy did not appear to negatively affect MS course, nor did MS adversely impact maternal or neonatal outcomes. Findings support safe pregnancy management in women with MS with appropriate monitoring and care.

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P588
Analysis of Pregnancy Complications and Offspring Outcomes in Multiple Sclerosis Using National Health Care Data in Korea

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Introduction: Multiple Sclerosis (MS) is a rare CNS demyelinating disease in Korea. Pregnancies in patients with MS are often considered high risk due to a higher incidence of obstetric complications and an increased likelihood of relapse. However, the pregnancy related complications and fetal outcomes in patients with MS remain uncertain.
Objectives/Aims: We investigated pregnancy-related and fetal complications in patients with MS using data from the National Health Insurance Service (NHIS) in Korea.
Methods: We analyzed NHIS claim data, including information from National Health Screening Examination (NHSE) and National Health Screening Program for Infants and Children in Korea. Our cohort consisted of pregnant women with MS (pgMS) and matched controls, selected based on age and Charlson Comorbity Index. This study included women with singleton pregnancies with live births from 2011 to 2020 who had participated in the NHSE within 4 years prior to pregnancy. We assessed pregnancy complications (e.g., gestational hypertension) and offspring outcomes (e.g., congenital malformations). Propensity score matching and multivariable logistic regression were used to estimate the risk of maternal complications and fetal outcomes. All statistical analyses were performed using SPSS (ver 23.0), and p value <0.05 was considered statistically significant.
Results: A total of 3,904,808 women who delivered between 2011 and 2020, 481 (0.012%) were diagnosed with MS. PgMS had higher rates of hypertension (2.49% vs 0.98%, p=0.0002) and diabetes mellitus (DM) (7.48% vs 2.37%, p<0.0001). However, no significant differences were observed in obstetric complications, including gestational DM (p=0.06), placental abruption (p=0.64), and postpartum hemorrhage (p=0.64). However, preterm birth (p=0.002) and placenta previa (p=0.03) were higher observed in pgMS. The offspring of MS patients had a higher incidence of congenital malformations of respiratory system (1.25% vs 0.44%, p<0.01) and muscular skeletal system (6.86% vs 4.39%, p=0.01). In the analysis of neonatal complications, there was no significant differences in respiratory distress syndrome (p=0.06), bronchopulmonary dysplasia (p=0.14) or hypoglycemia (p=0.60). In multivariable regression analysis, fetal outcomes showed significant differences in preterm birth (OR 2.46, 95% CI 1.35-4.48) and placenta previa (OR 1.788, 95% CI 1.01-3.15) after adjustment. Neonatal complications did not differ in pgMS after adjustment.
Conclusion: We evaluated maternal and fetal complications and neonatal systemic malformations in pgMS, compared to healthy pregnant women. PgMS did not show increased risks for most obstetric complications or neonatal congenital malformation compared to the general population. However, there was a higher risk of preterm delivery or placenta previa among pgMS. Further research through MS pregnancy registries or prospective studies is needed to better understand the risks associated with MS.

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Clinical Aspects of MS & Related Diseases – Clinical Assessment Tools

P1242
Identifying Gaps in Guideline-Based Care for Paediatric Multiple Sclerosis Through Informatics

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Introduction: MS is a chronic inflammatory demyelinating disease of the central nervous system, with paediatric onset (POMS) accounting for 10% of cases. The American Academy of Neurology (AAN) has established quality measures to optimize MS care, yet their implementation in POMS remains unexplored.
Objectives/Aims: To leverage clinical informatics to assess adherence to AAN-defined quality measures in a large cohort of POMS patients at a tertiary care center utilizing structured data from the electronic health record (EHR) and natural language processing (NLP) to extract clinically relevant information and identify current practice gaps.
Methods: A retrospective chart review was performed of patients with POMS at Texas Children's Hospital between 2015 and 2024. Clinical data, including clinical visits, medications, imaging, procedures, and laboratory results, was abstracted from structured EHR fields. NLP was applied to clinical documentation to evaluate adherence to key quality metrics, including documentation of medication side effects, bowel and bladder dysfunction, fatigue screening, and physical activity counseling.
Results: 189 patients with POMS were identified, 66% female, 34% male. 51% were of Hispanic or Latino origin, while 21% were White non-Hispanic, and 23% were Black non-Hispanic. These patients had over 1,600 unique neurology clinic visits and 986 MRIs performed. While 35% had neuropsychological evaluations and 17% had paediatric psychology or psychiatry visits, screening for bowel/bladder dysfunction, fatigue, and exercise counseling was notably underperformed. Monitoring practices varied by therapy type: patients receiving infusion therapies typically underwent medication monitoring during treatment sessions, while those on oral or injectable therapies were predominantly monitored during routine clinic visits.
Conclusion: Leveraging structured data and NLP, we identified significant gaps in adherence to AAN quality measures in paediatric MS care. These deficits may reflect limited time for screening, documentation burden, and challenges in adapting adult-focused metrics to paediatric practice. Integrating tailored EHR tools may enhance screening and documentation workflows, supporting the consistent application of quality metrics. Future efforts should also incorporate transition planning to adult MS care. These findings highlight the potential of clinical informatics to drive data-informed improvements in paediatric neuroimmunology.

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P1243
Assessing the risk of irreversible ambulatory impairment over the long-term: application of the Risk of Ambulatory Disability (RoAD) score in a real-world single-center multiple sclerosis cohort

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Introduction: The Risk of Ambulatory Disability (RoAD) score is a validated prognostic tool, ranging from 0 to 8, based on demographic and clinical prognostic factors at baseline - age, disease duration, Expanded Disability Status Scale (EDSS) - and 1-year predictors of treatment response - relapse assessment, presence of new T2 lesions gadolinium enhancement at follow-up magnetic resonance imaging (MRI) scans.
Objectives/Aims: To evaluate the RoAD score in a large real-world cohort, assessing the performance in prognosticating irreversible disability accrual.
Methods: A retrospective, monocentric analysis on the large cohort of patients followed at the MS Center of Bari was conducted. We included patients with a relapsing-remitting (RR) course, at least 5 years of follow-up, treated with at least one disease modifying treatment (DMT), an initial EDSS<4.0, annual neurological evaluations and MRI scans at baseline and after 1 year of treatment. To estimate the risk of reaching irreversible EDSS $\geq$6.0 a Cox regression model was performed by applying the RoAD score dichotomized (<4 vs $\geq$4) as the independent variable.
Results: After applying the inclusion criteria, we retrieved a cohort of 1051 RRMS patients, of whom 705 (67.1%) were female. The median (IQR) follow-up was 18.01 (12.76-23.01) years. Throughout the study period, 123 (11.7%) patients reached the disability milestone of irreversible EDSS 6.0 after a median (IQR) time of 9.47 (5.80-14.81) years. 1051 (97.5%) subjects were first treated with moderate efficacy (ME) DMTs (interferon-beta products, dimethyl fumarate, teriflunomide). A significantly lower percentage of patients treated with oral ME DMTs reached the outcome, compared to interferon-beta products (5.4% vs 12.1%, p=0.005). Stratifying by RoAD score <4 (874, 83.2%) vs $\geq$4 (177, 16.8%), the Cox model demonstrated an HR of 3.16 of reaching an irreversible EDSS $\geq$6.0 (95% CI 2.19–4.56, $p < 0.001$).
Conclusion: In patients with RRMS, the RoAD score is a valuable tool for predicting irreversible ambulatory disability at an early stage of the disease. Further studies are needed to test this score's applicability to MS cohorts treated with the newest DMTs.

Disclosure of interest: The authors report no conflicts of interest with respect to the contents of the current study, but note that the patients in the study were treated with a number of disease-modifying drugs and that the authors have received advisory board, membership, and speakers honoraria, travel support, research grants, consulting fees, or clinical trial support from the manufacturers of those drugs, including Actelion, Allergan, Almirall, Alexion, Bayer Schering, Biogen, Celgene, Excemed, Genzyme, Forward Pharma, Ipsen, Medday, Merck, Mylan, Novartis, Sanofi, Roche, and Teva, and their local affiliates.

P1244
A 20% change in the Timed 25-Foot Walk Test and 9-Hole Peg Test is clinically meaningful

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Introduction: Timed 25-Foot Walk Test (T25FWT) and 9-Hole Peg Test (9HPT) are commonly used in MS to assess lower and upper limb function. Clinically meaningful within-person changes are often defined as changes perceived by patients as being clinically important. For T25FWT and 9HPT, a threshold of a 20% change is often used, although it is not universally accepted. A 20% worsening in performance on either outcome is associated with an increased risk of long-term disability progression, as measured by Expanded Disability Status Scale.
Objectives/Aims: To consolidate existing research on clinically meaningful within-person change thresholds of 20% for T25FWT and 9HPT.
Methods: A targeted literature review was conducted to identify all English language articles on meaningful change estimation for T25FWT and 9HPT. Per industry standards, anchor-based approaches were considered the most robust methods, with distribution-based and qualitative methods used as supportive evidence. Relevant findings from each included study were systematically summarised.
Results: We identified 11 studies that provided key supportive evidence for a 20% change being considered clinically meaningful for T25FWT and/or 9HPT. Studies using anchor-based methods confirmed the clinical relevance of a 20% change as clinically meaningful for T25FWT, with changes of 20% or greater associated with meaningful changes in the Multiple-Sclerosis Walking Scale-12, Short-Form 36 physical component score (SF-36 PCS) and clinical global impressions of change. Other findings that supported this cut-point for T25FWT included an analysis of measurement variability in clinically stable patients, association with measures of patient-perceived disability including the Guy's Neurological Disability Scale (GNDS), SF-36 PCS and Multiple Sclerosis Impact Scale-29 physical and the distribution-based estimate of 17.8%. Fewer studies investigated a 20% change threshold for 9HPT; however, some studies provided supportive evidence for a 20% change on 9HPT. These included measuring testing variability in stable patients, association of a 20% change with meaningful change in patient-perceived disability on GNDS and SF-36 PCS and the distribution-based estimate of 15.3%.

Conclusion: Findings supported a 20% worsening in T25FWT and 9HPT as a clinically meaningful threshold. Incorporating these thresholds in composite outcome measures, such as composite confirmed disability progression (cCDP), may enhance the comprehensive assessment of disease progression in people with MS.

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P1245
Association Between Lower Extremity Reaction Time and Walking Function and Balance in People with Multiple Sclerosis: A Cross-Sectional Study

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Introduction: Reaction time involves the integration of cognitive and motor functions, which are commonly impaired in people with multiple sclerosis (pwMS). Walking function and balance problems are common in this population. To our knowledge, the association between lower extremity reaction time and walking function and balance has not been studied extensively. Exploring this may guide more comprehensive rehabilitation strategies aimed at improving walking function and balance.
Objectives/Aims: To investigate the association between lower extremity reaction time and walking function and balance in pwMS.
Methods: Sixty pwMS (mean age= 45.32±7.50 years; EDSS= 2.36±0.41) participated in this cross-sectional study. Lower extremity reaction time was measured using the BlazePod™ device, which required patients to extinguish four different sensors that flashed randomly with their dominant foot over a 10-second period. Walking function was assessed using the 6-Minute Walk Test (6MWT) and Timed Up and Go (TUG) test. Static (eyes open and closed) and dynamic balance were assessed using the Korebalance Balance Evaluation System, a computerized platform.
Results: The mean lower extremity reaction time was 0.95±0.25 seconds. It was negatively correlated with 6MWT ($r=-0.576$, $p<0.001$) and positively with TUG ($r=0.637$, $p<0.001$). No significant correlation was found with balance outcomes measured by the Korebalance system ($p>0.05$).
Conclusion: An increased lower extremity reaction time has been associated with reduced walking capacity in pwMS. Although there is no significant relationship between lower extremity reaction time and static and dynamic balance results, its relationship with walking function may indirectly affect balance. Reaction time and related factors should be examined in the evaluation processes of pwMS. Additionally, we believe that adding exercises that can improve reaction time to treatment programs may support walking function and potentially influence balance positively.

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P1246
A Fast and Novel Emoji-Based Patient-Reported Outcome Measure in Multiple Sclerosis

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Introduction: Incorporating the patient's perspective using patient-reported outcome measures (PROMs) is important in MS care. As a novel, emoji-based PROM, Mayo Clinic Electronic Emoji-Based Neurological Impairment Status (MEBNIS) is designed to track disability in MS in four symptom domains: Memory^{MEBNIS}, Mood^{MEBNIS}, Fatigue-Sleepiness^{MEBNIS}, and Ambulation^{MEBNIS}. Composite^{MEBNIS} is calculated as the sum of these four domains, reflecting the overall disability.
Objectives/Aims: To investigate the correlations of MEBNIS scores with established clinical and radiological markers of disease severity in persons with MS (pwMS).
Methods: A total of 195 pwMS were prospectively recruited between May 2021-May 2024 and completed MEBNIS, Expanded Disability Status Scale (EDSS), MS Functional Composite (MSFC) and its subtests [25-foot walk test (25FWT), 9-hole peg test (9HPT), paced auditory serial addition test (PASAT)], Beck Depression Inventory (BDI), Fatigue Questionnaire (FQ), Epworth Sleepiness Scale (ESS). Participants also underwent brain MRIs.
Results: The average age at MEBNIS administration was 48.5±13.4 years, the female-to-male ratio was 2.5:1, and 32.8%

had progressive MS. With aging, Memory^{MEBNIS} (r=0.17, p=0.017), Ambulation^{MEBNIS} (r=0.37, p<0.001), and Composite^{MEBNIS} (r=0.16, p=0.028) scores worsened. Memory^{MEBNIS} (r=-0.25 to 0.36) and Ambulation^{MEBNIS} (r=-0.59 to 0.69) scores correlated with all tested clinical metrics (p<0.05). Mood^{MEBNIS} and Fatigue-Sleepiness^{MEBNIS} scores correlated with ESS, FQ, and BDI (p<0.05). Composite^{MEBNIS} score correlated with all clinical tests/surveys [EDSS (r=0.47), MSFC (r=-0.42), 25FWT (r=0.49), 9HPT (r=0.36), PASAT (r=-0.26), ESS (r=0.38), FQ (r=0.64) and BDI (r=0.58) (p<0.001, all correlations)]. Memory^{MEBNIS} (r=-0.17, p=0.023), Ambulation^{MEBNIS} (r=-0.30, p<0.001), and Composite^{MEBNIS} (r=-0.20, p=0.007) scores inversely correlated with total cortical gray matter volume. These domains also inversely correlated with thalamic volume (p<0.05). Mood^{MEBNIS} and Fatigue-Sleepiness^{MEBNIS} scores did not correlate with any regions of interest on MRI (p>0.05).

Conclusion: MEBNIS demonstrated significant correlations with both clinical and radiological metrics across multiple domains. These findings support the potential of MEBNIS as a user-friendly, visual PROM to screen, triage, and follow-up pwMS with future longitudinal studies needed to further evaluate its clinical utility.

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P1247
Association between quality of life and brain volume in multiple sclerosis patients experiencing progression independent of relapse activity

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Introduction: Persons with relapsing remitting multiple sclerosis (PwRRMS) with progression independent of relapse activity (PIRA) have reduced quality of life (QoL) and accelerated brain atrophy. The relation between PIRA, brain volume (BV), and QoL needs further investigation.

Objectives/Aims: Explore the association between PIRA, BV, and QoL patient reported outcome measures (PROMS) among PwRRMS.

Methods: 125 newly diagnosed PwRRMS were included, and assessed annually with expanded disability status scale (EDSS), conventional magnetic resonance imaging (MRI), synthetic MRI, occurrence of relapses, and QoL PROMs: EuroQoL 5 Dimension 3 level (EQ-5D 3L), EQ visual analogous scale (EQ VAS), 29-item MS Impact Scale (MSIS-29). Linear mixed effects models (LMMs) where used to assess how BV measures (myelin [MYL]/intracranial volume [ICV], non-aqueous component [NAC]/ICV, brain parenchymal fraction [BPF], and grey matter [GM]/ICV) influenced QoL PROMs in PwRRMS with PIRA during five years of follow-up.

Results: 34% (43) PwRRMS in the cohort had PIRA, 72% (90) where female, median EDSS 2 (interquartile range [IQR] 1-2.5). Age and GM/ICV differed significantly at baseline between non-PIRA (mean age 33.59 years, SD 9.03; mean GM/ICV 48.80, SD 3.86) and PIRA PwRRMS (mean age 37.6 years, SD 11.39; mean GM/ICV 47.27, SD 2.75), with p-values of 0.033 and 0.037, respectively. LMMs found significant effects of BV on QoL PROMs among PwRRMS with PIRA: EQ VAS was affected by MYL/ICV (β1.19, 95%CI 0.146-2.235; p=0.026) and NAC/ICV (β1.681, 95%CI 0.362-3.001; p=0.013), indicating that higher values of MYL/ICV and NAC/ICV were associated with improved QoL. The physical subscale of MSIS-29 was affected by NAC/ICV (β-0.05, 95%CI -0.093-(-)0.008;

p=0.02) and BPF (β-1.346, 95%CI -2.287-(-)0.405; p=0.005), and the psychological subscale of MSIS-29 was affected by NAC/ICV (β-0.076, 95%CI -0.135-(-)0.017; p=0.011) and BPF (β-2.056, 95%CI -3.414-(-)0.699; p=0.003), indicating decreased QoL with lower NAC/ICV and BPF.
Conclusion: Reduced myelin, NAC, and BPF over five years are linked to worsened QoL PROMs in PwRRMS with PIRA. Thus, measuring QoL using PROMs in a clinical setting could be useful, as deteriorating QoL can be a sign of disease progression, particularly in the context of brain atrophy.

Disclosure of interest: Sarah Lindberg has nothing to disclose. Sofia Sandgren has received compensation for lectures from Novartis and Merck, and has served on scientific advisory boards for Merck. Markus Axelsson has received compensation for lectures and/or advisory boards from Biogen, Genzyme and Novartis. Igal Rosenstein has received compensation for lectures from Biogen, Novartis, Merck and Sanofi, and has served on advisory boards for Sanofi. Claes Malmeström has received honoraria for lectures and advisory board memberships from Biogen, Merck, Novartis, and SanofiAventis. Jan Lycke has received travel support and/or lecture honoraria and has served on scientific advisory boards for Alexion, Biogen, Bristol Myers Squibb, Celgene, Janssen, Merck, Novartis, Roche and Sanofi; and has received unconditional research grants from Biogen and Novartis, and financial support from Sanofi for an investigator-initiated study. Lenka Novakova has received lecture honoraria from Biogen, Novartis, Teva, Sanofi, Merck and has served on advisory boards for Merck, Janssen and Sanofi.

P1248
Reliability and Validity of the Psychomotor Vigilance Test to measure cognitive fatigability in Multiple Sclerosis

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Introduction: Cognitive fatigability differs from general feelings of cognitive fatigue. Fatigability is the decline in performance over short time periods indicating inattention and impaired alertness. While there are several self-reported questionnaires for MS-related fatigue such as the Fatigue Scale for Motor and Cognitive Functions (FSMC) and Visual Analog Scale (VAS) there are very few valid and reliable objective measures to index cognitive fatigability. Cognitive fatigability during The Psychomotor Vigilance Test (PVT) has been shown to be sensitive to sleep deprivation and alertness in people with brain injury, pilots, elite athletes and school children, but has yet to be validated in MS.
Objectives/Aims: This study examined the test-retest reliability of a computerized PVT (reaction time and number of mental lapses) and its associations with FSMC and VAS in individuals with MS. We expected that PVT outcomes would have stronger correlations with self-reported cognitive (convergent validity) than motor (divergent validity) fatigue.
Methods: Seventeen participants with MS completed three sessions (7-10 days apart) of a 10-minute PVT. Reaction time and lapses were measured during each session. Participants completed the FSMC and VAS questionnaires. Test-retest reliability for the PVT was assessed using Intraclass Correlation Coefficients (ICC). Validity was evaluated using Pearson's correlation coefficients between the PVT indices and FSMC and VAS scores.
Results: The PVT demonstrated excellent test-retest reliability for reaction time (ICC = 0.898, $p < 0.001$) and number of lapses (ICC = 0.913, $p < 0.001$). Convergent validity results showed a moderate positive correlation between FSMC cognitive fatigue and PVT reaction time ($r = 0.643$, $p = 0.004$) but not with PVT number of lapses ($r = 0.369$, $p = 0.132$). As expected, neither PVT reaction time nor number of relapses was significantly correlated with FSMC motor fatigue ($r = 0.435$, $p = 0.072$ and $r = 0.232$, $p = 0.355$ respectively). Notably, there were no significant correlations between PVT reaction time ($r = 0.321$, $p = 0.193$) or number of relapses ($r = 0.216$, $p = 0.389$) and feelings of overall fatigue measured using VAS.
Conclusion: The 10-minute computerized PVT demonstrated strong test-retest reliability and convergent validity with cognitive fatigue, supporting its use as a reliable tool to quantify cognitive fatiguability in individuals with MS.

Disclosure of interest: Nothing to disclose.

P1249
Physiotherapy and Confirmed Disability Improvement in People with Multiple Sclerosis

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Introduction: Confirmed disability improvement (CDI) is an emerging outcome in disease-modifying treatment (DMT) trials including people with multiple sclerosis (pwMS). A significant limitation is the inadequate consideration of physiotherapy's impact on disability improvement. Physiotherapy, proven to enhance mobility and dexterity, can significantly influence trial outcomes but is rarely incorporated into statistical models.
Objectives/Aims: Evaluate the occurrence of CDI in pwMS, and how it can be impacted by physiotherapy.
Methods: Data was extracted from the German Multiple Sclerosis Registry [data export: Sep. 2024]. Inclusion criteria were age ⩾18 and at least two years of continuous follow-up and physiotherapy

documentation. PwMS undergoing continuous physiotherapy ⩾6 months were matched to those who did not receive physiotherapy using a 1:1 matching for sex, DMT status, age at baseline, Expanded Disability Status Scale (EDSS), and disease duration. CDI was defined by reduction in EDSS of 1.5, 1.0, or 0.5 from a baseline level of 1.5, 2.0–5.5, and ⩾6.0, respectively, confirmed after ⩾3 months. Mean cumulative function (MCF) estimation for recurrent events assessed the occurrence of CDI related to, and independent from, physiotherapy, with results stratified by demographics and clinical factors.

Results: Records from 45,949 pwMS were screened and 1,430 participants with complete data and sufficient follow-ups were selected for matching. From those, 362 pwMS undergoing physiotherapy were matched to 362 without. In all participants (with and without physiotherapy), younger age (<48 years old, 17.0% vs 10.1%; p=0.075) and EDSS ⩾4 (18.6% vs 11.6%; p=0.030) were associated with significantly higher MCF for CDI compared to their counterparts. Physiotherapy was associated with a higher incidence of CDI (16.3% vs 11.1%; p=0.040) during up to 8 years of follow-up. Subgroup analyses revealed a statistically significant benefit of physiotherapy in pwMS with EDSS scores ⩾4 (25.3% vs 11.5%; with vs without physiotherapy, respectively, p=0.006) and with older age (12.3% vs 8.2%; p=0.031), while no significant benefit was observed in younger pwMS or those with lower EDSS scores.

Conclusion: This study leverages registry data to demonstrate the impact of physiotherapy on CDI occurrence. The findings underscore the importance of considering physiotherapy exposure in DMT trials and real-world studies, particularly for pwMS with higher EDSS scores and older age groups.

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P1250
A Generation Apart: Long-Term Outcomes of People with Multiple Sclerosis Diagnosed in the 1990s vs 2010s

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Introduction: Over the last three decades, the landscape of multiple sclerosis (MS) has changed dramatically due to earlier recognition of disease symptoms, advances in neuroimaging and diagnostic criteria, and the availability of increasingly effective disease-modifying therapies (DMTs).

Objectives/Aims: This study aimed to compare the clinical trajectories of patients diagnosed with MS in two distinct periods—1990–1996 and 2008–2014—to evaluate the real-world impact of evolving clinical practice on long-term disease outcomes.

Methods: A retrospective cohort design was used to compare patients diagnosed in two eras: Group 1 (1990–1996, n=133) and Group 2 (2008–2014, n=579). Demographic data, time from symptom onset to diagnosis, Expanded Disability Status Scale (EDSS) scores at diagnosis and 10-year follow-up, annualized relapse rates (ARR), and the rate of conversion to secondary progressive MS (SPMS) were recorded. Statistical analyses included independent and paired sample t-tests, chi-square tests, and Mann–Whitney U tests as appropriate.

Results: The total cohort included 712 patients (mean age: 50.7 ± 12.2 years; mean disease duration: 20.7 ± 8.8 years; 70.4% female). Time from symptom onset to diagnosis was significantly shorter in Group 2 (3.2 ± 4.6 years) compared to Group 1 (4.2 ± 4.7 years, $p<0.005$). The initial EDSS scores were lower in Group 2 (2.32 ± 1.52) than in Group 1 (2.95 ± 1.63; $p<0.001$). After 10 years, patients in Group 2 had significantly better disability outcomes (mean EDSS: 1.85 ± 2.02) compared to Group 1 (3.97 ± 2.23; $p<0.001$). ARR was also lower in Group 2 (0.18 ± 0.20) than in Group 1 (0.23 ± 0.20; $p<0.05$). While 52.6% of Group 1 patients had progressed to SPMS after 10 years, this figure was only 5.4% in Group 2.

Conclusion: This comparative analysis provides compelling evidence that major advances in MS diagnosis and treatment have substantially improved long-term outcomes. Patients diagnosed in more recent years benefited from earlier detection, more rapid initiation of therapy, and access to higher efficacy DMTs. These factors likely contributed to the significantly lower levels of disability, reduced relapse rates, and markedly lower rates of SPMS conversion observed in Group 2. Our findings highlight the importance of continued refinement in diagnostic strategies, early therapeutic intervention, and widespread access to potent DMTs in shaping the disease trajectory. Looking ahead, real-world data such as this not only validate

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P1251
Evaluation of Clinical and Digital Data Using Wearable Devices in Patients with Spasticity in Multiple Sclerosis

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Introduction: This study evaluates the suitability of digital measures for monitoring daily limitations caused by spasticity and compares these with established clinical scores (e.g., Modified Ashworth Scale (MAS), Expanded Disability Status Scale (EDSS)). Managing spasticity in MS is challenging, often requiring frequent therapy adjustments or discontinuation due to side effects. Wearable-based digital biomarkers enable continuous monitoring of movement, step counts, and sleep, potentially enhancing understanding of spasticity and treatment effects.
Objectives/Aims: The aim of the study is to evaluate whether digital measurements are suitable for monitoring spasticity-related limitations in everyday life and to compare them with established clinical scores.
Methods: A multicenter prospective study is being conducted with MS-related spasticity patients at University Hospitals Düsseldorf and Bochum as well as the MS specialist clinic Hachen. 50 patients will be monitored over six months, with three clinical visits at 3-month intervals. Each visit includes clinical exams (MAS, EDSS) and questionnaires on quality of life, symptoms, pain, mood, and MS-related impairments. Continuous activity, sleep, and cardiac data are recorded using the Withings® Scanwatch. A follow-up phone call after one week resolves technical issues.
Results: By the end of 2024, 48 patients (45.8% male, mean age 54.8 ± 10.3 SD) with a mean disease duration of 17.8 ± 10.3 SD years have been enrolled. Adherence was 93.4% (45/48 patients ⩾75% smartwatch recording time). The median EDSS score at baseline was 6 ± 2.5 IQR. First analyses showed a correlation between composite MAS between lower extremities and step data (Maximum MAS of 1. hip joint: r = -0.35; p = 0.047; 2. knee joint: r = -0.36; p = 0.043; 3. talocrural joint: r = -0.38; p = 0.032). Further data will be presented at ECTRIMS.
Conclusion: Initial findings indicate that digital monitoring correlates with clinical scores, offering insights into spasticity's daily impact and underscoring the potential of digital biomarkers in routine care.

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P1252
Impact of Menopausal Status and Gender on Disease Progression and Clinical Outcomes in Multiple Sclerosis

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Introduction: Sex and hormonal status are increasingly recognized as important modifiers of disease course in multiple sclerosis (MS). Hormonal fluctuations, particularly those associated with menopause, may impact both disease activity and long-term disability. Clarifying these differences may contribute to more personalized and effective management strategies in MS.
Objectives/Aims: To investigate clinical characteristics and EDSS progression in MS patients stratified by menopausal status and gender.
Methods: MS patients were stratified into three groups according to menopausal status and gender. Men were selected to match the age distribution of postmenopausal women. Demographic and clinical characteristics were compared across groups.
Results: The study included 864 individuals with MS, drawn from a larger cohort. Of these, 300 (34.7%) were postmenopausal women, 298 (34.5%) were premenopausal women, and 265 (30.7%) were men. The mean age was 64.77 ± 6.87 years in postmenopausal women, 40.86 ± 4.15 years in premenopausal women, and 61.01 ± 8.25 years in men. Disease duration was 24.17 ± 10.84 years in postmenopausal women, 19.49 ± 3.65

years in premenopausal women, and 21.09 ± 9.78 years in men. Age at disease onset was 40.60 ± 10.88 years in postmenopausal women and 39.91 ± 10.52 years in men.
In the total cohort, 592 patients (68.5%) had relapsing-remitting MS (RRMS), 181 (21.0%) had secondary progressive MS (SPMS), and 90 (10.4%) had primary progressive MS (PPMS).
At first clinical assessment, EDSS scores were significantly higher in men (3.79 ± 1.92) than in postmenopausal women ($p<.001$), while no significant difference was found between the two female groups (p=0.671). At the time corresponding to menopause, EDSS scores were similar between postmenopausal women (3.60 ± 2.32) and premenopausal women (p=0.555).
Premenopausal women reported using a significantly higher number of disease-modifying therapies (2.27 ± 1.22) compared to postmenopausal women (p=0.024), while medication use in men (2.20 ± 0.98) was similar to both female groups ($p>0.05$).
The annualized relapse rate (ARR) was highest in premenopausal women (0.25 ± 0.15), followed by men (0.20 ± 0.16) and postmenopausal women ($p<0.001$).
EDSS progression was observed most frequently in men (n=96, 36.8%), followed by premenopausal women (n=83, 28.6%) and postmenopausal women (n=78, 27.5%, p=0.039). Although premenopausal women had greater relapse activity and treatment intensity, disability worsening over time was more pronounced in the male group.
Conclusion: Men demonstrated the highest rate of EDSS worsening despite comparable disease duration and age at onset with postmenopausal women. Premenopausal women showed greater relapse activity and treatment intensity, while men exhibited more pronounced disability progression.

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P1253
Fist-Palm Test (FiPaT): a novel bedside test to screen for cognitive impairment in Multiple Sclerosis

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Introduction: Fist-Palm Test(FiPaT) is a novel non-verbalmotor task, able to screen for global cognitive status and to predict cognitive impairment.
Objectives/Aims: The aim of our study was to evaluate if FiPat could screen for cognitive status in patients with Multiple Sclerosis(pwMS)
Methods: One-hundred-eleven pwMS with mild disability (EDSS<2) and 28 age, sex and education matched Healthy-Subjects(HS) underwent:Neurological assessment with EDSS and nine-hole-peg test (9HPT), FiPaT (defined altered if final score was >=1); Brief Repeatable Battery of Neuropsychological tests.
Results: PwMS were more cognitive impaired than HS(28.8%pwMS vs0%HS,p=0.001).
FiPaT scores were higher in pwMS than HS (mean 0.69vs0.21, p=0.03); FiPaT was impaired in 30.6% pwMS and in 14.3%HS(p=0.08).
PwMS with altered FiPaT were older(46vs39.4years old, p=0.01) and showed higher times at dominant hand 9HPT (9HPT-DH) (23.2vs21.1, p=0.005) than pwMS with normal FiPaT, whereas the two PwMS groups displayed no differences in gender, EDSS, disease duration, treatment type, non-dominant hand 9HPT(9HPT-NDH).
Symbol digit modality Test (SDMT) (mean 0.24vs-0.46, $p<0.001$); Selective–Reminding-Test (SRT) Consistent Long-Term-Retrieval (SRT-CLTR) (-.51 vs -1.31, p=0.002), SRT-Long-Term-Storage (SRT-LTS) (-.64vs-1.17, p=0.03), SRT delayed (SRT-D) (-.52vs-1.11, p=0.02) 10/36 SPAtial Recall Test (SPART) (-.25vs-.88, p= 0.002) were significantly lower in pwMS with altered FiPaT.
In pwMS, FiPaT was a predictor of SRT-CLTR (FiPaT p=0.008; beta-.27) and SPART (FiPaT p=0.002; beta-.3), whereas FiPaT and 9HPT-DH were predictors of SDMT (FiPaT p=0.002; beta -.3; 9HPT-DH p0.004, beta -.24) independently from age, education, disease duration, EDSS,9HPT-NDH.
ROC analysis, to evaluate the accuracy of FiPaT in identifying cognitive impairment in MS, showed an Area Under the Curve of 0.59 (95%conf. int. 0.49-0.69) whit a sensitivity of 43.7% and specificity of 74.4%.
Conclusion: FiPaT could be a quick tool to screen cognitive status in pwMS.

Disclosure of interest: Umberto De Marca: nothing to disclose

P1254
Real-World Incidence and Risk Factors for IgE-Mediated Allergic Reactions to Ocrelizumab in Multiple Sclerosis: A Retrospective Single-Center Cohort Study

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Introduction: Real-world data on infusion-related allergic reactions during ocrelizumab (OCR) treatment in patients with MS are limited. .
Objectives/Aims: The aim of this study was to evaluate the incidence and characteristics of infusion-related allergic reactions to OCR in a real-life MS cohort and to identify potential associated risk factors
Methods: This retrospective cohort study was conducted at a tertiary care hospital. All patients who received at least one OCR infusion between 2018 and 2024 were included. Patients with grade-3 infusion-related reactions (IRRs) underwent allergologic evaluation—including skin prick tests (SPT), intradermal tests (IDT), patch tests (PT), and drug provocation tests (DPT)—performed according to EAACI guidelines, within 6 months of the reaction.
Results: The study cohort included 387 patients with a mean age of 41.2 years; 65.1% were female, 72.6% had relapsing MS, and 40.3% were treatment-naive. Patients received a mean of 5.6 OCR infusions. A history of known allergy was reported in 27.1% of patients, and 12.4% had previously been treated with other monoclonal antibodies (mAbs). Among patients treated with OCR, 16 (4.1%) experienced grade-3 IRRs, of whom 6 (37.5%) experienced an IgE-mediated allergic reaction to OCR, which was confirmed by DPT. All patients who experienced an IgE-mediated allergic reaction developed it after the first OCR infusion. IgE-mediated allergic reactions were more common in patients with a previous history of allergy ($p = 0.028$) and in those previously treated with mAbs ($p = 0.027$). Five of the six patients were switched to ofatumumab without recurrence of the allergic reaction.
Conclusion: IgE-mediated allergic reactions to OCR are uncommon. A previous history of allergy and prior treatment with mAbs are risk factors for developing IgE-mediated allergic reactions. Switching to ofatumumab appears to be well tolerated in these patients.

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P1255
Is PROM measurement useful in MS? Real-life experience from a tertiary hospital

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Introduction: Patient-Reported Outcome Measures (PROMs) provide direct insight from patients regarding their health status and quality of life. In Multiple Sclerosis (MS), where many symptoms are invisible or subjective, PROMs offer a complementary perspective to routine clinical evaluation.
Objectives/Aims: This work aims to present our experience after one year of PROM implementation in a tertiary hospital, report preliminary findings, and reflect on their real-world applicability.
Methods: Since March 2023, PROMs have been collected digitally every six months from patients with MS at Hospital Universitari Son Espases, a tertiary centre in the Balearic Islands. The selected tools include the Beck Depression Inventory-II (BDI-II), the Modified Fatigue Impact Scale (MFIS-5), the Multiple Sclerosis Impact Scale (MSIS-29), and the Multiple Sclerosis Quality of Life questionnaire (MSQOL-54). We present the initial data, focusing on scores obtained and on the evolution of participation over time.
Results: A total of 280 patients were included, with a mean age of 45.4 years; 69.3% were women. In the initial round, the mean BDI-II score was 11.9, with 18.8% of patients in the moderate-to-severe range. The mean MFIS-5 score was 7.5. Psychological impact on the MSIS-29 (mean 32.2) was greater than physical impact (mean 23.7). In the MSQOL-54, the mean quality of life score was 67.6 in women and 64.9 in men, with a mean mental health subscale score of 73.3. While initial adherence was high, a progressive decline in participation was observed across subsequent follow-ups.
Conclusion: PROMs provide valuable information to identify symptoms that often go unnoticed in clinical visits and contribute to a more patient-centred approach. However, sustained implementation faces challenges: questionnaire burden, declining adherence, and lack of integration into routine care. These findings encourage further reflection on how to optimise PROM use in everyday clinical practice so that they truly enhance personalised and efficient care for people with MS.

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P1256
Expanded Monitoring of Patients with MS: Insights from the Vienna MS-Nurse Pilot Project in Clinical Practice

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Introduction: Continuous monitoring of clinical metrics in multiple sclerosis is crucial for detecting subclinical disability and subtle disease progression but is often limited by constraints that impede systematic measurement in clinical practice.
Objectives/Aims: This study evaluated the relevance of expanded assessments by a specialized MS-nurse within clinical routine.
Methods: The Department of Neurology at the Vienna General Hospital allocated personnel resources to employ a specialized MS-nurse to administer clinical measures and questionnaires including the Symbol Digit Modalities Test (SDMT), Nine-Hole Peg Test (9HPT), and Timed 25-Foot Walk (T25FW), alongside the Fatigue Scale for Motor and Cognitive Functions (FSMC), Hospital Anxiety and Depression Scale (HADS) and Multiple Sclerosis Impact Scale (MSIS-29), based on referral by the treating neurologists following a standard operating procedure. Data from the assessments conducted between July 2024 and January 2025 was descriptively analyzed, with abnormal results defined according to normative standards.
Results: Among seventy-three pwMS (mean age 33.6 [SD±12.7] years, 62% female, RRMS 69.4%, median EDSS 3.0 [IQR 0-4.75]) SDMT was performed in 90%, 9HPT in 85% and T25FW in 89% of patients. Abnormal results were reported in 23/65 (35%) for SDMT, 26/62 (42%) for 9HPT and 25/64 (39%) for T25FW of patients.
Of note, even among patients with minimal or moderate clinical disability (EDSS <4), no reported neurologic deficit of the upper extremity and no reported cognitive deficit, the corresponding clinical measures were still frequently found to be abnormal (T25FW 7/40 [18%], 9HPT 8/37 [22%] and SDMT 12/42 [29%]). Questionnaires were completed in more than half of patients (FSMC 55/72 [75%], HADS 53/72 [73%] and MSIS-29 37/73 [51%]). Notably, FSMC and HADS were often moderately to severely abnormal in patients without reporting symptoms of fatigue or depression prior to testing (11/31 [36%] for FSMC and 15/34 [44%]).
Conclusion: Routine monitoring by a specialized MS-nurse frequently identified subclinical deficits, underscoring the value of expanded testing. Employing specialized MS-nurses enhances detection of MS-related impairments while reducing physician workload.

Disclosure of interest: Fabian Föttinger: nothing to disclose related to this study.

P1257
Assessment of General Health, Sleep Health and Polysomnographic Parameters in Naive MS; Preliminary results of the study

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Introduction: Poor sleep is a common symptom in people with MS. Studies have shown that people with MS have a lower quality of life than the general population.
Objectives/Aims: The aim of this study was to examine the relationship between sleep quality, overnight polysomnography (PSG) findings and overall quality of life in naïve MS patients.
Methods: PSG was performed in 18 consecutive naive patients with newly diagnosed MS in this prospective study. Pittsburgh Sleep Quality Index (PSQI), Epworth sleepiness scale (ESS) and Short Form (36) Health Questionnaire (SF-36) were applied to the patients.
Results: The mean age was 33.6 ± 10.9 years with an EDSS of 1.35 (0-5) in the 18 patients, 11 women and 7 men. Compared with the general population, SF-36 scores are lower in women than in men. In MS patients, vitality and role emotional were significantly lower in women than in men (p=0.015 and 0.020, respectively). The mean global PSQI score was 6.11 ± 4.07. Half of the patients had a poor score (>5). There was no significant association between poor score and sleep stages, sleep efficiency and latency to sleep onset. Patients with poor sleep quality had lower vitality and general health among SF-36 subparameters (p=0.013 and 0.042). According to ESS, normal daytime sleepiness was 16, 2 patients had mild sleepiness. There was no relationship between ESS and PSG parameters.
Conclusion: In naive MS patients, quality of life is lower in women. There was no significant relation between sleep quality and PSG parameters in naive MS patients. This may be due to the small size of our cohort. In addition, a good quality of sleep seems to be associated with feeling energized and with emotional well-being being in the foreground.Our findings need to be supported by broader studies of sleep quality, especially at disease onset in MS, where many variable symptoms are observed.

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P1258
Digital Remote Monitoring Improves the Prediction of Cognitive Performance After One Year in People with Progressive Multiple Sclerosis

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Introduction: The Symbol-Digit Modalities Test (SDMT) is a quick screening tool sensitive to cognitive impairment in MS. Many digital SDMTs have been developed, to enable remote cognitive monitoring for longer follow-ups and on a wider scale. However, evidence of their ability to predict cognitive status at follow-up is still scarce.
Objectives/Aims: To leverage remote cognitive monitoring data obtained via a digital SDMT to improve the prediction of cognitive performance at one-year clinical follow-up.
Methods: We used a validated electronic SDMT (eSDMT) to monitor cognition in a sample of people with progressive MS (pwPMS) over one year. Participants were recruited at the end of an inpatient multidisciplinary rehabilitation cycle (T0), during which they performed the oral SDMT. Upon discharge, they were instructed to perform the eSDMT independently from home, on a weekly basis, using their own PC/laptop. After one year (T12), participants repeated the SDMT.We applied smoothing to reduce random variability of repeated eSDMT scores. Then, we used custom algorithms based on the slope of repeated scores in the first month and nonlinear regression to detect the end of the initial learning (i.e., scores improving with repeated exposure) phase for each participant. A hierarchical linear regression was used to predict oral SDMT score at T12. In block 1, we entered age and oral SDMT score at T0 as predictors. In block 2, we added the mean of remote eSDMT scores. Results were evaluated via explained variance (R^2) and root mean squared error (RMSE).
Results: N=23 participants who completed T12 follow-up were included, of which 16 (69%) female, with mean±SD age=54.1±9.46 years, education=14.26±4.18, and median (interquartile range) EDSS=6.5 (6-6.5). The median learning duration was 21 (0-42) days. Block 1 predicted SDMT score at T12 (R^2=0.569, $p<0.001$, RMSE=8.57), and SDMT score at T0 was a significant independent predictor (β=1.26, $p<0.001$). Adding mean remote eSDMT score in block 2 significantly improved model fit (R^2=0.754, $p<0.001$) and lowered prediction error by 26% (RMSE=6.32). Mean remote eSDMT score was a significant individual predictor in block 2 (β=0.88, p=0.001), while SDMT score at T0 was no longer significant (β=0.44, p=0.133).
Conclusion: Remote monitoring with a digital SDMT performed autonomously by pwPMS can improve the prediction of cognitive performance after one year, thus raising the standard of care. Further studies are needed to validate these preliminary results on larger and more heterogeneous samples.

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P1259
Socioeconomic Profiling for Estimation of Multiple Sclerosis Outcomes (SCOPE-MS)

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Introduction: Socioeconomic factors significantly impact not only quality of life of people with MS (pwMS), but also disease severity and outcomes.
Although various validated instruments exist to assess these factors, they are often impractical for clinical use due to limited MS specificity and low efficiency. This underscores the need for a reliable, MS-specific tool that is both comprehensive and feasible for routine application.
Objectives/Aims: The SCOPE-MS AT project aims to develop and validate a practical questionnaire for the multidimensional assessment of socioeconomic factors in pwMS in Austria.
Methods: The project comprises two phases: (1) development and (2) validation of the questionnaire. Phase 1 involved a structured process including literature review, expert input, and construct definition (e.g., income, education, access to care, financial burden, social support, geographic setting, health literacy, housing). Items were designed for clarity and brevity, aiming for a completion time under 15 minutes. Content validity was assessed via expert review (alpha testing), followed by cognitive pretesting with patients (beta testing) and iterative refinements. The final version consists of 64 items and is available in both paper and digital formats (PC, tablet, smartphone).
Phase 2, launched in April 2025, uses a prospective, randomized cross-over design involving 300 pwMS from three Austrian centers. Participants are randomized into four groups to evaluate test-retest reliability and cross-format equivalence (paper/digital) over a two-week interval. Key outcomes include ICC, Cohen's Kappa, and System Usability Scale (SUS). Validation metrics comprise internal consistency (Cronbach's α), construct validity (factor analysis), test-retest reliability, and sensitivity across formats and devices. DIF and bias analyses explore the influence of demographic and clinical factors. Usability is assessed via completion time, error rates, and SUS scores.

Results: Phase 1 is complete, resulting in a 64-item questionnaire covering eight core domains of socioeconomic status (educational level, income and employment status, housing and living conditions, geographic location, access to medical care, financial burden, social support networks, health literacy) with an average completion time of 15 minutes. Phase 2 is ongoing.
Conclusion: SCOPE-MS AT has the potential to fill a critical gap in MS care by enabling accurate, efficient assessment of socioeconomic status – supporting research, clinical decision-making, and individualized treatment planning.

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P1260
The Migraine Screen Questionnaire (MS-Q): A Valid Tool for Identifying Migraine in Persons with Multiple Sclerosis

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Introduction: Despite the high prevalence of migraine in persons with multiple sclerosis (pwMS) and its impact on quality of life, there is a lack of validated screening tools tailored for this population. This study addresses this gap by validating the Migraine Screen Questionnaire (MS-Q) as a brief and practical tool for migraine identification in clinical and research settings.
Objectives/Aims: The objective of this study is to evaluate the diagnostic accuracy and reliability of MS-Q in pwMS.
Methods: A total of 210 pwMS (EDSS ranged from 0 to 7.5) were included in the study. The MS-Q was compared to clinical judgment and the International Headache Society (IHS) diagnostic criteria for identifying migraine. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive probability ratio (PPR), and negative probability ratio (NPR) were calculated for the overall cohort and stratified by sex. Additionally, the internal consistency of the MS-Q was assessed using the Kuder-Richardson 20 (KR-20) coefficient.
Results: According to clinical judgment and IHS criteria, there were 63 pwMS (30%) with migraine, while the MS-Q identified 61 pwMS (29%) as having migraine. The MS-Q demonstrated a Kappa of 0.68 ($p < 0.001$) for overall agreement with clinical diagnosis. For the overall cohort (n=210), the sensitivity was 0.76 (95%CI 0.64–0.86), specificity was 0.91 (95%CI 0.85–0.95), PPV was 0.79 (95%CI 0.66–0.88), NPV was 0.90 (95%CI 0.84–0.94), PPR was 8.62 (95% CI 5.04–14.74), and NPR was 0.26 (95%CI 0.17–0.41). When stratified by sex, males (n=46) showed a sensitivity of 0.80 (95%CI 0.30–0.99) and specificity of 0.93 (95%CI 0.79–0.98), whereas females (n=164) had a sensitivity of 0.76 (95%CI 0.63–0.86) and specificity of 0.91 (95%CI 0.83–0.95). The KR-20 for internal consistency was 0.67, suggesting questionable reliability.
Conclusion: The MS-Q shows good diagnostic accuracy in identifying migraine in pwMS, particularly in females. While the internal consistency is questionable, the tool demonstrates promising potential as a screening instrument for migraine in pwMS. Further validation studies are needed to confirm its reliability and clinical utility.

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P1261
Predictive Value of Oculomotor Metrics for Cognitive Impairment in MS

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Introduction: The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) evaluates processing speed, verbal memory, and visuospatial memory using the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT), and Brief Visuospatial Memory Test (BVMT), respectively. While effective, these tools are time-consuming and require active patient participation.
Objectives/Aims: Assess whether specific eye movement parameters correlate with cognitive performance on the BICAMS tests. Additionally, it explores their potential as predictors of cognitive dysfunction in Multiple Sclerosis (MS) patients.
Methods: A standardized protocol using the Dx 100 portable device measured oculomotor metrics, such as saccadic performance (speed, accuracy, latency), smooth pursuit (target capture and deviations), vergence movements (convergence/divergence accuracy), and visual reaction time. Spearman's correlations were conducted between cognitive scores and these metrics, with significance set at $p < 0.05$. Participants included 100 MS patients diagnosed according to the 2017 McDonald criteria, aged 18-65, with an EDSS score $\leqslant 3.0$, and corrected visual acuity of at least 20/100 in one eye. Exclusion criteria encompassed coexisting psychiatric or neurological disorders affecting eye movement, and prior ocular pathologies.
Results: Significant positive correlations were observed between SDMT performance and oculomotor variables. SDMT scores correlated with vertical saccade final accuracy mean ($\rho = .273$, $p = .006$) and accuracy undershoot ($\rho = .277$, $p = .005$), along with other metrics ($p < .05$). These findings suggest impairments in saccadic precision and visuomotor control may reflect slower processing speed. Further analysis of correlations between eye movement metrics and CVLT/BVMT is ongoing.
Conclusion: Our preliminary data suggest that oculomotor metrics may serve as an objective and efficient proxy for traditional cognitive testing, particularly in evaluating processing speed through SDMT. These findings support further studies to integrate such assessments into clinical workflows for early detection and monitoring of cognitive impairment.

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P1262
Clustering analysis of cognitive impairment and its association with physical disability in multiple sclerosis: a cross-sectional study in two countries

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Introduction: In people with Multiple Sclerosis (pwMS), cognitive impairment (CI) is a frequent and disabling symptom. However, the exact relationship between cognitive and physical disability remains not fully understood. One of the most commonly used tools to assess CI in MS is the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS).
Objectives/Aims: To examine the associations between the BICAMS tests and physical disability, as well as other disease-related factors, in pwMS from two different European countries.
Methods: We conducted a cross-sectional study in Greece (two centers in Thessaloniki and Serres) and Switzerland (Basel). All pwMS fulfilled the 2017 revised McDonald criteria and underwent a neurological examination, including the Expanded Disability Status Scale (EDSS), on the same day as the BICAMS tests (Symbol Digit Modalities Test, California Verbal Learning Test - Second Edition and Brief Visuospatial Memory Test - Revised). Statistical analyses (Mann-Whitney U-test, t-test, logistic regression) were performed using R, with significance set at $p<0.05$.
Results: We included 129 pwMS (n=100 from Switzerland, n=29 from Greece; mean age: 49.4 years; female: 65.9%; mean years of education: 13.8; mean disease duration: 17.9 years; treated: 75.2%; EDSS median: 3.0).

AI-assisted K-means clustering grouped patients into high and low cognitive performers based on the three BICAMS tests. These two groups had significant differences: lower-performing patients were older ($p<0.001$), had longer disease duration ($p=0.012$), fewer years of education ($p=0.021$), and were more frequently from Greece ($p=0.023$), while no differences were observed in sex and treatment status. In a multivariate logistic regression model, age (beta=0.056, $p=0.02$) and country (beta= 1.45, $p=0.012$) remained significantly associated with the cognitive performance.
Regarding physical disability, lower-performing patients had higher EDSS scores and higher scores in most functional systems (FS): cerebral, cerebellar, pyramidal, bowel/bladder and sensory (all $p<0.01$). In a multivariate logistic regression model, adjusted for age and country, cerebral (beta=0.69, p= 0.009), cerebellar (beta=0.52, $p=0.01$) and pyramidal FS (beta=0.5, $p=0.01$) remained significantly associated with the cognitive performance.
Conclusion: Clustering based on BICAMS cognitive performance identified distinct patient groups differing in age and country. The cerebral FS of the EDSS, along with motor disability (pyramidal and cerebellar FSS), were strongly associated with cognitive impairment. AI-based clustering on larger datasets could further enhance cognitive stratification in pwMS.

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P1263
Patient Reported Outcome Measures (PROMs) to shape clinic consults: impact on patient satisfaction

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Introduction: Patient-reported outcome measures (PROMs) in MS are mainly used to assess the effectiveness of interventions in clinical practice or clinical trials. There has been little focus on whether PROMS can enhance routine clinic reviews for people with MS (pwMS).
Objectives/Aims: To investigate whether electronic collection of PROMs (ePROMs) prior to routine MS outpatient appointments improved patient satisfaction with consultations.
Methods: Over 9 months, pwMS attending routine annual outpatient appointments with their MS neurologist were invited to complete ePROMs prior to their consultation. The ePROMs included self-reported disability, the Multiple Sclerosis Impact Scale (MSIS-29), quality of life (EQ-5D-5L, EQ-VAS), and the patients' preferred top three areas for discussion. Anonymous patient satisfaction surveys were performed during the period of ePROMs use, and a control period without.
Results: 398 pwMS were invited to complete ePROMs and 228 (57%) completed them. 373 patient satisfaction surveys were collected; 102 from pwMS who had completed ePROMs and 271 from pwMS who had not. Overall satisfaction was high in those with and without ePROM screening (98.0% satisfied/very satisfied versus 94.8% respectively, $p=0.253$ (Fisher's exact test)). Of pwMS who completed ePROMs, 62.7% reported that overall it enhanced their consultation, and 70.6% agreed that it helped them raise the most relevant issues during their consultation. The most common topics pwMS identified for discussion were fatigue/tiredness, balance/walking, and pain. The main barriers to completion of ePROMs were problems accessing/navigating the online PROMs portal.
Conclusion: MS patient satisfaction with outpatient appointments was high and was not impacted by completion of ePROMs

(likely due to a ceiling effect). However, patients reported that ePROMs enhanced their consultation, and their use in routine follow-up of pwMS should be further explored.

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Introduction: Understanding symptoms that impact people with MS (pwMS) is crucial for selecting patient-relevant outcomes for clinical assessment of new therapies. PwMS consistently report that lower and upper limb symptoms frequently impact their daily life activities. The Timed 25-Foot Walk Test (T25FWT) and 9-Hole Peg Test (9HPT) are commonly used in MS to assess lower and upper limb function.
Objectives/Aims: The purpose of this review was to summarise the patient-reported literature on MS-related lower and upper limb function, consolidate the findings and develop conceptual models describing the symptoms, impacts and abilities affected in pwMS.
Methods: A literature search was conducted in PubMed to identify qualitative studies published between 2014 and 2024 that captured the symptoms and associated impacts that pwMS experienced. Findings were summarised and used to refine conceptual models for lower and upper limb function.
Results: We identified nine studies that contributed to the conceptual models. For the lower limb model, the most common symptoms were balance problems, numbness/tingling in feet, fatigue, spasm/tightness and weakness/heaviness in limbs; walking impairment affected up to 79% of pwMS and standing difficulties up to 57% of pwMS. For the upper limb model, the most common symptoms were numbness/tingling in hands, spasm/tightness and weakness/heaviness in limbs; 50% of pwMS reported loss of hand dexterity/fine motor skills. Lower and upper limb symptoms affected daily activities such as dressing, eating, writing, carrying or lifting and household chores, work and playing sport. The importance of these symptoms was consistent across MS subtypes and levels of disease severity.
Conclusion: Conceptual models of disease informed by patient interviews provide a deep understanding of the patient perspective in a specific disease and can form the basis for measure selection in trials. Findings from the patient-reported outcomes literature supports the conceptual relevance of T25FWT and 9HPT in assessing MS disability.

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P1266
Symptoms related to lower and upper limb function frequently impact daily activities in people with multiple sclerosis

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P1267
Evaluating Backward Walking as a Sensitive Marker of Functional Mobility and Disability in Multiple Sclerosis

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Introduction: Mobility impairments in multiple sclerosis (MS) significantly affect quality of life.
Objectives/Aims: This study evaluated the clinical utility and sensitivity of the backward Timed 25-Foot Walk Test (B-T25FW) and its associations with key clinical measures in MS.
Methods: A cross-sectional study was conducted with 129 ambulatory MS patients from two centers. Disability (Expanded Disability Status Scale, EDSS), cognition (Symbol Digit Modalities Test, SDMT), manual dexterity (Nine-Hole Peg Test, 9HPT), fatigue, and forward and backward walking were assessed. Correlation and receiver operating characteristic (ROC) analyses were performed.
Results: The participants included in the study were 76% female, with a mean age of 38 years, and the majority were diagnosed with Relapsing-Remitting MS (86.8%). Backward and forward walking times significantly correlated with key clinical measures, including EDSS, SDMT, and 9HPT. Backward walking times showed moderate correlations with EDSS ($r = 0.469$) and weaker but significant correlations with 9HPT ($r = 0.452$) and disease duration ($r = 0.245$). Both walking tests were negatively correlated with SDMT scores. For prognostic purposes, forward walking exhibited slightly higher predictive power compared to backward walking.
Conclusion: The B-T25FW is a clinically relevant, practical, and sensitive tool for assessing mobility impairments in individuals with MS. Its integration into clinical practice could complement forward walking assessments, enhancing disease monitoring and guiding interventions. Future research should validate its longitudinal utility.

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P1268
Relapse-Free Time in MS: A Potentially Reliable Indicator of Disease Activity

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Introduction: In the current era of multiple sclerosis (MS), the incidence of relapses continues to decline due to the widespread use of high-efficacy therapies. This trend underscores the need for consistent and sensitive outcome measures. While the annualized relapse rate (ARR) remains the most widely used, it presents inherent variability and limitations. We propose relapse-free time (RFT) as a potentially alternative for monitoring disease activity.
Objectives/Aims: To assess the utility of a potential novel indicator, the RFT, in a population-based cohort of relapsing-remitting MS patients over a 5-year period.
Methods: We conducted a population-based analysis of patients with relapsing-remitting MS followed prospectively at a tertiary centre between 2019 and 2024. RFT and ARR were assessed annually.
Results: A total of 215 patients were included (mean age 48.2 ± 13.8 years; 67% female). By 2024, 11% had transitioned to secondary progressive MS. The proportion of patients with high-efficacy treatment each year from 2019 to 2024 was 13.5%, 15.9%, 16.9%, 18.6%, 22.6%, and 24.0%, respectively. Proportion of relapse-free patients was 81.1%, 82.4%, 84.4%, 81.7%, 90.5%, and 90.5%. The mean ARR for each year was 0.22, 0.22, 0.18, 0.22, 0.10, and 0.09, respectively ($p = 0.001$). The median RFT for the same time points was 3.90, 4.29, 4.87, 4.75, 5.72, and 6.12 years ($p < 0.001$).
Conclusion: RFT could be a viable and robust outcome measure to assess disease activity in the current MS treatment landscape.

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P1269
Do Multiple Sclerosis Patients Perceive the Effectiveness of Relapse Treatment? A Comprehensive Evaluation Through the Expanded Disability Status Scale and Patient Determined Disease Steps Correlation

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Introduction: Multiple sclerosis (MS) is a chronic demyelinating disease marked by relapses and remissions, affecting motor, sensory, and cognitive functions. Relapse treatment aims to reduce inflammation and promote recovery. This study compares clinician-based (EDSS) and patient-reported (PDDS) measures to evaluate the effectiveness of relapse treatment.
Objectives/Aims: To evaluate the effectiveness of relapse treatment in MS patients by comparing clinician-assessed (EDSS) and patient-reported (PDDS) disability scores, and to assess accompanying changes in cognitive and motor functions.
Methods: This study retrospectively analyzed clinical data from MS patients who were given steroids in 2025 due to relapse. Neurological disability was assessed using both the Expanded Disability Status Scale and the Patient Determined Disease Steps.
Results: A total of 25 patients included in the study. The cohort consisted of 64% females, with a mean age of 38 years and a mean disease duration of 11.04 years. Among these patients, 72% had relapsing-remitting MS, and 28% had secondary progressive MS. Following relapse treatment, both objective and patient-reported disability scores showed significant improvement. The Expanded Disability Status Scale score decreased from a mean of 2.96 to 2.00 ($p<0.001$), while the Patient Determined Disease Steps score decreased from 1.44 to 1.28 (p=0.043). These findings indicate that patients not only experienced clinical improvement but also perceived functional recovery in their daily lives. Cognitive test scores showed numerical improvement, but they did not reach statistical significance. The Symbol Digit Modalities Test scores rose from 45.36 to 49.88 (p=0.197), the California Verbal Learning Test scores increased from 47.12 to 53.04 (p=0.081), and the Brief Visuospatial Memory Test scores increased from 27.64 to 28.56 (p=0.355). These modest changes suggest that cognitive functions may recover more slowly or may require different intervention strategies. In terms of motor function, a significant improvement was observed in the 9-Hole Peg Test, with a decrease in time from 22.89 seconds to 22.07 seconds (p=0.017), indicating enhanced fine motor coordination. However, no significant changes were observed in the Timed 25-Foot Walk (from 5.71 to 5.58 seconds, p=0.752) or the 2-Minute Walk Test (from 161.85 meters to 164.04 meters, p=0.654).
Conclusion: The improvements observed in both the Expanded Disability Status Scale and the Patient Determined Disease Steps suggest that patients' perceptions of functional recovery align with the clinical assessments conducted by neurologists. Although cognitive and motor improvements were limited in this short-term analysis, the significant improvement in fine motor skills points to a positive impact of relapse treatment. Long-term, larger-scale studies are necessary to further investigate the durability and scope of these functional improvements.

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P1270
Association between treatment decision and personality, coping strategies, and impulsivity in patients with multiple sclerosis

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Introduction: The availability of various disease-modifying treatments (DMTs) allows for greater integration of personal preference into the shared decision-making process for treatment decisions in patients with MS (pwMS). However, the influence of psychological characteristics on these decisions has not been extensively explored.
Objectives/Aims: To investigate the influence of personality traits, coping strategies, and risk perception as potential factors affecting the selection of high efficacy DMTs (H-DMT) in pwMS.
Methods: In an ongoing prospective study at the Department of Neurology of the Medical University of Vienna, patients completed the Big Five Trait inventory (B5T), the Impulsive Behaviour Scale (UPPS), and the Brief COPE questionnaire at treatment initiation. Their influence on choice of H-DMT (natalizumab, antiCD20 monoclonal antibodies) vs. low/moderate efficacy DMT (L/M-DMT) was analysed using logistic regression first for each dimension separately, then combined with key variables. Propensity scoring was used to adjust for MS-associated determinants of DMT choice (sex, age, disease duration, DMT prior to baseline, relapse in the year before baseline, and Expanded Disability Status Scale (EDSS) at baseline).
Results: Of 137 pwMS (75.9% female, mean age 36.2 [SD 8.7], median EDSS 1.0 [IQR, 0-2]) included, 54% started HE-DMT and 46% started L/M-DMT. Higher scores for supportive coping (adjusted odds ratio [aOR] 1.59 [95% CI 1.07-2.42], $p = 0.024$) and active coping (aOR 3.37 [95% CI 1.36-8.95], $p = 0.011$) were significantly associated with a higher chance of choosing an H-DMT, while there were also trends towards an association

with extraversion (aOR 1.44 [95% CI 0.97-2.20], p = 0.076), openness to new experiences (aOR 1.46 [95% CI 0.98-2.23], p = 0.069), and higher perseverance (aOR 1.45 [95% CI 0.98-2.22], p = 0.071). After these factors were integrated into a single model, the directions of each association remained unchanged, although their statistical significance was lost.
Conclusion: Beyond MS specific factors, individual differences in personality structure, especially supportive and positive coping, may influence treatment decisions among pwMS. Recognizing these psychological factors could improve the shared decision-making process and contribute to more personalized treatment strategies.

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P1271
Cognitive Impairment Screening Tests in Multiple Sclerosis: SDMT, CogEval, and BICAMS

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Introduction: Cognitive impairment (CI) is highly prevalent in Multiple Sclerosis (MS) and contributes to disability, as well as reduced work and social quality of life.
Assessing CI is crucial in MS monitoring. However, neuropsychological testing requires time and personnel, which are often unavailable in daily practice.
Objectives/Aims: This study aimed to evaluate whether the Symbol Digit Modalities Test (SDMT) and CogEval can be used as screening tools for CI in MS, and their usefulness as compared to BICAMS.
Methods: A cross-sectional study was conducted with 102 MS patients in Guadalajara, Jalisco. The SDMT, CogEval, and BICAMS scales were administered, and their correlation was analyzed using Pearson coefficients and Bland-Altman plots. Test sensitivity and specificity were also assessed.
Results: There was a correlation between the Z-scores of CogEval and SDMT (r=0.715). These differences were clinically acceptable according to Bland-Altman analysis.
CogEval showed a sensitivity of 39.70% and specificity of 95.34%.
SDMT demonstrated a sensitivity of 81.35% and specificity of 100%.
The BICAMS test was used as the gold standard for cognitive screening in MS.
Conclusion: CogEval correlates well with SDMT, but it has not yet been validated in the Mexican population; therefore, it is not recommended as a standalone screening tool for MS-related cognitive impairment. In contrast, SDMT exhibits high sensitivity and specificity compared to BICAMS, making it the most cost-effective screening option for daily MS clinical practice. Further validation of CogEval in our population is required. Whenever possible, the full BICAMS test should be administered for comprehensive cognitive impairment screening in MS. We suggest validating cognitive screening tests in each population to enhance their applicability in cognitive screening

Disclosure of interest: Fernando Cortés Enríquez: I have received a travel grant from Roche Mexico to attend the meeting. Roche did not participate in the study in any way.

P1272
Patient-reported perception of self-monitoring after discontinuation of the self-administered Multiple Sclerosis Performance Test

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Introduction: Within MS PATHS (Multiple Sclerosis Partners Advancing Technology and Health Solutions), each person with MS (PwMS) at the Multiple Sclerosis Centre Dresden, Germany performed the Multiple Sclerosis Performance Test (MSPT), an expanded, digitalized version of the Multiple Sclerosis Functional Composite at each routine visit and were shown their results. In June 2023, MS PATHS and MSPT were discontinued.
Objectives/Aims: To assess the perceived impact of MSPT discontinuation among PwMS.
Methods: In October 2024, an anonymous web-based survey was emailed to PwMS of the MS Centre Dresden to assess potential subjective consequences. PwMS who previously performed the MSPT were included. Descriptive statistics were calculated for all responses.
Results: 145 PwMS (79.31% females) had performed the MSPT for up to six years within their clinical routine. Among them, 89 PwMS (57.05%) reported negative impact related to discontinuation, mostly related to the absence of feedback for self-monitoring (97.8%), followed by reduced contact with study staff (29.2%), and the need to rely on alternative monitoring tools, such as apps or diaries (6.7%). Of the 56 PwMS (38.6%) reporting no negative impact, reasons included reliance on physician feedback (67.9%), not using MSPT results for personal assessment (23.2%), preference for shorter visits (17.9%), and perceived pressure to succeed and stress (17.9%).
A total of 124 PwMS supported the resumption of regular MSPT-like monitoring (85.5%). Preferred features included maintaining the original format (66.9%), more test variety (27.4%), and greater gamification (21.8%).
Additionally, 114 PwMS (78.6%) were open to home-based self-assessments. Among those not in favor, reasons included

time demands (52.4%), stress associated with testing (19.1%), and avoidance of regular MS confrontation (61.9%).
Conclusion: Digital self-monitoring tools such as the MSPT were perceived as valuable. Most PwMS would welcome home-based reintroduction of similar tools.

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P1273
Robust, Longitudinal, Qualitative Patient Assessment Underpins Valid Clinical Measurement: The Smouldering Associated Worsening (SAW) Index Study

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Introduction: People with MS (pwMS) continue to experience subtle disability worsening across various clinical domains despite the absence of focal disease activity, so-called Smouldering Associated Worsening (SAW). Clinical assessment and measurement of SAW requires clarity on what is changing in exactly what way and should be grounded in patient experience. However, previous studies showed that understanding the specifics of complex clinical issues is challenging and requires a detailed approach to the longitudinal qualitative assessment of the patient experience to increase the probability that measured change will reflect actual change.
Objectives/Aims: The aim is to establish an index for assessing SAW from which measurements can be derived. Here, the objective is to describe the characteristics, areas that were most commonly identified as worsening, and the severity of MS impacts in the study sample at baseline.
Methods: Of the forty-three pwMS who consented, forty were recruited, three have withdrawn. All will be interviewed by two interviewers, four times each, over several months. Inclusion criteria were age 18-55; diagnosis of MS; evidence of worsening over time; Expanded Disability Status Scale (EDSS) score range 2.0-5.0; no relapses for two years; no MRI evidence of recent inflammatory disease activity. PwMS were scored for symptom severity at baseline using the self-assessment questionnaire SymptoMScreen (range 0 [minimum] to 72 [maximum]).
Results: Recruitment has been completed with 40 active participants across North America, the United Kingdom, Europe, and Oceania. Participant baseline characteristics: 80% female, mean age (SD); range: 50 years (7.5); 31-60, mean time since MS diagnosis (SD); range: 9.8 years (6.9); 2-27, and mean EDSS (SD); range: 4.0(0.7); 2.0-5.0. Common areas of worsening: walking (75%), cognition (79.2%), fatigue (66.7%) and balance (62.5%). SymptoMScreen responses [mean score (SD); range: 24(9.5); 6-45] implied symptoms were mild to moderately limiting. Interviews completed: baseline (24), longitudinal (10) and final (2).
Conclusion: Sensitive measures to capture disability worsening independent of focal disease activity will be enhanced by incorporating the most clinically relevant domains and their severity impact into instrument development. The SAW index study aims to contribute significantly to our understanding of SAW. The study is likely to be extended to enhance the robustness of its longitudinal nature.

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P1274
Validating a Norwegian version of the Neurogenic Bladder Symptom Score - Short Form

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Introduction: Neurogenic lower urinary tract symptoms (nLUTS) are common in neurological disease. Patient reported outcome measures (PROMs) can be useful in evaluating nLUTS and is recommended by guidelines. The Neurogenic Bladder Symptom Score – Short Form (NBSS-SF) is a 10-item PROM that measures symptoms and consequences of nLUTS. It has been validated in a population of patients with nLUTS caused by multiple sclerosis (MS), spina bifida and spinal cord injury, has good psychometric properties and has been translated into several languages.
Objectives/Aims: The aim of our study is to translate the NBSS-SF into Norwegian and demonstrate that it is valid for use in Norwegian patients.
Methods: NBSS-SF was translated into Norwegian in accordance with international guidelines for translating self-report measures, using forward and backward translation by two pairs of bilingual translators - each pair being native in either English or Norwegian. Different versions were compared and evaluated by thorough review, and following feedback from patients a final version was made.
To validate the final Norwegian version, MS patients treated with NTZ at 4-to-6-week intervals were invited to participate. They completed the Norwegian NBSS-SF and International Prostate Symptom Score (IPSS) at two consecutive visits. Data from electronic patient journals was gathered.
Results: 69 patients completed the PROMs. Mean age was 47 (range 21-68), median disease duration was 10 years (range 3-41), and median Expanded Disability Status Scale (EDSS) was 2.0 (range 0-8). The Norwegian NBSS-SF has good internal consistency (Cronbach's alpha=0.88) and test-retest reliability (intraclass correlation coefficient=0.88). There was a good correlation (r 0.58, $p<0.001$) between the NBSS-SF and IPSS.
Median NBSS-SF-score was 4 (range 1-19). NBSS-SF-score correlated positively with EDSS ($p<0.001$). Patients receiving treatment for nLUTS had higher scores ($p<0.001$).
Conclusion: The Norwegian version of NBSS-SF retains acceptable psychometric properties and can be used in a Norwegian context.

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Clinical Aspects of MS & Related Diseases – MS Burden & Comorbidities

P1275
Multiple Sclerosis greatly impacts family members/partners: evidence using the Family Reported Outcome Measure (FROM-16)

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Introduction: Multiple sclerosis (MS) may have a major impact on the physical, social and psychological wellbeing of people with MS (pwMS) and their family members/partners.
Objectives/Aims: To measure the impact of a person's MS on the quality of life (QoL) of their family members and partners using the validated generic Family Reported Outcome Measure-16 (FROM-16).
Methods: An online cross-sectional study was conducted to recruit family members/partners of pwMS through UK patient support groups.
Results: 219 family members/partners (mean age=49.3 years, SD=13.7; females=55.3%) of pwMS (mean age=50.1, SD=12.5; females=56.6%) completed the FROM-16. The FROM-16 mean total score was 16.9 (SD=7.8), indicating "a very large effect" on family members' QoL. The increasing age of pwMS, being a male pwMS and being a female carer were significant predictors of family impact. 50.7% of family members had FROM-16 scores ⩾17. Spouses/partners (170/219) of pwMS reported a significant impact on their sex life compared to other relationships (p=0.001).
Conclusion: MS substantially impacts the QoL of family members/partners of pwMS, indicating a need to assess this impact routinely. FROM-16 could be used to measure MS family impact in routine practice to support family members appropriately and to include this impact in health economic appraisal and therapeutic clinical trials.

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P1276
Comparing the Economic and Societal Impact of Using a High-Efficacy Therapy Early for Relapsing Multiple Sclerosis: A Cost-Consequence Analysis of Ofatumumab From a Societal Perspective in Italy

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Introduction: Ofatumumab (OMB) is a high-efficacy disease-modifying therapy (HE-DMT) with a favourable benefit-risk profile for the treatment of relapsing multiple sclerosis (RMS). The ALITHIOS trial showed that continuous OMB use reduced disability worsening and progression independent of relapse activity compared with switching from teriflunomide to OMB (TER-OMB).
Objectives/Aims: This analysis aimed to compare from an Italian perspective the economic and societal impact of naive use of high-efficacy OMB treatment versus switching from moderate-efficacy TER to OMB after 1–2 years, using 5-year ALITHIOS data.
Methods: Economic and societal outcomes were analysed from two treatment scenarios: patients initiating OMB as first-line therapy and patients initiating TER before switching to OMB after 1–2 years. A cost-consequence analysis was conducted using a 5-year Expanded Disability Status Scale (EDSS)–based Markov model. Cycle transitions included EDSS progression, improvement or stabilisation, treatment discontinuation, relapse and death. The efficacy parameters used were 6-month confirmed disability progression, annualised relapse rate and treatment discontinuation rate. Direct and indirect costs data were analysed from an Italian perspective. Direct costs included healthcare expenses, such as the drug, disease management, relapse, drug administration, monitoring and adverse event management costs. Indirect costs were related to multiple sclerosis–associated productivity loss.
Results: Early initiation of OMB, versus switching from TER to OMB, reduced annual healthcare costs by approximately 44%. Most of the savings were due to reduced year-on-year monitoring costs (~70%) and reduced relapse-associated costs (13.0%) for OMB versus TER-OMB. Initiating OMB early versus switching from TER to OMB also reduced annual indirect costs (€35,977 vs €37,066) and caregiver cost savings (€3795 vs €4074) due to lost productivity. Additionally, a 2.0% reduction in hospitalisation rates, a 2.5% reduction in need for wheelchair use (EDSS 7.0) and increased employment rates (40.0% vs 38.7%) were observed for OMB than for switch from TER to OMB.

Conclusion: This analysis demonstrates that even a brief delay of 1–2 years in transitioning from a moderate-efficacy DMT to a HET can influence economic and societal outcomes. It also affirms the favourable impact of early initiation with a HET such as OMB, especially in mitigating patient care costs and productivity loss for patients with RMS.

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P1277
Measuring Comorbidity in Multiple Sclerosis: A Systemic Review of Current Comorbidity Scales

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Introduction: Comorbidity assessment in multiple sclerosis (MS) is crucial due to its impact on disability progression and quality of life. However, comprehensive and systematic methods for assessing comorbidities in MS populations remain underexplored.
Objectives/Aims: This systematic review aimed to identify current comorbidity scales used in MS populations and assess their suitability for clinical implementation based on the quality of evidence.
Methods: A systematic review was conducted following PRISMA methodology. Studies published between 2014 and 2024 that reported original data or systematic reviews on measures of comorbidity in patients with multiple sclerosis (pwMS) were included. Studies solely involving healthy individuals, patients with other diseases, or measures unrelated to comorbidity were excluded. Information sources included MEDLINE, EMBASE, and the Cochrane Library. The search strategy combined the terms "multiple sclerosis" with "comorbidity". Quality of evidence was assessed by four raters using the GRADE approach.
Results: From 3,178 screened studies, 31 met the inclusion criteria, analyzing data from 234,089 MS patients. Four comorbidity scales were identified: Charlson Comorbidity Index (CCI), Elixhauser Comorbidity Index (ECI), Self-Administered Comorbidity Questionnaire (SCQ), and Self-Reported Comorbidity Questionnaire for MS (SRQ-MS). The CCI was the most frequently used measure (n= 14 studies with a total sample size of n = 180,001 pwMS) and showed relevant associations with MS-specific outcomes but had moderate to low evidence quality due to limited validation and reliance on retrospective study designs. Similarly, the ECI and SCQ lacked direct validation and demonstrated very low evidence quality. The SRQ-MS, while validated for MS populations, showed moderate evidence quality but faced inconsistencies across studies.
Conclusion: Of the currently available comorbidity scales, no single scale has displayed sufficient evidence to warrant routine use in MS populations. While potentially useful for research purposes, further validation and standardization is required to ensure their applicability in real-world use. Future studies should focus on developing and validating MS-specific comorbidity scales.

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P1278
Environmental Risk Factors and Relapses in Multiple Sclerosis: An Umbrella Review of Systematic Reviews and Meta-Analyses

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Introduction: People with MS continue to experience relapses despite the use of disease-modifying therapies. This has motivated growing interest in the potential of non-pharmacological interventions to reduce relapse risk. However, previous studies have been heterogeneous, and current clinical guidelines lack clarity on which measures should be incorporated into routine care.
Objectives/Aims: To conduct an umbrella review of systematic reviews with meta-analyses to determine the current evidence on non-pharmacological exposures associated with relapse risk in MS.
Methods: We searched PubMed, Embase and Cochrane from inception to March 20th, 2025, to identify systematic reviews with meta-analyses that evaluated the association between non-pharmacological exposures and relapse risk. We included observational studies that compared exposed and unexposed individuals and reported on relapses as an outcome. The effect sizes (relative risk [RR] or standardized mean difference [SMD]) and quality of evidence were assessed using the GRADE framework, considering whether associations remained after excluding studies at high risk of bias, the presence of imprecision (confidence intervals excluding 1 and more than 1000 participants), inconsistency ($I^2 > 50\%$), and publication bias (Egger test). Lack of reporting on these aspects was considered a reason for downgrading the certainty of evidence.
Results: We screened 3359 articles and identified 11 systematic reviews for inclusion. Protective factors were: breastfeeding (RR 0.63, high certainty), pregnancy (SMD -0.52, moderate certainty), menopause (SMD -0.5, low certainty), and autumn months (RR 0.97, moderate certainty). Risk factors were: early postpartum period (RR 1.87, moderate certainty) and stress, particularly war-related stress (RR 3.0, low certainty). Influenza vaccination (low certainty), COVID-19 infection (low certainty), and vitamin D levels >50 nmol/L (low certainty) were not associated with relapse risk.

Conclusion: Our umbrella review highlights the need for more robust studies to strengthen the certainty of evidence regarding non-pharmacological exposures and relapse risk in people with MS. Current findings support careful disease management during the pregnancy–postpartum cycle and the importance of stress mitigation strategies. No evidence of increased relapse risk was found for influenza vaccination or vitamin D levels, though further studies are needed to confirm these findings.

Disclosure of interest: No author has anything to disclose regarding this abstract

P1279
FOCAL-MS2 study: establishing the test-retest reliability of the Multiple Sclerosis Autonomy Scale (MSAS) questionnaire

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Introduction: Despite achieving no evidence of disease activity (NEDA), many MS patients have symptoms that impact on their autonomy, defined as being able to perform the roles that are most important to oneself, with or without help.
The Multiple Sclerosis Autonomy Scale (MSAS) is a new Patient Reported Outcome (PRO) aiming to evaluate patient autonomy in multiple sclerosis. This questionnaire has been developed in collaboration with MS patients and Healthcare Professionals.
Objectives/Aims: This abstract describes methods and results for the reliability of the questionnaire.
Methods: The FOCAL-MS2 study was launched to confirm the psychometric properties of the short version of the questionnaire. 210 pairs of healthcare professionals and patients were recruited to test the questionnaire. The MSAS questionnaire contains 10 dimensions in a 35-items short form and has been completed by patients at inclusion, D15, D30 and up to one year after inclusion. MSAS scores are standardized on 0-100 scale, higher scores representing higher burden of autonomy. Test-retest reliability was evaluated using a 2-way, random-effects, single-measurement intraclass correlation coefficient (ICC), with agreement between D0 and D15 also visualized with a Bland-Altman plot. A sensitivity analysis was performed between D0 and D30. Based on the ICC, the test-retest reliability could be described as per Cicchetti (1994) as poor (ICC$<$0.40), moderate (0.40-0.59), good ($>$0.60-0.74), or excellent ($>$0.75).
Results: From the 210 patients included from January to April 2024, 199 completed the MSAS questionnaire at baseline: 74% women, mean age at diagnosis 34.3 +/- 9.9 years; 132 (66.3%) had a relapsing remitting form of MS (RRMS), 23 (11.5%) with primary progressive (PPMS) and 44 (22.1%) with secondary progressive (SPMS). Between D0 and D15: Overall MSAS score had an ICC of 0.72 (CI95%:[0.65 -0.79]) considered as good.6 out of 10 dimension's score had an ICC considered as excellent 2 out of 10 dimension's score had an ICC considered as good 2 out of 10 dimension's score had an ICC considered as moderate In the sensitivity analysis between D0 and D30, similar results were observed in the subscales and overall MSAS score had an icc of 0.75 (CI95%:[0.68 -0.81]) considered as excellent.
Conclusion: The population included in the study covers the different profiles of MS patients. Overall, the MSAS questionnaire has a good test-retest reliability. Each of the MSAS subscales had moderate to excellent test-retest reliability. The final MSAS questionnaire will be available by the end of 2025.

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P1280
UK MS Domestic Violence and Abuse Research Initiative: experiences of victim-survivors with MS and healthcare professionals

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Introduction: Domestic violence and abuse (DVA) is more common among women and disabled people (ONS, 2020; ONS, 2023). During the COVID-19 pandemic, multiple sclerosis (MS) healthcare professionals (HCPs) became aware of a

significant increase in DVA in people with MS (pwMS) but found there was limited research on the issue. We established the MS DVA Research Initiative at two UK regional university MS centres to address this gap.
Objectives/Aims: To investigate the experiences of victim-survivors with MS and MS HCPs.
To gain perspectives on current support systems and how to improve the support journey.
Methods: Victim-survivors with MS were identified by MS HCPs in Leeds Teaching Hospitals and Nottingham University Hospital, through posters in clinics and a day-case unit, as well as through social media. Semi-structured interviews were conducted in a safe setting. Key themes were identified using reflexive thematic analysis.
We recruited HCPs through professional networks, social media and referrals. Semi-structured interviews were conducted online, by telephone or face-to-face. Key categories were developed using grounded theory methods.
Results: Sixteen women with MS were identified and seven consented to be interviewed. The women who chose not to participate did so for various reasons, including their involvement in court proceedings or deciding an interview would be too distressing. Key findings include coercive and controlling DVA experiences and the importance of support services creating meaningful interactions.
Forty HCPs from a range of professions were recruited and interviewed. Key findings include their experiences of DVA in MS, and the aspects of MS that make this an important issue for their practice. They also identified barriers and facilitators for addressing DVA in their role.
Conclusion: DVA is a major and under researched problem in people with MS. Victim-survivors with MS experience a range of violence and abuse and there can be a delay in realisation. They see HCPs as trusted professionals and would welcome them asking about their safety. MS HCPs value relationship building as a key part of addressing DVA in pwMS and see multiprofessional working as an important tool in identification and support.
The findings of this study are guiding the development of a Toolkit for MS HCPs to understand, identify, and support people with MS who experience DVA.
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P1281
Aging in Hispanic People with Multiple Sclerosis: Emerging Demographic, Clinical, and Healthcare Related Insights

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Introduction: Hispanic people with MS (HpwMS) in the US exhibit worse disease trajectories compared to White pwMS. Research is remarkably limited for this patient group, and even more so for older HpwMS. This creates a significant problem given pwMS and Hispanic people in the US (generally) experience accelerated aging and experience healthcare-related social determinants of health (SDOH). Thus, this study fills a substantial gap by providing critical initial characterizations across multiple levels for older HpwMS.
Objectives/Aims: The primary aim of the study is to characterize demographic, clinical, and healthcare-related SDOH in an older cohort of HpwMS.
Methods: Sixty-seven older (>50 years) HpwMS were recruited from a large academic medical center in an urban setting. Demographic and clinical information were collected via interview and medical record review. Healthcare-related SDOH were evaluated via PhenX toolbox questionnaires, including Access to Health Services, Disparate Healthcare Quality, and Access to Health Technology. Lastly, the Kurtzke Expanded Disability Status Scale (EDSS) measured level of disability. Participants were evaluated in their preferred language (English/Spanish).
Results: The mean age of the sample was 59.54 years (SD=7.45, range 50-81) with 73% identifying as women and a disease duration of 14.45 years (SD=8.18). Mean education level was 13.52 years (SD=1.99). Fifty-nine percent were US-born, and half of the sample identified Spanish as their first language, with 20.9% continuing to prefer Spanish as their primary language. All individuals reported having some type of health insurance, though 36.6% were on Medicare/Medicaid. Most were on DMT but 25.4% were not currently on a DMT. Five individuals (7.5%) reported disparate healthcare due to race/ethnicity. After controlling for sex, partial correlations revealed significant relationships between age and both symptom (r=.27, p=.031) and disease duration (r=.32, p=.010) but not disease severity (EDSS). Regarding accessibility to technology and providers, participants reported high rates of online health record access (76.1%) while sharing health information online was lower (37.3%). Additionally, 58.2% reported participating in online support groups, 55.2% watched health-related videos online, and 70.1% communicated with their doctors via text. Medical comorbidities were also examined.
Conclusion: To the authors' knowledge, this is among the first studies to characterize older HpwMS demographically, clinically, and psychosocially. Results offer unique insights into this patient group and provide a foundation for future research and clinical care for HpwMS.

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P1282
Unveiling the Hidden Burden: A Registry-Based Study of Comorbidities in Multiple Sclerosis from Iran

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Introduction: Comorbidities are highly prevalent among individuals with multiple sclerosis (MS), significantly influencing disease diagnosis, progression, treatment outcomes and quality of life. Despite their clinical significance and the variability in comorbidity prevalence across different populations and regions, there remains a notable lack of comprehensive research on comorbidities in MS at the national level in Iran.
Objectives/Aims: To address this knowledge gap by exploring the prevalence of comorbidities and their relationship with clinical outcomes in Iranian MS patients, providing insights for improved patient care and management strategies.
Methods: This cross-sectional study targeted all patients with multiple sclerosis (PwMS) in Tehran registered in the Nationwide MS Registry of Iran (NMSRI). Data were extracted from the registry and supplemented with additional information obtained through telephone follow-ups. All registered participants were evaluated by trained neurologists and diagnosed with MS based on the McDonald 2017 criteria. Comprehensive questionnaires were used to collect data on demographics, disease history, diagnosis, progression, and treatment details, as well as prevalent comorbidities. Comorbidities were divided into two categories: pre-MS diagnosis and post-MS diagnosis. Statistical analyses were performed using R software (v 4.4.1; R Core Team 2024), with the significance level set at $p \leqslant 0.05$.
Results: Among 2,771 participants (mean age: 37.07 ± 9.45), 1,133 had comorbidities, with a higher prevalence in women (n=921, 81.2%, $p < 0.001$). The age of MS diagnosis was higher in those with comorbidities (29.8 ± 9.3 vs. 27.9 ± 8.3, $p < 0.001$). Comorbidities were more common after MS onset than before (n= 886, 78.2% vs. n=401, 35.4%, $p < 0.001$). Pre-MS comorbidities most commonly included thyroid diseases (25.4%) and migraines (13.7%), while post-MS comorbidities were predominantly urinary disorders (32.5%), depression (26.3%), and anxiety (14.8%). Patients with progressive MS and those with mobility limitations exhibited significantly higher rates of post-MS comorbidities ($p = 0.007$ and $p = 0.001$, respectively). This trend was also observed in patients with severe disease (EDSS ⩾ 5.5), who had a higher prevalence of post-MS comorbidities compared to those with milder forms. Notably, these patterns were not observed for comorbidities diagnosed prior to MS onset. Furthermore, the EDSS score was significantly higher in patients with post-MS comorbidities compared to those without (2.71 ± 2.11 vs. 2.20 ± 2.11, $p < 0.001$), but no significant difference was found for patients with pre-MS comorbidities.
Conclusion: Comorbidities are more prevalent in severe forms of MS and significantly influence disease management and outcomes. Addressing these comorbidities, particularly those occurring post-MS diagnosis, is essential for tailored management strategies and improved clinical care.

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P1283
Potential Occult Hepatitis B Infection in MS Patients Receiving Ofatumumab: Prevalence,Risk Stratification, and Implications for Lamivudine Prophylaxis

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Introduction: Ofatumumab is a highly effective anti-CD20 monoclonal antibody used in treating relapsing forms of Multiple Sclerosis (MS), exerting its action by depleting B cells. Like other anti-CD20 therapies, ofatumumab carries a risk of hepatitis B virus (HBV) reactivation in patients with previously resolved or inactive infections. To mitigate this risk, prophylactic antiviral treatment with lamivudine may be indicated in selected patients, without unnecessarily limiting the use of ofatumumab.
Objectives/Aims: This study aimed to assess the prevalence of potential occult HBV infection (pOBI) in MS patients initiating ofatumumab therapy and to determine the proportion requiring lamivudine prophylaxis.
Methods: We evaluated 215 MS patients at our center, including 93 (43.25%) with relapsing-remitting MS and 122 (56.75%) with active progressive MS. The median EDSS score was 4.0 (range 2.5–6.5). Baseline HBV screening included anti-HBs, HBsAg, anti-HBc, and HBV DNA testing. Serological testing was performed using ELISA, and HBV DNA was quantified via real-time PCR.
Results: Among the cohort, 24 patients (11.2%) tested positive for anti-HBc, indicative of pOBI. Of these,
10 (41.7%) were classified as high-risk for HBV reactivation due to absent vaccination history or
low anti-HBs titres (<100 UI/mL), and consequently received lamivudine prophylaxis alongside
ofatumumab. The remaining 14 patients (58.3%) had protective anti-HBs levels and undetectable
HBV DNA, thus did not require antiviral prophylaxis.
Conclusion: The presence of antibodies to hepatitis B core antigen in the peripheral blood of MS patients reflects
a risk of HBV reactivation in patients treated with Ofatumumab but not all pOBI patients require
Lamivudine treatment and only about 10% of treated patients need infectious disease consultations
after appropriate HBV screening. Therefore, the impact of liver screening is necessary to prevent
HBV reactivation and to select, together with infectious disease specialists, a subgroup of patients
who need lamivudine prophylaxis.

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P1284
A Pilot Study on Advanced Care Planning in People with MS: Perspectives of Patients, Caregivers and Healthcare Professionals

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Introduction: Multiple sclerosis (MS) is a chronic neuroinflammatory condition that progressively impairs cognitive functions and decision-making capacity. Advance Care Planning (ACP) allows individuals to express their preferences for future care and end-of-life decisions, promoting self-advocacy and autonomy, which are relevant factors in the context of progressive illnesses. In Chile, a recent law was promulgated, but the implementation of ACP has not been explored in this population.
Objectives/Aims: To explore the perspectives of patients (P), caregivers (CG), and healthcare professionals (HP) on ACP in the context of MS, and the feasibility of its implementation in Chile.
Methods: This qualitative study used purposive sampling to recruit participants for semi-structured interviews conducted at two hospitals in Santiago, Chile. Thematic analysis was used to examine participants' experiences, perceived benefits and concerns, implementation strategies, and barriers to ACP. Interviews were audio-recorded, transcribed verbatim, and analysed inductively to identify key patterns and meanings.
Results: Twenty-two participants (P=8, CG=6, HP=8) were recruited. ACP was considered a meaningful and necessary process for people with MS. All the participants emphasised that ACP should be performed far from the diagnostic process. They highlighted the involvement of the care team (including physicians, psychologists, nurses, physiotherapists, and social workers). ACP should include preferences for both medical treatment and care, such as the place of care, the primary caregiver, and the option of spiritual support. Two P expressed that ACP could include the option of euthanasia. Participants suggested that ACP documents should be attached to the medical record, remain confidential, yet accessible to healthcare providers, family, and other designated individuals. Identified barriers included costs, lack of time, limited awareness, and legal conflicts. All HP indicated they would engage in ACP themselves if diagnosed with a neurodegenerative illness.
Conclusion: This pilot study provides valuable insights. The findings reveal strong support for ACP and the need to broaden its scope beyond medical decisions. Addressing identified barriers could enhance ACP integration into care pathways. These findings represent a starting point to promote the use of ACP in patients with neurodegenerative diseases.

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P1285
Investigation of Working Difficulties and Coping Strategies in Multiple Sclerosis Patients

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Introduction: Multiple sclerosis is a chronic neurologic disease that primarily affects adults in their working age. Symptoms related to the disease can lead to unemployment and challenges in the workplace.
Objectives/Aims: This study aims to review the challenges associated with work life in actively working adult MS patients, investigate the relationship of these challenges with disease-related factors such as cognitive, emotional, and physical disability, and to assess the strategies that patients employ to cope with these work-related difficulties.
Methods: One hundred fifty patients with a definitive diagnosis of relapsing-remitting multiple sclerosis (RRMS) were included in the study. We evaluated fatigue, cognition, mood, extremity functions, disability and coping strategies with difficulties at work.
Results: A total of 150 patients with a definitive diagnosis of MS were included in the study. In our study, as patients' cognitive levels decreased, their scores on psychological/cognitive barriers, physical barriers, and total barriers increased. We found a negative correlation between work-related difficulties and patients' cognitive levels. As patients' scores on depression, fatigue, and hopelessness tests increased, their scores across all work-related barriers also increased. Additionally, it was observed that as patients' extremity function deteriorated, their scores on psychological/cognitive barriers, physical barriers, and total barriers increased.
Conclusion: Our findings indicate that MS patients with better cognitive function experience fewer difficulties in the workplace. Furthermore, higher levels of depression, fatigue, and hopelessness were associated with greater challenges at work. It was found that patients' upper extremity functions, as well as walking and balance problems, are closely related to cognitive and physical difficulties encountered in the workplace. Workplace difficulties increased as the annual relapse rate and EDSS scores rose.

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P1286
Using fMRI machine learning and structural brain connectomics to identify neurobehavioral mechanisms of fear and anxiety in multiple sclerosis

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Introduction: Despite the high prevalence of comorbid anxiety in multiple sclerosis (MS), its specific neurobehavioral mechanisms have not been elucidated. In other conditions, altered fear processing is considered a key mechanistic hallmark. A critical question in MS is whether MS-related anxiety is merely a result of the accumulating disease burden or if it stems from active underlying neurodegenerative changes.
Objectives/Aims: In this study, we examined the role of neurobehavioral mechanisms, particularly fear generalization, in MS-related anxiety.
Methods: Eighteen persons with MS (PwMS) and anxiety, 36 PwMS without anxiety, and 23 healthy individuals were included in the study. All participants performed a functional MRI (fMRI) task to investigate fear generalization and underwent diffusion-weighted MRI scans to conduct a graph-based analysis of the structural brain connectome.
Results: PwMS with anxiety interpreted non-threating stimuli as threatening, which suggests fear overgeneralization, similar to what is observed in anxious individuals without MS. In the fMRI task, behavioral fear generalization was assessed based on participants' ratings of the risk of receiving an electric shock. A machine learning model, trained on whole-brain grey matter fMRI fear response patterns from healthy individuals, was used to predict the shock-risk ratings in both MS groups with high accuracy. Further analysis through regional fMRI predictions and graph-based methods revealed that behavioral overgeneralization of fear in MS relies on altered functional activity patterns and reduced structural network integrity of overlapping brain regions, including the hippocampus, amygdala and inferior temporal gyrus.
Conclusion: These results underscore the relevance of fear overgeneralization in the anxiety experienced by PwMS. The fact that a machine learning model trained on healthy individuals can predict fear generalization in MS suggests that MS-related anxiety is primarily driven by generic fear mechanisms, acting as an accompanying effect of the disease.

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P1287
High adherence to the Mediterranean diet and Physical activity influence Cognitive outcomes in Multiple Sclerosis

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Introduction: Dietetic and exercise counselling is a high priority for people with Multiple Sclerosis (PwMS). Previous studies have suggested an association between better Mediterranean diet alignment and lower objective and patient-reported disability. While PwMS historically were advised to avoid physical activity, they are now encouraged to remain active. Here we evaluated the impact of Mediterranean diet and exercise on disease control in early MS beyond NEDA-3 (No Evidence of Disease Activity – 3).
Objectives/Aims: To evaluate the possible effect of adherence to the Mediterranean diet and physical activity on cognition outcomes and serum neurofilaments levels (NfL) in PwMS.
Methods: Adherence to the Mediterranean diet was assessed using the Mediterranean Diet Adherence Screener, physical activity through the Global Physical Activity Questionnaire and cognitive performance using Brief International Cognitive Assessment for MS battery. These instruments were administered to a cohort of relapsing-remitting Multiple Sclerosis (RRMS) patients aged 18–55 years, with disease duration under 5 years and fulfilling NEDA-3 criteria for at least one year.
Results: A total of 30 patients, 70% women; aged 37,57±10,74 years; median Expanded Disability Status Scale of 1,5 (range 1,0-4,0) were included. Most participants were in the category of moderate adherence to the Mediterranean diet (56.7% within 6 and 9 points), followed by high adherence (36.7% more than 10 points) and only 6.7% had low adherence (below 5 points). 33.3% patients reported high levels of physical activity, corresponding to a total score of ⩾3000 MET (Metabolic Equivalent of Task)-minutes/week. High adherence to the Mediterranean diet was associated with better cognitive performance in the tests performed ($\chi^2 = 8.743$; $p = 0.013$). High physical activity was significantly associated with the absence of cognitive impairment ($\chi^2 = 10.429$; $p = 0.005$). A preliminary assessment of serum NfL levels in a subset of this cohort (n=23) showed no significant association with adherence to the Mediterranean diet or exercise.
Conclusion: High adherence to the Mediterranean diet and physical activity might be associated with better cognitive performance in RRMS, reinforcing the potential role for lifestyle interventions in MS management. Longitudinal studies and interventional clinical trials are needed.

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P1288
Longitudinal course of restless legs syndrome in multiple sclerosis - a controlled study

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Introduction: Multiple sclerosis (MS) leads to various symptoms, including restless legs syndrome (RLS), which is often underdiagnosed despite its high prevalence and impact on quality of life. Moreover, little is known about the longitudinal course of RLS in MS.
Objectives/Aims: Hence, the aim of this work is to investigate RLS prevalence and severity in MS over time.
Methods: Through this case-control study, people with MS (pwMS) and control persons (CP) from a previous cross-sectional study were followed up with face-to-face interviews in 2022-2023. Collected data included demographics, scores of the International RLS Study Group Rating Scale (IRLSSG), the Epworth Sleepiness Scale (ESS) as well as the Pittsburgh Sleep Quality Index (PSQI) and, for pwMS, the Expanded Disability Status Scale (EDSS) alongside magnetic resonance imaging (MRI).
Results: A total of 64 pwMS and 27 CP were analysed, with pwMS suffering significantly more often from RLS (27% pwMS, 4.2% CP, p=0.019). From the 43 pwMS with no RLS in the first assessment, 8 developed RLS over a median follow up period of 62 months (IQR = 40-81), leading to a RLS conversion rate of 19%, compared to a conversion rate of 0% in CP ($p = .025$). No significant correlation between changes in EDSS and IRLSSG scores ($rs= -0.180$; $p = 0.177$) could be found. RLS severity was associated with increased daytime sleepiness ($OR = 1.058$, $p = 0.003$), though not with impaired sleep quality. Furthermore, changes in EDSS did not significantly predict sleep quality or daytime sleepiness. Brainstem and spinal cord lesions significantly influenced RLS severity ($OR = 6.233$, $p = 0.033$ for brainstem lesions; $OR = 0.355$, $p = 0.006$ for spinal lesions).
Conclusion: Our study confirms the clearly higher prevalence of RLS in pwMS in comparison to CP. Moreover, RLS risk seems to increase over time in pwMS, Thus, active screening of RLS in pwMS is highly recommended. In addition, this study shows a clear correlation of RLS severity and daytime sleepiness, however, not in terms of sleep quality. Concerning MRI, this study provides contradictory results on the association between brainstem and spinal lesions and RLS in pwMS. Hence,

future prospective studies with larger sample sizes are warranted to investigate RLS in pwMS more in depth.

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P1289
Functional dependence in people with multiple sclerosis and its association with caregiver quality of life

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Introduction: The Pfeffer Functional Activities Questionnaire (FAQ) is a relevant tool to assess functional dependence in people with Multiple Sclerosis (PwMS). This scale, completed by the caregiver, provides a score reflecting the level of functional dependence. Caring for PwMS can impact caregiver quality of life, particularly for informal caregivers who provide daily support without compensation.
Objectives/Aims: To explore the relationship between PwMS functional dependence and caregiver quality of life. To analyse the association between functional dependence and clinical and cognitive variables in PwMS.
Methods: A cross-sectional study was conducted including 73 PwMS and their 73 informal caregivers. PwMS: 75.8% Relapsing-Remitting MS, 9.7% Secondary Progressive, 8.1% Primary Progressive; 67.7% female; mean age 45.9 $\pm$ 13.0 years; mean education 13.89 $\pm$ 3.11 years; Expanded Disability Status Scale (EDSS) 3.69 $\pm$ 2.47; disease duration 19.03 $\pm$ 25.39 years; Beck Depression Inventory (BDI-II) 15.32 $\pm$ 11.11; Fatigue Severity Scale (FSS) 4.2 $\pm$ 1.7. Caregivers: 61.6% female; mean age 51.27 $\pm$ 14.3 years; mean education 14.38 $\pm$ 3.16 years.
Assessment tools: PwMS - EDSS, BDI-II, Fatigue (FSS), Multiple Sclerosis Neuropsychological Questionnaire (MSNQ-P), and the Brief International Cognitive Assessment for MS (BICAMS). Caregivers - FAQ, Caregiver Quality of Life Questionnaire (CAREQoL-MS), Montreal Cognitive Assessment (MoCA), BDI-II, MSNQ-I, and the Hospital Anxiety and Depression Scale (HADS). Statistical analyses included descriptive and Spearman's correlation analyses.
Results: For caregivers, FAQ scores showed a strong positive correlation with CAREQoL-MS (rho $=$ 0.71, $p < 0.01$), while correlations with BDI-II, HADS-Anxiety, and MSNQ-P were not significant. For PwMS, FAQ strongly correlated with EDSS (rho $=$ 0.77, $p < 0.01$), moderately with FSS (rho $=$ 0.367, $p <$ 0.01), and MSNQ-I (rho $=$ 0.357, $p < 0.01$). FAQ scores also showed moderate-to-strong correlations with cognitive measures (CVLT-I, SDMT, and BVMT-R).
Conclusion: Functional dependence in PwMS is associated with both caregiver quality of life and PwMS clinical-cognitive variables. Including measures of functional dependence in clinical practice may improve care strategies for both PwMS and their caregivers.

Disclosure of interest: Author's name: nothing to disclose.

P1290
An Investigation of Headache Characteristics and Their Correlation with Serum Total Antioxidant Capacity in Multiple Sclerosis patients

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Introduction: Severe headaches and migraine, along with Multiple sclerosis (MS) which is prevalent in young adults, contribute significantly to disability in this age group. Oxidative stress and neuroinflammation are key mechanisms in headaches, with serum total antioxidant capacity (TAC) serving as a marker.
Objectives/Aims: This study aims to explore headache and migraine features in PwMS and their correlation with serum TAC.
Methods: This cross-sectional study assessed headache and migraine in PwMS using the International Classification of Headache Disorders, 3rd edition (ICDH-3) ICDH-3. Serum TAC levels were measured colorimetrically in (mM) unit, and statistical analyses (chi-square, Mann-Whitney U, logistic regression) were conducted to evaluate its correlation with migraine/headache risk.
Results: The study involved 73 PwMS, predominantly female 54 (74%) and with relapsing-remitting MS 44 (60.3%), with most 50 (68.5%) receiving ocrelizumab treatment. They have mean age of 39.0 ± 9.1 years, a mean disease duration of 10.73 ± 5.73 years, and a mean serum TAC quantity of 0.6 ± 0.12 mM. of all PwMS, 43 (58.9%) reported headaches > 4 hours in their life and 24 (32.9%) of all fulfilled migraine criteria. The mean duration of headache was 13.44±20.59 hours. Associated symptoms included nausea/vomiting 21(28.8%), photophobia/phono phobia 24(32.9%), or both17 (23.3%), with characteristics such as unilateral location 25(34.2%), pulsating quality 26(35.6%), and moderate-severe pain 40(54.8%) often leading to avoidance of routine activity25 (34.2%). Among migraine patients, 7(29.2%) reported aura, predominantly visual 5 (71.4%).
There was a significant correlation between sex and the presence of all types of headache, with females being more likely to report headaches compared to males ($p = 0.023$). Additionally, higher serum TAC levels prior to headache onset were correlated with a reduced risk of experiencing headaches, both in unadjusted (OR < 0.001, 95% CI: 0.0–0.069, $p = 0.003$) and adjusted models (OR < 0.001, 95% CI: 0.0–0.116, $p = 0.008$). Moreover, headache duration (in hours) was inversely correlated with pre-headache serum TAC levels ($p = 0.009$, $r = -0.30$).
Conclusion: Higher pre-headache serum TAC levels appear protective against headache occurrence and duration, deserving further investigation into its mechanisms for potential preventative or therapeutic strategies.

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P1291
Frailty, mental health, and quality of life in people with multiple sclerosis: a cross-sectional study

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Introduction: With the increasing median age of people with multiple sclerosis (MS), age-related syndromes such as frailty have emerged as new challenges to patient well-being. Prior research on frailty in MS has primarily focused on physical aspects, leaving the relationship between frailty and mental health unexplored.
Objectives/Aims: To investigate the associations between frailty, mental health, and quality of life (QoL) in people with MS.
Methods: A convenience sample of 204 patients with MS (median age: 51 [IQR 18] years, 74% women) from the KU Center for MS Care completed validated measures of frailty (Tilburg Frailty Indicator), anxiety and depression (Hospital Anxiety and Depression Scale), QoL (Multiple Sclerosis Quality of Life-54), and disability level (Patient-Determined Disease Steps).
Results: Overall, 50.5% of respondents were classified as frail. Frail participants were significantly older than their non-frail counterparts and had higher levels of anxiety and depression (both $p < 0.001$). Frailty status was also associated with lower QoL scores across physical and mental health domains ($p < 0.001$). In logistic regression analyses adjusted for age, sex, and disability, higher anxiety (OR=1.45, 95% CI [1.28, 1.65], $p < 0.001$) and depression scores (OR=1.58, 95% CI [1.365, 1.843], $p < 0.001$) were associated with greater odds of being frail.
Conclusion: This study revealed a strong association between frailty, mental health, and QoL in people with MS. Recognizing the interplay between frailty and mental health highlights the importance of integrated, multidisciplinary care strategies that address both physical vulnerability and psychological well-being in the MS population.

Disclosure of interest: Nothing to disclose

P1293
Pain in people with MS

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Introduction: Persons with multiple sclerosis indicate the presence of pain as one of the symptoms that
bothers them the most, leads to a lower quality of life, also affects mental health and often
limits them in the performance of employment.
Objectives/Aims: The aim was to map the incidence, severity and localization of pain in group of people with MS in Czech Republic.
Methods: Persons with MS were approached during their routine medical visit at the MS centre. The Visual Analogue Scale (VAS) and McGill Pain Questionnaire were used to assess pain. In addition, patients were asked about pain location and possible pain relieving factors.
Results: A total of 185 people with MS (75 % women) completed the questionnaire. The mean age of respondents was 46 years, disease duration 17 years and mean disability 3.5 (range 1-7.5). The survey showed the prevalence of pain in 60% (n=111) of people with MS. There was only a weak correlation of pain with EDSS (r=0.297**) and a moderate correlation with pain duration (r=0.486**). Patients most often experience pain at rest, reported by 56% of respondents. The second most common trigger is pain, occurring after exertion in 50%. The highest incidence of pain was recorded in spine, with 28% (n=31) of patients reporting lumbar spine pain, 24% (n=27) reporting cervical spine pain, and 21% (n=23) thoracic spine pain. Pain in the tibial region, specifically 28% (n=31), thigh pain 8% (n=9), and plantar pain in 8% (n=9) were most common in lower limb.
Conclusion: Pain in MS can be caused by the primary disease or other comorbidities. Understanding it can help to improve rehabilitation and overall comprehensive treatment and therefore the recognition that up to 60% report the presence of pain is important for clinicians.

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P1294
Patient Age and Healthcare systems are associated with HTN awareness in Hispanic Americans with MS

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Introduction: Hypertension (HTN) is associated with worse disability in MS. Hispanic people with MS (HpwMS) have

significant HTN unawareness; only 7% report having HTN, while 27% meet the American Heart Association (AHA) criteria for HTN diagnosis (dx). Lack of HTN awareness has been linked to socioeconomic challenges and healthcare access. Understanding the risk factors for HTN unawareness may help improve diagnosis and treatment in this population.

Objectives/Aims: To identify the risk factors for HTN unawareness in HpwMS.

Methods: We retrospectively analyzed individuals with at least two BP readings in a cohort of 450 HpwMS in southern California. HTN was defined by AHA dx criteria requiring a BP reading of ⩾130 Systolic (SBP) or ⩾80 diastolic (DBP) on at least two visits. People meeting AHA dx criteria were defined as HTN aware if they had a HTN ICD-10 code, documentation or treatment of HTN or self-reported having HTN. People without ICD-10 codes, documentation, treatment or self-report of HTN were considered HTN unaware. Age, sex, disease duration, place of birth, education level, number of comorbidities besides HTN, and healthcare access (integrative versus not) were used to examine HTN awareness using multivariable logistic regression.

Results: A total of 195 individuals had follow-up data with BP readings. Most were young (mean 35 years), women (59%), with RRMS (94%). Using vital signs, 43.9% of the cohort (n=86) met AHA dx criteria. HTN awareness was confirmed by self or physician documentation in 14 individuals (7.1%) and 18 took antihypertensives (9.2%). Only 22% of people with HTN were aware of the dx (n=19). Older age and being seen at an integrative healthcare system were associated with higher odds of being aware of a HTN dx. For every year older an individual was, they were 1.085x more likely to be HTN aware (95%CI 1.026-1.146, p=0.004). HpwMS under the care of an integrative public healthcare system were 4.94x more likely to be HTN aware (95%CI 1.110-22.021, p=0.036).

Conclusion: HpwMS have low rates of HTN awareness. Older people and those receiving MS care at public facilities may reflect better primary care access which underscores the benefits of integrative healthcare systems. Attention to HTN screening in younger pwMS are needed.

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P1295
Health Technology Utilization and Disability in People With Multiple Sclerosis

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Introduction: Hispanic people with MS (pwMS) in the United States (US) face healthcare access barriers and worse MS-related disability compared to White pwMS. Access to healthcare technology has been shown to improve communication and increase patient engagement, which can lead to better patient outcomes.

Objectives/Aims: To describe the preferences for and patterns of health technology utilization that could impact MS outcomes among Hispanic pwMS in the US.

Methods: Hispanic pwMS from the Alliance for Research in Hispanic MS were invited to participate. The PhenX Social Determinants of Health (SDOH) toolkit and Access to Health Technology survey were administered via phone. Demographic and clinical characteristics and health technology utilization were compared by geography (California, CA; Florida, FL; and Puerto Rico, PR). Multivariable logistic regression was used to assess the relationship between diverse SDOH, online health technology (OHT) access and utilization, and disability in the past 12 months.

Results: Of the 500 participating Hispanic pwMS, most were female (n=367, 73.4%). Mean age was 48.0 (SD 12.5) years and mean disease duration was 14.6 (SD 8.7) years. Mean Patient-Determined Disease Steps (PDDS) was 3.1 (SD 2.4), and 117 (23.4%) had a PDDS of ⩾ 6. 250 (50.0%) were US-born. Differences in place of birth and language preference were observed by geography. Utilization of OHT was highest in CA (75.6%), followed by FL (69.2%) and least in PR (14.6%). The majority of those who lacked utilization of OHT preferred to speak with healthcare providers (67.9%, 86.1%, and 92.8% for CA, FL, and PR respectively). Compared to those who utilized OHT, a larger proportion of those not utilizing OHT were not on MS disease-modifying treatment (24.5% and 17.2% respectively; p=0.044) and had PDDS ⩾ 6 (29.4% and 18.6% respectively; p=0.006). Being employed full-time [OR 95% CI 1.82 (1.07-3.11), p=0.028] and having education beyond high school or equivalency [1.70 (1.03-2.79), p=0.036] were associated with higher OHT utilization while male sex [0.50 (0.30-0.84), p=0.008] and low household income [0.44 (0.26-0.73), p=0.001] were associated with lower OHT utilization.

Conclusion: Patterns of health technology utilization by Hispanic pwMS differ by geography, possibly reflecting accessibility and sociocultural differences and preferences. Importantly, those with greater physical disability and socioeconomic disadvantage were less likely to use OHT. Enhancing OHT access may improve MS outcomes.

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P1296
Work-related quality of life and resource utilization in Italian Workers with Multiple Sclerosis

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Introduction: The early onset of Multiple Sclerosis (MS) significantly impacts both professional and personal life, leading to job retention difficulties and reduced employability. Work-related challenges negatively affect the quality of life (QoL) of individuals with MS, influencing both physical and mental health and consequently impairing occupational performance.
Objectives/Aims: This study aims to evaluate work-related quality of life and healthcare and social resources utilization in workers with MS (WwMS), investigating the influence of work difficulties.
Methods: This cross-sectional study included Italian WwMS recruited from two rehabilitation centers in Italy. Data were collected through an online survey assessing work difficulties (Multiple Sclerosis Questionnaire for Job Difficulties, MSQ-Job), work-related quality of life (Work-Related Quality of Life Scale, WRQoL), healthcare and social resources utilization (Needs and Provision Complexity Scale, NPCS). Differences between workers with and without work difficulties (according to the MSQ-Job cut-off score) were analyzed using Chi-square or Fisher's exact tests for categorical variables and t-tests or Mann-Whitney tests for continuous variables.
Results: A total of 160 WwMS (mean age: 48.2±9.5 years; 66.3% female; disease duration: 16.5±10.2 years; EDSS: 3.2±2.3) were included in the analysis based on survey completeness. Among them, 73.8% reported work difficulties according to the MSQ-Job cut-off (>15.8). The WRQoL subscales analysis indicated that stress at work was the most affected factor (score: 2.7±1.1). Significant differences ($p<0.002$) were found between workers with and without work difficulties across all WRQoL subscales (control at work, general well-being, home-work interface, job career satisfaction, stress at work, working conditions, and employee engagement). Regarding resource utilization, medical care, rehabilitation therapy, and advocacy were the most frequently used services. Individuals reporting work difficulties had significantly higher ($p<0.05$) demands for advocacy services, aids and equipment, and adapted accommodation.
Conclusion: This study highlights impact on work-related difficulties on work-related quality of life of PwMS. Moreover, it underscores the increased need for advocacy, assistive aids, and adapted accommodations within this specific population. These findings emphasize the importance of targeted interventions to address work difficulties, improve work-related quality of life, and optimize the utilization of healthcare and social resources

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P1297
Demographic and Neurocognitive Disparities in a Sample of Egyptian Multiple Sclerosis Patients; effect of treatment versus no tratment with disease-modifying therapies

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Introduction: Consideration of disease-modifying therapy (DMT) for all multiple sclerosis (MS) patients well established in the current treatment guidelines, but logistic barriers to access have begun to be identified. Prior studies have found that people with higher socioeconomic status, particularly education level, have better access to DMTs, perhaps explained by the association of higher education with higher income. And while most people with MS are women, being male is also associated with higher income. These factors argue for the need to better

understand whether there are differences in DMT uptake based on sex and education. Finally, in addition to well-documented benefits of DMTs for slowing disease progression, particularly silent cognitive impairment, there is growing evidence to suggest benefits of DMTs for cognitive functioning.
Objectives/Aims: Determine whether rates of DMT treatment differ based on socioeconomic status, particularly education and sex. Secondarily, we explore whether neurocognitive test performance differs in treated versus not treated groups.
Methods: This is a cross-sectional study that was carried on 643 patients with clinically definite MS at the neuroimmunology and MS unit at Al-Azhar University Hospitals. The regression models evaluated differences in education and sex of those treated versus not treated with DMTs. Models included the following predictors: age, gender, residence, disease duration, MS phenotype, socioeconomic status, education level, disability status, current DMT, compliance and adherence to DMT. Propensity score weights were extracted to obtain unbiased estimates of the relationship between DMT status and each outcome of interest. The same models evaluated performance differences between groups on an iPad-based processing speed test (PST), other cognitive batteries, and manual dexterity test (MDT).
Results: Controlling for covariates, individuals with low socioeconomic status particularly lower education level (OR=1.09, 95 % CI= [1.03, 1.14], $p = 0.003$) and female sex (OR=0.80, 95 % CI= [0.72, 0.90], $p < 0.001$) were less likely to be currently treated with DMTs. Small effect size association was shown for DMT treatment with better performance on cognitive batteries specifically the PST (beta=0.09, CI= [0.06, 0.13], $p < 0.001$) and MDT (beta=0.05, CI= [0.01,0.08], $p = 0.011$).
Conclusion: Multiple sclerosis patients with low socioeconomic status particularly lower education level and female patients had a lower likelihood of being currently treated with DMTs. After controlling all relevant variables, an independent (small) association of DMT treatment to better performance on cognitive tests specifically processing speed and fine motor dexterity was found. Reasons for disparities remain to be investigated in future work, and may include employment status, health insurance coverage, residence or sex differences in risk tolerance.

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P1298
Sleep quality and insomnia in people with multiple sclerosis

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Introduction: Sleep disorders, in particular insomnia, are common in people with multiple sclerosis (pwMS) and have a significant impact on the quality of life of pwMS. Sleep tends to be neglected in routine neurological practice. We, therefore, surveyed pwMS to document the unmet need concerning the diagnosis and management of sleep disorders.
Objectives/Aims: To assess (1) how pwMS rate their sleep quality, (2) how often they are diagnosed as having a sleep disorder or insomnia, and (3) whether or not they have used pharmacological and non-pharmacological interventions for their sleep disorders.
Methods: Subscribers with MS to the MS-Selfie self-management portal (www.ms-selfie.org) were invited to complete an online survey. The survey was opened on 9th September 2024 and remains open.
Results: As of December 10, 2024, there have been 172 responses from subjects with MS. 81.9% were female with a mean age of 53 years (range 32-70). 50.9% of respondents rated their sleep quality as poor or very poor. The most commonly diagnosed sleep problems were insomnia (47%), restless legs syndrome (33.7%), bruxism (21.7%) and obstructive sleep apnoea (12%). Only 12.8% of respondents did not complain of interrupted sleep. Nocturia (43.6%), pain (38.5%), anxiety (37.2%), leg spasms (36.5%), restless legs (28.2%) and menopausal symptoms (26.3%) were the most commonly reported symptoms interrupting sleep. Only 15.9% of respondents had had a formal sleep study. 51.2% reported never being asked about sleep during their MS clinic visits. 45% had tried over-the-counter medication to help with sleep, and 34% had used prescription drugs with variable success. Only 11 respondents had tried cognitive behavioural therapy and 11 mindfulness to improve their sleep.
Conclusion: This survey shows that most pwMS self-report MS-related sleep dysfunction. The survey indicates that MS-related sleep disorders are neglected clinically, poorly documented, poorly diagnosed and poorly managed in routine clinical practice. There is a significant unmet need to educate pwMS about sleep disorders and how to diagnose and self-manage these problems. In parallel, HCPs must incorporate screening tools for sleep disorders into routine clinical practice as an adjunct to proactively managing MS-related sleep disorders.

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P1299
Investigation of the Relationship Between Stigmatization and Upper Extremity Function in Mild-to-Moderate Disabled People With Multiple Sclerosis

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Introduction: Stigmatization refers to the negative labelling of an individual, group, or event, resulting in exclusion, rejection, blame, or devaluation. People with chronic illnesses such as multiple sclerosis (MS) tend to experience a heightened perception of stigmatization, which is associated with lower self-esteem, reduced perceived social support, increased depression and anxiety, greater social conflict, and more pronounced psychological distress. Stigmatization in chronic illnesses leads to adverse physical and psychological outcomes, negatively

impacting work and family life. Upper extremity dysfunction can occur in people with MS (pwMS) from the early stages of the disease, regardless of the Expanded Disability Status Scale (EDSS) score and disease duration.

Objectives/Aims: This study aims to investigate the relationship between coping mechanisms and upper extremity function, quality of life, neuropsychological symptoms, and depression-anxiety in pwMS.

Methods: This cross-sectional study involved a total of 67 pwMS. Hospital Anxiety Depression Scale (HADS) and The Preference-Based Multiple Sclerosis Index (PBMSI) were used to measure depression-anxiety levels and health-related quality of life. The Multiple Sclerosis Neuropsychological Screening Questionnaire (MSNQ) assessed neuropsychological competence during daily activities. While the Manual Ability Measure (MAM-36) questionnaire evaluated patient-reported upper extremity usage ability in daily activities, the Nine-Hole Peg Test (N-HPT) was employed to measure upper extremity skills based on performance. Stigma was assessed using the Neuro-QoL. Information such as EDSS, disease duration and age of the participants were also recorded.

Results: The participants had a mean disease duration of 8.85±5.56 years (range: 0–24), a mean age of 32.22±7.60 years (range: 19–49), and a mean EDSS score of 1.39±1.41 (range: 0–5.5). Regarding gender distribution, 46 were women (68.7%) and 21 were men (31.3%). Correlation analyses showed significant relationships between stigma (measured by Neuro-QoL) and various factors: MSNQ ($p < 0.01$, $r = 0.533$), depression ($p = 0.05$, $r = 0.343$), anxiety ($p = 0.07$, $r = 0.328$), quality of life-fatigue ($p = 0.03$, $r = 0.357$), quality of life-mood ($p = 0.04$, $r = 0.345$), quality of life-roles and responsibilities ($p < 0.01$, $r = 0.500$), total quality of life score ($p < 0.01$, $r = -0.447$), and MAM-36 ($p = 0.018$, $r = -0.310$). However, there was no relationship between stigma and age, disease duration, EDSS score, and N-HPT results.

Conclusion: The findings suggest that while stigmatization was linked to patient-reported upper extremity function (MAM-36), it did not correlate with objective performance-based upper extremity function (N-HPT). This discrepancy may reflect the subjective nature of stigmatization and its influence on self-perception and daily functioning.

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P1300
Sexual Function and Reproductive Intentions in Demyelinating Diseases: Insights from a Colombian Cohort

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Introduction: Multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) primarily affect young adults between the ages of 20 and 40. These conditions can lead to sexual dysfunction (SD), which, along with other disease manifestations, may significantly impact quality of life and influence reproductive decisions.

Objectives/Aims: To assess the perception of sexual function and reproductive intentions among individuals diagnosed with MS or NMOSD in Bogotá, Colombia.

Methods: This cross-sectional study employed both quantitative and qualitative analyses. Adults with a confirmed diagnosis of MS or NMOSD were included, and data were collected through an online survey. The study was approved by an ethics and research committee.

Results: A total of 89 patients (NMOSD: n=9, MS: n=80) completed the survey. The mean age was 40 ± 10 years. Sexual dysfunction was reported by 48.3% of patients, with the most common concerns being decreased sexual desire, mood changes, and difficulty with lubrication. Respondents perceived themselves to be mostly uninformed concerning sexual function. Nearly half (47.2%) reported to be not informed and 29.2% said they had been provided with little to no information concerning sexual function. Following diagnosis, 31% of patients reconsidered their decision to have children, while four patients (three females, one male) had children post-diagnosis. Additionally, 14 patients were advised by their physician not to conceive. Thematic analysis identified four key areas impacted by MS or NMOSD: low sexual desire, current symptoms of sexual dysfunction, self-image, and emotional expectations surrounding sexuality. Patients expressed concerns about both current symptoms and the uncertainty of future disease progression affecting their sexual health and reproductive decisions. Other common themes included the impact of the disease on relationships and concerns about the genetic risk of passing it on to their children.

Conclusion: Through this research, we provide a broader comprehensive understanding of sexual function and reproductive intentions among patients affected by MS or NMOSD and address the existing knowledge gap in Latin-American contexts.

Disclosure of interest: nothing to disclose.

P1301
Multiple sclerosis and neoplasms: a retrospective cohort characterization of treatment selection on dual diagnosis

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Introduction: The increased longevity in multiple sclerosis (MS) implies that some MS patients will suffer from neoplasms during their lifetime. As both pathologies stand at opposite ends of immune dysregulation spectrum, the first related to autoimmunity and the latter to escape from immune surveillance, this dual diagnosis imposes challenges regarding treatment decisions.
Objectives/Aims: Characterize a population with a dual diagnosis of MS and neoplasms and analyze the influence of these diagnosis in treatment approach in both diseases.
Methods: Retrospective single-center cohort characterization of outpatients managed in the MS Department of a secondary-care hospital with both MS and neoplasm diagnosis. We followed the National Institute of Health definitions for cancer and neoplasm. Data was collected from patient recordings. Descriptive statistics were conducted with IBM/SPSS®.
Results: From a population of 486 MS patients, 6,9% (N=31) had a diagnosis of at least one neoplasm during their lifetime, totalizing 36 neoplasms, 66,7% (N=24) of which were malign (cancer). Most of the neoplasms (66,7%; N=24) were diagnosed in patients with a prior MS diagnosis, while the remaining preceded the diagnosis of MS. Regarding antineoplastic treatment, in the group of patients whose neoplasm preceded MS (33,3%; N=12), surgery was the sole treatment in 58,3% (N=7) of cases, whereas 41,7% (N=5) underwent multiple oncologic therapies. In the group of patients whose neoplasm occurred after MS diagnosis, surgery was the sole treatment in 75,0% (N=18) of cases, whereas 16,7% (N=4) were not subject to any kind of treatment. In patients with a prior MS diagnosis, 38,7% (N=12) had a cancer diagnosis in the follow-up, totalizing 16 cancers, since 4 patients had multiple cancers. At cancer diagnosis, 31,3% (N=5) were not under MS disease modifying treatment (DMT), 25,0% (N=4) stopped and did not restart immunosuppression and 43,7% (N=7) maintained current DMT, including those of high efficacy. Median EDSS at time of cancer diagnosis was 4 (interquartile range 5.5) and did not differ from last follow-up. Mean follow-up since cancer diagnosis was 10,5 years [standard deviation (SD) 6,7 years], and mean follow-up since first symptoms of MS 19,5 years (SD 9,8 years).
Conclusion: In our cohort, MS diagnosis in patients with cancer may have influenced oncologic treatment decisions. However, most cancer diagnosis did not result in changes in MS DMT strategy and apparently cancer diagnosis had no impact on patient disability.

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P1302
Comorbidity and Health Status in People with Multiple Sclerosis: A Prospective Observational Study

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Introduction: Comorbidity is prevalent among people with multiple sclerosis (pwMS) and may contribute to the heterogeneity of clinical outcomes. We explored whether the presence of comorbidity is associated with health status in pwMS.
Objectives/Aims: To explore the impact of comorbidity on the health status in PwMS.
Methods: A prospective observational study was conducted in a real-world setting at a hospital-based MS clinic from June 2024 to January 2025. All eligible pwMS were scheduled to attend following a predefined algorithm: clinical examination and assessment of comorbidities, determination of walking capacity using the 6-minute walk test (6MWT), patient-reported health status questionnaires including the European Quality of Life–5 Dimensions index (EQ-5D-5L) and visual analogue scale (EQ VAS) and the Pittsburgh Sleep Quality Index (PSQI). Adjustment for patient age was performed.
Results: A total of 73 pwMS participated and 45 (62%) had at least one comorbidity while 33 (45%) had multiple comorbidities i.e. $\geqslant$ 2, including vascular risk factors (n=29, 87.9%), other autoimmune diseases (n=11, 33.3%), depression (n=6, 18.2%) and chronic obstructive lung disease (n=5, 15.2%). PwMS having a single comorbidity or multiple comorbidities had higher mean Expanded Disability Status Scale (EDSS) of 3.1 (SD 1.4) and 4.6 (1.7)

compared to those without comorbidity, 2.5 (1.4) (p=0.030, p=0.048), respectively. Mean 6MWT were lower in the groups with a single comorbidity (474 m (147)) or multiple comorbidities, 353 m (151) when compared to the non-comorbidity group (518 m (116), p=0.019, p=0.024), respectively. Patient-reported outcomes showed diminished overall health status (EQ VAS) 64 (19) vs. 73 (20), (p=0.042) and impaired sleep quality 9.5 (5.4) vs. 6.9 (5.2), p=0.031, in the comorbidities group compared to the non-comorbidity group.
Conclusion: Nearly half of pwMS had multiple comorbidities, associated with lower levels of functional capacity, increased disability, impaired sleep quality and overall health status. Our results suggest that pwMS with comorbidities have worse health status requiring specific attention in the clinic.

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P1303
Emerging Comorbidities and Malignancies in People with Multiple Sclerosis After the COVID-19 Pandemic: A Comparative Study

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Introduction: The COVID-19 pandemic has presented unprecedented challenges to healthcare systems and vulnerable populations, including people with multiple sclerosis (pwMS). As the pandemic unfolded, concerns emerged regarding its potential long-term impact on the overall health profile of pwMS. This study aimed to explore whether a history of COVID-19 infection was associated with differences in the frequency and types of newly reported comorbidities and malignancies in this population.
Objectives/Aims: To investigate the spectrum and frequency of comorbidities and malignancies reported after the COVID-19 pandemic among pwMS with and without a history of COVID-19 infection.
Methods: This retrospective study included pwMS with and without a history of COVID-19 infection, selected from a large cohort regularly followed at a tertiary MS center. Age- and sex-matched groups were formed to allow for appropriate comparisons.
Results: The study included 646 pwMS with confirmed COVID-19 and 646 pwMS without a history of COVID-19. In the COVID-19 group, 69.3% were female (n = 448), and the mean age was 44.41 years (SD = 11.58). The average disease duration was 13.12 years (SD = 8.29), and the mean age at MS onset was 31.29 years (SD = 9.12).
In this group, a total of 194 comorbidities were identified: psychiatric disorders (n = 65; 25.2%), neurological disorders (n = 61; 23.6%), cardiovascular diseases (n = 32; 12.4%), endocrine/metabolic disorders (n = 17; 6.6%), respiratory diseases (n = 10; 3.9%), rheumatologic/autoimmune diseases (n = 5; 1.9%), and gynecological/urogenital conditions (n = 4; 1.6%).
In the control group, 293 comorbidities were reported: neurological disorders (n = 61; 16.9%), psychiatric disorders (n = 25; 6.9%), cardiovascular diseases (n = 20; 5.5%), endocrine/metabolic disorders (n = 17; 4.7%), and respiratory diseases (n = 7; 1.9%). Although the total comorbidity burden appeared numerically higher in the control group, there was no statistically significant difference between the groups (p = 0.063).
Regarding malignancies, 16 cancer cases (2.5%) were identified in the COVID-19 group. Breast cancer was the most frequent (n = 7; 43.8%), followed by thyroid cancer, invasive ductal carcinoma, colorectal cancer, laryngeal cancer, cervical cancer, prostate cancer, lymphoma, and ovarian cancer (n = 1 each; 6.3%). In the control group, 7 malignancy cases (1.1%) were reported, including breast cancer (n = 5; 71.4%) and colorectal cancer (n = 2; 28.6%).
Conclusion: The findings indicate a possible shift in comorbidities and malignancies among pwMS after the COVID-19 pandemic. While not statistically significant, the higher frequency and variety of conditions in those with prior infection highlight potential emerging risks. These results emphasize the need for ongoing, multidisciplinary follow-up focused on both physical and mental health in the post-pandemic period.

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P1304
Effectiveness of disease management across health providing settings: the Multiple Sclerosis Center is a pillar for multi-disciplinary practices that promote quality of life for people with Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS) is a chronic neurological disorder, prevalent in young adults. MS leads in disability accrual, thus affecting overall patients' quality of life. Moreover, the management of MS poses significant burden on health systems worldwide.
Objectives/Aims: The present study delves into the impact of different health providing settings (e.g. private office / Clinic vs. specialized MS Center) on the effectiveness of MS management, as well as on patient-reported outcomes related to the quality of life (Axis A). Moreover, the study addresses their relative effectiveness in a health crisis, such as the COVID-19 pandemic (Axis B).
Methods: Data were collected based on questionnaires administered to pwMS. Upon the pandemic and prior to the COVID-19 vaccines being available, all data were collected via online questionnaires. Since March 2021, data were collected both online and in person.
Results: Overall, 776 pwMS participated in the study and answered Axis B questionnaire. Of those, 215 additionally answered Axis A questionnaire. Regarding Axis A, disease management by a specialized MS Center was associated with increased access to healthcare professionals ($p<0.001$) and/or MRI examinations ($p<0.001$) and was also linked to improved time-to-diagnosis following symptom onset, compared to the disease management in a private office / Clinic ($p<0.001$). Regarding Axis B, specialized MS centers demonstrated remarkable adaptability during the pandemic, swiftly implementing telemedicine and other remote care solutions to ensure continuity of care.
Conclusion: These findings underscore the importance of specialized care structures in maintaining patient well-being both in everyday practice conditions and during healthcare crises.

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P1305
West Nile Virus Encephalitis Following Ocrelizumab Therapy in a Patient with Multiple Sclerosis: A Case Report

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Introduction: West Nile virus (WNV) is a neurotropic flavivirus transmitted by mosquitoes. While most infections are asymptomatic, neuroinvasive disease can occur, especially in immunosuppressed individuals. Anti-CD20 therapies such as ocrelizumab may increase susceptibility due to humoral immune suppression.
Objectives/Aims: We present a case of encephalitis in a person with multiple sclerosis undergoing treatment with ocrelizumab.
Methods: Case report.
Results: We report a 30-year-old woman with relapsing-remitting multiple sclerosis (RRMS), receiving ocrelizumab infusions biannually for two years. She presented with acute confusion, fever, and focal neurological deficits shortly after returning from travel. Neurological examination revealed encephalopathy without meningeal signs. Brain MRI demonstrated demyelinating lesions, but no active MS activity. Cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis, elevated protein, and normal glucose. Initial serologic and PCR tests for common viral and bacterial pathogens were negative.
Despite broad-spectrum antimicrobial treatment, no etiology was identified until day six, when CSF PCR confirmed WNV infection. A second MRI revealed right thalamic involvement. No systemic manifestations or skin lesions were observed. Remarkably, the patient improved clinically within two weeks without long-term sequelae. Follow-up MRI showed resolution of thalamic lesions.
Conclusion: This case highlights the risk of neuroinvasive WNV in patients receiving anti-CD20 therapy. Diagnostic delays may occur due to impaired antibody responses, emphasizing the importance of early CSF PCR testing in suspected cases. Despite the immunosuppressed status, our patient experienced a mild course with full recovery. Clinicians should maintain a high index of suspicion for arboviral encephalitis in anti-CD20-treated patients presenting with encephalopathy, particularly in endemic or travel-associated exposure settings.

Disclosure of interest: nothing to disclose

P1306
Dyslipidemia among patients with multiple sclerosis

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Introduction: Dyslipidemia is a relevant comorbidity among patients who suffer from multiple sclerosis (MS).
Objectives/Aims: The aim of our study was to evaluate prevention of dyslipidemia in patients with different fenotypes of MS and its influence on the degree of disability according to EDSS scale.
Methods: 52 patients diagnosed with MS according to McDonald's criteria (2017), treated in the Neurology Clinic in Zabrze, Poland were included in a study. The motor disability

degree was evaluated based on EDSS. The blood samples were taken from each member of a study due to assess lipid profile. We accomplished an agreement of Bioethics Committee of Medical University of Silesia in Katowice, Poland to perform a study.
Results: 63,46% of a study members were diagnosed with dyslipidemia, the most often in case of secondary – progressive MS (SPMS), but the differences between several disease types were not statistically relevant/ significant. We found a positive correlation between triglicerydes concentration in a blood serum and the EDSS score ($R = 0.345$, $p<0.05$), as well as a negative correlation between HDL cholesterol levels and the EDSS score ($R = -0.438$, $p<0.05$).
Conclusion: Occuring of dyslipidemia is associated with a higher degree of disability according to EDSS. Monitoring of lipid profile parameters and a lifestyle modification in people who suffer from dyslipidemia is crucial in case of patients with MS. Further studies are needed to explain an influence of disrupted lipid profile on MS course.

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P1307
Epidemiology of common comorbidities in patients with Multiple Sclerosis using electronic healthcare records from 2007 to 2016 in Iran

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Introduction: Research interest in the impact of comorbidities in multiple sclerosis (MS) has been steadily increasing. Certain comorbidities, such as depression, anxiety, cardiovascular diseases (including hypertension and hypercholesterolemia), diabetes, and hypothyroidism, are more prevalent in the MS population. However, the epidemiology and burden of these comorbidities remain largely unassessed in many countries.
Objectives/Aims: This study aims to examine the prevalence of comorbidities in the MS population using healthcare records data.
Methods: This retrospective database analysis utilized patient-level medical and pharmacy claims data from a major insurance provider (Iranian Health Insurance) covering the years 2007–2016. Due to the lack of diagnostic data, MS patients were identified based on their prescriptions for Disease-Modifying Therapies issued by neurologists. Comorbidities in both MS and non-MS populations were determined through prescription data. Crude and age-standardized prevalence rates of comorbidities across different sex and age groups, as well as their odds ratios compared to the non-MS population, were analyzed.
Results: The most common comorbidities were depression (15.50%) and anxiety (10.1%). Hypercholesterolemia, diabetes, hypertension, and hypothyroidism were prevalent at rates of 6%, 3.6%, 3.5%, and 2.7%, respectively. Anxiety and depression were more common among the middle-aged group (45–65 years), whereas other comorbidities were more prevalent in older age groups. All comorbidities were more prevalent in females, except for hypertension in patients aged 45 years or older. The odds of all comorbidities were higher for male MS patients compared to their counterparts in the non-MS population. This pattern also applied to female MS patients aged 18–44 years, with the exception of hypertension.
Conclusion: Using electronic healthcare records, the prevalence of selected comorbidities in the MS population and their associations with sex and age can offer valuable insights for patients and healthcare providers. Furthermore, this study provides evidence for policymakers to develop policies aimed at enhancing the well-being of MS patients.

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P1308
Anxiety, depression, fatigue, and daytime sleepiness in Tunisian MS cases: a cross-sectional study

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Introduction: Anxiety, depression, fatigue, and daytime sleepiness (DTS) are frequent in MS. Despite their high prevalence, the specific underlying factors related to MS that contribute to these symptoms are not yet fully understood.
Objectives/Aims: To explore the sociodemographic, clinical, and radiological factors associated with anxiety, depression, fatigue, and DTS in MS cases.
Methods: We conducted a cross-sectional study on MS patients followed at the Neurology Department of Gabes University Hospital from 2020 to 2023. Anxiety and depression were assessed using HADS; fatigue and DTS using FSS and ESS, respectively. Data were analyzed with SPSS 26, with $p < 0.05$ considered significant.
Results: We included 53 MS patients with a mean age of 37.83 ± 11 years and a sex ratio of 0.43. Anxiety, depression, fatigue, and DTS were observed in 69.81%, 81.13%, 28.3%, and 64.15% of cases, respectively. The age of patients was negatively correlated with anxiety ($r = -0.21$; $p = 0.01$) and positively correlated with fatigue ($r = 0.31$; $p = 0.02$). The analysis showed that a higher number of relapses ($\geqslant 3$) and use of corticosteroids ($\geqslant 3$) were associated with a higher likelihood of depression. Subtentorial and cerebellar peduncle involvement were associated with lower HADS anxiety scores, while parietal involvement was linked to higher scores. Fatigue was associated with longer MS duration, delayed diagnosis, relapses$\geqslant 3$, corticosteroid courses$\geqslant 3$, and higher disability. Cerebellar peduncle and dorsal spinal involvement were linked to lower FSS scores. Fatigue correlated significantly with depression, but not anxiety. There was also an association between anxiety, depression, and DTS.
Conclusion: Our study revealed that anxiety, depression, fatigue, and DTS are prevalent and interrelated in MS patients.

Certain clinical and radiological features may be risk factors for these symptoms. Further research is needed to better understand the underlying pathophysiological mechanisms.

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Pathology & Pathogenesis of MS – Pathology

P1309
Impaired cerebral oxygen metabolic response to moderate hypoxia in patients with multiple sclerosis or myelin oligodendrocyte glycoprotein antibodies is associated with marker of brain inflammation but not impaired vasodilatory capacity

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Introduction: Patients with MS exhibit cerebrovascular dysfunction that may impact cerebral oxygen metabolism, though the underlying mechanisms remain unclear. Whether patients with myelin oligodendrocyte glycoprotein (MOG) antibodies also exhibit cerebrovascular impairments is not known.
Objectives/Aims: The aim of the study was to examine whether cerebrovascular dysfunction in patients with MS or MOG antibodies affects cerebral oxygen metabolism. We evaluated the cerebral physiological response to hypoxic exposure as a stress test of brain oxygen metabolism. The vasodilating capacity was assessed as the cerebrovascular reactivity to a vasodilating hypercapnic challenge. Blood-brain-barrier (BBB) permeability was measured as a marker of brain inflammation.
Methods: 49 patients participated (25 relapsing-remitting MS, 6 secondary progressive MS, and 18 with MOG antibodies) and 22 matched healthy controls (HC). Global cerebral blood flow (CBF) was obtained by measuring blood flow in the carotids and basilar arteries using phase-contrast mapping MRI. Cerebral metabolic rate of oxygen ($CMRO_2$) was calculated by Fick's principle: $CMRO_2$=CBF•[Arterial saturation-Venous saturation]. The venous oxygen saturation of the blood leaving the brain in the sagittal sinus was measured using susceptibility-based oximetry MRI. BBB permeability in thalamus was measured by dynamic contrast-enhanced MRI. The CBF response to hypercapnic exposure was evaluated by participants inhaling air containing ~5% CO_2 in the MRI scanner. Similarly, the CBF and $CMRO_2$ responses to hypoxic exposure were measured by participants inhaling hypoxic air (~12% O_2) in the scanner.
Results: CO_2 inhalation increased CBF and with no differences between patient groups and HC ($p>0.54$). Hypoxic air increased CBF in all groups, but the response was significantly lower in both the MS ($p=0.041$) and MOG ($p=0.003$) patients compared to HC. Both patient groups also exhibited a reduction in $CMRO_2$ (MS: $p=0.022$, MOG: $p=0.024$), in contrast to HC who maintained $CMRO_2$ during inhalation of hypoxic air. BBB permeability in thalamus was significantly higher in both the MS ($p=0.025$) and MOG group ($p=0.035$) compared to HC. The reduction in $CMRO_2$ correlated with abnormally high BBB permeability in the thalamus ($p=0.029$) across the patients.
Conclusion: The normal CBF response to CO_2 indicates preserved vasodilatory capacity in the patients. However, the blunted response to hypoxia and its correlation with abnormally elevated BBB permeability indicate that the inflammatory milieu in the brains of the patients may disrupt the cerebrovascular signaling. The similarly impaired $CMRO_2$ response observed in both MS and patients with MOG antibodies suggests common pathophysiological mechanisms.

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P1310
The Cytokine TWEAK Modulates Expression of MS Susceptibility Genes in Human Brain Microvascular Endothelial Cells

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Introduction: Multiple sclerosis (MS) is associated with temporal and spatial blood brain barrier (BBB) dysfunction and immune cell infiltration in the central nervous system (CNS). We found that, serum TNF-Related Weak Inducer of Apoptosis (TWEAK) is upregulated and associated with neuroinflammation during the disease, and also engenders permeabilization of an *in vitro* BBB model. In 2019, the *International MS Genetics Consortium* (IMSGC) published a genome-wide association study (GWAS) which identified over 230 genetic susceptibility variants associated with MS risk, predominantly enriched in peripheral and CNS-resident immune cells. Interestingly, some of these genes encode proteins that could also be regulated in human brain microvascular endothelial cells (BMEC) in the context of neuroinflammation (i.e., cell adhesion, trafficking, and BBB degradation).
Objectives/Aims: We sought to determine whether TWEAK or TNFα (as a control) exposure could modulate the expression of MS susceptibility genes in the human cell line hCMEC/D3, which, when conditioned, models the BBB *in vitro*.
Methods: Our database of differentially expressed genes (DEG; $|FC| \geqslant 1.0$) in TWEAK- or TNFα-stimulated hCMEC/D3 at 3h, 12h, and 24h was probed against MS risk genes (200 autosomal non-MHC loci, 410 mapped genes) published by IMSGC to highlight overlaps/congruities/matches.

Results: The cross-referencing yielded 271 interpretable genes. Of these, 126 genes (~46%) were significant DEGs ($|FC| \geqslant 1.5$) in response to TWEAK or TNFα at at least one timepoint. Notably, 26 genes were exclusively modulated by TWEAK, 54 by TNFα only, and 46 genes were responsive to both. TWEAK had a more pronounced effect at 24h, with 53 DEGs (36 upregulated, 17 downregulated), compared to other timepoints and TNFα at the same timepoint. Of the 64 TWEAK-responsive genes that overlapped with MS susceptibility loci, several genes play known roles in endothelial activation/inflammation or BBB integrity/cytoskeletal rearrangement.
Conclusion: Our findings indicate that TWEAK modulates the transcription of a subset of MS risk genes in human BMECs. To our knowledge, this is the first study to examine the transcriptional responsiveness of MS risk genes to inflammatory cues in the human brain endothelium.

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P1311
Unraveling cholesterol metabolism in multiple sclerosis: Gender-specific patterns and predictive biomarkers

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Introduction: Multiple Sclerosis is a chronic, immune-mediated, and heterogeneous disease characterized by demyelination, axonal damage, and both physical and cognitive impairment. An increasing body of evidence suggests that disruptions in cholesterol metabolism are linked to the clinical progression of MS. Cholesterol, along with non-cholesterol sterols and oxysterols plays a crucial role in immune regulation and signaling. Additionally, cholesterol is an essential constituent of myelin.
Objectives/Aims: To analyze sterol profiles in individuals with different types of multiple sclerosis and controls to better understand their potential role in the disease.
Methods: In this study, cholesterol concentrations, cholesterol-standardized levels of non-cholesterol sterols and oxysterols were determined in serum and cerebrospinal fluid samples from 127 individuals with clinically isolated syndrome, relapsing-remitting multiple sclerosis or primary progressive multiple sclerosis as well as 49 control subjects. Additionally, we quantified serum Neurofilament light chain, a protein indicative of axonal injury in the same patients.
Results: Our findings revealed significant alterations in cholesterol metabolism in patients. Serum cholesterol and cholesterol synthesis markers were elevated, while an opposite trend was observed in cerebrospinal fluid, indicating a contrasting pattern between the peripheral and central nervous system cholesterol metabolism. Cholesterol absorption was notably reduced in MS. The levels of neurofilament across different forms of multiple sclerosis followed a similar trend to serum cholesterol levels but were opposite to those found in cerebrospinal fluid, suggesting a link between axonal damage and disease progression. The serum-cerebrospinal fluid correlation pattern varied according to the disease type and the individual's gender.
Conclusion: Based on our results, we propose that reduced endogenous cholesterol synthesis in the brain may underlie or at least play a role in the pathological developments in multiple sclerosis, with cerebrospinal fluid cholesterol levels potentially serving as a marker of demyelination but not necessarily axonal damage. Furthermore, certain serum (oxy)sterols emerged as potential biomarkers for multiple sclerosis diagnosis and progression.
These outcomes contribute to a deeper understanding of multiple sclerosis pathophysiology and may facilitate the identification of novel biomarkers for diagnosis, as well as potential targets for treatment strategies.

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P1312
The Association of Serum Carnitine Levels with Fatigue Severity in a Sample of Egyptian Multiple Sclerosis Patients; A case-control study

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Introduction: Fatigue is one of the most common debilitating symptoms of multiple sclerosis (MS), affecting approximately two-thirds of patients and adversely affecting their quality of life throughout the course of the disease. Although the pathophysiology of fatigue in MS has not been understood well, it is hypothesized that the involvement of both CNS and musculoskeletal components is responsible for developing this symptom. There is a lot of evidence showing that carnitine deficiency is linked to fatigue development and severity in some conditions.
Objectives/Aims: Hence, considering the deteriorating impact of fatigue on the quality of life of patients with MS and mentioned role of carnitine in modulating energy homeostasis, the present study aimed to evaluate the contribution of serum

L-carnitine level and fatigue development and severity among patients with MS.
Methods: This case-control study was carried out at neuroimmunology and MS unit at Al-Azhar University Hospitals and included 560 patients diagnosed with relapsing-remitting MS (RRMS) based on the McDonald criteria in two age-matched equal-number groups according to the presence or absence of fatigue. Fatigue was scored using the valid questionnaire of Fatigue Severity Scale (FSS) according to the cut-off value of 35 for FSS (FSS $<$ 35 as "without fatigue" and FSS $\geqslant$ 35 as "with fatigue") and serum level of free L-carnitine was measured simultaneously. Patients with MS with known anemia, vitamin D deficiency, a history of inflammatory diseases, other autoimmune diseases, severe depression, and those being on antidepressant medication did not enroll in the study. Finally, the association between serum level of free L-carnitine and fatigue severity was evaluated in both groups.
Results: The mean value of FSS in patients with fatigue was 46.80 ± 7.55, which was nearly two-fold higher than the group without fatigue. There was a considerable correlation between the serum levels of free L-carnitine and FSS (Spearman rank correlation $= 0.76$, $P < 0.001$). We found a significant correlation between the serum level of free L-carnitine and FSS and showed that the patients with fatigue had significantly lower serum values of free L-carnitine compared to patients without fatigue (24.54 ± 16.84 vs. 75.46 ± 53.98, $P < 0.001$).
Conclusion: We showed that MS patients with fatigue had lower serum carnitine levels than those without fatigue. It suggests that MS patients with lower serum carnitine levels might experience more severe fatigue. This study also recommends that a higher dietary intake of carnitine might be an effective complementary treatment for fatigue in patients with MS.

Disclosure of interest: "Elsayed Abed: nothing to disclose."

P1313
Nano-silymarin Enhances Antioxidant Defense in stem cells from Secondary Progressive MS Patients: Focus on SOD Activity and Oxidative Stress Markers

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Introduction: Oxidative stress plays a major role in the progression of multiple sclerosis (MS), damaging cells and limiting the effectiveness of regenerative therapies. Stem cells (SCs) have shown therapeutic promise, but their performance can be compromised under oxidative conditions. Nano-formulated herbal compounds like silymarin may enhance antioxidant defenses and help improve the therapeutic potential of these cells.
Objectives/Aims: This study explored how nano-silymarin affects antioxidant responses in MSCs, focusing on changes in superoxide dismutase (SOD) activity and the levels of nitric oxide (NO) and malondialdehyde (MDA), which are key indicators of oxidative stress.
Methods: SCs were cultured and exposed to nano-silymarin at concentrations of 1, 2.5, 5, and 10 μM for 24 hours. SOD enzyme activity was assessed in the culture medium using a colorimetric assay. NO levels were measured to estimate nitrosative stress, and MDA levels were analyzed as a marker of lipid peroxidation. Each test was repeated in triplicate using cells from ten different MS patient samples.
Results: Nano-silymarin significantly enhanced SOD activity at 2.5 μM, suggesting improved antioxidant capacity. The highest dose (10 μM) resulted in a noticeable reduction in NO levels, indicating decreased nitrosative stress. MDA levels remained relatively unchanged across all concentrations. Overall, the strongest antioxidant response was observed at moderate nano-silymarin doses.
Conclusion: Nano-silymarin supports antioxidant function in SCs by increasing SOD activity and reducing NO production. These effects could enhance the therapeutic value of stem cells in oxidative stress-related conditions like MS, positioning nano-silymarin as a promising adjunct in regenerative medicine.

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P1314
Effects of resistance training on blood-brain barrier integrity in multiple sclerosis patients: a pilot study

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Introduction: The repulsive guidance molecule A (RGMa) is a glycosylphosphatidylinositol-anchored glycoprotein that plays a crucial role in the autoimmune-mediated pathological processes associated with central nervous system diseases, including MS. RGMa is involved in axon guidance and regeneration, but it also serves as a potent modulator of immunoregulatory molecules and the integrity of the blood-brain barrier (BBB). Physical exercise-based interventions (PE) are known as the main non-pharmacological treatment for MS through different mechanism such as decreasing the permeability of the BBB.
Objectives/Aims: This study aims to evaluate the effects of a resistance training (RT) program on plasma levels of RGMa in a group of MS patients.
Methods: Patients were included based on inclusion criteria: a confirmed MS diagnosis, age over 18, mild disability (EDSS $<$ 3), absence of new demyelinating lesions in the last brain MRI

and no relapse or MS treatment change during the previous six months. Participants with a high level of physical activity at baseline according to the International Physical Activity Questionnaire (IPAQ) were excluded. RGMa were assessed in plasma by commercial ELISA before the exercise intervention (1 week before RT program) and after intervention (1 week and 4 weeks after RT program). PE intervention consisted of a supervised 6-weeks RT program, performed 3 session times a week per week (18 sessions) consisted of 3 sets of 8-10 repetitions of 7 exercises.
Results: Eleven participants (9 females, 2 males) with a mean age of 40.8 years and a median EDSS of 0 (range: 0-2) were included. Circulating plasma RGMa levels showed a significant decrease following a RT intervention (dropped a 27%). Plasma RGMa decreased from 3.72 pg/ml at baseline to 2.69 pg/ml one week after training, and this reduction was maintained at 2.83 pg/ml after 4 weeks of detraining ($p<0.05$).
Conclusion: The results from this pilot study suggest that resistance training may impact on BBB permeability through decreasing different immunoregulatory molecules as RGMa in MS patients.

Disclosure of interest: Maria Nieto: nothing to disclose

Pathology & Pathogenesis of MS – Genetics/ Epigenetics

P1315
Using extremes in MS susceptibility to expose the functionally altered B and T cell in people with optic neuritis

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Introduction: Optic neuritis (ON) is an acute optic nerve inflammatory attack that often presents as first symptom in and affects approximately half of people with multiple sclerosis (MS). MS onset involves a complex interaction between Epstein-Barr virus (EBV) and genetic risk variants, which likely interferes with T-cell-dependent selection and promotes the maturation of B cells that become antibody-secreting cells (ASCs) in the central nervous system (CNS).
Objectives/Aims: We used the extremes in EBV-based and genetically determined disease risk to expose early alterations in B and T cell from people with or without MS after experiencing ON.
Methods: We measured anti-EBNA1 IgG levels and genotyped 372 participants of the PROUD study with relapsing-remitting MS (RRMS) or clinically isolated syndrome (CIS). Using PRSice-2 and the discovery GWAS (IMSGC 2019), we calculated the weighted genetic risk scores (wGRS) with 173 SNPs. Participants were followed a median of 6.45 years (3.30-10.78). PBMCs collected within 6 months after first symptom presentation were used to perform *ex vivo* spectral flow cytometry screens and *in vitro* T cell-dependent (CD40L/IL-21) stimulation assays to explore B- an T-cell interplay among groups.
Results: In CIS presenting with ON (N=161/372) participants in the highest quartiles of wGRS and anti-EBNA1 IgG were more likely to develop McDonald 2017 MS during follow-up (OR=3.99 and p-value=0.04, OR=1.36 and p-value=0.06, respectively). This cohort was used to select participants with ON, low wGRS and low anti-EBNA1 IgG not developing MS (Low, N=6) and participants with ON, high wGRS and high anti-EBNA1 IgG level developing MS (High, N=6). The high risk group presented lower abundance of circulating Th17.1 cells, supporting an enhanced migration towards the CNS in people with MS-associated ON. Moreover, in the high risk group, naïve B cells had a lower capacity to express granzyme B and memory B cells were more prone to differentiate into ASCs that strongly express IgG.
Conclusion: By analyzing the extremes in both wGRS and EBV Ig responses, we reveal subtle changes in disease-relevant B- and T-cell programs in people who develop MS after experiencing ON. This underlines the relevance of our previously identified mechanisms and subsets as a hallmark and provides a critical layer to further elaborate on in order to understand the cause of MS.

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P1316
Effect of BDNF Val66Met polymorphism on brain volume changes and disability progression during disease course in Multiple Sclerosis patients

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Introduction: Brain-Derived Neurotrophic Factor (BDNF) plays a key role in neuronal survival, proliferation, differentiation, synaptic plasticity and repair, contributing to neuroprotection and neuroplasticity. The Val66Met polymorphism alters BDNF function; however, its impact in multiple sclerosis (MS) remains uncertain, with conflicting evidence regarding its protective or detrimental effects.
Objectives/Aims: We aim to identify the effect of the Val66Met BDNF polymorphism on disability accrual and brain volume changes over time in relapsing-onset MS patients.
Methods: The presence of the *BDNF* Val66Met polymorphism was determined using polymerase chain reaction on blood samples. Patients underwent 3T MRI at baseline and annually throughout the follow-up period, along with neurological evaluation on the same day, including assessment using the Expanded Disability Status Scale (EDSS). Brain volumes were assessed using WMH-SynthSeg segmentation software. Linear mixed effects models adjusted for age, sex and disease duration at the study entry were used to assess and compare EDSS and brain volume changes over time among patients with and without Val66Met polymorphism.
Results: We included 97 relapsing onset MS patients; 29 were carriers of Val66Met BDNF polymorphism. Val66Met BDNF polymorphism were older at disease onset and more frequently male. Over a median follow-up of 7.38 (IQR: 4.90–9.87) years, compared to wild type, Val66Met polymorphism carriers exhibited more severe disability worsening over time (Beta=0.05; C.I.95%: 0.02, 0.07; p=0.001). They also showed larger increase in T2-lesion volume (Beta= 0.129; C.I. 95%: 0.028, 0.229; P=0,017) and more sever atrophy in deep gray matter volume (Beta -0.078; C.I. 95%: 0.031, -0.139; p=0,013) while no differences were observed in normalized brain, white matter and cortical gray matter volumes.
Conclusion: The Val66Met BDNF polymorphism, which impairs neuroprotection, was associated with greater white matter damage and Wallerian degeneration, resulting in increased deep grey matter atrophy over time. These findings support BDNF as a potential early biomarker for guiding treatment and as a target for neurorepair strategies.

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P1317
Do progression in multiple sclerosis share neurodegenerative mechanisms with other neurodegenerative diseases

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Introduction: While genetic predisposition to multiple sclerosis (MS) is well established, the pathogenic mechanisms underlying progression in MS remain elusive.
Objectives/Aims: Given the shared neurodegenerative features among neurological disorders, this study aimed to investigate the genetic overlap and causal relationships between progression in MS and two prototypical neurodegenerative diseases: Alzheimer's disease (AD) and Parkinson's disease (PD).
Methods: We performed cross-trait genetic analyses using genome-wide association study (GWAS) data from the International Multiple Sclerosis Genetics Consortium (14,581 MS cases) and the ENIGMA consortium (AD: 488,285 individuals; PD: 482,730 individuals; all European ancestry). Linkage disequilibrium score regression (LDSC) was applied to estimate the genetic correlations (rg). Two-sample Mendelian randomization (MR) analyses were conducted to infer causality between MS progression and neurodegeneration.
Results: Genetic correlation analyses revealed no substantial associations between progression in MS and AD ($rg = -0.494 \pm 1.091$, $p = 0.651$) or PD ($rg = -0.024 \pm 0.244$, $p = 0.921$). MR analyses further showed null causal effects of progression in MS on AD (IVW $\beta = -0.004$, 95% CI: -0.062-0.054, $p = 0.891$) or PD (IVW $\beta = 0.012$, 95% CI: -0.026-0.050, $p = 0.548$).
Conclusion: This large-scale genetic study provides evidence that progression in MS lacks shared genetic architecture or causal links with AD and PD, despite their overlapping neurodegenerative phenotypes. These findings underscore the necessity to explore non-genetic determinants including epigenetic regulation and environmental triggers in future mechanistic investigations of progression in MS.

Disclosure of interest: Zhang Yang yang:nothing to disclose

P1318
Distinct Genetic Mechanisms Converging on Immune Dysregulation in NMOSD: The Role of Post-Translational Modulation and Cytoskeletal Signaling according with AQP4 serostatus

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disease mediated by aquaporin-4 autoantibodies (AQP4-Ab). AQP4-Ab seropositive NMOSD is

characterized by autoimmune astrocytopathy, whereas seronegative cases predominantly display an inflammatory demyelinating pattern. In the era of targeted NMOSD therapies, understanding the biological pathways shaping disease across different AQP4 serostatus has become increasingly relevant.
Objectives/Aims: To explore biological pathways potentially implicated in NMOSD pathophysiology by identifying enriched functional categories associated with genes harboring predicted pathogenic or ambiguous variants within AQP4-Ab seropositive and seronegative groups
Methods: Whole-exome sequencing was performed in 29 AQP4-Ab seropositive and 11 seronegative NMOSD patients. Variants were evaluated for pathogenicity using in silico prediction tools. Gene Ontology (GO) overrepresentation analysis (ORA) was applied to genes with potentially pathogenic or ambiguous variants in ⩾70% of individuals per serogroup (adjusted $p<0.05$).
Results: In AQP4-Ab seropositive patients, enriched GO terms included "serine-type endopeptidase inhibitor activity" (SPINT3, SPINT4, SERPINB8, SERPINB11) and "Cul2-RING ubiquitin ligase complex" (PRAMEF8, PRAMEF10, PRAMEF18), highlighting pathways of post-translational protein regulation. In seronegative patients, enriched terms related to cytoskeletal organization, including "intermediate filament organization" and "keratin filament" (KRT3, KRT13, KRT78, EPPK1), and "cell periphery" (EPPK1, ARHGEF5, FBLIM1). Both serogroups showed suggestive enrichment for "immune response-regulating signaling pathway" (LILRB3, LILRA6, GP6).
Conclusion: Our findings reveal distinct, yet functionally convergent, molecular mechanisms in NMOSD pathogenesis. In AQP4-positive patients, genetic variation affecting post-translational protein modulation emerges as a key immune regulatory layer. In contrast, AQP4-negative patients harbor variants in cytoskeleton-associated genes increasingly recognized for modulating immune signaling. A functional convergence on immune response-regulating pathways is observed across both serogroups, suggesting a shared immunoregulatory axis underlying neuroimmune dysfunction in NMOSD. These results highlight the biological heterogeneity between seropositive and seronegative patients, with potential implications for therapeutic implications. Further studies are warranted to clarify the functional relevance of these molecular mechanisms.
Disclosur: All authors declare no conflicts of interest related to this study.

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P1319
Vitamin D treatment modulates the Interferon-Gamma pathway in Multiple Sclerosis

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Introduction: The inflammatory nature of Multiple Sclerosis (MS) highlights cytokine genes as key risk factors in its development. Interferon-gamma (IFN-γ) and vitamin D (VD) are two critical factors involved in MS, with IFN-γ promoting inflammation and VD playing a regulatory, potentially protective role. Emerging evidence also underscores the involvement of long non-coding RNAs (lncRNAs) in modulating the immune response and influencing the IFN-γ pathway.
Objectives/Aims: The primary aim of this study was to investigate the role of vitamin D and long non-coding RNAs, with a specific focus on NeST, in regulating the IFN-γ pathway in MS using bioinformatics analysis, cellular and animal models, as well as a pilot VD clinical trial. We sought to understand how vitamin D influences the expression of these regulatory elements and their involvement in the inflammatory processes that drive MS progression.
Methods: We administered 8 weeks of vitamin D supplementation (50,000 IU/week) to 42 patients with relapsing–remitting MS (RRMS) and 32 age- and gender-matched healthy controls. Clinical parameters, along with transcriptomic and epigenetic factors, were measured before and after supplementation. MS patients were diagnosed based on McDonald's criteria and had confirmed vitamin D deficiency (levels <20 ng/ml) prior to the trial. In addition, in silico analysis was conducted to explore the potential interactions between vitamin D-responsive elements and NeST-regulated components of the IFN-γ pathway.
Results: Our findings suggest that NeST-mediated regulation of the IFN-γ pathway plays a significant role in MS pathogenesis, particularly in the context of inflammation. Vitamin D supplementation modulated the expression of NeST and other lncRNAs associated with IFN-γ, as well as several key inflammatory molecules involved in MS progression. Vitamin D treatment reduced VD receptor expression unexpectedly. NeST Variant 1 increased, while Variant 2 decreased insignificantly. IFNG showed no major changes but differed between treated and controls. NTT increased significantly; IFNGR was unaffected. Ets-1 decreased significantly, while T-bet showed no differences. Notably, Nest expression was significantly elevated in the spinal cord of EAE mouse model compared to controls.
Conclusion: Genes and non-coding RNAs involved in the IFN-γ pathway appear to play a significant role in MS pathogenesis. Vitamin D may exert its immunomodulatory effects, in part, by influencing the expression and function of these genetic components.

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P1321
Differentially expressed miRNAs in Multiple Sclerosis patients stratified for NEDA status

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Introduction: Multiple Sclerosis (MS) is an autoimmune and neurodegenerative disease of the Central Nervous System (CNS). Multiomics is gaining increasing attention as a promising approach for studying complex diseases. In this context, microRNAs (miRNAs), small non-coding RNA molecules involved in post-transcriptional gene regulation, represent an attractive field of investigation due to their potential as diagnostic biomarkers, therapeutic targets and tools for elucidating disease-related biological pathways.
Objectives/Aims: To identify miRNAs differentially expressed according to disease activity in a population of patients with MS.
Methods: A cohort of 69 treatment-naïve patients with relapsing-remitting MS (RRMS) was recruited and sampled prior to initiation of first-line therapy. PBMCs were collected in absence of concomitant treatment and total RNA was extracted. MiRNA sequencing profiles were obtained (TruSeq® Small RNA Libraries Prep Kit). Patients were stratified based on their NEDA-3 status (No Evidence of Disease Activity – 3) at 2 years and comparison between EDA and NEDA patients was performed according to DESEq2, to identify differentially expressed miRNAs. Network analysis was performed with MiRNet tool.
Results: 15 miRNAs were found to be differentially expressed ($p < 0.05$ and FDR <0.05), 13 of which have been previously

associated with MS or with immunological pathways in the literature. According to the network analyses, hsa-miR-335-5p and hsa-miR-19a-3p were found to be the most connected miRNAs.
Conclusion: Our findings suggest the existence of miRNAs differentially expressed according to disease activity in RRMS patients. These miRNAs appear to be involved in immunological processes, potentially contributing to a better understanding of disease mechanisms and aiding in the identification of novel biomarkers. A replication phase on an independent cohort of 45 patients selected with the same inclusion criteria is currently ongoing.

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P1322
Unique Transcript Profiles of Microglia/Macrophages in Iron-Positive and Iron-Negative Chronic Active Lesions

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Introduction: Chronic active lesions (CALs) contain a dense rim of microglia/macrophages bordering demyelinated white matter (WM) lesions. A subset of CALs can be pathologically identified by an iron-enhanced microglia/macrophage rim. This iron-enhancing rim of microglia/macrophages can be detected by MRI as paramagnetic rims (PRLs). PRLs have been associated with lesion expansion and increased neurological disability. Here we present a spatial transcriptomic profile of microglia/macrophages associated with iron-positive and iron-negative CALs. Understanding specific genes and pathways altered in these cells may help design more precisely targeted therapies.
Objectives/Aims: The purpose of these studies is to compare transcript profiles of iron-positive and iron-negative CALs utilizing spatial transcriptomics.
Methods: We identified a rare tissue section which contained both Iron-positive and Iron-negative CALs. Spatial transcriptomics of microglia/macrophages from myelinated WM (NAWM), lesion rim and lesion core were performed. To validate the approach, transcript profiles were obtained from 4 adjacent sections followed by transcript and pathway analysis. The profiles of differentially expressed genes (DEGs) were utilized to build a predictive model to differentiate iron-positive and iron-negative CALs in our larger spatial transcriptomic dataset of CALs.
Results: We profiled microglia/macrophages from normal appearing white matter, iron+-positive and iron-negative lesion rims, and lesion cores. Unsupervised transcript profiles showed consistent clustering of ROIs across the 4 sections. Compared to NAWM, iron-positive DEGS were enriched for IL-12 production, while iron-negative DEGS were enriched in immune related pathways. We are investigating the utility of this approach to develop a transcript predictive model that distinguishes iron-positive and iron-negative CALs.
Conclusion: The profiles used to differentiate iron+ or iron- rims and lesions have potential to help target therapies towards more specific pathology.

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P1323
Common miRNAs between Multiple Sclerosis and EBV infection: common functions and mechanistic interactions

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Introduction: Common miRNAs between Multiple Sclerosis and EBV infection: common functions and mechanistic interactions
Objectives/Aims: EBV infection is considered as a predisposing factor of developing Multiple Sclerosis. There is rising supporting evidence of a stronger connection between two diseases through an epigenetic modulation and regulation of Multiple Sclerosis. miRNAs act as epigenetic modulation's transmitters and they are involved in both diseases. Our research's objective was to find common miRNAs and associated mechanisms between two diseases.
Methods: We deployed data from Human MicroRNA Disease Database (HMRDD, link: http://www.cuilab.cn/hmdd) searching for miRNAs associated with (1) Epstein Barr Virus infection and (2) Multiple Sclerosis. Commons found miRNAs were analyzed for annotations associated with common biological functions and transcription factors targets. We used TAM 2.0 and Enrichr enrichment analysis tools. For each trial acceptable False Discovery Rate was set up <0.05.
Results: We found 17 common miRNAs between EBV infection and Multiple Sclerosis according to data from HMRDD. TAM 2.0 analysis showed statistically significant annotations of multiple pathways associated with innate immunity's epigenetic modulation and cell cycle regulation. Transcriptional factors-targets analysis showed statistically significant annotations for

molecular pathways associated with regulation of IL4 and IL13 production. In between these common miRNAs, miRNA-146 and mi-RNA-155 seem having a more mechanistic correlation with remyelination/demyelination. One of commons found miRNAs is associated with BHRF1 gene.
Conclusion: Current study showed common miRNAs which act as a network of cell differentiation's epigenetic modulation and cytokines signaling both in Multiple Sclerosis and EBV infection. These common miRNAs could potentially showcase common pathophysiologic mechanisms which characterize the correlation between two diseases. These common miRNAs could also potentially indicate new therapeutic or prognostic biomarkers.

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P1324
Genetic Variants of Folate Metabolism and the Risk of Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) of unknown cause. Alterations in one-carbon metabolism have impact in the pathophysiology by genetic susceptibility to MS and increased the risk of MS.
Objectives/Aims: The aim of this study was to investigate the contribution of the gene polymorphism on Methylenetetrahydrofolate Reductase (*MTHFR*), Methionine Synthase Reductase (*MTRR*), Methionine Synthase *(MTR*) enzymes and of the essential factors (homocysteine, *Hcy*; cysteine, *Cys*; and vitamin B12, *VitB12*) in folate metabolism.
Methods: Eligible MS patients ($n = 147$) and health controls ($n = 127$) were participated. The gene polymorphisms were analyzed by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) and the levels of plasma *Hcy, Cys* and *Vit*B12 were measured by Enzyme Linked Immunuabsorbent Assay (ELISA).
Results: Our results showed that the levels of *Hcy* and *VitB12* were lower and the levels of *Cys* were higher in MS compared to controls.
Conclusion: The observation of high *Cys* values in all 3 gene polymorphisms suggests that the transsulfiration pathway of *Hcy* is directed towards *Cys* formation since the methionine synthesis pathway does not work. We could not find any association with all gene polymorphisms with the risk of MS. The *T* allele of *MTHFR C677T* and *G* allele of *MTR A2756G* are risk factors for serum *Cys* level on MS. As for *MTR A2756G*, serum vitB12 was observed in MS patients with *G* allele.

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P1325
Familial Multiple Sclerosis in Brazil: The Role of PRS and HLA in Disease Susceptibility

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Introduction: Multiple sclerosis (MS) is a complex autoimmune disease influenced by both genetic and environmental factors. Identifying individuals at high risk of developing MS is critical for understanding disease pathogenesis and guiding early intervention strategies. Polygenic risk score (PRS) models and HLA typing have emerged as promising tools for risk stratification. To date, no study has systematically evaluated PRS and HLA associations in Brazilian familial MS patients.
Objectives/Aims: To calculate the MS PRS and analyze HLA associations in a Brazilian cohort with familial MS, comparing affected individuals with unaffected family members and healthy controls without a history of demyelinating diseases.
Methods: Whole-genome sequencing was performed on 363 Brazilian individuals with samples stored in the Biobank of the Sociedade Beneficente Israelita Brasileira Albert Einstein (305 controls without a history of demyelinating disease, 39 familial MS patients, and 19 unaffected first-degree relatives). All available MS PRS from the PGS Catalog were computed, and the best-performing score (PGS002726) was selected for analysis. HLA typing was conducted in 168 individuals (39 familial MS patients, 19 unaffected relatives, and 111 unrelated controls).
Results: The mean PRS was significantly higher in MS patients compared to controls (MS: 0.475, SD = 0.735; Controls: -0.047, SD = 1; $p = 0.0093$). No significant difference was observed between the PRS of unaffected relatives and controls (unaffected relatives: 0.345, SD = 1.09; $p > 0.05$). The HLA-DRB1*04:01 allele was significantly more frequent in MS patients (OR 20.0; 95% CI 9.64 - 41.47; $p < 0.001$) and their relatives (OR 18.72; 95% CI 8.73 -40.1; $p < 0.001$) when compared to the general Brazilian population. However, no significant difference in HLA-DRB1*04:01 frequency was observed between MS patients and their unaffected relatives (OR 1.07; 95% CI 0.37 - 3.07; $p > 0.05$).
Conclusion: In this first study evaluating PRS in a Brazilian familial MS cohort, we demonstrated that affected individuals have significantly higher genetic risk scores compared to controls. Additionally, the HLA-DRB1*04:01 allele was more prevalent among familial MS patients and their unaffected relatives than in the general population.

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P1326
HLA association study in Brazilian Neuromyelitis Optic Spectrum disease according to AQP-4 autoantibody status

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Introduction: The complex genetic background of NMOSD has been associated with overexpression of immune-related genes, mainly the cytokine coding genes and those that coding cytokine receptors. A multi-ethnic HLA analysis including Asians, Latin Americans and Europeans, showed that NMOSD have 2.46 more chances of having the DRB1*03 allele than controls, and the main allelic association was the DRB1*03:01 in Western and DPB1*05:01 in Asians, confirming differences in African descendants. The NMOSD exome analyse identified rare inherited variants in the complement pathway and potassium channel genes, and confirmed DRB1*03 allelic association besides HLA-A*01, B*08, HLA-A*01, B*08, C*07, DQB1*02 but not with HLA:DPB1:05:01. The haplotype HLA-A*01, -B*08, and -DRB1*03 presented strong association with AQP4 seropositive NMOSD patients of European ancestry.
Objectives/Aims: Here we aimed to evaluate whether specific HLA subtypes were associated with Brazilian patients according to serostatus to AQP-4 antibody and severity outcome.
Methods: Whole-exome sequencing (WES) was performed in 29 AQP4(+) and 11 AQP4(-) NMOSD patients using the NovaSeq 6000 platform (Illumina). Raw sequencing data (FASTQ files) were processed with the HLA Explorer software for high-resolution HLA typing, aligning reads to the GRCh38 human reference genome. HLA allele calling was conducted for class I (HLA-A, HLA-B, HLA-C) and class II (HLA-DPB1, HLA-DQB1, HLA-DRB1) loci. Allelic frequencies were compared between AQP4 serostatus groups, and statistical significance was determined using Fisher's exact test ($p < 0.05$).
Results: The most frequent risk allele for AQP4 (+) status were HLA-DRB1*03:01 (13.8%) and HLA DRB1*15:01 (12.07%) and in AQP4 (-) were DRB1*15:01 (22.73%) and DRB1*03:01 (13.64%). Susceptibility of AQP4 (+) NMOSD was significantly associated with HLA-DPB1*04:01 and in AQP4 (-) with HLA-C*03:03:01. Patients AQP4 (+) showed high frequency of spinal cord involvement and a shorter time to reach higher EDSS.
Conclusion: In a cohort of Brazilian NMOSD patients divided according to serostatus for AQP4 antibody, the HLA class II alleles more frequent in both groups were not significantly associated with serological status. HLA-DRB1*0301, reported across different ethnic groups, showed high frequency association with patients AQP4 (+) at the same time that HLA-DRB1*1501 was more frequent associated with the seronegative group, suggesting that other biological pathways need to be searched for better understanding these phenotypes.

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P1327
ZFP36L1 as etiological gene in MS patients

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Introduction: The identification of the precise genes associated to the MS risk variants discovered by GWAS has proved challenging but is essential to uncover the full potential of genetic studies. The majority of these variants lie outside protein-coding genes and are enriched in enhancer regions, which are both cell-type and stimulus specific.
Objectives/Aims: This study evaluates the role of *ZFP36L1* as a putative MS etiological gene. ZFP36L1 is a zinc-finger RNA-binding protein that recognizes conserved AU-rich elements (ARE) located in 3' untranslated regions to mediate mRNA decay. Many ARE-containing transcripts have a prominent role in proliferation, metabolism, and survival in adverse conditions such as hypoxia. We aimed to ascertain the biological pathways related to *ZFP36L1* that may be perturbed in MS.
Methods: Proliferation and activity of PBMCs isolated from healthy controls and pwMS treated with anti CD20 therapies in basal and PHA-stimulated conditions, as well as the different lymphocyte subpopulations, were characterized by flow cytometry. Sera levels of EBNA1 quantified by ELISA. Mitochondrial respirometry assess by Seahorse (Agilent).
Results: The MS risk variant (rs2236262A) led to a significantly reduced *ZFP36L1* mRNA expression ($p = 0.015$) in healthy controls, but this eQTL effect was absent in PPMS, and

RRMS also showed diminished *ZFP36L1* expression. The homozygous mutant genotype showed significantly lower EBNA1 levels ($p = 0.014$), consistent with the capacity of ZFP36 RNA-binding proteins to restrain IFN-b and anti-viral immunity. The *ZFP36L1* mutant genotype promoted a significantly lower proliferation of T cells upon PHA stimulation ($p = 0.01$ and 0.05 in CD4 and CD8, respectively) in healthy controls but not in pwMS. The mutant genotype suppressed early and late activation of control lymphocytes in basal conditions, and upon PHA-stimulation showed significant increases when compared with either PPMS and RRMS patients. In controls, the allele specific differences observed in CD8 central memory in basal and stimulated conditions ($p = 0.009$ and 0.044, respectively) were not found in pwMS. Similar discrepancy manifested for CD8 effector memory. Dysfunctional mitochondria seem to cooperate in these altered T cell homeostasis.
Conclusion: Our results with the proposed MS risk allele allow the identification of *ZFP36L1* as a causal gene, with perturbed control of EBNA1 levels, T cell activity and proliferation, and mitochondrial energetic profile.

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P1328
Genetic Architecture of Progressive Multiple Sclerosis: Causal Relationships with Comorbidities and Identification of Potential Therapeutic Targets

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Introduction: Progressive MS (PMS) is recognized as being influenced by both genetic and environmental factors. While environmental factors such as viral infections have been extensively studied, few investigations have examined the genetic correlations and causations between PMS and other modifiable factors. Understanding these relationships is crucial for both early identification and effective management of PMS.
Objectives/Aims: This study aims to assess the genetic correlations and causations between PMS and 1,681 traits across diverse domains. Additionally, the genetic basis of molecular alterations during PMS was examined.
Methods: Genome-wide association studies (GWAS) summary data on PMS were obtained from the International MS Genomics Consortium. Data on other traits were acquired from the OpenGWAS Project. Linkage disequilibrium score regression (LDSC) and latent causal variable (LCV) models were employed to evaluate the genetic correlations and potential causations between PMS and other conditions. Summary-data-based Mendelian Randomization (SMR) was employed to investigate the potential influence of specific proteins on PMS, with subsequent validation performed within a longitudinal cohort.
Results: Significant genetic causality relationships were identified between PMS and inflammatory bowel disease and schizophrenia (false discovery rate [FDR] < 0.05), suggesting that both inflammatory processes and neurodegeneration contribute to the pathogenesis of PMS. Additionally, anxiety (genetic causality proportion[gcp] = -0.88, FDR = $1.99\times10\text{-}17$) and the use of certain medications including tramadol (gcp = -0.92, FDR = $2.22\times10\text{-}5$), were found to significantly affect PMS onset. Conversely, PMS demonstrated genetic effects on cognitive performance (gcp = 0.97, FDR = $9.25\times10\text{-}235$), multisite chronic pain (gcp = 0.93, FDR = $1.01\times10\text{-}50$), cholesterol (gcp = 0.72, FDR = 0.0006) and HbA1c levels (gcp = 0.65, FDR = 0.005). Through SMR analysis, we identified IL12RB1 as one of the key causal proteins influencing PMS onset. Within the longitudinal cohort, we validated that IL12RB1 protein levels were significantly associated with multiple domains of cognitive dysfunction, deep white matter hyperintensities, and subjective chronic pain.
Conclusion: Our findings suggest that anxiety and the use of certain medications may serve as early indicators preceding MS progression, while symptoms including pain and cognitive dysfunction could represent consequences of PMS. IL12 signaling represents a potential novel therapeutic target for managing the symptomatic manifestations of PMS.

Disclosure of interest: Xiaofei Wang and Hongyu Zhou: nothing to disclosure.

P1329
Cerebrospinal fluid exosomal Epstein-Barr virus microRNA BART19-3p is reduced in untreated patients with multiple sclerosis compared with treated patients and symptomatic controls

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Introduction: Recent evidence suggests Epstein-Barr virus (EBV) may be crucial for MS development. EBV encodes 44 microRNAs (miRNAs) in the BHRF1 and BART clusters, which inhibit apoptosis and regulate proliferation of infected cells. In exosomes, these miRNAs can act as cell-to-cell messengers and cross the blood-brain barrier (BBB).
Objectives/Aims: This exploratory study aimed to investigate EBV miRNAs in cerebrospinal fluid (CSF) exosomes and their association with clinical and biological markers.
Methods: EBV miRNAs were analyzed in 50 newly diagnosed patients with relapsing-remitting MS (RRMS), 24 clinically isolated syndrome (CIS) patients, 45 symptomatic controls (SC), paired samples from 15 anti-CD20-treated patients, and 24

unpaired samples from natalizumab (NTZ)-treated patients. miRNAs were profiled from CSF exosomes by quantitative PCR. Plasma anti-EBNA1 antibody and various CSF biomarkers were measured by immunoassays.
Results: Of the 44 EBV miRNAs, ebv-miR-BART13-5p and ebv-miR-BART19-3p were confidently measured in CSF exosomes. ebv-miR-BART19-3p was significantly lower in RRMS compared to SC (p=0.03), CIS (p=0.002), and NTZ-treated RRMS (p<0.0001). It correlated positively with the age-related multiple sclerosis severity (ARMSS) score in treatment-naive RRMS (p=0.02), and with disease duration in NTZ-treated RRMS (p=0.04) and anti-CD20 antibody-treated patients (p=0.02). In NTZ-treated patients, ebv-miR-BART19-3p was negatively correlated with a memory B cell and plasma-blast biomarker (p=0.04), and a tight junction marker (p=0.04). No significant correlations were found in anti-CD20-treated patients. ebv-miR-BART13-5p was only identified in a subset of individuals but was higher in CIS compared to SC (p=0.005). Anti-EBNA1 anti-body titers were higher in RRMS (p=0.0008), and NTZ-treated patients (p=0.03) compared to SC. In CIS patients, the titer correlated with markers of demyelination and inflammation.
Conclusion: The ebv-miR-BART19-3p, that is known to be associated with increased proliferation of EBV-infected cells, was higher in SC, CIS, and NTZ-treated patients compared to untreated RRMS patients. This may reflect higher intrathecal leukocyte cell counts in RRMS, resulting in fewer exosomes as they become internalized in recipient cells along with their EBV miRNA cargo. This is consistent with the observed correlations with disease duration, severity scores, and biomarkers.

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P1330
Establishing the role of ZNF638 isoforms in repair and progression

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Introduction: The recently identified MS-severity variant rs10191329 maps to a regulatory region (GH02J071448) adjacent to the ZNF638 gene. This gene is the main recruiter of the HUSH complex, which silences unintegrated viral DNA and is also an RNA-binding protein involved in the regulation of PPARG expression.
Objectives/Aims: To establish the impact of isoform-specific ZNF638 knockdown on wound-healing and transcriptome-wide expression.
Methods: Using a modified extended siRNA lipotransfection protocol, we undertook isoform-specific ZNF638 knockdown, by transfecting HEK293T cells with two siRNAs targeting different ZNF638 isoforms and negative-scrambled siRNA. RT-qPCR, Western blot, and immunofluorescence were used to assess the knockdown efficiency. The wound-healing assay was performed on three technical replicates of the four conditions: wild-type, negative-scrambled siRNA, ZNF638 siRNA-1 and -2. Three images/replicates were taken at 0 and 12 hours post-scratch and analysed in ImageJ. To explore the impact of the knockdown on the transcriptome-wide regulation expression, three independent technical replicates of RNA samples from the four conditions were sent for rRNA-depleted, deep-stranded bulk RNA-sequencing aiming for 100 million read/sample.
Results: RT-qPCR and western blotting confirmed the successful knockdown of the canonical long ZNF638 isoforms, a canonical HERVK22E-containing short ZNF638 isoform, and two novel short ZNF638 isoforms. The wound-healing assay showed that decreased expression of different ZNF638 isoforms improved cell migration and wound closure. Currently, we are waiting for the Bulk RNA-sequencing results to comprehensively establish the impact of the different ZNF638 isoforms on gene expression.
Conclusion: Decreased expression of *ZNF638* isoforms improved cell migration and wound healing. Identifying the impact of *ZNF638* isoforms knockdown on transcriptome-wide expression will hopefully pave the way towards potential neuroprotective therapies.

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P1331
Screening for Undiagnosed Genetic Immunodeficiencies in Neuroimmunologic Diseases: Pursuit of Precision in the Clinic

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Introduction: The contribution of genetic susceptibility to the onset of neuroimmunologic diseases and MS-mimics is increasingly recognized, yet accessibility, expertise, and costs related to genetic testing present significant barriers to their use in clinical practice. We have previously observed a significant burden of neurologic symptoms in people living with common variable immune deficiency (CVID). In addition, we created a database of patients seen at the University of Utah Autoimmune Neurology clinic who received targeted genetic screening, determining that this testing had an impact on patient management in about one third of cases.
Objectives/Aims: To illustrate the complexities of interpreting genetic testing results in the clinical setting, using data from our CVID cohort with mutations in the TNFRSF13B gene.
Methods: Of 994 patients analyzed in the Autoimmune Neurology Clinic during the study period, 165 (16.6%) had one or more genetic panels performed. For this study, we focused on pathogenic variants in the *TNFRSF13B* gene, and collected data on demographics, clinical course, and treatment.
Results: To date, 139 variants in *TNFRSF13B* have been reported to ClinVar as pathogenic or likely pathogenic 34 of which have been specifically associated with CVID. In our cohort, we identified two phenotypically distinct presentations of neurologic autoimmunity related to heterozygous likely pathogenic variants in the *TNFRSF13B* gene. Both patients – a female with pediatric onset glutamic acid decarboxylase-65 (GAD65) epilepsy (c.542C>A; p.Ala181Glu heterozygous), and an adult male with optic neuropathy in the context of previously undiagnosed CVID-associated granulomatous disease (c.310T>C; p.Cys104Arg heterozygous) – illustrate the challenges increasingly faced by clinicians in navigating etiologic investigations and clinical application of results for complex autoimmune neurology and neuroimmunology patients.
Conclusion: Genetic panel testing has led to diagnosis and treatment modifications in only a small number of patients in our clinics; many genetic changes identified through this testing remain of uncertain significance. It remains important, nonetheless, to pursue a genetic diagnosis in patients with suspicion for CVID-associated neurologic autoimmunity as immunomodulation presents additional risks in this under-recognized population. Increased access to genetic counseling may improve interpretation and clinically actionable application of genetic panel testing in neurology practice, but there are significant pragmatic complexities associated with bringing an emerging technology into the clinic.

Disclosure of interest: There are no disclosures pertinent to the work performed in this abstract. Each author works for the affiliated institutions. Stanley Naides works for Labcorp, owner of Invitae, where the genetic testing was performed in this study.

Pathology & Pathogenesis of MS – Experimental models

P1332
Impact of vitamin D on acute Epstein-Barr virus infection in the rabbit model: Implications for multiple sclerosis pathogenesis

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Introduction: The aetiology of multiple sclerosis is complex and not fully-known. However, genetics and several environmental factors have been implicated in disease pathogenesis. Of the environmental factors, Epstein-Barr virus (EBV) and low vitamin D levels have been implicated. Although numerous studies demonstrated that vitamin D supplementation could help to control EBV infection and diminish disease activity in MS patients, the interaction of these two risk factors remains poorly understood. One major obstacle in addressing EBV-associated questions has been the lack of a suitable animal model of EBV infection.
Objectives/Aims: The aim of this study was to investigate the impact of vitamin D on EBV infection using a novel rabbit model of EBV infection we have recently established.
Methods: The study was conducted on 39 New Zealand white rabbits, randomly divided into two major groups: vitamin D positive (VD+) and vitamin D deficient (VD-). Each group was further subdivided into EBV+ and EBV- groups. EBV+ groups received 1ml of cell culture-derived virus via the marginal ear vein of the rabbit. On day 0 of virus inoculation, VD- group was fed with vitamin D-deficient diet, and VD+ group was supplemented with vitamin D. 15 days post-infection, all the animals were euthanized. Blood and all major organs were harvested and stored for downstream analysis.
Results: Macroscopic and microscopic examination of spleen revealed substantial differences between the VD+ and VD- groups. Surprisingly, qPCR analysis on PBMCs and spleen showed a significantly higher high viral load in the VD+ group compared to VD- group. Moreover, in situ hybridization and immunohistochemistry for EBV revealed that the VD+ animals had a much more extensive infection compared to VD- animals.
Conclusion: We show, for the first time in a controlled manner, that vitamin D levels correlate positively with the EBV infection. Contrary to what has been suggested, our data indicate that elevated vitamin D levels are associated with higher viral load. There are two possible explanations. High vitamin D could dysregulate the immune system via negative feedback mechanisms. Additionally, immune dysregulation could also occur by EBV blocking VDR gene expression. Thus, resulting in enhanced

survival and higher viral load in the VD+ group. The findings from this study reflect the complex relationship between EBV and vitamin D, and further work is required to unravel the molecular mechanisms involved.

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P1333
Aquaporin-4-IgG Causes Reduction of Proliferation in Human Müller Cell Line with Microfibrillar Associated Protein 4 Expression

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Introduction: Optic neuritis (ON) is a main symptom in aquaporin-4 (AQP4) antibody-positive neuromyelitis optica spectrum disorder (NMOSD) that can impair visual function. In AQP4-NMOSD-patients, dysfunction of Müller cells, the principal glial cells in the retina, is observed. Previously, we demonstrated a decrease in levels of microfibrillar associated protein 4 (MFAP4), an extracellular matrix protein, at acute ON relapse (1), and showed that MFAP4 is expressed by Müller cells and enhances vascular leakage in the retina (2).
Objectives/Aims: The objective of this study was to investigate the expression of MFAP4 following exposure to AQP4-IgG and evaluate its potential role in NMOSD pathology.
Methods: We examined an immortalized Müller cell line from human retina (MIO-M1) using immunocytochemistry (ICC) to detect the expression of glial fibrillary acidic protein (GFAP), glutamine synthetase (GS), AQP4, and MFAP4. Cell proliferation was assessed using the WST-1 assay after 48 hours of exposure to purified IgG from an AQP4-NMOSD-ON patient combined with human complement (C). As a control, IgG from healthy blood donors combined with complement was used. To examine the effect of MFAP4 on cell proliferation, cells were seeded on MFAP4-coated wells. Additional wells were treated with anti-MFAP4. Transcriptomic changes following AQP4-IgG+C exposure, MFAP4 coating, and anti-MFAP4 treatment were analyzed using bulk RNA sequencing.
Results: Endogenous expression of GFAP, GS, AQP4, and MFAP4 was observed by ICC. After 48 hours, cell proliferation was significantly reduced (p= 0,01) in MIO-M1 exposed to AQP4-IgG+C compared to controls (IgG+C). Results for MFAP4 coating, anti-MFAP4 treatment, and bulk RNA sequencing are still under analysis.
Conclusion: MFAP4 and expression of relevant markers in Müller cell line was established. Exposure to AQP4-IgG+C resulted in a reduction of cell proliferation. The potential role of MFAP4 on Müller cell dysfunction in NMOSD, as well as the therapeutic potential of anti-MFAP4, is currently under further investigation.

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P1334
TGFB2 enhances oligodendrocyte differentiation and myelination ex vivo, but worsens EAE severity in vivo following ubiquitous TGFB2 expression via systemic gene therapy

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Introduction: Regeneration of myelin (remyelination) is a putative target for novel therapies to promote clinical recovery in MS. Previously, we identified TGFβ1 and TGFβ2 as promising remyelination-promoting targets. TGFβ1 and TGFβ2 are upregulated in remyelinated and/or active MS lesions with non-foamy microglia/macrophages, which we found to be associated with high remyelination potential *(Chen et al., Brain 2024)*.
Objectives/Aims: In this study, we tested the potential of TGFβ1 and TGFβ2 gene therapy to promote remyelination as a putative therapeutic intervention in MS.
Methods: TGFβ1 and TGFβ2 were functionally tested in *in vitro* oligodendrocyte precursor cell (OPC) monoculture using Oli-Neu cells, *ex vivo* mouse cerebellar slice cultures and in *in vivo* experimental autoimmune encephalomyelitis (EAE) model of neuroinflammation. For the Oli-Neu monoculture, recombinant TGFβ1 and TGFβ2 (0, 0.1 ng/ml, 1.0 ng/ml and 10 ng/ml) were added to differentiating OPCs after which myelin and the oligodendrocyte maturation genes Plp, Mbp and Apc were quantified using qPCR. The *ex vivo* slice cultures and *in vivo* EAE models were treated with adeno-associated viral (AAV) vectors

encoding TGFβ1 and TGFβ2 under an ubiquitous CAG promoter.
Results: First, the effect of recombinant TGFβ1 and TGFβ2 on oligodendrocyte maturation and myelination was assessed in monoculture using qPCR. For different concentration of recombinant TGFβ1 and TGFβ2, we did not observe a difference in Plp, Mbp and Apc expression compared to differentiated OPCs with vehicle. However, in *ex vivo* developing mouse cerebellar slice cultures, we found that AAV-CAG-TGFβ2 induced an increase in myelination, compared to controls. AAV-CAG-TGFβ1 did not impact myelination in the slice cultures. Together, these findings suggest that TGFβ2 enhances OPC maturation and myelination, but axon-like structures may be required in order to mature and produce myelin further. In EAE, we surprisingly observed a worse neurological score, as well as worse outcomes using the functional basso mouse scale and catwalk gait analysis, of mice treated with AAV-CAG-TGFβ2 only and/or AAV-CAG-TGFβ1 and AAV-CAG-TGFβ2 combined. AAV-CAG-TGFβ1 alone had no impact on neurological scores and functional readouts.
Conclusion: Together, these data indicate that TGFβ2 may promote oligodendrocyte maturation and myelination, but may need axon-like structures in order to do so. However, ubiquitous TGFβ2 expression is detrimental *in vivo*. Next, we will focus on CNS-specific targeting of TGFβ2 using AAV-gene therapy with CNS-specific promoters.

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P1335
Development of Cerebral Organoid-Based Model to Study Neuro-Immune Crosstalk in Human CNS Diseases

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Introduction: The increasing burden of neurodegenerative and neuroinflammatory diseases, such as multiple sclerosis (MS), highlights the need for human-specific central nervous system (CNS) models that capture the complex interactions driving demyelination and neuroimmune dysfunction.
Objectives/Aims: We aimed to develop and optimize a human induced pluripotent stem cell (hiPSC)-derived cerebral organoid (hCO) model that integrates existing strategies to replicate postnatal CNS cellular composition. We further assessed its long-term maturation, potential for modeling age-related neurodegeneration, and applicability for studying autologous neuroimmune interactions.
Methods: hCOs were generated from hiPSCs reprogrammed from peripheral blood mononuclear cells (PBMC) of two healthy donors and two MS patients using an optimized protocol. Organoid morphology was assessed via multiplex fluorescence microscopy. Co-culture conditions with autologous PBMC were optimized using live imaging. To investigate interactions between immune cells and aged hCOs, we performed Xenium spatial transcriptomics following a 24-hour co-culture with resting or polyclonally activated PBMC.
Results: Implementation of myelination-inducing steps yielded hCOs containing mature neurons, astrocytes, and myelinating oligodendrocytes by day 140. To introduce microglia, $CX3CR1^+/CD14^+$ microglia progenitors (MGPs) were co-cultured with 30–50-day-old hCOs. While MGPs attached to the hCOs and interacted with neurons, mature microglia ($TMEM119^+$ or $Iba1^+$) were not detected at three or six months post co-culture, indicating that the hCO microenvironment is insufficient for microglial maturation and maintenance. Given that vascularization supports CNS microglial colonization, we fused early-stage hCOs with vessel organoids containing $CD31^+$ vessel-like structures and $Iba1^+$ microglial cells. By day 45, fusion resulted in successful, though focal, integration of $CD31^+$ and $Iba1^+$ cells into DCX^+ neuronal tissue. To model aging, fully matured, myelinated hCOs were maintained in long-term culture (>500 days). At day 540, multiplex imaging revealed demyelination, axonal loss, and reactive astrogliosis, marked by a dense rim of $GFAP^+$ cells. At day 750, spatial transcriptomics confirmed progressive neurodegenerative signatures. Co-culture with activated autologous PBMC exacerbated these features, particularly inducing oligodendrocyte loss. Transcriptomic analysis revealed upregulation of type I interferon signaling across CNS cells, contributing to apoptosis of both oligodendrocytes and neurons.
Conclusion: This hCO model recapitulates aging and immune-driven neurodegeneration, offering a platform for studying neuro-immune interactions in CNS disorders.
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P1336
Could reduced cerebral blood flow associated with inflammation be causing hypoxia in MS?

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Introduction: We detected hypoxia in the cortex of ~33% of people with MS (Ann. Neurol. v94, 2023), and the EAE inflammation induced autoimmunity model (PLoS One v11, 2016). Reduced cerebral blood flow (CBF) has been reported in pwMS. However, the cuprizone (CPZ) model of demyelination, showed hyperoxygenation with reduced metabolic rate, and no change in CBF (Neuroimage v250, 2023).
Objectives/Aims: We hypothesize that reduced CBF may cause hypoxia and be associated with inflammation and oxidative damage. We studied hypoxia in the hippocampus of the LPS model using implanted pO2 probes. We measured hypoxia, perfusion, metabolic rate, cytochrome C oxidase redox and total cytochrome C in the cortex of EAE using MRI/NIRS.
Methods: In the LPS model, fibre optics were implanted in hippocampus 1 week before quantifying pO2 in awake freely moving mice using an Oxylite. EAE was induced with standard protocols. Controls included saline injected and CFA/PTX with no MOG. MRI was done on at 9.4T. NIRS/MRI was using 9.4 TMRI and a broadband NIRS. Perfusion was quantified with arterial spin labeling. Brains were frozen, and sections labeled with IBA1 for microglia/macrophages.
Results: Most LPS animals had baseline pO2's near 20mmHg. All (n=7) had periodic pO2 below 2xSD post induction. Both CFA/PTX and EAE showed decreased CBF ($p < 0.05$) and S_tO_2 ($p < 0.01$), increased OEF ($p < 0.01$) and no change in $CMRO_2$ compared to naïve. A high oxidation state and increased cytochrome C oxidase was observed in CFA/PTX and EAE. Iba1 staining supported microglia/macrophage related inflammation in EAE and LPS but not CFA/PTX.
Conclusion: There was hypoxia in LPS, EAE and CFA/PTX mice. The reduction of CBF in EAE, CFA/PTX and pwMS suggests abnormal blood flow regulation as a mechanism causing hypoxia. A combination of previous work on cuprizone showing demyelination with no hypoxia or reduction in CBF (Neuroimage v250, 2023), and the current work, suggest reduced CBF and changes in oxidative metabolism may relate to inflammation.

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P1337
Hippocampal Hyperexcitability in Experimental Autoimmune Encephalomyelitis (EAE): High-Density MEA Mapping for Functional and Pharmacological Profiling

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disorder characterised by neuroinflammation and demyelination, frequently accompanied by cognitive impairment. The hippocampus, essential for memory and learning, is increasingly recognised as a site of MS-related dysfunction. While behavioural and immune-related aspects of MS are well documented, the impact of neuroinflammation on hippocampal network function remains poorly understood. Experimental Autoimmune Encephalomyelitis (EAE), the most widely used animal model of MS, provides a platform to investigate such functional alterations.
Objectives/Aims: This study aimed to characterise hippocampal network excitability during EAE progression and to assess the suitability of high-density multielectrode array (HD-MEA) recordings as a platform for functional and pharmacological studies in neuroinflammatory disease models.
Methods: EAE was induced in C57BL/6 mice using a standard immunisation protocol. At defined disease stages (pre-symptomatic, peak, and remission), acute horizontal brain slices containing the hippocampus were prepared. Electrophysiological recordings were conducted *ex vivo* using a HD-MEA system with 4096 electrodes, enabling high-resolution mapping of local field potentials (LFPs) and spiking activity across hippocampal subregions (CA1, CA3, and dentate gyrus).
Results: The HD-MEA system proved highly effective for functional mapping and pharmacological assessment, revealing significant electrophysiological changes in hippocampal excitability. These alterations were responsive to pharmacological modulation, highlighting the system's utility for preclinical drug screening.
Hippocampal slices from EAE mice displayed consistent signs of hyperexcitability compared to healthy controls, including increased spontaneous activity and altered local field potential dynamics. Distinct zones of heightened excitability were identified across the hippocampus. These changes correlated with disease progression and remained detectable even during remission, suggesting a persistent disruption of hippocampal network function.
Conclusion: EAE induces sustained alterations in hippocampal excitability, likely contributing to cognitive dysfunction in MS. The HD-MEA platform offers a sensitive and high-resolution approach for assessing these electrophysiological changes and is particularly valuable for screening pharmacological compounds aimed at modulating network stability and reducing neuroinflammation. This makes it an essential tool for advancing therapeutic strategies for MS and other neuroinflammatory disorders.

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P1338
Vesicular microRNAs as Astrocytic Messengers of Neuroinflammation

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Introduction: Astrocytes are emerging as key modulators of neuroinflammation in multiple sclerosis (MS), actively shaping the CNS environment. One mechanism involves the release of extracellular vesicles (EVs) carrying microRNAs (miRNAs), which may regulate inflammation and serve as biomarkers of glial activation. Investigating the miRNA cargo of astrocyte-derived EVs offers insight into the molecular programs underlying glial responses in MS.
Objectives/Aims: To identify inflammation-induced changes in astrocyte EV miRNAs with potential as biomarkers of glial activation in MS.
Methods: Human iPSCs from a healthy donor and a relapsing-remitting MS (RRMS) patient were differentiated into astrocytes. Cells were characterized by immunofluorescence for astrocytic markers and glutamate uptake assay. Inflammatory responsiveness was confirmed by NF-κB nuclear translocation (IF) and induction of inflammatory genes (RT-qPCR) upon stimulation. Astrocytes were exposed to a pro-inflammatory cytokine cocktail (TNFα, IL-1α, C1q), and EVs were subsequently isolated from the culture medium using size-exclusion chromatography (SEC). EV-containing fractions were identified by CD63 flow cytometry and protein quantification, pooled, and further assessed for astrocytic markers by flow cytometry. Vesicular RNA was extracted, quality-checked by Bioanalyzer, and subjected to small RNA sequencing. Bioinformatic analysis identified inflammation-regulated miRNAs; candidates with consistent regulation in both lines were selected and validated by RT-qPCR in RRMS ADEVs-derived RNA.
Results: iPSC-derived astrocytes expressed canonical markers and showed functional responses to stimulation. EV-enriched fractions expressed GLAST and variable levels of GFAP, AQP4, and CD49f. Small RNA-seq identified 24 significantly regulated miRNAs in the RRMS line and 9 in the control line (adjusted $p < 0.05$). Only miR-146a-5p and miR-27a-3p were significantly upregulated in both lines; no commonly downregulated miRNAs were detected. RT-qPCR confirmed only miR-146a-5p upregulation in EVs from RRMS astrocytes ($p < 0.001$), supporting its role as a conserved astrocytic response to inflammation.
Conclusion: Astrocyte-derived EVs carry inflammation-responsive miRNAs. The consistent upregulation of miR-146a-5p in both lines suggests a conserved glial signature with potential relevance for MS.

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P1339
A Potential Role of GABAergic Immunosuppression in EAE Following High Dose Alcohol Administration

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Introduction: Multiple sclerosis (MS) is an autoimmune demyelinating disease with incompletely understood pathophysiology. While numerous environmental and lifestyle factors may influence the MS disease course, alcohol's immunomodulatory effects are particularly intriguing. Our group has previously demonstrated that low-moderate alcohol consumption (2.6% alcohol by volume (ABV)) confers anti-inflammatory effects in experimental autoimmune encephalomyelitis (EAE). We identified upregulation of $GABA_A$ receptor ($GABA_AR$) transcripts in splenic tissue, suggesting peripheral GABAergic signaling in alcohol's immune modulation. However, it remains unknown how high dose alcohol (HDA) may modulate MS-related neuroinflammation.
Objectives/Aims: Here, we sought to determine the effects of HDA in EAE and to characterize the underlying cellular mechanisms of alcohol-mediated immunomodulation.
Methods: C57Bl/6 male and female mice received a Lieber-DeCarli liquid diet containing 5% ABV alcohol or control diet for three weeks prior to EAE induction and for 42 days post-induction. We assessed the disease course via EAE clinical scoring, $GABA_AR$ expression in splenic tissue by immunohistochemistry, T-cell calcium signaling dynamics through in vitro calcium imaging of T-cells, and hepatic histopathology.

Results: HDA administration significantly attenuated EAE clinical severity in male mice compared to control-fed counterparts and alcohol-fed females. Immunohistochemical analysis revealed markedly increased GABAAR expression throughout splenic white and red pulp regions in alcohol-treated animals. Functional studies using calcium imaging demonstrated that CD3+ T-cells from wild-type mice exhibited elevated intracellular calcium following pretreatment with the GABAaR antagonist gabazine prior to CD3/CD28 application and exhibited diminished intracellular calcium following pretreatment with the GABAaR agonist muscimol prior to alcohol application. Histopathological examination revealed significant hepatocellular damage characterized by increased inflammatory infiltrates in alcohol-treated mice, indicating significant steatohepatitis.
Conclusion: Our findings demonstrate that HDA alleviates EAE symptoms through enhanced peripheral GABAAR expression in the peripheral immune system. While the associated hepatotoxicity negates any therapeutic potential of HDA, our mechanistic insights suggest that targeted GABAAR modulators could offer a promising MS immunomodulatory treatment strategy without alcohol's liver-damaging effects.

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P1340
Selective non-competitive AMPA receptor blockade in neuroinflammation

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Introduction: Changes in the glutamatergic system within the central nervous system (CNS) have been shown to influence neuronal and oligodendrocyte pathology in people with multiple sclerosis (MS). So far, studies on the role of glutamate and glutamate-related pathways in MS have focused only on the nervous system.
Objectives/Aims: Here, we discovered highly beneficial effects of the selective alpha-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA)-receptor blocker perampanel on the disease course of experimental autoimmune encephalomyelitis (EAE), the mouse model of MS. Of note, this was based on a yet undescribed non-canonical AMPA receptor-mediated signalling pathway in T cells.
Methods: Upon receptor blockade, we identified G_i-protein-coupled signalling induced CD69 expression in T cells converging on sphinogosine-1-phosphate (S1P) receptor-mediated control of T cell egress from lymph nodes. Furthermore, the inhibition of AMPA receptor reduced S1P blood levels in mice and patients.
Results: These mechanisms led to the retention of T cells in lymph nodes, resulting in reduced T cell numbers within the CNS. The combination of perampanel and S1P receptor-inhibitor fingolimod showed additive disease ameliorating effects in EAE models.
Conclusion: Our findings highlight novel targets originating from non-canonical AMPA receptor functions, opening the door for new therapeutic approaches to combat neuroinflammation.

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P1341
Assessing the Influence of In Vitro Differentiated Macrophages from MS Patient Monocytes on Cortical Network Connectivity Using a Humanized Model

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Introduction: The interplay between infiltrating innate immune cells, such as monocytes and the central nervous system (CNS)-resident cells, including microglia has been suggested as a possible trigger for MS disease progression and smoldering MS pathology. Monocytes differentiate into macrophages within the CNS and play a crucial role in the inflammatory processes that damage myelin and axons. Yet little is known about the direct effects of these cells on neuronal function in different stages of MS.
We have previously reported that Neurogenin-2 (NGN2) neurons develop patterns of functional connectivity and network topology on microelectrode array (MEA) systems which can potentially be used to study CNS disease pathology in vitro.
Objectives/Aims: Utilizing our humanized in vitro neuronal model for mechanistic evaluation of the effect of MS monocytes and macrophages on functional connectivity of cortical neurons.

Methods: We cultured healthy human induced pluripotent stem cell (iPSC)-derived NGN2 cortical neurons and primary healthy human astrocytes in vitro on MEA systems (on 6-well and 48-well, 64 and 16-electrode plates, respectively). This allowed repeated recordings of spontaneous network activity from each developing culture network. Monocytes from relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and healthy controls (n=4 per group) were retrieved and co-cultured with cortical neurons on MEA or differentiated to macrophages using Human Recombinant Macrophage Colony-Stimulating Factor (MCSF) for six days and then co-cultured with cortical neurons on MEA. Recordings were performed before and after adding monocytes or macrophages to the neuronal culture for 72 hours. The neuronal activity was analyzed using our unique network analysis pipeline.
Results: The number of active electrodes significantly increased in NGN2 cortical cultures (p=3e-7), mean firing rate (p=7e-6), and mean network burst rate (p=0.01) from days-in-vitro 14 to 35. The cortical cultures (n=35000 NGN2 cells/well) and primary astrocytes (n=12000 cells/well) were plated on MEA plates. The addition of monocytes was not toxic to the cortical neurons. We were not able to detect a significant difference in cortical activity when MS or healthy monocytes (n=150000 cells/well in 48well plate, 750000cells/well in 6well plate) were added to the cultures. In our preliminary study, we detected a suppression of neuronal connectivity by 60% in SPMS macrophages compared to RRMS (n=150000 cells/well in 48well plate).
Conclusion: We have previously reported that NGN2 neurons develop patterns of functional connectivity and network topology on MEA systems, similar to what has been seen in the brain. Our study aims to use our humanized in vitro platform to study the effect of human-derived MS monocytes/macrophages on cortical function. This model has the potential to provide both mechanistic insights and be utilized for screening developing therapeutics.

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P1342
Molecular underpinnings of choroid plexus enlargement during MS-related neuroinflammation

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Introduction: Choroid plexus (ChP) function is critical for central nervous system neuroinflammation and brain immune response during neurodegeneration. For example, in patients with multiple sclerosis (MS), recent studies described a massive ChP enlargement as a possible marker of ongoing neuroinflammation. Nevertheless, the exact basis and pathophysiology behind ChP hypertrophy remains unclear.
Objectives/Aims: We aimed to provide a mechanistic view of the ChP in a classic mouse model of inflammation, namely the experimental autoimmune encephalomyelitis (EAE), to reveal the underlying molecular characteristics of the ChP abnormalities based on proteomic analysis.
Methods: EAE was induced in C57BL6J mice. Disease severity was scored daily in a blinded fashion by two independent investigators using a scale from 0 to 5 (EAE score). Mice were scanned at the demyelination peak. ChP tissue was manually dissected for bulk RNA sequencing analyses from the lateral, third, and fourth ventricles of EAE and wild-type mice. We performed a protein-related gene search to assess protein-interaction networks.
Results: In the EAE, the peak of demyelination was reached 10–15 days after injection. MRI imaging depicted increased ChP volumes at day 16 ($t = 6.8$; $p = 0.00045$) and day 12 ($t = 3.4$; $p = 0.038$) in comparison to baseline. The transcriptomic-derived proteomic analyses from isolated ChP at the peak of disease revealed pathways closely related to mechanisms of cellular communication, function (e.g. transmembrane tyrosine receptor signalling (RTK) and vascular endothelial growth) and pathways involved in the regulation of cellular plasticity (e.g. neuron differentiation, axonal remodelling and myelin regulation).
Conclusion: We provide conclusive new evidence for the role of ChP in the context of neuroinflammation and demonstrate the existing relationship between ChP enlargement and CSF dynamics during the development of neuroinflammatory disease. Our findings highlight the possibility of new therapeutic avenues targeting RTK signalling.

Disclosure of interest: GGE: nothing to disclose related to this study

P1343
Retinal degeneration in brain-derived neurotrophic factor deficient mice

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Introduction: To date, the causes of many neurodegenerative diseases, including MS, are not fully understood, and therapies often fail to stop progression. The brain-derived neurotrophic factor (BDNF) is known to play a pivotal role in the development and maintenance of the central nervous system.
Objectives/Aims: Little is known about the impact of a BDNF deficiency in immune cells on the retina, a tissue also affected by MS. Hence, we investigated the possible effects of this deficiency in 3- and 7-month-old mice.

Methods: Wildtype C57BL/6 mice served as controls. While CLF animals had a BDNF deficiency in T-cells, macrophages, and myeloid cells, LF mice were deficient of BDNF only in myeloid cells. At 3 and 7 months of age, retinas of all groups were processed for immunohistology (n=6 eyes/group) and RT-qPCR (n=4-5 samples/group). Different retinal cell types were evaluated, namely retinal ganglion cells (RGCs), macroglia, and microglia/macrophages.
Results: Already at 3 months of age, a severe loss of RGCs was observable in CLF (48.7±3.4%; $p<0.001$) as well as LF mice (45.7±4.4; $p<0.001$) compared to controls (100.0±8.6%). While no changes in the mRNA expression of *Pou4f1* (RGCs) was notable in CLF mice, a significant downregulation was revealed in LF animals ($p=0.019$). At 7 months, the number of RGCs was also significantly decreased in CLF (63.8±3.5%; $p<0.001$) and LF retinae (58.1±6.0%; $p<0.001$) in comparison to controls (100.0±3.6). *Pou4f1* mRNA levels were downregulated in CLF ($p=0.001$) and LF mice ($p=0.003$) at this age. The $GFAP^+$ staining area was significantly larger in 3- and 7-month-old CLF and LF mice when compared to controls (all: $p<0.050$). Accordingly, the *Gfap* mRNA levels were upregulated in CLF and LF retinae at both ages (all: $p<0.010$). Interestingly, while the number of $Iba1^+$ microglia/macrophages was increased in 3-month-old CLF ($p<0.014$) and LF mice ($p<0.001$) compared to controls, no changes were observable in 7-month-old animals. Contrary, the *Iba1* mRNA expression was upregulated in both groups at both ages (all: $p<0.050$).
Conclusion: Overall, these findings indicate that BDNF deficiency in immune cells drives an early onset of RGC loss accompanied by persistent gliosis and microglial activation. The differential patterns of mRNA regulation between different time points and groups highlight the complexity of the retinal response to BDNF loss. Therapeutic strategies targeting BDNF and its receptors could help mitigate MS and other neurodegenerative diseases in the future.

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P1344
Inhibition of a cytoplasmic phospholipase-a prevents the accumulation of citrullinated myelin basic protein in multiple sclerosis myelin

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Introduction: The reasons behind white matter (WM) lesion in multiple sclerosis (MS) remains unknown. Before demyelination and autoimmune attack, citrullination of myelin basic protein (citMBP) might be involved in primary myelin destabilization, due to an aberrant Ca2+ influx emerging from an altered axon-myelinic communication and the activation of a cytoplasmic phospholipase A (cPLA2).
Objectives/Aims: To study whether citMBP is increased prior to demyelination and whether cPLA2 inhibition is able to affect, and possibly halt, this process.
Methods: In this pilot study we induced an in-vitro imbalance in axon-myelinic signal in acute post-mortem human organotypic WM slice cultures (hOSCs, n=15) via local application of the node of Ranvier Na+-channel 1.6 stimulator β-mammal scorpion toxin (Cn2, 35 nM), and measured the level of citMBP after 16 hours in presence or absence of the selective cPLA2 blocker CAY10502 (2 μM). To understand the role of destabilizing mechanisms in-vivo, we pretreated a group of mice intoxicated with the demyelinated agent cuprizone (n=12; 0.3% for 3 weeks) with the cPLA2 inhibitor ASB14780 (20 mg/kg i.p.).
Results: Cn2 application slightly increases hOSC citMBP expression compared with post-autopsy and basal measurements ($p=0.1$), while CAY10502 pretreatment overall suppressed this signal enhancement ($p<0.01$). Cuprizone intoxication elicits profound MBP hypercitrullination in the medial corpus callosum ($p<0.01$ versus controls), without affecting WM myelination ($p>0.05$). Pretreatment with ASB14780 annuls citMBP increase in the same WM tract ($p<0.01$).
Conclusion: These preliminary results suggest that MBP citrullination may partake in MS demyelination via activation of a Ca2+-dependent cPLA2. This is of importance to further investigate the in-vivo and in-vitro role of cPLA2 in MS pathogenesis in order to identify possible strategies to halt pre-lesional phases of myelin loss in this disease

Disclosure of interest: Nothing to disclose

P1345
Clostridium perfringens epsilon toxin disrupts the integrity of myelin sheaths in corpus callosum tissue in in vitro and in vivo models, reinforcing its link to multiple sclerosis

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Introduction: Epsilon toxin (ETX) is produced by *Clostridium perfringens* types B and D and can cross the blood-brain barrier (BBB) producing cytotoxic effects. In vitro models have demonstrated that ETX binds to myelin structures in mice and other species, including humans, leading to demyelination in mouse

cerebellar organotypic cultures. These findings, together with the detection of ETX antibodies in the sera of Multiple Sclerosis (MS) patients, suggest a potential link between ETX and MS. The myelin and lymphocyte (MAL) protein is currently the most accepted putative receptor.
Objectives/Aims: To investigate the role of ETX as a demyelinating agent in the corpus callosum from mice in *in vitro* and *in vivo* models.
Methods: We evaluated the time-dependent effects of ETX and pETX (non-toxic) in an acute *in vitro* model by incubating fresh adult mouse brain slices for 20 minutes, 1 hour, 2 hours, and 4 hours with 150 nM of either ETX or pETX. After each exposure period, slices were washed with PBS, fixed with 4% paraformaldehyde (PFA), and analyzed by immunohistochemistry (IHC). To investigate the demyelination process *in vivo*, mice (n=4) were intraperitoneally injected with ETX or pETX at a dose of 300 ng/kg. Injections were administered for three consecutive days, followed by a 15-day resting period. This cycle was repeated once, and in some animals, it was repeated again, resulting in exposure durations of 1, 2, or 3 months by the end of the experiment. Locomotor activity was recorded for one minute at the conclusion of the study. Mice were then anesthetized, perfused with 4% PFA, and their brains were analyzed by IHC.
Results: *In vitro* assays using the MAG antibody revealed morphological changes at the oligodendrocyte–neuron interface in specific hippocampal regions, suggesting oligodendrocyte impairment.
In vivo, locomotor tracking showed significant impairment in some ETX-injected mice compared to pETX-injected controls. IHC assays revealed a reduction in the myelin marker MAB328 in ETX-injected mice, potentially indicating a demyelinating effect of ETX on oligodendrocytes. Additionally, an increase in astrocytic and microglial markers was observed in ETX-treated mice attributable to neuroinflammation.
Conclusion: Our results demonstrate that ETX induces morphological changes in oligodendrocyte sheaths, which correlate with oligodendrocyte impairment. Moreover, locomotor tracking of ETX-injected animals was impaired compared to pETX-injected controls, and demyelinated areas were observed in the corpus callosum, further linking ETX effects to multiple sclerosis.

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P1346
Rethinking MS models: When Multiple Sclerosis Meets Schwannoma

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Introduction: MS is a central nervous system chronic autoimmune disease that leads to inflammation, axonal damage, and demyelination. It is predominantly driven by autoreactive CD4+ T lymphocytes that release cytokines such as IFN-γ and IL-6. Schwannoma is a benign tumor of peripheral nerve Schwann cells. Although the two conditions differ anatomically and mechanistically, recent hypotheses suggest that tumor antigens in schwannoma may trigger systemic immune dysregulation or paraneoplastic syndromes that breach CNS tolerance, potentially amplifying neuroinflammatory cascades involved in MS becoming a better biological model for MS instead of EAE.
Objectives/Aims: We describe the fourth case of concurrent MS and a non-operated vestibular schwannoma and explore the potential role of peripheral nerve tumors in modulating CNS-directed immune responses.
Methods: A 74-year-old woman presented to the clinic complaining of diplopia, short-term memory loss, loss of orientation in time, and signs of depression. Neurological exam, revealed red color desaturation, afferent pupillary defect, left hemiparesis, Hoffman's and Marinescu's signs, frontal release signs, hyperreflexia (DRTs: 5/4) and ataxia when performing tandem walking. MOCA score was 18/30 indicating cognitive impairment.
Results: Brain MRI revealed demyelinating frontoparietal lesions and a right vestibular schwannoma. Laboratory findings showed elevated alkaline phosphatase, CYFRA 21-1 antigen, and antinuclear antibodies with a fine speckled pattern. The patient initially declined treatment, but finally, accepted to receive corticoids, dextromethorphan, and alpha lipoic acid improving some of her symptoms.
Conclusion: The present case, of a simultaneous presentation of MS and a vestibular schwannoma supports a novel immunopathological model in which peripheral tumors might enhance central immune activation. This case challenges the conventional dichotomy between CNS and PNS pathologies, advocating for a more integrated clinical and diagnostic approach in complex neuroinflammatory syndromes.

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PATHOLOGY & PATHOGENESIS OF MS – Immunology

P1347
Identifying and characterising antigenic epitopes for developing tolerogenic dendritic cell-based therapy for multiple sclerosis

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Introduction: Identification and characterisation of autoantigens in multiple sclerosis (MS) has been challenging, but if successful, could lead to the development of autoantigen-specific tolerogenic therapies. Immune tolerance is re-established by exposing antigen presenting cells to tolerogenic stimuli with cognate autoantigens specific to the human leukocyte antigen (HLA) haplotype of people with MS. RASGRP2, a calcium- and diacylglycerol-regulated nucleotide exchange factor expressed by lymphocytes and striatal neurons, is a putative autoantigen in HLA-DRB1*15:01 (DR15)-positive individuals.
Objectives/Aims: We aimed to identify antigenic RASGRP2 epitope(s) that could be used to induce autoantigen-specific immune tolerance.
Methods: RASGRP2-derived peptides with strong, moderate and weak predicted binding affinity to DR15 were synthesised and incubated with peripheral blood mononuclear cells (PBMCs) from people with MS. Peptide presentation by cell surface HLA-DR was assessed using immunopeptidomic techniques. Changes in co-stimulatory molecule expression and cytokine secretion were assessed by flow cytometry and Fluorospot assays respectively. HLA-DR15-RASGRP2 peptide tetramers were synthesised to characterise frequency and phenotype of antigen-specific CD4+ T cells and autoantigen-specific proliferative responses.
Results: Multiple strong and moderate binding affinity RASGRP2 peptides could be presented by HLA-DR on DR15+ and DR15- patients' PBMCs. Stimulation by moderate binding affinity peptides produced the greatest increase in PBMC co-stimulatory molecule expression and pro-inflammatory cytokine secretion, particularly in DR15+ patients, but also in some DR15- patients. A novel RASGRP2 peptide eliciting the highest pro-inflammatory cytokine responses was used to synthesise HLA-DR15 tetramers. This peptide was confirmed to be a moderate binder to DR15 based on fluorescence polarisation. CD4+ T-cells specific for this peptide were four-fold higher in frequency in DR15+ patients versus controls and contained a higher proportion of pro-inflammatory T-effector cells. CD4+ T cells demonstrated increased proliferation when stimulated with the RASGRP2 peptide compared to control conditions.
Conclusion: We identified a novel immunogenic RASGRP2 peptide with relative selectivity for DR15+ people with MS, which has the potential to form the basis for autoantigen-specific tolerogenic therapy. Our approach could also be used to test other putative MS autoantigens.

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P1348
Unraveling the Interplay of Age and the Immune System in People with Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease in which immune dysregulation is a key factor. Given the increasing life expectancy of people with MS (pwMS), it is crucial to understand the impact of aging on the immune system, collectively termed immunosenescence.
Objectives/Aims: We characterized the immunosenescence process in pwMS by analyzing age-related changes in immune cell populations, thymic involution, inflammatory mediators, neurodegeneration, and telomere attrition.
Methods: Blood samples were collected from pwMS and healthy controls (HCs). The PBMCs cohort (n=110) was used to assess immune populations by flow cytometry. The DNA cohort (n=150) was used for the thymic involution study by signal joint T cell receptor excision circles (sjTREC) quantification and telomere length measurement using terminal restriction fragment (TRF) analysis. The plasma cohort (n=146) was used for inflammation and neurodegeneration analysis using automated ELISAs.
Results: The study of immunological populations with age revealed distinct correlations between pwMS and HCs in key immune populations, like B and NK cells. Moreover, pwMS exhibit a positive correlation with age in CD8 T cells expressing CD28 and CD57, along with an increase in active and senescent subpopulations in both CD8 and CD4 cells. sjTREC measurement showed the expected reduction with age and revealed that thymic involution is more pronounced in younger pwMS

compared to HCs. Furthermore, inflammaging in pwMS is marked by the positive correlation of IL-6, TNF-α, and CRP levels with age. When comparing individuals under/over 50 years, IL-6 increases with age in both groups. Besides, TNF-α is elevated in MS in people under 50 and over 50 years compared to HCs. In the case of IL-10, it is higher in pwMS, with an increase only in those over 50 years. Similarly, NFL levels are elevated in pwMS, and have a positive correlation with age in both pwMS and HCs. Notably, only in pwMS, NFL correlates with IL-6 and TNF-α. Finally, telomere attrition with age was reported in both pwMS and HCs, but no differences were found between groups.

Conclusion: Our findings reveal age-related immune changes in pwMS, including early thymic involution and an increase in senescent and CD28 Tc cells, inflammaging, neurodegeneration and telomere attrition. These results highlight the importance of considering age as a critical factor in MS clinical management and therapeutic strategies and open the door for further research.

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P1349
Viral Immune Profiles in Multiple Sclerosis and HIV Co-Infection: Insights into Antiretroviral Treatment-Induced Immunomodulation

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Introduction: Multiple sclerosis (MS) and human immunodeficiency virus (HIV) infection are both prevalent and extensively studied clinical conditions. Multiple clinical evidences suggest a potentially reduced rate of MS relapse in HIV-infected individuals. MS pathogenesis has been associated with various human herpesviruses (HHVs) and human endogenous retroviruses (HERVs). Several researchers have hypothesized that HIV infection itself and/or the antiretroviral therapy (ART) for HIV might coincidentally treat or prevent the progression of MS.

Objectives/Aims: Explores the potential immunomodulatory effects of HIV and ART on HHVs and HERVs in MS patients, providing insights into viral involvement in the pathogenesis and progression of the disease.

Methods: ELISA was employed to investigate the IgG and IgM profiles against HHVs and HERV-W in HIV-infected individuals with (n 14) and without (n 21) MS, compared to MS patients (n 21) and healthy controls (n 21). Patients with HIV and MS were further classified based on whether MS developed *prior* or after HIV infection. The HERV-W protein was also assessed by flow cytometry, through a specifically synthesized monoclonal antibody (mAb).

Results: These are the associations identified: (1) The IgG viral profiles reveled both a significant higher anti-CMV incidence in HIV (95%) and HIV/MS (100%) compared to MS patients (45%, $p < 0.01$) and HC (63%, $p < 0.02$) and a significant greater anti-EBNA1 frequency in MS (95%, $p = 0.02$) and HIV/MS (100%, $p < 0.02$) than HIV patients (67%). (2) Correlation analysis revealed a negative association between EBNA1 and HHV-6 IgG levels and the duration of HIV infection in both the HIV and HIV/MS cohorts. (3) HIV/MS patients showed a significant difference in mAb anti-HERV-W response, with lower positivity in monocytes and B/T cells in those developing MS after HIV infection. (4) Discriminant analysis identified strong discriminatory power of IgG response to CMV and EBNA1 in predicting cohort membership with an accuracy of 81% (80% for MS, 75% for HIV, and 93% for HIV/MS), identifying of unique viral profiles.

Conclusion: The viral responses detected suggest a specific profile for HIV and HIV/MS patients strongly CMV associated, differing from that of MS patients. Furthermore, chronic HIV infection and treatment with ART could induce immunomodulation that potentially alter the viral response in MS patients,

attenuating the clinical course of the autoimmune disease. Therefore, the higher prevalence of CMV associated with ART may be contributing to explain the lower rates of MS observed in HIV patients.

Disclosure of interest: All Author: nothing to disclose

P1350
Impaired AIRE-Mediated Peripheral Tolerance in Relapsing–Remitting Multiple Sclerosis: Influence of Androgens and Age

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Introduction: The autoimmune regulator (AIRE) gene is essential for central immune tolerance by promoting tissue-specific antigen expression in medullary thymic epithelial cells facilitating deletion of autoreactive T cells. AIRE may also enhance peripheral tolerance by supporting regulatory T cell (Treg) development. Recent findings indicate that AIRE is also expressed in secondary lymphoid organs and peripheral antigen-presenting cells, referred to as extrathymic AIRE-expressing cells (eTACs). Animal models showed that androgens can upregulate AIRE expression.
Objectives/Aims: To investigate the role of AIRE in immune regulation in patients with relapsing–remitting multiple sclerosis (RRMS) and its modulation by sex hormones
Methods: Sixty RRMS patients (40 female) and 60 age- and sex-matched controls were studied. Participants were stratified by age into two groups: <50 years ($n = 35$; 22 female) and $\geqslant 50$ years ($n = 25$; 16 female).Tregs and eTACs ($CD11c^{low}$ $CCR7^{+}$ $AIRE^{+}$ $ROR\gamma t^{+}$) were isolated by flow cytometry. Cytokines production was assessed by ELISA, and AIRE gene expression following hormone exposure by RT-PCR.
Results: RRMS patients had significantly fewer eTACs compared to controls ($p < 0.01$). This reduction was more pronounced in males and younger individuals than in women and older subjects ($p < 0.001$). Treg numbers were similar in RRMS and controls, but FoxP3 expression was lower in RRMS ($p < 0.01$). eTACs from RRMS patients demonstrated impaired suppressive function, as evidenced by reduced inhibition of proliferation and diminished suppression of IFN-γ and IL-17 secretion by MBP-specific T cells. Androgens significantly increased AIRE expression in eTACs, which was associated with an increase in indoleamine 2,3-dioxygenase (IDO), IL-10, and TGF-β production. By contrast, 17β-oestradiol had no effect. Circulating testosterone positively correlated with AIRE expression ($r^2 = 0.65$; $p < 0.01$).
Conclusion: AIRE-expressing eTACs contribute to immune regulation in MS. Reduced eTACs numbers and function in RRMS, especially among younger males, may impair peripheral tolerance. The androgen-mediated upregulation of AIRE may help explain the lower MS prevalence in males before andropause

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P1351
CD52 depletion enhances peripheral B cell tolerance function in a subset of MS patients

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Introduction: The anti-CD52 monoclonal antibody (mAb) alemtuzumab is highly effective in treating relapsing-remitting multiple sclerosis (RRMS) but often leads to secondary autoimmunity. Understanding its impact on B cell tolerance mechanisms is crucial for deciphering both B cell involvement in RRMS and development of secondary autoimmunity. Previous investigations indicate that between the two B cell tolerance checkpoints, only the peripheral checkpoint is dysfunctional in RRMS.
Objectives/Aims: To evaluate peripheral B cell tolerance checkpoint integrity in alemtuzumab-treated RRMS patients and healthy/disease controls.
Methods: Using an established approach, we constructed 128 recombinant mAbs from single IgM+CD27-CD19+CD10- mature naïve B cells and tested their poly- and autoreactivity. We examined mAbs from three healthy donors (HDs), three immunotherapy-naïve MS patients, and six patients treated with alemtuzumab at comparable time points post-treatment (mean ± SD 3.7 ± 0.67 years); of those, three had developed secondary autoimmunity. In parallel, we investigated BCR repertoire

parameters associated with tolerance mechanisms in the same subject groups.
Results: Polyreactivity of mAbs did not differ among subject groups. In mAb autoreactivity measurements that define peripheral checkpoint integrity, we observed that two of three immunotherapy-naïve RRMS patients had a defective peripheral checkpoint. Among patients treated with alemtuzumab, a bimodal distribution was noted: three of six patients had a high fraction of autoreactive mAbs, pointing to a defective peripheral checkpoint, and three had an autoreactive fraction significantly lower than that of HDs (P=0.027). This bimodal distribution did not align with presence of secondary autoimmunity. Further, alemtuzumab-treated patients showed lower mean naïve B cell CDR3 net charge than HDs (P=0.036), with no major differences in the other eight CDR3 properties. No differences were found in naïve B cell IGKJ1 usage frequency (a measure of the extent of secondary VJ recombination) among the three subject groups.
Conclusion: Treatment with alemtuzumab is associated with a very low frequency of autoreactive naïve B cells -pointing to a highly functional peripheral tolerance checkpoint- in a subset of patients. This could be attributed to its effect on T regulatory cells, known to influence peripheral checkpoint function, as well as to a deep depletion of B cells up to the pre-B cell stage.

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P1352
Targeting pyruvate kinase M2 (PKM2) reduces T cell pathogenicity in multiple sclerosis

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Introduction: Pyruvate kinase M2 (PKM2) is a metabolic enzyme with moonlighting functions that controls murine T cell activation and pro-inflammatory potential. Recent studies highlighted that targeting PKM2 represents a valuable therapeutic strategy in experimental models of T cell-driven inflammation. In particular, blocking PKM2 moonlighting activity in T cells limited their pro-inflammatory and pathogenic profile in a murine model of multiple sclerosis (MS). However, no study analyzed in detail the expression of PKM2 in human T cell subsets, and whether targeting PKM2 may limit the inflammatory potential of T cells from MS patients is unknown.
Objectives/Aims: In this study, we evaluated the expression of PKM2 in circulating T cells from two separate cohorts of healthy control individuals (HCs) and MS patients. In parallel, we analyzed the impact of PKM2 targeting on the inflammatory profile of HC and MS T cells.
Methods: We assessed PKM2 expression in T cells from HCs and MS patients by flow cytometry, and evaluated its potential correlation with demographics and clinical parameters associated with disease development. In parallel, we analyzed the effect of the PKM2 allosteric activator TEPP-46 on HC and MS T cell proliferation and cytokine production by flow cytometry. Additionally, cytokine levels in HC and MS T cell culture supernatants were quantified using a multiplex assay.
Results: Our data reveal that circulating effector and memory T cells express higher PKM2 levels compared to naïve T cells, and that PKM2 expression in effector and memory T cell subsets may correlate with age and disease duration in MS individuals. In particular, among effector/memory T cells, the Th17/Tc17 subsets display the highest PKM2 expression. Surprisingly, while PKM2 levels were comparable between HC and MS T cells, PKM2 targeting preferentially or exclusively inhibited interferon-gamma (IFN-γ), interleukin-5 (IL-5), IL-13 and IL-17 production by MS T cells.
Conclusion: Overall, our data suggest that PKM2 may represent a novel therapeutic target to limit T cell-driven inflammation in MS and potentially other human autoimmune diseases.

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P1353
Is Telomere Length a Marker of Immune Dysregulation and Neurodegeneration in Multiple Sclerosis?

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Introduction: Telomere length (TL) plays a key role in cellular aging and chronic inflammation. It varies across MS subtypes and is linked to disease activity and progression.
Objectives/Aims: In this study, we aimed to evaluate the effect of lecocyte telomere length (LTL) on the disease course of multiple sclerosis by comparing leukocyte telomere length in relapsing-remitting MS (RRMS) and progressive MS (PPMS) patients with healthy individuals, and to investigate the potential of telomere length as a biological marker.
Methods: Peripheral blood from healthy controls, RRMS and PPMS patients was analyzed. LTL was measured by qPCR after DNA extraction. Flow cytometry was used to assess leucocyte profile via biomarkers (CD3, CD4, CD25, CD28, CD45Ra, CD127, CD197, FoxP3). Brain volumetry was performed via 3D MPRAGE MRI in Freesurfer. Clinical, immunological, imaging, and telomere data were compared across groups.
Results: A total of 33 PPMS, 33 RRMS patients and 31 healthy controls were enrolled. Groups were similar in age and gender (p=0,4). Disease duration (years) was comparable between PPMS (11±6) and RRMS (10±6) (p=0,4). EDSS scores were significantly higher in PPMS (median 4.5) than RRMS (median 1) ($p<0.01$). All patients were on disease-modifying therapies. The most frequent leukocyte subset was $CD28^+CD4^+$ T cells. LTL showed a non-significant negative trend with age. LTL was significantly shorter in MS patients compared to controls (p=0.001), and tended to be lower in PPMS than RRMS (p=0.41). In ANCOVA including disease group as covariate, LTL was significantly shorter in patients with EDSS $\geqslant 4$ ($p<0.05$). A negative correlation was found between the percentage of $CD4^+$ Treg cells and telomere length (rho= -0.261, p = 0.001). A significant positive correlation was observed between LTL and thalamus volume (rho = 0.36, p = 0.001). Furthermore, thalamic volume was significantly higher in the control group compared to MS patients ($p<0.05$).
Conclusion: In MS, LTL was found to be associated with disease phenotype, disability status dand volumetric changes in certain brain regions. These findings suggest that telomere shortening may be considered a potential biomarker for understanding neurodegeneration and progression in MS.

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P1354
Novel mechanisms in regulatory B cells and antigen presentation in Multiple Sclerosis

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Introduction: While MS research has traditionally focused on T cells, recent evidence highlights the crucial role of B cells in both driving inflammation and mediating immune regulation. In particular, regulatory B cells (Bregs) produce anti-inflammatory cytokines such as IL-10, IL-35 and TGF-beta, suppressing T cell activity and modulating myeloid and glial responses. However, the functional heterogeneity of Bregs and their interplay with antigen-presenting cells (APCs) in MS remain poorly understood, particularly in the context of B-cell depleting therapies.
Objectives/Aims: This study aims to investigate the regulatory roles of B cells and their interactions with APCs in MS.
Methods: We analysed longitudinally collected blood samples from MS patients assigned to receive anti-CD20 therapy (rituximab or ocrelizumab), starting before treatment continuing at later time points. Age- and sex-matched healthy controls were included. Samples were stained in two advanced multicolor marker panels to assess B cells, monocytes, and dendritic cells, and analyzed using the BD FACSSymphony A3.
Results: When comparing B cell across different maturation and activation stages, as well as regulatory markers, we detected no significant alterations in untreated MS patients. However, analysis of repopulating B cells after B-cell depletion revealed striking differences. These reappearing B cells exhibited significantly higher expression of activation markers and reduced expression of regulatory markers. Additionally, they showed enhanced expression of antigen presentation markers, suggesting altered functional profile.
Moreover, circulating myeloid cells displayed significantly increased levels of major histocompatibility complex (MHC) class II and a higher frequency of pro-inflammatory cytokine-secreting cells in the absence of B cells. This indicates that blood myeloid cells gain pro-inflammatory properties when B cells are depleted, highlighting that pan-B cell depletion inadvertently eliminates pre-existing Breg-mediated regulatory functions.
Conclusion: This study provides novel insights into the dual role of B cells as both immune regulators and drivers of inflammation in MS. It reveals the impact of Bregs on APC function and establishes that B-cell depletion reshapes the immune landscape by promoting myeloid cell activation. These findings could help identify immune signatures associated with treatment efficacy and inform clinical decision-making for MS therapies.

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P1356
Exploring the relation between APOE and peripheral inflammation in MS

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Introduction: Apolipoprotein E (APOE) plays a critical role in lipid metabolism, immune modulation, and neuroinflammation—processes that are central to the pathogenesis of Multiple Sclerosis (MS). Changes in *APOE* expression and its interaction with key inflammatory and neurodegenerative pathways may reflect or influence disease mechanisms in MS.
Objectives/Aims: This study investigates *APOE* expression and its relationship with peripheral immune markers in treatment-naïve MS patients compared to healthy controls (HC), with the goal of better understanding its role in disease-related immune alterations.
Methods: RNA was extracted from blood of treatment-naïve individuals with MS (n=29) and non-inflammatory healthy controls (n=36). Gene expression was analyzed by qPCR. Cohort differences and correlations were assessed using Mann-Whitney and Spearman tests.
Results: The expression of *APOE* ($p < 0.001$) along with its major receptor *LRP-1* ($p = 0.014$) and the anti-inflammatory cytokine IL-10 ($p = 0.033$) were significantly reduced in MS compared to HC. In contrast, MS samples showed significantly increased expression of pro-inflammatory and myeloid cell markers including *NLRP3* ($p < 0.001$), *P2RY12* ($p = 0.044$), *RIPK1* ($p < 0.001$), *IL-6* ($p = 0.028$), and *TREM2* ($p < 0.001$). In relapsing-remitting MS (RRMS), subgroup analysis revealed a significant decrease of *APOE* ($p < 0.001$), *LRP-1* ($p = 0.014$), and *IL-10* ($p = 0.018$), while *IL-6* expression was increased ($p = 0.024$) when compared to HC. In progressive MS (PMS) gene expression of *RELA* and TNFα was significantly lower ($p = 0.04$ and $p = 0.034$) and *P2RY12* was higher relatively to HC ($p = 0.021$).
Furthermore, *APOE* expression negatively correlated with that of inflammatory markers in HC: *RELA* ($p = 0.001$), *IL-1B* ($p = 0.023$), *RIPK1* ($p < 0.001$), and *RIPK3* ($p = 0.001$). *TNF*α showed a consistent negative correlation in both HC ($p = 0.006$) and MS ($p = 0.003$). *APOE* positively correlated with *IL-10* in both groups (HC: $p < 0.001$; MS: $p < 0.001$). Unique to MS, positive correlations were observed in *NLRP3* ($p = 0.001$), *BTK* ($p = 0.012$), and *P2RY12* ($p = 0.001$). Moreover, in a subgroup analysis *APOE* positively correlated with *IL-6* in RRMS ($p = 0.002$).
Additional analysis of age at onset in our MS cohort revealed positive correlations for several markers, including *TLR4* (p =

0.011), *RELA* (p = 0.015), *BTK* (p = 0.020), *LRP-1* (p = 0.004), and *MMP9* (p = 0.047).
Conclusion: Our data show reduced *APOE* expression in the periphery of MS, accompanied by distinct changes in inflammatory markers. Differential correlations between *APOE* and immune markers in MS and HC suggest a shift in the regulatory role of *APOE* under disease conditions. These findings implicate a potential role of *APOE* in the pathophysiology and disease course of MS and therefore underscores its relevance as a candidate biomarker and therapeutic target.

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P1357
Immune profiles in Multiple Sclerosis: Kappa free light chain index correlates with CXCL 13

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Introduction: Whether the complex cytokine network nor its interplay with established biomarkers like κ-Free Light Chain (κ-FLC) index or neurofilament light chain (NfL) is yet not fully understood in Multiple Sclerosis (MS).
Objectives/Aims: To investigate whether cytokines, chemokines and related proteins correlate with κ-FLC index or NfL Z score in two independent cohorts.
Methods: In two independent cohorts of newly diagnosed MS patients 65 cytokines, chemokines, and related molecules as well as κ-free light chain (κ-FLC) index and NfL Z scores were measured. Cytokines were quantified by multiplex bead-based immunoassays, κ-FLC by nephelometry and NfL by by single-molecule array technique. κ-FLC index was calculated as (CSF κ-FLC/serum κ-FLC)/albumin quotient, NfL Z scores by using age- and body-mass-index adjusted reference data.
Results: Eighty-two (cohort I: 38, cohort II: 44), predominantly female (68% / 64%) patients were included. Clinical, radiological and routine laboratory baseline and follow-up characteristics did not differ significantly between the cohorts. In cohort I, κ-FLC index correlated with 5 serum molecules, 12 CSF molecules and 9 CSF/ serum ratios, NfL Z score with 3 serum molecules. Only the correlation between CSF BLC/CXCL 13 and κ-FLC index was validated in cohort II. Cytokine, chemokine and related molecule concentrations differed significantly between cohort I and II in >50% of all analytes, logarithmic ratio of reference values and medians revealed a strong correlation (σ=0.503, $p<0.001$).
Conclusion: Evaluation of cytokine networks in neuroinflammation is hampered by a high complexity and limited reproducibility of measurements. Nevertheless, BLC/CXCL 13 robustly correlates with κ-FLC index further substantiating its potential as a biomarker in neuroinflammatory disorders.

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P1359

The Prognostic Role of Type 2 and Type 3 Oligoclonal Bands in Multiple Sclerosis: AFive-Year Clinical Outcome Comparison

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Introduction: Oligoclonal bands (OCBs) in the cerebrospinal fluid are key biomarkers in multiple sclerosis (MS), reflecting intrathecal immunoglobulin synthesis. Although their diagnostic utility is well established, the prognostic significance of different OCB patterns—particularly Type 2 and Type 3—remains unclear. While both patterns indicate central nervous system immune activation, it is uncertain whether they differ in their association with long-term clinical outcomes. This study aimed to compare the five-year clinical trajectories of patients with Type 2 versus Type 3 OCBs, focusing on disability progression, relapse activity, and conversion to secondary-progressive MS (SPMS).

Objectives/Aims: This study aimed to investigate whether different oligoclonal band (OCB) patterns—specifically Type 2 and Type 3—are associated with distinct long-term clinical trajectories in patients with multiple sclerosis. By comparing five-year outcomes related to disability progression, relapse activity, and conversion to secondary-progressive MS (SPMS), the study sought to determine the potential prognostic relevance of OCB subtypes beyond their established diagnostic role.

Methods: This cross-sectional study evaluated the five-year clinical outcomes of MS patients with either Type 2 or Type 3 OCB positivity. Demographic and clinical parameters—including age at onset, sex, Expanded Disability Status Scale (EDSS) scores, annualized relapse rate, and conversion to secondary-progressive MS—were analyzed at two distinct time points: year two and year five following diagnosis.

Results: The study included a total of 1,270 patients, with 1,090 patients positive for Type 2 OCBs and 180 patients positive for Type 3 OCBs. At year two, patients with Type 3 OCBs exhibited significantly lower mean EDSS scores compared to those with Type 2 OCBs, suggesting a milder early disease course. However, by year five, the EDSS scores had increased in both groups, and the difference between them was no longer statistically significant. There were no notable differences between the groups in terms of relapse rates or conversion to SPMS during the five-year follow-up.

Conclusion: Type 3 OCB positivity appears to be associated with lower disability in the early stages of MS; however, this

benefit does not persist in the long term. By year five, disability progression, relapse rates, and conversion to SPMS were similar between Type 2 and Type 3 OCB groups. These findings suggest that OCB subtype alone may have limited prognostic value when assessed with standard clinical measures.

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P1360
Dynamic Relationship Between CSF Immune Cells and Tissue Damage Markers in Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is characterized by immune-mediated demyelination and neurodegeneration. While cerebrospinal fluid (CSF) biomarkers can track tissue damage, the relationship between immune cell populations and tissue damage markers remains poorly understood.
Objectives/Aims: This study aims to characterize the relationships between CSF cell populations and tissue damage biomarkers in multiple sclerosis, with particular focus on how these associations vary with disease subtype and activity state.
Methods: We performed comprehensive immunophenotyping of CSF samples from 63 participants (29 relapsing-remitting MS [RRMS], 7 primary progressive MS [PPMS], 27 patients with other suspected neurological diseases [OND]). CSF levels of neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) were measured using single molecule array technology. Relationships between immune cell populations and biomarkers were assessed using partial correlation and multiple regression analyses, adjusting for age and sex.
Results: RRMS patients exhibited expanded lymphocyte populations compared to OND, with elevated CD3+ T cells (+5,062 cells/mL, $p<0.0001$) and CD19+ B cells (+180 cells/mL, $p<0.0001$). Patients with MS showed an age-related shift in monocyte subsets, marked by increased CD14+CD16+ cells (r_{SP} =0.670, [95% CI: 0.44-0.81], p=0.0029). During active relapse, naive CD4+ T cells demonstrated the strongest association with NfL (cumulative geometric mean ratio=2.892 [95% CI: 1.352-6.188], $p<0.0001$), contrasting with non-relapse states (GMR=0.689 [95% CI: 0.449-1.057], p=0.101).
Conclusion: This study identifies distinct immunological signatures in MS and demonstrates disease activity-dependent associations between specific immune cell populations and tissue damage markers. The relationship between classical monocytes and GFAP in controls suggests a previously unrecognized role for myeloid cells in physiological CNS homeostasis.

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P1361
Serum Inflammatory Protein Levels in Untreated Relapsing-Remitting Multiple Sclerosis Patients as Potential Biomarkers for Disease Diagnosis and Prognosis

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Introduction: Reliable blood-based biomarkers for multiple sclerosis (MS) diagnosis and prognosis remain limited.

Objectives/Aims: To quantify a broad panel of serum protein biomarkers in MS patients and healthy donors (HD) using a sensitive proteomic immunoassay, and to evaluate their association with demographic, clinical, and radiological features.
Methods: A cross-sectional study was conducted in 352 untreated relapsing-remitting MS patients and 86 HD. Clinical (e.g., EDSS) and radiological (e.g., T2 and gadolinium (Gd)-enhanced magnetic resonance imaging lesions) parameters were assessed. Forty-five inflammatory proteins were measured in serum using the Olink Target 48 cytokine panel (proximity extension assay).
Results: Levels of oxidized low-density lipoprotein receptor 1 (OLR1) (p=1.5E-5), protransforming growth factor alpha (TGFA) (p=1.3E-7), interleukin 2 (IL-2) (p=1.6E-6), IL-1b (p=3.7E-7), and oncostatin-M (OSM) (p=2.8E-4) were significantly elevated in MS compared to HD, while thymic stromal lymphopoietin (TSLP) levels were higher in HD (p=5.1E-6). OSM strongly correlated with OLR1 (r=0.779), TGFA (0.776) and IL-1b (r=0.566); similarly, OLR1 and TGFA also correlated (r=0.624).
Regarding the association with different outcomes of the disease: a) Demographic: After grouping HD and MS patients based on their age (<29 or >44 years old), we observed higher IL-15 levels in the youngest group of HD (p=1E-3); whereas among MS, C-C motif chemokine 11 (CCL11), CCL13 and interstitial collagenase (MMP1) levels were elevated among the oldest group (p= 1.7E-5, p=4.5E-4 and p=5.6E-4 respectively). Female MS patients showed higher levels of Granulocyte colony-stimulating factor (CSF3) and fms-related tyrosine kinase 3 ligand (FLT3LG) than males (p=4.2E-5 and p=3.8E-4). b) Clinical: In MS patients older than 44 years old, EDSS positively correlated with C-X-C motif chemokine 8 (CXCL8) (r=0.312), CXCL11 (r=0.302) and CCL7 (r=0.330). c) Radiological: We did not observed any association of the levels of the analyzed proteins with the presence of Gd-enhancing lesions; however T2 lesion counts correlated with: OLR1 (r: 0.303), IL-1b (r:0.335), CCL3 (r:0.393), CXCL8 (r: 415), EGF (pro-epidermal growth factor) (r:505) and OSM (r: 0.303).
Conclusion: Specific serum proteins are altered in MS and associate with clinical and radiological parameters. Further studies are warranted to study their role in MS pathology and their potential as biomarkers for the diagnosis and/or prognosis of MS disease, and therapeutic targeting.

Disclosure of interest: All authors: nothing to disclose

P1362
Cerebrospinal fluid single-cell cellular transcriptome, proteomic profile and intercellular communication inference suggest dysfunctional SPP1 pathway underlying disability progression in multiple sclerosis

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Introduction: Progression independent of relapse activity (PIRA) in MS is one of the major determinants of disability accumulation. We performed single-cell RNA sequencing (scRNA-seq) to characterize the cellular compartment of cerebrospinal fluid (CSF) in relation to presence of PIRA, along with a complementary proteomic approach.
Objectives/Aims: To identify molecular correlates of PIRA by comparing CSF transcriptome of patients with and without PIRA, infer differential cell-cell communication, and correlate scRNA-seq findings with protein analysis of paired samples.
Methods: Eight patients with PIRA, 9 without PIRA and 1 control with NMOSD were included for transcriptomic and paired proteomic analysis. All patients were clinically stable, free from MRI activity and not on therapy in the last 6 months. PIRA was defined as confirmed EDSS progression independent of relapse activity. ScRNA-seq libraries were prepared with 10X Genomics platform. Cell types were annotated and visualized in a UMAP. Differentially expressed genes, enrichment analysis and cell-cell communication were analyzed among cell groups. CSF levels of 69 inflammatory molecules were evaluated with Multiplex technology in paired CSF samples.
Results: Within CSF monocytes/macrophages, two subclusters were increased in patients with PIRA: the first showed a microglia-like phenotype with upregulation of genes like TREM2, APOE, SPARC; the second had a similar gene pattern but with higher expression of HLA-DRA and HLADPB1. Both subclusters had high expression of SPP1 gene, which was significantly upregulated in the PIRA group. Gene ontology analysis of upregulated genes in microglia-like cells in PIRA yielded terms including positive regulation of immune response, cell-cell adhesion, and regulation of lymphocyte activation. Communication strength analysis between cells identified enrichment of SPP1-pathway in patients with PIRA. Comparing communication probabilities, SPP1 signaling between the abovementioned myeloid subclusters and CD4 T central memory cells was typical of PIRA. SPP1 protein levels correlated with its higher gene expression in paired samples from the scRNA-seq cohort.
Conclusion: Our data suggests myeloid cells dysregulation, in particular of microglia-like cells, in the CSF of patients with PIRA. The SPP1 pathway appeared to be involved in mediating PIRA as reflected by cell-cell communication and proteomic analysis.

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P1363
Cytomegalovirus is linked to T cell senescence and to disease course in multiple sclerosis

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Introduction: MS is an immune-mediated disease in which age strongly determines disease course and clinical response to disease-modifying treatment (DMT). However, the interplay of immune ageing and MS disease course remains largely unexplored.
Objectives/Aims: To investigate the associations between immunosenescence and disease course in a cohort of persons with MS (pwMS), in relation to infection with cytomegalovirus (CMV) and DMT.
Methods: Patients from the Swiss Multiple Sclerosis Cohort (SMSC) study at the University Hospital Basel, Switzerland, were prospectively enrolled. 229 pwMS were included in the study. 88 patients (37%) had positive CMV status. Patients were undergoing the following treatments: 39 untreated, 88 B cell depletion therapy (BCDT), 36 dimethyl fumarate (DMF) and 66 fingolimod. Blood T cell subsets were functionally and phenotypically characterized using multiparameter flow cytometry. Plasma concentrations of anti-CMV IgG, and inflammatory molecules MCP-1, MMP-1, and GDF-15 were measured. Cross-sectional analyses were performed using the Mann-Whitney-U test, Kruskal-Wallis test, Fisher's exact test, and bivariate and partial nonparametric correlations.
Results: We describe CMV-related and age-related T cell profiles in all treatment groups. JAK-STAT pathway functionality in naïve T cells differs and differentially correlates with neurofilament light chain (NfL) serum levels based on CMV status. In DMF-treated patients, a differential association between T cell senescence and disease activity is seen based on CMV status.
Conclusion: CMV is a main driver of T cell senescence in pwMS, independent of DMT. CMV modulates the relationships between blood T cell immunosenescence and MS disease course.

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P1364
Immune-checkpoint expression in multiple sclerosis regarding the presence of infections and disease progression

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Introduction: Immune checkpoint molecules play a crucial role in regulating immune activation. Multiple sclerosis is a demyelinating disease of the central nervous system where the immune system plays a crucial pathogenic role, involving both B lymphocytes (BL) and T lymphocytes (TL).
Objectives/Aims: The aim of this study is to explore the expression of immune-checkpoints of patients with relapsing-remitting multiple sclerosis (MSRR) and their relationship with the occurrence of infections and disease progression.
Methods: We conducted a prospective study of 118 RRMS patients, assessing immune checkpoint expression before and three months after treatment using spectral flow cytometry to analyze the expression of 16 stimulatory and inhibitory molecules across 22 immune cell subpopulations.
Results: The average age of the sample was 42.82 years, with 59.7% women. Nearly half (49.2%) of the patients developed infections, mainly viral (64.4%).
In patients with recurrent infections, significant immune dysregulation was observed: memory B cells showed elevated CD70 ($p=0.02$) and PD-L1 ($p=0.008$), while helper T cells had reduced PD1 ($p=0.008$) and altered OX40 ($p=0.03$). Regulatory T cells displayed lower CD70 ($p=0.02$) and decreased CD28 ($p=0.02$) and OX40 ($p=0.01$) at 3 months, alongside reduced CTLA in naive regulatory T cells ($p=0.003$). Monocytes exhibited elevated CD40 ($p=0.01$), while NK bright cells had lower CD70 ($p=0.01$) and NK dim cells showed increased BTLA ($p=0.01$) and PD1 ($p=0.003$). Disease progression (6.7% of patients) correlated with reduced B cells ($p=0.043$), memory B cells ($p=0.035$), and CTLA expression in memory B cells ($p=0.015$) and plasma cells ($p=0.029$), alongside elevated monocyte CD40 ($p=0.01$). Notably, 87.5% of progressive cases had concurrent infections, with infection onset linked to progression ($p=0.031$)
Conclusion: Different patterns of immune checkpoint expression, both at baseline and at 3 months after treatment initiation, have been identified in patients with disease progression and concurrent infections. The presence of infections in patients with RRMS seems to be associated with disease progression. These biomarkers offer promising tools for risk stratification and monitoring disease progression to improve patient outcomes.

Disclosure of interest: Alicia Garcia Leal: nothing to disclose

P1365
Biomarkers of gut barrier function in multiple sclerosis patients receiving oral disease modifying therapies

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Introduction: A link between gut barrier dysfunction and MS pathophysiology has been proposed. Alterations of zonulin and intestinal fatty acid-binding protein (I-FABP), respectively biomarkers of intestinal permeability and enterocyte damage, have been associated with MS disease activity and blood-brain barrier integrity.
Objectives/Aims: This study aims to evaluate longitudinally serum concentrations of zonulin and I-FABP in MS patients receiving oral disease-modifying therapies (DMTs) and to assess their potential role in disease monitoring, as well as their relationship with demographic, lifestyle, and anthropometric variables.
Methods: Serum samples were collected from 24 MS patients undergoing oral DMT (7 males and 16 females) including 5 treated with teriflunomide and 19 with dimethyl fumarate. Zonulin and I-FABP were measured at baseline (T0), before treatment initiation, and after 3 (T1) and 6 months (T2). Sex, age, smoking status, and body max index (BMI) were also considered as variables.
Results: In the overall population, I-FABP serum levels increased significantly over time (T1 Vs T0, $p = 0.022$; T2 Vs T0, $p = 0.020$) while Zonulin levels showed no significant changes. Stratification according to smoking habit revealed a significant increase in I-FABP levels among ever smokers at T1 ($p = 0.016$) and T2 ($p=0.041$), while zonulin increased significantly at T2 ($p=0.039$). Disaggregating our population by sex, there was a significant increase in I-FABP levels at T1 ($p=0.021$) and T2 ($p=0.020$) in women. Using a cut-off of 40 years, it was shown that in subjects $\leqslant$40 years, I-FABP levels increased significantly compared to baseline at T2 ($p = 0.021$), while the increase in I-FABP was not statistically significant in subjects $>$40 years. A significant increase at T2 in zonulin ($p = 0.030$) and at T1 in I-FABP ($p = 0.044$) were observed in subjects with a BMI$<$25. In patients with BMI $\geqslant$25, zonulin showed no significant changes over time. However, I-FABP increased significantly at T2 ($p = 0.028$). No correlation was found between the levels of the two molecules at any time point.
Conclusion: This longitudinal study on MS patients receiving oral DMTs suggests that while zonulin levels remained essentially stable, changes in other intestinal integrity markers, particularly I-FABP, may occur over time and vary based on individual characteristics such as smoking status, sex, age, and BMI. Further studies are needed to better understand the clinical implications of these findings.

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P1366
Understanding MOGAD pathogenesis: Does MOG have an immunoregulatory effect on microglia?

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Introduction: MOG antibody disease (MOGAD) is the commonest cause of demyelination in children, but its pathophysiology is not well understood. Myelin oligodendrocyte glycoprotein (MOG) is expressed on all mammalian CNS myelin yet its function is unknown. MOG interacts with receptor 'DC-SIGN' on dendritic cells, increasing immunoregulatory cytokine IL-10 release when toll-like receptor 4 is co-stimulated with lipopolysaccharide (LPS) (García-Vallejo JJ et al., 2014). Dendritic cells are not abundant in the CNS, but DC-SIGN is also found on microglia, the resident macrophage of the brain. Microglia are implicated in both MOGAD and MS pathology. Further understanding the MOG-microglia interaction is important for MOGAD, and also other demyelinating diseases, such as MS, where loss of MOG may contribute to both acute inflammation as well as smouldering inflammation in chronic lesions.
Objectives/Aims: To investigate whether (1) myelin, via a MOG-DCSIGN interaction, may have a homeostatic immunoregulatory effect on microglia, and whether (2) disrupting this interaction (either due to autoantibodies against MOG, or loss of MOG by demyelination) increases microglial inflammation.
Methods: We assessed microglial phagocytosis and morphology in 3 forebrain hypomyelinated Myrf knockout mice and 3 control mice, to assess of the impact of hypomyelination. We used a human iPSc-derived neuron-microglia co-culture system to stimulate microglia with myelin and MOG, and quantified IL-10 release by ELISA.
Results: Microglia phagocytose MOG in the control mouse and this is reduced in the hypomyelinated mouse (total microglia n=6, mean volumes 50.3 vs 11.9 respectively, $p<0.05$). Microglia in the hypomyelinated mice were larger and more ramified (n=15, mean sum filament length 498μm; mean sum scholl intersections 291) compared with control mice (n=15, mean sum filament length 324μm, mean sum Scholl intersections 193); $p<0.05$). Microglial IL-10 release is synergistically increased by co-stimulation with human myelin and LPS (711pg/ml), and with MOG and LPS (637pg/ml), compared with LPS alone (400pg/ml), MOG alone (8.7pg/ml) or myelin alone (0.4pg/ml) in our preliminary experiments.
Conclusion: The absence of myelin changes microglial structure, which may indicate a change in function. Microglia increase IL-10 secretion, both in response to myelin, and also MOG specifically, when co-stimulated with LPS. These results suggest

that MOG may be important for immune regulation in the setting of inflammation. This finding is important for understanding the role of microglia in all diseases where MOG is lost as a consequence of demyelination, including MOGAD and MS.

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P1367
VSIG4 Expression on Mononuclear Phagocytes in Cerebrospinal Fluid of Patients with Relapsing-Remitting Multiple Sclerosis

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Introduction: Mononuclear phagocytes, including monocytes, macrophages, and microglia, have pro-inflammatory and immunoregulatory functions in the central nervous system (CNS). V-set and immunoglobulin domain-containing protein 4 (VSIG4) is a complement receptor with immunomodulatory properties restricted to tissue-resident macrophages, but its expression in the central nervous system and role in multiple sclerosis (MS) remains elusive.
Objectives/Aims: To investigate VSIG4 expression on mononuclear phagocytes in cerebrospinal fluid (CSF) and peripheral blood, and to evaluate whether soluble VSIG4 (sVSIG4) in CSF reflects innate immune activation in MS.
Methods: VSIG4 expression on peripheral blood monocytes was analysed in 36 untreated patients with relapsing-remitting MS (RRMS), 31 patients treated with anti-CD20 therapy, 22 symptomatic controls (SCs), 9 with non-inflammatory neurological disorders (NINDs), and 26 healthy controls. In CSF, VSIG4 expression on mononuclear phagocytes and sVSIG4 levels were analysed in 19 untreated patients, 18 anti-CD20-treated patients, 12 SCs, and 4 NINDs using flow cytometry and ELISA. Monocyte-derived macrophages from 2 healthy individuals were stimulated in vitro with cell-free CSF from 12 untreated patients, 12 anti-CD20-treated patients, and 12 SCs to assess VSIG4 expression by flow cytometry.
Results: VSIG4 expression was minimal on blood monocytes, and present on CSF mononuclear phagocytes with significantly higher frequencies on the $CD16^-$ subset than on the $CD16^-$ subset across all groups. sVSIG4 was detectable in all CSF samples but concentrations did not differ between groups or correlate with surface VSIG4 expression. In vitro, stimulation with cell-free CSF markedly induced VSIG4 expression on monocyte-derived macrophages, regardless of CSF origin.
Conclusion: VSIG4 is expressed on CSF mononuclear phagocytes, particularly on the $CD16^-$ subset. Its expression appears to be influenced by the local CSF microenvironment but is not altered in RRMS or by anti-CD20 therapy.

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P1368
A potential role of Epstein-Barr Virus in modulating complement system proteins and compromising Blood-Brain Barrier integrity in Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is a multifactorial chronic inflammatory disease characterized by the autoimmune destruction of myelinated axons in the central nervous system (CNS), with a highly unpredictable course. Its pathogenesis is complex, and the complement system is believed to play a crucial role. In particular, senescent microglia and activated astrocytes have been shown to produce complement proteins such as C1q, C3a, Factor B, and C4, whose increased expression has been observed in MS patients. Epstein-Barr Virus (EBV), strongly implicated in MS, may interact with this innate immune system, although its precise role remains unclear.
Objectives/Aims: To investigate the role of EBV in the dysregulation of complement protein production by microglia and astrocytes, and to evaluate its effect on the integrity of the blood-brain barrier (BBB) using an Organ-On-Chip model.
Methods: Primary healthy microglia and astrocyte cell lines were co-cultured with EBV-positive lymphoblastoid cell lines derived from healthy individuals (LCL-B95.8-HD) and MS patients (LCL-B95.8-MS), as well as with an EBV-negative control cell line (BJAB). The expression of complement proteins (C1q, C3a, Factor B, and C4) was evaluated via qPCR and Western Blot, while their secretion was assessed through ELISA assays. Lipopolysaccharide (LPS) stimulation was used as a control to induce complement protein expression. A brain-chip model (Emulate Organ-On-Chip) was then developed to study BBB functionality and permeability after incorporation of EBV-positive or EBV-negative cell lines, by analyzing the diffusion of fluorescent molecules of different molecular weights.
Results: Co-culture with LCL-B95.8 cell lines (from both healthy donors and MS patients) led to a significant increase in C4 and Factor B expression compared to the BJAB cell line, indicating that EBV infection may contribute to aberrant complement protein production. Ongoing Organ-On-Chip experiments aim to determine whether EBV-infected cells, particularly

those from MS patients, are more capable of compromising BBB integrity than EBV-negative cells.
Conclusion: Preliminary results suggest that EBV may contribute to MS development and progression by acting on CNS-resident cells and causing dysregulation of complement protein production. This dysregulation could impair BBB integrity and exacerbate the neuroinflammation characteristic of MS.

Disclosure of interest: Martina Chiacchiarini: nothing to disclose.

P1369
Distribution of circulating lymphocyte subsets in MS: from disease specificity to progression

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Introduction: Besides for differences in antibody specificity, central nervous system (CNS) demyelinating autoimmune diseases may be classified by B cells that differently behave and interact with other lymphocytes inside and/or outside the CNS.
Objectives/Aims: To study whether this has potential as a disease-specific cellular hallmark, we assessed the distribution of B-cell versus other lymphocyte subsets in the blood from people with different types of CNS demyelinating autoimmune diseases.
Methods: We assessed the presence and features of circulating lymphocyte subsets from treatment-naive MS, MOGAD/NMOSD, autoimmune encephalitis and matched healthy control groups using spectral flow cytometry.
Results: In contrast to autoimmune encephalitis, B-cell frequencies were significantly elevated in both the MS and NMOSD/MOGAD groups compared with age-matched healthy control and autoimmune encephalitis groups. CD4+/CD8+ T-cell ratios were only higher in people with MS. Focusing on B-cell subsets, T-bet and CXCR3 as markers of CNS homing and interaction with CD4+ T cells were especially downregulated on B cells from people with progressive MS. The latter was not influenced by age and corresponded to less antibody-secreting cell outgrowth under CD4+ T cell-dependent in vitro conditions. Moreover, people with progressive MS showed lower frequencies of circulating ASCs, and memory B cells from these people were less capable of differentiating into ASCs under T helper cell-dependent conditions compared to the relapsing subgroup.
Conclusion: These findings show that a relative increase of circulating B cells and CD4+ T cells is characteristic for MS and suggest that the enhanced CNS-homing potential of the CXCR3+ memory B-cell subset is associated with MS disease progression.

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P1370
Macrophage-to-Mesenchymal Transition (Macro-MT) in Multiple Sclerosis: Transcriptional Reprogramming and Proinflammatory Myeloid Cell Phenotypic Shifts

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Introduction: Myeloid cells are pivotal players in the pathogenesis of multiple sclerosis (MS), yet the extent to which peripheral monocytes are transcriptionally and functionally altered upon entering the central nervous system (CNS) remains unclear.
Objectives/Aims: This study investigates transcriptional and functional alterations in myeloid cells from paired samples of cerebrospinal fluid (CSF) and peripheral blood (PB) in MS.
Methods: $CD14^{+}CD11c^{+}$ myeloid cells were isolated from CSF and PB of MS patients (n=6) and disease controls (n=3). Bulk

RNA sequencing (Smart-seq2) was performed to identify differentially expressed genes. Flow cytometry assessed microglial markers (TMEM119, P2RY12) in CSF. Monocyte-derived microglia-like cells (MDMi) were cultured with IL-34 and GM-CSF for 14 days to evaluate morphology and cytokine profiles (healthy controls: n=9; MS: n=15).
Results: In MS, CSF-derived $CD14^{+}CD11c^{+}$ cells showed upregulation of microglial related genes such as relevant transcription-factors MAFB and SPI1 (PU.1), and genes involved in immune activation (C1QA, HLA-DRB5, SPARC), while homeostatic genes (P2RY12, MERTK, ARHGAP15) were downregulated. Pathway analysis revealed alterations in extracellular matrix organization and epithelial-to-mesenchymal transition in both CSF and PB. Flow cytometry analysis revealed the downregulation of two-hallmark homeostatic microglial markers, TMEM119 and P2RY12 in CSF myeloid cells from MS patients versus controls (p=0.0258; p=0.0696, respectively). Unstimulated MDMi from MS patients had more branch junctions (p=0.0017), triple points (p=0.0145), greater branch length (p=0.02), and more total branches per cell (p=0.0087) compared to controls. These cells secreted higher baseline levels of TARC/CCL17 (p=0.0084), IL-6 (p=0.049), and IP-10/CXCL10 (p=0.0184), and less IL-4 (p=0.0287).
Conclusion: Myeloid cells in MS patients undergo significant transcriptional and functional reprogramming, characterized by a shift toward a pro-inflammatory phenotype. The observed phenotypic and transcriptional alterations suggest that Macro-MT may drive neuroinflammation in MS. These findings provide valuable insights into potential therapeutic strategies for targeting myeloid cell plasticity in MS.

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P1372
The relationship between oligoclonal band status and serum viral antibodies with cerebrospinal fluid viral load in newly diagnosed multiple sclerosis

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Introduction: Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system characterized by inflammatory and autoimmune processes. Oligoclonal bands (OCBs) in cerebrospinal fluid are among the most specific biomarkers supporting MS diagnosis. However, the relationship

between OCB status and systemic immune markers, including viral serologies and autoantibodies, remains unclear.
Objectives/Aims: This study aimed to investigate the relationship between oligoclonal band (OCB) status and IgG index value in cerebrospinal fluid (CSF) and serum viral antibodies with CSF viral load in newly diagnosed MS.
Methods: Two hundred-sixty one newly diagnosed MS patients were included in the study and evaluated retrospectively in between December 2022 and March 2024. Serum IgM-IgG antibodies for Epstein-Barr virus (EBV), herpes simplex virus (HSV) 1-2, cytomegalovirus (CMV), and varicella-zoster virus (VZV) were assessed at the time of diagnosis, additionally, PCR analysis was performed in CSF to detect these viruses. Serum antinuclear antibody (ANA) levels were also recorded. The relationship between the CSF OCB status and IgG index value and serum viral antibodies and presence of CSF viral PCR, as well as the correlation of these parameters with age, gender, first attack clinic, lesion location and number on MRI were examined.
Results: 86.2% of the patients were OCB positive, with 87.1% classified as Type 2 and 12.9% as Type 3. Serum EBV VCA and EBNA IgG, HSV1, HSV2, CMV, VZV IgG antibodies were positive at a frequency of 80/82 (%97.6), 59/76 (%77.6), 6/76 (%7.9), 46/47 (%97.9) and 91/93 (%97.8), while serum IgM antibodies were negative in all cases. All CSF PCR results were negative. There was no significant relationship between CSF OCB positivity and type, increased IgG index, and all serum viral IgG positivity ($p>0.05$). However, serum ANA positivity was significantly higher in OCB-positive patients (32.6%) compared to OCB-negative patients (11.1%) ($p=0.035$), suggesting a potential involvement of both central and peripheral immune activation in MS pathogenesis.
Conclusion: In newly diagnosed MS patients, no significant association was found between OCB positivity, serum viral antibodies, or CSF viral load. However, the higher ANA positivity in OCB-positive patients suggests a possible link between systemic autoimmune processes and MS pathogenesis. Further research is needed to clarify the immunological mechanisms underlying these findings and their potential implications for MS diagnosis and management.

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P1373
EBV Modified Extracellular Vesicles in people with MS

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Introduction: EBV can lay dormant in latent form following primary infection. Whilst the underlying cause of MS is undetermined, EBV has been strongly associated with MS pathogenesis. Extracellular Vesicles (EVs) are lipid bilayer delimited particles that play a role in cell-cell communication and are important for normal functioning of the immune system. They carry cargo such as virally derived miRNA and proteins. We set out to investigate whether EBV modified (EVs) can shed light on pathological pathways underpinning MS.
Objectives/Aims: To examine Extracellular Vesicles (EVs) from people with MS (pwMS) and matched controls with a focus on Epstein Barr Virus (EBV) serostatus, in order to determine potential differences in EBV derived proteins and miRNA between groups.
Methods: We have recruited participants with MS (pwMS) from Barts Health NHS Trust and age and sex matched 1:1 controls from the surrounding area. Blood samples were taken at a single time point to obtain plasma for downstream analysis. EVs were isolated using ExoSpin size exclusion chromatography kits and concentrated further using Amicon® 10kDa filters. To compare size and concentration of EVs between pwMS vs controls, EVs were characterised using Nanosight NS300 and Spherical morphology of isolated EV were confirmed by Transmission Electron Microscopy. EBV serostatus was determined using EBV VCA (viral capsid antigen) IgG ELISAs.
Results: To date we have recruited 45 pwMS (Median age= 43, IQR= 17) and 46 controls (Median age= 40, IQR= 22). Of the 45 pwMS, 36 (80%) were female and 9 (20%) were male with a median BMI of 27.025 kg/m^2, IQR=9.8. Of the 45 pwMS, 36.3% were on no disease modifying therapy at the time of recruitment, 4.54% had previously received Alemtuzumab, and 6.6% Cladribine. Current DMTs were 45.45% Natalizumab, 4.45% Dimethyl Fumarate and 2.22% Copaxone. Most, 93.3%, had RRMS (relapsing remitting MS) and 6.6% had converted to SPMS (secondary progressive MS).
Results from the NTA showed that EVs were slightly smaller in size (96.1 vs. 127.5 nm) in PwMS compared to controls, with similar concentrations (5.08 x 10^10 vs. 5.56 x 10^10 particle/mL). VCA IgG antibodies were measured in diluted plasma samples. VCA EBV seropositivity was similar between groups, with 43 (100%) pwMS testing positive for VCA EBV IgG antibody vs 41 (89%) controls.
Conclusion: Future Plans: We are going to further characterise EV with ExoELISA (CD63) kits and determine EV origin through flow cytometry MACSPlex Kit. We will determine the presence of EBV specific proteins within EVs and explore any differences in pwMS vs controls. We will explore the presence of EBV miRNA using sensitive digital PCR on EVs and examine if this differs to controls.

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P1374
Breaking inflammatory cycles: cladribine targets pathogenic B cell subsets in Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disease in which B cells play a centralpathogenic role by presenting autoantigens and secreting proinflammatory cytokines. Cladribine, an oral purine analog, shows durable efficacy in MS and is hypothesized to actvia selective depletion of pathogenic B-cell subsets.
Objectives/Aims: Here, we aimed to characterize cladribine's selective effects on peripheral B-cell subsets inMS. In a longitudinal cohort of 40 relapsing MS patients, we used multicolor flow cytometryto track the frequencies of B-cell subsets (transitional, naive, classical memory, marginalzone-like (MZ-like) memory, and double-negative (DN) memory B cells) over 36 months ofcladribine treatment. We also assessed B-cell cytokine production and measured serumneurofilament light chain (NfL) as a biomarker of neuroaxonal damage.
Methods: Peripheral immune cells were profiled by flow cytometry immunophenotyping. Serum neurofilament light chain (sNfL) was quantified by SIMOA (Quanterix). B-cell cytokine production was evaluated by multicolor flow cytometric intracellular staining.
Results: Cladribine induced rapid depletion of circulating B cells followed by differential reconstitution: transitional and naive B cells predominated early, whereas memory B cells (classical, MZ-like, and DN) were nearly absent. Memory reconstitution was uneven: DN memory B cells re-emerged partially by 2–3 years and classical memory B cells recovered only minimally, whereas MZ-like B cells remained profoundly depleted long-term. MZ-like Bcells were uniquely proinflammatory and polyfunctional, producing granulocyte- macrophage colony-stimulating factor (GM-CSF), interleukin-6 (IL-6), and tumor necrosis factor α (TNFα) simultaneously, and expressing high levels of the lipid antigen-presenting molecules CD1c and CD1d. During sustained MZ-like B-cell depletion, serum NfL levels decreased and remained low, indicating reduced axonal damage.
Conclusion: Long-lasting depletion of proinflammatory MZ-like B cells may underlie cladribine's durableefficacy in MS. Notably, cladribine was originally developed for hairy cell leukemia (HCL), aB-cell malignancy, and its efficacy in MS may reflect the shared immunophenotype betweenHCL cells and MZ-like or DN memory B cells. The work has been partially supported by Merck.

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P1375
MicroRNA-142-3p carried by extracellular vesicles from regulatory T cells marks disease severity in relapsing-remitting multiple sclerosis

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Introduction: Starting in the late 20th century, extracellular vesicles (EVs) (lipid bilayer particles able to transfer their molecular cargo) have gained significant attention for their role in cellular communication and are now recognized for their involvement in key processes such as immune responses. Recent studies have shown that regulatory T cells (Treg), involved in the control of immunological self-tolerance, utilize EVs to regulate immune responses, potentially contributing to the pathogenesis of autoimmune conditions such as multiple sclerosis (MS). However, the mechanisms by which Treg-EVs exert their suppressive functions and the potential pathogenic role of EVs in autoimmunity remain largely unexplored.
Objectives/Aims: To investigate the dysregulated molecular phenotype and function of T_{reg}-EVs from pwRR-MS and their correlation with clinical disability.
Methods: Treg cells from HDs and pwRRMS were isolated by magnetic cell separation from the blood of either healthy controls or treatment-naïve MS subjects and cultured in vitro; EVs were purified by precipitation followed by size exclusion chromatography (SEC) and tested in vitro in proliferation assays, by flow cytometry. EV-associated microRNAs were extracted and quantified by qRT-PCR.
Results: Human Treg-EVs have been demonstrated to exert a significant and selective inhibitory effect on
$CD4^+$ T cell proliferation *in vitro* and are enriched in microRNAs, with miR-142-3p being of particular interest. Here we found that Treg-EVs from people with relapsing remitting multiple sclerosis (pwRR-MS) contained lower amounts of miR-142-3p and were functionally dysregulated as compared to healthy donors (HDs), as evidenced by their inability to dampen TCR-stimulated $CD4^+$ T cell proliferation and activation *in vitro*. Moreover, we found that the shuttling of miR-142-3p by Treg-EVs inversely correlated with EDSS and with the number of brain gadolinium-enhancing lesions, thus revealing a direct association between the miR-142-3p shuttling capability of Treg cells and inflammatory activity in patients' brains.
Conclusion: Our results identified an important pathophysiological role for the miR-142-3p shuttled by Treg cells *via* EVs in the pathogenesis of MS. Indeed, pwRR-MS displayed a reduced capacity to shuttle miR-142-3p as compared to HDs and this miRNA showed an inverse correlation with MS disease severity, thus suggests its potential as a biomarker for monitoring disease activity.

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P1376
The synergic effects of natural-nano- drug formolation and stem cells on cytokines balances and immune cells of multiple sclerosis in secondary progressive patients

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune condition that targets the central nervous system, often leading to inflammation and immune system imbalances. In the effort to maintain immune tolerance and control autoimmunity, regulatory T cells (Tregs) and cytokines with immunomodulatory roles are crucial. Among various natural compounds, silymarin—especially in its nano-form—has emerged as a potential candidate for supporting immune regulation.
Objectives/Aims: This study aimed to investigate the impact of nano-silymarin on Treg cell proliferation and cytokine gene expression in a co-culture system consisting of adipose-derived mesenchymal stem cells (AD-MSCs) and PBMCs obtained from MS patients.
Methods: Stem cells were isolated from adipose tissue samples of female patients diagnosed with Secondary Progressive MS. After expansion in culture, the cells were co-cultured with PBMCs and exposed to nano-formulation at concentrations of 1, 2.5, 5, and 10 μM for a 24-hour period. Flow cytometry was used to determine the frequency of Treg cells characterized by the $CD4^+$ $CD25^+$ $CD127^+$ $FOXP3^+$ phenotype. In addition, mRNA expression of cytokines including IL-4, IL-10, TGF-β, FOXP3, IL-6, and IL-17 was quantified using real-time PCR techniques.
Results: Nano-formulation significantly enhanced Treg cell frequency at low doses (1 and 2.5 μM), with maximal expansion observed at 1 μM. Expression levels of anti-inflammatory cytokines (IL-4, IL-10, TGF-β, FOXP3) were markedly increased in nano-formulation-treated groups, while pro-inflammatory cytokines (IL-6, IL-17) were significantly downregulated compared to untreated controls.
Conclusion: Low concentrations of nano-formulation effectively promote Treg expansion and shift cytokine profiles toward an anti-inflammatory state. These findings suggest that nano-formulation may serve as a promising adjunct to stem cell-based therapies for immune regulation in MS

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P1377
Virus antibody responses in patients with MOGAD

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an antibody mediated inflammatory disorder of the central nervous system, characterized by demyelination targeting the optic nerve, brain and spinal cord.
Objectives/Aims: The etiology of MOGAD still remains to be determined. We performed a retrospective study comparing virus antibody levels in sera of MOGAD patients to relapsing-remitting multiple sclerosis (RRMS) patients. Additionally, cerebrospinal fluid analyses to Epstein-Barr virus (EBV) antigens were determined in MOGAD patients and compared to RRMS patients, as EBV plays a central role in the development of MS.
Methods: We enrolled 19 patients with MOGAD and 30 patients with RRMS referred to the Department of Neurology at Rigshospitalet. Moreover, 15 healthy controls (HCs) were included. Patients and HCs were matched according to age and gender when possible. Virus antibody levels to EBV, HHV6, JCV and CMV were measured by enzyme-linked immunosorbent assay.
Results: No differences in virus antibody levels to HHV6, CMV and JCV were observed between MOGAD patients and HCs. Similarly, no significant differences in antibody levels to HHV6, CMV and JCV were found for MOGAD patients and RRMS patients. However, RRMS patients presented with significantly increased EBV EBNA1 IgG levels compared to MOGAD patients and HCs.
Conclusion: Our findings suggest that development of MOGAD not is associated with neither HHV6, CMV nor JCV. Furthermore, results presented describe that EBV serology is different in MOGAD patients compared to RRMS, suggesting that the etiology of MOGAD is different from RRMS.

Disclosure of interest: The authors have nothing to disclose

P1378
Anti-Neurofascin 155, 186, and 140 Antibodies and Their Association with Clinical Subtypes of Multiple Sclerosis: A Prospective, Real-World, Multicenter Study

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Introduction: Anti-neurofascin antibodies (ANFA) have been reported in people with Multiple Sclerosis (PwMS). In this study, we investigated the association between ANFA positivity and different clinical subtypes of MS
Objectives/Aims: To evaluate anti-neurofascin antibodies targeting neurofascin isoforms 155, 186, and 140 in individuals with multiple sclerosis (MS) and correlate their presence with MS subtypes.
Methods: In this multi-centre prospective study, we tested ANFA155, ANFA186, and ANFA140 in a cohort of MS patients who met the McDonald 2017 criteria. Anti-neurofascin antibodies (ANFA) targeting neurofascin 155, 186, and 140 were measured using a competitive ELISA technique. Descriptive statistics were performed using Microsoft Excel, while comparative statistical analyses were conducted using Jamovi software.
Results: During the 17-month period (November 2023 to March 2024), we tested ANFA in 84 patients with multiple sclerosis (MS). Of these, 63 patients (75%) tested positive for at least one anti-neurofascin antibody, and 15 (17.86%) were positive for two antibodies. Isolated ANFA140 was detected in 29 patients (34.52%), isolated ANFA186 in 14 (16.67%), and isolated ANFA155 in 3 (3.57%). Combined ANFA186/140 positivity was found in 14 patients (16.67%), while combined ANFA155/140 was observed in 1 patient (1.19%). Among the ANFA155-positive patients, all three had relapsing-remitting MS (RRMS). In the ANFA186-positive group, 15 patients (93.75%) had RRMS, and 1 (6.25%) had secondary progressive MS (SPMS). Among those positive for ANFA140, 21 patients (72.41%) had RRMS, 6 (20.69%) had SPMS, and 2 (6.90%) had primary progressive MS (PPMS). Although the proportion of patients with progressive MS was higher in the ANFA140-positive cohort, the difference was not statistically significant when compared to other ANFA-positive groups. NF140 titers were significantly higher in progressive MS (671.38 ± 193.39 ng/mL) than in RRMS (439.81 ± 163.32 ng/mL; $p = 0.007$).
Conclusion: Anti-neurofascin 140 and 186 antibodies are detected in a high proportion of Indian patients with multiple sclerosis. The proportion of patients with progressive MS appears higher in the ANFA140-positive cohort. Higher ANFA titers were also observed in patients with progressive MS. These observations warrant validation through larger, multicentre studies.

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P1379
Influence of oral and skin microbiota on Multiple Sclerosis risk and severity: a Mendelian Randomization analysis

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Introduction: Recent research on the impact of gut microbiota on multiple sclerosis (MS) has been extensive; however, the role of microbial composition across several other key interfaces, such as the mouth and the skin, has received much less attention. To address this gap, we used Mendelian Randomization (MR) analyses, using genetic variants as proxies for environmental exposures to estimate the causal relationship between a risk factor and an outcome.
Objectives/Aims: Here we performed a two-sample MR analysis to assess the causal link between oral and skin microbiome composition and both MS risk and severity. We aimed to explore the influence of dysbiosis from other body sites on MS, moving beyond the gut, and to investigate its impact not only on susceptibility but also on disease course.
Methods: Exposure data were extracted from summary statistics of two large genome-wide association studies (GWAS) assessing the influence of host genetics on the microbiome composition of the oral cavity and of the skin. Outcome data were extracted from summary statistics of the 2019 GWAS on MS susceptibility and of the 2023 GWAS on MS severity. We applied inverse-variance-weighted (IVW) and Wald's ratio as primary MR methods, but also MR Egger to control for horizontal pleiotropy, and checked directionality through the Steiger's test.
Results: We found that the relative abundance of *Veillonella* genus in the skin enhanced MS risk, while no significant association between oral composition and MS susceptibility was highlighted. Furthermore, we found the *Gammaproteobacteria* class in the skin associated with MS severity, while we caught protective signals from different oral microbial strains (*Veillonella dispar* species, *Porphyromonas* genus, *Bacilli* class, and *Proteobacteria* phylum).
Conclusion: Our findings suggest the implication of skin microbiota on MS risk and of both oral and skin microbial composition on disease severity, reinforcing the relevance of dysbiosis in disease etiopathogenesis and broadening our insights beyond the gut. Exploring the influence of host-environmental interactions on susceptibility and disease course may inform the development of novel preventive and therapeutic strategies.

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P1380
EBV detection in saliva of MS patients across different treatments and in relapses

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Introduction: The Epstein-Barr virus (EBV) has been strongly implicated in MS pathogenesis, appearing to be a necessary condition for disease development. However, little is known about its contribution to the course of the disease, particularly regarding a possible relation between EBV reactivations and MS relapses.
Objectives/Aims: This study aims to assess the association between EBV detection in saliva and disease activity in patients with Relapsing-Remitting Multiple Sclerosis (RRMS), while also investigating whether different treatments influence viral detection.
Methods: Patients diagnosed with RRMS, in relapse and remission, were recruited between May2024 and February 2025. Saliva samples were collected from all participants, and EBV DNA detection was performed using commercial real-time PCR (EBV Real-Quant, SACACE). Statistical analyses included contingency tables and Fisher's exact test to compare EBV detection between groups, as well as logistic regression models to assess associations with clinical and demographic variables.
Results: We collected samples from 136 patients (including 19 in relapse). EBV was detected in the saliva of 32.4% of participants. However, no significant association was found between virus detection and MS activity ($p = 0.608$) or between EBV presence and the use of disease-modifying treatment (DMT) ($p = 0.417$). Despite this, certain treatments, particularly anti-CD20 monoclonal antibodies, appeared to influence viral presence.
Conclusion: No significant association was found between EBV reactivation and MS clinical activity. However, due to the scarcity of similar studies, further research is essential to explore

the potential relation between EBV reactivation and disease progression, as well as the impact of different therapies on its expression. Longitudinal studies and use of other sources of genetic material (blood, CSF) may provide a deeper understanding of this potential pathophysiological mechanism.

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P1381
Environmental Risk Factors in Familial vs Non-Familial Multiple Sclerosis: A Comparative Case-ControlStudy

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Introduction: MS arises from a complex interplay of genetic and environmental factors. The distinct environmental risk profiles between familial (FMS) and non-familial multiple sclerosis (NFMS) remain poorly characterized.
Objectives/Aims: To identify and compare environmental RFs in FMS and NFMS patients.
Methods: We conducted a population-based case-control study in Sina MS research center, Tehran, Iran during 2022-2024 including 460 participants across four groups: FMS patients (n=113), their unaffected relatives (n=147), NFMS patients (n=100), and healthy controls (n=100). Data were collected via structured questionnaires assessing demographics, lifestyle, previous infections, supplements, stress level and sun exposure. Adjusted odds ratios (AORs) were calculated using multivariate logistic regression.
Results: Shared risk factors included Vitamin D supplementation, it showed consistent protection (FMS: AOR=0.28,95%CI=0.13-0.59; NFMS:0.39,0.20-0.76) as did sun exposure during adolescence in winters (FMS: AOR=0.74, 95%CI=0.61-0.89; NFMS: AOR=0.73, 95%CI=0.59-0.90).FMS-specific factors included Stressful life events which increased FMS risk (AOR=1.89,1.05-3.40) while marriage was protective (AOR=0.37, 95%CI=0.16-0.82). Antibiotic effects varied temporally (recent use: AOR=2.96,1.29-6.80; chronic use:0.45,0.21-0.97).NFMS-specific factors included smoking (AOR=2.75, 95%CI=1.24-6.10) and vitamin C (AOR=0.39, 95%CI=0.19-0.79).Divergent factors were Iron supplementation, as they increased FMS risk (2.41, 95%CI=1.07-5.41) but protected against NFMS (AOR=0.30, 95%CI=0.13-0.67). Alcohol showed inverse associations (beer: FMS= AOR=0.32, 95%CI=0.13-0.77; NFMS= AOR=4.50, 95%CI=1.85-10.94).
Conclusion: Environmental RFs differentially influence FMS and NFMS, with shared (vitamin D), divergent (iron, alcohol use), and unique (antibiotic usage, vitamin C) associations. These findings underscore the need for tailored prevention strategies and further research into gene-environment interactions.

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P1382
Association between the presence of heavy metals in Biological Fluids and Multiple Sclerosis in North-Western Sardinia: A Pilot Study

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Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative disease of the central nervous system with a multifactorial etiology. Recent studies suggest that environmental exposure to heavy metals may contribute to the onset and progression of the disease. Notably, the northwestern region of Sardinia - characterized by both a high MS prevalence and significant environmental pollution - provides an ideal setting to investigate potential associations between heavy metal contamination and MS.
Objectives/Aims: This pilot study represents the first step of a broader research project aimed at exploring the interactions between heavy metals and epigenetic regulation, as well as their influence on cellular metabolic and molecular pathways, and how these factors may act as cofactors in the pathogenesis of MS.
Methods: Forty-four MS patients residing in the same geographical area were enrolled. Clinical data - including disease course, duration, and disability level - were collected. Serum and urinary concentrations of heavy metals and antioxidants were measured using inductively coupled plasma mass spectrometry (ICP-MS). Statistical analyses were performed to identify potential associations.
Results: Preliminary findings indicate that cadmium (Cd) and lead (Pb) concentrations are significantly higher in MS patients compared to the general population ($p < 0.05$). Elevated levels of these metals were also associated with more severe disease progression.
Conclusion: These data suggest that exposure to heavy metals may influence the clinical course of MS, underscoring the need for environmental pollution monitoring in high-risk areas. Further studies are warranted to confirm these findings and to elucidate the underlying biological mechanisms.

Disclosure of interest: All authors: nothing to disclose.

P1383
Alcohol Administration and Fecal Microbiota Transplantation Ameliorates EAE and Shifts Gut Microbiome and Metabolome in a Sex-Specific Pattern

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Introduction: Alcohol is widely consumed among multiple sclerosis (MS) patients, yet research on its effects, particularly in modulating MS neuroinflammation, remains limited. A potential link between alcohol and MS is the gut microbiome and its associated metabolites, such as Volatile organic compounds (VOCs). Our previous studies in Experimental Autoimmune Encephalomyelitis (EAE) have shown that low/moderate alcohol dose administration shifts gut microbial networks in a sex-specific pattern and ameliorates neuroinflammation in males; however, it remains unknown whether alcohol's beneficial effects on EAE are directly mediated via the gut microbiome and metabolome.
Objectives/Aims: Evaluate the efficacy of Fecal Microbiota Transplantation (FMT) from alcohol-drinking to alcohol-naïve mice in mediating EAE neuroinflammation.
Methods: Male and female C57BL/6J donor mice were fed a 2.6% alcohol by volume (ABV) Lieber-DeCarli diet or isocaloric control diet for 3 weeks. Recipients were administered non-alcoholic Lieber-DeCarli control diet containing antibiotics to ablate gut microbiota, followed by sex-matched FMT prior to myelin oligodendrocyte glycoprotein $(MOG)_{35-55}$ EAE induction. Weight and clinical scores were assessed daily from Day 7 to 42 post-EAE induction. Fecal samples were collected for 16S rRNA sequencing and VOCs analysis.
Results: FMT from alcohol-fed donors ameliorates EAE in a sex-specific pattern similarly to direct alcohol administration. Males receiving FMT from alcohol-fed males showed significantly greater EAE disease remission compared to other groups. 16S rRNA sequencing analysis revealed sex differences in gut microbiome composition at Day 42 post-EAE. Specifically, alcohol FMT female recipients displayed increased levels of *Bacteroidota, Verrucomicrobiota, Akkermansia, Firmicutes* CAG:41 and *Prevotella* sp. CAG:485, whereas alcohol FMT male recipients displayed increased levels of *Actinobacteriota, Firmicutes_A, Proteobacteria, Terrisporobacte*r, *Clostridium* and *Niameybacter*. VOCs differed significantly among alcohol FMT recipients, with females exhibiting higher levels of acetone compared to males, a metabolite known for its proinflammatory activity.
Conclusion: In this study, using FMT from low/moderate alcohol-drinking mice to alcohol-naïve mice, we demonstrate that alcohol can directly modulate gut microbiome and metabolome in a sex-specific pattern, contributing to EAE disease amelioration.

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P1384
Cold Stress Attenuates Experimental Autoimmune Encephalomyelitis Severity via Endothelial Semaphorin 6D Regulation of Sympathetic Innervation: Implications for MS Pathophysiology

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Introduction: MS is a temperature-sensitive disorder, as evidenced by Uhthoff's phenomenon, whereby elevated body temperature worsens symptoms. Cooling therapies have shown symptomatic benefits in some patients with MS, yet the underlying mechanisms are poorly understood. Cold exposure activates the sympathetic nervous system, which may impact MS pathophysiology. In an experimental autoimmune encephalomyelitis (EAE) model, the principal animal model of MS, cold exposure reprogrammes bone marrow immune cells, though peripheral responses remain underexplored.
Objectives/Aims: This study examines how cold exposure ameliorates EAE severity, focusing on the cold-activated sympathetic nervous system and the role of semaphorin 6D (Sema6D), an axon guidance molecule.
Methods: To assess immune responses under cold exposure, mice were housed at room temperature (22°C) or exposed to cold (10°C). MS-like autoimmunity was modelled by inducing EAE using myelin oligodendrocyte glycoprotein in wild-type and Sema6D-deficient (*Sema6d*$^{-/-}$) mice with global or conditional deletion. Disease progression, central nervous system (CNS) pathology, and peripheral immune responses were evaluated via immunophenotyping and histology
Results: At room temperature, EAE progression was similar in wild-type and *Sema6d*$^{-/-}$ mice. However, cold exposure attenuated disease severity in *Sema6d*$^{-/-}$ mice, with reduced CNS inflammation and demyelination. This effect was replicated in endothelial-cell-specific *Sema6d*$^{-/-}$ (*Sema6d*Δ^{VEcad}) mice but not in neuron- or microglia-specific knockouts. Mechanistically, cold-exposed *Sema6d*Δ^{VEcad} EAE mice exhibited reduced T cell responses in lymph nodes, with CD4^{+} T cell adoptive transfer experiments confirming that endothelial Sema6D is essential for proper T cell priming. Anatomically, *Sema6d*Δ^{VEcad} mice displayed a normal retinal vascular network but abnormally increased perivascular sympathetic innervation in lymph nodes, accompanied by elevated local norepinephrine levels, enhanced tissue hypoxia and cellular stress under cold exposure. Notably, chemical peripheral sympathectomy reversed the cold-mediated protection in *Sema6d*Δ^{VEcad} mice, confirming the causative role of sympathetic innervation.
Conclusion: Endothelial Sema6D regulates sympathetic nerve distribution in lymphoid organs, ensuring immune competence under cold stress. This regulatory mechanism indicates how cold-induced sympathetic activation influences autoimmunity through neuroimmune signalling, revealing a temperature-dependent checkpoint in immune regulation. Our findings demonstrate how environmental factors shape neural-immune interactions to modulate autoimmunity, suggesting Sema6D-mediated sympathetic-immune interactions as a potential target for MS therapy.

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P1385
Investigation of EBNA2-regulated genes in multiple sclerosis in blood and CNS tissue

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Introduction: We identified a specific allele of the Epstein-Barr nuclear antigen 2 (EBNA2) linked to multiple sclerosis (MS). The 1.2 EBNA2 allele significantly downregulates the CD40 gene, associated with MS, and disrupts other genes related to B cell activation and antigen presentation in lymphoblastoid cell lines carrying this allele.
Objectives/Aims: Our aim was to study the role of MS-associated EBNA2 variants in peripheral blood and CNS of people with MS and controls
Methods: We used a digital droplet PCR approach (QX200, Bio-Rad) to assess gene expression and flow cytometry analysis (LSR FortessaTM X20 SO Cell Analyzer- BD Biosciences) to measure protein levels in CD19+ B cells obtained from peripheral blood. We also examined the presence, extent, and distribution of cells expressing EBNA2 and related human proteins, in 4% formaldehyde-fixed frozen brain tissues from post-mortem cases with pathologically confirmed MS (n=10). Statistical analysis using GraphPad Prism (version 10.4.1) integrated laboratory, clinical, and demographic parameters.
Results: We found reduced levels of PTGER4 (prostaglandin E receptor 4 EP4) and an increased levels of PLXND1 in spLCLs infected with the 1.2 allele (associated with MS risk; n=8) compared to the 1.3B allele (not associated with MS risk; n=13). In CD19+ B cells from individuals with relapsing-remitting MS (pwMS) free from immunomodulatory treatment, we observed significantly increased Plexin-D1 (p=0.018) and reduced EP4 (p=0.025) levels in pwMS (n=10) compared to healthy donors (HD; n=36). Analysis of CD19+ cells expressing EP4 revealed a population of naïve B cells (HLA-DR+ and CD27 negative).
Further analysis of CD19+ cells expressing EP4 revealed a population of naïve B cells (IgM+ IgD+ CD38low CD24low) that were HLA-DR+ and CD27 negative.
Logistic regression, indicated that the presence of the EBV genome, low levels of CD40 and EP4, and high levels of PLXND1 were associated with an increased risk of developing MS (AUC = 0.85, p=0.01).
Furthermore, in post-mortem brain tissues from MS cases (n=10), we identified EBNA2+, EP4+, and Plexin-D1+ cells in the leptomeninges, correlating with increased meningeal inflammation and the formation of tertiary lymphoid-like structures. EP4 was rarely expressed in CD19+EBNA2+ cells, which showed a naïve immunophenotype.

Conclusion: These findings suggest that EBNA2 significantly affect the virus-host interaction in MS, potentially altering mechanisms that control infection in the peripheral blood and central nervous system.

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P1386
Macrophage-Intrinsic Defects as a Potential Contributor to Impaired Remyelination

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Introduction: Multiple sclerosis (MS) is one of the demyelinating disorders that is considered an autoimmune inflammatory disease due to immune system-based oligodendrocyte death. After myelin destruction, the process of remyelination by the migration of oligodendrocyte precursor cells (OPCs) to the area of damage and their subsequent transformation into mature oligodendrocytes is called remyelination. One of the critical aspects in MS pathology is the failure of effective remyelination, potentially due to inflammatory signals from the lesion microenvironment. Infiltrating peripheral immune cells especially monocyte-derived macrophages (MDM) play a dominant role in shaping lesion dynamics.
Objectives/Aims: HSPA5 protein raised as a potential biomarker for MS based on our *interactome* analysis for protein-protein interactions between macrophages and oligodendrocytes. We aimed to determine the expression level of HSPA5 in the blood of MS patients and to validate the finding in experimental autoimmune encephalomyelitis (EAE) mouse model.
Methods: Blood samples were collected from Relapsing Remission MS (RRMS) patients and healthy controls matched by age and gender (n:34 for RRMS; n:24 for health individuals). Monocytes classification was carried out by identifying the expression levels of CD14 and CD16 surface receptors in flow cytometry (FC) ($p<0.05$). HSPA5 protein expression levels were examined in subgroups of monocytes ($p<0.05$, $p<0.01$). To establish the chronic EAE model, 6-10 weeks old C57BL/6 female mice were used (n:6). Clinical scoring was recorded according to symptoms of mice. Spleen monocytes and macrophages ($F4/80^+$) were analyzed for HSPA5 protein levels by FC and confocal imaging.
Results: The $CD14^+CD16^+$ monocyte population was significantly higher in MS patients compared to healthy individuals We determined a significant decrease in HSPA5 expression in $CD14^-CD16^+$ and $CD14^+CD16^+$ monocyte population of the RRMS. More F4/80+ cells expressing HSPA5 were detected in control mice spleen cells compared to EAE mice. Upon M-CSF stimulation, monocytes from EAE mice differentiated into macrophages with lower HSPA5 expression compared to those from control mice.
Conclusion: Understanding the intrinsic mechanisms of MDM governing remyelination failure is crucial for developing effective therapeutic interventions.

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P1387
Immune– Extracellular Matrix Interactions in Chronic Active Cortical Lesions: Insights from a Preclinical Model of Cortical Multiple Sclerosis

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Introduction: Extracellular matrix (ECM) disruption alters the balance between inflammation, damage, and repair in chronic active white matter lesions in MS. Its role in cortical lesions remains unexplored.
Objectives/Aims: To analyse ECM dynamics and their interaction with glial reactivity and peripheral inflammation in a model of chronic active cortical lesions.
Methods: We developed an animal model of focal chronic active cortical pathology by administering a cortical and peripheral injection of an adenovector chronically expressing interleukin-1 beta (AdIL-1β) (Silva et al., 2018; PMID: 29378262 and 2025; PMID: 40018028). An adenovector expressing β-galactosidase was used as a control. The expression of thrombospondin-1 (TSP-1), tissue inhibitor of metalloproteinases-1 (TIMP-1), neutrophil gelatinase-associated lipocalin/lipocalin-2 (NGAL/LCN2), chemokine (C-X-C motif) ligand 1 (CXCL1), and monocyte chemoattractant protein-1 (MCP-1) was measured in serum and cerebrospinal fluid (CSF) using multiplex ELISA assays, and in brain tissue via immunohistochemistry. Microglial activation was assessed using major histocompatibility complex class II (MHC-II), anti-CD68 (ED1), and ionised calcium-binding adaptor molecule 1 (IBA1), and astroglial activation using glial fibrillary acidic protein (GFAP). Peripheral inflammation was analysed through blood smears and spleen profiling by flow cytometry.
Results: We observed a significant increase in CSF TSP-1, TIMP-1, NGAL/LCN2, CXCL1, and MCP-1 ($p = 0.0006$, $p = 0.0003$, $p = 0.0002$, $p = 0.03$, and $p = 0.03$, respectively) and serum compared with control animals ($p = 0.003$, $p < 0.001$, $p < 0.001$, $p = 0.02$, and $p = 0.002$, respectively). CSF concentrations of these markers correlated with their serum concentrations ($r = 0.78$, $p = 0.0003$; $r = 0.81$, $p = 0.002$; $r = 0.82$, $p = 0.0003$; $r = 0.81$, $p = 0.002$; $r = 0.69$, $p = 0.001$, respectively). Cortical microglial activation correlated with both CSF and

serum levels of NGAL/LCN2, CXCL1, and MCP-1 (CSF: r = 0.76, p = 0.005; r = 0.83, p = 0.001; r = 0.75, p = 0.004; serum: r = 0.72, p = 0.007; r = 0.83, p = 0.001; r = 0.88, p = 0.0001, respectively) and cortical astroglial activation correlated with serum and CSF TIMP-1 levels (r = 0.69, p = 0.0002; r = 0.70, p = 0.004, respectively). Peripheral inflammation analysis revealed increased $CD8^+$ and decreased $CD4^+$ splenic cells after intravenous AdIL-1β. $CD3^+$ $CD8^+$ cells showed reduced naïve and increased effector memory subsets. In $CD3^+$ $CD4^+$ cells, all subsets differed significantly, with fewer naïve and more central and effector memory populations.

Conclusion: A distinct blood and CSF ECM-related profile was identified in animals with chronic active cortical lesions, correlating with cortical damage. These findings may inform therapies targeting remyelination and chronic neuroinflammation, and hold potential as biomarkers pending validation in MS patients

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P1388
Sphingosine-1-phosphate receptor 5 mediated oligodendrocyte protection

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Introduction: Siponimod, a selective Sphingosine-1-phosphate receptor 1 and 5 (S1PR1 and S1PR5) modulator, significantly reduces disease progression in patients with secondary progressive MS. The precise role of the S1PR5 and its endogenous ligand Sphingosine-1-phosphate (S1P) in Siponimod's mode of action is yet poorly understood. Our group demonstrated that Siponimod is highly effective in reducing cuprizone-induced demyelination and protecting oligodendrocytes from metabolic-toxic degeneration. These effects are independent of T and B cell modulation and are lost in mice lacking the S1PR5, indicating that S1PR5 is essential for Siponimod's oligodendrocyte protection.

Objectives/Aims: We assume that, under cellular stress, S1P binds to the S1PR5 expressed on oligodendroglia and thereby protects oligodendrocytes as an endogenous regulator. We therefore hypothesize that S1PR5-deficient mice exhibit an increased susceptibility compared to wild-type mice under metabolic stress conditions.

Methods: Metabolic oligodendrocyte degeneration was induced in C57BL/6J mice by intoxication with cuprizone (0.25%) for three weeks. Paraffin-embedded brain sections were processed for immunohistochemistry and immunofluorescence.

Results: Following cuprizone intoxication, S1PR5-deficient mice exhibit significantly higher densities of apoptotic cells in the *corpus callosum* compared to wild-type mice ($\gamma H2aX^+$ cells 320 vs. 137 /mm^2). Co-labeling with oligodendrocyte lineage markers reveals a marked increase in apoptosis specifically among mature oligodendrocytes in S1PR5-deficient mice. Overall, S1PR5-deficient mice show a more severe pathology, including significantly greater myelin loss (PLP^+ area 44% vs. 66%), increased microglia activation ($IBA1^+$ area 36% vs. 21%) and more pronounced axonal damage (APP^+ spheroids 1955 vs. 539 /mm^2). Notably, higher densities of oligodendrocyte progenitors are observed in S1PR5-deficient mice ($GPR17^+$ cells 134 vs. 70 /mm^2), potentially reflecting a compensatory regenerative response and indicating that oligodendrogenesis is not impaired in S1PR5-deficient mice.

Conclusion: S1PR5-mediated signaling pathways appear as important regulators in the protection of oligodendrocytes against metabolic-toxic *noxae* and are therefore a highly relevant therapeutic target. These findings and further follow-up studies on the signaling pathways involved are not only relevant for developing new treatment options for MS, but also for a broader range of neurodegenerative disorders involving oligodendroglial dysfunction.

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P1389
Loss of Oligodendrocyte transcription factor 2 Protein Expression in Metabolically Stressed Oligodendrocytes

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Introduction: Oligodendrocyte transcription factor 2 (OLIG2) is a sequence-specific deoxyribonucleic acid-binding factor essential for oligodendrocyte lineage progression and early differentiation. Although widely used as a pan-oligodendrocyte marker, its stability and functional role in oligodendrocytes under pathological conditions remain incompletely understood. Previous *in vitro* studies suggest that oligodendrocyte lineage-enriched transcripts are highly sensitive to suppression during integrated stress responses, potentially contributing to oligodendrocyte dysfunction and myelin degeneration.

Objectives/Aims: We hypothesize that oligodendrocytes lose OLIG2 protein expression as an adaptive or maladaptive response to cellular stress.

Methods: We analyzed OLIG2 protein expression in the metabolic-toxic cuprizone mouse model and in post-mortem brain tissue from MS patients. Brain sections were processed for immunohistochemistry and immunofluorescence. OLIG2 messenger ribonucleic acid (mRNA) levels were quantified

using quantitative real-time polymerase chain reaction (qPCR).
Results: Following cuprizone intoxication, we observed a significant increase in OLIG2 low-expressing ($OLIG2^{low}$) cells in the corpus callosum, accompanied by an increased number of Activating Transcription Factor 3 positive ($ATF3^{+}$) and DNA damage-inducible transcript 3 positive ($DDIT3^{+}$) cells, reflecting activation of the integrated stress response pathway. Immunofluorescence double labeling revealed a marked increase in 2',3'-cyclic-nucleotide 3'-phosphodiesterase positive and OLIG2 negative oligodendrocytes ($CNPase^{+}OLIG2^{-}$) during demyelination, signifying that oligodendrocytes can completely lose OLIG2 protein expression in a metabolically stressed state. When cuprizone intoxication was paralleled by treatment with siponimod, the number of $OLIG2^{low}$ oligodendrocytes was significantly reduced, highlighting siponimods oligodendrocyte-protective effect. In MS tissue, we detected a significant accumulation of $OLIG2^{low}$ cells within the active-demyelinating lesion rim, reinforcing OLIG2 protein downregulation as a stress-associated phenotype as well in human pathologies. Notably, OLIG2 mRNA levels remained unchanged after cuprizone intoxication, indicating a post-transcriptional regulation of OLIG2 protein loss.
Conclusion: Our findings suggest that OLIG2 protein expression is dynamically regulated in oligodendrocytes under metabolic stress. This has methodological implications, as stressed oligodendrocytes may evade detection using OLIG2-based linage markers. Functionally, loss of OLIG2 may contribute to transcriptional instability and myelin dysfunction. Targeting stress response pathways may offer a strategy to preserve oligodendrocyte identity and function in demyelinating diseases.

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P1390
Ozanimod Normalizes Pro-Inflammatory Astrocyte Marker Gbp2 in MS Patient iPSC Derived Cerebral Organoid Models

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Introduction: Ozanimod, a selective S1P1,5 modulator, has been approved for treating relapsing MS since 2020. It reduces relapse rates by blocking lymphocyte egress from lymph nodes. However, the direct effects of ozanimod on the central nervous system (CNS), where S1P receptors are also abundant, remain largely unknown.
Objectives/Aims: We sought to understand how ozanimod impacts human CNS cell types, including neurons, interneurons, astrocytes, and oligodendrocytes.
Methods: We used induced pluripotent stem cells (iPSC)-derived cerebral organoids from MS patients and healthy controls to study CNS cells. These *in-vitro* derived brain tissues were treated with ozanimod and analyzed for gene expression to understand the drug's effects on individual cell types.
Results: Cerebral organoids from both MS patient and healthy iPSCs developed neurons, interneurons, astrocytes, and oligodendrocytes over three months. Gene expression analysis showed increased excitatory neuron *(SLC17A7/VGLUT1)* production in MS-derived organoids from day 60, with no differences in neural progenitor cell *(PAX6)*, interneurons (*NKX2.1, DLX2*), oligodendrocyte progenitors (*PDGFRA*), or myelination markers (*PMP22, PLP1*). MS-derived organoids also had higher proinflammatory astrocyte marker *(GBP2*) expression on day 75, which was reversed by ozanimod treatment.
Conclusion: Our work shows that iPSC-derived cerebral organoids are valuable for evaluating drug impacts on human CNS cells. Comparing organoids from healthy and MS patient iPSCs can help characterize disease pathophysiology, as we found a bias towards excitatory neuron production in MS.
Most excitingly, we found a potential new mechanism of action of ozanimod as it relates to MS astrocyte biology. The elevated level of reactive astrocyte marker *GBP2* in MS versus healthy organoids implies a contribution of these inflammatory astrocytes to chronic CNS inflammation that is independent of lymphocyte infiltration. Ozanimod's ability to normalize *GBP2* expression will be studied in greater detail at the individual astrocyte cell level going forward.

Disclosure of interest: Authors are employees and shareholders of Bristol Myers Squibb

P1391
Cytotoxic CD8 T cells are expanded in Cerebrospinal Fluid of patients with Progression Independent of Relapse Activity

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Introduction: Brain-infiltrating cytotoxic CD8+ T cells are detected in the cerebrospinal fluid (CSF) of people living with Multiple Sclerosis (PwMS), persist over several years, and may contribute to disease progression. Granzyme B+ (GZMB) CD8+ T cells in the blood have been associated with disability and could effectively distinguish relapsing-remitting from progressive Multiple Sclerosis (MS). To our knowledge, no study has investigated whether specific cell types may also contribute to Progression Independent of Relapse Activity (PIRA).
Objectives/Aims: To investigate whether single cell RNA sequencing can identify specific cell clusters in the CSF associated with the future development of PIRA.
Methods: We identified four PwMS who experienced PIRA over 5 years and four age, sex, and disease modifying

treatment-matched PwMS who did not. We performed single cell RNA sequencing with the 10x Genomics' single cell RNA-seq 5' kit with TCR profiling on cryopreserved CSF pellets.
Results: We identified 9 cell clusters including monocytes, brain border macrophages, early activation CD4+ T cells, naïve/central memory CD4+ T cells, Th1 CD4+ T cells, γδ T cells and cytotoxic GZMB+ CD8+ T cells. GZMB+ CD8+ T cells can be detected in the CSF and are expanded in PwMS who experienced PIRA. We could not detect specific PIRA-associated TCR clones.
Conclusion: GZMB+ CD8+ T cells in the CSF may be biomarkers of subsequent PIRA. Selectively targeting this cellular population could be a novel strategy for treating this worsening that affects PwMS.

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P1392
Assessment of the parameters of brain injury in the cerebrospinal fluid in smoldering multiple sclerosis

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Introduction: Inflammatory demyelination and impaired recovery processes in multiple sclerosis (MS) result in permanent neurodegeneration and neurological disability.
Objectives/Aims: The aim of this study was to determine the concentration of markers of neurodegeneration in the cerebrospinal fluid (CSF) of MS patients during relapse (RPG) and without MS exacerbation (WPG).
Methods: A single-center prospective observational study was performed. We evaluated the concentrations of the parameters of brain injury: neurofilaments (NF-H), glial fibrillary acidic protein (GFAP), S calcium-binding protein (S100B) and ubiquitin C-terminal hydrolase (UCHL1) in the CSF of 123 relapsing–remitting MS and 88 progressive MS patients divided into 30 RPG and 181 WPG.
Results: In RPG active lesions were more frequent compare to WPG in the brain magnetic resonance imaging (MRI) (80% vs.18%, $p<0.001$) as well as in cervical and thoracic MRI (30% vs. 6.1%, $p<0.001$). Compared to RPG among WPG was found higher Expanded Disability Status Scale [score] (3.25 [3.0, 3.25] vs. (4.0 [2.5, 4.5) and longer MS symptoms duration [years] (1 [0,1] vs. 2 [0,6], respectively. The concentrations of GFAP and NF-H [pg/mL] were higher in RPG than in WPG (3.055 [1.55, 4.45] vs. 2.03 [1.36, 2.83], p= 0.042 and 4 ([3,25] vs. 3 [3, 4)], p=0.010, respectively. In the whole MS cohort EDSS correlated positively with the concentrations of GFAP (R= 0.19, p=0.006) and with NF-H (R= 0.14, p= 0.046) while MS symptoms duration correlated positively with the levels of S100B ($R = 0.21$, $p = 0.002$) and with UCHL1 (R= 0.27, $p<0.001$).
Conclusion: The concentrations of selected parameters of brain injury were higher in MS patients during relapse and correlated positively with EDSS compared to the individuals without MS exacerbation. These results confirm the concept of smoldering MS, in which focal inflammatory lesions related to the relapses are secondary to the loss of axons and neurons.

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P1393
Cerebrospinal fluid and plasma HDL (dys) function in Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is a multifactorial neurodegenerative disease in which cholesterol plays a key role. Cerebral cholesterol transport is mediated by lipoproteins similar to plasma HDL and observed in human cerebrospinal fluid (CSF); the first step of this process is the efflux of cholesterol from astrocytes, occurring through the major efflux transporters ABCA1 and ABCG1. Dysregulation of cholesterol transport in the central nervous system has been associated with neurodegenerative disorders. However, whether dysfunctions also occur in MS has not yet been clarified.
Objectives/Aims: The aim of this study was to investigate the relationship between cholesterol homeostasis and MS, focusing on CSF and serum HDL capacity to promote cholesterol efflux.
Methods: We conducted an observational study including CSF and serum from people with MS (pwMS) (n=45) and age- and sex-matched controls (n=14). Cerebral and serum HDL cholesterol efflux capacity was evaluated with a standardised radioisotopic technique using central and peripheral cell models.
Results: CSF HDL-cholesterol efflux capacity from astrocytes was significantly lower in pwMS compared to control subjects

(p=0.0003), with a specific impairment of the ABCG1-mediated pathway (p=0.0196). No significant differences were observed between the groups for serum HDL-cholesterol efflux capacity ABCA1- and ABCG1-mediated. The stratification of pwMS by the presence of oligoclonal bands (OCB) showed significantly lower CSF HDL-cholesterol efflux from astrocytes (p=0.0374) and specifically serum HDL-cholesterol efflux capacity ABCA1-mediated (p=0.0086) in OCB+ pwMS.
Conclusion: MS is associated with a defect in CSF HDL capacity to promote the first step of cerebral cholesterol transport, suggesting cerebral HDL as a potential pharmacological target in this condition. In addition, the observation that CSF and serum HDL-cholesterol efflux capacity are lower in OCB+ pwMS suggests that HDL (dys)function may be mechanistically correlated with the presence of OCB and could be investigated as a potential biomarker of the disease.

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P1394
Drebrin plasma levels in Secondary Progressive Multiple Sclerosis Patients treated with Anti CD-20 Drugs in comparison to healthy population

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Introduction: Drebrin, a cytoskeletal protein involved in synaptic plasticity and neuronal stability, has attracted attention for its role in neuroinflammatory and neurodegenerative processes.
Objectives/Aims: The aim of this study was to compare plasma drebrin levels in Secondary progressive multiple sclerosis (SPMS) patients treated with anti-CD20 drugs and healthy volunteers, and to investigate the association between drebrin levels and cognitive performance.
Methods: A total of 82 participants, including 40 SPMS patients and 42 healthy subjects, were enrolled in this study. Drebrin plasma levels were measured and cognitive function was assessed using the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II) and the Brief Visuospatial Memory Test-Revised (BVMT-R). Statistical analyses included independent t-tests, Mann-Whitney U tests and linear regression to assess group differences and associations.
Results: The mean age of healthy subjects was 43.65 ± 9.38 years, which was significantly higher than that of SPMS patients (35.57 ± 9.52 years, $p < 0.001$).SPMS patients had significantly higher plasma drebrin levels (0.37 ± 0.11) compared to healthy subjects (0.24 ± 0.13, $p < 0.001$). No significant difference in Drebrin levels was observed between ocrelizumab and rituximab groups. SPMS patients scored significantly lower on cognitive tests compared to healthy control: SDMT (patients: 42.78 ± 12.19; healthy: 66.54 ± 11.33, $p < 0.001$), CVLT-II (patients: 36.08 ± 11.01; healthy: 54.41 ± 9.29, $p < 0.001$) and BVMT-R (patients: 24.73 ± 10.11; healthy: 33.79 ± 2.78, $p < 0.001$). Linear regression showed no significant association between Drebrin levels and cognitive status in either group.
Conclusion: Elevated plasma drebrin levels in SPMS patients may reflect a compensatory response to neuroinflammation or neuronal injury. However, the lack of association between Drebrin levels and cognitive status suggests that other factors, such as oxidative stress or synaptic loss, may play a more fundamental role in cognitive decline. These findings highlight the complex interplay between Drebrin, neuroinflammation and neurodegeneration in SPMS and underline the need for further investigation in larger, longitudinal studies.

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Imaging & Non-Imaging Biomarkers – MRI

P1395
Predictive Value of Serum Biomarkers and MRI-based Volumetric Measurements of Hippocampus and Thalamus for Cognitive function in patients with Multiple Sclerosis

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Introduction: The prevalence of cognitive impairment in people with MS ranges from 35% to 65%. Thalamic atrophy, as well as elevated serum levels of neurofilament light chains (sNfL) and glial fibrillary acidic protein (sGFAP), can be detected even in the early stages of MS. However, their specific impact on cognitive function in clinically stable MS and their association with long-term disability progression remain incompletely understood. Ongoing neuro-axonal and astrocytic damage, along with thalamic atrophy, may contribute to the cognitive impairment in MS.

Objectives/Aims: We performed a linear regression analysis to assess whether thalamic and hippocampal volumes (V_{Thal}/V_{Hipp}), as well as levels of sNfL and sGFAP, serve as predictors of cognitive function in MS.
Methods: In this cross-sectional, retrospective study, 65 MS patients (age M=46.3±13.2; female 61.5%; EDSS M=3.1±2.2; years since diagnosis M=11.03±9.21, educational years M=14.8±3.1; 53.9% with high efficacy therapy) were examined in the University Hospital Ulm (Germany) using the Brief International Cognitive Assessment for MS (BICAMS). In a linear regression analysis, we investigated whether volumetric automated MRI measurements for V_{Thal} and V_{Hipp} (z-scores, Biometrica, jung Diagnostics GmbH), sNfL and sGFAP (z-scores, Ella platform) were predictors of cognitive function (BICAMS composite score) and accounted for variance in cognitive performance among MS patients.
Results: V_{Thal} (β=.282, t(62)=5.430, p<.001) and V_{Hipp} (β=.515, t(62)=5.975, p<.001) were significant predictors of the BICAMS in MS, explaining 32.2% (V_{Thal}) and 36.5% (V_{Hipp}) of the variance. In contrast, sNfL and sGFAP were no significant predictors of the BICAMS (p=.271 and p=.585).
Conclusion: In our cohort, thalamic and hippocampal volumes emerged as significant predictors of cognitive function in MS patients, accounting for 32.2% and 36.5% of the variance, respectively, in contrast to the serum biomarkers sNfL and sGFAP. These findings align with previous cross-sectional studies reporting a lack of correlation between sNfL and cognitive function in clinically and radiographically stable MS. This supports the notion that imaging and biochemical markers reflect different aspects of the disease pathology, with sNfL and sGFAP being more closely associated with disease activity. Longitudinal studies are warranted to clarify these relationships further.

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P1396
Radiomics Detects ^{1}H-MRS–Linked Metabolic Signatures in the Thalamus

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Introduction: Radiomics offers a powerful, non-invasive approach for quantifying subtle patterns in medical images, demonstrating significant clinical relevance. However, the molecular underpinnings of them in MS remain unclear. Proton magnetic resonance spectroscopy (^{1}H-MRS) quantifies brain metabolite levels, providing a crucial insight into the neuroinflammatory and neurodegenerative processes that characterize MS.
Objectives/Aims: To investigate the associations between spectroscopy-derived metabolic profiles and radiomic features (RF), focusing on the thalamus, a key region affected in MS.
Methods: This study included 20 individuals with MS (15 Female, mean age = 48±12) and 29 healthy controls-HC (19 Female, mean age = 38±10). MRI scans were conducted using a 3T scanner. ^{1}H-MRS spectra were acquired from a single bilateral voxel (21 × 34 × 14 mm^3) positioned to encompass both the left and right thalamus. Spectral processing was performed using MRspa and LCModel-6.3. Metabolite concentrations, including N-acetylaspartate (NAA), glutamate (Glu), glutamine (Gln), total choline (tCho), and myo-inositol (mIns), were quantified as ratios relative to total creatine (tCr). Only metabolites with mean Cramér-Rao Bounds ⩽20% were considered reliable.
RF extraction was performed using PyRadiomics, generating over 1700 features from 3D T1-weighted and FLAIR images based on the thalamic spectra mask from ^{1}H-MRS. LASSO regression was applied for each metabolite ratio, adjusting for age, sex, and disease status. The top 25 most frequently retained RF were selected. Pearson correlations were calculated between each metabolite ratio and its corresponding RF. We also examined associations between RF and clinical measures, including the MS Functional Composite and Expanded Disability Status Scale.
Results: In the MS group, two T1-derived RF were significantly correlated with the mIns/tCr and seven FLAIR-derived features with the Glu/tCr (FDR < 0.05). These features capture the intensity, variability and spatial organization of voxel values. In HC, ten T1-derived RF showed significant associations with the Glu/tCr.
Seven T1and five FLAIR-derived features were significantly associated with 25-Foot Walk Test in MS (FDR < 0.05, with r values ranging from -0.81 to +0.87).
Conclusion: Radiomic features, particularly those reflecting voxel intensity variability, can reveal metabolite levels. This pattern is not random as it specifically captures only the Glu and mIns to tCr ratios in both MS and HC populations. This finding is a step toward highlighting the potential of radiomics as a non-invasive imaging biomarker in MS.

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P1397
Intracranial volume loss and skull thickening in metachromatic leukodystrophy and multiple sclerosis

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Introduction: Intracranial volume (ICV) is often used as a normalization factor for brain volume measurements and considered to be stable in adults. We regularly noticed thick skulls on MRI scans of leukodystrophy patients, suggesting potentially changed skull morphology. This observation raised questions about ICV stability and whether such changes were also present in a non-genetic disease such as MS.
Objectives/Aims: To evaluate the ICV and skull thickness in participants with metachromatic leukodystrophy (MLD), people with MS (pwMS), and controls.
Methods: We retrospectively analyzed cross-sectional and longitudinal MRI scans of participants with MLD (n=32, scans=136), pwMS (n=232, scans=431), and controls (n=140, scans=319). Skull thickness and ICV were determined using automated segmentation techniques. The MLD and control groups were split into participants below and above 20 years to account for natural ICV and skull growth. In the pwMS group, all participants were older than 20 years.
Results: Both ICV and skull thickness increased over time in controls below 20 years. In young MLD participants, ICV decreased (-18.8 ± 22.4 mL/year, $p<0.001$). Above the age of 20 years, ICV and skull thickness remained stable in controls. In comparison to controls, we observed ICV loss in MLD participants (-4.01 ± 8.29 mL/year, $p=0.004$) and in pwMS (-2.99 ± 2.69 mL/year, $p<0.001$), as well as skull thickening (MLD: 0.16 ± 0.14 mm/year, $p<0.001$, pwMS: 0.04 ± 0.09 mm/year, $p=0.013$). In both adult groups negative correlations were found between ICV and skull thickness (MLD: -19.39mL/mm, $p<0.001$, pwMS: -13.16 mL/mm, $p<0.001$), but not in controls ($p=0.222$).
Conclusion: ICV shrinkage and skull thickening in participants with MLD and pwMS challenge the assumption of a stable ICV after reaching adulthood and suggest an active adaptive response of the skull to pathological processes, possibly atrophy. These morphological changes appear most pronounced in MLD patients, where atrophy may develop at an early age. ICV shrinkage may lead to underestimations of atrophy when using ICV as a normalization factor, emphasizing the need to refine volumetric methodologies to more accurately assess and predict brain atrophy progression. Further research is needed to explore the responsible mechanisms and potential differences between MS subtypes.

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P1398
The relationship between white matter lesions and fatigue in multiple sclerosis: A multi-center MAGNIMS study

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Introduction: Fatigue is one of the most frequent and disabling symptoms for people with MS. The role of white matter lesions in causing fatigue is still not fully elucidated.
Objectives/Aims: In this retrospective multicenter study we investigated the relationship between strategic white matter lesion location and fatigue in a large cohort of MS patients.
Methods: MRI, clinical data and self-reported fatigue scores from within 3 months of MRI were collected from 8 different MS research centers across Europe. White matter lesions were automatically segmented using LST-AI and transformed to MNI152 space. Relationships between log-transformed white matter lesion load and fatigue scores were tested using linear regression models. The strategic location of lesions related to fatigue was assessed with voxelwise lesion symptom mapping (VLSM) using NiiStat and structural lesion disconnectome mapping using the BCBtoolkit. Specificity analyses correcting for EDSS, age, sex and disease duration were conducted for all analyses.
Results: We analyzed data from 1047 patients with MS (mean age 43.9 (11.4) years, 710 (67.8%) female, median EDSS 2.5 (0-8), mean disease duration 12.2 (0-46) years, SPMS: 143, PPMS: 54, RRMS: 831, CIS: 19). We found a significant but very weak relationship between white matter lesion load and fatigue. For each 10-fold increase in lesion volume, fatigue score increased 8.02 points (scale 0-100) explaining less than 3% of data variability (adjusted R^2=0.0286, $P<0.001$). When controlling for confounding the relationship disappeared (estimate = 1.2 +/- 1.58, P=0.45). VLSM did not reveal significant voxels associated with fatigue (10000 permutations, one-tailed $P>0.05$). Disconnectome mapping revealed a network of white matter connections which were associated with fatigue severity (10000 permutations, $P<0.05$, familiy-wise error rate corrected). The network had peaks near the right precentral gyrus, left frontal pole and right visual cortex. Looking at individual disconnectomes, people with a high overlap of their individually affected network and the fatigue network had an 8.4 (+/- 1.42) point higher fatigue score ($P<0.001$). The effect was still significant after controlling for confounding factors (P=0.011).
Conclusion: MS related fatigue is only weakly associated with white matter lesion load and not with spatial lesion location. However, lesion connectivity to specific white matter tracts was associated with fatigue severity.

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P1399
Choroid plexus volume: its relation to lateral ventricle volume and potential as an imaging biomarker in multiple sclerosis

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Introduction: Choroid plexus volume (CPV) has recently emerged as an imaging surrogate for various (para)clinical

measures in persons with multiple sclerosis (pwMS). The location of the plexus inside the lateral ventricles is problematic as ventricular enlargement is an established component of brain atrophy in MS. So far, it is unclear whether brain atrophy impacts CPV and whether CPV is independently associated with clinical endpoints.

Objectives/Aims: – To investigate the relation between CPV and lateral ventricle volume (LVV) in pwMS and healthy controls (HC). To determine whether CPV shows (para)clinical associations independent from LVV.

Methods:

– An automatic segmentation network was trained on 70 manually segmented brain MRI scans (both pwMS and HC) using nnUNet with FLAIR and T1w inputs. CPV and LVV were normalized for intracranial volume.

– From our large MRI database (n = 10,872 scans), 292 HC and 292 pwMS were matched for age, sex and LVV. Wilcoxon-Mann-Whitney tests were used for between-group comparisons. Linear and nonlinear models of the relation between CPV and LVV were compared using analysis of variance (ANOVA).

– Regression models with brain white matter lesion volume/Expanded Disability Status Scale (EDSS) scores as dependent variables and either LVV only or LVV + CPV as independent variables were compared via ANOVA for all scans of pwMS (n = 10,558 scans, 63.9% female, median age at scan = 37.9, median EDSS = 1.5).

Results: CPV was significantly higher among pwMS (median = 1746 mm^3) than among HC (median = 1574 mm^3; $p < 0.001$). This difference disappeared on individual matching for age, sex and LVV ($p = 0.17$). The general relation between CPV and LVV was best described by a square root function (linear: R^2 0.284 vs. nonlinear: R^2 0.408, $p < 0.001$).Higher LVV was moderately but significantly associated with higher white matter lesion volume ($R^2 = 0.248$) and EDSS score ($R^2 = 0.110$) in pwMS. Although the addition of CPV formally improved both models ($p < 0.001$), the numerical improvement in model fit was very small (white matter lesion volume: $R^2 = 0.249$; EDSS: $R^2 = 0.120$).

Conclusion: CPV and LVV are positively correlated in a nonlinear fashion. After correcting for LVV, we did not observe a difference in CPV between pwMS and HC, nor did we find a meaningful independent association of CPV with EDSS or white matter lesion volume. Although our findings do not rule out any potential of CPV as an MS surrogate, they stress the importance of correcting for LVV when dealing with the parameter.

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P1400
Automated assessment of perivascular spaces differentiates MS from its MS mimics

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Introduction: Perivascular spaces are compartments in the brain surrounding blood vessels that are involved in neuroimmune functions. In brains afflicted by MS, prior work has shown inflammatory cells become sequestered in PVS. Enlargement of PVS may contribute to or be reflective of MS disease pathology. While some studies have demonstrated enlarged PVS are more prevalent in MS compared to healthy controls, conflicting data has shown more PVS in subjects without MS. Thus the relationship between PVS and MS warrants further study.

Objectives/Aims: To quantify PVS and assess PVS volumes with an automated detection tool in subjects with MS and

patients with disorders mimicking MS known to potentially influence PVS, such cerebrovascular disease.
Methods: T1-weighted and FLAIR sequences were obtained on 3T MRI from 40 participants: 10 with MS, 10 with MS and a known comorbidity associated with MRI white matter abnormalities, 10 with migraine and MRI T2 hyperintense lesions, and 10 who were previously misdiagnosed with MS due to a variety of diagnoses. MRIs were analyzed using a previously validated automated segmentation pipeline. Primary outcomes included number of PVS and PVS volume, which were evaluated separately in each model.
Results: MS diagnosis was inversely associated with the number of PVS ($t(23.99) = 3.92$, $p < 0.001$) and PVS volume ($t(22.49) = 3.64$, $p < 0.001$). ROC analysis demonstrated an AUC above 0.8 for both the number of PVS and PVS volume, for differentiating the MS and non-MS cohorts. In logistic regression, the number of PVS ($OR = 0.98$, *95% CI* [0.97, 0.99], $p < 0.01$) and volume of PVS ($OR = 1.00$, *95% CI* = [0.998, 1.00], $p < 0.05$) remained significantly associated with MS diagnosis after controlling for age.
Conclusion: These findings suggest that a higher number of PVS and larger PVS volume are associated with lower odds of MS diagnosis and perhaps higher risk of cerebrovascular disease. The degree to which cerebrovascular disease influences PVS in patients with MS and other diagnoses warrants further study in larger longitudinal cohorts.

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P1401
Longitudinal atrophy measures in MS differ between scanners: implications for trials and clinical implementation

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Introduction: Brain atrophy is a key marker of disease progression in MS, driving growing interest in its adoption as a routine clinical and trial metric. However, scanner and protocol variability remain a challenge in clinical practice and multi-center studies. While cross-sectional reliability has been studied, longitudinal analyses are lacking.
Objectives/Aims: To evaluate volumetric change reproducibility between scanners in people with MS (pwMS) and healthy controls (HCs).
Methods: Twenty-eight pwMS and 10 HCs underwent a scan and immediate rescan, including 3D T1-weighted imaging, on three MRI scanners (GE Discovery MR750 [3T], Siemens SOLA [1.5T], and Siemens VIDA [3T]) within a four-hour window at baseline (BL) and identically repeated at 1.5 year follow-up (FU). Images were bias-field-corrected and processed with HD-BET for brain extraction followed by cross-sectional FreeSurfer. For each participant, for each scanner, the BL-scan and FU-scan pair and the BL-rescan and FU-rescan pair were then independently processed using the longitudinal FreeSurfer pipeline to compute volume change (Δvolume) for whole brain, total gray matter (GM), deep gray matter (DGM), lateral ventricles (LaV), and the thalamus. Between-scanner differences were determined by repeated-measures ANOVA with post-hoc pairwise tests. Within-scanner repeatability of Δvolume was then assessed by intra-class correlation coefficients (ICC) for absolute agreement. Between-scanner reproducibility was assessed by ICC for consistency.
Results: Annual brain Δvolume in MS was: -0.48%±0.52 on GE, -0.73%±0.50 on SOLA, and -0.75%±0.60 on VIDA (HC: -0.28%±0.37, -0.21%±0.59, -0.57%±0.27, respectively). Larger Δvolume were found on VIDA than on GE ($p<0.01$) for whole brain, GM, and DGM, which was also true for SOLA vs GE for GM and DGM ($p<0.05$). LaV Δvolume was higher for SOLA (2.4% ± 3.1) than for GE (1.7% ± 2.7) and VIDA (1.7% ± 3.1) ($p<0.001$). Within-scanner reliability varied between regions (mean ICC_{GE}=0.72 (range 0.49-0.95), mean ICC_{SOLA}=0.75 (0.65-0.98), mean ICC_{VIDA}=0.76 (0.60-0.98). Between-scanner agreement ranged poor-excellent, and lower between GE and the Siemens scanners: (mean $ICC_{GE\text{-}SOLA}$=0.51 (range 0.28-0.92), mean $ICC_{GE\text{-}VIDA}$=0.56 (0.39-0.94), mean $ICC_{VIDA\text{-}SOLA}$=0.71 (0.56-0.96).
Conclusion: FreeSurfer-assessed longitudinal volume changes were consistent within scanners but varied between them. These differences may mask true biological change and should be accounted for in multi-center MS studies. Harmonization may be needed for reliable analysis.

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P1402
Cortical magnetic susceptibility in patients with MS: MRI characterization of sensorimotor areas

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Introduction: Quantitative Susceptibility Mapping (QSM) is an advanced MRI technique used in MS research for its ability to detect white matter demyelination and iron accumulation in deep gray matter (GM) nuclei. However, no studies to date have investigated its potential for assessing cortical regions affected by MS pathology.
Objectives/Aims: This study aims to investigate QSM in cortical regions involved in sensorimotor functions, comparing susceptibility distributions between people with MS (PwMS) and healthy controls (HCs). Additionally, QSM were correlated with SANDI (Soma and Neurite Density Imaging), an advanced diffusion model enabling the in-vivo assessment of tissue microstructure, also in the GM.
Methods: A total of 145 PwMS and 38 HCs underwent 3T MRI. For all PwMS, the Expanded-Disability-Status-Scale (EDSS) score was assessed. The precentral (PrCG) and postcentral gyrus (PoCG) were extracted from lesion-filled T1 images using FreeSurfer. QSM maps and SANDI metrics (the fractions of soma, neurite, and extracellular space) were computed. Group comparisons of QSM values were performed using a General Linear Model (GLM) adjusted for age and sex, with both voxel-wise and ROI-based approaches. Spearman correlation analysis assessed associations between QSM and SANDI metrics in PwMS.
Results: Voxel-wise analysis revealed significantly increased QSM values in the right PoCG of PwMS compared to HCs ($p < 0.05$, family-wise error corrected). No significant QSM differences were found in the PrCG or PoCG using ROI-based analysis. However, PwMS in the highest EDSS tertile showed elevated QSM in the right PrCG compared to HCs ($p = 0.02$). QSM values in the left and right PrCG negatively correlated with soma fraction ($r = -0.2$, $p = 0.007$; $r = -0.2$, $p = 0.002$) and positively with extracellular fraction ($r = 0.2$, $p = 0.01$; $r = 0.3$, $p < 0.001$), respectively. Similar correlations were observed in the right PoCG (soma fraction: $r = -0.2$, $p = 0.001$; extracellular fraction: $r = 0.3$, $p < 0.001$).
Conclusion: Increased QSM values were observed in sensorimotor areas, with a negative correlation to soma density and a positive correlation to extracellular space. These findings support the hypothesis that elevated cortical QSM is associated to cortical degeneration in MS.

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P1403
Identification of paramagnetic rim lesions in a standard university hospital clinical setting in Finland

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Introduction: Paramagnetic rim lesions (PRLs) are an emerging MRI biomarker in multiple sclerosis (MS), with both diagnostic and prognostic value.
Objectives/Aims: To identify PRLs in a standard university hospital setting and to explore the associations between PRL burden and clinical/imaging parameters
Methods: We retrospectively reviewed all 3T brain MRI studies performed as a part of routine MS monitoring at Turku University Hospital, Finland, between 1.9.2021 and 31.12.2023. Exclusion criteria were neurological diseases other than MS, age <18 years and insufficient MRI data. PRLs were visually identified on filtered phase images from susceptibility-weighted imaging (SWI) sequences used. Brain volumetric data were extracted from post-contrast 3D T1-weighted images using the cNeuro® (Combinostics Ltd, Tampere, Finland) cMRI quantification tool, which is in routine clinical use at our hospital. Clinical variables were obtained by manual chart review from electronic medical records.
Results: The final cohort included 206 people with MS (pwMS). The overall person-level prevalence of PRLs was 34%. Among participants, 183 had 0-2 PRLs and 23 had $\geqslant 3$ PRLs. These groups did not differ significantly in terms of age or disease duration. However, the $\geqslant 3$ PRL group had significantly higher EDSS (Expanded Disability Status Scale) and MSSS (Multiple Sclerosis Severity Score) at the time of imaging ($p < 0.05$). The number of PRLs demonstrated a positive correlation with EDSS and MSSS in the subgroup of pwMS with $\geqslant 1$ PRL ($p < 0.05$). Additionally, the $\geqslant 3$ PRL group had significantly lower total brain parenchymal and thalamic volumes ($p < 0.05$). No significant differences were observed between the groups in terms of clinical MS phenotype, class of disease modifying therapy, cerebrospinal fluid parameters at MS diagnosis, or number of gadolinium-enhancing T1-lesions at MS diagnosis.
Conclusion: PRLs can be successfully identified using conventional SWI in a routine clinical setting. PRL burden was associated with more aggressive disease.

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P1404

The myelin content of the cortico-spinal tract is associated with physical disability and information processing speed in Multiple Sclerosis patients

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Introduction: *Myelin Streamline Decomposition (MySD)* is a method that extracts the myelin signal (obtained with myelin-sensitive contrasts) along white matter tracts– as reconstructed with diffusion tractography. Recently, MySD was extended to account for focal lesions along fiber tracts (*MySD-lesion)*.
Objectives/Aims: We extracted the cortico-spinal tract (CST) streamlines and the corresponding myelin weights using *MySD-lesion* in people with MS (pwMS) to assess the relationship between myelin content, (i) clinical disability (Expanded Disability Status Scale (EDSS)), and (ii) information processing speed (Symbol Digit Modalities Test (SDMT)).
Methods: We analyzed 122 pwMS (72 f, 51 PMS; 46.9 ± 14.1 years; median DD: 7.34 years; median EDSS: 3) that underwent 3D FLAIR, MP2RAGE, multi-shell diffusion and magnetization transfer saturation imaging at 3T MRI. White matter lesions (WMLs) were segmented using a deep learning tool, followed by manual correction. Whole brain tractography was performed

using iFOD2 MRtrix3. We computed whole-brain network metrics from myelin volume fraction (MVF) along brain tracts using MySD-lesion, including global efficiency, mean strength, clustering coefficient, network density, and modularity. We also extracted the myelin content of the CST in both hemispheres. A subset of 81 patients (46 f, 34 PMS; 46.9±13.2 years; median DD: 8.36 years, median EDSS: 3) underwent SDMT testing. SDMT z-scores were corrected for age and education. Correlations between CST myelination and brain MVF connectomes were assessed. We used linear regression models to assess the relationship between CST myelination and (i) EDSS and (ii) SDMT z-scores. Covariates included log-transformed WML volume, phenotype, age (only for EDSS), sex, and handedness.
Results: We found correlations between the left CST and whole-brain MVF-weighted mean strength (cor= 0.428, p<0.001) and MVF-weighted efficiency (cor= 0.430, p<0.001). The right (β= −0.372, p= 0.015, Adj. R^2= 0.559) and left (β= −0.370, p= 0.046, Adj. R^2= 0.552) CST myelin content was associated with EDSS. Also, the myelin content in the left CST was significantly associated with SDMT (β= 0.569, p= 0.001, Adj. R^2= 0.205).
Conclusion: The left CST integrity is linked to global WM integrity, as reflected by MVF mean strength and efficiency, which might explain the association of myelin content in the left CST with processing speed. Also, left and right CST integrity were associated with EDSS, showing in vivo a strong relationship between physical disability and CST myelination.

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P1405
Discrepancies in PRL Detection Methods and Their Association with Cognitive Performance in MS

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Introduction: Paramagnetic rim lesions (PRLs) are chronic active lesions and have been increasingly recognized as important biomarkers of disease progression in MS. While prior work has shown links to physical disability and inflammation, their relationship to cognitive performance, remains less well understood.
Objectives/Aims: Examine the relationship between PRL status, determined by multiple methods, and cognitive outcomes in people with MS.
Methods: Seventy-one participants underwent structural magnetic resonance imaging (MRI) and completed four cognitive measures: Symbol Digit Modalities Test (SDMT), Expanded Disability Status Scale (EDSS), California Verbal Learning Test (CVLT), and Brief Visual Memory Test-Revised (BVMTR). PRL status was assessed via two methods: manual counts by three expert raters and an automated tool, APRL (Lou et al., 2021). We examined associations between cognitive outcomes, as both continuous and binary variables, and PRL count and probability using linear and logistic regression, mixed effects models, and functional regression.
Results: Manual PRL counts were not significantly associated with any cognitive measure (all p's > 0.22). However, higher PRL count from APRL was associated with lower SDMT scores both continuously (β = -0.35, 95% CI [-0.59, -0.11], $p < 0.01$) and categorically ($OR = 1.12$, 95% CI [1.04, 1.21], $p < 0.01$). With APRL, we also calculated PRL probability, a ratio of PRLs to all white matter lesions. Here, a greater PRL probability was seen in those with abnormal SDMT scores (OR = 1.07, 95% CI [1.01, 1.15], p < 0.05). We also evaluated these relationships with lesion-level PRL probability from APRL but again did not see any significant relationships with disability outcomes (all p's > 0.07). Finally, we used functional regression to ask how people with higher PRL probabilities perform cognitively, and

we again saw no relationship with any of the cognitive measures (all p's > 0.28).
Conclusion: PRL status, particularly when assessed with APRL, showed an association with SDMT performance. However, the lack of consistency across methods highlights the need for improved PRL detection strategies and further evaluation of statistical approaches used to link imaging biomarkers with cognitive outcomes.

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P1406
Association Between Quantitative Susceptibility Mapping (QSM) Lesion Types and Choroid Plexus Volume: A Correlational Study

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Introduction: Multiple sclerosis (MS) is a chronic neuroinflammatory disease characterized by diverse lesion types and neurodegeneration. Quantitative susceptibility mapping (QSM), an MRI technique, helps classify MS lesions based on iron and myelin content. Recent studies indicate that the choroid plexus (CP), which plays a role in immune surveillance and cerebrospinal fluid production, may affect lesion development and repair.
Objectives/Aims: This study explores the relationship between QSM-defined lesion types and choroid plexus volume in MS patients.
Methods: A five-year study involved 46 MS patients (44 with RRMS and 2 with PPMS), using 3D FLAIR, MPRAGE, and ME-GRE sequences to create QSM maps. Lesions were segmented with FreeSurfer's SAMSEG, categorized as iso-intense (remyelinated), hyperintense (chronic inactive), hypointense (remyelinated), and paramagnetic rim lesions (PRLs). Whole-brain parcellation and choroid plexus segmentation were performed to evaluate regional associations, with correlations between lesion subtypes and CP volume analyzed using Spearman's rho and Mann-Whitney U tests.
Results: Among 898 lesions, 57% were iso-intense, 32.4% hyperintense, and 7.2% hypointense. PRLs accounted for 5.48% periventricular, 4.95% subcortical, and 3.58% juxtacortical lesions. Remyelinated lesions (iso- and hypointense) showed moderate positive correlations with choroid plexus volume (right: $r = 0.37$–0.42; left: $r = 0.32$–0.42, $P<0.05$), suggesting a role in neuroinflammatory modulation and tissue repair. PRLs and chronic inactive lesions volumes had low to moderate positive correlations with total choroid plexus volume change ($r = 0.309$ and $r = 0.286$, $P<0.05$), indicating a possible link to CP-related inflammatory processes. No meaningful correlation was found with intracranial volume change ($r = 0.009$ and $r = -0.124$, $P<0.05$), suggesting their burden may be independent of global brain atrophy.
Conclusion: Our findings show a new link between remyelinated lesions and choroid plexus volume, highlighting its potential role in MS lesion repair and supporting further research into targeted therapies.

Disclosure of interest: Elnaz Asadollahzadeh nothing to disclose

P1407
Multiparametric normative human brain atlases of R1, R2, proton density, and myelin volume fraction using synthetic quantitative MRI: application to patients with early or late-onset MS

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Introduction: Quantitative magnetic resonance imaging (qMRI) using Synthetic MRI is increasingly applied in MS. We constructed normative synthetic 3D-MRI brain atlases of the relaxation rates R1, R2, proton density (PD), and Myelin (MyC) for the comparison with individual patient data or group analyses. In this proof-of-concept study, we evaluate two MS groups of patients at their first diagnosis of MS with early onset (EOMS, age$<$30 years) or late onset (LOMS, age $>$ 45 years) with similarly low lesion loads and brain atrophy, to show that the multiparametric atlases can depict specific disease-related differences. Typically, MS is diagnosed in young adults, however the incidence of LOMS is increasing. Thus, research on the pathophysiology of this population is required.
Objectives/Aims: To investigate microstructural brain alterations of MyC, R1, R2, or PD by applying the quantitative normative atlases to EOMS and LOMS.

Methods: Quantitative 3D-brain atlases of R1, R2, PD, and MyC derived from 58 healthy controls (HC) based on the single-scan Synthetic MRI sequence were compared with EOMS (n=18) and LOMS (n=18) patient groups who also received Synthetic MRI. Quantitative parameters were extracted from 23 white matter (WM) regions (ROI). T-tests between patient groups and the normative data in each ROI and between the averages of all ROI, and z-score maps for visual comparison at exemplary individual patients were used to show differences between both MS groups and quantitative atlases.
Results: Averaged across all ROIS, significant differences in R1 were found between both MS groups and the standard atlases (EOMS/LOMS/HC: 1.25/1.23/1.49 s^{-1}, all $p < 0.001$). In MyC, PD, and R2 significant average aberrations were seen in LOMS (LOMS/HC: 22.3/25.7%, 71.6/69.6%, 12.51/12.91s^{-1}). This tendency was confirmed by the single ROI analyses; for example, in GCWM deviations were significant in EOMS and LOMS for R1, while in MyC, R2, and PD aberrations were seen only in LOMS (all $p<0.05$). The z-score maps showed localized differences between individual patients and the atlases.
Conclusion: The quantitative atlases were suited to highlight specific tissue changes in EOMS and LOMS patients with similar macroscopic lesions and GCWM volumes. R1 seemed to be more sensitive than R2, PD, and MyC. Overall qMRI suggested less severe structural alterations in EOMS compared to LOMS.

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P1408
Parasagittal dural volume is associated with cerebral pathology and neuroinflammation

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Introduction: The parasagittal dura (PSD) is a structure of recent interest, suggested to represent a neuro-immune interface potentially playing a role in chronic neuroinflammation.
Objectives/Aims: The aims were to develop a general automated method for volumetric segmentation of the PSD on 3D FLAIR images, and determine clinical and MRI associations with this structure. We hypothesized that the volume of the PSD would be increased in MS versus non-MS disease, and would be pathologically associated with disease severity.
Methods: T1 images were processed in CAT12 to obtain brain segmentations and cortical thickness (CT). FLAIR images were bias corrected and then intensity normalized using Z-scores to the (1) whole brain, (2) the ventricles, and (3) the normal-appearing white matter; (4) fuzzy C-means, and (5) WhiteStripe (WS). The meningeal space was defined between the pial surface and dural-osteal junction using Freesurfer's *mri_synthstrip*, followed by intensity thresholding, region-growing, and median filtering, all constrained by masking applied from standard space superior to the Torcula. Intensity thresholds were chosen empirically given a lack of gold standard. Resulting PSD volumes were log-transformed and associations modeled with multivariable linear regression in R.
Results: A retrospective cohort of 360 patients with relapsing MS (RMS, age 45±12), 96 with progressive MS (PMS, age 58±9), and 89 with other inflammatory (OIND: N=41, age 50 ±12) or non-inflammatory (NIND: N=48, age 49±11) neurological disease. PSD volumes obtained by different normalization methods agreed moderately to strongly (r~0.4-0.9). Across all normalization methods, PSD volumes correlated with age (r=0.29-0.47, $p<0.001$) and intracranial volume (ICV; r=0.30-0.45, $p<0.001$). Contrast administration prior to the FLAIR correlated with larger PSD (r=0.1-r=0.2, $p<0.01$). In multivariable models adjusting for age, ICV and contrast, PSD volumes were 22-30% greater in RMS vs NIND ($p<0.001$) but not RMS vs OIND ($p>0.05$). All methods except WS showed significant pathological associations with higher PSD and lower brain volumes, and decreased CT (all $p<0.01$), regardless of diagnosis. Inconsistent findings were observed between normalization methods in association with lesion volumes, paramagnetic rim lesion number, and disability scores, with only Z-brain showing consistent associations ($p<0.01$) with all three. No association with concurrent treatment were observed.
Conclusion: Automated determination of PSD volumes using a threshold-based approach is feasible but limited by lack of a "gold standard"; the choice of normalization method can affect clinical correlations. The PSD is enlarged in MS versus non-inflammatory controls but not other CNS inflammatory conditions, and is associated with greater loss of cerebral volume and lower cortical thickness across all disease states; this is suggestive of a nonspecific pathological association.

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P1409
Optimizing T1 hypointensity threshold for detecting white matter demyelination in multiple sclerosis: a postmortem in situ MRI study

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Introduction: In multiple sclerosis (MS), the radiological correlate of severe tissue damage is hypointensity on T1-weighted images, but the definition of T1 hypointensity has not been well established. Examination of postmortem MRI T1 hypointensity and macroscopic demyelination on MS specimens provides the opportunity to quantitatively evaluate T1 hypointensity to detect white matter (WM) demyelination.
Objectives/Aims: To optimize the threshold for T1 hypointensity to detect WM demyelination using postmortem MRI.
Methods: We analyzed MS brain autopsy specimens and corresponding postmortem in situ MRIs. T2 hyperintensities were segmented semi-manually on FLAIR and T2-weighted images. T1-weighted MPRAGE images were normalized using the mean values in normal-appearing WM and lateral ventricles and these values were set at 100 and 0, respectively. T1 hypointensities were defined as hypointense regions within T2 lesions on normalized T1w images. Demyelination was determined macroscopically as discoloration in WM on the photos of fixed brain slices. Thresholds for T1 hypointensity detection were calculated using the following formula: Threshold = [Mean T1 intensity of grey matter] – $k \times$ [SD of gray matter T1 intensity], where k is a scaling factor. Fixed brains were sliced in a custom cutting box, and MRIs and photos of brain slices were co-registered. Various thresholds were applied, and receiver operating characteristics (ROC) curves were generated to identify the threshold yielding the highest sensitivity and specificity for demyelination. Correlation between T1 hypointensity areas with optimal threshold from MRI and demyelination areas from brain slice was analyzed.
Results: Six brain slices from four donors (2 females; mean age at death = 51.8 ± 8.5 years; 4 secondary progressive MS; mean disease duration = 23.5 ± 10.5 years) were analyzed. From the ROC analysis, the optimal scaling factor was k=0.4 or the normalized T1 intensity of 73.9. This threshold yielded 79.7% sensitivity, 80.0% specificity, 80.3% accuracy, and a Dice coefficient of 74.6%. The mean demyelinated WM area per slice was 1.48 ± 0.50 cm^2 while the corresponding T1 hypointensity area was 1.37 ± 0.46 cm^2. The Pearson correlation between T1 hypointensity areas and demyelination areas was 0.54.
Conclusion: The optimized T1 hypointensity threshold showed accurate identification of WM demyelination within T2 lesions. Applying this threshold to in vivo MRI may help monitor the evolution of WM demyelination and MS progression.

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P1410
Frequency-Specific Dynamics of Node Entropy and Centrality Reveal Complex Functional Reorganization Across Multiple Sclerosis Stages at 7T

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Introduction: We explored dynamic functional brain reorganization in People with Multiple Sclerosis (PwMS) using high-resolution 7 Tesla (7T) resting-state fMRI (rs-fMRI). Specifically, edge Functional Connectivity (eFC) graphs were used to derive to measure node entropy (NE), describing connection diversity across communities, and Node Degree Centrality (NDC), the average connection strength. The goal of calculating these measures was to map brain network alterations in MS.
Objectives/Aims: We compared NE and NDC in major resting state networks of Healthy Controls (HC), Relapsing-Remitting MS (RRMS), and Secondary Progressive MS participants (SPMS). This was done in three different fMRI frequency bands while leveraging 2-year follow-up, longitudinal 7T imaging data.
Methods: 7T rs-fMRI data (10 min, 1.25s TR; 105 scans from 46 subjects: 17 HC/17 RRMS/12 SPMS with scans acquired at baseline and longitudinally over up to 4 years). The corresponding time series data from 100 Regions of Interest (ROI) were evaluated to measure dynamic eFC graphs. This was done with a sliding window design. Consensus clustering of eFC eigenvectors identified communities (k=20). NE and NDC were then calculated per node and averaged for 7 major rs-fMRI networks. Linear Mixed Effects (LME) models were then applied to measure group-specific NDC and NE values in the 7 brain networks, as well as the change in NDC and NE in conventional (0.008-0.1Hz), Low-Frequency (LF, 0.008-0.027Hz), Medium-Frequency (MF, 0.027-0.073Hz), and High-Frequency (HF, 0.073-0.1Hz) bands for MS participants and HC over 4 years.
Results: Distinct, frequency-specific patterns emerged. NE increased broadly in MS participants, supporting compensatory mechanisms and potentially less segregated connectivity. This effect was strongest in the LF band (RRMS/SPMS>HC in Attention [Attn]/Visual [Vis] networks; $p<0.001$) and HF band (MS>HC across Vis/Motor [Mot]/Control/Default Mode Network [DMN] regions; $p<0.05$). NDC increases were observed in SPMS for the MF band of the Salience/Ventral Attention and Temporal Parietal networks ($p<0.05$). Compared to controls, SPMS participants showed accelerated, age-related NE decreases (Conventional: Vis; p=0.008; MF: Mot; $p<0.003$),

accelerated NE increases (MF: Attn; $p<0.003$), and accelerated, age-related NDC increases (MF: Attn; $p<0.05$).
Conclusion: Our broad observation of increased Node Entropy (particularly in LF/HF bands) suggest shifts towards less specialized functional roles in certain brain networks in MS. Increases in NDC and decreases in NE over time in SPMS may relate to network-dependent functional alterations unique to progressive MS that are distinct from healthy aging. Analyzing complementary, frequency-specific dynamic network properties appears to offer valuable insights into the functional rs-fMRI signal reorganization in PwMS.

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P1411
Preliminary results of AI-based harmonization of brain MRIs from several MS clinical trials

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Introduction: Brain Magnetic Resonance Imaging (MRI) is essential for diagnosing and monitoring MS, but variability in scanners, acquisition protocols, and reconstruction techniques across multi-centric, multi-scanner brain MRIs introduce differences that hinder the possibility of pooling data and limit results generalization.
Objectives/Aims: To develop an artificial intelligence (AI)-based solution to harmonize multi-trials T1-weighted brain MRIs of people living with MS to minimize contrast differences.
Methods: A dataset of 147 brain scans acquired at baseline was retrospectively selected from 7 trials included in the Novartis-Oxford Multiple Sclerosis (NO.MS) dataset, which is comprised of MS clinical trials, managed and analysed by various MRI evaluating centres. A reference dataset of 10 scans was manually selected and used to synthetically generate the training dataset. A total of 200 modifications were applied to each 2D image in the frequency domain (absolute k-Space data), simulating contrast alterations. A convolutional neural network (CNN) based on a U-Net3+ architecture with an additional skip connection between the first and last convolutional layer was trained using the synthetically generated images as input, and the original reference image as ground-truth. Mean square error with L2 regularization was used as loss function. The image quality of the remaining 137 scans was evaluated using the MRIQC tool. Metrics were compared among the CNN-harmonized images, the original ones, and the denoised images (using an N4 bias field correction filter).
Results: A total of 12,000 2D images were synthetically generated to train the CNN. Our solution showed an improvement in MRIQC metrics, particularly in those related to contrast artifacts. Significant improvements were observed with respect to N4 and original images in intensity non-uniformity (CNN-harmonized vs N4: 19.4%, CNN-harmonized vs original: +55.2%), coefficient joint variation (CNN-harmonized vs N4: +21.6%, CNN-harmonized vs original: +43.4%), and contrast-to-noise ratio (CNN-harmonized vs N4: +14.7%, CNN-harmonized vs original: 29.1%). Signal-to-noise ratio/Dietrich's signal-to-noise ratio, which was not manipulated with the harmonization, remained similar across all scans, with N4 achieving slightly better results (+2% improvement) relative to the AI-harmonization.
Conclusion: Image harmonization is crucial to minimize heterogeneity in multi-centric studies. Our solution competes with well-established algorithms in generating high-quality images.

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P1412
Thalamic atrophy in multiple sclerosis appears to be primarily driven by lesion pathology rather than by axonal damage within the thalamus itself

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Introduction: Axonal pathology in MS can be characterized by quantification of T1-relaxation rate (R1) with multiparametric magnetic resonance imaging (MRI). R1 is reduced in axonal loss and disease progression in MS. The origin of thalamic atrophy, known as a robust marker of neurodegeneration in MS, remains unclear since lesion pathology as well as microstructural affection of the thalamus itself are potential causes.
Objectives/Aims: To investigate the association between thalamic volume and thalamic R1 compared to lesion volume (LV) and lesional R1 in RMS and SPMS
Methods: Control subjects (CS n=50), patients with secondary progressive (SPMS n=71) and relapsing (RMS n=49) MS received multiparametric MRI to calculate thalamic volume(ThV, _left/right/bilateral) and LV as well as R1 within thalamic (R1Th) and lesion (R1L) regions. Group differences and correlation between the parameters were calculated and in patients, correlation with logarithmized serum neurofilament light chain levels (sNfl) corrected for age was performed.
Results: Significant thalamic volume reduction corrected for age could be shown in MS (ThV_l RMS= 5.82ml$^{+/-0.7}$;SPMS 5.29ml$^{+/-0.8}$) compared to CS (ThV_l 6.57ml$^{+/-0,4}$;$p<0.001$) and in between patient subgroups ($p<0.02$). sNfl-levels did not differ significantly comparing RMS (2.68pg/ml$^{+/-0,1}$) with SPMS 2,86pg/ml$^{+/-0,08}$). In RMS ThV_l was correlated with LV(ρ-.732, $p<0.001$) and R1L (ρ+,382, $p<0.007$) but not with R1Th_l and sNfl. In SPMS ThV_l was correlated with Nfl(ρ-.263, $p=0.029$), LV(ρ-.619, $p<0.001$) and R1L (ρ+,3, $p<0.01$) but also not with R1Th. Unlike in RMS, in SPMS R1L was not correlated with sNfl.
Conclusion: The lack of association of the ThV_l in RMS and SPMS with the R1 within the thalamus while having evidence for association with LV and lesional R1, suggests that thalamic atrophy seems to be driven by lesion pathology rather than axonal degeneration of thalamus itself. In SPMS other competing axonal damage besides lesion pathology seems to affect thalamic atrophy reflected by the association of ThV_l with sNfl in combination with missing association of R1L with sNfl in SPMS.

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P1413
Association Between Volume and Microstructural Damage in MS Lesions

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Introduction: MS lesions vary in size and evolve over time; yet, the relationship between lesion volume and underlying microstructural damage remains poorly understood.
Objectives/Aims: To assess whether lesion size at baseline and volume change over time are associated with distinct microstructural characteristics.
Methods: People living with MS (plwMS) that underwent the Swiss MS Cohort (SMSC, annual visits with conventional Magnetic Resonance Images, MRIs) and the INsIDER study protocols (two timepoints two-year apart, including qT1 for microstructural integrity, MTsat for myelin content, and multi-shell diffusion MRI for neurite density, NDI) were selected. Follow-up images were co-registered using FSL MMORF and white matter lesion (WML) masks were manually corrected after automatic segmentation. Quantitative MRI (qMRI) measures were calculated as weighted mean within each lesion. The first analysis focused on the association between baseline lesion volume (identified on SMSC visit closest to the first timepoint of INsIDER) and qMRI measures. Based on volume and the density derived from the volume data, lesions were clustered by K-means and qMRI measures in those clusters were compared. The second analysis assessed lesion evolution and qMRI measures changes. Lesions were clustered by hierarchical clustering using baseline volume, percentage volume changes between 3 consecutive visits, and the volume change from the first to last visit. qMRI measure changes in the clusters were compared using a linear model.
Results: A total of 1151 WMLs was identified in 61 plwMS (mean age = 43; female = 64%; mean EDSS = 2.8). Based on baseline volume, 3 clusters divided WMLs into small (n = 924, median = 30.5 mm3), medium (n = 222, median = 429.8 mm3), and large (n = 5, median = 39,662.5 mm3) size. Mean qT1, MTsat, NDI in medium WMLs differed significantly from those in small WMLs (b = 79.4, -0.21, -0.07; all $p < 0.001$, respectively). Longitudinal changes in WML volume were clustered in 6 groups. Compared to the lesions with a steady volume decrease, lesions with a steady volume increase showed increasing qT1, decreasing MTsat and NDI (b = 2.4, -2.3, -3.7; $p < 0.001$, $p=0.002$, $p<0.001$, respectively).
Conclusion: We found that WMLs with larger volume had qMRI values compatible with greater demyelination, axonal damage, and reduced neuronal integrity compared to smaller lesions. Our results also showed that expanding lesions exhibited progressive microstructural damage over time, whereas shrinking lesions displayed potential signs of repair.

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P1414
Soma and Neurite Density Imaging Model applied to Multi-shell Diffusion-weighted MRI data to assess Microstructural Damage in Multiple Sclerosis

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Introduction: The in vivo assessment of the pathological mechanisms underlying disability progression in multiple sclerosis (MS) is challenging. Soma and neurite density imaging (SANDI) is a quantitative MRI model that has revealed cellular alterations in the brain normal-appearing white matter (WM) and grey matter (GM) in vivo in MS, but the evidence supporting SANDI metrics as biomarkers in clinical practice and trials is limited.
Objectives/Aims: To evaluate the potential of SANDI metrics as biomarkers for MS through assessing: differences between people with MS (pwMS) and healthy controls (HCs) across various regions of the brain and cord; their association with clinical measures; and their ability to reflect concurrent clinical worsening.
Methods: We included pwMS and HCs who underwent, at baseline (BL) and 1-yr follow-up (FU), structural (T2-FLAIR; T1-weighted) and diffusion-weighted (DW) 3T MRI scans, including multi-shell brain (b={0, 500, 1000, 2000, 3000, 4000, 5000}s/mm2; 2.2×2.2×2.2mm3) and cervical cord (b={0, 50, 1000, 2000, 3000, 4000, 5000}s/mm2; 1×1×6mm3) acquisition. The SANDI model was fitted to obtain maps of fsoma and fneurite, representing the density (signal fraction within the voxel) of neuronal soma and neurites, respectively. pwMS were assessed on the expanded disability status scale (EDSS), walking speed test, 9-hole peg test and symbol digit modalities test, at BL and 1-yr FU. Age/sex-adjusted linear regression models were used.
Results: We included 52 pwMS (age: 47.8yrs, 28 female, 77% on disease modifying therapy, disease duration: 10.2yrs) and 27 HCs (49.7yrs, 15 female). At BL, as compared to HCs, pwMS showed lower fsoma and fneurite in several brain GM structures, including cortex (fsoma 0.298 vs 0.312, p=0.039; fneurite 0.096 vs 0.101, p=0.028) and thalamus (fsoma 0.199 vs 0.211, p=0.007; fneurite 0.183 vs 0.189, p=0.044); and lower fneurite in the brain WM (0.541 vs 0.555, p=0.007). At BL, higher fsoma and/or fneurite in brain cortex and WM, thalamus, and cord GM and WM were associated with lower disability scores (p-values: <0.001 to <0.05). In pwMS, cortical fsoma and fneurite and brain WM fneurite significant decreased ($p<0.05$) over the 1-yr FU period, without differences between the few EDSS worseners during FU (N=6) and stable pwMS.
Conclusion: Based on BL results, SANDI metrics seem to reflect long-term disability accumulation in pwMS and can help understand its mechanisms; however, their sensitivity to short-term clinical changes requires further investigation.

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P1415
Spinal Cord Damage in African American and White People with Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) has a more severe course in African American people with multiple sclerosis (AA-PwMS) in comparison with non-Hispanic White PwMS (NHW-PwMS).

Objectives/Aims: The aims of our study were to measure cervical spinal cord (CSC) damage in AA-PwMS using clinical MRI and to investigate its impact on motor disability.

Methods: Subjects underwent 3T MRI with brain and CSC coils; T2-hyperintense lesion volumes were identified and measured on FLAIR images. Normalized total brain volumes were extracted from the T1 images using Freesurfer. CSC lesions were identified on cervical 2D-T2w-TIRM images. CSC cross sectional area (CSA) at C2-C3-C4 was calculated using spinal cord toolbox. Sensory-motor evaluation was performed including EDSS, 9-hole peg test (9-HPT) and 25-foot walk test (25-FWT). The Mann-Whitney U test was used to compare variables between groups. The correlation between C2 CSA and EDSS, 9-HPT and 25-FWT scores were analysed using the Spearman correlation coefficient.

Results: 54 AA-PwMS and 56 sex- and age-matched NHW-PwMS were enrolled. EDSS (2 vs 1.5, p=0.014), 9-HPT (dominant hand 25.1 vs 22 seconds, non dominant hand 25.8 vs 23 seconds, $p < 0.01$ for both) and 25-FWT (5.66 vs 2.77 seconds, $p < 0,01$) were significantly worse in AA-PwMS than in NHW-PwMS. Normalized total brain volume (0.707 and 0.715, p=0.15) and T2-hyperintense lesion volumes (4.4 and 4.0 mL, p=0.63) did not differ between groups, as well as the number of cervical spinal cord lesions (median= 1 in both groups). The C2 and C3 segment CSA was significantly smaller in AA-PwMS (73.7 and 72.6 mm^2 vs 77.3 and 76.6 $mm^{2;}$ p=0.03 for both). EDSS and 25FWT were negatively correlated with C2 CSA (p =0.03 and p =0.02).

Conclusion: AA-PwMS experience higher motor disability, despite similar brain burden. Spinal cord atrophy could explain the difference in clinical status.

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P1416
Clinical disability predictors over the disease course

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Introduction: Over recent decades, several Magnetic Resonance Imaging (MRI) biomarkers have been identified as correlates of clinical disability throughout the course of multiple sclerosis (MS). However, emerging evidence suggests that the pathological substrates underlying MS may vary over time.
Objectives/Aims: To identify and compare the relevance of MRI predictors of clinical disability (Expanded Disability Status Scale scores, EDSS) across different disease epochs.
Methods: We stratified MS patients into three groups based on disease duration: 0–5, 5–10, and >10 years. Within each epoch, Bayesian linear mixed-effects models were fitted using the brms package, with EDSS as the dependent variable. Scaled MRI-derived measures—including normalised brain, cortical grey matter, white matter, deep grey matter, thalamic, brainstem and cerebellar volumes, as well as T1/T2 ratio of T2-hyperintense lesions and normal-appearing white matter—were included as fixed effects. A random intercept for patient was added to account for repeated measures. Semi-partial R^2 values were computed to quantify the unique variance explained by each predictor.
Results: We analysed data from 245 MS patients who underwent annual 3 Tesla (3T) MRI and clinical assessments over a median follow-up of 14.4 years (interquartile range: 6.7–21.3). In the early stage (0–5 years), thalamic volume contributed most strongly to disability ($R^2 = 0.05$). During the intermediate phase (5–10 years), lesion-related metrics—T2-hyperintense ($R^2 = 0.11$) and T1-hypointense lesion volume ($R^2 = 0.08$)—explained the greatest variance, suggesting a stronger link between lesion burden and disability. In the later stage (>10 years), no predictor accounted for substantial unique variance (all semi-partial $R^2 < 0.02$), indicating a more complex and diffuse pattern of disability accumulation not attributable to any single imaging marker.
Conclusion: Our results suggest that different MRI biomarker should be monitored over the disease course, paving the way towards treatment strategies aimed to counteract specific pathological mechanisms.

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P1417
Distribution of brain lesions in MS patients and their relation to spinal cord atrophy

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Introduction: Lesion burden is a basic conventional metric for evaluating disease severity and making predictions used in routine clinical practice. Spinal cord atrophy is an important outcome measure in MS. The median upper cervical spinal cord area (MUCCA) serves as a valuable metric to quantify spinal cord atrophy. The relationship between MUCCA and the detailed topography of intracranial lesions has not been fully characterized.
Objectives/Aims: To assess the correlation between MUCCA and the distribution of intracerebral lesions, including leptomeningeal enhancement.
Methods: We examined 58 MS patients (all phenotypes): 42 females, with a mean EDSS 3.34, and disease duration of 10.31 years; and 16 males with a mean EDSS 4.17 and disease duration of 13.49 years. All MRI scans were performed on the same 3T MRI scanner (MAGNETOM Skyra, Siemens Healthcare, Forchheim, Germany). The MRI protocol included 3D: MPRAGE, FLAIR, DIR, T2, postcontrast MPRAGE and FLAIR. Spinal cord volume was assessed by measuring the MUCCA using a semi-automatic edge-detection tool. Detection of the number and localization of the intracerebral lesions were manualy evaluated by two experienced neuroradiologists (one with 24 years of experience in MS imaging) according to consensus recommendations (periventricular, deep white matter, juxtacortical, pure cortical, brain stem, cerebellum and leptomeningeal

enhancement. Linear mixed-effects model with multiple comparisons adjustment (Holm's method) was used to analyze associations between distribution of intracerebral lesions and MUCCA.
Results: Patients with presence of pure cortical lesions (adjusted p=0.0018), cerebellar lesions (adjusted p=0.0253) and brainstem lesions (adjusted p=0.0491) had lower MUCCA compared to subjects without lesions in this area.
Conclusion: The study shows the importance of detailed evaluation of the localization of the lesion by radiologists. Spinal cord atrophy evaluated with MUCCA is associated with the presence of cortical, cerebellar and brainstem lesions. If validated, these findings could enhance our understanding of the myelocortical subtype of MS and explain greater disability in patients with infratentorial lesions.

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P1418
Spinal Cord Reserve as a Novel Magnetic Resonance Imaging-Based Prognostic Marker in MS: a Multi-Center Validation Study

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Introduction: Spinal canal area (SCaA) is a proxy for maximal lifetime spinal cord growth. Recent studies suggest that a smaller cervical SCaA, as quantified with the Spinal Cord Toolbox, is associated with higher Expanded Disability Status Scale (EDSS) scores and EDSS worsening over 5 years in patients with MS.
Objectives/Aims: To validate this novel concept of spinal cord reserve in MS, using an (i) independent multi-center cohort, (ii) alternative quantification technique, and (iii) enriched set of clinical disability measures.
Methods: Our retrospective longitudinal study was conducted at the National MS Center in Melsbroek, using data from a multi-center Belgian cohort. SCaA and spinal cord area (SCoA) were measured in 714 brain MRI scans from 426 MS patients (median age 45 years, 68.2% women). Image processing relied on a deep learning model for spinal canal and cord segmentation, and vertebral labeling (icometrix, Leuven, Belgium). Two distinct quantification methods were applied: i.e., averaging values over the entire C2-C3 level (method 1) and over 10 slices centered around the C2-C3 intervertebral disk (method 2). Disability measures were repeatedly collected during clinical routine, and included EDSS, Timed 25-Foot Walk Test (T25FWT), 9-Hole Peg Test (9HPT) and Symbol Digit Modalities Test scores. For each individual, associations of SCaA with concurrent clinical disability, as with change in disability over the longest available interval, were assessed with multivariate linear regression models, adjusted for age, sex, calculated spinal cord parenchymal fraction (=SCoA/SCaA), brain T2 lesion load, and, where applicable, follow-up duration and baseline clinical scores.
Results: Mean SCaA and SCoA were 209.6 ± 32.9 mm^2 and 62.7 ± 9.0 mm^2 (method 1) and 203.5 ± 35.0 mm^2 and 61.5 ± 9.8 mm^2 (method 2), respectively. The intraclass correlation coefficient between both methods was 0.95 for SCaA and 0.96 for SCoA. SCaA was associated ($P < 0.001$) with concurrent EDSS (β -0.02, -0.02), T25FWT (β -0.41, -0.38) and 9HPT (β -0.36, -0.33) scores. Additionally, SCaA predicted ($P < 0.007$)

worsening of T25FWT (β -0.27, -0.25) and 9HPT (β -0.43, -0.44) scores over a mean follow-up of 74 ± 30 months.
Conclusion: Both SCaA quantification methods yielded highly similar results, in line with values from previous studies. Our findings reinforce the novel concept of spinal cord reserve and its association with clinical disability worsening in MS. We support the use of SCaA at C2-C3 as a prognostic factor in affected patients.

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P1419
Glymphatic dysfunction in neuromyelitis optica spectrum disorder: association with disability and brain atrophy

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a central nervous system autoimmune disease primarily mediated by anti-aquaporin-4 (AQP4) antibodies. Emerging evidence suggests that dysfunction of the glymphatic system may contribute to its pathogenesis.
Objectives/Aims: This study aimed to assess glymphatic function in NMOSD patients and explore its associations with clinical disability, brain structural alterations, and neuropsychiatric symptoms.
Methods: A total of 39 NMOSD patients and 21 age- and sex-matched healthy controls (HCs) were prospectively recruited. All participants underwent 3.0T MRI including structural and diffusion tensor imaging (DTI). Glymphatic function was evaluated using the diffusion tensor image analysis along the perivascular space (DTI-ALPS) index. Choroid plexus (CP) volume was manually segmented, and perivascular spaces (PVS) were quantified. Clinical assessments included the Expanded Disability Status Scale (EDSS), Hamilton Anxiety and Depression Scales (HAMA/HAMD), Fatigue Impact Scale (FIS), and Pittsburgh Sleep Quality Index (PSQI). Partial correlation and logistic regression were used to explore associations between imaging metrics and clinical features.
Results: In NMOSD patients, CP volume was positively correlated with lateral ventricular volume ($r = 0.46$, $p = 0.008$) and negatively with thalamic volume ($r = -0.55$, $p = 0.023$). Larger CP volume was significantly associated with higher EDSS scores ($r = 0.44$, $p = 0.002$), suggesting a potential link between glymphatic dysfunction and clinical disability. EDSS also correlated positively with HAMA ($r = 0.36$), HAMD ($r = 0.56$), and PSQI ($r = 0.53$) (all $p < 0.05$). No significant group differences were found in DTI-ALPS index or PVS volume, possibly due to limitations in imaging sensitivity.
Conclusion: Enlarged CP volume in NMOSD patients is associated with brain atrophy and increased disability, supporting the hypothesis that glymphatic system dysfunction may contribute to disease progression. Further longitudinal and dynamic imaging studies are needed to clarify its pathophysiological and therapeutic relevance.

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P1420
ConfLUNet: Instance-Level MS Lesion Segmentation in the Presence of Confluent Lesions

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Introduction: Accurate segmentation and identification of individual (i.e, instances) white matter lesions (WML) is critical for MS diagnosis, monitoring, and prognosis. Current approaches rely on semantic segmentation followed by connected components (CC) to delineate lesions. However, CC fails to separate pathologically distinct but spatially merged lesions—termed confluent lesion units (CLUs)—limiting lesion-level analyses.
Objectives/Aims: This work formally validates ConfLUNet (Wynen et al., ISBI, 2024), a novel end-to-end framework designed to directly address instance segmentation (IS) in the presence of CLUs.
Methods: The study included 63 MS patients (40 females; age 42.4 ± 12.1 years) with 3D Fluid-Attenuated Inversion Recovery (FLAIR), Magnetisation-Prepared RApid Gradient Echo (MPRAGE) (1.0 mm^3) and Echo Planar Imaging (EPI) (0.67 mm^3) scans acquired on a GE 3T scanner. Manual IS masks performed on EPI-registered FLAIR and refined using MPRAGE/EPI for challenging cases identified 1,104 WMLs (⩾3 mm), including 221 CLUs.
ConfLUNet extends a 3D nnU-Net architecture and builds on Panoptic DeepLab approach to perform IS by predicting 1)

lesion masks, 2) lesion centre prediction and 3) offset vector to the lesion centre. Inference combined predicted lesion centres and voxel offsets to directly assign voxels to lesion instances. Evaluation included panoptic quality (PQ), dice score (DSC), detection metrics F1, Recall and Precision for all lesions and CLU-wise ([CLU]). 5-fold cross-validation (CV) and inference on held-out test set was used to validate ConfLUNet.

Results: CV showed ConfLUNet outperforming CC with higher PQ (51.2% vs. 48.9%), lesion-wise F1 (77.3% vs. 74.7%), F1[CLU] (84.4% vs. 78.8%), Recall[CLU] (86.4% vs. 71.8%), and Precision[CLU] (95.8% vs. 94.8%). On the held-out test set (n=13), it maintained superior PQ (38.9% vs. 35.9%), F1 (62.4% vs. 59.1%), Recall[CLU] (83.3% vs. 71.2%), and F1[CLU] (80.2% vs. 78.9%), while CC showed higher Precision[CLU] (96.2% vs. 88.1%). DSC remained similar (70.4% vs. 69.8%). When considering all lesions in the test set, CC's recall dropped to 43.9%, whereas ConfLUNet sustained 78.0%. ConfLUNet also corrected CC's increasing undercount bias with higher lesion load.

Conclusion: ConfLUNet, the first end-to-end framework for lesion IS in MS, enhances CLU detection without compromising segmentation quality, enabling more precise lesion quantification, thus more reliable clinical correlations and more accurate treatment response monitoring. ConfLUNet's code is open source.

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P1421
Clinical Quantitative Susceptibility Mapping in Multiple Sclerosis using Inline Reconstruction

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Introduction: Quantitative Susceptibility Mapping (QSM) is increasingly utilized to assess underlying tissue magnetic susceptibility (S), reflecting paramagnetic iron or diamagnetic calcium or myelin, enabling new pathological insights into Multiple Sclerosis (MS). However, QSM typically requires complex and time-consuming offline post-processing. Here, we employed a Siemens research package for fast inline reconstruction at the scanner of skull-stripped QSM images, generating quantitative susceptibility maps [ppb] from phase/magnitude maps. The underlying Total Generalized Variation algorithm handles phase unwrapping, background field removal and dipole inversion. Thus, QSM maps become readily available for clinical use.

Objectives/Aims: We validated inline reconstructed QSM in patients with relapsing-remitting MS (rMS) and secondary progressive MS (pMS), focusing on the basal ganglia and deep grey matter (DGM), and comparing the results with published literature.

Methods: Diagnostic MR-imaging was performed in 76 MS patients (rMS=62,pMS=14), including 3D-EPI (resolution: 0.8x0.8x0.6mm³, TR/TE/FA: 71ms/35ms/10°, EF9, duration: 4:17 minutes) used for inline QSM reconstruction. QSM and T1w images were co-registered and combined into hybrid images with improved contrast. DGM regions (ROI) - including thalamus (THA) putamen (PUT), caudate (CAU), globus pallidus (GP), substantia nigra (SN), red nucleus (RN) and dentate nucleus (ND) - were segmented on the hybrid images using the HybraPD atlas. Mean and standard deviation of S in the ROI were extracted from the QSM maps, with the global brain S as reference.

Results: Mean S values across DGM regions were consistent with previous literature (in ppb: PUT=55.1, CAU=47.2,GP=103 .3,SN=94.1,RN=60.2,ND=54.5), with slightly higher S in the THA (10.8 ppb vs. -7.5 ppb in Zivadinov et al., 2018). In the GP, higher S was significantly associated with greater disability (beta=.03 P=.0002) and longer disease duration (beta=.09 P=.0008). Compared to rMS, pMS exhibited higher mean S values in the CAU, PUT, GP, SN, and ND.

Conclusion: Inline reconstructed QSM maps substantially simplify the clinical application of this quantitative technique. Compared to previous literature, we obtained consistent results for S in the DGM nuclei of patients with rMS and pMS. The diagnostic and prognostic value of the method requires further investigation in future studies.

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P1422
T1-weighted/fluid-attenuated inversion recovery ratio as a potential marker of demyelination: comparison with R1, R2 and proton density in healthy human brain

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Introduction: 3D fluid-attenuated inversion recovery (FLAIR) imaging is often preferred over T2-weighted imaging for detecting MS lesions via magnetic resonance imaging (MRI). The T1-weighted/FLAIR ratio (T1w/FLAIR) has emerged as an alternative to the T1w/T2w ratio, a marker of myelin integrity in patients with MS (pwMS). However, its relevance to white matter (WM) microstructure and myelin remains unclear. Axonal damage and demyelination can be accessed via the longitudinal relaxation rate (R1), while the transverse relaxation rate R2 reflects both myelin and iron content. Proton density (PD) indicates free water and brain tissue density, as well as edema in various disease processes.
Objectives/Aims: To assess associations between T1w/FLAIR and R1, R2 and PD as measured by multiparametric MRI in different WM regions of interest (ROI) to evaluate microstructural correlates of T1w/FLAIR.
Methods: N=56 healthy controls received 3D-T1w, 3D FLAIR and multiparametric Synthetic MRI at 1.5 Tesla. T1/FLAIR maps were calculated using a nonlinear calibration method, and registered to the interpolated and bias-corrected R1, R2 and PD maps. ROI data from 23 atlas-based WM regions (using JHU White Matter Tractography and Harvard-Oxford Cortical Atlases) were averaged in each ROI across all HC. Partial correlation analyses controlling for age were used to assess associations between T1w/FLAIR and the quantitative measures.
Results: Out of the 23 ROIs, T1/FLAIR correlated significantly with the R1 maps in 14 of the ROIs (r: 0.27 – 0.63). The comparison to the R2 maps revealed strong correlation as well (r: 0.33 – 0.64) in 20 ROIs. PD maps showed a strong negative correlation with the T1/FLAIR maps in 11 ROIs (r: -0.27 – -0.62). The overall correlation of all ROIs taken together revealed strong significant correlation for R1 ($r = 0.54$; $p < 0.0001$), R2 ($r = -0.66$; $p < 0.0001$) and PD ($r = -0.44$; $p < 0.0001$) maps.
Conclusion: T1w/FLAIR showed strong associations with R1, PD, and moreover R2, notably in highly myelinated fiber tracts. Given R1 and R2's sensitivity to myelin content in the brain and PD's link to tissue density, these findings support T1w/FLAIR as a marker of myelin content in healthy controls. Further validation with established myelin measures and in demyelinating conditions is warranted.

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P1423
Association of Sulcal Morphometry with Psychological Factors and Cognition in Multiple Sclerosis

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Introduction: Psychological factors are highly prevalent in people with multiple sclerosis (pwMS). Cognitive impairment is also pervasive. Structural neuroimaging markers have been linked to all these factors in MS, but they are limited in their predictive power. Measures of sulcal morphometry have demonstrated greater sensitivity for predicting outcomes in several neurological groups, though their utility in MS has not yet been investigated.
Objectives/Aims: Investigate the association of sulcal measures (i.e., sulcal span, surface area, mean depth) with depression, anxiety, psychosocial fatigue, and processing speed.
Methods: Sixty-nine pwMS (56 women) completed structural neuroimaging, psychological questionnaires (Chicago Multiscale Depression Inventory- Mood subscale; State-Trait Anxiety Inventory; Modified Fatigue Impact Scale- Psychosocial subscale), and the Symbol Digit Modalities Test (SDMT). Structural T1 MRI scans were segmented using FreeSurfer 6.0 and outputs were imported into BrainVisa's Morphologist toolbox to obtain sulcal measures. Six sulci (left (L), right (R) hemispheres separate)- superior frontal sulcus, central sulcus, anterior and posterior lateral fissure, superior temporal sulcus, and intra-parietal sulcus- were selected based on previous literature examining reliability, universal presence, size, and ease of identification. Raw scores for all variables were used in analyses.
Results: To account for collinearity among sulci, linear ridge regressions were conducted within RStudio. Age, sex, and estimated intracranial volume were included as covariates for psychological outcomes; education was added for SDMT analysis. Greater sulcal span in the L/R posterior lateral fissure was associated with higher reported mood, anxiety (state, trait), and psychosocial fatigue. The latter was also associated with greater sulcal span in the L superior frontal sulcus. Greater mean sulcal depth in the L posterior lateral fissure was associated with higher reported mood, anxiety (state, trait), and psychosocial fatigue. Greater mean sulcal depth in the L intraparietal sulcus and R

superior temporal sulcus were also positively associated with mood and psychosocial fatigue, respectively. Greater sulcal span in the L posterior lateral sulcus and L intraparietal sulcus were associated with poorer SDMT performance.
Conclusion: To the authors' knowledge, this is the first study to examine sulcal morphometry in relation to psychological and cognitive factors in MS. Examining sulci in MS advances the field by providing unique, detailed information of cortical folding as it relates to critical outcomes that impact the everyday lives of pwMS. Also, based on work in other neurological groups, sulcal measures may provide a more sensitive and nuanced picture of structural brain changes in MS compared to more conventional measures (e.g., cortical thickness), providing the foundation for a novel MRI biomarker for this patient group.

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P1424
Mind the Gap: Bridging Missed Monitoring with Data-Driven Intelligence in MS Care

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Introduction: Magnetic Resonance Imaging (MRI) plays a vital role in the diagnosis and ongoing monitoring of multiple sclerosis (MS). Timely imaging informs decisions on disease-modifying therapies (DMTs) and disease activity management. However, missed or delayed scans are common and can lead to suboptimal care. National guidelines from the Association of British Neurologists (ABN) and NICE recommend regular imaging to support clinical decision-making. Increasing demand often strains routine scheduling, resulting in delays, missed opportunities, and inefficient resource use.
Objectives/Aims: To develop and implement a real-time data dashboard to streamline MRI scheduling for people with MS, reduce missed scans, and improve service efficiency. The project also aimed to establish a digital infrastructure for future integration of agentic artificial intelligence (AI) to support automated monitoring.
Methods: In collaboration with the Information Department, a live Tableau dashboard was created to integrate patient data from multiple sources. This tool identifies patients due or overdue for MRI based on predefined criteria and facilitates monthly administrative sessions to efficiently review and process scan requests. The system was embedded into clinical workflows using a dedicated four-hour monthly admin slot.
Results: Missed MRI appointments dropped significantly from 30.9% to 1.80% within the MS service. The structured model reduced clinician time spent on MRI requests from an estimated 113–170 hours per year to 48 hours, representing a 71% time saving. Radiology departments were also able to allocate scan slots more efficiently and minimise financial losses from unused appointments.
Conclusion: The implementation of a data-driven MRI tracking tool significantly improved workflow efficiency and reduced missed imaging in MS care. This project provides a foundation for integrating agentic AI systems capable of autonomously detecting missed investigations, prompting timely action, and enhancing personalised, proactive care. Expansion of this model to monitor blood tests for patients on DMTs is currently underway.

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P1425
Transverse myelitis in AQP4-antibody NMOSD is associated with structural changes in the cerebral somatosensory pathway

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Introduction: Transverse myelitis (TM) linked to AQP4-antibody-positive neuromyelitis optica spectrum disorder (AQP4-NMOSD) poses a considerable risk for severe motor and sensory impairments. TM in AQP4-NMOSD typically affects multiple segments of the spinal cord, inflicting significant localized damage. However, the broader implications of this damage on motor and sensory pathways in both the brain and spinal cord remain largely unknown.
Objectives/Aims: The aim of this study is to examine the microstructural changes in the motor and somatosensory pathways of the spinal cord and brain in AQP4-NMOSD patients with a history of TM.
Methods: We used advanced MRI techniques, including NODDI and MP2RAGE, to assess the integrity of the motor and somatosensory tracts at various locations in the brain and spinal cord of 18 AQP4-NMOSD patients who have a history of TM compared to 20 healthy controls (HC).

Results: In patients with AQP4-NMOSD, the average age was 50.13 years, with a disease duration of 8.8 years (ranging from 0.5 to 29 years). These patients experienced a median of 2.5 attacks and had a median Expanded Disability Status Scale (EDSS) score median of 4 (1 to 7.5). Comparative analyses revealed a notable reduction in cross-sectional area (mean: 63.62 vs. 70.75, $p = 0.016$) and fractional anisotropy in the cervical spinal cord's dorsal columns (mean: 0.59 vs. 0.65, $p = 0.018$) and lateral columns (mean: 0.57 vs. 0.62, $p = 0.021$) when compared with healthy controls. In the brain, AQP4-NMOSD patients had an increased isotropic volume fraction in the ventral posterolateral nucleus (VPL) (0.06 vs. 0.05, $p = 0.03$), decreased neurite density index in several segments the superior thalamic radiation, and reduced T1 relaxation rates in the primary somatosensory cortex when compared with HC (mean: 0.72 vs. 0.74, $p = 0.04$). No significant differences in these metrics between study groups were observed in the cerebral motor pathway. Additionally, a significant correlation was found between neurite density in the VPL and EDSS in AQP4-NMOSD patients ($r = -0.469$, $p < 0.05$).
Conclusion: Patients with AQP4-NMOSD who experienced TM demonstrate significant structural changes in the somatosensory pathway in both the brain and spinal cord, which are closely linked to clinical outcomes. Future research will examine the temporal dynamics of these changes after TM and investigate their potential as significant endpoints in clinical trials for AQP4-NMOSD.

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P1426
Analysis of the Inflammatory Metabolic Component of Lesions in Patients with Multiple Sclerosis using Multivoxel Spectroscopy and Histograms in an IMMS Tertiary Referral Public Hospital, Puebla, Mexico

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Introduction: Multiple Sclerosis (MS) is a neurodegenerative autoimmune disease affecting the central nervous system. While Magnetic Resonance Imaging (MRI) identifies active inflammatory lesions, the MAGNIMS criteria, crucial for diagnosis, do not include more sensitive techniques to quantify inflammation. Multivoxel Spectroscopy (MVS) and histogram analysis have demonstrated efficacy in detecting subtle inflammatory activity in other neurological diseases, suggesting potential utility for MS.
Objectives/Aims: To demonstrate the effectiveness of MVS and histogram analysis in identifying inflammatory activity during the treatment of patients with MS.
Methods: A prospective longitudinal study was conducted at a tertiary referral centre. Clinical and radiological data were collected, including Multivoxel Spectroscopy (MVS) and histogram analysis. The MVS data underwent post-processing and fusion with the DIR sequence to assess metabolic activity in regions of interest. The analysis specifically focused on the inflammatory metabolites Lactate and Lipids (L-L). Descriptive and inferential statistics were used for analysis.
Results: Thirty-three MS patients were included (22 women, 12 men), with 75.75% having Relapsing Remitting MS. While 94.12% showed no contrast enhancement on MRI, MVS detected inflammatory activity in 76.4%. Based on L-L behaviour, four MVS inflammatory activity groups were defined: Null (inverted/below average L-L peaks), Mild (elevated L-L but below creatine), Moderate (L-L above creatine but below N-acetyl aspartate), and High (lipid/lactate above creatine and N-acetyl aspartate). Each drug treatment group was further classified according to their inflammatory activity. No inflammatory activity was detected in patients treated with Natalizumab (n=3). Logistic regression showed a higher odds ratio for inflammation with Interferon (n=19; OR=8.5) and a lower odds ratio with Rituximab (n=7; OR=0.16). Predicted probabilities of inflammation were highest for Interferon Beta (89%) and lowest for Rituximab (57%).
Conclusion: MVS and histogram analysis proved to be effective biomarkers for detecting inflammatory metabolic activity and evaluating pharmacological responses, outperforming contrast-enhanced MRI. A larger and more treatment-diverse sample is required.

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P1427
Automated MS Lesion Detection with NeuroQuant: Comparing the Hybrid Machine and Deep Learning Version to Its Predecessor

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Introduction: NeuroQuant® MS (NQ-MS) is software for detecting and analyzing multiple sclerosis (MS) lesions and lesion burden, categorized by brain regions based on McDonald criteria. When NQ-MS was updated to 4.0, a hybrid machine and deep learning (ML/DL) algorithm was integrated, evaluated in this study for visual and statistical performance against its predecessor.
Objectives/Aims: We hypothesized that ML/DL integration enhances lesion detection, assessed visually and through statistical analysis.
Methods: Fifty-one subjects with MS were scanned with NQ-MS compatible T2w-FLAIR and T1w-MPRAGE data on a 1.5T Siemens Aera MRI with a 20-channel head coil, as a part of a larger study. In NQ-MS, lesion detection volume was set to a minimum of 3 mm^3 with 1 mm separation. In the previous NQ-MS version 3.1, sensitivity thresholds (scale 0–2) were applied. First with the default of 1.0, then adjusted to 1.2 for periventricular lesions to avoid detecting non-lesion structures. Segmentation results will be reviewed by an MS-specialized neuroradiologist. Statistical analysis with R Software (v4.3.0) compared both NQ-MS versions using paired t-tests for each brain region.
Results: Lesion counts and volumes were higher in version 4.0 compared to 3.1: juxtacortical ($p<0.001$); deep white ($p< 0.001$); infratentorial ($p< 0.001$), except for periventricular lesions, which showed a significant reduction ($p< 0.001$). Version 4.0 also had a larger total lesion burden for all brain regions ($p< 0.001$). Visual inspections did not reveal more lesions segmented by version 4.0. The lesions detected looked more precisely filled and delineated compared to earlier versions. Recalculating with adjusted sensitivity for periventricular lesions (1.0 vs 1.2) removed the statistical difference between version 4.0 and 3.1.
Conclusion: This study compared two software versions using identical imaging data. The latest version, incorporating a neural network trained on MS data, exhibited higher sensitivity without needing sensitivity adjustments, along with improved lesion detection. These findings underscore the impact that different post-processing tools can have on results. They also emphasize the advancements achieved through ML and DL integration.

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P1428
Correlation of Choroid Plexus Volume with clinical, CSF, and neuroradiological characteristics in early-stage Relapsing-Remitting Multiple Sclerosis

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Introduction: An emerging factor in MS is the alteration of blood-cerebrospinal fluid barrier (BCSB), which seems to play a significant role in the early stages of MS. The choroid plexuses (ChP) volume is considered a marker of BCSB activation and correlates with disease severity.
Objectives/Aims: This study aims to evaluate whether the volume of the ChP correlates with clinical, cerebrospinal fluid (CSF) and neuroradiological characteristics in relapsing-remitting MS patients naïve to disease-modifying therapies.
Methods: A retrospective sample of 10 controls and 50 MSRR patients was analysed. All subjects underwent blood sampling, lumbar puncture, and 3T brain MRI. CSF was examined for Q_{Alb} (Alb_L/Alb_S), oligoclonal bands, NfL and YKL-40. The analysis included the EDSS score at baseline, brain volumes and cerebral lesion volume. The volume of the ChP was obtained from manual segmentation at the level of the lateral ventricles in 3D-T1 sequences. All brain volumes were normalized for total intracranial volume.
Results: The ChP volume was higher in patients compared to controls (p=0,035) and in MS patients it correlates positively with Q_{Alb} (ρ=0,338, p=0,016) and negatively with total brain volume, grey matter volume, and white matter volume (ρ=-0,379, ρ=-0,283, ρ=-0,353, $p<0,05$). No correlation was detected with the other variables under analysis.
Conclusion: The volume of the choroid plexuses correlates with disease progression defined by the degree of brain atrophy.

Disclosure of interest: Nothing to disclose.

P1429
Depression in MS is associated with functional and effective connectivity disruptions of the dopaminergic reward circuit

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Introduction: Although depression is one of the most common and debilitating comorbidities in MS, its neurobiological mechanisms remain still poorly understood. Increasing evidence highlights that impaired functional connectivity (FC) within the reward circuit plays a key role in the pathophysiology of major depressive disorder (MDD). On this basis, a similar functional dysconnectivity has been proposed as a potential mechanism underlying depression in MS.
Objectives/Aims: The present study aimed to investigate functional and effective connectivity of key nodes of the reward circuit in MS patients with depression (MS-D), as compared with MS patients without depression (MS-nD) and patients with major depressive disorder without MS (MDD). Specifically, the study had two main objectives: (1) to assess how depression

affects FC in patients with MS by comparing MS-D and MS-nD; (2) to assess whether MS-related depression presents distinct neurobiological features relative to MDD in the absence of MS by comparing MS-D and MDD.
Methods: Firstly, we carried out a FC analysis with ventral tegmental area (VTA) and nucleus accumbens (NAcc) as regions of interest. Secondly, Dynamic Causal Modelling (DCM) was applied to fMRI data in order to investigate how MS-related depression could impact, besides FC of the reward circuit, the direct causal influences of its nodes (i.e. effective connectivity, EC).
Results: Results showed a reduced FC in MS-D compared to both MS-nD and MDD. Additionally, DCM revealed increased inhibitory self-connections, a negative modulation of the VTA in MS-D vs. MS-nD, and a negative modulation between the VTA, NAcc, and right amygdala as effect of having depression.
Conclusion: These findings provide new insights into the neurobiological mechanisms underlying depression in MS and highlight the potential of combined FC-EC investigation as MRI biomarker for understanding the onset of core depressive symptoms and supporting the development of personalized therapies.

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P1430
Bridging the MRI Divide: Impact of National Standardisation on MS Imaging Quality in Czechia

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Introduction: MRI is central to MS care, a role further reinforced by the 2024 revision of the McDonald criteria. Although MS care is centralised in Czechia, MRI is often performed by external providers, contributing to variability. Unfortunately, the clinical impact of MRI remains limited by inconsistent protocols and reporting. In response, Czech experts issued national MRI guidelines in 2024 (Vaneckova et al.), introducing core protocols and structured reporting, with an initial focus on MRI units within MS centres.
Objectives/Aims: To evaluate the impact of MRI standardisation in Czech MS care and identify remaining barriers to quality and consistency.
Methods: All 15 Czech MS centres completed a 27-item survey before and again 6 months after the 2024 national implementation of MRI standardisation guidelines. Between both rounds, national recommendations were published, and an educational campaign was conducted. The survey assessed, e.g. protocol adherence, use of DIR and SWI sequences, spinal cord imaging, DIS/DIT, structured reporting, and collaboration with external radiology providers. Results were analysed descriptively.
Results: Following the initiative, DIR and SWI sequence usage increased by 20%, and follow-up scheduling at recommended timepoints (baseline, 6 months, annually) improved by 25%. Internal MRI departments achieved 100% consistency in assessing DIS/DIT, reporting lesion count and localisation, and comparing with previous scans. Most reports from both internal and external providers included assessments of MS-typical findings and prognostic markers. External MRI reports also showed improvement but remained more variable. Spinal cord imaging was often incomplete, with full sagittal coverage in 2 sequences present in only a minority of cases. Overall, 84% of external reports were considered clinically insufficient due to missing sequences, limited spinal cord imaging, or vague conclusions. On average, each MS centre collaborated with three external MRI departments (range 1–16).
Conclusion: MRI standardisation led to measurable improvements in imaging quality and monitoring, with particularly strong gains in internal radiology units. While peripheral MRI sites also improved, variability persists. Although greater centralisation remains a desirable goal, full centralisation is not feasible. The next phase of the initiative focuses on supporting external radiologists through training and implementation of structured reporting tools to ensure high-quality MRI access for all patients with MS.

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P1431
Comparison of two methodologies for measuring lesion volume evolution in Multiple Sclerosis

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Introduction: Assessing lesion volume evolution (LVE) in MS patients is important to evaluate disease progression. This can be done using various methods, including calculating the volume of white matter lesion (WML) masks at each time point and summing the Jacobian determinant (JD) within the baseline WML mask after longitudinal nonlinear registration. It is unclear which method is more closely linked to pathologic changes. MS pathological features can be assessed using quantitative MRI (qMRI) and fluid biomarkers such as serum neurofilament light chain (sNfL), a measure of neuroaxonal damage.
Objectives/Aims: To evaluate the correlation between LVE assessed using two different methods (JD and WML) and markers of tissue integrity from two methods: (i) qMRI and (ii) sNfL.
Methods: 1151 lesions from 61 people with MS who were part of both the Swiss MS Cohort (annual conventional MRI scans) and the INsIDER study (baseline and 2 years follow-up scans with quantitative T1 (qT1) for microstructural integrity, MTsat for myelin content, and neurite density index (NDI) for axonal integrity) were included. Fluid attenuated inversion recovery (FLAIR) images were co-registered using FSL MMORF. WML masks were automatically generated and manually refined by an

expert. The LVE was derived using both WML and JD methods. qMRI measures were computed as the percentage change of the qMRI mean values within each registered WML. WMLs were hierarchically clustered by baseline volume and volume change over time points. We found six JD-based clusters, including one with steady increases and one with steady decreases in WML volume (JD_+ and JD_-). In contrast, nine clusters were found based on longitudinal changes in WML masks, including two with steady increases (one steeper) and two with steady decreases (one steeper) ($Long_+$, $Long_{+steep}$, $Long_-$, and $Long_{-steep}$). To compare the methods, $Long_+$ and $Long_{+steep}$ were combined ($Long_+$ thereafter), as 59% of their lesions overlapped with JD_+. Linear regression models were applied to compare the qMRI metrics between JD_+ and JD_-, as well as $Long_+$ and $Long_{-steep}$. Two linear regression models were applied between age- and BMI-adjusted Z-scores of sNfL at the second INsIDER timepoint, and the number of increasing lesions (JD_+ or $Long_+$), adjusting for new lesions and sNfL Z-scores from the first timepoint.

Results: For both the methods, the lesions decreasing in volume showed decreasing qT1 (β=-2.4/-1.9, $p<0.001$), increasing MTsat (β=2.3/1.88, p=0.003/0.022) and NDI (β=3.8/2.6, $p<0.001$/0.01) when compared to lesions increasing in volume. Z-score sNfL correlated positively with the number of lesions increasing in volume per patient when using both methods (β=0.07/0.08, p=0.012/0.006).

Conclusion: The associations between volumetric lesion changes over time and microstructural changes were evident even when different methods were used for measuring LVE and across various methods used to assess tissue damage, including qMRI and sNfL.

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P1432
Assessing Structural Differences in Late-Onset compared to Adult-Onset Multiple Sclerosis: A Multiparametric MRI Study

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Introduction: The prevalence of people with multiple sclerosis (PwMS) with onset at or after age 50 (late-onset, PwLOMS) is increasing. Previous studies have identified MRI differences between PwLOMS and people with adult-onset MS (PwAOMS), but a comprehensive analysis of global and regional white matter (WM) and gray matter (GM) metrics is lacking.

Objectives/Aims: By using a multiparametric approach, we compared the structural MRI profiles of PwLOMS and PwAOMS, focusing on global and regional assessment of WM lesions, GM volume and diffusivity abnormalities in the WM.

Methods: Brain 3T MRI scans were acquired for 40 PwLOMS, 195 sex- and disease duration-matched PwAOMS and 175 sex- and age-matched healthy controls (HC) divided in two groups (HC-AOMS=125 and HC-LOMS=50). We applied false discovery rate (FDR) for conventional MRI analysis and family-wise error correction (FWE) for voxel-wise analysis, with a $p<0.05$ considered statistically significant.

Results: Both PwAOMS and PwLOMS showed higher T2 lesion volume (T2-LV) compared to their HC-groups, with PwLOMS showing higher T2-LV than PwAOMS (FDR-$p\leqslant0.004$). Compared to their HC-groups both PwLOMS and PwAOMS showed significant reductions of all volumetric measures (FDR-$p\leqslant0.006$), except for the pallidus in PwLOMS. In addition, PwLOMS showed a significantly higher lesion frequency than PwAOMS in the left superior longitudinal fasciculus (FWE-p=0.003). Both MS groups had lower fractional anisotropy and higher mean diffusivity, axial diffusivity and radial diffusivity values in the majority of WM tracts (all FWE-$p<0.05$) compared to respective HC-groups, without any age×disease interaction effect. Compared to their HC-groups

both PwAOMS and PwLOMS showed widespread GM atrophy (FWE-p$<$0.05), and a significant age$\times$disease interaction effect was found, with a larger effect of MS on lowering GM volume in the left paracentral lobule, insula, bilateral putamen, and right pre- and post-central gyrus occurring in PwLOMS compared to PwAOMS (all FWE-p$\leqslant$0.040).

Conclusion: Compared to sex- and disease duration-matched PwAOMS, PwLOMS had a worse structural profile, mostly characterized by more severe GM atrophy and higher WM lesion burden, highlighting the need for targeted assessments and interventions.

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P1433
Whole brain volume loss (BVL) is associated with a short-term disability progression in relapse-activity free multiple sclerosis

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Introduction: Reliable biomarkers for disability progression independent of relapse activity in multiple sclerosis (MS) are needed.

Objectives/Aims: This study reports initial results from a multicenter, prospective, observational study in Germany investigating the association between brain volume loss (BVL) and short-term disability progression under routine clinical care.

Methods: A total of 544 active relapsing remitting patients with baseline (BL) and one-year follow-up (FU) visits were enrolled across 21 sites. Medication, relapse activity, and EDSS were recorded at each visit. MRI included 3D-T1 and 2D/3D-FLAIR. BL scans provided T2-lesion volume and number and brain parenchymal volume (BPV, z-scores); from FU scans new/enlarged T2-lesions and BVL (annualized) was computed. In addition to EDSS, the SUM-EDSS (sum of sub-scores) was applied. Disability progression was defined as ΔEDSS$>$0 or ΔSUM-EDSS$>$0. Pearson/Spearman correlations and logistic regression assessed associations with BVL/year.

Results: At BL mean(std): EDSS: 2.0(1.3), SUM-EDSS: 5.2(4.6), disease duration:7.6(7.1) years, T2-lesion volume: 7.0(9.9) ml, BPV z-score: -1.0(1.2). Change (FU-BL): ΔEDSS: 0.0(0.6), ΔSUM-EDSS: 0.0(2.1), BVL/year: -0.3(0.5) %, age-adjusted: -0.1(0.5) %, new/enlarged T2-lesions 0.5(1.4). At FU, 71% were relapse activity-free during the observation period, 70% had no new/enlarged T2-lesions, and 51% were free of both. Strongest BL correlations (Pearson/Spearman) (p$<$0.001) were observed between BPV z-scores and EDSS (r=-0.33/ρ=-0.29) and SUM-EDSS (r=-0.40/ρ =-0.33). BVL/year correlated with ΔEDSS (r=-0.12/ρ=-0.11, p$<$0.05) and ΔSUM-EDSS (r=-0.21/ρ=-0.19, p$<$0.001). Correlations remained significant in the relapse activity-free sub-cohort.

Patients with progression (ΔSUM-EDSS>0) showed higher BVL/year (-0.26%) vs. stable patients (-0.09%, p<0.001). BVL/year was a significant predictor in logistic regression (p<0.001), 1% increase in BVL/year was associated with a 90% increase in the odds of disability progression.
Conclusion: BVL over one year was significantly associated with disability progression in the absence of relapses or new lesions, supporting its value as a short-term risk marker in MS. These findings underscore BVL as a potential biomarker of neurodegeneration and silent disease progression, and support its integration into clinical monitoring

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P1434
Structural Markers of Cognitive Decline in MS

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Introduction: While physical symptoms in persons with MS (PwMS) are widely recognized, cognitive impairment in MS remains underappreciated, despite having significant impacts on quality of life. Recent evidence has linked cognitive deficits with grey matter neurodegeneration. To this end, MRI has become essential for quantifying atrophy and demyelination in PwMS through volumetric analysis and the T1w/T2w ratio, respectively.
Objectives/Aims: To investigate the relationship between performance on the Symbol Digit Modalities Test (SDMT) and MRI indicators of neurodegeneration in PwMS.
Methods: Subjects with a confirmed MS diagnosis, recruited as part of a longitudinal study which the SDMT was the primary outcome, also had a 3T MRI completed at baseline. T1-weighted images were processed with Freesurfer to obtain cortical thickness, and thalamic nuclei volumes were derived using Thalamus Optimized Multi-Atlas Segmentation (THOMAS) was used to obtain thalamic nuclei volumes. The T1w/T2w ratio was sampled on the midthickness and used as a surrogate measure for cortical myelin content. We compared MRI outcomes in subjects impaired vs. not impaired on SDMT (Canadian norms), defined as z-score worse than 1.5 SD below the mean. Specifically, Welch's t-test was implemented for the subcortical mask volumes while general linear models enabled vertex-wise comparison of cortical thickness and T1w/T2w values.
Results: There were 100 subjects with both SDMT and MRI data available: age 46.2 (SD 12.4), 75 females, with 14.2 (SD 2.3) years of education. The median EDSS was 2.0 (range 7.0). The mean SDMT was 58.9 (SD 11.0) corresponding to a z-score of 0.1 ± 1.0. Only 7 subjects were found to be impaired on the SDMT. MRI revealed statistically significant greater cortical thinning and thalamic atrophy in the cognitively impaired group. Cortical thinning was localized to the superior frontal regions, particularly in the left hemisphere. Thalamic atrophy was localized to the anteroventral, pulvinar, and lateral geniculate nuclei of the left thalamus. There were no significant differences in cortical myelin content between groups.
Conclusion: Impairment on the SDMT in PwMS was marked by predominantly left-lateralized cortical and thalamic atrophy, while differences in cortical myelin content were not statistically significant. Our findings suggest that MRI markers of grey matter atrophy may support early prediction of cognitive outcomes.

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P1435
Amygdala volume changes as a potential marker of multiple sclerosis progression - about the relationship between the atrophy pattern, Expanded Disability Status Scale (EDSS) and progression independent of relapse activity (PIRA)

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Introduction: Assessment of brain atrophy may be a promising marker of relapsing-remitting multiple sclerosis (RRMS) progression, but it is currently not widely used in clinical practice.
Objectives/Aims: The study aimed to assess the correlation of disability measured by the Expanded Disability Status Scale (EDSS) and progression independent of relapse activity (PIRA) with volumetric changes in patients with RRMS treated with cladribine tablets (CLAD) and alemtuzumab (ALEM).
Methods: Clinical and magnetic resonance imaging (MRI) data from patients with RRMS were retrospectively analyzed at 4 time points (pretreatment and 3 years of follow-up). Volumetric data were obtained from MRI using the FreeSurfer. Annual volumetric and EDSS changes were pooled together to examine short-term associations and patient-wise analyses were performed. Simple linear regression was performed, and two-sided p-values were reported.
Results: 33 patients treated with CLAD (mean age 41.4 years; 77% women) and 19 patients treated with ALEM (mean age 33.3 years; 100% women) were included. Analysing year-to-year correlations, significant positive correlation was found between EDSS and amygdala volume changes ($p = 0.00007$, $R = 0.39$) in both treatment groups and with a similar strength. It was also observed for the pallidum ($p = 0.0152$, $R = 0.25$). When comparing annual percentage volume changes across three groups—years with EDSS progression ($n = 10$), regression ($n = 11$), and no changes ($n = 74$)—significant differences were found in amygdala ($p < 0.01$; 1.98%, -4%, -0.8%), thalamus ($p = 0.03$; -0.54%, 2.98%, 0.1%) and pallidum ($p = 0.02$; 1.98%, -6.96%, -0.23%). Additionally, among the 10 patients with EDSS progression, an increase in amygdala volume was observed in 3 patients with PIRA, whereas it was not seen in the 7 patients whose EDSS progression was associated with relapsing activity ($p = 0.0188$; 4.60% vs. 0.004%).
Conclusion: The study showed association of EDSS progression with an increase in amygdala (and to a lesser extent pallidum) volume in RRMS patients during a 3-years follow-up. Conversely, progression of disability measured by EDSS was associated with a decrease in the thalamus volume. Interestingly, an increase in amygdala volume was observed in patients with PIRA-related progression compared to patients with relapse-associated worsening. This could suggest the possibility of using this area as a volumetric marker of disease progression. However, further research are needed to fully understand these relationships.

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P1436
Investigating the Early Pathogenesis of Multiple Sclerosis: Insights from 7T MRI in Patients with Earliest Monofocal Demyelinating Events

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Introduction: Understanding the earliest pathophysiological mechanisms underlying MS remains a major challenge. In the large majority of cases, the diagnosis of MS is currently established after a first clinical event based dissemination in space and time on MRI (presence of lesions of different ages). This supports the hypothesis that this first event does not represent the real onset of the disease. In rare cases, patients present with a single lesion on brain or spinal cord MRI that expresses the symptom but without meeting the MRI criteria for dissemination in time and space (Earliest Monofocal Demyelinating Events-EMDE). In this condition, the clinical onset might correspond to the earliest manifestation of the inflammatory demyelinating process.
Objectives/Aims: To investigate i) Focal and diffuse White (WM) and Grey Matter (GM) damage in a cohort of patients assessed on brain 7T MRI within 6 months of an EMDE, ii) the potential relationship between WM and GM injury, iii) their clinical impact.
Methods: 30 patients have been included (optic nerve (ON), spinal cord (SC short myelitis), brain hemisphere (BH), or brainstem (BS) presented with a single lesion related to the inaugural symptom without additional lesions identified on brain and spinal cord MRI, and with the presence of oligoclonal bands on CSF analysis. All subjects underwent brain ultra-high-field 7T MRI (MP2RAGE, FLAIR, FLAWS, T2*, T1Gad, DTI and 23Na sequences) to assess focal and diffuse WM and GM damage (WM lesions, intracortical (IC) and leukocortical (LC) lesions, qT1, WM and GM fraction, volume and total sodium accumulation). EDSS, MSFC and cognitive scores have been obtained the same day. A group of 30 matched controls has also been included for cognitive testing and 7T MRI comparisons.
Results: Patients characteristics: 21 females and 6 males (3 patients have been excluded), mean age = 31.2yo; mean disease

duration = 4.7 months; mean EDSS = 0.2. First event: SC=8, ON=6, BS=7, BH=6.
Main findings: 70% have no ICLs and 70% no LCLs (60% had neither ICLs nor LCLs, and 100% in case of inaugural SC lesion). A central vein sign (CVS) was present in all identifiable HC lesions, but no paramagnetic rim lesion (PRL) was detected. A significant correlation (p=0.1) was observed between WM and LC lesions but no significant correlation was found between IC and WM injury, nor between WM and GM damage and clinical evaluations. No significant diffuse WM and GM damage was observed when comparing patients to controls.
Conclusion: We first evidenced that the prevalence of cortical lesions is very low at the earliest stage of MS. Our findings also suggest that pathophysiological mechanisms underlying WM and GM damage at this early phase of the disease are distinct. Longitudinal follow-up of this cohort will offer further insights into the dynamics of WM and GM damage and their clinical impact.

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P1437
Dynamic Causal Modelling revealed altered effective connectivity between primary visual cortex and lateral geniculate nucleus in AQP4-NMOSD patients with optic neuritis

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Introduction: Visual dysfunction following attacks of optic neuritis (ON) represents a severe clinical manifestation of neuromyelitis optica spectrum disorder (NMOSD). Neuroimaging studies linked such visual impairment to functional disruptions, such as increased functional connectivity (FC) within the visual network in NMOSD testing positive for specific IgG auto-antibodies targeting aquaporin-4 (AQP4) compared to healthy controls (HC). Although this enhanced FC is thought to reflect a compensatory response to visual damage, the effective connectivity (EC) between visual areas and other key regions involved in visual processing, such as the lateral geniculate nucleus (LGN) of the thalamus, remains unexplored.
Objectives/Aims: The present study aimed to investigate whether and how increased resting-state FC in AQP4-ON patients within the visual network is accompanied by altered causal interactions between key nodes of the visual pathway.
Methods: Resting state FC analysis was carried out on 12 HC and 12 AQP4-ON patients. Firstly, seed-based analysis was used to generate FC maps of the visual network. Secondly, FC values of the primary visual cortex (V1) were extracted and compared between HC and AQP4-ON. Finally, Dynamic Causal Modelling (DCM) was applied to fMRI data to assess EC between V1 and LGN.
Results: AQP4-ON exhibited a significant FC increase within the visual network, including V1 and lateral occipital cortex (peak coordinates: x=+06, y=-92, z=+34; cluster size k>2000; p<0.05 with Family Wise Error correction). On the contrary, FC between V1 and LGN was significantly lower in AQP4-ON patients compared to HC (p=0.03). Additionally, the EC analysis revealed inhibitory self-connection of LGN and inhibitory modulation from LGN to V1 with posterior probability >95% (strong evidence).
Conclusion: The altered EC observed in AQP4-ON suggests that a pronounced FC increase within the visual network could also be associated with maladaptive processes such as inhibitory modulation between regions. These findings highlight how DCM can provide deeper insights into the neural mechanisms underlying FC changes in AQP4-ON.

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P1439
Lesion Distribution Criteria on Conventional MRI for MS, NMOSD, and MOGAD Differentiation

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Introduction: Multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) can share similar clinical and radiological features which, depending on disease course and serologic tests' timing/availability, may pose diagnostic challenges.

Objectives/Aims: We aimed to identify sets of conventional MRI lesion distribution criteria proposed for disease differentiation and to investigate their clinical utility.

Methods: We searched MEDLINE, SCOPUS, Web of Science, ProQuest, Google Scholar (from inception to January 2025) for English-written and peer-reviewed diagnostic accuracy studies examining sets of lesion distribution criteria and including at least brain MRI. Screening, data extraction and quality assessment (QUADAS-2) were done in duplicate, complying with the PRISMA statement. Diagnostic accuracy meta-analysis was performed using hierarchical and univariate random-effects logistic regression models. We conducted subgroup analyses on race/ethnicity and MRI timing. Certainty of evidence was assessed with the GRADEpro tool.

Results: We identified three sets of criteria ("Matthews", "Cacciaguerra", "MS lesion checklist"), investigated in 11 studies totally (2041 patients; MS, n=1037; NMOSD, n=862; MOGAD, n=142), with low applicability concerns. Sequences included T1, and T2-weighted fluid-attenuated inversion recovery. Pooled sensitivity and specificity of the Matthews brain

MRI criteria were: 0.92 [0.86, 0.96] and 0.85 [0.79, 0.90] for MS vs seropositive-NMOSD; 0.93 [0.84, 0.97] and 0.90 [0.80, 0.95] for MS vs seronegative-NMOSD; 0.86 [0.81, 0.90] and 0.87 [0.76, 0.93] for MS vs MOGAD. Results were sustained among subgroups, with higher diagnostic values in non-Caucasian populations and during follow-up. Diagnostic performance was strongest in Asian populations (positive likelihood ratio = 7.08 [4.89, 10], negative likelihood ratio = 0.17 [0.13, 0.23]). Pooled sensitivity and specificity of the Cacciaguerra brain-spinal cord criteria for NMOSD vs MS differentiation were 0.96 [0.75, 0.99] and 0.83 [0.71, 0.90], respectively. The MS lesion checklist was evaluated in one study, showing lower sensitivity and specificity (0.74, 0.79, respectively) for MS vs NMOSD/MOGAD differentiation. Among all sets of criteria, the Matthews criteria provided the strongest moderate certainty evidence.

Conclusion: Lesion distribution criteria can accurately discriminate between MS, NMOSD and MOGAD. Further optimized validation studies, revisions, and extensions may support sustained implementation.

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P1440
Support vector machine predicts 2-year MS disease progression using MRI, blood serum biomarkers, and clinical data

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Introduction: Multiple sclerosis (MS) disease progression is difficult to predict. There is currently no unique imaging or blood serum biomarker to reliably determine if and when the disease will worsen. Combining potential biomarkers and training a machine learning model may provide a more accurate prediction of personalized disease worsening.

Objectives/Aims: Predict the 2-year risk of MS progression using a support vector machine (SVM) trained on baseline imaging, blood serum biomarkers, and clinical data.

Methods: Clinical data were collected at baseline, year 1 and year 2, and were used to identify patients progressing in their clinical disease based on predefined criteria.
Baseline diffusion tensor imaging (DTI) data was used to calculate the fractional anisotropy (FA), which reflects tissue integrity, and myelin water imaging (MWI) was used to extract the mean myelin water fraction (MWF, myelin content), standard deviation (SD, myelin heterogeneity), and myelin heterogeneity index (MHI=SD/MWF, myelin damage composite measure). 71 immune-related proteins were quantified by nELISA in blood serum samples at baseline. An SVM was trained to classify patients as progressor or non-progressor at 2 years. The accuracy, sensitivity, and precision were calculated with 5-fold cross-validation. Bagging and recursive feature elimination with cross-validation (RFECV) were implemented to reduce bias and variance and improve model accuracy.
Results: The cohort of 107 (79 F) participants included 73 with relapsing-remitting MS, 15 primary progressive MS, and 19 radiologically isolated syndrome. 44 people with MS were identified as progressing in their clinical disease. The mean age was 42yrs (24-63), disease duration 3yrs (1-13), and median EDSS was 1.5 (0-6). SVM achieved an AUC of 0.80, accuracy 0.85, sensitivity 0.67, and precision of 0.87. The discriminant features selected by RFECV included mean MWF, SD, and MHI, as well as FA. The most discriminant proteins were Eotaxin, FLT-3L, IP-10, and TRAIL. Clinical features predictive of MS progression included age, disease duration, EDSS, and sex.
Conclusion: SVM trained on multimodal clinical data, MRI, and blood biomarkers showed promising results in predicting 2-year risk of disease progression, which demonstrates the clinical utility of MWI, DTI, blood serum biomarkers, and clinical data. SVM could become a tool facilitatingin the delivery of personalized treatment recommendations for people with MS.

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P1441
Age-Dependent Divergence of FLAIR and QSM Lesion Volumes in Multiple Sclerosis: A Longitudinal and Stratified Analysis

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Introduction: Quantitative susceptibility mapping (QSM) provides iron-specific contrast for MS lesions, while Fluid Attenuated Inversion Recovery (FLAIR) captures mixed pathologies including vascular lesions and gliosis.
Objectives/Aims: We hypothesized an age-dependent volumetric divergence in lesion composition, with FLAIR becoming increasingly nonspecific in elderly.
Methods: FLAIR images of relapsing MS (n=138, 60% females, mean age: 40.0y, median MS-duration: 2.0y, median Expanded Disability Status Scale [EDSS] score: 1.5) were coregistered to QSM by reorientation, N4 correction, affine (magnitude-to-T1), boundary-based registration (QSM-to-T1), and T1-to-QSM by inverted matrix transformation. Analyses incorporated 2-year longitudinal follow-up (n=49) and cross-sectional controls (n=89) for variance estimates. FLAIR/QSM differences (ΔV) were compared via Wilcoxon, Cliff's Delta, and Levene's test. Mixed-effects models (age, disease duration, and EDSS interactions) included subject-specific random effects. Segmented regression identified ΔV breakpoints, and in K-means, we clustered by age, ΔV, and disease duration.
Results: FLAIR lesion volumes were 4.4x larger than on QSM (0.79[0.95]mL vs 0.18[0.25]mL, threshold at >20ppb; Cliff's δ=0.484), with 7.4× greater variance (11.22 vs 1.52 mL^2; $p<0.001$). Longitudinal mixed modeling demonstrated age- (β=0.053,p=0.010) and disease duration-dependent (β=0.082,p=0.026) ΔV increases, with a significant age×disease duration interaction (β=0.010,p=0.013). The effect of disease duration on ΔV was positive with aging (β=0.198,p=0.039 for >50y). We found curvilinear relationships to EDSS (linear: β=4.61,

p=0.025; quadratic: β=4.98,p=0.006), explaining 78% of ΔV variance. Segmented regression found a ΔV breakpoint at 30.9y±3.79. K-clustering confirmed triphasic stratification: (1) younger (<30.9y, minimal ΔV), (2) middle-aged (30.9-50y, moderate ΔV), and (3) older (⩾50y, maximal ΔV), with divergence exceeding +1SD by 51y. This progression paralleled the escalating variance ratio of FLAIR, suggesting progressive nonspecificity beyond the 50y threshold. A mixed-effects model fit favored quadratic age relationships (AIC=540.4), with high between-subject variance (3.6 vs. residual 1.0), consistent with cross-sectional heterogeneity.
Conclusion: FLAIR/QSM divergence emerges at 30.9, then amplifies, and peaks at ⩾50y. Quadratic EDSS effects and age-duration interactions suggest evolving lesion composition, highlighting the specificity of QSM and nonspecificity of FLAIR in the elderly.

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P1442
Paramagnetic Rim Lesion (PRL) in a Patient with Neuro-Behçet: A Diagnostic Challenge

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Introduction: Behçet's Disease (BD) is a systemic inflammatory vasculitis with a broad clinical spectrum. Neuro-Behçet (NBD) occurs in 5%–10% of cases, more frequently in young men. The parenchymal form predominates, affecting the brainstem, basal ganglia, and spinal cord. On magnetic resonance imaging (MRI), asymmetric T2/FLAIR hyperintense lesions are seen, with mild enhancement, diffusion restriction, possible hemorrhagic foci, and venous dilatation on susceptibility-weighted imaging (SWI). Advances in imaging have contributed to differentiating demyelinating from vasculitic central nervous system diseases.
Objectives/Aims: In multiple sclerosis (MS), a paramagnetic rim lesion (PRL) on SWI is a marker of chronic inflammation. However, whether PRL is exclusive to MS or also present in other neuroinflammatory diseases such as NBD remains under discussion.
Methods: Male, 49 years old, diagnosed with BD in 2020. Clinical features included panuveitis, retinal vasculitis, oral/genital ulcers, erythema nodosum, and thrombophlebitis; treated with azathioprine and prednisone. Referred to neurology after a 3T brain MRI showed periventricular and infratentorial demyelinating lesions. One periventricular lesion exhibited a PRL.
Results:
Conclusion: NBD and MS share clinical and radiological features, often with a relapsing-remitting course. Concomitance is more expected in patients previously using anti-TNF alpha. PRL is considered highly specific for MS, with Susac syndrome as the main differential diagnosis. The 2024 McDonald criteria included PRL as a relevant paraclinical finding, though its real-world application is still under evaluation. In this case, despite the BD diagnosis, the PRL and dissemination in space would fulfill MS diagnostic criteria. Given the limited data on PRL in NBD, this case raises the hypothesis that paramagnetic rim may not be exclusive to MS and Susac, becoming a relevant topic for future research and diagnostic refinement

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P1443
A Multi-Scanner Study of Region-Specific MS Lesion Detection Using AH-1

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Introduction: Multiple sclerosis (MS) lesion detection software requires robust validation across diverse imaging conditions before clinical implementation. While previous studies have evaluated automated detection tools in controlled research settings, real-world clinical validation across multiple scanner types remains limited.
Objectives/Aims: This study evaluates the region-specific performance of AH-1, an automated MS lesion detection software, in a multi-scanner clinical environment at Coimbra Local Health Unit using data acquired from five different magnetic resonance imaging (MRI) systems.
Methods: A total of 101 cases were analysed using AH-1 and subsequently validated by expert neuroradiologists. Among these, 32 cases (32,67% of the dataset) were classified as active, defined as having at least one new or enlarging lesion confirmed by expert evaluation. The complete dataset contained 169 lesions. Each detected lesion was systematically categorised as true positive (TP), false positive (FP), or false negative (FN). Performance metrics were calculated for the entire dataset and stratified by anatomical brain region.

Results: Overall, AH-1 demonstrated excellent performance with a sensitivity of 0,91, precision of 0,85 and false negative fraction of 0,09. Deep white matter lesions were the most frequent (141 of 169 total lesions, 83,4%) and showed high detection sensitivity (91,60%) with a moderate false positive rate (16,79%). Deep grey matter, leukocortical, infratentorial, and periventricular regions showed promising results (83,33-100% sensitivity); however, these findings are limited by low sample sizes in these regions.
Conclusion: This real-world validation across multiple scanners demonstrates AH-1's robust performance in detecting new/enlarging MS lesions, particularly in deep white matter regions where most lesions occur. The software showed promising performance in deep grey matter and infratentorial regions—areas traditionally challenging for automated systems due to complex anatomy and imaging artifacts—though larger region-specific datasets are needed to confirm these preliminary findings.

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P1444
Deep learning-based Segmentation of the Choroid Plexus in Multiple Sclerosis Using MPRAGE, FLAIR, and MP2RAGE

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Introduction: The choroid plexus (CP) appears enlarged on MRI in people with MS (PwMS) and its volume increase has been linked to inflammation in postmortem studies. However, assessing CP volume in vivo in pwMS requires time-consuming manual segmentation. While deep learning (DL) tools exist for automatic CP segmentation on T1-weighted images, their performance requires further improvement.
Objectives/Aims: To develop a DL tool for CP segmentation in the lateral ventricles on T1-weighted images in PwMS, compare its performance with existing methods, and extend its application to MPRAGE+FLAIR and MP2RAGE+FLAIR sequences.
Methods: Two 3T MRI datasets, each comprising 177 PwMS, were used, one from the Swiss Multiple Sclerosis Cohort study with MPRAGE+FLAIR and the other from the INsIDER study with MP2RAGE+FLAIR. Images had a 1mm³ isotropic resolution, and FLAIR was co-registered to MPRAGE/MP2RAGE. Each dataset was split into a test set (n=36) and a dataset (n=141) for five-fold cross-validation (CV). CP were manually segmented by two raters. CP segmentation masks on MPRAGE using two publicly available DL-based methods, FastSurfer and ASCHOPLEX, were used as comparison. ASCHOPLEX was fine-tuned on ten subjects in the CV dataset before segmentation, as recommended by its authors.We trained UNETR, a transformer-based U-Net for medical image segmentation, leveraging CP localization and size. MPRAGE images were bias-field corrected with ANTs and skull-stripped with HD-BET. Regions within a bounding box around ventricles segmented by SAMSEG were extracted, and patches of 32x32x32 voxels were subsequently sampled. Data augmentation was applied. A combined Dice and Focal loss was optimized using AdamW. Clusters < 100 voxels in the predicted CP masks were removed. The same pipeline was applied to MPRAGE+FLAIR and MP2RAGE+FLAIR.
Results: The mean and standard deviation of Dice scores of our UNETR on the CV dataset were 0.76 ± 0.01 (MPRAGE), 0.84 ± 0.01 (MPRAGE+FLAIR), and 0.81 ± 0.01 (MP2RAGE+FLAIR). The mean Dice scores for CP segmentation on MPRAGE in the test dataset were 0.38 (FastSurfer), 0.70 (ASCHOPLEX), and 0.77 (our UNETR).
Conclusion: Our UNETR model, which leverages CP location and size, outperformed existing methods. When used with FLAIR, it achieved remarkable performance and also demonstrated strong applicability to MP2RAGE+FLAIR. This approach can be valuable in supporting the analysis of the CP in PwMS.

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P1445
Predictors of Variability in Brain Volume Loss Measurements in Multiple Sclerosis: A Longitudinal MRI Study

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Introduction: High variability in longitudinal MRI measurements of brain volume loss (BVL) challenges its clinical application. Identifying factors influencing this variability could help determine which patients have more reliable BVL assessments, improving its utility for individual-level evaluation.
Objectives/Aims: To identify demographic, clinical, or radiological factors predicting high or low intra-individual variability in BVL measurements in multiple sclerosis (MS) patients.
Methods: This single-center longitudinal study analyzed 896 MS patients (4,348 time points) scanned using the same protocol on a single 1.5T scanner without major hardware upgrades. Whole brain volume was derived from T1-weighted 3D scans and assessed using SIENA software. Inclusion required ⩾3 MRI scans, intervals between scans ⩾10 months, disease-modifying treatment (DMT) duration ⩾12 months, and last high-dose corticosteroid treatment or relapse >30 days before scanning. A multivariate linear mixed-effects regression model predicted BVL variability over time. First, a linear trend of BVL was estimated. Next, the absolute deviation of measured BVL from the expected trajectory was calculated, with greater discrepancies indicating higher BVL variability. Finally, associations between demographic, clinical, and imaging factors (independent variables) and BVL variability (dependent continuous variable) were tested.
Results: The strongest predictors of greater BVL variability were lower brain parenchymal fraction (BPF) (B=-0.06 per % point; $p<0.0001$) and female gender (B=0.10; p=0.0003). Weaker predictors included higher EDSS (B=0.029 per status point; p=0.006), younger age (B=-0.004 per year of age; p=0.017), and greater T2 lesion volume (B=0.005 per volume unit; p=0.037). Patients treated with first-line DMTs (B=-0.09; $p<0.0003$), but not second-line DMTs, had lower BVL variability than those without DMTs. Time of day, interval between MRI scans, and time since last relapse were not associated with BVL variability. On average, females had 0.1 percentage points higher BVL variability than males. A 1%-point decrease in BPF corresponded to a 0.06%-point increase in BVL variability.
Conclusion: Lower disease burden, younger age, and male gender are linked to lower BVL variability. These findings may improve the interpretation of brain volumetric measures in clinical practice and research.

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P1446
Cerebellar 7T imaging at mesoscale resolution in multiple sclerosis

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Introduction: Cerebellar injury is common in people with multiple sclerosis (pwMS), but visualizing its thin, highly foliated cortex is challenging and typical 1-3mm MRI resolutions are inadequate for accurate gray matter delineation and subtle pathology detection.
Objectives/Aims: Our aim is to utilize 7T MRI, state-of-the-art MRI sequences and submillimetre images to better characterize cerebellar tissue damage, even within the thin cortical layers.
Methods: Seven pwMS (3 females, age=55±7yrs) and five healthy controls (HC, 4 females, age=60±11yrs) from the Amsterdam MS cohort were scanned using a 7T (Phillips, 8Tx/32Rx rf-coil) and 3T (GE, 8Tx/Rx rf-coil) MRI-scanner. 7T MRI included: 1) cerebellar-layer 0.19×0.19×0.5mm3 T2*-weighted 3D-FLASH sequence with prospective motion correction (realigning reconstructed fat navigators in real time), 2) whole-head 1.0mm-isotropic MP2RAGE. 3T MRI: 3DT1 FSPGR, 0.9×0.9x1.0mm resolution, collected 21±10 months prior to 7T. 3T and 7T images were visually compared on lesion pathology. Cerebellar layers were segmented in the left Crus I using LayNii (Huber et al, 2021, NeuroImage). Local field values were extracted for WM, granular and molecular layer, averaged, and compared between groups using independent t-tests ($p<0.05$).
Results: Some pwMS showed visible cerebellar damage (lesion pathology), with improved contrast on 7T and one lesion not visible on 3T. As to the cortical layers, the iron-rich granular layer and molecular layer were visible due to the susceptibility differences in both in both HC and MS data. Visually, pwMS have a slightly brighter signal in the granular cell layer, but quantitative assessment of the phase differences showed that this was not significant (MS=0.020±0.008 ppm, HC=0.016±0.005 ppm). Additionally, the WM (MS=-0.042±0.012ppm, HC=-0.041±0.029 ppm) and molecular layer (MS=0.003±0.008 ppm, HC=-0.004±0.012 ppm) did not differ between groups.
Conclusion: To conclude, to the best of our knowledge, this is the first time the cerebellar cortical layers were visualized in-vivo in pwMS. PwMS showed a slightly increased intra-cortical contrast, potentially indicating an affected granular layer with increased iron deposition. These analyses rely heavily on semi-automatic segmentation, future analyses will involve full manual segmentation and more participants. Besides the layers, the visibility of lesions improved on 7T, together highlighting the advantages of using ultra-high field MRI to image anatomy at an unprecedented resolution.

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P1447
Continuous Learning for Multiple Sclerosis Lesion Segmentation in Domain-Incremental Scenarios

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Introduction: Multiple sclerosis (MS) lesion segmentation is crucial for monitoring disease progression. Deep learning methods have shown promising results but suffer from domain shift problems when applied to data from different scanners or protocols. Transfer learning (TL) can address this issue but leads to catastrophic forgetting, where the model loses performance on the original domain. Continuous learning approaches aim to maintain knowledge from previous domains while adapting to new ones.
Objectives/Aims: To investigate the effectiveness of Elastic Weight Consolidation (EWC) in mitigating catastrophic forgetting during domain adaptation for MS lesion segmentation, and to evaluate its performance in few-shot learning scenarios.
Methods: We implemented a 3D U-Net architecture for MS lesion segmentation and trained it on two datasets: WMH2017 public dataset (n=60, mean lesion load 29.87 ml [1.1, 118.35]) and an in-house dataset from Vall d'Hebron Hospital (VH) (n=57, mean lesion load 4.01 ml [0.13, 23.52]), both containing T1-weighted and FLAIR sequences. The WMH2017 dataset included images from three scanners (3T Philips Achieva, 3T

Siemens TrioTim, and 3T GE SignaHDxt), while the VH dataset contained images from a single scanner (3T Siemens TrioTim). The baseline model trained on WMH2017 was fine-tuned on the VH dataset using both TL and EWC. Performance was assessed using lesion detection metrics on both source and target domains. We also conducted few-shot learning experiments with 1, 2, 3, 5, and 10 target domain images to determine the minimum number required for effective adaptation.

Results: EWC significantly reduced catastrophic forgetting compared to TL, preserving source domain knowledge while successfully adapting to the target domain. The performance drop on the source domain was reduced by 8-19% in terms of detection F-score compared to TL, where forgetting ranged from 20% to 37%. In few-shot scenarios, using only 3 target domain images with EWC led to a 10% improvement in F-score, while using 5 images achieved results comparable to using all available training data.

Conclusion: EWC enables models to adapt to new domains while preserving knowledge from previous ones, both in full-training and few-shot scenarios, making it ideal for clinical settings with multiple scanners and limited labeled data. Moreover, it eliminates the need to store source domain data for target domain training, addressing both storage requirements and potential privacy concerns associated with medical data.

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P1448

Cortical myelin repair and enhanced local neuronal activity prevent cognitive impairment in multiple sclerosis

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Introduction: Cognitive impairment is a common manifestation of MS, significantly affecting the daily functioning and quality of life of people with MS (PwMS).

Objectives/Aims: To explore the role of cortical myelin loss in contributing to cognitive impairment in MS, as well as the impact of adaptative changes in local neuronal activity and cortical myelin repair in compensating the effect of cortical demyelination on cognitive function.

Methods: We included 82 subjects from two longitudinal multimodal studies: 56 PwMS (25 females, 31 males) and 26 age- and sex-matched healthy controls (HC). Cognitive function was assessed through a battery of neuropsychological tests covering five cognitive domains, and PwMS were classified as cognitively impaired (CI) or cognitively preserved (CP) based on a composite score. All subjects underwent a 3T-magnetic resonance imaging (MRI) protocol, repeated after 12 months in patients only, that included magnetization transfer imaging and resting-state functional MRI. Magnetization transfer ratio (MTR) was used to generate individual maps of cortical myelin content changes, while maps of local functional connectivity density (lFCD) were computed from resting-state functional MRI. These maps were used to calculate individual indices of cortical demyelination, remyelination, and local functional connectivity change in patients compared to HC.

Results: In patients, a greater extent of cortical demyelination was significantly associated with an increased risk of cognitive impairment ($p = 0.007$; odds ratio [OR] 1.65; area under the curve [AUC]: 0.77). We observed that IFCD progressively increased with greater cortical myelin loss ($p<0.001$). However, this compensatory mechanism effectively protected against cognitive impairment only in patients with extensive cortical myelin loss (p=0.005; OR: 0.79, AUC 0.70). Interestingly, structural compensation through cortical myelin repair had a strong protective effect on cognitive function in the whole patient cohort, independently of IFCD enhancement (p=0.03, OR=0.61; AUC=0.72). Specifically, a 10% increase in cortical myelin repair nearly halved the risk of developing cognitive impairment in PwMS.

Conclusion: Cortical demyelination plays a crucial role in MS-related cognitive impairment. However, while both structural and functional compensatory mechanisms can mitigate its impact on cognitive function, cortical remyelination emerged as the most decisive mechanism, drastically reducing the risk of cognitive impairment in PwMS. Therefore, targeting myelin repair through therapeutic strategies shows great potential to prevent cognitive impairment in MS.

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P1449
Comparing Deep Learning Models for MS Lesion Segmentation in Brain MRI: AClinically-Oriented Evaluation of UNet, CDCG-UNet, and Swin-UNet

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Introduction: Efficient monitoring and accurate detection of lesions associated with multiple sclerosis (MS) on magnetic resonance imaging (MRI) scans is essential for diagnosis, treatment, and planning, which is often difficult due to the heterogeneity of lesions and the intricate nature of volumetric data. Automated segmentation of lesions using deep learning techniques has shown potential, yet automated segmentation using different networks has not been comprehensively evaluated. Comparison of standard UNet, CDCG-UNet, and Swin-UNet architectures serves as the basis for this study. These architectures have been used for cancers, herein the same architecture is used for lesions.
Objectives/Aims: This study compares three deep learning models—UNet, CDCG-UNet (a CNN enhanced with attention mechanisms), and Swin-UNet (a newer transformer-based model)—to determine which is most effective for segmenting MS lesions in brain MRIs.
Methods: Two MRI datasets were used:

- MSSEG 2016, manually annotated lesions from 53 patients and
- Shifts 2.0, simulating variability in scanners and imaging protocols.

Pre-processing: bias correction, intensity normalization, and conversion to a uniform orientation. Slices were analyzed in coronal, axial, sagittal, with segmentation results fused using majority voting. Assessment metrics: Dice score, Intersection over Union (IoU), Precision, Recall, and F1 score.
Results: Across all views and datasets, Swin-UNet consistently outperformed the other models:
Coronal view: Swin-UNet (IoU: 0.6262, F1: 0.6857), CDCG-UNet (IoU: 0.4706, F1: 0.6346), UNet (IoU: 0.4378, F1: 0.6034).
Axial view: Swin-UNet (IoU: 0.7015, F1: 0.7417), CDCG-UNet (IoU: 0.4509, F1: 0.6054), UNet (IoU: 0.4191, F1: 0.5755).
Sagittal view: Swin-UNet (IoU: 0.5715, F1: 0.6368), ahead of UNet and CDCG-UNet.
Conclusion: Swin-UNet, a transformer-based architecture, showed superior accuracy and robustness in segmenting MS lesions across multiple brain planes and imaging conditions. Its ability to capture both local and global features likely contributes to its high performance. This makes it a promising tool for future clinical integration, potentially enhancing radiological workflows and lesion monitoring. Future directions include applying the model to spinal MRIs and exploring its role in clinical decision support systems.

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P1450
Cladribine tablets-treated multiple sclerosis patients show different spatio-temporal patterns of acute, chronic and resolving brain inflammatory activity

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Introduction: Cladribine tablets (CladT) have been shown to reduce acute inflammation in the brain of people with MS (pwMS). However, the dynamics of inflammatory activity, including chronic and resolving inflammation, remain unclear.
Objectives/Aims: To evaluate the spatio-temporal patterns of acute, resolving and chronic lesional activity in pwMS treated with CladT over a 4-year period.
Methods: MRI data (T1-w/T2-w images) of 178 pwMS from the MAGNIFY-MS Extension (NCT03369665) study were analysed. For each pwMS, MRI was acquired 12 times over a 4-year period. New + enlarging (N+E) lesions, slowly expanding lesions (SELs) and shrinking + disappearing (S+D) lesions were assessed at each time point and served as markers of acute, chronic and resolving inflammation, respectively. N+E and S+D maps were obtained using subtraction images. SELs were detected using an in-house developed tool able to provide the time of occurrence, determined as the time point when lesion intensity differed from white matter. Differences in accrual

trajectories (both volume [V, in cm³] and number [N]) across lesion types were assessed using a linear mixed-effects model, with subject included as a random factor and a lesion type-by-time interaction term. For each lesion type, mean yearly accrual rate of volume (V/y) and number (N/y) were reported. Spatial differences in lesion accrual were assessed using the FMRIB software library "randomise" tool.
Results: SELs showed lower accrual rate (0.06 V/y; 0.3 N/y) than N+E (0.16 V/y; 1.15 N/y; $p<0.01$) but a higher accrual rate than S+D (0.03 V/y; 0.15 N/y; $p<0.01$). SELs showed their highest accrual rate at year 1 (0.12 V/y; 0.5 N/y), whereas N+E and S+D accumulation rate was highest at month 1 (N+E: 2.31 V/y; 11.87 N/y; S+D: 0.26 V/y; 1.29 N/y). Voxel-wise analyses at year 4 revealed a higher N+E activity compared to SELs across the entire brain (significant voxels: 47308). No difference was observed between SELs and S+D. N+E and S+D showed a more widespread distribution in the white matter while SELs mostly concentrated in the periventricular region.
Conclusion: CladT efficacy in pwMS followed distinct temporal patterns across lesion types. Acute and resolving lesions showed a reduced accrual rate within the first months of treatment. In contrast, the effect on SEL accrual became evident after one year. Notably, for all types of brain inflammatory activity, the growth rate was lower in the fourth year compared to the first, suggesting that CladT's effects are sustained over time.

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P1451
Concomitant Iron and Myelin Investigation in the Thalamus of Primary Progressive Multiple Sclerosis: A 7T MRI Study

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Introduction: Primary progressive multiple sclerosis (PPMS) remains an understudied MS phenotype. The thalamus, a key relay deep-brain structure, displays a specific pattern of iron loss with disease duration, differently from other deep-brain nuclei and has been implicated in MS-related neurodegeneration. However, the extent and role of concomitant iron and myelin changes in the thalamus of PPMS patients remains unknown. Ultra-high-field (UHF) MRI offers a unique opportunity to detect such subtle microstructural changes that may contribute to disease progression.
Objectives/Aims: We aimed to utilize 7T quantitative magnetic resonance imaging (qMRI) to assess contaminant iron and myelin alterations in PPMS.
Methods: Using 7T MRI (Philips Achieva, Best, The Netherlands), we assessed iron and myelin alterations in 28 PPMS patients and 16 healthy controls (HCs) via quantitative susceptibility mapping (QSM), myelin water fraction (MWF) and magnetization transfer ratio (MTR) imaging.
Thalamic lesions were identified manually under blinded conditions and classified as either confined or crossing thalamic borders. Pearson correlations between qMRI metrics and thalamic volume, as well as group differences in qMRI measures, lesion burden, interthalamic variance, and asymmetry (using Welch's t-tests), were analyzed. Due to the exploratory design of the study, uncorrected p-values are reported.
Results: 28 PPMS patients (mean age: 54.8 years, range: 32–76 years; 61% female) were compared to 16 HCs (mean age: 57.5 years, range: 36–78 years; 50% female). Thalamic lesions were present in 16 PPMS patients (53 total; 31 crossing borders) and in 1 HC (6 total; 4 crossing borders). Lesions appeared more frequently in the right thalamus (right: 34, left: 25), though qMRI measures were similar across hemispheres. PPMS patients showed significant thalamic atrophy ($p = 0.012$) and reduced QSM values ($p = 0.011$) compared with HCs. A trend toward increased interthalamic MTR variance was observed in PPMS ($p = 0.068$). Thalamic volume correlated positively with MTR ($r = 0.48$, $p = 0.001$), and MTR correlated negatively with MWF ($r = -0.45$, $p = 0.002$).
Conclusion: This is the first UHF-(q)MRI study to detail thalamic iron and myelin alterations in PPMS, showing extensive thalamic lesions and atrophy along with reduced QSM values, indicating iron loss similarly to that seen in relapsing-remitting MS. The negative MTR–MWF correlation may reflect contributions from other non-myelin macromolecules, influenced by the low myelin content of the thalamus

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P1452
Peripheral Blood T Regulatory Cell Frequencies Correlate with Normal-Appearing White Matter Integrity in Relapsing-Remitting MS, but Not in Secondary Progressive MS

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Introduction: Multiple sclerosis (MS) is characterized by immune-mediated and neurodegenerative damage within the central nervous system. Regulatory T cells (Tregs), which modulate immune responses, have been proposed to play a key role in MS pathophysiology by regulating inflammation and promoting myelin repair. However, the relationship between Treg levels and MRI-based measures of brain pathology remains uncertain.

Objectives/Aims: To investigate associations between Treg frequencies in peripheral blood and Synthetic MRI-derived white matter integrity measures in both relapsing (RRMS) and secondary progressive MS (SPMS).

Methods: 47 patients with RRMS and 70 with SPMS underwent a quantitative multislice, multiecho, multisaturation delay acquisition sequence (Synthetic MRI) on a 1.5 Tesla scanner for the quantification of myelin volume fraction (MVF) and relaxation rates (R1, R2). MS lesions, normal-appearing white matter (NAWM), and gray matter (GM) were segmented using the SAMSEG pipeline. Peripheral blood mononuclear cells (PBMCs) were isolated, and the frequencies of CD4+CD25+Foxp3+ Tregs were analyzed by flow cytometry (BD FACS-Canto TMII). Spearman correlation analyses were conducted to assess statistical relationships.

Results: NAWM metrics (MVF, R1, and R2) and white matter (WM) volume demonstrated significant correlations with the frequencies of CD4+CD25+Foxp3+ Tregs in the RRMS group (rho coefficients for WM volume: 0.466, p=0.001; MVF: 0.379, p=0.009; R1: 0.386, p=0.007; R2: 0.310, p=0.034). No significant associations were observed between GM or lesional microstructural MRI parameters and Tregs. Additionally, no significant correlations between Synthetic MRI-derived parameters and Tregs were identified in the SPMS group.

Conclusion: The frequencies of Tregs in peripheral blood appear to play an important role in maintaining NAWM integrity in RRMS. In contrast, lesional and GM pathology may be mediated by alternative pathophysiological mechanisms. The absence of correlations between Tregs and NAWM metrics in the SPMS group may be attributable to the functional decline of Tregs and the predominant impact of neurodegeneration at this disease stage.

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P1453
Effect of Immunomodulatory Therapies on Imaging Measures of Remyelination in the ADVANCE and ASCEND Trials

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Introduction: Remyelination is a critical yet unmet therapeutic need in multiple sclerosis (MS). Current immunomodulatory therapies primarily target immune dysfunction, but they may also influence remyelination.
Objectives/Aims: We aimed to assess the effect of peginterferon β-1a and natalizumab on tissue repair in chronic white matter lesions, as measured by changes in T1-weighted over T2-weighted ratio (T1w/T2w) derived from magnetic resonance imaging (MRI).
Methods: Brain MRI data from the phase-3 ADVANCE (1512 RRMS patients, NCT00906399) and ASCEND (889 SPMS patients, NCT01416181) trials were analyzed. Among supratentorial white matter voxels that were T2-hyperintense at baseline, those located at least 3 millimeters away from any area of gadolinium enhancement (detected at baseline or follow-up) were selected. In selected voxels, after allowing for resolution of baseline sub-acute lesion activity, the change in T1w/T2w signal from week 24 to the last placebo-controlled study timepoint was measured. The effect of each therapy on MRI changes was assessed using a separate linear regression model, adjusted for subject age and gender, as well as for baseline lesional MRI signal and distance to the lateral ventricles.
Results: In ADVANCE, peginterferon β-1a promoted T1w/T2w signal recovery in chronic white matter lesions of RRMS subjects, relative to placebo (P=0.022). In ASCEND, natalizumab promoted T1w/T2w signal recovery in chronic white matter lesions of SPMS subjects, relative to placebo (P=0.046). Treatment effect was preferentially expressed in the deep white matter (WM) relative to juxtacortical and periventricular WM ($P<0.03$ in both trials). Treatment effect was also preferentially expressed in chronic lesion areas with a baseline T1-weighted signal intensity above the subject-level median ($P<0.03$ in both trials). Lastly, T1w/T2w recovery in chronic lesions treated with peginterferon β-1a was significantly greater in chronic lesions that were <1 year old relative to lesions that were >1 year old (P=0.002). This differential effect was greater in younger subjects (<34 years old) (P=0.043).
Conclusion: Current immunomodulatory therapies may promote remyelination in chronic white matter lesions. This effect is greatest in young chronic lesions showing less baseline T1-weighted signal abnormality, detected in the deep white matter of young MS patients.
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P1454
AssistMS – Artificial intelligence-assisted magnetic resonance imaging for quality, efficiency and equity in the NHS care of multiple sclerosis

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Introduction: There are >130,000 people with MS (pwMS) in the UK, costing the National Health Service (NHS) >£1billion annually. Most pwMS are treated with disease modifying treatments (DMTs). DMT treatment failure is however common, and these are amongst the highest cost drugs regularly prescribed in the NHS. Effective treatment monitoring is therefore essential, with early identification of treatment failure and treatment optimisation expected to improve long-term outcomes. Magnetic resonance imaging (MRI) is used to detect sub-clinical disease activity, but current practice - eyeball assessment of MRI - is time consuming, tiring and error prone. Icobrain ms is a validated/CE-marked artificial intelligence (AI) technology supporting visual assessment of brain MRI in pwMS.
Objectives/Aims: To test icobrain-ms for superiority in detecting MS disease activity; to assess the impact on DMT prescribing decisions; to undertake health-economic analysis to evaluate impact on healthcare resource use and quality of life outcomes.

Secondary analysis will explore impact on time from MRI acquisition to review and time for review by radiologists.
Methods: Randomised (1:1) UK multi-centre trial (recruitment: 12 months; follow-up 12 months) to compare eyeball assessment of MRI brain with and without icobrain ms assistance. Health economic analysis will use an individual-level microsimulation model with lifetime horizon.
Results: N=1336 participants will be recruited across three sites to detect 8% "treatment" effect between the two arms assuming 40% standard-of-care proportion with disease activity (80% power, 5% 2-sided significance, 10% drop-out). Set-up challenges encountered in lack of clear pathways at sites for the installation of necessary software (icobridge) on NHS picture archiving and communication systems have been overcome. However, hurdles have been overcome, and opening of the first site for recruitment is imminent.
Conclusion: AssistMS will be the first randomised UK clinical trial of an AI MRI tool in pwMS. The study has broad support from the MS community, including pwMS.
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P1455
Myelin and Neurite Pathology Varies Distinctly Across MS, NMOSD, and MOGAD

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Introduction: Differentiating MS from neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) remains clinically challenging due to overlapping features on conventional MRI. Quantitative and tissue-specific magnetic resonance imaging (MRI) biomarkers may reveal microstructural abnormalities not captured by standard imaging, offering greater disease specificity.
Objectives/Aims: To compare brain microstructural features across MS, NMOSD, MOGAD, and healthy controls (HC), focusing on both focal lesions and normal-appearing tissue.
Methods: A total of 39 individuals with NMOSD [AQP4+ (N=21; 95% female; mean age 52.2±17.4), seronegative (N=8; 75% female; 44.3±10.3)], 10 with MOGAD (60% female; 41.2±17.3), 79 persons with MS (pwMS; 62% female; 45.3±5.5), and 65 HC (72% female; 42.5±14.0) were enrolled. All participants underwent 3 Tesla MRI (Siemens PrismaFit). Myelin content was quantified using Rapid Estimation of Myelin for Diagnostic Imaging (REMyDI), neurite microstructure using Neurite Orientation Dispersion and Density Imaging (NODDI), and myelin thickness via g-ratio mapping (higher values representing thinner myelin sheaths). Quantitative metrics were extracted from cortical gray matter, lesions, and normal-appearing white matter (NAWM). Group comparisons were performed using the Mann-Whitney U-test or unpaired t-test, as appropriate.
Results: Compared to HC, individuals with NMOSD had lower NAWM myelin content (24.0±2.8% vs. 25.7±2.6%, $P<0.0001$), thinner NAWM myelin sheaths (g-ratio 0.78±0.02 vs. 0.76±0.02, $P=0.0005$), and higher neurite orientation dispersion (ODI 0.24±0.01 vs. 0.23±0.01, $P=0.014$), largely driven by the AQP4+ subgroup. Compared to pwMS, those with NMOSD had lower cortical myelin content (6.0±0.9% vs. 6.4±0.8%, $P=0.003$), thinner NAWM myelin sheaths (g-ratio 0.78±0.02 vs. 0.77±0.02, $P=0.003$), thicker lesional myelin sheaths (g-ratio 0.74±0.11 vs. 0.78±0.06, $P=0.006$) and lower lesional neurite density (0.27±0.07 vs. 0.31±0.03, $P=0.002$). Compared to pwMS, MOGAD patients exhibited thicker myelin sheaths in lesions (g-ratio 0.68±0.12 vs. 0.78±0.06, $P=0.0006$) and lower lesional neurite density (0.26±0.06 vs. 0.31±0.03, $P=0.0009$). No statistically significant differences were observed between MOGAD, AQP4+, and seronegative NMOSD subgroups.
Conclusion: Distinct patterns of myelin and neurite pathology were identified across MS, NMOSD, and MOGAD. NMOSD was characterized by diffuse myelin thinning and neurite disruption, while MOGAD exhibited increased lesional myelin thickness despite axonal compromise. These findings suggest that myelin- and neurite-sensitive imaging can provide novel insights into disease-specific pathophysiology and provide informative outcome measures in future clinical trials targeting demyelination and neuroaxonal damage.

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P1456
Nutrient intake and advanced imaging/laboratory markers in MS: an exploratory cross-sectional study

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Introduction: There is growing interest in the role of diet as a potential environmental factor influencing the pathogenesis and progression of MS.
Objectives/Aims: To investigate associations between nutrient intake and advanced biomarkers of MS-related neuroinflammation and neurodegeneration.
Methods: A cross-sectional cohort of 112 MS patients was screened for average food intake over the past 12 months using the validated French MetaCardis food frequency questionnaire. Daily nutrient intake was quantified, along with the percentage (pct) of ultra-processed food (UPF) using the NOVA classification, and the pct of alcoholic energy intake. All patients underwent 3T brain MRI and matched serum sampling, including glial fibrillary acidic protein (sGFAP) analysis. Normalised brain volumetrics, cortical lesions (CL), paramagnetic rim lesions (PRL), enlarged perivascular space in the centrum semiovale (EPVS-CSO) and brain-predicted age difference (brain-PAD) were assessed (Borrelli et al. 2024). Regression models were adjusted for total energy intake (Willett et al. 1997) as well as age, sex, and body mass index (BMI).
Results: After adjusting for total energy intake, age, sex, and BMI, a higher dietary intake of saturated fatty acids (SFA)—particularly lauric (C12), myristic (C14), and palmitic (C16) acids—and trans fatty acids (t-FA) were associated with several MRI biomarkers of greater MS burden. Specifically, increased intake of C14, C16, and t-FA was associated with greater PRL volume (in mL; β=424, p=0.047; β=131, p=0.029; β=2305, p=0.007; respectively). Higher t-FA intake was linked to an increased CL count (β=23, p=0.019), while increased C12 intake was associated with reduced total brain volume (β=-8x10^{-3}, p=0.038), and higher brain-PAD (β=2.8, p=0.036). Additionally, after adjusting for age, sex and BMI, higher %UPF consumption was associated with greater CL count (β=0.5, p=0.009), and reduced thalamic volume (β=-2x10^{-5}, p=0.024). A higher pct of alcoholic energy intake was associated with increased sGFAP levels (β=3, p=0.002) and EPVS-CSO scores (β=0.02, p=0.009).
Conclusion: Higher dietary intake of SFA, t-FA, UPF and alcohol is associated with brain MRI and fluid biomarkers of MS-related neuroinflammation and neurodegeneration, suggesting a potential role in disease progression. Dietary modifications may represent a potential strategy to mitigate disease burden. Future longitudinal and interventional studies are needed to establish causality.

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P1457
Deep Learning-Driven Prognosis of Multiple Sclerosis Using Multimodal MRI and Clinical Features

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Introduction: Multiple Sclerosis (MS) is a chronic, heterogeneous disease of the central nervous system, where the trajectory of disability progression varies significantly across individuals. Accurately

forecasting disease progression is critical to tailoring patient-specific treatment strategies. While conventional magnetic resonance imaging (MRI) interpretation remains reliant on expert clinical judgment, recent advances in artificial intelligence offer new avenues for automating and enhancing predictive capabilities.
Objectives/Aims: This study aims to develop a deep learning framework that combines multimodal MRI with longitudinal clinical data to predict disability progression in MS. By capturing both spatial and temporal disease patterns, the goal is to provide accurate and interpretable prognostic insights that can support early intervention and guide individualized treatment planning in clinical practice.
Methods: The patient cohort consists of 193 patients with Relapsing Remitting MS (RRMS) followed yearly over 10+ years, and has been thoroughly characterized. Each visit includes T1- and T2-weighted brain MRI and clinical assessments such as the Expanded Disability Status Scale (EDSS) and Multiple Sclerosis Functional Composite (MSFC) scores. Our architecture combines a 3D ResNet to capture spatial features in MRI with a bidirectional GRU network enhanced by time-aware attention mechanisms to learn disease evolution over time. The model is optimized for robustness in the presence of limited and imbalanced data. To ensure interpretability, we apply CAM-based saliency mapping to localize image regions contributing most to the prediction.
Results: In a preliminary analysis of a subset of patients (n = 104), our model was trained to predict Sustained Accumulation of Disability (SAD) using EDSS-derived labels. Triplets of consecutive visits were constructed to capture temporal progression. Our results indicate that including temporal context and focusing on earlier visits improves predictive performance. The model demonstrated training accuracy of 90% and validation accuracy up to 88% when trained on a subset of the total visits, highlighting the model's potential to support early prediction of MS progression.
Conclusion: These findings support the feasibility of deep learning models to predict MS progression from conventional clinical MRI and longitudinal data. Ongoing work focuses on expanding the multimodal scope by integrating additional clinical metrics (e.g., MSFC), refining model interpretability, and modularizing training for spatial and temporal sub-networks. The larger objective is to deliver an interpretable, clinically deployable decision-support tool for individualized MS prognosis.

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P1458
AH-1 Software Performance in MS Lesion Detection: Validation Against Expert Neuroradiologist Assessment

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Introduction: Accurate detection of new or enlarging T2 lesions is crucial for monitoring disease activity in patients with multiple sclerosis (MS). While automated detection tools show promise, their real-world performance compared to expert neuroradiologists remains incompletely characterized, particularly regarding their ability to correctly identify both active and stable cases.
Objectives/Aims: To evaluate the performance of AH-1, an artificial intelligence-based lesion detection software, against expert annotations by an expert neuroradiologist at Hospital Vall d'Hebron, with particular focus on its accuracy in identifying both disease activity and stability.
Methods: We analyzed 196 validated MRI cases (57 active, 139 stable) acquired across nine different MRI scanners at a single institution. Performance metrics included True Positive Fraction (TPF), False Positive Fraction (FPF), and False Negative Fraction (FNF). Cases were classified as active or stable based on expert validation, and patterns of disagreement were systematically analyzed.
Results: For active lesion detection, AH-1 achieved a TPF of 0,98, FPF of 0,05, and an F1 score of 0,95. Notably, the software correctly identified 98% of active cases but misclassified 16% of stable cases as active. The overall agreement between AH-1 and expert assessment was 83,7%. Error analysis revealed that 65,7% of false positives stemmed from misclassification of existing lesions, while only 1,0% of cases presented false negatives. The software demonstrated excellent performance in correctly identifying truly stable cases, with 99% of cases identified as stable by AH-1 being confirmed as stable by the expert.
Conclusion: H-1 demonstrates high sensitivity for detecting MS lesion activity and excellent reliability in confirming disease stability. Its high negative predictive value suggests particular utility as a screening tool to confidently rule out disease activity. The identified error patterns, primarily related to misclassification of existing lesions, provide clear direction for future software refinements. These findings support the integration of AH-1 into clinical workflows to enhance radiologist efficiency while maintaining diagnostic accuracy in MS monitoring.

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P1459
Choroid plexus volume changes in multiple sclerosis and neuromyelitis optica spectrum disorder: a longitudinal MRI study

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Introduction: Choroid plexus enlargement has been reported in multiple sclerosis (MS), possibly reflecting underlying inflammatory processes. While choroid plexus volume appears greater in MS than in healthy controls or in neuromyelitis optica spectrum disorder (NMOSD), comparative longitudinal studies are lacking.
Objectives/Aims: To examine longitudinal changes in choroid plexus volume in patients with MS and NMOSD, and to assess whether the change over time differs between the diseases.
Methods: A total of 140 patients, including 88 patients with MS (87 with relapsing-remitting MS and one with secondary progressive MS) and 52 with NMOSD (38 seropositive for anti-aquaporin4 antibody), were enrolled for this study and underwent brain MRI scans at baseline and follow-up (mean interval of 52.5 months). Choroid plexus volume and other regional tissue volumes were extracted automatically on 3D T1-weighted images using FastSurfer. A linear mixed effects model was used to evaluate the longitudinal changes in choroid plexus volume.
Results: The patients with MS were younger (34.7±8.7 vs. 47.4±14.6 years) and had lower EDSS scores (1.5, IQR 0.0-2.0 vs. 3.0, IQR 1.5-3.5) compared to those with NMOSD. At baseline, normalized choroid plexus volume did not differ significantly between the groups (MS, 1.19±0.25 mL vs. NMOSD, 1.19±0.29 mL). Although choroid plexus volume increased in MS, the delta volume between the baseline and follow-up scans did not significantly differ (MS, 0.0768±0.170 mL vs. NMOSD, 0.0593±0.191 mL, $p = 0.641$). In relapse-free patients, the linear mixed effects model revealed a significant interaction between time and disease group ($\beta = -0.00144$, $p = 0.023$), indicating that the trajectory of choroid plexus volume change over time differed between patients with MS and NMOSD: MS patients showed a significant increase in normalized choroid plexus volume over time ($\beta = 0.00196$, $p < 0.001$), whereas no significant change was observed in NMOSD patients.
Conclusion: These findings suggest that choroid plexus volume increases progressively over time in MS, even in the absence of clinical relapse, whereas NMOSD shows no significant longitudinal change. The differential trajectories observed between the two diseases suggest that choroid plexus involvement may reflect distinct underlying inflammatory mechanisms in MS compared to NMOSD.

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P1460
Choroid plexus volumetry and multi-echo ASL analysis in multiple sclerosis (MS) and neuromyelitis optica spectrum disorders (NMOSD)

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Introduction: Recent studies highlight the role of choroid plexus (CP) inflammation and enlargement in the pathology and progression of multiple sclerosis (MS). However, the impact of CP characteristics in neuromyelitis optica spectrum disorders (NMOSD) remains poorly understood. An important physiological information that may contribute to the changes in the CP is the blood-brain barrier (BBB) permeability. In that sense, novel arterial spin labeling (ASL) developments have been proposed to measure the time of exchange (Tex) for the arterial blood to cross the BBB and reach the brain tissue. Tex is based on water exchange, being potentially sensitive for subtle BBB changes.
Objectives/Aims: To assess changes in CP volume and permeability in MS and NMOSD.
Methods: A total of 30 subjects (10 healthy controls HC, 12 MS and 8 NMOSD) were evaluated by MRI using a 3T Scanner (Achieva, Philips). Acquisition included 3D-T1 images with 1mm^3 isotropic resolution and a multi-echo (10-400ms), arterial spin labeling multiple postlabeling delays acquisition (ME/PLD-ASL) for evaluation of the exchange of water from blood

to brain across the BBB in the CP. Automatic CP segmentation was performed by FreeSurfer based on the 3D-T1 images, improved with the application of a Gaussian Mixture Model. ME/PLD-ASL images were used to calculate mean Tex maps. ME/PLD-ASL images were co-registered with T1-weighted images, and the segmented CP was used as a region of interest to extract quantitative values of Tex in ms. CP volumes and Tex results were compared among the three groups using ANCOVA, co-variating by age and sex. Intracranial volume was also considered in CP volume comparisons.

Results: We observed a significant increase in CP volume in the MS group (2.44ml ± 1.18) compared to NMOSD (1.49ml ± 4.14) and HC (1.46ml ± 3.91) (p= 0.019). Although the Tex was higher in the MS group (32.3ms ± 22.9) in comparison to NMOSD (28.2ms ± 16.6) and HC (23.9ms ± 12.5), indicating a potential decrease the BBB permeability, this finding did not reach statistical significance (p= 0.847).

Conclusion: The significant CP enlargement observed in MS, absent in NMOSD, suggests that CP alterations may serve as a specific marker of inflammatory processes in MS. While we noted an increase in Tex for the MS group, further investigations are warranted to clarify the relationship between CP size and BBB permeability changes, which may enhance our understanding of disease mechanisms and potential therapeutic targets in MS.

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P1461
Does interrater variation influence the classification according to the diagnostic criteria for multiple sclerosis?

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Introduction: Studies on interrater agreement regarding the magnetic resonance imaging (MRI) analysis of patients presenting with the first clinical episode suggestive of multiple sclerosis (MS) are limited and outdated.

Objectives/Aims: The purpose of this study was to assess the interrater agreement regarding lesions in the brain, optic nerve and spinal cord in patients presenting with a first clinical episode suggestive of MS and the interrater variability on the classification of the 2017 and 2024 revisions of the McDonald criteria.

Methods: Seventy-eight patients underwent a standardized multisequence 3 Tesla MRI of the brain, optic nerves, and spinal cord, analyzed by three readers with varying expertise. Lesions were categorized according to lesion location as defined by McDonald diagnostic criteria. Interrater variability was calculated by Cohens κ for pairwise reader comparisons, and Fleiss κ for the overall degree of agreement.

Results: The interrater agreement was slight to fair regarding the total number of lesions and moderate to substantial regarding the presence of lesion. Highest agreement was observed for spinal cord ($\kappa = 0.84$) and periventricular T2 lesions ($\kappa = 0.7$) and Gd-enhancing brain lesions ($\kappa = 0.75$). The agreement regarding the classification according diagnostic criteria was substantial, being similar for the 2017 and the proposed 2024 revisions of the McDonald criteria ($\kappa = 0.65$).

Conclusion: Despite advanced standardized imaging protocols at 3T, interrater agreement regarding lesion counts does not lead to a better interrater agreement. However, agreement in classifying lesions according to diagnostic criteria is consistent between the 2017 and proposed 2024 criteria.

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P1462
Distribution of Cerebral Lesions in Primary Central Nervous System Vasculitis

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Introduction: Primary central nervous system vasculitis (PCNSV) is a rare autoimmune disease that exclusively affects the brain and spinal cord, without systemic involvement. Its clinical presentation is highly heterogeneous and can often mimic other neurological disorders. The literature concerning the frequency and localization of radiological findings at the onset of PCNSV is limited.
Objectives/Aims: This study aims to determine the distribution of cerebral lesions present at the onset of the disease in PCNSV.
Methods: In this multicentre study, lesions on the patients' first brain MRIs were marked using axial FLAIR sequences with the ITK-SNAP software to create a lesion heat map. Subsequently, using SPM12 software, the FLAIR sequences were aligned with T1 sequences and spatially normalized according to the ICBM MNI-152 atlas. Heat maps illustrating lesion density were generated using MRIcroGL software.
Results: A total of 32 patients with PCNSV were included in the study (17 male, 15 female). The median age of the patients was 45 years (interquartile range [IQR]: 43–60). The median follow-up period was 5 years (IQR: 2–7). The median baseline and final mRS (modified Rankin Scale) scores were 2 (baseline mRS IQR: 1–3, final mRS IQR: 1–2). A monophasic course was observed in 15 (46%) patients and a multiphasic course in 17 (54%). Diagnosis was made in 10 patients via brain biopsy, in 20 via conventional angiography, in 1 via vessel wall MRI, and in 1 via MR angiography. Among the 32 patients, 24 had both a brain lesion and a brain MRI of adequate quality, and the lesion heat map analysis showed the most frequently affected regions as the centrum semiovale, deep grey matter, and the frontal and occipital horns of the lateral ventricles. In contrast, cortical grey matter, brainstem, and cerebellum involvement was limited.
Conclusion: This study demonstrates that in PCNSV, lesions primarily occur in the centrum semiovale and deep grey matter, with comparatively little involvement of the cerebral cortex and brainstem. This unique distribution pattern of lesions may assist in distinguishing PCNSV from other neurological conditions that share similar clinical features.

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P1463
Choroid Plexus Enlargement in Secondary Progressive MS: phenotype comparison

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Introduction: The choroid plexus (CP) is increasingly recognised as a contributor to chronic inflammation in multiple sclerosis (MS). While CP enlargement is reported in early

MS, its role in secondary progressive MS (SPMS) is poorly understood.
Objectives/Aims: We aimed to quantify CP volume in SPMS and compare it to relapsing-remitting MS (RRMS) and clinically isolated syndrome (CIS), and to assess associations with disease severity and progression.
Methods: CP volumes were manually segmented and normalised to intracranial volume. Age correction was applied using a healthy control cohort. Cross-sectional and longitudinal analyses evaluated relationships with ventricular volume, lesion burden, and brain atrophy.
Results: CP volume increased significantly across MS phenotypes: SPMS patients showed 26% higher CP volume than CIS (p=0.010) and 17% higher than RRMS (p=0.034). CP enlargement in SPMS was independent of ventricular size, indicating distinct underlying mechanisms. While lesion burden was the primary determinant of brain atrophy in SPMS, longitudinal data revealed significant associations between CP volume, chronic lesion expansion (r^2=0.31), and brain volume loss (r^2=0.52).
Conclusion: CP enlargement is a progressive feature of MS, not driven by ventricular expansion. In SPMS, it may reflect ongoing inflammation contributing to tissue damage, supporting its role as a biomarker.

Disclosure of interest: Samuel Klistorner: Nothing to disclose

P1464
Interhemispheric connectivity is compromised in Radiologically Isolated Syndrome

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Introduction: The corpus callosum (CC) is a neuro-axonal structure that facilitates the transfer of information between the cerebral hemispheres. Its role in integrating and transferring information between the two hemispheres is particularly significant in the development of cognitive disorders in multiple sclerosis (MS).
Objectives/Aims: This study aimed to correlate the volume and lesion load of the CC with cognitive performance in subjects with radiologically isolated syndrome (RIS).
Methods: We conducted a monocentric retrospective study in which all RIS participants underwent magnetic resonance imaging (MRI), including 3D T1 and 3D FLAIR sequences, along with a standardized neuropsychological assessment including patient-reported outcomes (PROs) assessing alexithymia, mood disorders, fatigue, and quality of life. The CC volume (CCV) was segmented using voxel-based morphometry with MATLAB SPM12. Lesion volume was semi-automatically segmented from 3D FLAIR images using Assembly-NET. All volumes were normalized by total intracranial volume.
Results: 50 RIS were included, with 41(82%) women, mean age of 42.4 $\pm$ 13.8 years. Of the 50 subjects, 14 (28%) converted to clinical MS during follow-up. The CCV of the subjects who converted (11.80 $\pm$ 1.53 $\times$ 10^3 mL) was statistically lower than that of the pre-symptomatic subjects (12.74 $\pm$ 1.26 $\times$ 10^3 mL) with p=0.031, but we observed no difference in cognitive assessment results between the two groups. A positive correlation was observed between the CSCT z-score and CCV (ρ=0.28; r^2=0.131; p=0.048), while the CC lesion load was negatively correlated with the CSCT z-score (ρ=-0.34; r^2=0.115; p=0.015).
Conclusion: These results demonstrate that CC atrophy partially contributes to subjects' performance on information processing speed tasks, even in the preclinical stage of the disease. Focal callosal lesions reduced cognitive performance, confirming that attentional disorders and slower processing speed are significantly associated with lesion damage in RIS.

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P1465
Myelin Bilayer Mapping: A Novel MRI Approach for Quantifying Myelin Macromolecular Content

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Introduction: Demyelination is one of the main hallmarks of MS, yet, access to reliable information on the extent and progression of demyelination across the central nervous system remains a challenge. Several magnetic resonance imaging (MRI) methods with sensitivity to myelin exist, but image intensities often reflect a combination of tissue properties rather than the myelin content specifically. A solution to this problem is to capture and isolate magnetic resonance signals stemming directly from the macromolecular structure of the myelin sheath, the lipid-protein bilayer. In the presented work, this is enabled by specialised imaging techniques and hardware capable of targeting nonaqueous signals, which exhibit much shorter lifetimes (10s–100s μs) than the aqueous signals targeted by standard MRI methods ($>$ 1 ms).
Objectives/Aims: We present an overview of a novel MRI technique for direct mapping of myelin bilayer content in the brain.
Methods: A specialised imaging system based around a 3T Philips Achieva scanner is used to target the short-lived bilayer signals. The system is equipped with a high-performance, custom-built gradient coil for rapid spatial encoding and fast radiofrequency components for early data collection. Head images are acquired at multiple echo times to study the time evolution of the signals. Based on a time-domain signal model describing

human white matter (WM), the relative amplitude contributions of three signal components are isolated per image voxel using a fitting procedure. The signal component with the shortest lifetime represents the myelin bilayer, and so the amplitude map of this component quantifies myelin macromolecular content across the brain. [Baadsvik, MRM 2024;91]

Results: The imaging technique has so far been tested in seven healthy volunteers, yielding myelin maps with three-dimensional whole-brain coverage at 1.4 mm resolution. High myelin amplitudes are observed for WM, as expected. Also ex vivo MS brain has been mapped [Baadsvik, Sci Adv 2023;9], exhibiting varying (intermediate to low) amplitudes in locations of MS lesions. Histological staining was performed to validate the MS myelin amplitudes, with strong correlations found.

Conclusion: Quantitative maps of myelin bilayer content can be obtained using a specialised MRI approach. The maps are expected to aid in disease monitoring and the development of remyelinating therapies, as well as facilitate studies into the mechanisms behind demyelination and myelin repair. As a next step, a first in vivo MS study is planned.

Disclosure of interest: ELB, MW, BVI, KPP: Nothing to disclose

P1466
Association of Pretreatment Lateral Ventricular Volume and Medulla Oblongata Volume with Cognitive Function After 1 Year of Ozanimod in Early Relapsing MS

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Introduction: Spinal cord volume (SCV) and whole brain volume (WBV) atrophy are associated with cognitive impairment in relapsing multiple sclerosis (RMS). The medulla oblongata is included in routine brain MRI and is a biomarker for SCV. The ENLIGHTEN study is evaluating effects of ozanimod on cognition and brain volume in patients with early RMS.

Objectives/Aims: Determine whether the proportion of ENLIGHTEN participants with cognitive impairment after 1 year (y) of ozanimod varies by baseline lateral ventricular volume (LVV) and medulla oblongata volume (MOV) (proxies for WBV and SCV respectively).

Methods: ENLIGHTEN (NCT04140305) is an open-label, multicentre, phase 3b study of ozanimod 0.92 mg in adults with early RMS. In this exploratory analysis (cutoff 7 Feb 2024), we divided patients into tertiles based on LVV or MOV at baseline and calculated the proportion with cognitive impairment at 1 y for each tertile. Cognitive impairment was defined as a score of ⩽44 on the Symbol Digit Modalities Test (SDMT), ⩽39 on the California Verbal Learning Test, Second Edition (CVLT-II), or ⩽17 on the Brief Visuospatial Memory Test, Revised (BVMT-R).

Results: Of 188 ENLIGHTEN participants (78.7% female; mean age 39.5 y; mean 4.1 y since symptom onset; median Expanded Disability Status Scale 2.0; 70.7% naive to disease-modifying therapy), 158–170 had available data. For the largest (worst), middle, and smallest (best) LVV tertiles respectively, proportions (95% confidence intervals [CI]) with cognitive impairment at 1 y were 21.1% (10.5, 31.6), 16.1% (6.5, 25.7), and 7.0% (0.4, 13.6) on the SDMT; 14.8% (5.3, 24.3), 11.1% (2.7, 19.5), and 3.6% (0.0, 8.4) on the CVLT-II; and 20.8% (9.8, 31.7), 9.1% (1.5, 16.7), and 14.5% (5.2, 23.9) on the BVMT-R. For the smallest (worst), middle, and largest (best) MOV tertiles, proportions (95% CI) with cognitive impairment at 1 y were 20.0% (9.4, 30.6), 8.8% (1.4, 16.1), and 17.0% (6.9, 27.1) on the SDMT; 13.2% (4.1, 22.3), 7.3% (0.4, 14.1), and 9.8% (1.6, 18.0) on the CVLT-II; and 17.3% (7.0, 27.6), 14.3% (5.1, 23.5), 12.0% (3.0, 21.0) on the BVMT-R.

Conclusion: Trends suggested patients with early RMS who had smaller LVV and larger MOV at baseline were less likely to be cognitively impaired after 1 y of ozanimod than patients who started with larger LVV or smaller MOV. For some outcomes, middle tertiles were inconsistent with the trend (although 95% CIs overlapped), which may in part stem from unidentified factors preferentially impacting cognitive function in one tertile or another.

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P1467
Cervical Cord Atrophy Correlates with Intracranial Lesion Load in Tumefactive Multiple Sclerosis Spectrum

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Introduction: Spinal cord atrophy is associated with motor disability in multiple sclerosis (MS) and may be related to intracranial lesion burden. Tumefactive MS (TMS) has a broad radiological spectrum, making it an attractive model for studying the contribution of intracranial lesion load on spinal cord atrophy and progressive disease.

Objectives/Aims: To determine the relationship between upper cervical spinal cord (UCC) area, intracranial lesion load, and a progressive clinical course in TMS.

Methods: This was a retrospective observational study of individuals with tumefactive demyelinating disease (TDD) that underwent automated cervical spinal cord area analysis from C1 to C3 using a 3D T1-weighted magnetization prepared rapid gradient echo (MPRAGE) brain MRI sequence. Individuals were stratified into three groups based on lesion load: single-lesion tumefactive demyelinating disease (SL-TDD), multiple-lesion tumefactive demyelinating disease (ML-TDD), and TMS fulfilling 2005 dissemination in space (DIS) criteria. Descriptive characteristics and UCC area were compared across radiological and clinical phenotype, using the Kruskal-Wallis and chi-square test as appropriate.

Results: A total of 111 individuals were included, 60% were female and the median age was 45.6 years (IQR 34.2, 54.7). Seven (6%) were classified as SL-TDD, 28 (25%) as ML-TDD, and 76 (68%) as TMS. Seven (6%) developed a progressive disease course, all of whom met criteria for TMS. The TMS cohort had more UCC lesions (TMS 62% vs. ML-TDD 26%; $p = 0.003$), lateral tract lesions (TMS 53% vs. ML-TDD 14%; $p=0.001$), and had a higher final EDSS [median 2.5 (IQR 1.5,3.0) vs. 2.0 (0.0,2.0); $p=0.01$] than the ML-TDD cohort, despite a similar median age and follow-up duration. After excluding 31 patients with UCC lesions, a stepwise decrease in UCC area was observed across the three radiological groups: SL-TDD, median (range) 57 mm^2 (47.9,70.2); ML-TDD, 53.4 mm^2 (37.2,63.2), and TMS, 51 mm^2 (32.0,64.3); $p=0.04$. There was no statistically significant difference in UCC area between progressive and non-progressive TMS patients.

Conclusion: Across the TMS spectrum, intracranial lesion load inversely correlates with upper cervical cord area, independent of UCC lesions. Individuals with TDD that fulfill DIS criteria have an increased frequency of UCC and lateral tract cord lesions, increased disability, and higher likelihood of progressive disease. Spinal cord atrophy and associated disability in TMS may be related to both cerebral and spinal cord disease.

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P1468
Relationship between brain volume and microstructural integrity of NAWM and lesion localization in MS patients

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Introduction: Lesion volume and number are key biomarkers for MS in routine clinical practice, but it has its limitations. The integrity of normal-appearing white matter (NAWM) and the volume of specific brain regions are other critical markers of disease progression. This study uses quantitative MRI techniques to assess T2 z-scores, providing insight into microstructural changes in the NAWM.

Objectives/Aims: We investigate the relationship between the volume of targeted brain regions and the microstructural integrity of NAWM, assessed by T2 z-scores from quantitative brain MRI, and how these factors are influenced by lesion presence and localization.

Methods: We examined 58 MS patients of various MS phenotypes, including 42 females (mean EDSS: 3.34, mean duration: 10.31 years) and 16 males (mean EDSS: 4.17, mean duration: 13.49 years). All MRI scans were conducted on a 3T MRI system (MAGNETOM Skyra, Siemens Healthineers, Forchheim, Germany). The protocol included 3D: MPRAGE, FLAIR, DIR, MP2RAGE, and 2D GRAPPATINI. We segmented lesions and brain regions using research applications, T2 deviations for each patient's NAWM were calculated as median absolute T2 voxelwise z-scores. Two neuroradiologists evaluated lesions based on consensus recommendations, classifying lesions into periventricular, deep white matter, juxtacortical, pure cortical, brainstem, cerebellar regions and leptomeningeal enhancement. Using a hierarchical cluster analysis, patients were divided into 3 clusters based on lesion location and its quantification (cluster 1 low number of lesions, cluster 2 high number of lesions cortically, cluster 3 high number of lesions periventricularly and cortically).

Results: We observed differences among 3 clusters of lesion distribution in the corpus callosum volume ($p<0.005$) and the number of different voxels in T2 maps of the cerebellum ($p=0.016$). Patients with the smallest lesional volume/number in all locations (cluster 1) showed the highest changes in T2 mapping in the cerebellum.

Conclusion: The work suggests association between the distribution of microstructural brain damage and the localization of lesional pathology. This finding could help in better describing the MR phenotype of the patient and thus refine the extent of involvement obtained in clinical practice by dominant evaluation of the lesional pathology.

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P1469
A vision transformer-based framework for longitudinal new lesion detection in multiple sclerosis

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Introduction: Detecting new lesions is crucial for monitoring disease progression and assessing treatment response in MS. Existing methods for new lesion detection are limited, with few robust methods that consistently identify subtle changes over time.
Objectives/Aims: To develop a deep learning framework based on transformers that comprises a model for accurate and generalizable detection of new lesions from longitudinal imaging data in MS .
Methods: We collected an in-house longitudinal dataset of 352 people with MS presenting new lesions. Two Vision image Transformer (ViT)-based models, SegMamba and SwinUNETR, were adapted to detect new lesions from longitudinal FLAIR images using Dice loss for optimization. In our framework, preprocessing techniques included skull stripping and rigid registration to follow-up space. Model validation was performed through Dice metric on the public MSSEG2021 dataset, which includes heterogeneous MRI acquisitions. Additional evaluations focused on lesion overlap and lesion cluster count to assess spatial consistency.
Results: On the MSSEG2021, SwinUNETR achieved a Dice score of 0.583, while SegMamba obtained a 0.575. In terms of lesion detection, SwinUNETR identified 66.37% of new lesions and recovered 67.2% of the lesion volume, whereas SegMamba detected 66.04% of lesions and recovered 73.1% of the lesion volume. Further evaluations of lesion overlap and lesion cluster count confirmed consistent performance across both models in capturing new lesion patterns.
Conclusion: Our framework robustly addresses longitudinal new lesion detection using longitudinal FLAIR images while maintaining good accuracy and generalizability.

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P1470
Quantitative indices based on tract density statistics for potential MS phenotypes differentiation

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Introduction: Extensive research is gained to find out quantitative index or even group of indices to enhance remitting-relapsing (RR) and active secondary progressive (ASP) MS differentiation. Tractography is rather new method for study the peculiarities of spatial tract distribution, which differs greatly in normal appearing white matter, lesion, locations with sufficient neurodegeneration. From viewpoint of MS phenotypes differentiation, corpus callosum (CC) is another very perspective signal transport region. But the main difficulty is need of analysis of huge number of tracts in complicated anatomical surrounding. In order to obtain human analyzable results, tract density (TD) is used.
Objectives/Aims: To provide MS phenotypes differentiation quantitatively, normalized sum of TD over the whole brain (NSTD), normalized sum of TD in CC (NSCC) and normalized entropy of TD in CC (NECC) are studied.
Methods: By means of GE MR750w 3T (DTI routine), 13 patients (7 – RRMS, 6 – ASPMS) are examined with axial slice thickness of 5.0 mm, 128 directions of b-value 4000 s/mm^2. Tractography is realized by DSI Studio (10^8 tracts). Whole brain tracts are recalculated into TD distribution, multiplanar reconstruction to sagittal plane is performed in order to match the spatial position of the CC. For CC slice, the state of disorder is evaluated with Shannon entropy, which is normalized on number of brain containing slices (NECC), NSTD and NSCC are calculated as sum of TD over a whole brain and CC normalized on number of brain containing slices. We used expended disability status scale (EDSS) to assess neurological status.
Results: All tracs are calculated under condition of identical quantity, each tract influence the finite number of voxels, thus longer and denser tractы enforce higher sum of TD. As a result, more massive network of tracts in whole brain or CC will result in a higher value of the NSTD or NSCC. In the RRMS case, NSTD = 40.5 – 45 million tracts/voxel, ASPMS is characterized by NSTD = 37.5 – 39.2 million tracts/voxel. NSCC is typically higher for low EDSS, but NECC statistical meaning is need to studied in depth in future work.
Conclusion: More massive network of tracts in RRMS provide higher NSTD in comparison with ASPMS (40.5 – 45 vs 37.5 – 39.2 million tracts/voxel). NSTD is shown to be potential quantitative index for MS phenotypes differentiation. NSCC is typically higher for low EDSS, further studies of the TD statistical properties are needed.

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P1471
Relationship Between CSF Cellular Populations and MRI Biomarkers of MS Disease Severity: Insights from the CLOCK-MS Study

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Introduction: Multiple sclerosis (MS) activity and burden can be estimated using magnetic resonance imaging (MRI)-based biomarkers which are accessible and non-invasive. However, the relationship between MRI biomarkers and the underlying immune dysregulation is unclear.

Objectives/Aims: To explore the relationship between brain MRI biomarkers and the immunologic underpinnings of disease in patients with relapsing MS (RMS).

Methods: CLOCK-MS is an open-label, phase IV, randomized, multicenter study exploring the mechanism of action of cladribine tablets (CladT) in RMS (NCT03963375). At baseline (prior to initiation of CladT), patients (N=47) underwent blood and cerebrospinal fluid (CSF) sampling and MRI. MRI biomarkers included lesion volume, thalamic volume, total gray matter and white matter (WM) volumes, and gadolinium enhancing (Gd+) lesions. Blood and CSF samples were analyzed via flow cytometry to yield absolute counts of immune cell subsets. Univariate relationship with the number of Gd+ lesions was assessed. Canonical correlation analysis characterized the relationship between MRI volumetric measurements and cell counts in the CSF and blood.

Results: Baseline assessments are presented here. There was a positive relationship ($p<0.05$, uncorrected) between Gd+ lesions and number of CSF CD4 central memory T cells ($r=0.30$), as well as CD4 regulatory T cells ($r=0.29$), and CD8 T cells ($r=0.41$). There was a positive correlation between Gd+ lesions and the number of circulating transitional B cells ($r=0.35$) and a negative correlation with the number of circulating CD8 regulatory T cells ($r=-0.32$). While canonical correlation between the MRI biomarkers and cell counts identified no significant relationship with cell subsets in the blood ($F=1.0$, $p=0.43$), there appeared to be a relationship between thalamic and cerebral WM volume with CSF CD4 T cells, CD4 central memory T cells, and CD8 T cells ($F=1.4$, $p=0.044$). An assessment of the relationship between MRI, CSF and blood changes 1-year post-CladT treatment is planned.

Conclusion: Acute inflammation (Gd+ lesions) correlated with particular B and T cell subsets in both CSF and blood. MRI volumetric measures, likely reflecting the longer term consequences of MS injury, correlated only with CSF T cell populations. These results suggest that CSF analysis is valuable for identifying contributors to central nervous system compartmentalized processes that may extend beyond focal inflammatory lesions, while acute inflammation may also be reflected in blood measures.

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P1472
Diagnostic Accuracy of Central Vein Sign on Magnetic Resonance Imaging in Pediatric-Onset Multiple Sclerosis: A systematic review and meta-analysis

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Introduction: Multiple sclerosis (MS) diagnosis in pediatric populations presents unique challenges due to overlapping clinical and radiological features with other conditions. The Central Vein Sign (CVS) has emerged as a promising diagnostic biomarker in adult MS, but its utility in pediatric populations remains inadequately characterized.
Objectives/Aims: The aim of this systematic review is to evaluate the diagnostic accuracy of the Central Vein Sign (CVS) in pediatric-onset multiple sclerosis (MS) through a comprehensive analysis of existing literature.
Methods: A systematic search was performed on publicly available databases (PubMed, Embase, and Scopus) up to November 2024. Studies measuring the CVS accuracy on MRI in pediatric MS patients were included. Meta-analysis was performed using Open Meta-Analyst software to calculate the pooled proportions of CVS positivity per patient, per lesion number, the CVS mean positive rate, and lesion distribution patterns across different brain regions. The study was performed according to PRISMA 2020 guidelines.
Results: Four studies with a total of 118 pediatric patients (mean age 11.4-15.6 years, 13.6-40% male, disease duration 0.8-1.6 years) were included. The pooled proportion of CVS-positive patients was 0.643 (95% CI: 0.253 to 1.032, $p<0.001$), while the pooled proportion of CVS-positive lesions was 13.851 (95% CI: 11.260 to 16.442, p=0.829). The mean of the CVS-positive rate ratio was 0.531 (95% CI: 0.346 to 0.715, $p<0.001$). Regional analysis revealed varying CVS lesion distribution: juxtacortical (mean=1.082, 95% CI: 0.044 to 2.120, p=0.028), deep white matter (mean=6.037, 95% CI: 4.698 to 7.377, p=0.445), periventricular (mean=4.621, 95% CI: 3.391 to 5.852, p=0.249), and infratentorial (mean=0.989, 95% CI: -0.018 to 1.996, $p<0.001$).
Conclusion: The meta-analysis performed suggests that CVS could serve as a valuable diagnostic tool in pediatric MS, potentially improving diagnostic accuracy in this challenging population. Further prospective studies with standardized imaging protocols are needed to establish definitive diagnostic thresholds.

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P1473
Correlation Between Spinal Cord Cross-Sectional Area (CSA) and Multiple Sclerosis Types:: A Longitudinal Study

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disorder that affects the central nervous system and leads to neurological disability. In the past decade, there has been increasing interest in monitoring disease progression through cord cross-sectional area (CSA) and lesion metrics.
Objectives/Aims: This study evaluated changes in cervical CSA among patients with relapsing-remitting multiple sclerosis (RRMS) and secondary progressive multiple sclerosis (SPMS).
Methods: Eighty-five patients with multiple sclerosis (MS), diagnosed with either relapsing-remitting MS (RRMS) or secondary-progressive MS (SPMS), were recruited from neurology clinics and MS centers. Baseline assessments included clinical evaluations, neurological examinations, and spinal cord MRI scans to measure cross-sectional area (CSA). Participants were organized based on sex, MS type, and lesion' presence. Follow-up assessments were conducted after one year to monitor changes in CSA scores, the number of lesioned segments per participant, total lesion length, and the overall number of lesions. Statistical analyses were performed using SPSS 26, including descriptive statistics, paired t-tests, and generalized estimating equations to account for repeated measures within subjects over time.
Results: Eighty-five patients with multiple sclerosis participated in the study, comprising 90.6% females and 9.4% males, with a mean age of 35.13±7.7 years. The majority of participants had relapsing-remitting multiple sclerosis (RRMS), accounting for 90.6% of the cohort. Longitudinal analysis showed a significant decrease in the mean spinal cord cross-sectional area (CSA), which declined from 74.87±8.77 mm^2 to 73.19±8.62 mm^2 (p=0.01). Patients with secondary progressive multiple sclerosis (SPMS) experienced a more pronounced decline in CSA compared to those with RRMS (p=0.035). Additionally, neither sex nor treatment with disease-modifying therapies (DMDs), whether platform or high-efficacy, significantly influenced the progression of CSA during the one-year study period.
Conclusion: These results emphasize the importance of ongoing and extended observation to assess the impact of various types of DMDs on spinal cord atrophy.

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P1474
Brain Atrophy as an Indicator of Progression Independent of Relapses in MS

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Introduction: Progression independent of relapse activity (PIRA) contributes significantly to long-term disability in relapsing-remitting multiple sclerosis (RRMS). While its mechanisms remain poorly understood, central nervous system (CNS) atrophy is believed to play a key role. No definitive biomarkers for PIRA currently exist, but brain atrophy assessed via MRI may aid in its identification.
Objectives/Aims: To evaluate the association between atrophy of specific CNS structures and the presence of PIRA in people with MS (PwMS).
Methods: This cross-sectional study included PwMS with an RRMS phenotype. Brain volumes were assessed using MRI and compared with age- and sex-matched controls. EDSS scores from routine visits were used to classify patients into three groups: (a) stable EDSS; (b) worsening EDSS with clinical/MRI evidence of relapses (relapse-associated worsening, RAW); and (c) worsening EDSS without relapses or MRI activity (PIRA). Brain volumes were compared between groups using effect size (ES) analysis. Firth's penalised logistic regression (FPL) was performed to assess the association between brain atrophy and MS progression.
Results: Among 47 PwMS, 35 (74.5%) remained stable and 12 (25.5%) experienced worsening. Brain atrophy was absent in 15 (32%), with only 26.6% of these showing progression. PIRA was identified in 7 patients (14.8%). PwMS with PIRA exhibited greater atrophy than those with RAW, particularly in the left thalamus and cingulum, bilateral insula, bilateral frontal white matter, right temporal and parietal white matter, and cortical grey matter. Expansion of the third ventricle was also observed, all findings demonstrating large ES. FPL showed that brain atrophy was significantly associated with progression (OR = 5.1; 95% CI: 2.82–10.03; $p < 0.001$). No significant differences in atrophy were found between the stable and RAW groups ($p = .13$), whereas differences were significant in the PIRA group ($p = .001$).
Conclusion: PIRA is associated with increased atrophy in brain regions commonly affected by MS-related neurodegeneration. MRI-detected brain atrophy, along with third ventricle expansion, may serve as useful imaging biomarkers for identifying PIRA.

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P1475
Two-Year Brain Atrophy Predicts Long-Term Disability Progression in Progressive Multiple Sclerosis

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Introduction: Only a few studies evaluated the predictive value of brain atrophy for long-term disability progression in progressive MS.
Objectives/Aims: The aim is to investigate the predictive value of short-term brain volume loss (BVL) for long-term disability

progression in patients with relapsing-remitting MS (RRMS) and progressive MS (PMS).
Methods: A cohort of 156 patients (prospective, observational study) with (pw) MS (103 pwRRMS and 53 pwPMS either primary or secondary PMS) was analyzed. Patients underwent MRI at baseline (BL) and after 2 years (2yFU). Clinical assessments included the Expanded Disability Status Scale (EDSS) and the MS Functional Composite (MSFC, z-scores) at BL and after approximately 8 years after initial BL (8yFU). MRI included 3D-T1 and 3D-FLAIR sequences. T2-lesion load and brain parenchymal volume (BPV, z-scores) were derived from BL MRI. 2yFU MRIs were used for new/enlarged T2-lesions and for the annualized, age-adjusted BVL. Disability progression was defined as change in EDSS (ΔEDSS=EDSS at 8yFU – EDSS at BL) and change in MSFC (ΔMSFC accordingly). To test the predictive value of BVL patients were dichotomized according to annual age-adjusted BVL into those with pathological BVL ($< -0.4\%$) and those with normal BVL ($\geq -0.4\%$) at 2yFU. Pearson's correlations were used to assess associations between BVL/year and ΔMSFC, ΔEDSS.
Results: EDSS and MSFC scores (BL and 8yFU) were available for 100 pwRRMS and for 35 pwPMS. The RRMS and PMS groups had the following BL characteristics [mean (SD)]: age: 39.1(9.6)/47.2(12.4), disease duration: 9.5(6.4)/12.3(8.6) years, EDSS: 2.2(1.3)/3.8(1.9), MSFC z-score: 0.6(1.4)/-0.2(1.0), T2-lesion volume: 6.5(7.3) /11.9 (10.0) ml, BPV z-score: -1.6(1.3)/-1.8 (1.1). MRI scans at 2yFU: age-adjusted BVL/year: -0.1(0.3) /-0.2 (0.6) %, new/enlarged T2-lesions 1.1(2.1)/2.6 (4.8). Disability progression at 8yFU: ΔEDSS: 0.2(1.0)/1.4(1.3), ΔMSFC: -0.2(1.4)/-1.1(1.9). There was no association between new/enlarged T2-lesions at 2yFU and ΔMSFC, ΔEDSS in either group. However, BVL/year at 2yFU correlated with both ΔEDSS ($r=-0.38$, $p<0.05$) and ΔMSFC ($r=0.50$, $p<0.005$) at 8yFU in pwPMS, but not in pwRRMS. The pwPMS and pathological BVL at 2yFU experienced greater disability progression compared to those with normal BVL: ΔEDSS: 2.09 (1.28) vs. 1.06 (1.07), $p=0.02$; ΔMSFC: –2.01 (2.38) vs. –0.60 (1.43); $p = 0.04$ This difference could not be observed in the RRMS group.
Conclusion: BVL over two years, but no new or enlarged T2-lesions, was predictive of long-term disability progression in pwPMS, but not in pwRRMS.

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P1476
Expert panel consensus guidelines of the German Society of Neuroradiology on the use of magnetic resonance imaging in the diagnosis and monitoring of multiple sclerosis

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Introduction: The 2021 MAGNIMS-NAIMS-CMSC consensus recommendations for magnetic resonance imaging (MRI) in patients with multiple sclerosis (MS) provided authoritative guidance on standardization and harmonization of MRI applications for MS diagnosis and treatment monitoring in clinical routine settings world-wide. The recent draft on the 2024 revisions of the McDonald criteria suggested additional MRI measures such as the optic nerve (ON) and paramagnetic rim lesions (PRLs) as well as the central vein sign (CVS) for the diagnosis of MS. Furthermore, certain MRI measures such as slowly expanding lesions (SELs), particularly with paramagnetic rims, are increasingly used in the clinical trial setting and may enter in routine clinical imaging in the near future. These developments suggest a further expanding role of MRI in the management of patients with suspected and proven MS.
Objectives/Aims: To establish Expert panel consensus guidelines of the German Society of Neuroradiology in collaboration with the German Society of Neurology (DGN on the use of magnetic resonance imaging in the diagnosis and monitoring of multiple sclerosis in the context of the German health care system.
Methods: Guidelines were developed based on literature research and consensus sessions.
Results: We suggest the continuous use of the acquisition protocol established by the 2021 MAGNIMS-NAIMS-CMSC consensus recommendations for the patients with a conclusive MS diagnosis. For patients with inconclusive imaging findings to diagnose MS, we recommend changes in MRI acquisition protocols incorporating susceptibility weighted imaging (SWI) sequences for demonstration of PRLs and CVS as well as ON imaging. Additionally, we provide updated recommendations regarding the use of MRI for treatment monitoring purposes including the follow-up of progressive MS patients.
Conclusion: These guidelines will provide a guidance on standardization and harmonization of MRI applications for MS diagnosis and treatment monitoring in clinical routine setting in Germany and elsewhere.

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P1478
Reliable Evidence of Altered Functional Connectivity in Multiple Sclerosis: An Rrgion-to-Rrgion and Region-to-network Analysis Using a 1 5 T MRI Scanner

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Introduction: MS is a neurodegenerative disease that disrupts brain connectivity, impacting cognitive and motor functions. Resting-state functional magnetic resonance imaging (rs-fMRI) is a powerful tool for assessing brain functional connectivity (FC) and understanding how brain regions interact in both healthy and diseased states, thus offering insights into disease mechanisms and potential biomarkers for progression. This study focuses on alterations of connectivity between specific regions of interest (ROIs) in patients with MS (pwMS), and their detection using a clinical 1.5 Tesla MRI scanner.
Objectives/Aims: To examine alterations in region-to-region (ROI-to-ROI) and ROI-to-network FC in pwMS using resting-state fMRI, and to demonstrate that a 1.5 Tesla MRI scanner provides reliable results for assessing these connectivity changes.
Methods: rs-fMRI and structural data were acquired from 17 pwMS (relapsing/progressive subtypes: 10/7; age/disease duration:37±8.5/6.0±3.2 years) using a 1.5 T Philips scanner. DPABI toolbox was used for the preprocessing pipeline and to compute the FC matrices by extracting the mean of the BOLD signal time series from 25 ROIs/network, followed by the computation of Pearson's correlation coefficient between each pair of ROIs/ network. Fisher r-to-z transformation was performed to improve the normal distribution. A two-sample unequal variance t-test was used to compare the FC differences between pwMS and healthy control (HC) groups.
Results: Compared to HC pwMS exhibited significant connectivity alteration in both ROI-to-ROI and ROI-to-network connectivity (all $p<0.01$). Increased FC was observed between the supplementary motor cortex and the Default Mode Network (DMN). Also, significant FC reductions were found between the Salience Network (SN) and thalamus, and between the DMN and thalamus. Additional reductions were observed between the frontal pole and supramarginal gyrus (SMG), the left lateral parietal lobe and cerebellum, and between the supplementary motor cortex and SN. In contrast, increased FC was detected between the occipital pole and frontal pole, hippocampus and insula, posterior parietal cortex and thalamus, and between the SMG and rostral prefrontal cortex.
Conclusion: This study shows that a 1.5 Tesla MRI scanner can reliably detect functional connectivity alterations in MS patients, with results aligning with findings from studies using 3T scanners. These consistent patterns highlight the value of 1.5T MRI as an accessible and effective tool for investigating brain network disruptions and monitoring disease progression in clinical settings.

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P1479
Longitudinal Assessment of Brain Volume Changes in Rituximab-Treated Indian MS Patients: A Two-Year Follow-Up Study

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Introduction: Rituximab is increasingly used as a high-efficacy disease-modifying therapy (DMT) in Indian patients with MS. However, its effect on brain volume loss—an important marker of disease progression—remains underexplored, especially in low-resource settings.
Objectives/Aims: To evaluate brain volume changes following rituximab initiation and examine their correlation with clinical disability
Methods: This retrospective cross-sectional study included MS patients diagnosed per the 2017 McDonald criteria who underwent 3T MRI (GE SIGNA™ Architect) both before and after rituximab initiation. Brain volumes—including whole brain (WBV), grey matter (GM), subcortical GM (SGM), cortical GM (CGM), cerebellum and brainstem—were quantified using vol2Brain. Annualized volume change was calculated by dividing the absolute volume difference by the MRI interval. Post-treatment volume increase was defined as improvement. Correlations with clinical and demographic variables (EDSS, disease subtype, lesion volume) were analyzed using non-parametric tests in SPSS.
Results: Thirty patients were included (median follow-up: 2 years; 70% female; median age: 35). Of these, 73% had relapsing-remitting MS (RRMS), and 27% had secondary progressive MS (SPMS). Mean EDSS at last follow-up was 2.1 ± 1.2. Annualized volume change (cm^3/year) showed reductions in WBV (-1.19), GM (-0.902), and cerebrum (-0.806), with slight increases in SGM (+0.045), cerebellum (+0.094), and brainstem (+0.018). Thirteen patients (43%) showed WBV improvement, associated with earlier rituximab initiation (mean 12 vs. 36.8 months; $p = 0.04$). No association was found between positive or negative volume change group and age, sex, EDSS, lesion burden, or disease subtype. However, SGM volume gains were linked to RRMS phenotype ($p=0.04$) and EDSS improvement ($p = 0.02$).
Conclusion: Early rituximab initiation may mitigate or reverse brain volume loss in MS irrespective of baseline disability. Subcortical GM volume gains may reflect clinically meaningful benefits and could serve as potential imaging biomarkers

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P1480
Central vein sign and paramagnetic rim lesions in differentiating multiple sclerosis from anti-myelin oligodendrocyte glycoprotein Ab associated disease (MOGAD)

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Introduction: In patients with MOGAD, brain lesions analysis shows perivenous lymphocyte infiltration and demyelination typical of multiple sclerosis (MS). However, in these patients the presence of the MRI correlate of this marker thus far has been explored only in few patients whereas never it was presence paramagnetic rim lesions (PRLs).
Objectives/Aims: Aim of this study is to assess presence of > 50% PVL frequency, corresponding to the MS specific central vein sign (CVS), and of PRLs in MOGAD patients and in MS.
Methods: MOGAD patients (n=14), with at least one brain lesion, and MS (n= 15) patients were included. Isotropic and submillimetric EPI 3D FLAIR* images, were acquired by MRI (3 T) to assess perivenular lesions (PVL) frequency according to the NAIMS criteria, for assessing CVS presence (> 50% PVLs with respect to total lesion number). PRLs presence was also assessed.
Results: Median PVLs proportion/patient in MS was 80%, in MOGAD 62% (p=0.005). 36% MOGAD patients, were CVS+ vs 100% MS. None of the MOGAD patients had PRLs - versus 52 % of the MS (p=0.001).
Conclusion: Some MOGAD shows the MS specific CVS, supporting the hypothesis that these cases may carry a disease similar to MS. However, no MOGAD patient had PRLs lesions, suggesting that in this disease entity smoldering lesions are not frequent.

Disclosure of interest: Nothing to disclose related to this abstract

P1481
Spinal Cord Lesions as Predictors of Conversion to Secondary Progressive Multiple Sclerosis

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Introduction: Secondary progressive multiple sclerosis (SPMS) is marked by a gradual accumulation of disability, often occurring without overt relapse activity. While relapse-associated worsening (RAW) is a recognized contributor to disease progression, progression independent of relapse activity (PIRA) has emerged as a pivotal mechanism in the transition from relapsing multiple sclerosis (RMS) to SPMS. Spinal cord lesions, particularly within the cervical region, have been implicated in more rapid progression and earlier SPMS conversion. Their identification may be crucial for predicting SPMS onset and recognizing patients at heightened risk of PIRA.
Objectives/Aims: This study aimed to evaluate the predictive value of spinal cord lesions, particularly cervical lesions, in the transition from RMS to SPMS; to compare progression patterns between PIRA and RAW phenotypes; and to assess the relationship between lesion burden and long-term disability.
Methods: We retrospectively analyzed 58 patients initially diagnosed with RMS who transitioned to SPMS over a minimum five-year follow-up period. Based on clinical progression patterns, patients were categorized into PIRA and RAW subgroups. Spinal cord lesions were assessed using MRI, and disability progression was measured using the Expanded Disability Status Scale (EDSS).
Results: Patients with three or more spinal cord lesions at baseline had a significantly higher risk of converting to SPMS (OR = 4.1, $p < 0.001$). Among converters, 71% exhibited a PIRA pattern, while 29% followed a RAW trajectory. Cervical spinal cord lesions correlated with more rapid disease progression (median time to conversion: 6.9 years) and higher disability levels (EDSS ⩾ 6.0 in 67% of cases).
Conclusion: Spinal cord lesions, particularly in the cervical region, are strong predictors of SPMS conversion, predominantly through the PIRA mechanism. Early spinal cord MRI screening could help identify high-risk individuals, supporting more timely and tailored therapeutic interventions.

Disclosure of interest: lakri nabila: nothing to disclose

P1482
Towards Metabolic Biomarkers of Aging

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Introduction: Ageing is influenced by both lifestyle and diseases. Multiple Sclerosis (MS) contributes to chronic low-grade inflammation ("inflammaging") and neurodegeneration, thereby affecting ageing processes. To date, brain ageing in MS has mainly been studied using volumetric MRI approaches
Objectives/Aims: We aimed to investigate metabolic markers of biological brain ageing using advanced MRI sequences, specifically chemical exchange saturation transfer (CEST).

Methods: This is an interim analysis of an ongoing investigator-initiated trial (NCT06221631), with approximately 13% of the target participants enrolled (25% of healthy controls and 2% of people with MS [pwMS]). We evaluated age-related variations in CEST pools in 7T MRI of healthy individuals (n=25, aged 18-65 years) as potential biomarkers of ageing, and compared them to two pwMS (aged 23 and 33). CEST contrast was quantified using Lorentzian fitting of denoised, normalised, and B0- and B1-corrected z-spectra (55 offsets). Correlation analyses between age and CEST pool amplitudes were performed for white matter (WM) and grey matter (GM), using Pearson correlations and a physics-informed deep learning model (PICAE – Physics-informed conditional autoencoder). As this is an interim analysis with a small sample size, no adjustments for covariates were applied. CEST pool concentration maps (amide, amine, magnetisation transfer [MT], and relayed Nuclear Overhauser Effect [rNOE]) of pwMS were compared to age-matched controls
Results: Correlations with chronological age were found in WM MT pools (p 0.02, R 0.49) using Lorentzian fitting and Pearson correlation. With PICAE, correlations with age were observed in GM amide (p 0.02, R 0.51), GM rNOE (p 0.05, R 0.42), WM rNOE (p 0.04, R 0.44), and WM MT (p 0.03, R 0.47) pools. The results were not adjusted for multiple testing.
Conclusion: CEST is an emerging, yet unestablished imaging modality with various processing approaches currently under discussion. Our preliminary data highlight the potential of CEST pools as biomarkers of biological brain ageing and underscore the need for systematic comparison of analysis approaches, as processing methods appear to influence the outcomes.

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P1483
Detection of active disease in non-relapsing Progressive Multiple Sclerosis Patients: the added value of spinal cord MRI

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Introduction: Spinal cord MRI is not routinely recommended in the monitoring of MS. In patients with progressive MS (pMS), presence of disease activity is an important predictor of treatment response to currently approved treatments.
Objectives/Aims: The aim of this study was to investigate the added usefulness of spinal cord MRI in the identification of active disease in patients with non-relapsing pMS.
Methods: MRI records were reviewed in a cohort of pMS patients. All patients with at least 2 years of follow-up with the same MRI scanner were included in the study. Patients with clinical relapses during follow-up were excluded from the study. Asymptomatic combined unique active lesions (CUA) were defined as any new T2/STIR lesion or any T1 Gd+ lesion, in absence of a clinical relapse.
Results: 185 non-relapsing pMS patients were included in the study (41 primary progressive, 144 secondary progressive; median EDSS 6.0), out of a cohort of 422 pMS patients. Mean length of MRI follow-up was 4.0 years (range 2-8). 28/185 (15.1%) patients showed new asymptomatic CUA brain lesions during follow-up, 14/185 (7.6%) patients showed new asymptomatic CUA spinal cord lesions, 4/185 (3.4%) patients showed new asymptomatic CUA lesions both in the brain and in the spinal cord. Overall, the addition of spinal cord MRI allowed to detect disease activity in +43.75% more patients than brain MRI only.
Conclusion: The addition of spinal cord MRI allows to detect active disease in a significantly higher proportion of non-relapsing pMS patients. This is important in stratifying expected response to treatment and to inform treatment choices.

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P1484
A Novel Imaging Classification of Iron-Related Lesions in Multiple Sclerosis

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Introduction: Susceptibility-weighted imaging (SWI) is an MRI sequence capable of detecting iron deposition, a hallmark of activated microglia in multiple sclerosis (MS). Paramagnetic rim lesions (PRLs) are well-established SWI findings indicative of chronic inflammation, particularly in progressive MS.
Objectives/Aims: This study aimed to explore the heterogeneity of iron-related lesions, including but not limited to PRLs, using SWI and clinical parameters.
Methods: We retrospectively analyzed MRI data including SWI acquired with a 3 Tesla scanner, from MS patients who visited our institution between January 1, 2018, and July 31, 2023. Lesions with central low signal on SWI, distinct from PRLs, were defined as central iron deposition lesions (c-IDLs), while lesions exhibiting diffuse low signal throughout were classified as diffuse iron deposition lesions (d-IDLs). Clinical variables including MS phenotype, Expanded Disability Status Scale (EDSS), disease duration, and third ventricular width were evaluated.
Results: Among 80 MS patients, 71 were included after excluding cases with incomplete data. The cohort included 50 females, with a mean age of 44.2 ± 11.8 years, and a median disease duration of 13.4 years (IQR 6.25–18.7). Relapsing-remitting multiple sclerosis (RRMS) and progressive MS (PMS) were diagnosed in 59 and 12 patients, respectively. PRLs were observed in 2 patients, c-IDLs in 2, and d-IDLs in 21. Notably, 8 patients had both PRLs and d-IDLs. PRLs were significantly more common in PMS than in RRMS (33.3% vs. 10.2%, $p = 0.036$). Among the 33 patients with iron-related lesions, those with c-IDLs had significantly shorter disease duration (median 0.042 years vs. 13.4 years, $p = 0.011$), lower EDSS scores (median 0 vs. 2, $p = 0.030$), and narrower third ventricular widths (median 3.5 mm vs. 5.5 mm, $p = 0.045$) compared to those with PRLs or d-IDLs.
Conclusion: PRLs are more prevalent in progressive MS and may serve as a useful imaging biomarker for disease progression. c-IDLs appear to occur in the early stages of MS and may reflect microglia-driven inflammation originating at the lesion core. This novel classification of iron-related lesions could provide deeper insights into the temporal and pathological heterogeneity of MS.

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P1485
Deep Learning driven prediction of Multiple Sclerosis using structural MRI data

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Introduction: Accurate and early diagnosis of MS is crucial for effective disease management. Magnetic Resonance Imaging (MRI) is a pivotal diagnostic modality due to its sensitivity in detecting pathological lesions. However, conventional diagnostic approaches heavily depend on manual interpretation, introducing variability and diagnostic delays.
Objectives/Aims: In this study, we propose a deep learning framework employing Convolutional Neural Networks (CNN) for automated prediction of MS using MRI scans.
Methods: The study setting was the MS clinic of a large integrated health care system serving south-eastern Michigan. Electronic data base was searched and patients with confirmed MS diagnosis and healthy controls of 150 subjects used from a dataset. MRI images were pre-processed to enhance lesion visibility. This was followed by training CNN models to classify images into MS and healthy control categories. The CNN architecture is optimized to detect intricate patterns specific to MS lesions, enhancing prediction reliability and diagnostic consistency. Data augmentation techniques was implemented to strengthen model robustness, addressing issues related to limited training data. Model performance is evaluated using metrics including accuracy, precision, recall, and F1-score, providing comprehensive insights into predictive capabilities.
Results: Of the 100 MS patients, 72 were female, 27 male, 42 were White, 57 were Black, and the mean age was 45.65 years. A custom convolutional neural network (CNN) was designed with three convolutional layers (32, 64, 128 filters), ReLU activation, and max pooling, followed by flattening and two fully connected dense layers (128 units and a final output neuron with sigmoid activation). The model was trained on 100 preprocessed MRI images using binary cross-entropy loss and the Adam optimizer, over 50 epochs with 100 iterations. Data augmentation and dropout (rate 0.3) were employed to reduce overfitting. The model achieved a validation accuracy of approximately 80%, demonstrating potential for MRI-based MS prediction on limited data.
Conclusion: Our preliminary findings demonstrate that CNN models effectively identify MRI features indicative of MS,

achieving high diagnostic accuracy and precision. This study highlights the potential of CNN-driven approaches to significantly enhance diagnostic accuracy and clinical efficiency. Future research will involve validation using larger datasets and exploration of CNN explainability techniques to improve clinician trust and encourage adoption in MS diagnosis.

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P1486
Paramagnetic rim lesions are associated with self-reported cognitive decline but not other psychiatric symptoms of multiple sclerosis

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Introduction: Paramagnetic rim lesion (PRL) is an emerging biomarker of chronic inflammation in multiple sclerosis (MS), which is related to higher physical and cognitive disability. However, it remains unclear whether the presence of PRL is also associated with psychiatric status and patient-reported outcomes.
Objectives/Aims: To elucidate the relationship of PRL to physical, cognitive, and psychiatric functions in MS.
Methods: Seventy-nine MS patients (61 relapsing and 18 progressive MS) were enrolled between May 2024 and February 2025, and simultaneously subjected to 3-Tesla head magnetic resonance imaging including susceptibility-weighted imaging, clinical evaluation by Expanded Disability Status Scale (EDSS) score, Timed 25-Foot Walk (T25-FW), 9-Hole Peg Test (9-HPT) and iPad®-based processing speed test (CogEval), and self-reported questionnaires (Apathy Scale [AS], Fatigue Questionnaire [FQ], Hospital Anxiety and Depression Scale [HADS], EuroQoL 5-Dimension 5-Level Test [EQ-5D-5L], Multiple Sclerosis Quality of Life-54 [MSQOL-54]).
Results: PRL was detected in 49 (62%) MS patients. The patients with one or more PRLs (PRL $\geqslant$ 1 group) tended to have higher EDSS scores than those without PRLs (No PRL group), although they were similar in age, gender, and disease duration. No differences were observed in T25-FW, 9-HPT, AS, FQ, HADS, EQ-5D-5L, and MSQOL-54 physical and mental health composite scores. However, the CogEval z-scores were lower in the PRL $\geqslant$ 1 group than in No PRL group ($p = 0.0086$). The number of PRLs was significantly correlated with EDSS scores ($r = 0.314$, $p = 0.0051$), as well as CogEval z-scores ($r = -0.397$, $p = 0.0007$). The self-assessed cognitive function as an MSQOL-54 subdomain was lower in the PRL $\geqslant$ 1 group than that in No PRL group ($p = 0.0294$).
Conclusion: PRL is linked to cognitive decline assessed by iPad®-based processing speed test and a self-report test, but not with psychological status or total QOL scores at the time of testing.

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P1487
Association between mogad clinical phenotype and changes in total brain and thalamic volumes: an exploratory cohort study

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) usually presents with optic neuritis or myelitis, while cerebral or brainstem involvement is less common in adults. Grey matter atrophy progresses with attack frequency. This cross-sectional study assesses total brain volume, total grey matter, and thalamic volumes in MOGAD, hypothesizing phenotype-specific differences.
Objectives/Aims: To test if (a) assesses total brain volume, total grey matter, and thalamic volumes and (b) cognitive function in individuals with MOGAD differ between clinical phenotypes.
Methods: We calculated total brain, total grey matter, and bilateral thalamic volumes from 3T MRI brain scans from MOGAD patients, expressed as logit-transformed percentiles relative to a normative dataset (mdbrain). Patients were stratified based on clinical phenotype: optic neuritis (MOGAD-ON) and encephalitis or brainstem syndrome (MOGAD-ENC/BSS). Clinical (Symbol Digit Modalities Test; age-, sex-, and education-adjusted z scores) and demographic data were collected.
Results: Thirteen patients were analyzed (MOGAD-ON: $n = 8$; MOGAD-ENC/BSS: $n = 5$). The median age at MRI scan was

higher (47.7 vs 30.2 years) and the number of attacks lower (2.0 vs 5.0) in the MOGAD-ON subcohort. Female predominance was noted in MOGAD-ENC/BSS (60.0%). Total brain volume (-0.3 vs -2.4, p = 0.02) and mean thalamic volume (-0.20 vs -2.9, p = 0.05, Mann-Whitney U test) was lower in the MOGAD-ENC/BSS subcohort. SDMT scores did not correlate with total brain, total grey matter, or thalamic volume, and did not differ between subcohorts (MOGAD-ENC/BSS: 1.1, MOGAD-ON: 0.7, p = 0.22, Mann-Whitney U test).
Conclusion: Our findings suggest phenotype-specific grey matter atrophy in MOGAD: Patients with encephalitic or brainstem manifestations may show lower total brain volume and lower thalamic volume compared to MOGAD-ON, despite preserved cognitive function measured with SDMT.

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P1488
AI-based multiparametric MRI analysis of patients with MS and Progression Independent of Relapse Activity

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Introduction: Progression independent of relapse activity (PIRA) represents the main driver of clinical disability accrual in MS. Pathological mechanisms underlying PIRA are likely various and still uncertain; however, most of them hesitate in neuronal damage/loss which appear visible in vivo on MRI as brain atrophy (BA). Although BA is widely used as outcome measure in clinical trials, it is still difficult to detect at a subject-level in the real-world practice. Also, its functional correlate/impact on the clinical performance remains unclear.
Objectives/Aims: The primary goal of this study was to identify the BA pattern (BAP) associated with PIRA using Artificial Intelligence (AI); secondarily, we aimed to assess the functional and microstructural connectivity correlated to PIRA-associated BAP.
Methods: We included 27 MS patients treated with Natalizumab presenting PIRA and clinically stable (CS) disease. Patients underwent a motor and cognitive evaluation (EDSS, Symbol Digit Modality test (SDMT)) and a brain MRI (MPRAGE, 3D-FLAIR, resting state (RS)-fMRI, DTI). Brain volumetrics was analyzed through an AI software (Pixyl) detecting global/regional atrophy. Comparisons of clinical/MRI volumetric measures were performed between PIRA and CS groups. We then assessed the RS functional connectivity (RS-FC) -by seed-based analysis- and the microstructural damage -through tract-based spatial statistics (TBSS)- of PIRA-associated BAP.
Results: Age, sex and disease/treatment duration resulted comparable between the two groups. PIRA group showed a higher proportion of patients with global/total white matter atrophy. No differences were found for total gray matter (GM) atrophy, however when analyzing the single GM regions, PIRA group showed a greater proportion of patients with left thalamus atrophy (leftTA) (88% vs. 40%; p-value=0.0324). From FC analysis, patients with leftTA resulted to have an abnormal anticorrelated activity ($p<0.0001$) between the posterior cingulum gyrus (a Default Mode Network (DMN) hub) and a cortical area including fusiform/parahyppocampal gyrus. Interestingly, patients with leftTA -showing those FC abnormality- had a lower score at SDMT compared to the group with no leftTA (median 40.5 vs. 56; p-value=0.0182). From TBSS analysis, leftTA group showed a greater microstructural damage ($p<0.05$), more evident in the posterior thalamic radiations.
Conclusion: AI enables to identify BAP associated to clinical phenotypes. PIRA is associated with leftTA, which correlates to a RS-FC alteration within the DMN, possibly involved in decreased cognitive performance.

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P1489
Ultra-High Field MRI-Based Myelin Water Fraction supports the identification of Active Remyelination in MS Post-Mortem Brains

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Introduction: Multiple Sclerosis (MS) lesions are the result of multiple waves of inflammation, myelin and axonal damage, repair and /or degeneration. Better characterization of these stages could improve our understanding of lesion biology and support the development of targeted therapies. Ultra-high-field MRI allows high-resolution assessment of MS lesions, and quantitative measures can sensitively reflect underlying pathology.
Objectives/Aims: To investigate the cellular composition of MS lesions during active remyelination and its detection through high-resolution Myelin Water Fraction (MWF) mapping.
Methods: Four lesion-containing post-mortem brain blocks from two patients with Secondary Progressive MS were scanned at Bruker a 9.4 T spectrometer with optimized 3D-Multiple Gradient Echo (3DMGE) and T2-weighted Multi-Slice-Multi-Echo (MSME) protocols. Based on the MSME, MWF was estimated. Lesions were classified by immunohistochemistry (IHC) based on myelin (anti-MBP) and activated microglia (anti-MHC II) staining. Active remyelination was identified in one block based on Brain Enriched Myelin Associated Protein 1 (BCAS1) staining, where Imaging mass cytometry (IMC) further profiled cellular composition. Regions of interest (ROIs) including lesion core, border, perilesional rim and surrounding white or grey matter, were manually segmented based on the GRE-magnitude and on IHC images and compared with MWF maps.
Results: Areas of potential remyelination, identified based on MBP-staining, showed increased MWF relative to the lesion core ($p=0.03$), although still lower than normal-appearing tissue ($p=0.0002$). In a selected cortical lesion, localized increases in MWF on regions of approximately 100x100 µm, correlated spatially with the presence of remyelinating BCAS1+ oligodendrocytes. Here IMC analysis revealed: reduced S100b+ astrocyte density, stable reactive GFAP+ astrocyte and neuronal density, unchanged activated microglia, and increased mature oligodendrocytes, relative to nearby normal-appearing grey matter.
Conclusion: We showed that ultra-high-field MWF might detect ongoing remyelination in post-mortem MS brain tissue at single-cell resolution. Our approach enables correlations between MRI signals and lesion cellular composition. Ongoing work aims to dissect cell-type-specific contributions to MWF and validate the findings in a larger cohort, potentially supporting the clinical adaptation of these metrics, and the further development of targeted therapies.

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P1490
Alterations in Brain Activity and Connectivity in Core Resting-State Networks of Multiple Sclerosis Patients Using a 15 T MRI Scanner: Evidence of Reliable Findings.

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Introduction: MS is a neurodegenerative disorder that causes demyelination and axonal damage, affecting brain function and connectivity. Resting-state functional magnetic resonance imaging (rs-fMRI) provides valuable insights into alterations in brain activity and connectivity in MS patients. Core resting-state networks (RSNs) involve the Default Mode Network (DMN),

Central Executive Network (CEN), and Salience Network (SN) are critical for cognitive, motor, and emotional processes. Understanding the disruptions within these networks in MS could help elucidate disease mechanisms and offer potential biomarkers for disease progression.
Objectives/Aims: This study explores alterations in brain activity and functional connectivity within Core RSNs in MS patients and examines their relationship to cognitive and motor dysfunction.
Methods: Rs-fMRI and structural (MPRAGE) data were collected from 16 Relapsing-Remitting and 4 Primary Progressive MS patients (disease duration 5.6±3.3 years) and 20 age-matched healthy controls (HC) using a 1.5 T Philips scanner. The DPABI toolbox was utilized to compute brain activity and connectivity, including degree centrality (global connectivity) and regional homogeneity (local connectivity) following preprocessing. Connectivity matrices were extracted from RSNs covering 18 brain regions. A two-sample equal variance t-test was performed to assess connectivity differences between MS patients and HC.
Results: MS patients exhibited significant alterations in brain activity and connectivity across several RSNs. The CEN showed significant reductions in local connectivity, particularly in the anterior cingulate cortex, lateral prefrontal cortex right (r), and posterior parietal cortex r. The Supramarginal Gyrus as a part of the SN shows a significant reduction in global and local connectivity in MS patients. Further, significant brain activity alterations were observed in the MS patients, in the CEN, particularly in the anterior cingulate, lateral prefrontal r, and posterior parietal cortex r.
Conclusion: This study reveals widespread disruptions in resting-state brain connectivity and activity within core networks in MS patients compared to healthy controls. Notably, these meaningful and robust results were obtained using a 1.5 T MRI scanner, emphasizing the potential of lower-field-strength systems to detect relevant functional alterations. These findings suggest that rs-fMRI could be a valuable tool for tracking disease progression and assessing motor impairments in MS.

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Imaging & Non-Imaging Biomarkers – OCT

P1491
Retinal hyperreflective foci as markers of inflammation and neurodegeneration in multiple sclerosis

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Introduction: Retinal hyperreflective foci (HRF) detected by optical coherence tomography (OCT) have been proposed as non-invasive biomarkers of activated microglia in multiple sclerosis (MS). HRF are increased in MS patients compared to healthy controls and correlate with radiological activity, cortical demyelination, and pro-inflammatory cytokines in the cerebrospinal fluid (CSF). Interestingly, HRF levels appear unaffected by therapies targeting adaptive immunity, such as Natalizumab, suggesting that microglial activation may occur independently. HRF have also been described in the outer retina of relapsing-remitting MS (RRMS) patients.
Objectives/Aims: This study aimed to: (1) examine the association between HRF and global brain volumes as markers of neurodegeneration; (2) explore the relationship between HRF and CSF biomarkers of neuroinflammation (YKL-40), neurodegeneration (neurofilament light chains, NfLs), and intrathecal inflammation (IgG index); and (3) assess HRF distribution in the outer retina in RRMS patients and healthy controls.
Methods: Sixty-six RRMS patients and 33 age-matched healthy controls underwent neurological assessment, lumbar puncture, brain MRI, and OCT. HRF were manually counted by two independent raters across all retinal layers. Brain MRI was used to quantify white matter (WM) and gray matter (GM) volumes. CSF YKL-40 and NfLs were measured by ELISA. Generalized estimating equations adjusted for age, sex, and optic neuritis history were used to assess associations
Results: HRF counts were significantly higher in all retinal layers in RRMS patients compared to controls ($p < 0.001$). GCPL HRF were positively associated with WM ($\beta = 0.0022$; $p < 0.001$), GM ($\beta = 0.0017$; $p < 0.001$), and CSF YKL-40 ($\beta = 0.11$; $p = 0.018$), but not with NfLs. OPL–ONL HRF showed a negative correlation with the IgG index ($\beta = -0.23$; $p = 0.017$).
Conclusion: HRF in the GCPL may reflect neuroinflammatory activity rather than neurodegeneration in RRMS, supporting their potential as imaging biomarkers of innate immune activation.

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P1492
Retinal layer atrophy reflects progression independent of relapse and radiological activity in relapsing multiple sclerosis

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Introduction: Progression independent of relapse activity (PIRA) is the main driver of disability accumulation in relapsing multiple sclerosis (RMS). Retinal layer atrophy measured by optical coherence tomography (OCT) reflects neuroaxonal damage, and has been associated with PIRA. However, it remains unclear whether this association is driven by subclinical inflammatory activity or reflects true progression independent of acute inflammation.

Objectives/Aims: To investigate the relationship between retinal layer atrophy and progression independent of relapse and MRI activity (PIRMA) to clarify the impact of subclinical inflammatory activity.

Methods: From an ongoing prospective observational study, RMS patients meeting the following criteria were included: an OCT scan conducted 3 to 6 months after treatment initiation (rebaseline) and at least one follow-up OCT after ⩾12 months. We evaluated associations between PIRMA and thinning of the peripapillary retinal nerve fiber layer (pRNFL) and the macular ganglion cell plus inner plexiform layer (GCIPL) using multivariate mixed-effects linear regression models adjusted for relevant covariates.

Results: A total of 210 RMS patients (mean age 30.5 years, SD 7.9; 74.1% female) were analyzed over a median observation period of 2.3 years (range 1–5.9 years).

PIRMA was observed in 33 (15.7%) patients, while PIRA was encountered in 61 (29.0%). Multivariate models revealed that PIRMA was associated with significantly more pronounced thinning of both GCIPL (0.72%/y, $p<0.001$) and pRNFL (1.05%/y, $p<0.001$).

Conclusion: Our multivariate findings indicate that retinal atrophy is significantly linked with PIRMA, reinforcing its potential as a biomarker of MS-related neuroaxonal degeneration that occurs independently of acute focal inflammation.

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P1493
Influence of OSCAR-IB criteria on test-retest reliability of Spectralis SD-OCT retinal layer thickness measurements in people with Multiple Sclerosis

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Introduction: Retinal optical coherence tomography (OCT) allows the assessment of inter-eye differences (IEDs) in macular ganglion cell-inner plexiform layer (GCIPL) and peri-papillary retinal nerve fiber layer (pRNFL) thicknesses, to identify unilateral optic nerve involvement (UONI), and support dissemination in space (DIS) as part of the 2024 revised McDonald MS diagnostic criteria. The OSCAR-IB criteria [(O) obvious problems, (S) poor signal strength, (C) centration of scan, (A) algorithm failure, (R) retinal pathology (I) illumination and (B) beam placement] are essential for identifying suboptimal-quality optic nerve OCTs, which could contribute to inaccurate UONI identification, although understudied in macular OCTs.
Objectives/Aims: To assess differences in test-retest reliability of GCIPL and pRNFL thicknesses between scans fulfilling (SFO) vs. scans not fulfilling (SNFO) OSCAR-IB criteria, acquired using Spectralis SD-OCT.
Methods: We recruited 98 PwMS, 31 healthy controls, and 35 people with other neurological diseases. Using macular volume and optic nerve head protocols, participants underwent Spectralis SD-OCT to measure GCIPL and pRNFL thicknesses, respectively. Two OCTs per eye per protocol were obtained and classified as SFO or SNFO. Reproducibility was evaluated with intra-visit intraclass correlation coefficients (ICCs), coefficients of variation (COVs), and mean absolute differences (MAD).
Results: SFO (GCIPL:n=199; pRNFL:n=216) demonstrated superior reliability, as compared to SNFO (GCIPL:n=97; pRNFL:n=72). For GCIPL thicknesses, SFO had a MAD of 0.49μm (SD 0.41μm) with an ICC of 0.997, and COV of 0.53%, while SNFO had a GCIPL MAD of 0.77μm (SD 0.9μm), ICC of 0.990, and COV of 0.83%. For pRNFL thicknesses, SFO showed a MAD of 1.5μm (SD 1.5μm), ICC of 0.991, and COV of 1.14%, while SNFO exhibited a pRNFL MAD of 4.11μm (SD 10.13μm), ICC of 0.827, and COV of 3.38%. Low signal strength and algorithm failure were the most impactful OSCAR-IB criteria on GCIPL (COV=3.34%) and pRNFL (COV=7.72%) thickness reproducibility, respectively.
Conclusion: GCIPL and pRNFL measurements demonstrated superior reliability in SFO, as compared to SNFO, with pRNFL reliability more diminished than GCIPL reliability by OSCAR-IB violations. GCIPL thicknesses may remain relatively reliable with lower-quality scans. These findings highlight the need to apply quality control criteria for interpreting pRNFL and GCIPL thickness measurements in order to reduce artifactual UONI and accurately support DIS for the diagnosis of MS.

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P1494
A view across time: OCTA parameters predict general disability in pwMS

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Introduction: Optical coherence tomography angiography (OCTA) is a promising tool that visualizes retinal vascular structures, revealing new metabolic and vascular elements driving multiple sclerosis (MS) disease pathology. While its role in assessing visual function has been increasingly explored, the association between retinal vascular changes and general disability in patients with MS (pwMS) remains underinvestigated.
Objectives/Aims: To assess the role of OCTA as a predictive biomarker of disability in pwMS.
Methods: 41 patients that had received relapsing-remitting multiple sclerosis (RRMS) diagnosis in the previous 6 months before inclusion underwent baseline OCTA evaluation and clinical evaluation at baseline, 6 months and yearly over a 4-year period. Correlations between OCTA parameters and Expanded Disability Status Scale (EDSS) scores were assessed by the means of linear mixed models, adjusting for age, gender and disease duration.
Results: Global reduction of vascular and perfusion densities (VD and PD) at the level of the superficial capillary plexus (SCP) consistently correlated with higher EDSS scores at all timepoints, independently of gender, age and disease duration (for global SCP VD: β = -0.34, p = 0.019, for global SCP PD: β = -0.19, p = 0.039). While no correlations were observed with baseline EDSS, a direct association was seen at 2 and 3 years follow up, suggesting retinal vascular changes might precede clinical observable disability by several years. Global SCP VD and PD strongly correlated with both the visual component of the EDSS score (SCP VD: β =-0.25, p=0.013), and subscores unrelated to visual function, such as the pyramidal (SCP VD: β = -0.23, p= 0.025) and cerebellar functional domains (SCP VD: β = -0.28, p= 0.003), suggesting a broader implication of vascular alterations in disability accrual.
Conclusion: Baseline retinal vascular integrity, as assessed through OCTA imaging, may provide valuable insights into general disability accrual in pwMS.

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P1495
Retinal hyperreflective foci: A new potential biomarker in optic neuritis

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Introduction: Retinal hyperreflective foci (HRF), presumed to represent aggregated microglial cells, have been detected on optical coherence tomography (OCT) in 70.5% of patients with relapsing-remitting multiple sclerosis (RRMS) who have no history of optic neuritis (ON).
Objectives/Aims: This study investigates the presence of HRF on OCT in patients with ON and examines their potential association with established biomarkers in RRMS.
Methods: In this cross-sectional study, patients with unilateral ON referred for evaluation of potential demyelinating disease, along with healthy controls, underwent high-resolution spectral-domain optical coherence tomography (SD-OCT). Exclusion criteria included any prior ophthalmic pathology, systemic condition affecting the visual system, and other etiologies for ON. HRF were defined according to the latest international consensus criteria as hyperreflective structures measuring less than 30 μm in diameter, without back shadowing, and located within the avascular outer nuclear layer (ONL) of the retina. Both affected (ON) and healthy (NON) eyes were examined in a dark room without the use of a mydriatic agent. A total of 121 macula volume scans, spaced 60 μm apart, were obtained from each eye. HRF were quantified within the macular region.
Results: A total of 21,538 OCT scans from 178 eyes were analysed in 93 patients with ON (RRMS = 60, CIS/idiopathic ON = 33) and 53 healthy controls. HRF were detected in at least one eye in 89.3% of patients compared to 1.8% in controls. HRF were present in the ON eye in 72% (median: 7, IQR: 1-18) and in the NON eye in 80.7% (median 4, IQR: 1-10). A higher prevalence of HRF were found in ON eyes ($p<0.001$). HRF count in the ON eye correlated negatively with ganglion cell and inner plexiform layer (GCIPL) thickness (p=0.033). Further analyses regarding MRI lesions and CSF are ongoing.
Conclusion: HRF are prevalent in both ON and NON eyes, suggesting a widespread inflammatory process. The negative correlation between HRF count and GCIPL thickness may

indicate early disease activity and neurodegeneration in multiple sclerosis.

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P1496
Association of retinal layer thinning with intrathecal inflammation in early Multiple Sclerosis

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Introduction: Retinal layer thinning, as measured by optical coherence tomography (OCT), serves as a reliable biomarker for assessing the extent of neuroaxonal damage. However, the degree to which it reflects chronic intrathecal inflammatory processes that may begin in the early stages of the disease remains unclear.
Objectives/Aims: To evaluate the correlation of cerebrospinal fluid (CSF) inflammatory markers measured at the time of diagnosis with retinal layers thinning.
Methods: Forty-eight patients from a single referral centre (the University of Verona) affected by RRMS, who did not have a clinical episode of optic neuritis or other ocular pathologies were included in the study. Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany, dilated pupils, eye tracking) was employed. For measurement of the peripapillary retinal nerve fibre layer thickness (RNFL), we used a ring scan around the optic nerve head (12°, 1536 A-scans, 16⩽Automatic Real-Time (ART) averaging ⩽100) using the device-internal segmentation module 6.0.14.0. A macular volume scan (25°×30°, 61 B-scans, 768 A-scans per B-scan, 12⩽ART⩽15) quantified the retinal volume. Macular retinal volume was segmented to obtain data on single layers, in particular ganglion cell layer (GCL) and inner plexiform layer (IPL) volume were obtained. Data on average pRNFL, superior sector, temporal sector, inferior sector, nasal sector (um), GCL and IPL (mm^3) were collected. For analysis, the OCT values of the right eye were included. CSF levels of 68 inflammatory molecules were evaluated with multiplex technology at the time of diagnosis.
Results: Of all 48 patients enrolled 35 (73%) were females. Median EDSS was 3 (range 0-4), and mean age was 37,5 ± 14. A lower GCL was significantly associated with higher levels of inflammatory markers including MMP1 (r = -0.424, p= 0.035), Osteopontin (r=-0.322, p= 0.048), CCL3 (r=-0.334, p=0.040), and a trend towards a negative correlation with many markers of smoldering disease activity including sCD163 (r=-0.217) and Chitinase3-like1 (r=-0.265). Similarly, lower IPLwas associated with increased values of MMP1 (r=-0.540, p=0.005), IFNalfa2 (r=-0.501, p= 0.041), CXCL2 (r=-0.439, p=0.036) and slightly associated with LIGHT levels (r=-0.378).
Conclusion: OCT performed at the time of diagnosis could represent a reliable marker of intrathecal inflammatory processes occurring since the early stages of MS.

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P1497
Inner retinal hyperreflective foci as predictors of early disease activity in newly diagnosed multiple sclerosis patients

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Introduction: Hyperreflective foci (HRF) in the inner retina (IR), detected via optical coherence tomography (OCT), are emerging as biomarkers of microglial activation in multiple sclerosis (MS). While their presence has been consistently reported, their prognostic value—particularly in identifying patients at risk of early inflammatory activity—remains unclear.
Objectives/Aims: This study aimed to evaluate whether baseline HRF count can predict disease activity and influence treatment response in newly diagnosed people with MS (pwMS).
Methods: We retrospectively included 57 pwMS from a single-center cohort. All patients were enrolled at clinical onset, with no prior evidence of disease activity or optic nerve inflammation, confirmed through clinical, radiological, and OCT parameters. At baseline, patients were stratified based on the initial disease-modifying therapy prescribed: platform therapies (PTpwMS) versus high-efficacy therapies (HETpwMS). HRF count was assessed in both eyes and summed across the ganglion cell–inner plexiform layer (GCIPL), inner nuclear layer

(INL), and inner retina (IR = GCIPL + INL). PTpwMS were followed longitudinally for ⩾24 months. The primary endpoint was time to treatment switch due to evidence of disease activity (clinical relapses or new/enlarging/gadolinium-enhancing lesions on MRI).
Results: At baseline, HETpwMS had significantly higher HRF counts in all retinal layers compared to PTpwMS (GCIPL: 25.8±4.4 vs 19.0±5.3; INL: 50.2±9.9 vs 37.1±9.4; IR: 76.0±12.2 vs 56.1±12.3; all $p < 0.001$). ROC analysis identified a threshold of 75 IR-HRF, above which PTpwMS showed a significantly shorter time to treatment switch (HR = 6.5; 95% CI: 1.5–28.8; $p = 0.007$).
Conclusion: Higher baseline HRF counts, particularly in the inner retina, may help predict early disease activity in MS. Quantifying HRF at diagnosis could support neurologists in selecting high-efficacy therapies earlier in the disease course.

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P1498
Toward Reliable Individual-Level Optical Coherence Tomography Biomarkers in Multiple Sclerosis: A Protocol Comparison Study

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Introduction: Inner retinal layer thickness, particularly the ganglion cell-inner plexiform layer (GCIPL), assessed via optical coherence tomography (OCT), is an established surrogate marker of neuroaxonal damage in multiple sclerosis (MS). For longitudinal monitoring – though valuable in group analyses – the small absolute changes over time often approximate inter-scan variability, limiting reliability and constraining utility in therapy monitoring and personalized management.
Objectives/Aims: To investigate whether the reliability of OCT-based GCIPL thickness measurements can be enhanced by modifying scan acquisition parameters.
Methods: This prospective study, enrolled people with MS (pwMS) diagnosed according to the 2017 McDonald criteria, along with age- and sex- matched healthy controls (HC). All participant underwent spectral-domain OCT at baseline, and after two and four weeks. At each visit, five macular scan protocols were performed in randomized order: standard (49 lines, high-speed [HS], automated real-time tracking [ART] 9), high-ART (49 lines, HS, ART 50), high-lines (97 lines, HS, ART 9), high-resolution (49 lines, high-resolution [HR], ART 9), and maximum (97 lines, HR, ART 50). The primary outcome was reliability of GCIPL thickness measurements, assessed via intraclass correlation coefficients (ICC) using a 2-way mixed-effects model with absolute-agreement. To assess the effect size of test–retest reliability, the mean absolute difference (MAD) between measurements was calculated.
Results: In total, 26 eyes from 9 pwMS and 4 HC were included. Mean baseline GCIPL thickness across the five OCT protocols were 69.2µm (5.6), 69.9µm (5.8), 69.5µm (5.7), 69.5µm (5.7), and 70.2µm (5.9) for the five protocols, respectively, demonstrating excellent inter-protocol reliability (ICC 0.99; 95% CI 0.98–1.00; $p<0.001$). Each protocol independently exhibited high test-retest reliability. Notably, the high-lines, high-resolution, and maximum protocols yielded marginally superior, yet statistically non-significant, reproducibility (ICC 1.00; 95% CI 0.99–1.00; $p<0.001$), with similar effect sizes reflected by MAD ranging from 0.4 to 0.5µm (SD 0.3–0.4). The shortest mean scan time was observed with the standard protocol (10.6s [1.6]), followed by the high-resolution (20.5s [2.3]), high-lines (21.0s [3.3]), high-ART (57.4s [11.2]), and maximum protocol (232.5s [35.0]).
Conclusion: All evaluated OCT protocols demonstrated excellent test-retest and inter-protocol reliability in measuring GCIPL thickness. Balancing reliability with time efficiency, high-lines and high-resolution protocols offer an optimal compromise between data quality and practical feasibility. Standardized acquisition parameters are strongly recommended to ensure reproducibility and comparability of findings across studies.

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P1500

Sex Differences in the Retina-Brain Connection in Adults with Relapsing-Remitting MS Following Optic Neuritis

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Introduction: Sex differences may influence MS pathophysiology; while females have a higher MS risk, males often experience worse progression. Trans-synaptic degeneration (TSD), triggered

by optic neuritis (ON) or brain inflammation, may drive widespread neurodegeneration, which may contribute to long-term disability. Whether TSD differs between sexes in relapsing-remitting MS (RRMS) following ON remains unclear.
Objectives/Aims: To investigate sex-related differences in TSD in early-stage RRMS.
Methods: People recently diagnosed (<6 months prior to baseline) with RRMS were recruited to FutureMS, a Scottish multicentre longitudinal cohort study. Cross-sectional 3T magnetic resonance imaging and optical coherence tomography were used. Thalamic volume was segmented with FreeSurfer-v6; Peripapillary retinal nerve fibre layer (pRNFL) and ganglion cell–inner plexiform layer (GCIPL) metrics were extracted using OCTolyzer software. Expanded Disability Status Scale (EDSS) was performed on all participants. Sex-related comparisons were performed separately for ON and non-ON groups using t-tests or Mann-Whitney U-tests. Generalised estimating equations assessed sex and ON effects on retina-brain associations, adjusted for age and imaging site, and multiple comparisons corrected.
Results: Data from 161 participants (120 Female: mean age ± SD yrs: 37.4±9.7; median EDSS: 2.0; 41 Male: mean age ± SD yrs: 36.2±11.5; median EDSS: 2.5) were analysed. ON history was more common in males (39%) than females (34%) ($\chi^2(4)=33.5$, $p<0.01$). In the ON group, males had significantly lower pRNFL thickness (temporal, superior-temporal), GCIPL thickness and volume (nasal), and thalamic volume (p.adjust<0.05). Lower thalamic volume was associated with lower nasal GCIPL measures in Males-ON than Females-ON (p.adjust<0.05). No sex differences were found in the non-ON group.
Conclusion: Males with RRMS may experience more severe TSD post-ON than females, with no sex differences in non-ON participants. Findings may support GCIPL and thalamic metrics as TSD markers and suggest greater visual pathway vulnerability in Males-ON. Longitudinal analyses will assess progression of sex-related TSD in MS.

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P1501
Baseline OCTA evaluation may improve prediction models for early disability progression in relapsing-remitting multiple sclerosis

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Introduction: Retinal microvasculature assessed using optical coherence tomography angiography OCTA has emerged as a potential biomarker for MS progression, reflecting underlying neurodegenerative processes.
Objectives/Aims: To evaluate if baseline OCTA metrics improve detection of early disease progression in patients with newly diagnosed relapsing-remitting MS (RRMS).
Methods: We performed a longitudinal analysis on 41 patients recently diagnosed with RRMS. Patients underwent neurologic examination, OCT and OCTA scanning and cerebrospinal fluid (CSF) and serum sampling at baseline and 1-year follow-up visit. Fluid biomarkers included neurofilament light-chain (NfL), glial fibrillary acidic protein (GFAP), and chitinase 3-like-1 (CHI3L1) from both serum and CSF. OCTA analysis provided global and sectorial parameters of vascular density in the deep (DCP) and superficial (SCP) capillary plexuses. The primary outcome was Extended Disease Status Scale (EDSS) - Plus Score confirmed progression at 1 year. Univariate binary regressions were performed to identify the best predictors of progression, followed by building multivariate regression models and ROC analysis to evaluate model performance.
Results: Eight patients met the EDSS-Plus progression criteria at follow-up. Baseline CSF-GFAP levels and retinal OCT metrics (retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL) thicknesses) presented significant correlations with EDSS-Plus progressor status, while NfL and CHI3L1 from both serum and CSF and serum GFAP showed no significant results. A two-variable model incorporating CSF-GFAP and GCIPL thickness achieved moderate accuracy for identifying patients with EDSS-Plus progression (AUC = 0.828, F1-score = 0.667). The addition of SCP small vessels vascular density in the superior quadrant enhanced the model's performance (AUC 0.895, F1-score 0.80), with an increase in sensitivity from 62.5% to 75% and in specificity from 93.8% to 96.9%.

Conclusion: Combining OCTA-derived metrics with traditional OCT and CSF biomarkers at baseline evaluation enhances the prediction of early disability progression in RRMS patients.

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P1502
Optical Coherence Tomography and Visual Pathway in Multiple Sclerosis Patients from Argentina

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Introduction: Over the last few years there has been growing interest in the use of visual measures as useful tools for multiple sclerosis (MS) prognosis and follow-up. Thus, it is important to recognize which visual measures might be more sensitive in representing patients' visual impairment.
Objectives/Aims: To compare the sensitivity of Low Contrast Letter Acuity (LCLA) with High contrast visual acuity (HCVA) for the assessment of optic nerve impairment objectified by structural damage observed in optical coherence tomography (OCT). To evaluate if there is progressive damage over time of LCLA, HCVA, RNFL and GCL in patients with MS
Methods: A prospective cohort study of two years of follow-up was conducted. Each patient had two assessments separated by 18 months. The retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness was measured using OCT (Heidelberg Spectralis), while HCVA (Snellen) and LCLA (Sloan 2,5%) were used to assess the visual function in each eye separately. Statistical analysis was performed using the SPSS package. Sensitivity of HCVA and LCLA for detecting structural damage was compared using chi-square analysis. Paired t-tests were used to examine intra-individual changes in HCVA, LCLA, average RNFL, and GCL.
Results: We included 136 eyes of 68 patients with MS. Out of 72 eyes with RNFL thinning we found 5.6% and 83.4% of HCVA and LCLA impairment respectively. Out of the 80 eyes with GCL thinning, we found 4% and 79% of HCVA and LCLA impairment respectively. We found a high correlation between LCLA and RNFL ($r=0.50$ $p<0.01$), LCLA and GCL ($r=0.53$, $p<0.01$). The HCVA correlates moderately with RNFL ($r=0.47$ $p<0.01$) and low with GCL (r=0.21 p 0.08). The sensitivity for detecting visual pathway impairment was 5% and 84% with HCVA and LCLA, respectively. HCVA remained unchanged (ΔVA OD: M=0.00, p=1.00; ΔVA OI: M=0.00, p=1.00), while LCLA improved (ΔLCVA M=0.03, 95% CI: 0.006–0.054, p=0.015). RNFL decreased slightly but significantly (ΔRNFL: –0.59 μm, p=0.031); GCL did not change (p=0.292).
Conclusion: We demonstrate that LCLA measurement is more sensitive than HCVA for assessing optic nerve impairment objectified by OCT. While HCVA remained stable, LCLA and RNFL showed measurable changes over times. These findings support the utility of LCLA and OCT as sensitive tools for monitoring progression in patients with MS.

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P1503
Connection between cognitive decline and retinal nerve fiber layer thickness measured by optical coherence tomography in patients with multiple sclerosis

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Introduction: Different biomarkers are under investigation to measure progression in Multiple Sclerosis (MS). The possible uses of the Optical Coherence Tomography (OCT) to assess neurodegeneration in neurological conditions have been widely investigated. Currently, its application as a biomarker in MS is being studied, but there is no consensus about it in clinical practice.
Objectives/Aims: To evaluate the use of OCT as a biomarker tool to detect progression of the disease in MS patients by analyzing the relation between cognitive impairment and retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness
Methods: A prospective cohort study of two years of follow-up was conducted. Each patient had two assessments separated by 18 months. The RNFL and GCL thickness was measured using OCT (Heidelberg Spectralis). The cognitive impairment was assessed using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS), and the Neuropsychological Screening Battery for Multiple Sclerosis (NSB-MS). Physical impairment was measured with Expanded Disability Status Scale (EDSS) and Multiple Sclerosis Functional Composite

(MSFC). Statistical analysis was performed using the SPSS package
Results: We included 61 patients with MS. Initial measurements revealed an average RNFL thickness of 89.91 μm (±16.75) in the right eye and 88.41 μm (±16.50) in the left eye, an average GCL thickness of 42.6 μm (±9.70) in the right eye and 42.12 μm (±8.81) in the left. No statistically significant differences were observed across RNFL quadrants or GCL values over time, except of the nasal quadrant of left eye, which had significant reduction in RNFL thickness ($p = 0.0401$). Patients with RNFL thickness with altered values exhibited poorer performance in the MSFC ($p = 0.0421$) and BICAMS ($p = 0.0177$). Similarly, for the GCL thickness with altered values significantly lower scores in BICAMS ($p = 0.0271$) were found.
Conclusion: This study revealed significant correlations between altered RNFL and GCL thickness and poorer performance cognitive domains and physical functions. Longitudinal analysis demonstrated stability in most OCT parameters, with a notable exception of nasal RNFL thinning in the left eye, indicating localized progressive degeneration over time. These findings support the incorporation of OCT into routine clinical assessments and its role in evaluating the efficacy of neuroprotective therapies in MS.

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P1504
Application of optical coherence tomography in multiple sclerosis – the 2025 update of the Austrian network (AN-OCT-MS) consensus recommendations

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Introduction: Optical coherence tomography (OCT) for measuring retinal layer thicknesses is a new modality relevant for diagnosis and prognosis of multiple sclerosis (MS) now anchored in clinical routine with the 2024 revision of the McDonald criteria.
Objectives/Aims: The aim of this consensus is to provide a comprehensive recommendation for the use of OCT in patients with MS (pwMS).
Methods: This consensus was developed by an expert committee (Austrian Network for Optical Coherence Tomography in Multiple Sclerosis [AN-OCT-MS]) set up under the auspices of the Austrian Society of Neurology and the Austrian Society of Ophthalmology following a formal consensus methodology. It covers indications as well as quality standards for conduction, interpretation and reporting of OCT in pwMS. As a living consensus, it was updated in March 2025.
Results: All 20 recommendations achieved a strong consensus (>90%) including:

1) OCT should be performed as part of diagnostic workup for suspected MS. If a pathological inter-eye-difference (IED) is detected in peripapillary retinal nerve fiber layer (pRNFL, IED ⩾5μm/⩾5%) and/or ganglion-cell-and-inner-plexiform-layer (GCIPL, IED ⩾4μm/⩾4%), involvement of the optic nerve for fulfillment of dissemination in space (DIS) is considered proven, provided other causes have been excluded.
2) OCT should be performed at diagnosis or before treatment decisions to stratify for progression risk: If there are signs of advanced neuroaxonal damage (pRNFL ⩽88μm and/or GCIPL<77μm), an increased risk of disability progression over the next 3 years can be assumed, provided other causes have been excluded.
3) The use of OCT in DMT monitoring cannot currently be generally recommended. At centers particularly familiar with OCT in MS, it may be used to monitor MS-associated neuroaxonal damage, whereby results should only be interpreted in the overall clinical context and never used as the sole decision criterion.
4) OCT scans should include a peripapillary ring scan and a multilinear macular scan according to AN-OCT-MS protocol to enable assessment of pRNFL and GCIPL.
5) OCT scans should undergo quality control based on the OSCAR-IB criteria and only be used if quality criteria are met.
6) Only Spectralis® (Heidelberg Engineering) or Cirrus® (Carl Zeiss Meditec) devices should be used in MS patients, as other devices are not currently validated in MS.
7) The report on findings of an OCT in pwMS should contain a summarizing interpretation.

Conclusion: The AN-OCT-MS guidelines provide a comprehensive framework to facilitate use of OCT in patients with MS.

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P1505
The diagnostic potential of retinal asymmetry in patients with relapsing remitting multiple sclerosis

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Introduction: The optic nerve has recently been included as 5th dimension for dissemination in space into the proposed McDonald 2024 diagnostic criteria of multiple sclerosis (MS). Here, retinal optical coherence tomography (OCT) represents one possible diagnostic modality to detect inflammatory lesions of the optic nerve. However, the effectiveness of retinal asymmetry as measured by OCT to discriminate individuals with MS from healthy controls (HC) and other neurological diseases (OND) remains to be further investigated.

Objectives/Aims: This study aimed to evaluate the diagnostic performance of intereye differences (IED) of the combined ganglion cell and inner plexiform (GCIP) and the peripapillary retinal nerve fibre layer (pRNFL) in detecting MS patients with and without a history of optic neuritis (ON) within a real-world dataset of OND and HC.

Methods: This cross-sectional study retrospectively included MS patients, patients with OND, and HC. We excluded eyes with acute ON $\leqslant$ 90 days before OCT imaging (Heidelberg Engineering Spectralis OCT2), non-ON ophthalmological diseases and poor image quality. Values are presented as median and interquartile range.

Results: We included a total of 425 patients with relapsing remitting MS, 225 patients with OND and 81 HC. MS patients presented a significantly higher IED (pRNFL 4 µm [2;9]; GCIP 1,8 µm [0,7;4,2]) as compared to HC (pRNFL 2 µm [1;4]; GCIP 1,1 µm [0,7;1,4]) and OND (pRNFL 2 µm [1;5]; GCIP 1,1 µm [0,4;1,4]); $p < 0.0001$ and $p < 0.0001$, respectively. Retinal asymmetry demonstrated good diagnostic performance in distinguishing patients with a history of ON from HC (IED pRNFL AUC = 0.84; IED GCIP AUC = 0.87) and those with OND (IED pRNFL AUC = 0.84; IED GCIP AUC = 0.88). Moreover, IED measures had the capability to differentiate MS patients with and without a history of unilateral ON (IED pRNFL AUC = 0.78; IED GCIP AUC = 0.8) and MS patients from OND and HC (IED pRNFL AUC = 0.65; IED GCIP AUC = 0.68).

Conclusion: Retinal asymmetry of the inner retinal layers as measured by OCT is a valuable diagnostic marker to detect axonal lesions of the optic nerve in MS patients within both real-world neurological patient populations and an MS cohort. The IED may serve as a useful tool for identifying RRMS patients within a general neurological cohort. Further longitudinal studies are needed to evaluate the dynamics of inter-eye difference in MS and its value in demonstrating dissemination in time.

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Imaging & Non-Imaging Biomarkers – PET

P1506
TSPO-PET-measurable increase in glial activation predicts later brain atrophy in multiple sclerosis

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Introduction: In multiple sclerosis (MS), accumulation of disability is driven by central nervous system (CNS)-compartmentalized inflammation. This inflammatory process involves activated microglia and astrocytes, which contribute to neuroaxonal damage which in turn accelerates disease progression. Activated glial cells express 18-kDa translocator protein (TSPO), and TSPO-binding radioligands and positron emission tomography (PET) imaging can be used to quantitate glial activation *in vivo*.
Objectives/Aims: The aim of this study was to evaluate the longitudinal evolution of glial activation in untreated cohorts of relapsing remitting MS (RRMS) and secondary progressive MS (SPMS) patients over one-year follow-up, and to explore how a change in glial activation associates with later imaging and clinical outcomes.
Methods: Eighteen untreated MS patients (RRMS n = 8, SPMS n = 10) were studied. Brain magnetic resonance imaging (MRI) and TSPO-PET scans using [^{11}C]PK11195 were performed at baseline and one year later. Distribution volume ratio (DVR) of [^{11}C]PK11195-binding, and the proportion of TSPO-high voxels at baseline in the normal appearing white matter (NAWM) were compared to the respective parameters in follow-up scans. Changes in TSPO-PET-definable chronic lesion phenotypes were quantified. Follow-up MRI was obtained from 13 patients after 4-11 years.
Results: TSPO-signal was higher among SPMS compared to RRMS patients at baseline measured either by DVR of TSPO radioligand binding or the proportion of active voxels in the NAWM. During follow-up, TSPO uptake remained stable in RRMS patients in all regions of interest. Among the SPMS patients, the proportion of active voxels in the NAWM increased significantly over one-year follow-up. Greater increase in the proportion of active voxels in the NAWM over one year associated with later development of brain atrophy.
Conclusion: Our study provides novel information about the natural evolution of CNS-compartmentalized inflammation and demonstrates an important link between NAWM TSPO-signal and later adverse outcomes among MS patients, supporting the notion that diffuse glial activation in the NAWM contributes to disease progression.

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P1507
Increased TSPO-binding Associates with Brain Atrophy in Multiple Sclerosis

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Introduction: In MS, chronic activation of microglial cells plays an important role. Microglial activation can be measured in vivo using positron emission tomography (PET) with the radioligand [^{11}C]PK11195, which specifically binds to the 18 kDa translocator protein (TSPO). Increased TSPO-PET measurable microglial activation associates with increased disability,

microstructural and neuroaxonal damage, and also predicts disease progression in MS.
Objectives/Aims: To study the association between diffuse microglial activation and brain atrophy in MS.
Methods: TSPO-PET with [^{11}C]PK11195 radioligand and 3T magnetic resonance imaging (MRI) scans were obtained. The volumes of whole brain, normal appearing white matter (NAWM), cortical GM(cGM), thalamus, ventricles, and T2 lesions were calculated as parenchymal fractions (PF). The specific TSPO-binding was quantified as distribution volume ratio (DVR). Patients were classified into two groups based on the percentage of TSPO-active voxels in white matter (WM). Greater than 9.6% was considered as HOT-PET positive and less than 9.6% as HOT-PET negative. Group comparisons, Pearson correlation analyses, and linear regression adjusted with age and disease type were performed to evaluate the associations between DVRs and volumetric brain measures.
Results: The study cohort included 50 MS patients (38 women, 12 men; 42 relapsing-remitting MS and 8 progressive MS), with mean age of 47 years (SD 6.74). The median disease duration was 18.9 (Q1-Q3 16.0-24.3) years. The median EDSS was 2.5 (range 1-6.5). The increased NAWM DVR correlated with decreased whole brain (r=-0.41, p=0.003), NAWM (r=-0.40, p=0.004), cGM (r=-0.34, p=0.015), and thalamus (r=-0.42, p=0.002) volumes, and increased ventricle volume (r=0.30, p=0.037) and T2 lesion load (r=0.33, p=0.018). In addition, increased thalamus DVR correlated with decreased thalamus volume (r=-0.54, p<0.001). All associations except for cGM and ventricle volume remained significant when adjusted with age and disease type. HOT-PET positive patients (n=25) were older (p=0.012) and had higher EDSS (p=0.016) than HOT-PET negative patients (n=25). HOT-PET patients had smaller NAWM and thalamus volumes and larger ventricles compared to HOT-PET negative patients (NAWM 31.98 vs. 33.69; p=0.049; thalamus 0.95 vs. 1.01; p=0.018; ventricles 2.46 vs. 1.76; p=0.018).
Conclusion: The association between increased microglial activation and brain atrophy among MS patients highlights the significance of diffuse WM inflammation in progression-promoting neurodegeneration.

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P1508
Systemic and Central Nervous System 18F-Fluorodeoxyglucose-Positron Emission Tomography Findings in Neuromyelitis Optica Spectrum Disorder and Myelin Oligodendrocyte Glycoprotein Associated Disease

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Introduction: Aquaporin-4 seropositive neuromyelitis optica spectrum disorder (AQP4+NMO) and myelin oligodendrocyte glycoprotein antibody associated disease (MOGAD) are rare inflammatory diseases of the central nervous system (CNS). Investigations during workup of these conditions may include ^{18}F-fluorodeoxyglucose-positron emission tomography (FDG-PET) to aid in the differential diagnosis by assessing for systemic inflammation or malignancy and can offer insights into CNS metabolic activity.
Objectives/Aims: To describe systemic, lesional, and regional brain FDG-PET findings in AQP4+NMO and MOGAD.
Methods: In this single-center retrospective study, we included individuals with AQP4+NMO and MOGAD with available FDG-PET after disease onset. FDG-PET were reviewed for systemic findings and metabolic abnormalities related to CNS lesions underlying clinical attacks within 30 days prior to FDG-PET. For those with dedicated brain FDG-PET, NeuroQ software was used to generate standardized Z-scores of FDG avidity in 47 brain regions.
Results: FDG-PET following disease onset was available for 26 AQP4+NMO and 9 MOGAD participants. Relevant systemic FDG-PET findings were found exclusively in patients older than 50 years old, and included 6 patients with AQP4+NMO with breast, thyroid, and appendiceal cancer, systemic vasculitis, and organizing pneumonia, and 1 MOGAD patient with a renal mass. In AQP4+NMO, 2/3 with acute optic neuritis and 1/8 with acute myelitis showed corresponding lesional optic nerve or spinal cord hypermetabolism, respectively. In MOGAD, this was observed in 1/3 cases with acute optic neuritis and the 1 case of acute myelitis. In those with acute optic neuritis, all 3 AQP4+NMO and 1/3 MOGAD cases had significant hypometabolism of the primary visual cortices. For those with acute myelitis, 6/8 AQP4+NMO had significant hypometabolism in various frontal lobe areas, whereas this was not observed in the 1 MOGAD case.
Conclusion: FDG-PET identified a number of systemic and lesion-related findings in AQP4+NMO and MOGAD. Malignancies were identified in several patients, exclusively though in people over 50 years of age. Hypermetabolic changes corresponding to lesions in the optic nerve and spinal cord were observed in cases of acute optic neuritis and acute myelitis. Regional brain hypometabolism was observed in areas interconnected to acute lesions, consistent with a diaschisis phenomenon.

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P1509
PET Imaging of Brain Microglial Activation Reflects Spinal Cord Atrophy and Clinical Decline in Multiple Sclerosis

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Introduction: Glial activation in normal-appearing white matter (NAWM) is a key feature of diffuse neuroinflammation in MS, undetectable by conventional MRI. PET imaging with ^{11}C-PBR28, a second-generation Translocator Protein (TSPO) radioligand, enables in vivo quantification of smoldering microglial inflammation. Although this process is thought to drive neurodegeneration and disability progression in MS, its relationship with spinal cord atrophy, a key biomarker of disease severity, remains unclear.
Objectives/Aims: This study investigates the association between brain microglial activation and both brain and spinal cord atrophy in MS.
Methods: Forty-one MS patients (24 relapsing-remitting, 17 secondary progressive) underwent simultaneous ^{11}C-PBR28 MR-PET and 3T MRI. Activated microglia density in brain NAWM was quantified using 60-90 min standardized uptake values (SUV). Brain and spinal cord volumes were measured using FreeSurfer and Spinal Cord Toolbox, respectively. Associations between NAWM ^{11}C-PBR28 binding, atrophy metrics, and Expanded Disability Status Scale (EDSS) were analyzed through regression models. All associations were adjusted for TSPO binding affinity due to genotype-dependent variability of ^{11}C-PBR28.
Results: Higher ^{11}C-PBR28 binding in NAWM was associated with reduced C2–C3 spinal cord cross-sectional area (R^2=209, β=-17.5, p=0.027), independently of age, disease duration, binding affinity, and white matter (WM) lesion volume. The NAWM TSPO expression also associated with brain WM atrophy (R^2=180, β=-0.44, p=0.011) and EDSS (R^2=312, β=4.27, p<0.001). Moreover, ^{11}C-PBR28 uptake in NAWM (β=3.2, p=0.006) and WM lesion volume (β=0.001, p=0.027) independently predicted EDSS (R^2=406).
Conclusion: Microglial activation in brain NAWM reflects a diffuse inflammatory process that extends beyond the brain, contributing to spinal cord atrophy and functional decline. These findings support the role of PET-detected microglial activation as a marker of widespread neuroinflammation in MS and highlight its contribution to MS disability, independent of lesion load.

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P1510
Comparison of glial activation between people with MS and people with post-COVID-19 condition using TSPO-PET

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Introduction: Multiple sclerosis (MS) is a prototypic neuroinflammatory disease, where compartmentalized inflammation contributes to disease progression. Persistent glial activation has similarly been suggested to contribute to neurological post-covid symptoms.
Objectives/Aims: The aim of this multimodal cross-sectional study was to interrogate the presence of microglial activation among individuals with MS and in people suffering from post-covid neurological symptoms.
Methods: Patients with MS (n = 13), participants with neurological post-covid symptoms (n = 14) and healthy controls (n = 11) underwent PET-imaging using the 18 kDa translocator protein (TSPO)-binding radioligand [11C]PK11195 for evaluation of glial activation and 3T MRI for brain volumetrics. Distribution volume ratio (DVR) was used to quantify specific [11C] PK11195-uptake. Freesurfer was used to analyze volumetric measures in various brain regions. Neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) were measured in blood using SIMOA. Additionally, clinical assessments including neurological examinations and mental health questionnaires were conducted in the MS and long covid groups. Group differences were assessed using Wilcoxon tests and correlations using Spearman's method in R programming language.

Results: MS patients had significantly higher [11C]PK11195-uptake compared to long covid participants in several brain regions. Compared to healthy controls, MS patients had higher uptake in thalamus ($p=0.026$) and caudate ($p<0.001$). However, post-covid participant DVRs did not differ significantly from healthy controls in any brain region. No statistically significant differences in NfL and GFAP serum levels were observed between the three groups. The post-covid cohort had higher fatigue than the MS patients ($p=0.039$) and the post-covid fatigue associated with elevated hippocampal radioligand uptake ($\rho=0.75$, $p=0.008$). Post-covid depression and anxiety similarly associated with greater uptake in the hippocampus ($\rho=0.88$, $p<0.001$) and amygdala ($\rho=0.83$, $p<0.003$), while better quality of life was associated with smaller DVR-values in hippocampus ($\rho=-0.83$, $p=0.002$) and amygdala ($\rho=-0.76$, $p=0.010$).
Conclusion: While people with MS exhibited increases in TSPO-binding compared to healthy controls, this could not be demonstrated in individuals with post-covid neurological symptoms. This suggests that persistent widespread glial activation may not be the major cause for post-covid symptoms but instead a variety of mechanisms are likely to contribute to the condition.

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P1511
Association between serum CHIT1 and glial activation measured with TSPO-PET

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Introduction: Microglia play a significant role in multiple sclerosis (MS) disease progression from early stages of the disease to the progressive forms of the disease. 18 kDa translocator protein (TSPO)-PET can be utilized to quantitate glial activation, but a soluble biomarker reflecting microglia activation would provide a more simple way to assess the MS-disease-associated glial activation. Chitotriosidase (CHIT1) is a protein which is expressed mainly by microglia, and which has been linked to various neurological diseases. In MS, CHIT1 is predominantly located in actively demyelinating lesions. CSF CHIT1 is a robust predictor for faster disability progression but only in few studies, CHIT1 has been measured in blood.
Objectives/Aims: To explore the association between microglial activation measured with TSPO-PET and serum CHIT1 in MS.
Methods: Study cohort consisted of 54 patients with MS (18 progressive MS [PMS] and 36 relapsing remitting MS [RRMS]) and 16 age and sex matched healthy controls (HCs). TSPO-PET imaging using [^{11}C]PK11195- ligand, 3T MRI, clinical evaluation and blood sampling were conducted concurrently. T1-hypointense lesions were classified as rim-active if the distribution volume ration (DVR) of [^{11}C]PK11195-binding was low in the plaque core and higher at the plaque edge, overall-active if the binding was high in both core and edge, and inactive if there was no significant ligand binding. Serum CHIT1 was measured using commercial ELISA.
Results: The mean (SD) age of patients with MS was 46.3 (9.3) years, disease duration was 10.3 (8.0) years, and the mean EDSS was 3.4 (1.7). There was a trend for higher serum CHIT1 concentration in PMS compared to RRMS (median [IQR] 30.4 ng/ml [19.1-39.6] vs. 18.8 ng/ml [9.5-31.8]; $p=0.056$). CHIT1 concentration correlated with the percentage of rim-active lesions (Spearman correlation $\rho=0.27$, 95%CI [-0.0011-0.51, $p=0.045$) and all active (rim-active and overall active) lesions ($\rho=0.27$, [-0.0053-0.51], $p=0.048$) in patients with MS. Furthermore, CHIT1 correlated with T1 DVR among RRMS patients ($\rho=0.39$, [-0.059-0.64], $p=0.019$).
Conclusion: Demonstration of correlation between serum CHIT1 concentration and prevalence of TSPO-active lesions in MS brain suggests that serum CHIT1 measurement could be considered a proxy soluble biomarker for chronic lesions with prevailing glial activation. This is significant, as chronic active lesions are known to associate with later adverse clinical outcomes in MS.

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P1512
Clinical Value of 18F-FDG-PET in Brain Nucleus Accumbens Network in Anti-LGI1 Encephalitis

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Introduction: Anti-leucine-rich glioma inactivated 1 (anti-LGI1) autoimmune encephalitis is a common form of encephalitis, primarily manifesting as limbic encephalitis. Clinical features include cognitive impairment, psychobehavioral abnormalities, mood disorders, seizures and hyponatremia.
T2 and/or FLAIR hyperintensities in basal ganglia (BG) and medial temporal lobe (MTL) is frequently detected on MRI in anti-LGI1 encephalitis patients. However, 36% of patients show no abnormalities in these regions, though ^{18}F-FDG PET can detect metabolic changes. ^{18}F-FDG PET outperforms MRI in diagnosing acute cases. Previous studies have reported hypermetabolism in BG and MTL, but the specific affected subregions remain unclear. Prefrontal hypometabolism has also been observed. However, the relationship between hyper- and hypometabolism in anti-LGI1 encephalitis patients, particularly within subregions, remains poorly understood. Research linking metabolic patterns to cognitive, hyponatremia, faciobrachial dystonic seizures and disease severity is also limited.
Our study aims to comprehensively analyze the brain metabolic patterns in anti-LGI1 encephalitis patients and subgroups. Additionally, we seek to investigate the correlation between metabolic patterns, clinical features, and disease severity to improve management.
Objectives/Aims: To explore the ^{18}F-FDG-PET metabolic pattern in anti-leucine-rich glioma inactivated 1 (anti-LGI1) autoimmune encephalitis and its relationship with disease severity.
Methods: ^{18}F-FDG PET CT scans from 50 anti-LGI1 encephalitis patients and 25 controls were analyzed using statistical parametric mapping software (SPM12) for voxel-wise analysis. The Scaled Subprofile Modeling (SSM) algorithm established an LGI1-specific metabolic pattern, and a metabolic covariant network was created based on the Brainnetom atlas. Correlations between the SSM pattern z-score and clinical scores were examined using SPSS.
Results: Subtle ^{18}F-FDG-PET metabolic characteristics were identified, with hypermetabolism in the hippocampal rostal, nucleus accumbens, and hypothalamus, and hypometabolism in the dorsolateral prefrontal cortex and cingulate cortices. Additionally, we found a metabolic covariant network extending from focused on the nucleus accumbens, projecting to the hippocampal head, dorsolateral prefrontal cortex and posterior cingulate cortex, demonstrating positive associations with disease severity and cognitive impairment. No significant correlation was observed between faciobrachial dystonic seizures and basal ganglia metabolism, nor between hyponatremia and hypothalamic metabolism.
Conclusion: Our findings have important implications for the early detection and evaluation of anti-LGI1 encephalitis. It also provides valuable insights into the underlying pathogenesis of clinical manifestations associated with anti-LGI1 encephalitis.

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P1513
Periventricular gradient of thalamic glucose metabolism in multiple sclerosis detected by 18FDG-PET

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Introduction: In MS, a reduced rate of regional cerebral glucose utilisation – as measured by [(18)F]-fluorodeoxyglucose-positron emission tomography (FDG-PET) – has been described in the thalamus and other deep gray matter structures. This hypometabolism may represent a neural correlate of MS-related neurodegeneration. Structural neuroimaging studies have shown that thalamic damage tends to follow a 'surface-in' gradient emanating from the lateral ventricles.
Objectives/Aims: Using FDG-PET, we assessed whether a similar periventricular gradient can be found in terms of thalamic glucose metabolism.

Methods: 31 patients with relapsing MS (PwMS) and 25 matched healthy controls (HCs) underwent 3T magnetic resonance imaging (MRI) and FDG-PET on a PET-MRI system. FDG-PET data were compared between both groups using a voxel-based method (statistical parametric mapping) with age and sex as co-variates of no-interest. Metabolic gradient maps were generated for each axis (x, y, z) and compared between groups. Correlation analyses were conducted between regional glucose metabolism and T2-lesion (T2L) and choroid plexus (CP) volumes derived from structural MRI.
Results: In comparison to HC, PwMS had a significant hypometabolism in bilateral medial thalami and caudate nuclei. A significant gradient increase in regional glucose metabolism was observed in the x-axis for both thalami ($p = 0.0002$) with increasing distance from the lateral ventricles. Thalamic metabolism negatively correlated with T2L and CP volumes.
Conclusion: Results likely represent a metabolic correlate of the underlying neurodegenerative process resulting in the thalamic atrophy observed in MS. These findings provide further support for the contributory role of a 'surface-in' gradient of thalamic damage on the ventricular sides that is likely to be mediated by soluble inflammatory mediators found in the cerebrospinal fluid.

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Imaging & Non-Imaging Biomarkers – Fluid biomarkers

P1514
Kappa Free Light Chain Index as a Diagnostic and Prognostic Biomarker in Multiple Sclerosis

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Introduction: Cerebrospinal fluid (CSF) analysis is crucial in MS diagnosis. The 2024 McDonald criteria incorporate kappa free light chains (KFLC) as additional CSF biomarkers. Beyond diagnostic utility, an elevated $KFLC_{index}$ may be associated with worse clinical outcomes in people with MS (pwMS).
Objectives/Aims:

1. -To evaluate the diagnostic performance of $KFLC_{index}$ compared against the 2017 and 2024 McDonald clinico-radiological (McD-cr) criteria, defined as clinical and magnetic resonance imaging (MRI)-based criteria without initial CSF biomarkers (oligoclonal bands or KFLC).
2. -To explore the prognostic significance of $KFLC_{index}$ in pwMS.

Methods: This was a retrospective cohort study including individuals who presented to our Neurology Department (2019−2024) with a suspected first MS relapse. Patients were followed biannually and underwent annual 3-Tesla craniospinal MRI. $KFLC_{index}$ was calculated as: $(KFLC_{CSF}/KFLC_{serum}) / (albumin_{CSF}/albumin_{serum})$.
Results: Among 150 participants, 64 met the 2017 McD-cr criteria and 67 the 2024 McD-cr criteria. Oligoclonal bands showed high sensitivity (85.9%[2017]; 86.6%[2024]) but moderate specificity (68.6%[2017]; 71.1%[2024]). Optimal $KFLC_{index}$ cutoffs were 9.5 and 12.0. At 9.5, sensitivity was higher (92.2%[2017]; 92.5%[2024]), but specificity lower (63.1%[2017]; 65.4%[2024]). At 12.0, sensitivity slightly decreased (87.5%[2017]; 88.1%[2024]), whereas specificity improved (67.9%[2017]; 70.4%[2024]).
In prognostic analysis (n=76 pwMS), $KFLC_{index}$ correlated with age (rho=−0.26) and was significantly associated with women (p=0.002) and new infratentorial or spinal lesions (p=0.005). A $KFLC_{index} \geqslant 100$ was associated with younger age (<40 years;OR=1.53;p=0.048), women (OR=1.53;p=0.037), and new infratentorial or spinal lesions (OR=6.90;p=0.003). Multivariate analysis confirmed $KFLC_{index} \geqslant 100$ as an independent predictor of new infratentorial or spinal lesions (aOR=8.07;p=0.019).
Conclusion: The $KFLC_{index}$ is a reliable diagnostic biomarker even when evaluated against the McD-cr criteria. Its diagnostic performance is comparable to oligoclonal bands, and it further offers prognostic value regarding the development of infratentorial or spinal lesions. These findings support the incorporation of $KFLC_{index}$ for diagnostic and prognostic assessments in MS.

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P1515
Disruption of the Blood-Brain-Barrier in Neuropsychiatric Disease in Down Syndrome

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Introduction: Down Syndrome Regression Disorder (DSRD) is a neuropsychiatric condition affecting young adults with Down syndrome causing insomnia, catatonia, encephalopathy, and obsessive-compulsive behavior. Studies have identified diagnostic abnormalities which have predicted immunotherapy responsiveness although yield on conventional CSF diagnostic testing is low, with abnormalities noted in 19% of individuals.
Objectives/Aims: This study sought to evaluate proteomic, metabolomic, and immune signatures in the cerebrospinal fluid

of individuals with DSRD and compare them to neurotypical controls and individuals with pediatric onset neuroinflammatory disorders.
Methods: A prospective case-control study comparing proteomic, metabolomic, and immune profiles in individuals with DSRD was performed. Samples were obtained from a biorepository of affected individuals and compared to clinically available data and previously obtained neurodiagnostic studies. Individuals with DSRD were compared to individuals with established neuroinflammatory conditions (e.g., multiple sclerosis), and neurotypical controls undergoing a lumbar puncture for headaches. Samples underwent high-throughput proteomic, metabolomic, and immune profiling. Data was compared across groups and clinical phenotypes. Gene set enrichment analysis and pathway analyses were utilized to analyze the data.
Results: In total, 34 individuals with DSRD, 22 neuroinflammatory controls, and 27 neurotypical controls were enrolled in the study. We observed a highly significant concordance in dysregulated proteomics signatures in DSRD and neuroinflammatory controls versus healthy controls, most prominently upregulation of many immunoglobulin sequences. In addition, individuals with DSRD displayed strong upregulation of liver-derived plasma proteins and erythrocyte proteins in the CSF, indicating poor blood-brain barrier integrity. The immune marker profile of DSRD is clearly similar to other neuroimmunological conditions, including strong elevation of MIP3-α, eotaxin, and IFN-γ.
Conclusion: Individuals with DSRD have unique CSF proteomic and metabolomic signatures consistent with neuroinflammation and increased blood-brain barrier permeability. The CSF of individuals with DSRD was comparable to individuals with neuroinflammatory disorders than neurotypical controls, indicating the potential for an immune-mediated etiology.

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P1516
The blood-brain barrier in MS: correlation between clinical, CSF, MRI signature and albumin quotient in naïve patients

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Introduction: The alteration of the blood-brain barrier (BBBD) plays a key role in the pathogenesis of MS and has been observed even before demyelinating lesions develop. The permeability of the BBB, measured as Q_{Alb} (Alb_L/Alb_S), correlates with central inflammatory load.
Objectives/Aims: This study aims to evaluate whether BBBD correlates with clinical, cerebrospinal fluid (CSF) and neuroradiological characteristics in relapsing-remitting MS (RRMS) patients naïve to disease-modifying therapies.
Methods: A retrospective sample of 166 RRMS patients and 30 controls was analysed. All subjects underwent blood sampling, lumbar puncture, and 3T brain and spinal MRI. Patients were divided into two groups: BBBD– and BBBD+, with BBBD defined by $Q_{Alb} > Q_{AlbLim}$. CSF was examined for NfL and YKL-40. The analysis included the EDSS score at baseline and during follow-up (maximum of 8 years), brain volumes and cerebral lesion volume. Spinal involvement was qualitatively characterized.
Results: Patients have higher Q_{Alb} values, and BBBD was detected in 38 patients (22.89%) and in none of the controls. The BBBD+ group had a higher proportion of men. The EDSS score was higher in pBBBD+ at baseline and during follow-up ($p<0.05$). No significant differences in clinical progression or occurrence of PIRA were found. CSF concentrations of NfL and YKL-40 correlated positively with Q_{Alb} (r=0.302 and r=0.237, $p<0.005$). pBBBD+ had a higher lesion load (p=0,036) and white matter volume (p=0,024), no other significant differences were found in brain volumetrics or contrast enhancement.
Conclusion: BBBD correlates with a higher neuroinflammatory burden, defined by brain lesion volume and CSF biomarkers, and is associated with worse clinical impairment.

Disclosure of interest: Nothing to disclose.

P1517
Microbiota-derived metabolome: towards a non-invasive biomarker of multiple sclerosis

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Introduction: Multiple sclerosis (MS) is associated with a dysfunction of immune cells, whose cause is unknown. We

hypothesize that gut microbiome affects the function of immune cells through release of specific metabolites modulating disease activity during different phases of disease.
Objectives/Aims: The objective of this study was to assess whether plasma concentration of different gut-derived metabolites derived from tryptophan (TRP) correlates with disease activity in MS.
Methods: Subjects with MS were included cross-sectionally at the Neurology Clinic, University of Genova and IRCCS Ospedale San Martino, Genova, Italy. Peripheral blood was collected by venipuncture and plasma was isolated through centrifugation and frozen at -80°C. A simple and sensitive liquid chromatography-tandem mass spectrometry (LC-MS/MS) method in PRM mode was developed to determine the levels of 12 key Tryptophan (TRP) compounds in human plasma samples. Binary classification was performed applying supervised methods such as Supervised partial least squares-discriminant analysis (PLS-DA) and orthogonal partial least squares-discriminant analysis (OPLS-DA) and predictive performance of specific metabolites was evaluated by receiver operating characteristic curves (ROC).
Results: The cohort included patients with relapsing-remitting (RR)MS (N=28), secondary progressive (SP)MS (N=13) and primary progressive (PP)MS (N=7). Mean age was 55 (SD=15.99, range=20-75). Patients were untreated (N=18) or treated with ocrelizumab (N=13), fingolimod (N=7), or other therapies (N=19).
Among the 12 key TRP metabolites examined, Indoxyl Sulfate demonstrated the strongest diagnostic accuracy (AUC = 0.72), displaying higher levels in the (SP)MS group compared to the (PP)MS group
The metabolite pattern changed with age, particularly regarding kynurenic acid (AUC>70%, p-value <0,05)After adjusting for age, treatments significantly influenced the metabolomic profile, marked by elevated concentrations of kynurenine and kynurenic acid, accompanied by a decrease in indole-3-carboxaldehyde levels.
Conclusion: This study demonstrates that targeted metabolomics can identify distinct metabolic profiles, associated to different ages, treatments and disease type in MS. If these results are confirmed in larger cohorts, microbiota-derived metabolites may become a non-invasive biomarker of MS.

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P1518
Ovarian aging in multiple sclerosis: Anti-Müllerian Hormone predicts disease activity independent of age

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Introduction: Ovarian aging, as measured by Anti-Müllerian Hormone (AMH), has been implicated in various health outcomes in women. While the effect of aging on the disease course of multiple sclerosis (MS) is well established, the role of ovarian aging remains less clear.
Objectives/Aims: This study aimed to investigate whether AMH levels predict relapse and disability worsening in women with MS.
Methods: This prospective longitudinal study including women with MS aged 18 to 65 years was conducted at the Medical University of Innsbruck. AMH levels were measured using an electrochemiluminescence immunoassay. Cox regression analysis was applied to investigate the impact of AMH on time to relapse as well as on time to disability worsening, defined as a 6-month confirmed increase in the Expanded Disability Status Scale (EDSS) score.
Results: A total of 104 women at a median age of 50 years (25^{th}-75^{th} percentile: 42-55), a median EDSS of 2.0 (1.5-4.0) at baseline, and a median follow-up time of 48 months (43-50) were included. Univariate analyses revealed that women who experienced relapses were younger (39 vs. 52 years), but also showed higher AMH levels (median 0.5 vs. 0 µg/l). Multivariable Cox regression analysis revealed that both higher age (Hazard Ratio [HR]: 0.95, p=0.039) and lower AMH levels (HR: 1.40, p=0.022) independently predicted longer time to relapse. Regarding disability worsening, in univariate analysis women were older (53 vs 48 years) and had lower AMH levels (0 vs 0.1 µg/l). Multivariable Cox regression analysis showed that lower AMH levels (HR: 0.54, p=0.0038) independent of age, predicted shorter time to disability progression.
Conclusion: Ovarian aging, as assessed by AMH, is a risk factor for MS disease course in addition to chronological age. These findings suggest that AMH may serve as a valuable biomarker for disease activity in women with MS.

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P1519

Evaluating the value of serum neurofilament light chain after DMT initiation for monitoring early treatment response

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Introduction: Serum neurofilament light chain (sNfL) is a well-recognized biomarker of axonal damage in multiple sclerosis (MS). Although sNfL levels typically decrease with effective disease-modifying therapy (DMT) and show good a correlation with inflammatory activity, it is uncertain whether sNfL change or height of absolute values shortly after DMT initiation can predict medium- to long-term outcomes.
Objectives/Aims: Therefore, the present study aimed to determine whether sNfL could serve as an early biomarker for evaluating treatment response.
Methods: From an ongoing prospective observational study at the Department of Neurology, Medical University of Vienna, we analyzed patients with relapsing multiple sclerosis (RMS) who were newly initiated on any DMT. Serum sNfL concentrations were measured before DMT initiation (baseline) and again six months later and calculated as age- and BMI-adjusted z-scores. Minimum required follow-up was 24 months. Treatment response was defined according to the occurrence of relapse. Diagnostic accuracy for prediction of relapse was determined by receiver operating characteristics (ROC) based on area under the curve [AUC] and negative predictive value (NPV). Multivariate logistic regression analysis was performed for all independent variables and adjusted for age, disease duration, baseline DMT and relapse in the prior year.
Results: Among 107 RMS patients (mean age 35 years [SD±9]; 64.5% initiated on high-efficacy DMT), 18 (16.8%) patients experienced at least one relapse during follow-up. Baseline sNfL was not significantly associated with higher rates of relapse (adjusted odds ratio [aOR] 1.36 [95% CI 0.90-1.99]; p=0.20)
At six months, median sNfL z-scores were significantly lower in individuals who remained relapse-free (0.52 vs. 2.41, p=0.008) during follow-up. The change in sNfL z-scores at 6 months compared to baseline (delta) also differed markedly (−0.98 vs. 0.26, p=0.014), indicating a more pronounced decline in the non-relapsing group. Both absolute six-month z-scores and delta z-scores were associated with relapse (AUC of 0.752 and 0.733, respectively) during follow-up, with a remarkably high negative predictive value (NPV) of 95.6% and 97.8%, respectively. Multivariate analysis indicated that absolute z-scores at six months after DMT initiation was a significant predictor of future relapse (aOR 2.04 [95% CI 1.21-4.02]; p=0.017), while delta z-scores did not remain statistically significant (aOR 1.26 [95% CI 0.98-1.69]; p=0.10).
Conclusion: These findings, aligning with prior research, highlight the utility of sNfL as an early biomarker of DMT response in RMS. Six-month sNfL z-scores, and in particular their normalization after DMT initiation, likely allow for robust identification of patients who respond favourably to treatment.

Disclosure of interest: Fabian Föttinger: nothing to disclose related to this study.

P1520

Using plasma neurofilament light chain to evaluate response during cladribine treatment in multiple sclerosis

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Introduction: Cladribine treatment in year 1 and 2 is expected to be highly-effective on multiple sclerosis (MS) outcomes over 4 years. However, some patients might experience residual activity and, thus, need additional treatment. As such, the use of biomarkers of neuro-axonal loss, such as plasma neurofilament light chain (pNfL), might support prognostication and treatment decisions.
Objectives/Aims: We aim to: 1) investigate pNfL variations over time in people with MS treated with cladribine; 2) compare pNfL levels during cladribine treatment to age- and sex-matched controls; 3) assess pNfL prediction of clinical and/or radiological activity.
Methods: In this retrospective study, we included 258 people with MS treated with cladribine and 304 age and sex-matched controls. Blood samples were collected al baseline and at 6 months follow-ups; pNfL was evaluated using Lumipulse™ fully automated chemiluminescent enzyme immunoassay. For MS cases, we collected evidence of disease activity during follow-up (including relapses, active MRI, and EDSS progression) (EDA3). Covariates of the statistical models were age, sex, presence of cardiovascular comorbidities, smoking, descriptor of disease progression (relapsing or progressive), and EDSS.
Results: On multivariate linear regression model using pNfL before treatment as reference, pNfL was lower after year 1 (Coeff=-211.39; 95%IC=-363.55, -59.03; p=0.008) and after year 2 of cladribine (Coeff=-167.70; 95%IC=-317.26, -18.14; p=0.028). On multivariate linear regression model using controls as reference, pNfL was higher in MS before cladribine treatment (Coeff=7.43; 95%IC=2.45, 12.40; p=0.004), but was similar after year 1 (Coeff=-1.04; 95%IC=-3.36, 1.27; p-value=0.376), after year 2 (Coeff=1.48; 95%IC=-0.60, 3.55; p=0.162), and after >3 years after cladribine start (Coeff=2.23; 95%IC=-0.47, 5.08; p=0.103). We observed EDA3 in 15 patients (5.8%), mostly driven by EDSS progression (n=11); on Cox regression model, higher pNfl was associated with a lower risk of EDA3 during follow-up (HR=0.32; 95%IC=0.11, 0.94; p-value=0.039).
Conclusion: Cladribine provided significant reductions of pNfL during treatment, suggesting reduced neuro-axonal loss, which ended-up to pNfL levels in line with age- and sex-matched controls. Higher pNfL likely corresponds to inflammatory activity, that was almost-fully controlled in our cohort, while other biomarkers should be used to predict disability progression.

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P1521
Monitoring Patients with Relapsing-Remitting Multiple Sclerosis Switching from Intravenous to Subcutaneous Natalizumab every 4 Weeks vs every 6 Weeks

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Introduction: Natalizumab (NTZ) is a humanized monoclonal antibody targeting α4-integrin (CD49d), preventing its migration to the central nervous system. CD49d receptor occupancy (RO) correlates with the clinical and radiological features in relapse-remitting multiple sclerosis (RRMS) patients (pts). NTZ can be administered intravenously (IV) or subcutaneously (SC). While CD49d RO remains stable in pts switching from IV to SC in a 4-week (w) regimen, data on a 6w regimen are limited.
Objectives/Aims: To evaluate CD49d RO in pts switching from IV to SC NTZ in both 4w and 6w regimens. Additionally, this study aimed to monitor serum neurofilaments light chain (sNfL) levels and clinical course.
Methods: This multicenter, observational, ambispective study included adult RRMS pts on IV-NTZ (4w or 6 w) for at least 6 months before enrolment. Three lymphocyte subpopulations (CD4+, CD8+, and CD19+) were analyzed before the first, third, and seventh SC-NTZ administration, with follow-up of 24 weeks (4w group) and 36 weeks (6w group). An interim analysis of sNfL levels is presented. A mixed model for repeated measures (MMRM) was used for statistical analysis.
Results: No significant differences in the CD49d RO were observed at any time point in the 4w (N=20) or 6w (N=28) groups. However, higher CD49d RO percentages were observed in lymphocyte subsets ($CD4^+$, $CD8^+$, and $CD19^+$) with the 4w regimen (76.5%, 66.7%, 67.6%, respectively) compared to 6w (69.9%, 58.3%, 56.7%). A significant LS mean difference of 13.08 (SE = 4.10; p = 0.028) was observed at the third administration for the $CD19^+$ subpopulation (95% CI: 4.90–21.26). sNfL levels showed no significant differences between regimens or across timepoints (4w: N=8; 6w: N=16), with mean values of 7.93 pg/mL (4w) and 10.63 pg/mL (6w). Patients remained sta-

ble throughout follow-up, with no significant MRI lesion activity or disability progression.
Conclusion: SC-NTZ administration in 4w and 6w regimens showed no differences in CD49d RO, sNfL levels, or clinical outcomes. The stable clinical and radiological activity observed during follow-up supports the consistency of these findings.

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P1522
The Value of Neuregulin-1 and sTREM-2 as Biomarkers in Serum and Cerebrospinal Fluid of Multiple Sclerosis Patients

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Introduction: Recent studies have explored biomarkers to facilitate MS diagnosis, prognosis, and treatment efficacy assessment. Among these, oligoclonal bands (OCB) in the cerebrospinal fluid (CSF), IgG index, and neurofilament light chain (NfL) are prominent, though they lack specificity for MS, and lumbar puncture can be invasive and limited in follow-up.
Objectives/Aims: This study aimed to evaluate sTREM-2 and NRG-1 as novel biomarkers in MS patients' CSF and serum, compared to NfL and GFAP.
Methods: Sixty patients with newly diagnosed relapsing-remitting MS (RRMS) and forty-eight subjects with a diagnosis of idiopathic intracranial hypertension for CSF and thirty healthy subjects for serum as control were included in the study. sTREM-2, NRG-1, NfL and GFAP in CSF and serum were analyzed using ELISA.
Results: Serum and CSF sTREM-2 level were significantly elevated in MS patients compared with controls respectively (p:0.049, p:0.006). Conversely, NRG-1 levels were significantly lower ($p < 0.001$) in serum but not in CSF of MS patients. Both serum and CSF NfL levels were significantly elevated in MS subjects ($p < 0.001$). Serum and CSF GFAP levels did not differ between groups. In the MS group, we found a highly significant correlation between CSF and serum levels of NfL, sTREM-2 and NRG-1. However, no significant correlations were observed between GFAP CSF and serum levels. Other than NRG-1 CSF levels which showed a significant positive correlation with 9-Holl Peg score and SDMT incorrect count (p=0.041, p=0.004), the other markers did not show any correlation to the scores.
Conclusion: This study indicates elevated sTREM-2 and reduced NRG-1 serum levels in MS, underscoring their potential as biomarkers. Further research is needed to validate these findings and understand the implications for MS management.

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P1523
Evaluation of oxidative stress-related gene expression in PBMCs and inflammatory serum markers in an MS cohort

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Introduction: Oxidative stress and inflammation play key roles in the pathophysiology of multiple sclerosis (MS). While the presence of oxidative stress has been extensively documented in central nervous system (CNS) tissues of MS patients, more recent evidence indicates systemic alterations in redox balance, particularly in peripheral blood mononuclear cells (PBMCs), as well as elevated inflammatory markers in serum.
Objectives/Aims: This study aimed to assess the expression levels of antioxidant and inflammatory pathway

markers—namely Nrf2, NF-κB, SOD1, HO1, and GCLC—in PBMCs, along with a panel of 13 inflammatory chemokines in serum, from a cohort of individuals with MS.
Methods: A total of 37 MS patients (27 relapsing-remitting [RRMS] and 10 progressive [PMS]) and 23 healthy controls were recruited. Clinical and demographic data were collected via self-assessment questionnaires. Blood samples were drawn to isolate PBMCs and serum simultaneously. Gene expression levels were quantified using qPCR, and serum cytokines/chemokines were measured via a multiplex assay.
Results: Our results revealed significantly increased expression of HO1 in both total MS ($p=0.02$) and PMS ($p=0.02$) patients. GCLC expression was elevated in total MS ($p<0.0001$) and RRMS ($p<0.0001$) groups. However, Nrf2 expression was decreased in total MS ($p=0.001$), RRMS ($p=0.004$), and PMS ($p=0.01$). NF-κB expression was higher in total MS ($p=0.01$) and RRMS ($p=0.005$). Correlation analysis revealed that Nrf2 positively correlates with GCLC, SOD1, and NF-κB, whereas NF-κB negatively correlates with HO1. ROC analysis demonstrated high diagnostic accuracy for combined oxidative stress markers, particularly Nrf2/GCLC (AUC=0.90). In contrast, inflammatory chemokine levels did not significantly differ between MS and controls.
Conclusion: These results suggest an altered antioxidant response in responses in PBMCs from MS patients. The correlations between oxidative stress markers highlight potential interactions between these pathways. This study reinforces the relevance of PBMCs in MS-related oxidative stress, with potential implications for biomarker research.

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P1524
Evaluating the role of CSF MOG-Ab testing in children with MOGAD

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Introduction: Myelin oligodendrocyte glycoprotein associated disease (MOGAD) is now a well recognize neuroinflammatory syndrome in both children and adults. MOG antibodies (Ab) are best detected using cell-based assays in serum, with high clinical syndrome specificity for MOGAD. Recent studies have shown that MOG-Ab in cerebrospinal fluid (CSF) can be used in diagnosis and prognosis of patients with MOGAD.
Objectives/Aims: The aim of our study was to evaluate the frequency of CSF MOG-Ab in patients with MOG-Ab in the serum and assess its impact on disease presentation, course and prognosis.
Methods: This was a retrospective study analysing data of 43 paediatric patients positive for serum MOG-Ab, all of whom had paired serum and CSF samples tested as part of their routine clinical care. Patients were divided into two groups based on the presence or absence of CSF MOG-Ab. Demographic data, clinical presentation, disease course, MRI findings, and CSF parameters were compared between the groups.
Results: CSF MOG-Ab were detected in 15/43 (34.8%) of patients. No significant differences were observed in demographic characteristics, including sex and age at onset. Acute disseminated encephalomyelitis (ADEM) was more frequent in the MOG-Ab serum+/CSF- group (17/28 (60.7%) vs 4/15 (26.7%), $p=0.05$). Other phenotypes were more common in the MOG-Ab serum+/CSF+ group, including cortical encephalitis (5/15 (33.3%) vs 3/28 (10.7%)), though the differences were not statistically significant. The MOG-Ab serum+/CSF+ group had higher CSF white blood cell count ($p=0.005$). No significant differences were observed in risk of relapses and disability scores (EDSS) at last follow-up (median follow up 1.3 years [IQR 0.6-2.2]). Persistent MOG-Ab seropositivity (median time from first to last sample 0.8 years [IQR 0.2-1.6]) was seen in both groups (8/28 (28.6%) vs 7/15 (46.7%)) with no statistical significance.
Conclusion: MOG-Ab in CSF were less frequently found in patients with ADEM, this is either due to (1) blood brain barrier permeability, (2) higher serum MOG-Ab or (3) intrathecal production. Further studies evaluating these factors may increase our understanding of disease mechanisms in MOGAD.

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P1525
Higher levels of neurodegenerative (NfL and GFAP) and inflammatory (CXCL10) biomarkers are associated with lower levels of fitness and strength in multiple sclerosis

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Introduction: Blood biomarkers have the potential to provide early and precise identification of inflammation, neurodegeneration and treatment response. However, it is likely that body mass and lifestyle influence these biomarkers, potentially expanding their use in lifestyle precision medicine.
Objectives/Aims: We aimed to determine whether MS patient characteristics (age, sex, type of MS, disease duration, Expanded Disability Status Scale [EDSS]) and/or modifiable characteristics (body mass index, fitness, and hand strength) were associated with biomarker levels.
Methods: We recruited 40 people with MS from a MS Neurology clinic. Patients underwent blood draws and then grip strength and cardiopulmonary fitness testing. We measured biomarkers of neurodegeneration and inflammation in plasma; neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP), and inflammatory cytokines CXCL10 and CXCL13. Using correlation analyses, we determined whether MS patient characteristics (age, sex, type of MS, disease duration, Expanded Disability Status Scale [EDSS]) and/or modifiable characteristics (body mass index, fitness, and hand strength) were associated with biomarker levels.
Results: Participants (median EDSS 2.0), with a mean age of 47.65 ± 9.87 years, were predominantly female (77.5%) and had relapsing-remitting MS (90%). There were no sex differences in biomarker levels. Higher plasma NfL was associated with lower body mass index (R= -0.37) and weaker hand strength (R= -0.39). Higher GFAP was associated with older age (R= 0.37) and lower maximum heart rate achieved during the fitness test (R= -0.33). GFAP levels were higher in those diagnosed with secondary progressive verses relapsing disease (p=0.013). Higher level of inflammatory cytokine CXCL10 was associated with higher body mass index (R= 0.34) and weaker grip strength (R= -0.36). CXCL13 was not related to any variables. Notably, none of the biomarkers were related to disease characteristics; EDSS or disease duration.
Conclusion: Higher levels of neurodegenerative (NfL and GFAP) and inflammatory (CXCL10) biomarkers were associated with lower levels of fitness and strength, suggesting that lifestyle can potentially modify the individual's inflammatory/neurodegenerative milieu. Other than higher GFAP in people diagnosed with progressive disease, biomarkers were not related to sex or MS-related disease characteristics; EDSS, MS type or disease duration.

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P1526
Perceptions and Adoption of NfL Biomarker Testing for Monitoring MS Patients in the EU4/UK and US

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Introduction: Neurofilament light chain (NfL) has emerged as a promising biomarker for monitoring disease activity, progression, and treatment response in Multiple Sclerosis (MS). Despite growing evidence supporting its use in MS, integrating NfL into routine clinical practice remains a challenge.
Objectives/Aims: Understand healthcare professionals' (HCPs) perceptions of NfL as a biomarker to monitor MS and evaluate the adoption rates of NfL testing in clinical practice in the EU4+UK and US.
Methods: A multi-centre online survey of treating neurologists (MS nurses included in UK), screened for duration in specialty and caseload, was conducted in Q4 2024 (10/2024 – 12/2024) across EU4+UK (FR, DE, IT, ESP, UK) and US. De-identified HCP perceptions were collected, and de-identified patient charts were recorded for eligible patients seen during the consultation period. 346 HCPs (EU4/UK=236; US=110) recorded their perceived importance of NfL and other clinical and radiological biomarkers to monitor the disease course, volume of NfL usage in practice and anticipated future usage of NfL. NfL testing status was collected on the 4510 de-identified patient charts (EU4+UK= 3435; US= 1075).
Results: NfL monitoring was perceived less important than other traditional measures of disease monitoring by sampled HCPs (59% citing a 4/5 importance on a 5-point Likert scale). This was reflected by low average usage rates recorded among HCPs familiar with NfL testing (n=321), with the HCPs stating that they tested NfL levels in 22% of their relapsing-remitting MS (RRMS) caseload, and 21% of their progressive caseload (secondary and primary progressive MS). Adoption rates were lower in the EU4+UK sample (20% RRMS and 19% progressive MS, n=215) vs US (25% in both MS types, n=106). Among the HCPs with current stated usage (n=125), 48% were uncertain of their future adoption of NfL testing.
Patient chart data illustrated similar patterns of low NfL adoption, with NfL testing deemed unapplicable for 54% of reported MS patients. This was driven primarily by the UK (71%, n=542) and France (68%, n=693), with the test less likely to be unapplicable for patients in Germany (42%, n=685).
Conclusion: In this study cohort, low adoption and perceived importance of NfL biomarker testing for monitoring MS patients was evident. Regional differences were observed, with recorded lower adoption in the EU4+UK vs US. Further investigation is needed to elucidate the potential barriers to NfL adoption and guide the development of standardised protocols to optimise NfL use in MS management.

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P1527

Cerebrospinal fluid α-internexin is increased in patients with multiple sclerosis compared to healthy controls and correlates strongly with neurofilament light protein

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Introduction: Alpha-internexin (α-internexin) is an intermediate filament protein predominantly found in the central nervous system (CNS) and is one of the core structural components of the neuronal cytoskeleton, along with neurofilaments. Its unique properties have spurred interest in its potential as a biomarker for neurological diseases, though it remains relatively underexplored compared to other neurofilament proteins.
Objectives/Aims: Investigating α -internexin as a potential biomarker for multiple sclerosis.
Methods: We measured cerebrospinal fluid (CSF) α-internexin in patients with MS and healthy controls (HC) using an in-house α-internexin SIMOA (single-molecule assay) developed and validated at the University of Gothenburg. The main outcome measure was the difference in α-internexin between patients with MS and HCs. We also calculated correlations with clinical (age, sex, MS disease course, MRI (magnetic resonance tomography) results, disease-modifying treatment (DMT)) and CSF biomarker data (cell count, albumin quotient, neurofilament light (NFL), glial fibrillary acid protein (GFAP), T-Tau, CXCL13).
Results: We included 34 patients with MS and 8 HCs in the analysis. α-internexin was detected in all samples (range; 0.16-38.4 ng/L). Median α-internexin was significantly increased in patients with MS (1.19 ng/L; IQR 0.69-2.34) compared to HCs (0.44 ng/L; 0.36-0.51) ($p<0.001$) and correlated strongly with concentrations of CSF NFL (R; 0.88; $p<0.001$). α-internexin correlated significantly with CSF cell count, expanded disability status scale (EDSS) score, and CSF CXCL13 ($p<0.05$), but did not correlate with age, sex, MRI T2 lesion burden, disease course, or csf/serum albumin quotient.
Conclusion: We conclude that CSF α-internexin, similarly to NfL, is a marker of axonal nerve injury in patients with MS.

Disclosure of interest: Magnus Johnsson: nothing to disclose

P1528

Real-world Utilization of a Novel Multi-analyte Blood-Based Biomarker Panel, the Octave® Multiple Sclerosis Disease Activity (MSDA) Test In Clinical Practice Across the United States

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Introduction: The complexity of multiple sclerosis (MS) underscores the urgent need for reliable and accessible biomarkers to improve disease management and patient care. Blood-based biomarkers offer a minimally invasive, cost-effective, and scalable solution for monitoring disease activity (DA) and guiding personalized treatment strategies. They hold potential for identifying inflammatory and neurodegenerative processes, treatment response, and subclinical disease activity. Incorporating blood-based biomarkers into routine care can enhance early diagnosis, optimize therapeutic interventions, and improve long-term outcomes for individuals living with MS.
Objectives/Aims: To describe the real-world utilization of the Octave® Multiple Sclerosis Disease Activity (MSDA) test, a clinically validated, multi-analyte blood-based biomarker panel for MS in clinical practice across the United States (US).
Methods: We conducted a descriptive analysis of data collected and reported from the Octave® MSDA Test and plan to characterize change in MSDA over time. Data on the test requisition form includes gender, age, race and ethnicity, current disease-modifying therapy (DMT), reason for test, and date of MS diagnosis.
Results: The Octave® MSDA Test has been commercially available since 2022. A total of 14,808 MSDA tests have been ordered from 137 institutions and 231 healthcare providers (HCP). As of March 2025, 11,411 MS patients have had completed tests. Baseline demographics include mean age 52 years, 77.3% female, mean disease duration 13.8 years, 79.5% White, 14.7% Black, and 4.3% Hispanic. A high efficacy DMT (anti-CD20s, natalizumab, cladribine, alemtuzumab) was used to treat 44% of patients, while 33.4% reported not being on a DMT at their latest test. The Octave® MSDA Test provides a quantitative, validated index DA score from 0-10 with 0.5 intervals and established thresholds for low (0-4), moderate (4.5-7) and high (7.5-10) disease activity. MSDA scores from this cohort are 64.4% low, 29.1% moderate and 6.5% high with a mean score of 3.8. 76.3% of patients had 1 MSDA test, 19.3% had 2 tests and 4.4% had 3 or more. The top HCP reported indications for use include routine/longitudinal monitoring, pre/post therapy, relapse assessment and baseline evaluation.
Conclusion: This report highlights the growing use of the MSDA in US clinical practice and its potential to transform MS care. Ongoing research is essential to fully realize the Octave® MSDA's impact and ensure its smooth integration into clinical workflows.

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P1529
Serum NOX5 as a Diagnostic and Pharmacodynamic Response Biomarker in Multiple Sclerosis

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Introduction: One mechanism of neurodegeneration in multiple sclerosis (MS) is likely related to oxidative stress (OS). Increased OS has been documented in MS patients, including elevated cerebrospinal fluid levels of reactive oxidative stress (ROS) markers.
Objectives/Aims: NADPH oxidases (NOXs) are major regulated sources of ROS. Based on prior studies we hypothesize that NOX5, a calcium-dependent NOX isoform, may serve as a serum biomarker for MS characterization, disease activity, and treatment response.
Methods: We analyzed serum samples from 64 participants enrolled in the UMass MS Biobank, stratified into four age- and sex-matched groups: noninflammatory neurological disease (NIND) controls (n=26), and MS patients either without treatment (n=14), on B-cell depleting therapies (BCD; n=16), or treated with Dimethyl Fumarate or Glatiramer Acetate (DMF/GA; n=8). Serum was stored at –80°C and NOX5 protein levels were quantified using a commercial ELISA kit (Elabscience) following the manufacturer's protocols. Statistical analysis included ANOVA and t-tests, performed in GraphPad Prism.
Results: Serum NOX5 levels were not associated with age or sex ($p>0.05$). NOX5 was significantly elevated in untreated MS patients compared to NIND controls (43% increase; t=3.909, p=0.0004), with an AUC of 0.82 (p=0.001), supporting its diagnostic potential. When treated MS patients were included in the analysis, the difference remained significant (t=3.459, p=0.001). Among treatment subgroups, untreated patients had a 12% increase in NOX5 levels (163.4 ng/mL) compared to those on BCD (145.4 ng/mL) and DMF/GA (147.0 ng/mL), although these differences did not reach significance ($p>0.05$), likely due to sample size limitations. In MS patients, NOX5 levels did not demonstrate a significant association with disease duration or expanded disability status scale (EDSS) scores ($p>0.05$).
Conclusion: OS is increasingly recognized as a likely contributor to MS and MS-related neurodegeneration. Our data support its potential use as a diagnostic indicator and pharmacodynamic response biomarker. These findings align with prior reports and support NOX5 as a marker of ROS and/or vascular dysfunction in MS. Further studies in larger cohorts are warranted to validate its clinical utility and mechanistic relevance.

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P1530
Serum protein biomarker combinations predict time to relapse and disability in MS (a validation cohort)

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Introduction: Long-term clinical outcomes are highly variable in multiple sclerosis (MS). High efficacy disease modifying treatments (DMTs) are now available, although carry an increased risk of serious adverse events. Serum biomarkers predictive of future MS activity would help identify people with MS who are likely to benefit most from high-efficacy therapy and limit risks to others.
Objectives/Aims: In this study, we aimed to validate previous work using a panel of serum-only protein biomarkers to predict prognostic features including time to relapse and time to disability milestones in a cohort of people with relapsing MS (pwRMS).
Methods: Sera were obtained from a regional Neuroscience research tissue bank comprising 90 pwRMS and 58 non-MS controls. PwRMS had prospective EDSS and relapse data available from disease onset. Simoa HD-X (neurofilament light (NfL) and glial fibrillary acidic protein (GFAP)), ELLA platform (CXCL12, sCD27, vitamin D binding protein and osteopontin (OPN)) and ELISA (C1s/C1inh; CCL27; C3 and C5) were used to measure serum concentration of 10 biomarkers. Raw concentrations were transformed to Z-scores allowing comparison between biomarkers in future combination analyses. Comparisons between MS and controls were undertaken using independent-samples Mann Whitney tests. Cox regression analyses were also used to measure association of each biomarker with time to next relapse and EDSS 6. Concordance (C) statistics for each Cox regression model were used to rank best fit (1.0=perfect fit).
Results: Comparison of RMS and controls showed 8 biomarkers to be significantly different in pwRMS versus controls; OPN and C1s/C1inh ($p=<0.001$) demonstrating highest significance. For time to next relapse univariate analysis identified the most significant predictive biomarkers in isolation to be C5 (p=0.03; C=0.72) and CXCL12 (p=0.07; C=0.74). The best combination was CXCL12+C3+C5 (p=0.03; C=0.74). The top biomarkers in isolation to predict time to EDSS 6 were sCD27 (p=0.00008; C=0.78) and CXCL12 (p=0.02; C=0.76). The most informative combinations were OPN+CXCL12+sCD27 ($p=9x10^{-8}$;

C=0.84) and OPN+CXCL12+sCD27+C5+CCL27 ($p=2x10^{-7}$; C=0.85).
Conclusion: These results suggest combinations of serum biomarkers improved prognostic values compared to biomarkers in isolation. In addition, Complement proteins show potential as biomarkers to predicting MS outcomes. May offer a more personalised approach to inform decisions on therapeutic intervention.

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P1531
Comparison of two analytical platforms for quantification of neuroglial biomarkers in blood samples: a single molecule array and an electrochemiluminescence assay

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Introduction: Advances in ultrasensitive immunoassays have enabled the reliable quantification of neuroglial biomarkers in blood, providing valuable insights into neurological disorders. However, cross-platform evaluations are necessary to ensure comparability and standardization.
Objectives/Aims: This study aimed to compare the analytical performance of a Single Molecule Array (Simoa) and an electrochemiluminescence (ECL) assay for quantifying neurofilament light chain (NFL) and glial fibrillary acidic protein (GFAP) in human serum.
Methods: Baseline serum samples from 175 patients with relapsing-remitting multiple sclerosis were analyzed in parallel using Simoa and ECL assays. NFL and GFAP concentrations were determined on both platforms, and direct comparisons were made using correlation analyses (Spearman), Bland-Altman plots, reproducibility and dilution linearity assessment.
Results: All 175 samples were quantifiable on both platforms. NFL concentrations correlated strongly between methods (Spearman correlation $r = 0.88$, $p < 0.0001$), whereas the correlation for GFAP was moderate ($r = 0.77$, $p < 0.0001$). Reproducibility for NFL was similar between assays, while GFAP measurements showed slightly better reproducibility with the ECL assay. The relationship between the two assays could be described with the following equations: $NFL_{ECL} = 7.63 \times NFL_{SIMOA} + 1.71$ and $GFAP_{ECL} = 0.332 \times GFAP_{SIMOA} + 4.22$.
Conclusion: Both Simoa and ECL assays demonstrated strong performance and feasibility for measuring neuroglial biomarkers in serum. While both methods were suitable for NFL quantification, the ECL assay showed a slight advantage for GFAP regarding reproducibility. These findings support efforts towards harmonizing biomarker measurement across platforms to ensure comparability in clinical and research applications.

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P1532
Serum Neurofilament Light Chain, but not GFAP, predicts No Evidence of Disease Activity at one-year follow-up in Radiologically Isolated Syndrome

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Introduction: Serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (sGFAP) are biomarkers of disease activity in multiple sclerosis (MS). We evaluated whether baseline sNfL and sGFAP levels predict no evidence of disease activity (NEDA) in a cohort of people with radiologically isolated syndrome (RIS) over a median follow-up of one year.
Objectives/Aims: To determine whether baseline serum sNfL and sGFAP levels are associated with NEDA status over one year in people with RIS (pwRIS).
Methods: Baseline sNfL and sGFAP levels were measured in 48 treatment-naïve pwRIS. NEDA was defined as the absence of new clinical symptoms, including relapses and disability progression, and the absence of new lesions on magnetic resonance imaging over one year. Fluid biomarker levels were corrected for age. Logistic regression models were used to assess the association between biomarker levels and NEDA status. Receiver operating characteristic curve analysis was performed to evaluate test performance using the area under the curve (AUC).

Results: Higher baseline sNfL levels were associated with lower odds of achieving NEDA (p = 0.009). Higher baseline sGFAP levels showed a trend towards reduced odds of achieving NEDA (p = 0.055). In a combined model including both sNfL and sGFAP, only sNfL remained a significant predictor of NEDA (p = 0.039). The AUC for sNfL was 0.79, while the AUC for sGFAP was 0.64. Combining sNfL and sGFAP did not improve model performance (AUC 0.79).
Conclusion: Baseline sNfL levels are a significant predictor of NEDA at one-year follow-up in pwRIS. sGFAP levels provide limited additional predictive value for short-term relapsing disease activity. Further research is needed to determine whether combining biomarkers improves predictive accuracy for long-term prognosis, including relapsing and progressive disease activity.

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P1533
Choroid Plexus Volume and Blood-based Protein Profiles to Monitor Brain Atrophy in Multiple Sclerosis

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Introduction: The choroid plexus (CP) plays a key role in central nervous system inflammation, and increased CP volume (CPV) in patients with multiple sclerosis (pwMS) has been shown to correlate with clinical and MRI-based indicators of disease progression. Given its role in cerebrospinal fluid (CSF) production and as the blood-CSF barrier, the CP is a promising imaging biomarker for disease monitoring. The MS Disease Activity (MSDA) panel, comprising 18 proteins, captures blood-based changes across critical biological pathways using a proximity extension assay on the Olink™ platform. This study examines CPV and the blood-based MSDA panel in relation to brain atrophy to improve MS monitoring.
Objectives/Aims: To assess the predictive value of CPV and blood-based biomarkers for indicating brain volume changes over a median follow-up time of 5.4 years (IQR: 4.5-6.3).
Methods: 88 pwMS and 48 age- and sex-matched healthy controls (HC) underwent 3T MRI to evaluate normalized brain volume and brain atrophy using FreeSurfer and SIENA. Protein levels were measured using the MSDA assay panel on the Olink™ platform. We compared serum MSDA scores and protein values between pwMS and HC using Mann-Whitney U tests, and calculated stepwise two-block multiple linear regression models to identify predictors of brain volume and change over time.
Results: CPV was significantly higher in pwMS compared to HC (median = 788.7mm³ vs 683.6mm³; $p = 0.034$). MSDA score and all pathways were elevated in pwMS ($p < 0.001$). NfL and MOG concentrations were increased, while 11 proteins were decreased compared to HC ($p < 0.05$). Five proteins did not have a significant difference. In pwMS, CPV correlated with CXCL9 (r = 0.233), GFAP (r = 0.275), CDCP1 (r = 0.231) and TNFS12B (r = 0.289) ($p < 0.05$). In multivariate regression analysis, CPV was associated with brain atrophy ($\beta = -0.261$; $p = 0.033$), while the MSDA scores and panel biomarkers showed no associations.
Conclusion: Our findings support CPV as a potential imaging marker for MS progression. Broader longitudinal serum proteomic analysis and a tailored multi-analyte algorithm may be warranted to identify serum signatures of CPV and disease progression.

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Serono, Biogen Idec, and Teva Pharmaceutical Industries Ltd./ Sanofi-Aventis; and serves on scientific advisory boards for Bayer Schering Pharma, Biogen Idec, Merck Serono, Novartis, Genzyme, Roche, and Teva Pharmaceutical Industries Ltd./ Sanofi- Aventis. M. Khalil has received travel funding and speaker honoraria from Bayer, Biogen, Novartis, Merck, Sanofi and Teva and serves on scientific advisory boards for Biogen, Bristol-Myers Squibb, Gilead, Merck, Novartis, Alexion, Amgen and Roche. He received research grants from Biogen, Novartis and Teva.

P1534
Serum Neurofilament Light Chain is Associated with Putamen Atrophy in Multiple Sclerosis

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Introduction: Deep grey matter (DGM) atrophy is a recognized marker of neurodegeneration in MS and is associated with disease progression and disability. Among DGM structures, the putamen may be particularly vulnerable to early MS-related atrophy. Serum neurofilament light chain (sNfL) is an emerging biomarker of neuroaxonal injury, but its relationship with regional DGM atrophy remains unclear.
Objectives/Aims: To investigate the association between sNfL levels and putaminal atrophy in patients with RRM, and to explore correlations between sNfL and other imaging parameters such as total DGM volume and lesion burden.
Methods: This cross-sectional, retrospective study included 103 RRMS patients followed at Hospital Israelita Albert Einstein, São Paulo, Brazil. Inclusion criteria required at least one brain MRI and a corresponding sNfL measurement within one month. MRI volumetrics were assessed using automated segmentation, and sNfL was measured using the Simoa NF-light™ Advantage Kit. Patients were stratified into low and high sNfL groups based on the median level. Correlations were analysed using Spearman's coefficient and multiple linear regression, adjusting for potential confounders.
Results: Mean age was 39.9 ± 10.1 years, and 81.6% were female. The mean putamen volume was 8.5 ± 1.5 mL. A significant negative correlation was found between sNfL levels and putamen volume [IC= -0.0785 (-0.141; -0.0161); p = 0,014]. No significant association was observed between sNfL and lesion volume or total brain volume. However, when analysing the data considering a multiple regression model, no significance was found between sNfL and regional brain atrophy.
Conclusion: Elevated sNfL levels are associated with putaminal atrophy, supporting sNfL as a potential biomarker of neurodegeneration in MS. The findings emphasize the importance of monitoring DGM integrity and highlight the potential of sNfL in guiding prognosis and treatment strategies beyond inflammatory activity alone.

Disclosure of interest: Nothing to disclose.

P1535
Astrocyte-derived extracellular vesicles as a source of biomarkers for Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS) is a chronic autoimmune disorder characterized by neuroinflammation and degeneration within the central nervous system (CNS). Current tools for diagnosis and disease monitoring, such as MRI and clinical scales, are limited in their ability to capture the underlying biological activity of the disease. There is an urgent need for minimally invasive biomarkers that reflect disease progression and therapeutic response. Extracellular vesicles (EVs), particularly those derived from CNS cells, offer a promising avenue as they carry proteins and nucleic acids reflective of their cellular origin. Among them, astrocyte-derived EVs (ADEVs) have gained attention due to the central role of astrocytes in MS pathology.
Objectives/Aims: We aimed to develop a novel blood-based technique to selectively isolate brain-derived EVs enriched in astrocytic markers from people with MS. Our goal was to evaluate their potential as a source of biomarkers indicative of MS disease activity.
Methods: We established a sequential isolation protocol targeting astrocyte-specific EVs. EVs were characterized for their quantity, size distribution, content in proteins and RNA to confirm their identity and cell-type origin. Proteomic profiling was then performed to quantify and compare the protein cargo of ADEVs from people with MS and healthy controls.
Results: Our isolation method achieved high enrichment of astrocyte -derived EVs carrying astrocyte-related cargo as compared to other EV subpopulation. ADEVs from people with MS showed elevated levels of proteins linked to neuroinflammation and neurodegeneration. Several of these proteins were differentially expressed between MS patients and controls, highlighting their potential as biomarkers for disease monitoring. Aggregating these protein levels into a unique scoring enable fair separation of people with MS from healthy individuals thus demonstrating the usefulness of ADEVs as biomarkers for MS.
Conclusion: Astrocyte-derived EVs isolated from peripheral blood represent a promising and minimally invasive source of biomarkers for MS. The developed protocol enables routine access to CNS-specific molecular signatures, providing new insights into MS pathogenesis and offering potential tools for more accurate disease tracking and personalized management.

Disclosure of interest: Sylvain Perriot: is a founder and owns shares of Lermed

P1536
Establishment and validation of normative values for serum glial fibrillary acid protein (sGFAP) in a healthy Italian cohort

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Introduction: Glial fibrillary acid protein (GFAP) is a type-III intermediate filament of mature astrocytes, essential for synaptic function and homeostasis. Serum GFAP has shown potential as monitoring biomarker for neuromyelitis optica spectrum disorder (NMOSD) activity and progressive MS (PMS) disease progression. To support clinical implementation, normative reference values are still needed.

Objectives/Aims:

1) To elaborate GFAP reference values on healthy controls (HC)
2) To validate these values on NMOSD patients

Methods: Serum samples were selected from CRESM Biobank: 139 HC (101 females; mean age= 40 years/old) and 99 follow-up samples from 15 NMOSD patients in an active (n=9, 6 patients with relapse or active imaging) or not-active (n=90, 15 patients) state; they were tested with Neuro 2-plex B Advantage kit (Quanterix). Association between biological variables and sGFAP were assessed via uni/multivariate linear regression. Normative values were obtained using a non-crossing, additive, semiparametric smooth quantile regression model. Generalized Estimating Equations (GEE) model was used to assess the relationship between sGFAP values and disease activity in NMOSD.

Results: In HCs, log-sGFAP correlated moderately with age (Pearson's $r = 0.439$, 1.38% yearly mean increase) and was lower in males ($p=0.023$). Blood volume (BV) adjusted for sex and age showed a weak negative association ($\beta= -0.095$, $p = 0.008$).

For establishing normative values, the best-performing model (especially in upper quantiles) was *QuantRegGrowth* package in R 4.4.1 using decade as predictor and log-sGFAP as outcome, estimating the 50th, 75th, and 90th percentiles. Active NMOSD patients showed a 1.55-fold increase in sGFAP levels compared to not-active ones (GEE, 95% CI: [1.30, 1.85], $p < 0.001$). Applying normative values revealed that samples above the 75° and 90° percentiles were more frequent in the active group (Fisher's exact test $p=0.03$ and $p=0.003$). Additionally, NMOSD patients with sGFAP levels above the 75th percentile were 4.7 times more likely to be classified as active at the time of sampling (GEE, 95% CI: [1.05, 20.94], $p = 0.043$).

Analysis of GFAP normative value application in PMS interpretation is ongoing.

Conclusion: We established decades-adjusted normative values for sGFAP (50th, 75th and 90th percentile). The validation on NMOSD samples supports their utility as reliable indicators of astrocytic damage in active disease phases. Implementing these references can improve clinical interpretation and patient management, upon broader validation.

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P1537
Serum neurofilament light chain levels reflect disease progression and disability in progressive multiple sclerosis

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Introduction: Serum neurofilament light chain (sNfL) has become a promising biomarker for acute and chronic neuroaxonal damage in relapsing and progressive multiple sclerosis (MS). Evidence is accumulating that sNfL levels have a predictive value for the risk of disability progression in MS.

Objectives/Aims: To assess serum neurofilament light chain (sNfL) levels in patients with progressive MS.

Methods: We analysed sNfL levels in a cross-sectional cohort study involving 181 patients with progressive MS (PMS). Additionally, we investigated the correlation between disease activity and sNfL levels in 341 patients with relapsing MS (RMS) using single molecule array technology.

Results: Serum NfL levels (pg/mL) were significantly elevated in patients with RMS and PMS compared to HC (29.4 vs 12.3, $p<0.05$; 38.4 vs 12.3, $p<0.001$, respectively). Additionally, higher sNfL levels were correlated with disability. A statistically significant difference in sNfL levels was observed between relapsing and progressive disease in individuals not receiving treatment (35.2 vs 42.0, $p<0.01$, adjusted for age). Furthermore, treatment significantly reduced sNfL levels in RMS compared to those not receiving treatment (24.4 vs 36.9, $p<0.01$, adjusted for age). Notably, a statistically significant difference was

observed only with natalizumab and fingolimod, but not with interferons or glatiramer acetate when compared to individuals not receiving treatment.
Conclusion: The findings support the utility of sNfL measurement to monitor MS disease activity and progression alongside magnetic resonance imaging.

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P1538
Cerebrospinal fluid molecular pattern at multiple sclerosis diagnosis predicts cognitive functioning after five years of follow-up

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Introduction: The cerebrospinal fluid (CSF) inflammatory markers reflect diffuse intrathecal inflammation, associating with meningeal infiltrates and damage in the adjacent grey matter (GM) in MS. Cognitive impairment (CI) is associated with brain damage in MS and is often present early in people with MS since the earliest stages of the disease. Some specific CSF molecules have been demonstrated to mirror cognitive functioning at time of diagnosis in a cross-sectional evaluation described in a previous study.
Objectives/Aims: To investigate whether a specific CSF inflammatory profile at the time of diagnosis is associated with cognitive functioning after a five-year follow-up period
Methods: Sixty-one patients with MS (47 females, mean±standard deviation SD age: 43.3±11.5, mean±SD education=14.5±3.3) underwent CSF withdrawal from lumbar puncture for diagnostic purposes and a comprehensive neuropsychological assessment after a period of follow-up. The cognitive evaluation was conducted using the Brief Repeatable Battery of Neuropsychological Tests and other additional tests (the Stroop Test (ST), the Trail Making Test, the Phonemic Semantic and Alternate Verbal Fluency Test (VF), the Modified Five Point Test (MFPT), and the Brief Visuospatial Memory Test–Revised (BVMT-R). We specifically evaluated the levels of 12 inflammatory mediators in the CSF which were significantly associated with cognitive functioning in a previous study.
Results: A statistically significant correlation between CSF molecules evaluated and cognitive tests were found, in particular: Word List Generation (WLG) with LIGHT (R=-0.28; p=0.029) and IL35 (R=-0.26; p=0.045); ST with CX3CL1 (R=0.30; p=0.019); Semantic VF with CCL8 (R=-0.26; p=0.045), LIGHT (R=-0.36; p=0.005), IL12 (R=-0.29; p=0.027), IL22 (R=-0.33; p=0.010), and IL35 (R=-0.26; p=0.049); Alternate VF with LIGHT (R=-0.28; p=0.040), IL12 (R=-0.30; p=0.026) and IL22 (R=-0.32; p=0.017). Furthermore, Osteopontin levels significantly correlated with Phonemic VF (R=-0.34; 0.008); SVF (R=-0.26; p=0.045) and with a composite index representing executive functioning (R=-0.26; p=0.042).
Conclusion: Specific CSF molecular patterns are associated with future cognitive functioning alterations accumulated after 5 years of follow-up from diagnosis. This further suggest the key role of intrathecal inflammation in driving compartmentalized MS disease pathology including cognitive impairment.

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P1539
Cerebrospinal fluid proteins associated with neuroaxonal damage in early active multiple sclerosis

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Introduction: Neuroaxonal damage underlies disease progression in multiple sclerosis (MS) and can be assessed by determining concentrations of neurofilament light (NfL) protein in cerebrospinal fluid (CSF) or serum.
Objectives/Aims: The objective here was to shed light on biological processes associated with neuroaxonal degeneration.
Methods: To quantify protein patterns associated with NfL in paired CSF and serum samples, a highly sensitive proximity-extension assay combined with next-generation sequencing (Olink Explore) was utilized.
Results: A discovery cohort (n=114) with treatment naïve early-stage active MS stratified into above or below median of CSF NfL demonstrated that 13 proteins were upregulated in CSF (LILRB4, CXCL6, CXCL5, CD38, CCL19, CXCL11, IMPA1, MSR1, CXCL10, MCP2, ITMA2, TNFRSF12A and CCL23). Importantly, associations to CCL19, CXCL11, MSR1, CXCL10, TNFRSF12A and CCL23 were replicated in a more heterogenous validation MS cohort (n=128) that also comprised later stages of MS with ongoing disease modulatory therapy. In contrast, no consistent serum protein profiles associating with serum levels of NfL could be discerned in this group-based analysis. Further, 75 CSF proteins showed a positive adjusted linear association with CSF-NfL, while no such significant association remained in the corresponding corrected analysis in serum.
Conclusion: The identified and replicated CSF protein profile indicates distinct inflammatory processes associated with ongoing neuroaxonal degeneration. All of these most robust six pro-inflammatory markers independently replicated and individually observed to be relevant in the context of MS, may thus serve as more MS-specific disease activity or treatment response biomarkers than NfL, which represents a generic marker of axonal damage.

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P1540
Brain-derived blood extracellular vesicles as potential treatment response biomarkers in multiple sclerosis patients receiving anti-CD20 therapy

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Introduction: Suppression of inflammatory activity with disease-modifying therapies is the cornerstone of multiple sclerosis (MS) treatment. However, many of these therapies are administrated as maintenance treatments, increasing the risk of infections and other immune-mediated side-effects over time. The ability of brain-derived blood extracellular vesicles (EVs) to cross the blood-brain-barrier into the bloodstream, thereby reflecting the current immune status of the central nervous system, has kindled interest in them as potential biomarkers.
Objectives/Aims: We aimed at defining the potential of MS-specific brain-derived blood EVs biomarker panel to tailor anti-CD20 therapy (rituximab) regimens to individual relapsing MS patients.
Methods: We analysed matched diagnostic cerebrospinal fluid (CSF) and serum from treatment-naïve relapsing-remitting MS (RRMS) patients (n=25), before and after six months of rituximab therapy from an ongoing randomized clinical trial OVERLORD-MS (https://clinicaltrials.gov/show/NCT04578639; REC West ID: 66391). Healthy serum controls (HC; n=15) were also examined. EVs morphology, size, and concentration (CellMask, Epstein–Barr virus nuclear antigen 1 (EBNA1) and L1 cell adhesion molecule (L1CAM)) were assessed for both total and $L1CAM^+$ (brain-derived) EVs using transmission electron microscopy (TEM), and nanoparticle tracking analysis (NTA). Further ongoing analyses include immunophenotyping of EVs surface receptors with conventional flow cytometry (MACSPlex exosomes kit) and label-free quantitative proteomics of EVs protein cargo (proximity extension assay).
Results: Our preliminary findings, from NTA analysis of the rituximab treatment cohort (n=25) showed a significantly increased L1CAM ($p < 0.0001$) concentration in total serum EVs at baseline (untreated) compared to HC. The L1CAM concentration in total serum EVs decreased ($p < 0.0001$) after rituximab treatment at month 6 compared to baseline. In addition, we found increased levels of EBNA1 concentration in $L1CAM^+$ serum EVs ($p < 0.01$) baseline compared to HC.
Conclusion: This study indicates the disease specificity and biomarker potential of $L1CAM^+$ blood EVs, as evidenced by

the significant changes observed before and after rituximab treatment.

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P1541
Proteomic profiling for novel biomarkers of risk of conversion to multiple sclerosis and disease severity

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Introduction: There is still a need for more sensitive and specific biomarkers to improve diagnostic and prognostic accuracy early in the course of the MS, in order to tailor treatment to patients' individual risk. The Sequential Window Acquisition of all Theoretical Fragment Ion Spectra (SWATH-MS) mass spectrometry method offers unsurpassed proteomic coverage and more reproducible quantification.
Objectives/Aims: Identify a proteomic signature of risk of conversion to multiple sclerosis and disease severity
Methods: Clinical data were collected retrospectively or prospectively. We use residual cerebrospinal fluid samples collected at initial presentation in a population of 17 CIS, 62 MS and 43 other non-inflammatory neurological diseases (ONIND) patients. Differentially expressed proteins (DEPs) between MSCIS vs ONIND, MS vs ONIND, MS vs CIS and CIS vs ONIND were identified with a false discovery rate (FDR) $<$ 0.05, except for MS vs CIS, the FDR was set $<$ 0.4. Network analysis was performed using the STRING protein-protein interaction (PPI) network. Relationships between DEPs, prognosis factors and short or mid-term disease activity were analysed by Mann-Whitney U test or Kruskal-Wallis test with multiple comparison correction. The classification power of DEPs in MSCIS vs. ONIND was evaluated by XGBoost with repeated stratified cross-validation by OmicLearn.
Results: SWATH-MS analysis identified and quantified 1257 proteins, 593 were selected for groups comparison, of which 73 were DEPs: 31 in MSCIS vs. ONIND, 55 in MS vs. ONIND, 16 in MS vs. CIS, and 3 in CIS vs. ONIND groups comparison. This 73 DEPs network has 3.5 more interactions than expected with a PPI enrichment p-value $<$ 1*10-16. CH3L2 is significantly higher in patients who have T2 spinal MRI lesions at onset (FDR $<$ 0.0002), and LAMP2 is significantly lower in patients who have a NEDA-3 at 5 years (FDR $<$ 0.0005). To classify MSCIS vs. ONIND, we used the 73 DEPs and achieved a receiver operating characteristic with a mean AUC (area under the curve) of 0.77 (0.07 std) and a precision-recall curve with a mean AUC of 0.62 (0.12 std).
Conclusion: SWATH-MS analysis is a powerful tool for investigating proteomic signatures of disease severity and diagnosis. The identification of these 73 DEPs may help to better understand the pathophysiology and define the best treatment strategy.

Disclosure of interest: Laure Bastide: nothing to disclose

P1542
Neurodegenerative, inflammatory and signaling biomarkers in early RRMS: Insights from CSF analysis

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Introduction: Neurodegeneration, inflammation and dysregulated cellular signaling are key factors in the pathogenesis of MS. Cerebrospinal fluid (CSF) biomarkers reflecting these processes may provide valuable insights into the underlying mechanisms of relapsing-remitting MS (RRMS) and serve as potential indicators of disease activity.
Objectives/Aims: Our study aimed to assess the levels of selected neurodegeneration, inflammatory and signaling parameters in the CSF of patients diagnosed with RRMS.
Methods: Sixty-two patients newly diagnosed with RRMS and twenty-six healthy individuals were enrolled in the study. We determined the concentrations of 18 molecules (amyloid beta 1-42, FGF-21, kalikresin-6, neurogranin, S100B, TDP-43, BDNF, GDNF, MIF, NF-H, Tau, UCHL1, CNTF, GFAP, NCAM-1, NGF beta, Tau (pT181), YKL-40 (CHI3L1)) in CSF. We analyzed relationships between selected markers' levels depending on the gender, presence of MRI lesions or comorbidities.
Results: We found increased levels of GFAP and NF-H in the RRMS group. In contrast, the concentration of Tau protein and MIF was higher in the control group. The number of T2 lesions in MRI decreased with the increasing levels of BDNF and FGF-21. No correlations were found for active Gd+ lesions. The concentration of GDNF, Tau protein, BDNF, S100B, and NF-H was higher in male patients. The levels of NRGN were significantly higher in women. In the RRMS group, positive correlations were found between the levels of IL-1, TNF-alfa, IL-17A and NCAM 1, IL-17A, IL-12 and Tau protein, as well as IL-17A and BDNF. A negative correlation was observed only between IL-17 and NRGN.
Conclusion: Our study highlights the role of selected factors in the development of neuroinflammation at the early stage of MS. Understanding the relationship between these molecules and the pathomechanism of the disease may be crucial in planning the most appropriate immunomodulatory therapy.

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P1543
Double Seronegative Optic Neuritis: Identification and Analysis of New Autoantibodies and Their Antigenic Targets

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Introduction: Although optic neuritis (ON) is commonly linked to multiple sclerosis (MS), the discovery of anti-aquaporin-4 (AQP4) and anti-myelin oligodendrocyte glycoprotein (MOG) antibodies in non-MS ON patients suggests an alternative antibody-mediated mechanism. About 15% of non-MS ON cases remain seronegative for both AQP4 and MOG, a condition termed "double seronegative" (DSN) ON. The pathophysiology of these cases is poorly understood, with clinical heterogeneity suggesting distinct mechanisms, possibly involving unidentified autoantibodies.
Objectives/Aims: The aim of this study is to better characterize non-MS DSN ON patients clinically and pathophysiologically, focusing on identifying and characterizing new antigenic targets that could help clarify the pathogenesis of this condition.
Methods: A French national cohort of DSN ON patients is being established as part of the "QUEST-ION" study (QUalitative Evaluation of SeronegaTive-Idiopathic ON) based on the NOMADMUS cohort, with the creation of a biobank. Purified serum IgG will be tested using immunofluorescence (IF) on murine and human optic nerve sections and cell cultures to assess IgG binding and potential pathogenic effects. Immunodetection techniques such as Western blot (WB), immunoprecipitation, and mass spectrometry will be used to identify antigenic targets.
Results: 44 DSN ON patients were included in QUEST-ION. IF analysis of 9 patient sera revealed positive staining in 5 cases, with specific IgG recognition of an oligodendrocyte cytoplasmic protein in one case. This protein was also expressed in other specific cells of kidney and liver. This recognition was confirmed by WB, showing a specific IgG binding to 20 kDa and 40 kDa proteins, likely dimeric. Proteomic analyses are ongoing to identify the target protein.
Conclusion: These results confirm the presence of unidentified autoantibodies in non-MS DSN ON patients. Identifying and characterizing these autoantibodies could improve diagnosis and management, providing a potential new biomarker and better understanding of the pathophysiological mechanisms, which may enhance clinical care and therapeutic strategies.

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P1544
Characterizing Protein and MSDA Score Correlations Amongst Stable Participants from the Measuring Outcomes and Value: an Integrated, Novel Solution for Generating insights in MS (MOVING MS) Study

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Introduction: The MOVING MS Study evaluates the Octave platform's impact on Multiple Sclerosis (MS) care, focusing on unplanned healthcare utilization and patient and physician satisfaction. Octave's platform features the Multiple Sclerosis Disease Activity (MSDA) Test, a validated multi-protein assay that measures the absolute concentration of 18 protein biomarkers, corrects for sex and age, and generates a Disease Activity (DA) score (1 to 10 in 0.5 increments), and is validated for MRI and clinical assessments of disease activity.
Objectives/Aims: Exploratory analysis to determine the correlation between DA scores at successive timepoints in clinically stable participants.
Methods: Eighty-six participants with relapsing remitting MS were enrolled in a 12-month randomized waitlist-controlled trial of the Octave platform, including MSDA testing at up to five timepoints (baseline, 3, 6, 9, and 12 months). Participants were evaluated for meeting criteria for clinical stability, defined by: 1) no gadolinium-enhancing or T2 new/enlarging lesions; 2) no clinical relapses; 3) no Expanded Disability Status Scale progression based on specific criteria and 4) no switch in disease-modifying therapy; and for completion of at least two MSDA Tests. Pearson correlation coefficients (r) were calculated between the first two successively collected DA scores and the individual log-transformed protein concentrations. Confidence intervals were cluster bootstrapped. The average DA score change per year, adjusted for age and sex, was estimated using a random slope and intercept linear mixed model.
Results: Thirty-four participants (108 samples) met clinical stability criteria for inclusion in the analysis (79% female, mean baseline age=41yrs). The median disease duration at baseline was 5yrs (IQR=10yrs). The DA score correlation between the first two successive timepoints was strong (r=0.92, 95%CI=[0.79, 0.97]), while NfL (r=0.75, 95%CI=[0.47,0.91]) and GFAP (r=0.71, 95%CI=[0.46, 0.89]) showed moderate correlation. On average, DA scores minimally changed over time, with a mean decrease of 0.47 score units/year (95%CI=[0.16, 0.79]).

Conclusion: Stable participants demonstrated strong DA score correlation across timepoints, with greater precision than moderate correlations observed for NfL and GFAP. These findings may indicate that the multi-protein DA Score is more stable and reliable than single proteins. The estimated DA score change per year provides a benchmark for assessing disease activity stability in future longitudinal studies

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P1545

Application of Serum Neurofilament Light Chain (sNfL) and Glial Fibrillary Acidic Protein (sGFAP) as Biomarkers in the Clinical Management of Multiple Sclerosis (NeuroFiLMS): a protocol of a prospective observational study

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Introduction: Advances in ultrasensitive assay techniques have enabled precise quantification of serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (sGFAP), highlighting its potential as a dynamic biomarker for detecting neuroaxonal injury and progression in multiple sclerosis (MS).
Objectives/Aims: In NeuroFiLMS, sNfL is being investigated as a prognostic biomarker for clinical and radiological disease activity in relapsing MS, and sGFAP for progression. The aim is to assess whether diagnostic and therapeutic decisions will be influenced by monitoring sNfL concentrations over time in people with MS (pwMS) and to evaluate the comparability of different assay methods.
Methods: NeuroFiLMS is a prospective, multicenter observational study that is conducted across multiple MS centers of the German Multiple Sclerosis Registry across Germany, enrolling 1,500 pwMS diagnosed with relapsing MS. Participants will be randomized in a 2 (n=1,000): 1 (n=500) ratio to either management with immediate sNfL reporting or with delayed sNfL reporting to treating physicians to assess how biomarker availability influences therapeutic decision-making in routine healthcare across Germany. Over a two-year follow-up period, pwMS will undergo three study visits during clinical routine care, involving blood sampling for sNfL sGFAP, comprehensive clinical evaluations, and MRI assessments. The study employs standardized protocols for sample collection (within clinical routine laboratory procedures and in research collaboration) prior to analysis by the Siemens assay (University Medicine Mannheim, Heidelberg University), and the SIMOA quanterix assay (University of Basel). Statistical analyses will include correlation studies, multiple regression models, and Receiver Operating Characteristic curve analyses.
Results: There is a paucity of validated serum biomarkers for the precise assessment of disease activity in MS. sNfL and sGFAP have the potential to be cost-effective biomarkers, potentially enabling faster and more precise therapeutic decisions. Additionally, the study will evaluate the intra-individual variability of sNfL measurements over time and across different laboratory testing methods, ensuring its robustness for clinical use.
Conclusion: sNfL and sGFAP have the potential to serve as cost-effective, easily accessible, and low-burden biomarkers in the future, contributing in a timely manner to diagnostic and therapeutic decision-making in relapsing MS.

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pecuniary interests to disclose, other than being the lead of the German MS Registry, which receives (project) funding from a range of public and corporate sponsors, recently including The German Innovation Fund (G-BA), The German Retirement Insurance, The German MS Trust, The German MS Society, Biogen GmbH, BristolMyersSquibb, Merck Healthcare Germany GmbH, Novartis Pharma GmbH, Roche Pharma AG and TG Therapeutics. None resulted in a conflict of interest. FP received research support from Neurosciences Clinical Research Center, German Ministry for Education and Research (BMBF), Deutsche Forschungsgemeinschaft (DFG), Einstein Foundation, Guthy Jackson Charitable Foundation, EU FP7 Framework Program, Biogen, Genzyme, Merck Serono, Novartis, Bayer, Roche, Parexel and Almirall; honoraria for lectures, presentations and speaker honoraria from Guthy Jackson Foundation, Bayer, Biogen, Merck Serono, Sanofi Genzyme, Novartis, Viela Bio, Roche, UCB, Mitsubishi Tanabe and Celgene; received compensation for serving on a scientific advisory board of Celgene, Roche, UCB and Merck; and is an Academic Editor of PLos One and Associate Editor of Neurology® Neuroimmunology & Neuroinflammation; all unrelated to the presented work.

P1546
Exploration of small non-coding RNAs in Multiple Sclerosis

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Introduction: Small non-coding RNAs (sncRNAs) have emerged as promising biomarkers due to their high stability and accessibility. In a previous study, we profiled sncRNAs across immune-related cells and fluids revealing Multiple Sclerosis (MS)-associated changes and opposing patterns in the central nervous system (CNS) compared to the periphery.
Objectives/Aims: Replication of previous findings and further exploration of sncRNAs as markers of MS disease activity and progression.
Methods: The Small-seq protocol was applied to profile sncRNAs in nearly 800 samples, with ~300 individuals with matching plasma and cerebral spinal fluid (CSF). The cohort encompassed various MS disease trajectories, assessed based on clinical information, as well as 91 non-inflammatory neurological disorders controls (NINDCs) and 48 healthy controls (HC). The stability of sncRNAs was assessed by leaving blood and CSF from three subjects for an extended period of time in room temperature (0, 1, 3, 6, 24, and 48 hours), followed by exposure to freeze/thawing conditions. Processing of the Small-seq data included filtering, mapping, deduplication, annotation, counting and normalization.
Results: Detected sncRNAs were categorized into microRNAs (miRNAs), tRNA-derived fragments (tRFs), small nucleolar RNAs (snRNAs), snoRNA-derived RNAs (sdRNAs), yRNA-derived fragments (ysRNAs). We found significant differences in sncRNA distribution between plasma and cerebrospinal fluid (CSF). Thus, miRNAs (88%) dominated in plasma, with smaller fractions of tRFs (10%) and ysRNAs (2%), while CSF displayed a more balanced profile of entities with tRFs at 47%, miRNAs at 45%, and ysRNAs at 7%. Importantly, sncRNA profiles remained generally stable across preanalytical conditions, including prolonged bench time (up to 48 hours) and repeated freeze-thaw cycles. Detailed comparisons between HC and disease groups, as well as correlations with clinical features in the MS group, will be included in the final presentation.
Conclusion: This multi-compartment study provides novel insights into distinct molecular and tissue-specific signatures linked to MS immunopathology, particularly the divergence between CNS and peripheral compartments. Additionally, the stability of sncRNA profiles under common preanalytical conditions supports the reliability of Small-seq for large-scale, translational applications.

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P1547
Blood Neurofilament Light Chains Assessed by Chemiluminescent Enzyme Immunoassay: Experience in a Large Cohort of Multiple Sclerosis Patients Treated with High-Efficacy Therapies and Correlation with Single Molecule Assay

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Introduction: Blood neurofilament light chains (NfL) are increasingly used as a biomarker in MS. Several new assays for plasma NfL (pNfL) have been proposed recently, among which the Lumipulse™ assay, a fully automated chemiluminescent enzyme immunoassay. More data are needed on the use of these new assays in the clinical setting.
Objectives/Aims: The aim of this study was to evaluate the Lumipulse™ assay for pNfL measurement in MS patients treated with high-efficacy therapies. We assessed correlations with clinical and demographic variables, compared pNfL levels between patients treated with anti-CD20 monoclonal antibodies and natalizumab. The degree of agreement between Simoa™ and Lumipulse™ for the determination of NfL levels was also evaluated in a subset of patients.
Methods: Plasma NfL were tested using the Lumipulse™ assay in a population of MS patients treated with anti CD20 mAbs (ocrelizumab, ofatumumab) and with natalizumab, every 6 months over a period of 1 year. pNfL levels were correlated with clinical and demographic variables in a generalized linear regression model. In the patients treated with anti CD20 mAbs, also lymphocyte subpopulations (CD4+, CD8+, CD19+, NK lymphocytes assessed every 6 months over 1 year) were included in the model. Furthermore, patients treated with natalizumab and patients treated with anti CD20 mAbs were matched for sex, age and EDSS using propensity score; patients with recent disease activity were excluded. In a subset of patients, NfL levels were simultaneously tested also with the Simoa™ assay and the two methods were compared.
Results: This study included 287 MS patients, treated with anti CD20 mAbs (162 ocrelizumab, 70 ofatumumab) and with natalizumab (75). Mean age was 48.4 years, mean duration of disease 12.4 years, median EDSS 3.5. In the linear regression models, pNfL levels correlated with age ($p<0.001$), EDSS ($p=0.011$) and recent disease activity ($p<0.001$).
Comparing patients treated with anti CD20 mAbs and patients treated with natalizumab (60 vs 60 after propensity score matching), no significant differences in pNfL levels were found.
In 25 patients simultaneously tested with both the Lumipulse™ and Simoa™ assay on the same blood sample, NfL levels were strongly correlated and Passing-Bablok regression showed high agreement in NfL levels between the two assays.
Conclusion: Plasma pNfL levels measured using Lumipulse™, in a population of MS patients treated with high efficacy therapies, confirm the known correlations with age and recent disease activity. Comparison of the Lumipulse™ and Simoa™ assays shows high agreement in the measurement of NfL.

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P1548
Association of neurofilament light chain and glial fibrillary acidic protein levels with comorbid depression in MS

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Introduction: Elevated levels of serum neurofilament light chain (sNfL) reflect neuronal injury, while elevated serum glial fibrillary acidic protein (sGFAP) levels indicate astrocytic activation. Both are elevated in people with multiple sclerosis (pwMS) compared to healthy individuals, and separately in those with depression. Understanding whether sNfL and sGFAP are particularly elevated in pwMS with comorbid depression may clarify how depression influences MS disease outcomes.
Objectives/Aims: To compare sNfL and sGFAP levels across four groups: MS without comorbid depression, MS with comorbid depression, depression (but no immune disease), and healthy controls.
Methods: Data were obtained from 260 participants in the IMID study conducted in Manitoba, Canada (mean age = 45 years, 78% female), including 52 with MS and depression (MS-Dep), 50 with MS without depression (MS-NoDep), 69 with depression but no immune-mediated diseases (Dep-noImmune), and 89 healthy controls. Sociodemographic characteristics and blood samples were collected at baseline. sNfL and sGFAP concentrations were quantified with Single Molecule Array immunoassay and then log transformed. Multivariable linear regression modelled sNfL and sGFAP levels separately as outcomes, with examination of the primary exposure (disease group: MS-Dep, MS-NoDep, Dep-noImmune, or healthy controls), and confounders (age, BMI, and

sex). Subgroup analyses of sNfL levels in MS assessed the effect of DMT (platform compounds, oral therapies, high-efficacy monoclonal antibodies, and other/untreated) on the associations.
Results: sNfL levels were significantly higher in MS-Dep (β=0.35, $p<0.001$), MS-NoDep (β=0.26, $p<0.001$), and Dep-noImmune (β=0.15, $p=0.03$) compared to healthy controls. GFAP levels were also elevated in MS-Dep (β=0.31, $p<0.001$) and MS-NoDep (β=0.36, $p<0.001$), but not in Dep-noImmune (β=0.042, $p=0.63$) compared to healthy controls. A significant positive correlation was observed between log-transformed sNfL and sGFAP levels (Pearson's r=0.59, $p<0.001$).
Conclusion: These findings potentially highlight a higher level of NfL with comorbid depression in MS compared to healthy controls, with GFAP levels elevated in MS but not in those with depression and no immune disease. This difference may suggest depression in MS is more closely linked to both axonal damage and glial activation, whereas depression alone may not be associated with significant glial activation. Longitudinal studies may clarify the role of neurodegeneration biomarkers in the context of comorbid depression in MS.

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P1549
Changes in GFAP expression reflect early Multiple Sclerosis severity and reveal gender variations

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Introduction: Glial fibrillary acidic protein (GFAP) is a fundamental structural protein of astrocytes and serves as a critical marker of astrocytic activation and glial injury. In multiple sclerosis (MS), elevated levels of GFAP in cerebrospinal fluid (CSF) have been associated with reactive gliosis, particularly in the neurodegenerative stages of the disease. Recent investigations have proposed GFAP as a promising biomarker for the monitoring of MS, especially in its progressive forms, where neurodegeneration and gliosis are more pronounced.
Objectives/Aims: This study aims to explore the potential of CSF GFAP as an indicator of early astrocytic damage by evaluating its levels concerning to various clinical variables, including disability as measured by EDSS, as well as sex and phenotype differences.
Methods: CSF samples from 101 patients with MS (80 RRMS, 15 PPMS, and 6 SPMS) were collected by lumbar puncture at the moment of diagnosis. All participants signed the informed consent. CSF levels of GFAP were measured using Milliplex® assay (Merck). Statistical analysis was performed using parametric tests and significance was set at 0.05.
Results: Significant sex differences were observed, within the MS patient group, with males (N=28) exhibiting significantly higher GFAP levels compared to females (N=67) (p=0.015). Although no significant differences were detected between disease phenotypes, Bonferroni correction shows a trend towards significance between PPMS and SPMS subtypes (p= 0.053), with GFAP levels higher in PPMS. Finally, linear regression revealed a positive and significant association between GFAP levels and baseline EDSS (β=0.213, 95% CI, 1.713 to 58.009, p=0.038), indicating that higher GFAP levels are associated with a greater degree of neurological disability at the time of diagnosis.
Conclusion: The results of this study support GFAP as a bio of early neurodegeneration in MS indicating astrocytic damage from disease onset. The significant association between GFAP levels and baseline EDSS in our cohort validates GFAP as a marker of clinical severity. Higher GFAP levels in males - who are more frequently affected by PPMS- point to sex-specific neurodegenerative patterns. These findings align with previous studies positioning GFAP as a relevant biomarker in progressive forms of MS with prognostic value.

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P1550
Increased kappa free light chain index in patients with late onset multiple sclerosis

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Introduction: Intrathecal immunoglobulin-G synthesis is a pathological hallmark of multiple sclerosis (MS). Cerebrospinal fluid (CSF) kappa-free light chain (κFLC) detection has emerged as a new biomarker in MS, but little is known about its expression and variance across distinct patient subgroups.
Objectives/Aims: To assess and compare intrathecal synthesis through the kFLC index between patients with early and late onset MS.
Methods: An exploratory retrospective single-center cohort study including consecutively diagnosed MS patients was conducted. Nephelometric kFLC measurements of paired serum/CSF samples collected at MS diagnosis were obtained. A cut-off for increased κFLC index was established at >6.1 as per previous published reports. Two groups were defined: early onset (EO) patients (first MS symptoms < 50 years) and late onset (LO) patients (first MS symptoms ⩾ 50 years).
Results: Sixty (60) patients were included, 42(70%) female, with a mean age of 48.3 years (±14.3; min18-max79) and a mean disease duration of 5.2 years (± 4.8; min 0.5-máx 23). 25 (41.7%) LO patients were included. Groups did not differ in demographic or clinical variables (gender, disease phenotype, disease duration, baseline EDSS, MRI findings at baseline). Although the prevalence of CSF-restricted OCB was similar between groups (EO n=31, 88.6%; LO n=22, 88,0%, p=1.000), the prevalence of a kFLC index >6.1 was significantly higher in LO MS patients (n=22, 88.0% vs EO n=22, 62,9% p=0.040). A tendency towards a higher CSF kFLC in LO was observed (3.35±4.24 vs EO 1.59±2.5, p=0.055), with no differences in serum kFLC (p=0.602) between groups.
Conclusion: In this cohort, a higher prevalence of increased kFLC index was found among patients with late-onset MS. This may reflect a longer period of intrathecal dysimune reactions connected to MS pathological onset, even if not clinically expressed until later stages (*ie* LO MS).

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P1551
Association of Ceramide Synthetases mRNA Expression with Imaging Outcomes in Multiple Sclerosis

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Introduction: The clinical course of multiple sclerosis (MS) is highly variable, highlighting the need for reliable biomarkers of disease activity. While ceramides (Cer) play a crucial role in MS pathophysiology, studies have reported inconsistent alterations in Cer levels, limiting their utility as potential biomarkers. In contrast, ceramide synthetases (CerS) regulate the selective synthesis of specific Cer species, offering a more dynamic and functionally relevant target for assessing disease activity. Evaluating CerS expression may provide deeper insights into their potential as biomarkers in MS.
Objectives/Aims: To investigate the association between mRNA expression levels of CerS2 and CerS6 in plasma and blood leukocytes with imaging outcomes, including the number of lesions and volumetric analysis, in patients with MS.
Methods: This cross-sectional study evaluated mRNA expression levels of CerS2 and CerS6 in plasma and peripheral blood leukocytes from patients with multiple sclerosis (MS). Imaging data included the number of T2/FLAIR and T1 gadolinium-enhancing lesions, as well as volumetric measurements obtained with SIENA and SPM12, including overall parenchymal fraction (OPF), gray matter parenchymal fraction (GMPF),

lesion volume (LV), along with the automated lesion count (ALC). Associations between CerS2 and CerS6 mRNA expression and clinical variables were evaluated using simple linear regression and Spearman rank-order correlation coefficients, as appropriate. Data management and statistical analyses were performed using REDCap and STATA version 17.0, respectively.

Results: A total of 34 patients (mean age 40± 10.40; 76.5% female) were included. No significant associations were identified between CerS2 or CerS6 mRNA expression and any radiological variable. Specifically, neither CerS2 nor CerS6 expression correlated with the number of T2/FLAIR lesions ($p = 0.71$ and $p = 0.76$), T1 gadolinium-enhancing lesions ($p = 0.95$ and $p = 0.07$), OPF ($p = 0.487$ and $p = 0.76$), GMPF ($p = 0.38$ and $p = 0.44$), LV ($p = 0.74$ and $p = 0.45$), or ALC ($p = 0.65$ and $p = 0.88$), respectively.

Conclusion: In this exploratory analysis, CerS2 and CerS6 mRNA expression levels were not associated with imaging outcomes in MS. While these preliminary findings do not support their utility as cross-sectional biomarkers, they highlight the need for longitudinal studies to further assess their potential role in tracking the course of MS over time.

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P1552
Cytokine Phenotype of Patients with Multiple Sclerosis: Towards Precision Medicine

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Introduction: This study stems from the increasingly essential need to optimize the diagnostic process and the early prognostic assessment of patients with Multiple Sclerosis (MS) to initiate, as quickly as possible, the most suitable Disease-Modifying Therapy (DMT) for a specific patient.

Objectives/Aims: The aim of this study is to describe a 'typical' cytokine profile characteristic of patients with MS and to predict the disease outcome on the base of cerebrospinal fluid (CSF) and serum cytokine levels, in order to achieve better patient stratification at the time of diagnosis.

Methods: We conduced a single-center retrospective study of 112 subjects, including 17 controls (subjects with gliotic lesions) and 95 diagnosed with MS between December 2021 and August 2024. Data relating to both CSF and serum cytokines were collected at the time of diagnosis, along with data concerning relapse rate between diagnosis and 6 month follow up after the initiation of DMT.

Results: Between 95 MS patients, 13 were diagnosed as Primary Progressive MS (PP-MS) and 82 as Relapsing Remitting MS (RR-MS). In RR-MS average CSF values of CXCL10, CXCL13, INFγ, IL10 and TNFα were significantly higher than in controls (respectively 352.01 pg/mL vs 163.27 pg/mL, 34.88 pg/mL vs 3.85 pg/mL, 0.21 pg/mL vs 0.04 pg/mL, 1.15 pg/mL vs 0.42 pg/mL, 0.9 pg/mL vs 0.51 pg/mL; p-values <0.001). In PP-MS CSF values of IL10 and TNFα were higher than in controls (respectively 1.05 pg/mL vs 0.42 pg/mL, 0.9 pg/mL vs 0.51 pg/mL; p-values <0.001). CSF ProADM levels were higher in PP-MS respect as RR-MS (0.79±0.16 pg/mL vs 0.67±0.14 pg/mL; p-value=0.03). Higher CSF IL8 levels were found in MS patients who had a relapse at 6 month follow up as compared to whom didn't have a relapse (60.64±26.9 pg/mL vs 43.18±14.45 pg/mL; p-value=0.03).

Conclusion: One of the study's major strengths lies in the high homogeneity in patient stratification, as cytokine analysis was consistently performed at the time of disease diagnosis and during a stable disease state (at least one month after symptom onset). We have found a CSF cytokine pattern that differs significantly between MS patient and healthy control, and our results are largely consistent with the data available in the literature. Moreover, we found that ProADM levels can aid in the differential diagnosis between RR-MS and PP-MS in more challenging cases. Another interesting aspect is that IL8 CSF values, measured out at diagnosis, can help in the prediction of an early relapse.

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P1553
Unraveling the associations between brain metabolic biomarkers and disease disablity in multiple sclerosis

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Introduction: High-resolution, whole-brain 3D proton MRSI (^{1}H-MRSI) presents a compelling non-invasive method for metabolic brain imaging, providing new insight to depict and investigate MS biology.
Objectives/Aims: To explore the association whole brain metabolic biomarkers and disease severity based on Expanded Disability Status Scale (EDSS) scores.
Methods: A total of 82 individuals diagnosed with multiple sclerosis (MS) were enrolled from the HS-MUSIC (HuaShan Multiple Sclerosis Imaging Cohort) study conducted at Huashan Hospital Fudan University, Shanghai. We stratified patients into three groups: with no disability (EDSS 0–1), with mild disability (EDSS 1.5–3), and with moderate to severe disability (EDSS $\geqslant$3.5). Employing high-resolution three-dimensional magnetic resonance spectroscopic imaging (3D ^{1}H-MRSI), we concurrently quantified N-acetylaspartate (NAA) as a marker of neuronal integrity and myo-inositol (mI) as an indicator of gliosis. Neurometabolite concentrations, normalized to water signals, were assessed across 22 bilaterally defined anatomical brain regions of interest (ROIs), delineated using FreeSurfer software in conjunction with the ICBM-DTI-81 white matter labels atlas. Neurometabolic profiles were subsequently compared among MS subgroups to elucidate patterns associated with disease severity.
Results: Among patients with mild disability based on EDSS scores, mI concentrations were significantly elevated across nearly all normal-appearing white matter subregions, with exception of the superior longitudinal fasciculus and the cingulum hippocampus. Similar elevations were observed in cortical gray matter subregions, including the insula, cingulate, and frontal cortex, as well as in deep gray matter structures such as the thalamus and caudate nucleus (all Ps < 0.05). The cingulum exhibited markedly increased mI levels in individuals with moderate to severe disability compared to those without disability. Furthermore, patients with moderate to severe disability demonstrated persistent reductions in NAA levels within the cingulate and frontal cortices relative to both the no-disability and mild-disability groups, and more pronounced declines in the thalamus and caudate compared to patients with EDSS scores of 0–1 (all Ps < 0.05).
Conclusion: High-resolution, whole-brain 3D proton MRSI (^{1}H-MRSI) presents a compelling non-invasive modality for metabolic brain imaging, facilitating the identification of potential biomarkers indicative of disease severity in patients with multiple sclerosis.

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P1554
Behaviour of MOG-IgG and AQP4-IgG Serostatus in Patients with NMOSD and MOGAD

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Introduction: Serostatus in Aquaporin-4 (AQP4)-IgG and Myelin oligodendrocyte glycoprotein (MOG)-IgG remains a novel but poorly understood aspect. The factors influencing serostatus stability or change are not yet elucidated, and its application in clinical practice for patients with Neuromyelitis Optic Spectrum Disorder (NMOSD) and MOG Associated Disease (MOGAD) is still under investigation.
Objectives/Aims: To determine how many patients present a serostatus change, how many of these changes are sustained across follow-up tests, and how many patients with initially stable serostatus remain consistent throughout follow-up tests. Additionally, to explore clinical factors that may influence seroconversion or seroreversion.
Methods: We conducted a retrospective observational study based on 140 clinical records from patients with NMOSD and MOGAD, at Hospital Ramos Mejía from 2000 to 2024. Patients with two or more AQP4-IgG and/or MOG-IgG tests were included. Serostatus was classified according to the second test as stable (positive or negative), or changed (seroconverted or seroreverted). For stable serostatus and additional follow-up tests with remaining results were classified as consistently stable. A sustainably changed serostatus was defined as a change followed by a subsequent test showing the same result. All the changed serostatus were analysed in relation to the antibody assay used, time since the last clinical attack and whether the patient was receiving immunosuppressive therapy. Additional variables included sex, disease duration and initial clinical phenotype.
Results: We included 45 patients with at least 2 AQP4-IgG and/or MOG-IgG test, 30 patients with NMOSD AQP4+, 8 patients MOGAD and 7 double-negative NMOSD. We found 22 stable serostatus, 11 positive including 1 MOGAD, and 11 negative; 5 consistently stable, 2 positive and 3 negative. 23 changed serostatus, 11 seroconverted and 12 seroreverted; 10 sustainably changed serostatus, 2 positive and 8 negative (one of them was seroconverted in follow-up test). We identified 31 cases with serostatus changes: 23.5% of seroconversions, 12 cases were associated with an improvement in the antibody assay used ($p = 0.0002$); and 22% of seroreversions, among which 5 cases were patients with MOGAD and 2 cases were explained by impaired assay performance. A statistically significant association was found between seroreversion and testing conducted more than six months after the last clinical attack ($p=0.02$). No significant associations were found with immunosuppressive therapy, sex, disease duration or initial clinical phenotype.
Conclusion: Serostatus change is not uncommon in NMOSD and MOGAD patients; however, repeat antibody testing is not routinely performed. While access to improved assay methods is

not always feasible, follow-up testing offers a valuable opportunity to detect seroconversion and to support diagnosis in initially seronegative patients.

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P1555
MRI and fluid biomarkers of clinical cognitive decline in early stages of relapsing-remitting multiple sclerosis: a 3-year prospective study

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Introduction: While radiologic surrogates of cognitive dysfunction in multiple sclerosis (MS) have been extensively explored, it remains crucial to combine MRI and fluid biomarkers to achieve a comprehensive understanding of the mechanisms underlying cognitive decline in MS.
Objectives/Aims: This longitudinal study investigated the association between radiological and biochemical variables in predicting noteworthy cognitive deterioration in a cohort of patients with relapsing-remitting MS (RRMS) over a three-year period.
Methods: A longitudinal assessment was conducted on 35 recently diagnosed RRMS patients and 22 healthy controls (HC). All participants underwent a comprehensive neuropsychological assessment, classifying 14 RRMS patients as cognitively stable (CS) and 21 as cognitively declining (CD). MRI scans were used to quantify lesion volumes, gray matter fraction (GMF), and cortical thickness (CT). Blood samples were collected to measure serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (sGFAP) levels using the single molecule array (SIMOA) platform. Annualized percentage changes between follow-up and baseline measures were calculated. A general linear model assessed the effects of group and time, and regression models were employed to examine predictors of cognitive decline.
Results: At baseline, CS patients did not show differences in any variable compared to controls, whereas CD patients exhibited lower GMF, reduced CT, and elevated sNFL levels than HC. Compared to CS, CD patients had higher baseline sNFL levels and higher annual rates of CT reduction. The binary logistic regression model retained baseline sNFL levels as the only significant predictor of future cognitive decline in the RRMS group ($R2 = 0.23$, $OR = 1.585$).
Conclusion: Elevated neuroaxonal damage and accelerated cortical thinning during early MS stages are associated with an increased risk of developing cognitive decline. Therefore, sNfL and CT may serve as early, non-invasive biomarkers for predicting future cognitive worsening in MS.

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P1556
Neurologists' perspectives on serum neurofilament light chain-guided therapeutic decisions in PIRA

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Introduction: In multiple sclerosis (MS), progression independent of relapse activity (PIRA) drives irreversible disability through neuroaxonal injury. Serum neurofilament light chain (sNfL) levels help identify underlying inflammatory activity in patients with PIRA, prompting treatment escalation.
Objectives/Aims: The objective of this study was to assess neurologists' attitudes toward sNfL testing in PIRA management.
Methods: A nationwide web-based study was conducted among neurologists involved in MS care in Spain. Participants reviewed a simulated case or vignette of a 36-year-old woman with relapsing-remitting MS treated with dimethyl fumarate, who had no relapses but an Expanded Disability Status Scale (EDSS) score increase from 2 to 3 over one year, suggesting PIRA. Her sNfL level was 13 pg/mL without confounding factors. Neurologists chose between three options: continuing current treatment, switching to glatiramer acetate, or escalating to high-efficacy therapy. For those who initially opted to maintain or adjust treatment to a less intensive approach, a reassessment was conducted at 12 months. This reassessment revealed that the patient's EDSS had increased to 4, with six new T2 lesions and an sNfL of 15 pg/mL. Bivariate analyses were used to identify factors influencing the neurologists' decision-making process.
Results: Among 116 neurologists (mean age [SD]: 41.9 [10.1] years; 53.4% male; mean practice experience: 16.0 [9.2] years), 66.4% considered sNfL testing useful for treatment decisions in this case. Initially, 36.2% of participants chose not to escalate treatment; by the second assessment, only 16.7% maintained this approach. Those who consistently opted for less intensive treatment strategies were more empathetic (p=0.012) and reported workplace restrictions on expressing concerns (p=0.014). Conversely, those who favored high-efficacy therapy from the start based on sNfL levels were more open to innovation (p=0.025) but reported feeling overwhelmed at work (p=0.024).
Conclusion: While most neurologists found sNfL testing useful, treatment decisions were associated with factors such as empathy, openness to innovation, and workplace constraints. Addressing these factors through tailored educational initiatives may optimize PIRA management.

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P1557
Plasma miRNA Profiling of Pregnancy-associated Immunomodulation in Multiple Sclerosis

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Introduction: In MS patients, pregnancy leads to a decreased relapse rate during the third trimester, possibly due to the transient immunotolerance induced during pregnancy, followed by a temporary worsening of the disease postpartum. MicroRNAs (miRNAs) are epigenetic modulators of gene expression and have been proposed as mediators of immune regulation and biomarker candidates for MS.
Objectives/Aims: To investigate the miRNA dynamics in patients with relapsing-remitting MS (RRMS) and healthy controls (HC) before, during and after pregnancy to identify miRNAs associated with improvement and worsening of the disease.
Methods: Next generation sequencing (NGS) was utilized to broadly assess miRNA expression dynamics in plasma samples of pregnant women with RRMS (n=8) and pregnant HC (n=8) in the first trimester, third trimester, and postpartum. Selected miRNAs were quantified by quantitative polymerase chain reaction (qPCR) in the full cohort, consisting of MS (n=27) and HC (n=14) sampled before, during and after pregnancy, followed by pathway enrichment analysis of differentially expressed miRNAs.
Results: Longitudinal analysis showed an overall upregulation of mainly placenta-associated miRNAs in the third trimester

compared to the first trimester and postpartum in both RRMS and HC. These dynamic changes were, however, more pronounced in MS patients than in HC, since a set of 17 miRNAs was found to be upregulated during pregnancy but to also have higher expression in MS patients than in HC in the second and third trimester. Pathway analysis of their mRNAs targets revealed association with immunomodulatory pathways.
Conclusion: Pregnancy strongly affects longitudinal miRNA expression profiles irrespective of the disease status, but MS-specific dynamics could be observed. Further studies may reveal whether miRNAs play a mechanistic role in the improvement of MS during pregnancy, and if so, could be used as biomarkers for disease improvement and worsening in MS in general.

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P1558
Advances in the Understanding and Measurement of a Predictive Autoantibody MS Signature Motif related to the Epstein Barr Virus

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Introduction: IgG serum and CSF autoantibodies directed to a motif P-(SA)-x-(SGA)-R-(SN)-(LRKH) found in hundreds of human and pathogen proteins, appears 5-6 years before symptom onset in approximately 10% of clinical diagnoses of MS. Understanding the predictive and specific nature of these autoantibodies may allow for earlier diagnosis and treatment, and inform mechanisms driving disease.
Objectives/Aims: To discover a monoclonal antibody (mAb) directed to the MS Signature motif from MS memory B cells, define a consensus peptide antigen, develop a diagnostic serological assay, and identify underlying candidate tolerance breaking antigens in Epstein-Barr virus (EBV) and the CNS.
Methods: Anti-IgG and three different peptide tetramers were used on the Beacon® Optofluidic system to identify an activated memory B cell secreting a broadly cross-reactive mAb to the MS Signature epitope. Technologies for antigen discovery, validation and assays included: Phage Immunoprecipitation Sequencing (PhIP-Seq), Luminex xMAP®, Biolayer Interferometry (BLI), human protein microarrays, transiently transfected human embryonic kidney cells (HEK293) and immunofluorescence staining of mouse brain neuronal cell cultures.
Results: A mAb to the MS Signature motif was cloned from an MS patient's memory B cells, binding a variety of peptides containing the motif with affinities from 2-25nM. Consensus peptides defined by alanine scanning PhIP-Seq were used to develop a diagnostic assay with a sensitivity equivalent to 0.5ng/mL mAb, a precision of $<11\%$ and a positivity rate of 12.6% among a cohort of n=380 MS patients (n=91 healthy and n=49 irrelevant neurological disease sera were negative). Suspected tolerance-breaking antigens containing the motif are the EBV envelope glycoprotein (gM) and tegument protein BRRF2. Human proteome PhIP-Seq and microarrays identified mAb binding to CNS synaptic proteins RIMS2, ZNRF2 and RTN2B. MS Signature mAb binding was validated against recombinant proteins on BLI and over-expression in HEK293 cells. Immunocytochemistry with mixed neuronal cells localized the majority of MS Signature mAb to the cytoskeleton with a minor fraction at the plasma membrane.
Conclusion: A mAb to the predictive MS Signature epitope was used to develop a precise, specific and sensitive diagnostic assay. Proteomic evidence suggests the common motif allows for a rare, EBV-mediated break in B cell tolerance to synaptic CNS proteins. The relationship of the mAb, EBV and CNS antigens to MS is being further investigated.

Disclosure of interest: Krista McCutcheon, Aaron Bodansky, Thomas Ngo, Jing Zhou, Daniela Moura, Iris Tilton, James Asaki, Greer Waldrop, Colette Caspar, Debanjana Chakravarty, Kelsey Zorn, Asritha Tubati, Stacy Caillier, Richard A. Cuneo, Jorge Oksenberg, Samuel J. Pleasure (nothing to disclose). Bruce A.C. Cree: has received personal compensation for consulting from Alexion, Alumis, Avotres, Biogen, Boston Pharma, EMD Serono, Hexal/Sandoz, Horizon, Immunic AG, Kyverna, Neuron23, Novartis, Sanofi, Siemens and TG Therapeutics; received research support from Genentech and Kyverna and is on an advisory board for Autobahn. Stephen L. Hauser: currently serves on the scientific advisory boards of Accure, Alector, Annexon, Hinge Bio; previously consulted for BD, Gilead, Moderna, NGM Bio, Nurix Therapeutics, Pheno Therapeutics; previously served on the Board of Directors of

Neurona and currently serves as an advisor. Has received non-financial support (travel reimbursement and writing support for anti-CD20-therapy-related meetings and presentations) from F. Hoffmann-La Roche and Novartis AG; and has received no personal compensation from any entity that sells or tests therapeutics for MS. Sasha Gupta: has received IIT funding from Kyverna Therapeutics and consulting funds from Legend, IGI, and Antheum. Joseph J. Sabatino Jr: has received research funding support from Novartis and Roche/Genentech and honoraria from Roche/Genentech, IgM Biosciences, and TG Therapeutics. Joseph L. DeRisi: is a founder and consultant of Delve Bio, Inc., and a consultant for PHC Global, Inc. Michael R. Wilson: has received research grant funding from Roche/Genentech, Novartis and Kyverna Therapeutics.

P1559
Baseline sNfL levels and MRI Markers of subclinical disease activity in a real-world MS cohort

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Introduction: It is a matter of debate how to interpret elevated sNfL levels in clinical routine and their association to established MRI metrics of subclinical disease activity.
Objectives/Aims: To assess whether patients with elevated age-corrected baseline sNfL z-scores show higher new and enlarging lesion volume (nT2LV) than patients with normal sNfL z-scores during annual routine clinical MRI monitoring.
Methods: We retrospectively analyzed MS patients from a single outpatient clinic. Blood samples and magnetic resonance imaging (MRI) were obtained during standardized routine clinical visits. Healthy controls were studied as a reference. All sNfL levels were analyzed using the SIEMENS Atellica platform. MRIs were evaluated using MSPie Prototype to assess nT2LV. Age-normative sNfL z-scores were modelled from controls. Patient sNfL was defined as normal (sNfL z-scores <2), and elevated (sNfL z-scores $\geqslant 2$). Group differences in nT2LV were investigated for sNfL z-score groups using Wilcoxon rank sum test.
Results: A cohort of n=277 MS patients (mean age 43 $\pm$12) and n=186 controls (mean age 43$\pm$ 11) were included in this analysis. Most patients had normal sNfL z-scores (92%), while 8% had elevated sNfL z-scores. Patients with elevated sNfL did not show significantly higher nT2LV compared to the patients with normal NfL z-scores during annual follow-up (mean $nT2LV_{sNfL\ elevated}$= 0.17 $\pm$ 0.27 ml vs. mean $nT2LV_{sNfL\ normal}$= 0.16 $\pm$ 0.88 ml, p-value= 0.076).
Conclusion: The number of patients with elevated sNfL z-scores was low in our cohort with standardized annual MRI monitoring. Patients with elevated baseline sNfL z-score showed similar nT2LV development like sNfL normal patients.

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P1560
Development of AHR-network depended potential biomarker in patients with neuromyelitis optica spectrum disorders

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Introduction: Neuromyelitis optica spectrum disorders (NMOSD) comprising anti-Aquaporin-4 (AQP4) antibody-positive (seropositive) and anti-AQP4 antibody-negative (seronegative) subgroups are severe autoimmune diseases characterized by recurrent central inflammation and high risk of persistent disability. The activity of the ligand-activated transcription factor aryl hydrocarbon receptor (AHR) is a key immune regulator correlating with disease course not only in MS, but presumably also in NMOSD. Due to the diagnostic uncertainty in seronegative NMOSD and the clinical need for monitoring tools in seropositive patients, there is a pressing demand for novel biomarkers.
Objectives/Aims: Using a protein-based, exploratory approach, we aimed to identify novel biomarkers relevant for diagnosis, prognosis and therapeutic monitoring in NMOSD. Additionally, we explored potential interactions between these proteins and AHR within the gut-brain-axis to better understand their role in disease activity and progression.
Methods: Following a systematic literature review to identify candidate proteins, we employed the Olink Target 96 Proximity Extension Assay to quantify their levels. We conducted both cross-sectional and longitudinal analyses using serum samples from 100 seropositive and 12 seronegative NMOSD patients, alongside 14 MS patients and 22 healthy controls.
Results: Differentiating seronegative NMOSD from both MS and seropositive NMOSD, interferon-gamma (IFN-γ) and lysosome-associated membrane glycoprotein 3 (LAMP3) showed significantly elevated serum levels compared to controls, MS

patients, and seropositive NMOSD patients. Similarly, CD83 antigen, a molecule involved in lymphocyte activation, was significantly increased in the seronegative subgroup compared to the seropositive patients.
Elevated interleukin-6 levels in NMOSD compared to MS and controls aligned with previous reports. CXCL13 was found to be elevated in proximity to a relapse, in contrast to stable disease phases. Besides, the protease MMP12 was found to be decreased during relapses compared to other stages and controls.
Conclusion: Our findings identify converging as well as distinct protein signatures with potential to improve disease monitoring, prognostic assessment, and diagnostic accuracy in conditions that often present with overlapping clinical features. Certain proteins, including IFN-γ, LAMP3, and CD83, suggest a broad immunological activity in seronegative NMOSD. CXCL13, a B-cell–associated chemokine, emerges as a promising biomarker for anticipating relapses.

Disclosure of interest: Ammon: nothing to disclose

P1561
Defining Reference Values for the Clinical Utility of Cerebrospinal Fluid Biomarkers

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Introduction: Reliable reference values ensure consistency and reliability in research findings, and are essential for supporting diagnosis and disease monitoring. Recently, neurofilament light (NfL) reference values in cerebrospinal fluid (CSF) and serum have been widely adopted by multiple sclerosis (MS) clinics to guide diagnosis, assess disease activity, and evaluate treatment response. However, a need for additional reliable and easily applicable biomarker use is evident.
Objectives/Aims: To establish reference values for MS-relevant biomarkers in CSF, that can be used to facilitate early diagnosis and monitoring of MS disease progression.
Methods: CSF samples from 100 symptomatic controls (SC), aged 19-67 years, selected according to Teunissen et al. (2013), were analysed for biomarkers using enzyme-linked immunosorbent assays, electro-chemiluminescence immunoassays, and a single molecule array. All calibration curves complied with ICH M10 criteria. Samples and inter-plate controls were run in duplicates in all but one assay. Lower limit of quantification (LLOQ) was defined as the lowest standard with a CV<25%, upper limit of quantification (ULOQ) as the highest standard with a CV<20%. CV<25% was accepted for samples within LLOQ and the second calibrator standard, and CV<20% for the remaining calibrator range. Values <LLOQ were assigned ½·LLOQ. Values >ULOQ were truncated to ULOQ. Data analysis was performed in Prism. Outliers (Q=0.5) were identified and excluded. Normality and lognormality tests, linear regression, and Runs test of residuals ensured data linearity. Reference values or age-specific equations were calculated based on the upper bound of the 95% confidence interval.
Results: Reference values, defined as the upper bound of the 95% confidence interval in SC, were established for age-independent CSF biomarkers; chitinase 1 (CHIT1), C-X-C motif chemokine ligand 13 (CXCL13), interleukin-12 subunit beta (IL-12) and vascular endothelial growth factor A (VEGF-A). Equations for age-adjusted reference values were determined for the age-dependent biomarkers; soluble B-cell maturation antigen (sBCMA), sCD27, glial fibrillary acidic protein (GFAP), myelin basic protein (MBP), interleukin 8 (IL-8) and interleukin 15 (IL-15).
Conclusion: Establishing reference values is a critical step in validating new biomarkers. The reference values established in this study are based on a solid control material, providing a reliable standard for easily assessing the clinical utility of the biomarkers in MS and related diseases.

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P1562
The Treasure of Biobanks: How CRESM Biobank Serves Multiple Sclerosis Research

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Introduction: One of the main challenges in clinical research, including in multiple sclerosis (MS) field, is poor data reproducibility and limited translation of research findings into clinical practice. This is often due to insufficient rigor in sample collection, lack of validated methods and limited data sharing.
Research biobanks play a key role in enabling high-quality scientific studies. They are legal entities established within public/

private institutions to support the scientific community and broader society, while respecting participants' rights and ethical principles. Biobanks ensure the systematic collection, storage and regulated access to biospecimens and associated data, according to informed consent and established quality standards.
The Regional Reference Multiple Sclerosis Center Biobank (BB-CRESM, San Luigi Gonzaga University Hospital, Orbassano, Italy) is the first institutional biobank in Italy dedicated to MS. It operates under a defined governance structure and a regulatory framework. It is part of BBMRI-ERIC, the European infrastructure for biobanking
Objectives/Aims: To highlight the role of biobanking to support high-quality research in MS
Methods: The institutional establishment of BB-CRESM within the University Hospital San Luigi Gonzaga following the approval of the required legal and ethical documentation, along with the definition of governance and the implementation/update of policies and procedures for the management and access to samples/data are fundamental to an effective biobanking.
Currently, BB-CRESM includes around 3200 MS and neurological patients and 250 healthy participants. Approximately 165000 aliquots of various biospecimens (serum, plasma, RNA, blood, cerebrospinal fluid) and associated data are available for access. These are pseudonymized and managed through a biobanking system, according to GDPR and national privacy laws. Quality is ensured through strict operating procedures, quality controls and continuous staff training.
Results: The access to samples and associated data represents a primary outcome in biobanking. Since 2020, BB-CRESM has provided over 1000 samples and dataset for MS research projects conducted by several institutions including University San Raffaele (Rome), University of Nottingham, ISS (Rome), IRCCS Besta (Milan), University of Turin, University of Basel, University of Naple, in addition to supporting CRESM's own research. These contributions have advanced the understanding of disease mechanisms and/or the identification of diagnostic, prognostic, or treatment-response biomarkers
Conclusion: BB-CRESM plays a crucial public role in advancing MS research, promoting transparency, quality, and collaboration, and ultimately contributing to the integration of research findings into clinical practice

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P1563
Evaluation of Patient-Reported Progression in Multiple Sclerosis: Correlations with MRI, OCT, and Fluid Biomarkers

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Introduction: MS is a chronic neuroinflammatory disease, and assessing its progression is crucial for patient management. Traditional tools like the Expanded Disability Status Scale (EDSS) and MRI may not fully capture disease activity, especially in progressive MS (PMS) forms. Novel biomarkers such as GFAP, NFL, and suPAR offer potential alternatives to monitor disease progression, but their correlation with self-reported progression remains unclear.
Objectives/Aims: This study evaluates the relationship between self-reported disease progression in Multiple Sclerosis (MS) and various biomarkers, including Glial fibrillary acidic protein (GFAP), neurofilament light chain (NFL), soluble urokinase plasminogen activator receptor (suPAR), optical coherence tomography (OCT) results, and MRI findings.
Methods: A total of 75 MS patients (all subtypes) were enrolled, with self-reported progression assessed across various symptoms. OCT scans, MRI imaging, and blood biomarkers (GFAP, NFL, suPAR) were collected and analyzed. Statistical analysis was performed using STATA-18, with group comparisons conducted using non-parametric tests.
Results: The cohort demonstrated significant differences in GFAP and NFL levels between patients reporting disease progression and those who did not. The median GFAP levels were significantly higher in the progression group (93.4 pg/ml vs. 67.96 pg/ml, p=0.0126), as were NFL levels (9.86 pg/ml vs. 7.19 pg/ml, p=0.0211). However, no significant difference was found for suPAR levels (2.99 µg/L vs. 2.88 µg/L, p=0.5606). MRI findings indicated a greater number of plaques in the progression group, and OCT revealed thinning of the retinal nerve fiber layer in those with reported progression.
Conclusion: GFAP and NFL are promising biomarkers for identifying MS patients experiencing disease progression, particularly in relation to self-reported symptoms. SuPAR, while not showing significant differences, warrants further exploration as a potential inflammatory biomarker. These findings suggest that integrating biomarkers, along with OCT and MRI, could provide a more comprehensive approach to tracking MS progression, especially in progressive subtypes.

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P1564
Cerebrospinal fluid NfL, CHIT1, sCD27, and sBCMA as predictors of inflammatory disease activity and PIRA in newly diagnosed patients with multiple sclerosis

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Introduction: Improved prediction of future disease outcomes could help guide initial treatment choices and inform newly diagnosed patients with multiple sclerosis (MS) about their prognosis. Fluid biomarkers have been linked to prognosis, but the added predictive value of these biomarkers remain unclear.
Objectives/Aims: We sought to investigate neurofilament light (NfL), chitinase 1 (CHIT1), soluble B cell maturation antigen (sBCMA) and soluble CD27 (sCD27) as predictors of inflammatory disease activity and progression independent of relapse activity (PIRA) in newly diagnosed patients, and evaluate the prognostic potential compared to demographic and clinical predictors.
Methods: We conducted a cohort study, included newly diagnosed MS patients starting teriflunomide, and analysed cerebrospinal fluid samples for NfL, CHIT1, sCD27, and sBCMA. We examined associations with disease activity (relapses, T2 and contrast-enhancing lesions), relapses, and PIRA, and compared the predictive accuracy of models with age, sex, Expanded Disability Status Scale, and T2 lesion load against models with added NfL or CHIT1.
Results: We included 154 patients (median time since lumbar puncture and onset [IQR]: 0.2 years [0.1-0.4] and 0.7 years [0.4-2.4]). Kaplan-Meier analysis showed that patients with age-corrected NfL levels above the median had a higher risk for disease activity, but not for relapses or PIRA. We observed no differences in Kaplan-Meier curves for CHIT1, sCD27, or sBCMA. Adding NfL did not improve predictive accuracy for 2-year risk of disease activity or relapse, and CHIT1 did not improve 5-year risk predictions for PIRA.
Conclusion: We found NfL associated with disease activity, consistent with previous studies. However, adding NfL to models for 2-year disease activity or relapse risk, or CHIT1 for 5-year PIRA risk, did not enhance predictive accuracy. This suggests that even though an association can be found in univariable or multivariable analyses, it may be explained by existing factors or be too weak to improve predictions.

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P1565
Effect of long-term Frozen Storage on Stability of Kappa Free Light Chain Index

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Introduction: Kappa free light chain (κ-FLC) index is a biomarker to assess intrathecal immunoglobulin synthesis supporting the diagnosis of inflammatory neurological diseases. The impact of frozen storage duration on the κ-FLC index is not known.
Objectives/Aims: To investigate whether frozen storage duration influences κ-FLC index.
Methods: CSF and serum samples of patients with multiple sclerosis collected for routine diagnostic purposes had been stored at -20°C. κ-FLC and albumin concentrations were measured at two different timepoints, i.e. before and after storage. The κ-FLC index was calculated as (CSF κ-FLC/ serum κ-FLC)/ (CSF albumin/ serum albumin).
Results: A total of 70 patients were included showing median CSF κ-FLC concentration of 0.25 (25^{th}-75^{th} percentile: 0.12-0.43) mg/dl, serum κ-FLC concentration of 1.05 (0.86-1.34) mg/dl, CSF albumin concentration of 17.7 (14.6-26.1) mg/dl and serum albumin concentration of 4230 (3898-4488) mg/dl. The κ-FLC index was 44 (25-108). With increasing frozen

storage duration, the absolute concentrations of CSF κ-FLC, serum κ-FLC, CSF albumin and serum albumin decreased, while the κ-FLC index remained stable. The observed changes in absolute concentrations evened out by using CSF/ serum ratios of κ-FLC and albumin when calculating the κ-FLC index.
Conclusion: Frozen storage duration has no relevant impact on κ-FLC index.

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P1566
Is Vitamin D a Key to Combating Oxidative Stress in Relapsing-Remitting Multiple Sclerosis?

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Introduction: Previous studies indicate that vitamin D (VitD) may play a role in reducing oxidative stress (OS) in patients with multiple sclerosis (MS).
Objectives/Aims: This research aimed to evaluate the effects of different VitD supplementation regimens on OS and to assess the prevalence and severity of VitD deficiency in individuals with relapsing-remitting MS (RRMS).
Methods: A total of 72 patients were enrolled in the study, with a 6-month supplementation protocol consisting of two dosing strategies: a high-dose group (HD) receiving 2,000 IU/day and a low-dose group (LD) receiving 15,960 IU/month. At follow-up, 52 patients (23 in a HD group and 29 in the LD group) were assessed for the impact on OS biomarkers. Statistical analysis was conducted to compare various parameters.
Results: The majority of participants were female (63.46%). The median ages were 39.5 [34.5–49.8] years for the HD group and 47 [40.0–55.0] years for the LD group. Significant differences were noted in age ($p = 0.028$), body weight ($p = 0.014$), and height ($p = 0.001$) between the groups; however, the generalized estimating equations (GEE) model showed no significant interactions of age and BMI with the assessed parameters. The median concentration of 25(OH)D [ng/mL] increased from 23.023 [15.578–25.76] in the HD group and 28.318 [20.644–32.232] in the LD group to 29.819 [24.937–38.064] and 30.837 [25.382–36.789], respectively ($p < 0.01$), with a notably greater increase in the HD group ($p = 0.01$). Initially, 71.2% of patients exhibited hypovitaminosis D, and at follow-up, 46.2% had serum VitD levels remaining below 30.0 ng/mL. A significant rise in the levels of IL-4, IL-6, IL-17A, IL-22, IL-23, and TNF-α [pg/mL] and a drop in IL-10 levels were noted throughout the study ($p < 0.01$). A significant positive correlation was found between serum levels of 25(OH)D and sCD40L ($R = 0.33$; $p < 0.05$) and TNF-α ($R = 0.28$; $p < 0.05$), while a significant negative correlation was observed between 25(OH)D and IL-23 ($R = -0.32$; $p < 0.01$) at baseline.
Conclusion: The data suggests that VitD supplementation may not be adequate to restore oxidative balance in RRMS patients, highlighting the necessity for further investigation into optimal dosing strategies.

Disclosure of interest: Martyna Lis, Natalia Niedziela, Robert Kwinta, Monika Adamczyk-Sowa: nothing to disclose.

P1567
Optimizing Immune Response: Vitamin D supplementation and Inflammation in Relapsing-Remitting Multiple Sclerosis

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Introduction: Emerging evidence suggests that vitamin D (VitD) supplementation may play a significant role in modulating inflammation in individuals diagnosed with multiple sclerosis (MS).
Objectives/Aims: This study aimed to assess the effect of varying doses of VitD on selected inflammatory markers in patients with relapsing–remitting MS (RRMS), while also evaluating the severity of vitamin D deficiency among participants.
Methods: The study included 72 patients who participated in a 6-month supplementation protocol with two different dosing approaches. The high-dose group (HD) received 2,000 IU daily, while the low-dose group (LD) was administered 15,960 IU per month. During the follow-up phase, 52 patients (23 from the HD group and 29 from the LD group) were assessed for their effects on selected inflammatory markers. Statistical analyses were conducted to compare different parameters.
Results:A median serum concentration of 25(OH)D was 24.26 nmol/L (IQR:16.99–30.39) where 53 individuals (73.6%) were classified as deficient. Differences in body weight, height, and age were observed between groups; however, a generalized estimating equation model indicated no significant interactions of age or BMI with the measured parameters. Following six months of supplementation, both groups exhibited a significant increase in serum 25(OH)D levels ($p<0.01$). Additionally, after supplementation, a significant increase in chemokine CXCL16, pentraxin 3 (PTX3), and osteoprotegerin (OPG) levels was noted ($p=0.02$, $p=0.01$, and $p<0.01$, respectively) and the increase in PTX3 and OPG was greater in the LD group ($p=0.04$ and $p=0.03$, respectively). Furthermore, a positive correlation was observed between 25(OH)D levels and PTX3 ($R=0.28$, $p<0.05$) and OPG ($R=0.28$, $p<0.05$) at baseline.
Conclusion: The findings imply that the administered doses of VitD may be insufficient for achieving significant improvements in inflammatory responses in RRMS patients, thereby highlighting the need for further investigation into optimal supplementation strategies.

Disclosure of interest: Martyna Lis, Natalia Niedziela, Robert Kwinta, Monika Adamczyk-Sowa: nothing to disclose.

P1568
Investigate potential metabolomic biomarkers for Epstein-Barr Virus (EBV) positive Relapse Remitting Multiple Sclerosis

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Introduction: Investigate potential metabolomic biomarkers for Epstein-Barr Virus (EBV) reactivated Relapse-Remitting Multiple Sclerosis (RRMS).
Objectives/Aims: EBV can invade B lymphocytes in lymph nodes and induce immune cell infiltration and inflammation in CNS causing multiple neurological disorders including encephalitis, multiple sclerosis, lymphoma, etc. The clinical manifestations and lab results of EBV+ RRMS might be difficult to diagnose without next-generation sequencing (NGS). Whereas, EBV may alter distinguished metabolic pathways of host cells, implicating potential methods for biomarker discovery to assist the diagnosis and prognosis for those patients.
Methods: Patients with EBV+ RRMS and RRMS without EBV reactivation were recruited under the ethic approvement of Southern Medical University in 2021. We totally collected cerebrospinal fluid (CSF) from patients with active EBV+ RRMS (n=15) validated by NGS and RRMS (n=6) in Nanfang Hospital from 2021 to 2023. A liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed to identify the CSF metabolomic profiles in *Novogene.lnc*. The metabolomic profile were analyzed by 2 statisticians. KEGG enrichment analysis and Ingenuity pathway analysis was performed to annotate related metabolic pathways.
Results: 164 metabolites were identified to be elevated and 115 downregulated in EBV+ RRMS. Gamma-Aminobutyric acid (GABA) (FDR-adjusted $p=0.003$) and 5-hydroxytryptamine (Serotonin, 5-HT) (FDR-adjusted $p=2.03e-06$) were significantly upregulated in patients with RRMS when EBV is activated. 5-HT was distinctively identified to be elevated in GFAPAb+ EBV+ RRMS cohort. 39 and 60 pathways were detected via KEGG enrichment analysis in the positive and negative modes. Tryptophan metabolism was identified to be altered in patients with EBV+ RRMS.
Conclusion: Metabolomic profiles may assist the evaluation and prediction of virus-associated RRMS. Serotonin and GABA might be useful to predict the development and severity of EBV+ RRMS.

Disclosure of interest: Pei Shang: nothing to disclose

P1569
Development and Validation of a High-Sensitivity serum ELISA for detection of Neurofilament Light Chain in patients with Multiple Sclerosis

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Introduction: Neurofilament light chain (NF-L) is a key biomarker for neurodegenerative diseases, including MS. UmanDiagnostics has developed a sensitive, cost-effective serum ELISA for NF-L detection that requires no specialized equipment. The assay provides an easy-to-use complement to high-throughput platforms for clinical and research use determinations of neurofilament in serum.
Objectives/Aims: This study aimed to evaluate the analytical performance of the novel assay, analyse serum NF-L

levels in MS patients, and correlate ELISA data to single-molecule array (Simoa) read-out.
Methods: The Uman serum NF-L ELISA uses a dual monoclonal antibody sandwich format optimized for
specificity and low background. Signal amplification was achieved through a proprietary enzymatic detection system, enhancing the assay's lower limit of quantification (LLoQ). Analytical performance was assessed through detection limits, linearity, variability, and parallelism. Clinical validation was performed in collaboration with two laboratories, using serum samples from MS patients. The correlation to the established Simoa NF-L assay was also evaluated.
Results: The developed ELISA demonstrated a dynamic range of 4 – 100 pg/ml with an LLoQ of 0.6 pg/ml.
Parallelism was demonstrated at 4.8% across dilutions ranging from 4x to 256x (0.30 – 19.77 pg/ml on calibrator curve). Dilution linearity was demonstrated at 83.8 – 109.7% (0.38 – 57.0 pg/ml on calibrator curve). Intra-assay and inter-assay CVs were $<5\%$, indicating high repeatability and reproducibility. Clinical validation revealed significantly higher NF-L levels in MS patients vs. controls ($p = 0.02$, $n = 78$) and between PP/SPMS and RRMS ($p = 0.0009$, $n = 75$), with higher levels as age increases (RRMS under vs. over 55 y.o. $p = 0.0243$). The assay correlated well with the Simoa method ($R^2 = 0.94$).
Conclusion: The new serum NF-L ELISA offers a cost-effective, sensitive, and reliable complement to high-throughput platforms, supporting clinical and research use in neurodegenerative disease monitoring. Further longitudinal studies will help determine its prognostic value, especially in MS.

Disclosure of interest: Maria Hörnberg: Nothing to disclose

P1570
Cerebrospinal fluid cytokines in paediatric neuroinflammatory conditions

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Introduction: Cerebrospinal fluid (CSF) cytokines may contribute to neuroinflammation across various neurological conditions.
Objectives/Aims: We evaluated the clinical utility of measuring CSF cytokines and associated phenotypes in children.
Methods: Between 2019-2024, CSF from children under 18 with suspected neuroinflammatory was analysed using the BD Biosciences cytokine bead array for interleukin-2 (IL-2), IL-4, IL-6, IL-10, interferon-alpha (IFN-α), and tumour necrosis-factor-alpha (TNF-α).
Results: 112 patients were included (median age at lumbar puncture: 6 years [IQR 3.6–11.2]; 54% male). CSF IL-6 was raised in 35/112 (31%; median 107 pg/ml, IQR 24-329). IL-6 was raised in 16/50 with acquired neuroimmune conditions (5 with myelin oligodendrocyte glycoprotein antibody-associated disease [MOGAD], 5 with seronegative demyelination, 2 with seronegative autoimmune encephalitis, 4 with febrile-infection-related epilepsy syndrome [FIRES]); 5/9 with central nervous system (CNS) infections; 9/17 with monogenic autoinflammatory syndromes (4 with hemophagocytic lymphohistiocitosis [HLH], 3 with interleukin-1 receptor-associated kinase 4 [IRAK-4] deficiency, 2 with interferonopathies); and 5/7 with cancer treatment-related neurotoxicity (5/6 with chimeric antigen receptor T-cell [CAR-T] therapy). No cytokine was elevated without IL-6; four had additional raised cytokines.
Elevated IL-6 was more frequent in acquired demyelination versus seronegative autoimmune encephalitis (10/23 versus 2/17, $p=0.04$), and within the demyelination group, IL-6 elevation was associated with higher CSF protein ($p=0.007$).
Among patients with raised CSF IL-6, serum IL-6 was elevated in 13/21 tested. No elevations were seen in MOGAD, seronegative demyelination or autoimmune encephalitis. In contrast, serum IL-6 elevations were observed in 2/3 FIRES, 1/2 CNS infections, and all cases of CAR-T neurotoxicity, HLH and IRAK-4.
Longitudinal data over a median of 34 days (IQR 14-90) showed persistent CSF IL-6 elevation in 7/16 patients (3 IRAK-4, 2 HLH, 1 tuberculous meningitis, 1 relapsing demyelination), while levels normalized in 9 (4 FIRES, 2 CAR-T, 2 non-relapsing demyelination, 1 CNS infection). Tocilizumab was used in 9 patients (3 seronegative demyelination, 3 IRAK-4, 2 CAR-T, and 1 HLH) with variable outcomes.
Conclusion: CSF IL-6 is a marker of neuroinflammation in children. While not specific, its elevation can aid in diagnosis and treatment decisions, especially in atypical cases. Clinicians should note that therapies targeting IL-6 or its receptor have limited CNS penetration unless the blood-brain barrier is disrupted.

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P1571
Preanalytical factors on CHI3L1 levels using an in-house SIMOA assay

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Introduction: Variability in preanalytical factors (i.e., sample type, processing, freeze-thaw cycles) contributes to inconsistent biomarker results across MS centers. Chitinase 3-like protein 1 (CHI3L1), a well-established prognostic biomarker, is produced both centrally and peripherally. This broader expression raises concerns about the reliability of blood-based CHI3L1 compared to cerebrospinal fluid (CSF), resulting in conflicting studies on its utility in monitoring MS progression. Furthermore, the absence of a standardized detection platform for CHI3L1 levels could contribute to these discrepancies.
Objectives/Aims: Here we aimed to assess the impact of preanalytical variables on serum CHI3L1 levels, using an *in-house* assay developed on the Single Molecule Array (SIMOA) platform.
Methods: CHI3L1 levels in serum, plasma and CSF were determined by SIMOA in samples from healthy controls (HC), and MS patients. Sample type experiments were performed with 29 MS paired plasma/serum/CSF samples. Freeze-thaw experiments were performed with 28 MS serum samples. To ensure consistency, each freeze-thaw cycle after the first was standardized to an 8-hour thaw at room temperature followed by a 16-hour freeze at −70 °C. Delayed processing time experiments were performed in serum from 20 HC whose blood sample processing (i.e., centrifuging and freezing) was delayed up to 2, 4, 6, and 24 hours. All samples for each preanalytical condition studied were analyzed together using a single reagent batch.
Results: The mean (standard deviation) concentrations of CHI3L1 along the three samples types were 31.2 (20.2) ng/ml for serum, 16.5 (11.6) ng/ml for plasma, and 100.9 (53.9) ng/ml for CSF. A significant correlation was observed between the three compartments ($r = 0.93$; $p < 0.0001$ serum vs. plasma; $r = 0.56$; $p = 0.0016$ serum vs. CSF; and $r = 0.54$; $p = 0.0026$ plasma vs. CSF). A statistically significant difference was observed in CHI3L1 levels across freeze-thaw cycles 1, 2, and 3 when compared to the fourth cycle. Likewise, statistically significant differences were found for the comparisons between the 2, 4, and 6-hour delays in sample processing compared to the 24-hour delay.
Conclusion: Our results indicate that up to three freeze-thaw cycles and a blood processing delay of 6 hours do not consistently alter CHI3L1 concentrations as measured by our *in-house* Simoa assay. Importantly, the strong correlation between blood and CSF CHI3L1 levels suggests the feasibility of using serum as a surrogate for CSF.

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P1572
Circulating MicroRNA Signatures as Potential Biomarkers for Treatment Response in Diroximel Fumarate-Treated Multiple Sclerosis Patients

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Introduction: Despite extensive research on Multiple Sclerosis(MS), reliable biomarkers for diagnosis and treatment monitoring remain elusive. miRNAs are small non-coding RNAs involved in crucial biological pathways. We hypothesize that a specific serum miRNA signature correlates with treatment efficacy.
Objectives/Aims: To identify circulating microRNAs (miRNAs) associated with treatment response in Multiple Sclerosis patients treated with Diroximel Fumarate (DRF).
Methods: We analyzed selected miRNAs identified in previous studies as showing significant results in assessing treatment effects and responses using LNA-SYBR green-based RT-PCR in 20 untreated MS patients. We compared expressions during a relapse and three months post-relapse. In a separate cohort of 20 patients, we evaluated miRNA expression at baseline and after six months of DRF treatment. Clinical and MRI data were collected over two years. We compared miRNA expressions between patients achieving NEDA 3 (No Evidence of Disease Activity) with those who did not. Ingenuity Pathway Analysis (IPA) software helped identify changes in associated pathways and functions.

Results: We validated 13 miRNAs differentiating relapse from remission ($p < 0.05$); notably, hsa-miR-484 was the most significantly decreased serum miRNA (fold change: 1.2, $p = 0.0043$). Additionally, hsa-miR-122-5p exhibited the largest change (fold change: 3, $p = 0.0061$). Three miRNAs (hsa-miR-103a-3p, hsa-miR-182-5p, hsa-miR-30e-5p) were differentially expressed post-DRF treatment. While none of the baseline miRNAs correlated with NEDA status, hsa-let-7d-3p, hsa-miR-320b, and hsa-miR-191-5p were associated with NEDA in treated patients. IPA highlighted the ID1 signaling pathway as crucial for immune response regulation in MS
Conclusion: Circulating serum miRNAs show potential as biomarkers for assessing disease activity and treatment response in MS.

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P1573
Association of Ceramide Synthetases mRNA Expression with Clinical Outcomes in Multiple Sclerosis

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Introduction: The clinical course of multiple sclerosis (MS) is highly variable, highlighting the need for reliable biomarkers of disease activity. While ceramides (Cer) play a crucial role in MS pathophysiology, studies have reported inconsistent alterations in Cer levels, limiting their utility as potential biomarkers. In contrast, ceramide synthetases (CerS) regulate the selective synthesis of specific Cer species, offering a more dynamic and functionally relevant target for assessing disease activity. Evaluating CerS expression may provide deeper insights into their potential as biomarkers in MS.
Objectives/Aims: To investigate the association between mRNA expression levels of CerS2 and CerS6 in plasma and blood leukocytes with clinical disease activity, including relapse frequency and disability progression, in patients with MS.
Methods: This cross-sectional study evaluated mRNA expression levels of CerS2 and CerS6 in plasma and peripheral blood leukocytes from patients with multiple sclerosis (MS). Clinical data included annualized relapse rate (ARR) and functional outcomes: Expanded Disability Status Scale (EDSS), Symbol Digit Modalities Test (SDMT), 9-Hole Peg Test (9-HPT), and Timed 25-Foot Walk (T25-FW). Associations between CerS2 and CerS6 mRNA expression and clinical variables were evaluated using simple linear regression and Spearman rank-order correlation coefficients, as appropriate. Data management and statistical analyses were performed using REDCap and STATA version 17.0, respectively.
Results: A total of 34 patients (mean age 40± 10.40; 76.5% female) were included. No significant associations were identified between CerS2 or CerS6 mRNA expression and any clinical variable. Specifically, neither CerS2 nor CerS6 expression correlated with ARR ($p = 0.71$ and $p = 0.65$), EDSS ($p = 0.31$ and $p = 0.22$), SDMT ($p = 0.76$ and $p = 0.72$), 9-HPT ($p = 0.79$ and $p = 0.42$), or T25-FW ($p = 0.31$ and $p = 0.68$), respectively.
Conclusion: In this exploratory analysis, CerS2 and CerS6 mRNA expression levels were not associated with relapse frequency or clinical measures of disability in MS. While these preliminary findings do not support their utility as cross-sectional biomarkers, they highlight the need for longitudinal studies to further assess their potential role in tracking the course of MS over time.

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P1574
The current use of Glial fibrillary acidic protein (GFAP) as an outcome in randomized clinical trials: a systematic review

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Introduction: Glial fibrillary acidic protein (GFAP), the main intermediate filament in astrocytes, is associated with disease progression in MS. Similarly, its potential for monitoring treatment response is increasingly recognized but unresolved.

Objectives/Aims: We aimed to systematically analyze the current use of GFAP as an outcome in RCTs including people with MS (pwMS).
Methods: We included all registered and/or published RCTs in pwMS that reported GFAP as an outcome. We systematically searched Clinicaltrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP), PubMed and Embase. For each eligible RCT, we extracted and analyzed study design characteristics, interventions, populations and GFAP effects. We summarized effect sizes as absolute mean differences (AMD). We are currently contacting trial authors to obtain missing data. Meta-analyses and meta-regressions are planned to explore the relationship between GFAP and other outcomes, such as neurofilament light chain (NfL).
Results: We identified 14 RCTs reporting GFAP as an outcome: 8 completed, 6 ongoing (including 3 scheduled for completion in 2025). The first was registered in 2012. Drugs were assessed in 8 RCTs, exercise in 6. GFAP was measured in serum in 12 RCTs (1 plasma; 2 cerebrospinal fluid). RCTs included (or planned to recruit) a median of 61 patients (IQR 50-166). Populations were all MS types (n=5), relapsing-remitting MS (n=4) and mixed subtypes (n=5). Patient-relevant primary endpoints were used in 5 RCTs (adverse events: n=4; fatigue/participation: n=1), while others used fluid, imaging and respiratory biomarkers. GFAP was a primary endpoint in 3 RCTs and a secondary in 4. Results were available for 5 RCTs (2 primary analyses; 3 secondary or post-hoc analyses using patient subsets). The AMD in GFAP levels between treatment and control arms ranged from -399 to -1.5 pg/mL (median -7.4, IQR -22 to -3.5). For data from one RCT a statistically significant decrease by 7.4 pg/mL with siponimod treatment ($p<0.0001$) versus placebo was reported.
Conclusion: GFAP is increasingly used as an outcome in randomized MS clinical trials. Although data remain limited, RCTs reporting results have shown reductions in GFAP levels due to treatment. This consistent trend raises the question of whether GFAP reductions align with other outcome measures – a focus of ongoing analyses which will be presented at the conference to inform the potential clinical utility of GFAP.

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P1575
Serum, CSF and MRI biomarkers predict contrast enhancement with gadolinium in multiple sclerosis

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Introduction: The presence of gadolinium enhancement on magnetic resonance imaging (MRI) is one of the principal criteria for diagnosis and disease activity of multiple sclerosis (MS). However, frequent use of contrast agents will cause concerns of long-term toxicity. Therefore, serum, cerebrospinal fluid, and non-invasive neuroimaging biomarkers may be served as promising parameter to assess MS activity.
Objectives/Aims: To evaluate the clinical applicability of serum, CSF and MRI biomarkers in the prediction of contrast enhancement (CE) in the MRI scans of MS patients.
Methods: Retrospective study of MS patients admitted to the Huashan Hospital named "the HS-MUSIC cohort" between year 2023 and 2024. CSF and serum samples were obtained from patients undergoing MRI 2 days before or after collection. Paired serum and CSF neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) levels were measured in parallel on ultrasensitive single molecule array (Simoa) HD-1 analyzers (Quanterix) using the Simoa Neurology 2-Plex B Advantage Kit. Serum Nfl levels were adjusted to Z-score concerning age and BMI. High-resolution 3D ^{1}H-MRSI was employed to map lactate levels as a surrogate marker of neuroinflammation.
Results: 62 Patients with confirmed MS were included from our cohort; n=28(45.2%) showed CE on MRI versus n=34(54.8%) without CE. Higher serum Nfl Z-scores ($p=0.028$) and CSF Nfl levels ($p<0.001$) were corrected with CE. Only CSF Nfl levels indicated CE on MRI, logarithmic transformed (odd ratio[OR]:21.214, 95% CI 3.71-121.21). Receiver operator characteristic analysis revealed a reasonable cut-off value for serum Nfl z-score at 2.15 (sensitivity 64.3%; specificity 82.2%) and CSF Nfl levels at 2041.74pg/ml (sensitivity 82.1%; specificity 47.5%). Elevated lactate concentrations within white matter lesions were observed in relapsing-remitting MS patients with CE lesions compared to those without CE lesions ($p = 0.004$).
Conclusion: Nfl levels are related and predictive of CE on MRI. Following further evaluation, CSF Nfl levels may help stratify the application of contrast agents for brain imaging in MS patients. High-resolution 3D ^{1}H-MRSI provides a promising tool for non-invasive metabolic imaging to characterize MS activity.

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P1576
Analysis of extracellular vesicles containing Clostridium perfringens epsilon toxin as a novel blood-based biomarker for multiple sclerosis

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Introduction: Clostridium perfringens epsilon toxin (ETX) has been proposed as an environmental trigger of multiple sclerosis (MS). Recent publications and our preliminary data demonstrate that ETX treatment induces increased extracellular vesicle (EV) secretion in cells that express the ETX receptor MAL including T-cells, CNS-endothelial cells, and myelin producing oligodendrocytes. ETX binding to MAL results in ETX oligomerization and formation of a transmembrane pore, resulting in ionic imbalance and cell death. To overcome this, we demonstrate cells remove ETX pore via EV secretion as a survival mechanism.
Objectives/Aims: The aim of this study was to determine if ETX induced EV and their molecular cargo can be used as a specific biomarker of ETX exposure in MS patients versus healthy controls (HC). We hypothesize that MS patients will have increased ETX-specific EV signature compared to HC.
Methods: We used a combination of in-vivo and in-vitro methods to study the mechanisms of ETX induced EV secretion. Circulating EV from MS patients and HC plasma were analyzed using previously established methods.
Results: We demonstrate that ETX treatment increases EV secretion both in-vivo and in-vitro and inhibition of EV biogenesis increases cell death. Interestingly, ETX induced EV contain a unique molecular cargo versus EV secreted when treated with other stimuli. Importanlty, ETX induced EV express higher levels of the ETX receptor MAL compared to other stimuli. Finally, analysis of EV isolated from patient plasma reveal increased circulating concentrations of MAL positive EV in MS patients versus HC, especially in MS patients with contrast enhancing lesions.
Conclusion: Taken together, these preliminary results indicate a possible increased exposure of MS patients to ETX versus HC, especially during active disease, and supports the hypothesis that ETX may be an environmental trigger of MS. Current studies are underway to further molecularly define this ETX specific EV signature via small RNA sequencing and compare detection in MS patients vs HC.

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P1577
Longitudinal Assessment of Serum Neurofilament Light Chain and Glial Fibrillary Acidic Protein in Patients with Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder

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Introduction: Serum neurofilament light chain (NfL) is a marker of axonal damage, with established relevance in monitoring disease activity in patients with multiple sclerosis (MS). However, in aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4-Ab NMOSD), its association with disease activity remains unclear. In contrast, glial fibrillary acidic protein (GFAP) is considered a more promising marker particularly in patients with AQP4-Ab NMOSD, as it is a primary astrocytopathy, than in MS.
Objectives/Aims: To assess the relationship between serum NfL and GFAP in patients with AQP4-Ab NMOSD.
Methods: A retrospective analysis was performed using prospectively collected longitudinal data from 32 patients between 2006 and 2023, with their serum samples stored throughout this period according to international biobanking guidelines. The Single Molecule Array platform (Simoa SR-X; Quanterix) was used to measure serum NfL and GFAP concentrations. Statistical analyses were performed using R software. Correlation between serum NfL and GFAP was assessed using repeated measures correlation (rmcorr). The relationship was further modeled using a linear mixed-effects model with a logarithmic transformation applied to both variables.
Results: A total of 380 serum samples from 32 patients (4 men, 28 women) were analyzed. The minimum number of analyzed samples per patient was 2, and the maximum was 34. The average follow-up duration was 6.8 years (range: 1–15 years). No significant correlation was found between serum NfL (mean = 13.52 pg/ml, SD = 16.45) and GFAP (mean = 480.53 pg/ml, SD = 1420.02) using repeated measures correlation ($r = 0.00005$, $p = 0.999$). In contrast, the linear mixed-effects model showed that a 1% increase in serum GFAP corresponded to an approximately 0.15% increase in serum NfL ($p < 0.0001$).

Conclusion: These findings suggest that serum GFAP may contribute to the modulation of serum NfL dynamics in patients with AQP4-Ab NMOSD. Further analyses are underway to clarify these interactions in the context of treatment and clinical disease activity.

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P1578
Long-Term Course of Serum GFAP Concentration in Patients with AQP4-Positive NMOSD

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Introduction: The rapid expansion of long-term immunotherapeutic options for relapse-prevention in aquaporin-4 IgG seropositive neuromyelitis optica spectrum disorders (AQP4+NMOSD) necessitates biomarkers for long-term monitoring of disease activity. Serum glial fibrillary acidic protein (sGFAP), a marker of astrocyte damage, is associated with disease activity in AQP4+NMOSD. However, data on the long-term course of sGFAP in AQP4+NMOSD is currently scarce.

Objectives/Aims: To characterize the long-term trajectories of sGFAP concentrations in patients with AQP4+NMOSD and to assess their value for the prediction of attacks.

Methods: 22 patients with AQP4+NMOSD were followed in a monocentric, observational, prospective study. Serum samples and clinical data were collected at least at three (median 7, IQR [7, 8]) visits within a minimum of five (median 9, IQR [7, 10]) years. sGFAP was measured using SIMOA technology. sGFAP change (ΔGFAP) was calculated as the difference between each two subsequent measurements. Linear mixed models with age and sex as covariates were performed and Cox regression analyses with time-dependent covariates and a frailty term were applied to model the risk of relapses.

Results: Eight of 22 patients experienced a total of 22 attacks during the study. Attacks during observation were not clearly associated with sGFAP (beta = -0.11, 95% CI: [-0.25, 0.03], p = 0.15), with a numerically higher median sGFAP concentration in patients without attack (117 (IQR [75.6, 172.0]) pg/mL vs. 64 (IQR [49.2, 85.1) pg/mL). ΔGFAP was substantial, but not clearly different between relapsing (median 2.0, IQR [-17.4 – 18.5] pg/ml) and non-relapsing (median 6.7, IQR [-10.1 – 33.9] pg/ml) patients (beta = -0.06, 95% CI: [−0.19,0.05], p = 0.31). Neither sGFAP concentrations (HR = 0.26, 95% CI: [0.09, 0.73], p = 0.08) nor ΔGFAP (HR = 1.64, 95% CI: [0.345, 2.81], p = 0.53) were clearly associated with the risk of attack.

Conclusion: Despite the well-recognized increase of sGFAP in acute attacks, the applicability of single sGFAP measurements for disease monitoring in AQP4+NMOSD may be limited due to relevant interindividual fluctuations even in clinically stable patients. Long-term fluctuations in sGFAP as well as its unexpectedly missing association with attacks in this investigation underscore the need for a better understanding of patient factors that influence sGFAP concentrations. Future research with larger cohorts is warranted to delineate the value and applicability of GFAP in relapse prediction.

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P1579
Comparison of SIMOA and VEUS technologies for serum glial fibrillary acidic protein measurement

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Introduction: Glial fibrillary acidic protein (GFAP) is a critical cytoskeletal component predominantly expressed in astrocytes, playing vital roles in maintaining structural stability, neuroprotection, and scar formation in central nervous system (CNS). Following astrocytic injury, GFAP is released into CSF and blood, serving as a biomarker for CNS disorders, including multiple sclerosis (MS).
Objectives/Aims: This study aimed to compare the performance of the newly developed VEUS technology for measuring serum GFAP (sGFAP) levels against the established single-molecule array (SIMOA) method in patients with relapsing remitting MS (RRMS) and non-inflammatory neurological disorders (NINDs) and symptomatic controls (SCs).
Methods: A single-center retrospective analysis was conducted at Department of Neurology, University Hospital Ostrava. Patients who met following inclusion criteria were enrolled: 1) diagnosis of RRMS according to the revised 2017 McDonald criteria, NINDs or SCs, 2) age $\geqslant$ 18 years. Samples were collected as part of lumbar puncture, which was carried out for diagnostic or therapeutic purpose. Samples were then stored at CSF biobank at a temperature of -70 °C until the commencement of the analysis. The determination of sGFAP concentration was conducted using the SIMOA GFAP Advantage PLUS Kit HD-X diagnostic kit (SIMOA, Quanterix) and the Duplex RUO Kit (GFAP/UCH-L1) (VEUDx, EZDiatech). The two methods were compared using Spearman correlation, Passing-Bablok regression and Bland-Altman analysis.
Results: A total of 59 patients were included, of whom 47 (79.7 %) were female. Median age was 39 years (IQR 29 – 50). 29 patients (49.2 %) were treated for RRMS. Significant differences between the results of the two methods were observed, with SIMOA measuring notably higher sGFAP levels (median 114 ng/L, IQR 83.3–186) compared to VEUS (median 6.26 ng/L, IQR 3.93–7.12). On average, sGFAP levels obtained using SIMOA were 370.37 ng/L (95 % CI -73.64 to 814.39) higher than those measured with VEUS, showing significant bias in sGFAP concentrations between the methods. No significant correlation between the measurements was observed ($rs = 0.14$, $p = 0.28$). There was no statistically significant difference in sGFAP concentrations measured by SIMOA between patients with MS and controls ($p = 0.87$).
Conclusion: The results of this study do not support the possibility of substituting sGFAP measurement between VEUS and SIMOA methods.

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P1580
MicroRNAs and clinical disability in multiple sclerosis

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Introduction: microRNAs have been proposed as possible biomarkers in multiple sclerosis (MS). Several candidates have been identified in previous studies in relationship with different clinical and radiological outcomes.
Objectives/Aims: we aim to corroborate these previous results in a larger cohort of MS patients, to measure their association with the clinical evolution of the disease through multivariate analysis.
Methods: cross-sectional study. Inclusion criteria: 1) MS subjects attending the demyelinating disease units of 4 university hospitals in Madrid (Getafe Hospital, Ramón y Cajal Hospital, QuironSalud Hospital and Torrejón Hospital); 2) MS diagnosis according to McDonald 2017 criteria, of any phenotype following Lublin 2013 definition, and radiological isolated syndrome (RIS) according to Okuda 2009 criteria; 3) age 18 years-old or older; and 4) no active treatment over the lats 6 months. Disability was quantified with the Expanded Disability Status Scale (EDSS). 8 microRNAs (miR-9.5p, miR-29b.3p, miR-34a.5p, miR-126.3p, miR-138.5p, miR-146a.5, miR200c.3p and miR-223.3p), selected from previous studies, were analysed. Sex, age at study, time of MS duration and clinical phenotype of MS were established as covariates for the regression multivariate model. Statistical significance was set at $p<0.05$. SPSS, version 21 was used for the statistical analysis.
Results: 93 patients. 62 women; 68 relapsing-remitting MS (RRMS); 8 secondary-progressive MS (SPMS); 6 primary progressive MS (PPMS); 6 clinical isolated syndrome (CIS) and 5 RIS; age of onset: mean=35.3 years (SD=10.6); time of MS duration: mean=3.8 years (SD=3.8); EDSS: median=2.0 (Interquartile range: 1.0-3.0). In univariate analysis miR-9.5p was associated with EDSS (b=0.28; P=0.04); and miR29b.3p, miR-34a.5p, miR-126.3p and miR-146a.5p were correlated with MS phenotype. MiR-29b.3p, miR-34a.5p and miR-146a.5p higher in CIS (p=0.001, p=0.041 and p=0.026, respectively); and miR-126.3p higher in RRMS ($p<0.001$). After multivariate adjustment 3 microRNAs were associated with EDSS status: miR-9.5p (b=0.37; p=0.048); miR-126.3p (b= - 1.14; p=0.009); and miR-146a.5p (b=0.4; p=0.026).
Conclusion: Our results reassure the potential use of microRNAs as biomarkers in MS to predict the disease course and improve the monitoring of our patients. MiR9.5p, miR-126.3p and miR-146a.5p, as in line with previous results, seem to be the most relevant, and a further study of them and their mechanisms of action would be recommended.

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P1581
A blood-based biomarker measuring degradation of biglycan is upregulated in patients with multiple sclerosis compared to healthy donors: Results from the VACCINE and EXIT studies

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Introduction: A typical multiple sclerosis lesion forms around blood vasculature and is associated with immune cell infiltration. The ensuing inflammation causes perivascular fibrosis through increased fibrillar collagen deposition as a physical barrier to the influx of immune cells. Biglycan is present in active and chronic lesions and involved in collagen fibril assembly, hence contributing to extracellular matrix organization in the perivascular space.
Objectives/Aims: We hypothesise that BGM is elevated in patients with MS compared to healthy matched donors and may be associated with disease severity by expanded disability status scale (EDSS).
Methods: The biomarker BGM reflecting degradation of biglycan mediated by matrix metalloproteinase-9 and -12 was quantified in serum samples collected from relapsing MS patients once prior to infusion (EXIT20, n=184) with matched healthy donors

(n=30) and longitudinal in MS patients prior to vaccination (VACCINE, n=58) with matched healthy donors (n=32). Differences between MS patients from the two clinical cohorts and the healthy controls were assessed with Welch's Two Sample t-test. Correlation to EDSS was performed using Pearson's correlation coefficient.
Results: For the EXIT20 study, the mean age was 45.2 years (63% female) for MS patients, while the mean age was 4.6 years in the matched healthy controls (56% female). For the VACC study, the mean age was 43.7 years (71% female) for the MS patients, and a mean age of 48.5 years in the matched healthy controls (65% female). MS patients in both cohorts have significantly higher levels of BGM detectable in blood serum compared to healthy controls (EXIT20 $p < 0.0001$, VACC $p < 0.0001$ with BGM $\bar{x}$ =10.4 ng/mL [3-25.6] and $\bar{x}$ =7.7 ng/mL [3.1-20], respectively). The correlation to EDSS was not significant.
Conclusion: We evaluated the biomarker BGM in two clinical studies of MS patients, and found the levels elevated compared to healthy donors, while there was no association with disease severity quantified by EDSS. These results indicate that changes in MS lesions may be observed serologically. Biglycan could potentially be a biomarker in disease monitoring at time of diagnosis as well as a biomarker for treatment response.

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P1582
Serum Neurofilament Light Chain as a Predictor of Disability and Lesion Burden in Multiple Sclerosis using ultrasensitive ELISA kits

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Introduction: Neurofilament light chain (NfL) is emerging as a potential biomarker of axonal damage in multiple sclerosis (MS), with increased serum levels reflecting disease activity and neurodegeneration.
Objectives/Aims: The aim of this study was to assess the predictive value of serum NfL levels in relation to functional status and lesion burden in MS patients.
Methods: We conducted a cross-sectional observational study in 2023 at the Hospital Dr. Rafael Ángel Calderón Guardia in San José, Costa Rica. Including 36 adult patients diagnosed with MS, excluding those with other neurological or systemic inflammatory conditions. Serum samples were analyzed for NfL concentration using an ultrasensitive enzyme-linked immunosorbent assay (ELISA) kit (MyBioSource, catalog #MBS9399603). Expanded Disability Status Scale (EDSS) scores and brain MRI (1.5T) were obtained within 3 months of sample collection. We analyzed correlations between sNfL and clinical/MRI parameters, and receiver operating characteristic (ROC) curves were generated to determine predictive thresholds for poor functional status (EDSS >2.0) and high lesion load (>20 T2 lesions).
Results: The median age of participants was 39.5 years, with a female predominance (77%). Patients with EDSS >2.0 had significantly higher sNfL levels (median 217 pg/mL) compared to those with EDSS ≤ 2.0 (median 133 pg/mL, $p<0.05$). A cut-off value of 180 pg/mL predicted EDSS >2.0 with sensitivity of 78% and specificity of 73%. Similarly, sNfL >180 pg/mL was associated with >20 T2 lesions (AUC: 0.80; p=0.002).
Conclusion: Elevated serum NfL is associated with greater disability and MRI lesion burden in MS. A threshold of 180 pg/mL may be useful for identifying patients at higher risk of clinical progression. These findings support the clinical utility of sNfL as a biomarker in MS management. Importantly, the use of ultrasensitive ELISA platforms such as PCR-based methods may offer a more accessible alternative to SIMOA technology, expanding biomarker availability in resource-limited healthcare settings.
Presentation Preference: Both oral and poster presentation.
Disclosure: Rafael Matamoros Sánchez & Dr Hubert Fernandez declares no conflicts of interest in the last 3 years.

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Imaging & Non-Imaging Biomarkers – Other Biomarkers

P1583
MSCopilot® digital biomarkers obtained in a real-world setting correlated with their clinical counterparts in the MS-DETECT study

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Introduction: Monitoring disability worsening in people living with multiple sclerosis (PwMS) traditionally relies on standardized clinical assessments. However, the Expanded

Disability Status Scale lacks sensitivity to capture subtle changes, while the Multiple Sclerosis Functional Composite with its four components (MSFC-4) is challenging to administer routinely in clinical practice. MSCopilot® is a Software as a Medical Device designed for at-home assessments of key functions: walking, dexterity, cognitive, and low-contrast visual acuity. Previous studies have shown that the MSCopilot® composite score correlates with MSFC-4 score, supporting its potential use for remote monitoring. The ongoing, prospective, longitudinal MS-DETECT study (NCT05816122) evaluates MSCopilot®'s ability to detect disability worsening during and between clinical visits in 336 PwMS across 7 countries over 18 to 24 months.

Objectives/Aims: This interim analysis describes patient demographics and clinical baseline comparisons between MSCopilot® digital biomarkers and individual MSCF-4 scores.

Methods: Baseline demographic and clinical data, including the MSFC-4 assessments, were collected in PwMS with relapsing or progressive MS during the in-clinic inclusion visit. Subsequently, the four MSCopilot® tests were self-administered at home within the following week. The association between the digital scores and their clinical counterparts was assessed using/with Pearson correlation coefficients.

Results: As of December 2024, 243 patients were included in the interim analysis. The cohort was 68.7% female, with a mean age of 49.15 ± 8.74 years and mean disease duration of 17.57 ± 8.04 years. MS phenotypes were distributed as follows: relapsing-remitting MS (RRMS: 83.9%), active secondary progressive MS (SPMS: 2.9%), and non-relapsing SPMS (13.2%). EDSS scores ranged from 2.5 to 6.5 (mean: 3.8 ± 1.3). We recorded high test completion (>98%) and at least 88% of these tests met quality criteria. Significant correlations were observed between digital and clinical components across all domains (all $p<0.001$) with dexterity having the lowest coefficient ($r=0.28$) and walking the highest ($r=0.68$).

Conclusion: MSCopilot® digital biomarkers demonstrated high data coverage and excellent quality criteria. Each digital test correlated with its clinical counterpart, emphasizing the potential value of digital biomarkers in remote monitoring of PwMS. Their potential use in early detection of disease worsening could supplement and/or improve clinical monitoring in MS.

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P1584
Exploring the relationship between visually-mediated word-finding and disability in a 4-year longitudinal study: preliminary findings

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Introduction: Yap et al. (2023) found that word-finding in MS was associated with information processing speed and largely independent of mood. They suggested that MS-related change in visual object meaning perception (visually-mediated lexical retrieval and confrontation naming) may hold promise as a cognitive biomarker of disability in MS.

Objectives/Aims: We present initial findings from a 4-year follow-up study examining the relationship over time between word-finding, information processing speed, and disability in relapsing remitting (RRMS) and progressive (PMS) MS.

Methods: So far, 21/44 persons with MS have been reassessed (9 male; 10 RRMS; mean age=52 years; mean education=16.5 years), completing measures of word-finding (Visual Naming Test, VAN; Auditory Naming Test, ANT; Rapid Automatised Naming, RAN), information processing speed (Symbol Digit Modality Test, SDMT), mood (Hospital Anxiety and Depression Scale, HADS), and MS-related disability (Expanded Disability Status Scale, EDSS).

Results: At follow-up, PwPMS experienced significantly greater disability than PwRRMS [EDSS, independent t(19)=-5.026, p<0.001], but they did not differ on anxiety or depression. Exploratory 2-tailed Pearson partial correlations, adjusted for age and years of education, indicated that greater disability was associated with slower information processing speed [r=-0.761; p<0.001], slower visually-mediated word retrieval [r=0.982; p<0.001], and slower visually-mediated object naming [r=0.684; p=0.001]. Disability was not associated with VNT or ANT naming errors, nor RAN object naming. Better SDMT performance was negatively correlated with response times on the VNT [r=-0.935, p=0.002]. Mood did not correlate with cognitive performance. Exploratory 2-way analyses of covariance, controlled for age, years of education, and information processing speed, did not reveal any significant main effects or interactions for RAN object naming or ANT performance. However, response times for visually-mediated word retrieval were significantly slower for PwPS [$F(1,16)=22.099$, $p<0.001$; $\eta^2=0.58$].
Conclusion: Initial longitudinal findings suggest that greater MS-related disability is associated with slower processing speed and performance on tasks measuring visual object meaning perception, with greater difficulties in visually-mediated object naming experienced by PwPMS. Data collection is ongoing, including healthy control follow-up. Increased statistical power will facilitate further testing of a word-finding biomarker of disability MS.

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P1585
Cortical Excitability Changes in Neuromyelitis Optica Spectrum Disorder: Insights from Transcranial Magnetic Stimulation and Clinical Correlations

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a severe inflammatory demyelinating disease of the central nervous system, primarily affecting the optic nerves and spinal cord. Although NMOSD is classically considered to spare the brain, emerging evidence suggests functional cortical involvement. Altered cortical excitability, assessed using transcranial magnetic stimulation (TMS), may provide insights into the pathophysiology of NMOSD and its clinical manifestations.
Objectives/Aims: To investigate cortical excitability changes in NMOSD using TMS and explore their correlation with clinical phenotype, including disease severity, relapse rate, and disability burden.
Methods: A cross-sectional study was conducted on 30 NMOSD patients and 30 age- and sex-matched healthy controls. TMS was used to assess key cortical excitability parameters, including resting motor threshold (RMT), short-interval intracortical inhibition (SICI), intracortical facilitation (ICF), and cortical silent period (CSP). Clinical data, including disease duration, Expanded Disability Status Scale (EDSS) scores, relapse history, and presence of brain lesions on MRI, were collected. Correlations between TMS measures and clinical parameters were analyzed.
Results: NMOSD patients exhibited significant cortical excitability alterations compared to controls, including increased RMT ($p < 0.05$), reduced SICI ($p < 0.01$), prolonged CSP ($p < 0.05$), and enhanced ICF ($p < 0.05$). Notably, reduced SICI correlated with higher EDSS scores ($r = -0.45$, $p < 0.01$) and greater relapse frequency ($r = -0.42$, $p < 0.05$), suggesting impaired GABAergic inhibition in patients with more severe disease. Additionally, patients with supratentorial MRI lesions showed greater cortical excitability changes than those without.
Conclusion: Our findings suggest that NMOSD is associated with significant alterations in cortical excitability, particularly impaired intracortical inhibition. These changes correlate with clinical severity and may reflect underlying neurophysiological dysfunction beyond the spinal cord. TMS could serve as a useful biomarker for cortical involvement in NMOSD and a potential tool for monitoring disease progression and therapeutic response.

Disclosure of interest: Iodice:nothing to disclose

P1586
Nominal Multimodal Evoked Potentials Indicate Clinical Progression While Qualitative Evoked Potentials Reflect Subclinical Deterioration In Multiple Sclerosis

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Introduction: While magnetic resonance imaging (MRI) is crucial for diagnosing and monitoring multiple sclerosis (MS) it sometimes fails to correlate with clinical progression. Evoked potentials (EP), particularly multimodal EPs, offer a valuable alternative by detecting early subclinical deterioration and predicting disease progression.
Objectives/Aims: This study evaluated how qualitative versus nominal EP scores reflect progression in relation to MRI activity and the expanded disability status scale (EDSS).
Methods: 118 MS patients were assessed using MRI and multimodal evoked potentials including visual, motor, and somatosensory EPs at baseline and annually for 3 years. EP progression was evaluated using a nominal score (EPPSn) indicating a transition from normal to pathological and a qualitative score (EPPSq) defined as progressive when the maximum side difference in latency exceeded a predefined threshold. MRI progression was determined by the appearance of new or enlarged lesions.

Statistical analyses were performed using chi-squared tests and binary logistic regression.
Results: Our cohort consisted of 84 women (71%) and 34 men (29%) with a median EDSS score of 2.0 at baseline and a mean age of 33 years. MRI activity significantly correlated with EPPSq (p=0.024) but no significant correlation was observed between MRI activity or EPPSq and EDSS change. However, EPPSn was significantly associated with EDSS deterioration (p=0.029). Logistic regression revealed that the likelihood of EDSS worsening was 2.4 times higher in patients with progression in EPPSn (p=0.032).
Conclusion: MRI progression did not correlate with EDSS deterioration. While EPPSn reflected clinical worsening, EPPSq and MRI progression appeared to capture subclinical changes not mirrored by EDSS. These findings suggest that both EP scoring methods offer complementary insights into MS disease activity and may support more comprehensive patient monitoring and treatment decisions.

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P1587
Prediction of Cognitive and Motor Impairment Progression in Multiple Sclerosis Patients With Oculomotor-Derived Digital Biomarkers

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Introduction: Early detection and disease monitoring in people with MS (PwMS) are ongoing challenges in clinical practice, research settings, and response to treatment studies. Major roadblocks include patient assessment time constraints and a lack of objective, cost-effective, disease-specific biomarkers.
Objectives/Aims: To build upon decades of established scientific literature linking eye movement abnormalities in PwMS to disease severity by developing oculomotor-derived digital biomarkers of Cognitive and Motor Impairment Progression.
Methods: PwMS in an ongoing longitudinal proof-of-concept study are undergoing eye-tracking testing and clinical assessments every 6 months in clinical settings while also undergoing weekly eye-tracking testing at home using a novel mobile eye-tracking technology developed by Innodem Neurosciences, whose patented gaze-tracking technology allows for oculomotor capture using the standard camera of iPads and outputs over two hundred distinct eye movement parameters. To determine if patients showed disease progression during the study, we identified those that exhibited a clinically meaningful change in at least one of the cognitive (e.g. SDMT) or motor (e.g. T25FW, EDSS) scores measured, using standard established change criteria from the scientific literature. Subsequently, oculomotor features were examined to determine if any had rates of change that differed between those that were shown to progress compared to those that had not based on the clinical data. In a final step, a machine learning classification analysis was conducted to determine if we could correctly identify progressors from non-progressors using only the eye tracking data.
Results: Longitudinal data was collected from more than 60 patients who had been followed for up to 18 months, of which more than 50% had shown progression based on cognitive or motor test score changes that were determined to be clinically meaningful. A machine learning classifier was built that could identify both cognitive and motor progressors with a high degree of sensitivity (>80%) and specificity (>85%).
Conclusion: The findings highlight the promise of oculomotor-derived digital signals as a novel biomarker of early and subtle disease progression in PwMS. Furthermore, such biomarkers are likely to improve physicians' access to non-invasive, sensitive and accessible disease progression markers.

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P1588
Robust Smartphone Placement Classification to Enhance Digital Biomarker Reliability

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Introduction: Smartphone-based assessment of motor capacity is increasingly used in people with Multiple Sclerosis (pwMS). As in real-life conditions the smartphone can be held in different locations and these can vary over time, a robust phone location detection method is needed to then select the best location-specific data processing algorithm. Previous phone-position detection methods, with an accuracy of about 87%, had limited generalisability and were not validated for MS.
Objectives/Aims: This paper presents a machine learning model for smartphone placement classification integrating multiple data types designed to overcome such limitations.
Methods: A training dataset included data from 83 healthy adults (Age 20-83 y) who performed a 30-second walk test, with two smartphones (one iPhone and one Android) simultaneously worn in left/right front- (FP, n=165 valid datasets) and back-pockets (BP, n=165 valid datasets), or waist-worn (WW, n=166 valid datasets). A pool of 465 features (time=201, frequency=66, motion-energy=198) were extracted from acceleration and angular velocity signals. A multiclass gradient-boosted random forest (RXGBoost) was trained using 100 random hyperparameter configurations, and each configuration was evaluated with a 10-group-user-out cross validation. The model was then tested on data from 61 pwMS (Age 26-72 y, EDSS: 0-3, FP, n=56 and WW, n=5). Its results were also compared to those from a gravity-based model.
Results: RXGBoost achieved excellent multiclass-classification performance (FP vs BP vs WW) in the training cross-validation process, F1-score (F1)=0.994±0.001, Accuracy (ACC)=0.992±0.001 and ROC-AUC (AUC)=0.999±0.001. Gravity and gyroscope-based features were critical for WW detection in the training dataset, while time and frequency-based features of linear acceleration and gyroscope signals distinguished FP from BP. On the MS test dataset, RXGBoost outperformed the gravity-based model, achieving higher F1 (0.991 vs. 0.945), ACC (0.984 vs. 0.903), and AUC (0.998 vs. 0.85).
Conclusion: The proposed model demonstrated outstanding performance in smartphone placement classification in pwMS, thereby enabling enhanced precision in using the right sensor location-adaptive algorithms for the extraction of smartphone-based digital biomarkers collected in a real-world unsupervised setting.

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P1589
The visual evoked potentials revisited for the follow up of Patients with multiple sclerosis In the era of new diagnostic criteria

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Introduction: Multiple sclerosis (MS) is a chronic demyelinating disease with a heterogeneous clinical course, making the prediction of long-term disability difficult. Visual evoked potentials (VEPs), especially amplitude-based parameters, may be sensitive biomarkers of neurodegeneration and functional deterioration not detected by conventional clinical measures.
Objectives/Aims: To investigate the clinical relevance of P100–N145 amplitude compared to conventional VEP parameters (P100 latency and N75–P100 amplitude) in predicting disability progression in patients with relapsing-remitting MS.
Methods: In this retrospective cohort study, 40 RRMS patients (80 eyes) were analyzed with VEP and EDSS data at baseline and at the end of the study over an average period of 48 months. Statistical analysis was performed using non-parametric methods, including Spearman correlation and Kruskal–Wallis tests.
Results: No significant association was found between P100 latency and EDSS progression. Although N75–P100 amplitude correlated with initial EDSS ($r = -0.276$, $p = 0.009$), its change longitudinally was not associated with disability worsening. In contrast, the reduction in P100–N145 amplitude over time was significantly correlated with EDSS progression ($r = -0.431$, $p < 0.001$), suggesting a stronger association with cumulative neurodegeneration.
Conclusion: P100–N145 amplitude appears to be a valuable and underutilized marker of disease progression in MS that more accurately reflects neuroaxonal loss than latency-based measures. These results argue for the inclusion of amplitude-based VEP analysis in routine monitoring and emphasize the need for multimodal strategies in treating MS

Disclosure of interest: Nothing to disclose

P1590
Increased short chain fatty acids during relapses in new onset MS compared to pre-existing MS – new information on the pathophysiology of the gut brain-axis?

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Introduction: The role of the gut microbiota in the development and progression of MS has become increasingly important in recent years. The prevailing paradigm in most cases is that of intestinal dysbiosis, which might also explain the finding of a reduced production of short chain fatty acids (SCFA). However, the direction of causality, i.e. whether the intestinal changes are the cause or consequence of chronic CNS inflammation, remains to be elucidated. The majority of previous studies have focused on treated or untreated, but long-term MS patients. The alteration in faecal SCFA concentrations in the early stages of the disease, particularly during relapses, remains to be extensively studied.
Objectives/Aims: Evaluation of changes in SCFA in the early stages of relapsing remitting MS (RRMS) compared to patients with longer course of disease and healthy controls (HC).
Methods: The prospective case-control study was conducted on a cohort of 22 RRMS patients (16 female, mean age 36 years) at the time of first relapse without prior immunosuppressive medication (early-RRMS). The study collected clinical and demographic parameters, as well as faecal SCFA concentrations measured by gas chromatography. Subsequently the parameters were compared with those of age- and sex-matched clinically stable RRMS patients under ongoing long-term immunotherapy (late-RRMS) as well as HC.
Results: The early-RRMS cohort showed significantly higher faecal SCFA concentrations than the late-RRMS cohort, especially for propionate ($p = 0.019$), butyrate ($p = 0.017$), isobutyrate ($p = 0.016$), valerate ($p < 0.001$) and isovalerate ($p < 0.001$). There were no statistically significant differences in SCFA concentrations compared to the HC.
Conclusion: The findings of this study indicate that a reduction in SCFA levels is exclusively observed in patients with RRMS during the further course of the disease, rather than at the onset. Consequently, it can be hypothesised that a decrease in intestinal SCFA concentration is rather a consequence than a cause of chronic CNS inflammation. Disease modifying treatment may also have an impact. A further investigation of this connection is urgently required.

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P1591
Do Visual Evoked Potentials Reveal Subclinical Neurodegeneration in Multiple Sclerosis? A Retrospective Cohort Analysis

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Introduction: Visual Evoked Potentials (VEP) are sensitive neurophysiological tests assessing visual pathway integrity. In multiple sclerosis (MS), latency prolongation reflects demyelination, whereas amplitude reduction indicates axonal degeneration. Evaluating VEP changes might provide insights into disease progression and treatment responses.
Objectives/Aims: To investigate relationships between VEP changes (latency prolongation and amplitude reduction) and clinical outcomes (disability progression, relapse activity, MRI findings) in MS patients.
Methods: We retrospectively evaluated 83 MS patients (79.5% female, median age 36 years) without acute optic neuritis. Median follow-up between two VEP assessments was 2 years. Latency prolongation (>1 ms increase) and amplitude reduction (>0.3 μV decrease) were analyzed alongside clinical measures including Expanded Disability Status Scale (EDSS), annualized relapse rate (ARR), MRI, and cerebrospinal fluid (CSF) findings. Statistical analyses included comparative tests, correlation analyses, and multivariate logistic regression.
Results: Significant latency prolongation was detected in 43.4% of patients and was associated with higher relapse rates ($p<0.001$) and lower baseline structural MRI lesion load. These patients also had lower median CSF IgG indices (0.7 vs. 0.9, $p=0.035$). Significant amplitude reductions occurred in 56.6%, correlating with higher disability progression (EDSS scores: median 1.5 vs. 1.0 at second VEP, $p=0.017$; last EDSS evaluation, $p=0.028$). Higher baseline amplitudes and shorter initial latencies predicted later amplitude decline. Any significant VEP change was associated with increased relapse activity ($p=0.014$), despite similar EDSS scores at baseline and follow-up. While latency changes did not significantly correlate with EDSS progression, amplitude reduction correlated modestly with worsening EDSS ($r=-0.225$, $p=0.041$). Multivariate analysis identified ARR as an independent predictor of latency prolongation (OR=2.91; 95% CI: 1.38–6.13, $p=0.005$).
Conclusion: Our findings support the utility of serial VEP assessment in capturing subclinical disease dynamics, and suggest that future prospective studies should explore its potential role in individualized monitoring strategies and long-term prognostication in MS.

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P1592
EDSS, Disability and Gait Analysis: Uncovering Ambulation Disability Variability in People with Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS), a relapsing and progressive central nervous system disorder, can impair multiple functional abilities such as gait and cognition. While Expanded Disability Status Scale (EDSS) was designed to standardize disability severity in people with MS (PwMS), it may not fully capture functional variability within "similar disability." The 25' timed walk provides information solely about gait velocity. This study examines the variability of additional critical gait parameters that underly "ambulation" hypothesizing that multiple gait parameters that are not specifically velocity dependent are also sequentially impaired with higher EDSS scores. This complex deconstruction of ambulation and reveals important disease related changes likely not detected by the EDSS or other standard ordinal gait measures.
Objectives/Aims: To assess the real-world validity of the EDSS as a measure of gait impairment related disability measure in PwMS.
Methods: Retrospective analysis of multiple objective critical gait parameters obtained by a digital gait analysis (GA, ProtoKinetics) obtained in the course of routine care. *Clinical instrument to retrospectively capture levels of EDSS* was used to calculate EDSS of chart notes obtained within 6 months of GA. Patients were stratified by EDSS score (0-1 to 6.5-7). GA parameters included preferred walking speed (PWS) and dual-task (DT) walks, measuring velocity, step length (SL), and double support (DS). Variability (coefficient of variation, CV) was assessed within each EDSS group.
Results: A cohort analysis (n = 196, 68% female) of PwMS demonstrated that left SL CV ranged from 10.53% (0-1 group) to 33.93% (6.5-7 group), and right SL CV ranged from 12.52% to 37.43%. DS CV ranged from 11.46% to 29.36% (left) and 12.07% to 30.41% (right). Gait velocity CV variability ranged from 16.51% (0-1 group) to 55.92% (6.5-7 group). For DT, left SL CV ranged from 8.93% to 35.15%, and right SL CV ranged from 10.25% to 44.23%. DS CV ranged from 10.13% to 30.09% (left) and 9.80% to 30.14% (right). Gait velocity CV ranged from 16.15% to 57.96%.
Conclusion: Gait velocity impairment with increasing EDSS is accompanied by increased variability in other critical gait parameters across PWS and DT. Lower variability was seen in lower EDSS groups, with a progressive increase in higher groups, indicating EDSS limitations in capturing full disease variability and potential for improved disease progression detection and therapy evaluation.

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P1593
Machine learning-based prediction of disability progression in multiple sclerosis using clinical, performance-based, and patient-reported outcomes

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Introduction: While clinical predictors of disability progression in people with multiple sclerosis (pwMS) are well-established, the contribution of patient-reported outcome measures (PROMs) remains underexplored.
Objectives/Aims: To develop a machine learning (ML) model for predicting disability progression—defined as a change in EDSS over three years—using clinical data, performance-based tests, and PROMs.
Methods: Data were collected at baseline and at a 3-year follow-up, including clinical&demographic outcomes (type of MS, baseline EDSS, sex), performance-based measures (Timed 25-Foot Walk, 9-Hole Peg Test, and Symbol Digit Modalities Test), and PROMs (MS Walking Scale, Modified Fatigue Impact Scale, Activities-specific Balance Confidence Scale, Beck Depression Inventory, Epworth Sleepiness Scale, and the Multiple Sclerosis International Quality of Life Questionnaire). Four machine learning models—Linear Regression, Decision Tree, Random Forest, and Support Vector Regression (SVR)—were applied. Model performance was evaluated using Mean Absolute Error (MAE), Mean Squared Error (MSE), Root Mean Squared Error (RMSE), and R^2 score.
Results: Data from 182 pwMS (mean EDSS±SD: 2.28±1.9, 69% female) were analyzed. Linear Regression demonstrated the best performance, achieving the lowest error rates and highest predictive accuracy (MAE: 0.321, MSE: 0.185, RMSE: 0.430, R^2: 0.951). It was closely followed by Random Forest, which also showed strong predictive power (MAE: 0.347, MSE: 0.246, RMSE: 0.495, R^2: 0.935. Decision Tree and SVR yielded less accurate predictions, with higher error rates and lower R^2 values (MAE: 0.432 and 0.547; R^2: 0.879 and 0.844, respectively). Visual inspection of prediction outputs confirmed that Linear Regression and Random Forest models closely tracked actual EDSS scores over time, particularly in the third year.
Conclusion: Linear Regression's superior metrics suggest a strong linear relationship, likely driven by baseline EDSS,

making it effective for general predictions. Random Forest, with comparable graph performance, also captured non-linear patterns, indicating robustness for MS progression. Decision Tree and SVR underperformed, reflecting overfitting and the need for tuning, respectively. Future work should explore hybrid models to enhance prediction accuracy.

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P1594
Evoked potentials as prognostic biomarker in early relapsing-remitting MS and clinically isolated syndrome: a 24-month analysis from a prospective German multicentre cohort

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Introduction: MS has an unpredictable disease course. Prospective data for evoked potentials (EPs) as predictors of disease activity, particularly in correlation with other biomarkers are lacking.

Objectives/Aims: To determine whether baseline somatosensory (SSEP), visual (VEP), and motor evoked potentials (MEP) correlate with and predict outcomes at 24 months in newly diagnosed MS and clinically isolated syndrome (CIS) patients. Here, we present an interim analysis of ProVal-MS (German Clinical Trials Register-ID: DRKS00014034), a multicentre prospective study conducted at five German university centres.

Methods: Besides clinical metrics (e.g., Expanded Disability Status Scale (EDSS), Fatigue Scale for Motor and Cognitive Functions (FSMC), Symbol Digit Modalities Test (SDMT)), assessments include SSEP, VEP, and MEP, along with cranial and spinal magnetic resonance imaging (MRI), serum neurofilament light chain (sNfL) and serum glial fibrillary acidic protein (sGFAP).

Results: The interim analysis included 73 patients (total cohort, n=367) with a mean age of 32.9±9.2 years with 67.6% females. Median EDSS was 1.0 (interquartile range (IQR) 1.0-2.0), median sNfL level 12.3 pg/mL (IQR 8.8-21.3), and median sGFAP 131.0 pg/mL (95.2-160.8). At baseline, abnormal tibialis nerve SSEP was associated with longer disease duration (p=0.004), while patients with abnormal abductor hallucis muscle MEP showed higher baseline EDSS (p=0.035). Abnormal VEP was associated with higher baseline EDSS (p=0.016), lower SDMT scores (p=0.015) and reduced visual acuity bilaterally (right eye, p=0.025, left eye, p=0.002). Baseline EPs were not associated with EDSS progression, MRI activity or fluid biomarkers over 24 months. However, patients with abnormal VEP at baseline, showed significantly greater improvement in SDMT over 24 months compared to those with normal VEP (median increase 7.0 vs. 3.0, p=0.033).

Conclusion: Here we present first data on EPs as potential biomarker in a prospective well-characterized cohort of CIS and

early MS patients. We could observe associations between EPs and disability, cognition and vision.

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P1595
Facial Palsy in Multiple Sclerosis Revisited: Prevalence of Movement Asymmetry Evidence from Objective, Video-Based Facial Analysis

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Introduction: The prevalence of facial palsy (FP) in multiple sclerosis (MS) is ambiguous in the literature; reports vary widely (3-20%) likely reflecting methodological differences in clinical assessment. On top of that, an autopsy series suggested evidence for facial nerve damage in over 50% of examined cases, implying FP may be underrecognized.
Objectives/Aims: Our aim was to objectively quantify and investigate the occurrence of facial movement asymmetry in MS from recordings of freely spoken monologues, using a single-camera setup.
Methods: We collected video recordings from 111 people with MS and analysed them using deep learning-based 3D facial landmark tracking. Ten facial asymmetry markers were calculated capturing dynamic, spatial and temporal features of the mouth and brows. We then subjected the markers to unsupervised k-means cluster analysis and related them to clinical scores and neuroimaging markers.
Results: Two distinct clusters emerged: LOW asymmetry (52.3%, $n = 58$) and HIGH asymmetry (47.7%, $n = 53$). The HIGH asymmetry group exhibited a significant increase across all asymmetry markers ($p < 0.001$). Clinically, this group consisted of older individuals with slightly higher overall EDSS scores as well as higher scores in the pyramidal, cerebellar and bowel bladder sub scores and for the timed 25-ft walk. The strongest clinical correlation was observed between asymmetric eyebrow movement and the EDSS pyramidal score ($r = 0.31$, $p < 0.001$). Concerning asymmetry- and neuroimaging markers, the strongest correlation was found between asymmetric fluctuations in the mouth corner movement and cerebral grey matter ($r = -0.19$, $p = 0.036$).
Conclusion: Our results suggest the existence of subclinical facial palsy in a large subgroup of MS, consisting of nearly 50% of the included cohort, exceeding prior clinical estimates. Our quantitative facial asymmetry markers reflect both disability and neuroanatomical changes, thus indicating facial asymmetry

as a novel digital biomarker in MS. The high sensitivity of our method to detect subtle facial asymmetry not only improves FP monitoring but may also enable early identification of neuronal degradation and smouldering disease activity in MS.

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P1596
Probing Motor Cortical Network Reactivity in Multiple Sclerosis with TMS–EEG: Clinical and Prognostic Correlates

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Introduction: Motor disability is a major contributor to long-term impairment in multiple sclerosis (MS) and is associated with early disruption of synaptic and network-level function. Transcranial magnetic stimulation combined with EEG (TMS–EEG) enables direct, non-invasive assessment of cortical reactivity and connectivity with high temporal resolution.
Objectives/Aims: To investigate whether TMS-evoked potentials (TEPs) and TMS-related spectral perturbations (TRSPs) from the primary motor cortex (M1) are altered in MS, relate to disease duration and disability, and predict long-term disease activity.
Methods: Forty-three relapsing-remitting MS patients and twenty-six healthy controls (HCs) underwent single-pulse TMS over the left M1 with simultaneous EEG recording. TEP components (P15, P30, N45, P60, N100) and TRSPs in beta and gamma bands were extracted. MS patients were clinically followed for two years and classified as NEDA or EDA based on the NEDA-3 criteria. Disability was assessed by Expanded Disability Status Scale (EDSS) and hand dexterity by the 9-Hole Peg Test (9HPT). Group comparisons, correlation analyses, and logistic regressions were performed.
Results: MS patients showed a significant reduction in P60 amplitude. A trend toward lower P15 amplitude was observed in EDA vs. NEDA patients. Gamma-band desynchronization (Gamma TRD) was reduced in MS, but not predictive of disease course. Only P15 amplitude significantly predicted NEDA status at 2 years (accuracy: 74.4%; sensitivity: 93.5%).
Conclusion: TMS–EEG detects alterations in motor cortical reactivity and oscillatory responses in MS. P15 amplitude may serve as a candidate predictive biomarker of motor network stability. TMS–EEG provides a privileged window onto network dysfunction in MS, with potential to guide early prognosis and treatment.

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P1597
Step by Step: Unlocking Accurate Smartphone-Based Gait Analysis in Multiple Sclerosis

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Introduction: Many validated algorithms are available for accurately detecting steps and strides from inertial sensor data recorded from a midline lower trunk position. In contrast, the state of the art is limited to only detecting strides when a device is located in a front pocket over the thigh, which is a scenario frequently encountered in unsupervised use of smartphone sensors. Moreover, little is known about how these algorithms would perform when applied to data collected in such a scenario from people with impaired gait.
Objectives/Aims: This work aims to present and validate the method "Frequency-Adaptive Iterative Robust Quantification" (FAIR-Q) specifically designed to handle different smartphone positions to accurately segment steps from accelerometer data collected in people with Multiple Sclerosis (pwMS).
Methods: FAIR-Q leverages on continuous wavelet synchrosqueezing to dynamically analyze vertical acceleration signals and identify varying motion-related frequencies, which are then used to perform an iterative filtering process optimising the signal-to-noise ratio. The method, previously tuned and validated for processing data from a sensor on the lower back, was here applied to 83 healthy adults (HA, age 20-83 y.o.) and 56 pwMS (age 26-72 y, EDSS: 0-3). Participants performed a 30s walking test with the smartphone in their front pocket, while simultaneously wearing a reference motion capture system (Xsens). The algorithm was applied to the smartphone data and its internal parameters were tuned using data from ⅓ of randomly selected participants from each group. Its performance was then assessed against the reference values using held-out data from the remaining ⅔.
Results: The translation from lower trunk to pocket data required the tuning of only one parameter, accounting for

expected differences in the main frequency content of the vertical acceleration signals. With this tuning, FAIR-Q proved highly accurate in detecting initial contacts (Median (IQR) F1-score = 0.99 (0.98-0.99) for HA and 0.99 (0.98-0.99) for pwMS) and in estimating step duration (Median (IQR) Relative Error = 0 (0.0-0.88)% for HA and 0 (0.0-1.75)% for pwMS).
Conclusion: Applying our robust method for step segmentation from data collected with a smartphone in the front pocket during a 30s walking task, reached accuracy levels equivalent to those obtained for lower trunk data. Future studies will focus on establishing the generalisability of the results to other motor tasks, including free-living and longer and more variable gait data.

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P1598
Analysis of the potential use of peripheral myeloid-derived suppressor cells as a biomarker of optic nerve damage in an animal model of multiple sclerosis

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Introduction: Multiple sclerosis (MS) is a highly heterogeneous neurodegenerative disease in terms of clinical severity and treatment response, demanding reliable biomarkers for therapy evaluation. Assessing remyelination in MS remains challenging due to both the absence of remyelinating therapies and biologically validated methods for its quantification. The optic nerve (ON) has been proposed as an informative pathway for remyelination monitoring, with visual evoked potentials serving as a measurable parameter in both animal models and patients. Although ON has been described to be affected in experimental autoimmune encephalomyelitis (EAE) MS model, its relationship with clinical severity remains elusive. Our group pioneered the characterization of monocytic myeloid-derived suppressor cells (M-MDSCs) as potential biomarkers of disease severity and relapse recovery in MS. In EAE, circulating M-MDSCs correlate with milder clinical severities and lesser tissue damage in the spinal cord.
Objectives/Aims: Analyze the relationship between EAE clinical severity and ON histopathological impairment.
Evaluate the potential of M-MDSCs as predictive biomarkers of ON myelin alteration in EAE.
Methods: M-MDSCs were quantified in the peripheral blood of each EAE mouse at both disease onset and peak. Animals were followed-up until disease peak or up to 35 days post-immunization, once clinical stabilization was achieved. Severity and recovery indices were determined for each mouse during the disease tracking, enabling their classification as severe/mild and poor/good-recoverers of the clinical course based on the median of these parameters, respectively. ONs were dissected out and processed for Ranvier node density quantification. Matched non-immunized mice (CT) were analyzed for comparison
Results: EAE mice at peak showed lower ON node density than CT regardless of the prior disease severity. Interestingly, at 35 dpi, good-recoverers EAE mice exhibited higher ON node density than those with poorer recovery, without reaching in both cases the density seen in CT mice. Elevated M-MDSCs levels at disease onset and peak correlated with higher ON node density at both peak and after recovery, respectively. ROC curve analysis revealed that a cut-off of 4.50 % of M-MDSCs at disease onset predicted a node density in the ON above the mean of the total population at peak with 70% specificity, while 5.24% of M-MDSCs distinguished high ON node density above the mean at recovery with a 90% specificity
Conclusion: Our findings underscore the strong correlation between lower disease severity, high-recovery clinical courses, and preserved ON Ranvier node density in EAE. Likewise, peripheral M-MDSCs appear to be a promising biomarker for predicting ON myelin damage throughout the clinical course of EAE.

Disclosure of interest: Nothing to disclose

P1599
Eye-Tracking Neurological Assessment technology in Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) is a central nervous system disease that causes demyelination and neurodegeneration, leading to disability progression and cognitive dysfunction. As MS can be diagnosed earlier and increasingly recognized as a continuum, there is a growing need for new methods to objectively measure MS below the current clinical threshold such as the Eye Tracking Neurological Assessment (ETNA™-MS).
Objectives/Aims: The goal of eye movement research in multiple sclerosis (MS) is to identify and monitor the disease status and progression by measuring oculomotor parameters. These parameters can reflect certain aspects of brain function related to mobility and/or cognitive impairment. This objective is addressed through three distinct and complementary studies described below.
Methods: The Validation study employed a multi-site, cross-sectional design to record eye movements of MS patients using patented eye-tracking technology, alongside functional and cognitive assessments. The Proof-of-Concept (PoC) study is an ongoing longitudinal clinical trial involving eye-tracking tests and clinical assessments every six months. Finally, the ELIOS study investigates early changes in novel investigational eye movement biomarkers from baseline to six months post-treatment initiation in Canadian patients with active relapsing-remitting MS (RRMS) prescribed ofatumumab.
Results: The Validation study demonstrated high accuracy and reliability of the ETNA™-MS in estimating EDSS and SDMT scores for MS patients, with 84.8% of AI model's EDSS estimates within ± 0.5 points of clinical data and a test-retest reliability of over 95%. Preliminary data from the PoC study found that over 50% of patients showed clinically meaningful changes in at least one score measured, identifying 10 distinct eye metrics with significant differences between progressed and non-progressed patients, and achieving a sensitivity of 82% and specificity of 88% in detecting progression.
Conclusion: The ETNA™ device offers a reliable and accurate tool for estimating clinical scores in MS patients, with performance comparable to human neurologists. Its impressive test-retest reliability and low mean absolute error highlight its suitability for integration into clinical practice. These findings suggest that eye movement biomarkers could serve as novel indicators for detecting early progression in MS, facilitating treatment optimization and improving patient outcomes.

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P1600
Predicting the Clinical Course of Multiple Sclerosis: A 10-Year Longitudinal Study of Biomarkers and Cognitive Status

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Introduction: Predicting the clinical course of multiple sclerosis (MS) at diagnosis is crucial in the current therapeutic landscape. Although several prognostic factors are recognized, distinct profiles differentiating benign from aggressive MS remain undefined.
Objectives/Aims: We studied a cohort with good clinical evolution and no treatment to assess whether astrocytic (GFAP) and axonal (NfL) biomarkers, alongside cognitive impairment (DC), could predict outcomes 10 years later.
Methods: Plasma GFAP and NfL levels were measured in samples collected in 2015 using the Lumipulse assay. At the time of sampling, patients had a mean disease duration of 14.2 years and a median score of 1.0 on the Expanded Disability Status Scale (EDSS). A total of 33 cases were included. After 10 years, clinical progression was assessed by EDSS increase and the need for disease-modifying therapy. Cognitive Status was also evaluated in 2015 to determine its predictive value for treatment by 2025. Descriptive analyses, correlation tests, and Chi-square tests were performed.
Results: Alterations in at least one biomarker (GFAP or NfL) were observed in 75.8% of patients. By 2025, 45.5% showed EDSS progression, of whom 52% had exhibited biomarker alterations in 2015. Among those with elevated GFAP or NfL levels, 56% were undergoing treatment after 10 years. In contrast, patients without biomarker alterations (24.2%; 8 cases) largely remained untreated (62.5%; 5 cases) and maintained EDSS scores below 3.0 (100%). Among patients with CI in 2015, 57.1% required treatment by 2025; however, no statistically significant association was found between CI and treatment status, nor between biomarker alterations and later treatment initiation.
Conclusion: Although no significant associations were observed between biomarker alterations, cognitive impairment, and treatment need after 10 years, the absence of biomarker abnormalities was linked to better clinical profiles. GFAP and NfL levels may aid in identifying MS patients with favourable prognoses or true benign MS.

Disclosure of interest: A. Gil has received collaborations for travel from Neuraxpharm and Roche.

P1601
Feasibility and Safety of Transcranial Magnetic Stimulation in Multiple Sclerosis

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Introduction: Variables derived using transcranial magnetic stimulation (TMS) applied over the motor cortex serve as neurophysiological biomarkers of the corticospinal tract; a heavily myelinated pathway commonly affected in MS. Like other types of non-invasive brain stimulation, there are associated risks with TMS. In order for the tool to be used as a biomarker, it must be feasible and safe in a clinical setting.
Objectives/Aims: Therefore, we examined the frequency and reasons for TMS session ineligibility (i.e., feasibility) and described adverse events (i.e., safety) in people living with MS.
Methods: We assessed eligibility using an international consensus screening form, and adverse events were categorized as mild/moderate or severe/life-threatening.
Results: Our sample included 316 TMS sessions involving single pulse stimulation to the motor cortex of 152 participants living with MS. On average, sessions included individuals who were 47.75 ± 11.1 years of age and had a disease duration of 14.06 ± 8.4 years. Relapsing-remitting was the most common disease subtype, and we included 219 (69%) females. In terms of feasibility, 21 participants (n = 295) were ineligible; the most common reasons included being prescribed a contraindicated medication (n = 7), having a history of seizures (n = 5) or a diagnosed seizure disorder (n = 4). Twelve participants did not complete TMS despite being eligible. With regards to TMS safety, of the 283 remaining TMS sessions, there were no serious adverse events, but seven sessions involved a mild adverse event (fatigue (n = 4) and discomfort (n = 3)). Peak stimulation intensity (but not session time or number of pulses provided) was significantly higher in those who experienced an adverse event (74.57% ± 13.8 versus 61.25% ± 17.7 maximum stimulator output; $p = .038$).
Conclusion: We conclude that TMS is feasible and safe in people living with MS if the proper screening procedures are followed - supporting its broader usage as a neurophysiological biomarker of corticospinal function.

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P1602
The role of hormones in MS progression: insights from a two-year prospective cohort

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Introduction: Hormonal factors have emerged as potential modulators of multiple sclerosis (MS) progression

Objectives/Aims: This study aimed to evaluate the associations between circulating hormone levels and clinical, radiological and biomarkers in MS patients.
Methods: A two-year prospective study was conducted in a cohort of 105 MS patients (63 females, including 27 postmenopausal, and 42 males). Participants underwent standardized neurological and cognitive evaluations as well as 3 Tesla (3T) brain MRI using deep learning-based volumetric software. Serum analysis included 25 (OH)-vitamin D, thyroid-stimulating hormone (TSH), neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), and sex-specific hormones (testosterone in men; estradiol, follicle-stimulating hormone [FSH], progesterone, and anti-Müllerian hormone [AMH] in women). Spearman correlations and age-adjusted partial correlations were computed, with subgroup analyses stratified by gender and age.
Results: In the overall cohort, testosterone showed a strong positive correlation with total gray matter volume ($\rho = 0.57$, $p < 0.001$) and a moderate correlation with whole brain volume ($\rho = 0.33$, $p = 0.001$). FSH was significantly associated with GFAP ($\rho = 0.26$, $p = 0.01$) and inversely correlated with gray matter volume ($\rho = -0.35$, $p = 0.0005$). Conversely, 25(OH) vitamin D, TSH, estradiol, progesterone, and AMH exhibited only weak correlations with Expanded Disability Status Scale (EDSS) progression and other imaging or biomarker endpoints. In age-stratified analyses, women under 50 years exhibited stronger association between FSH, estradiol, and progesterone levels and neuroprotective outcomes, which were attenuated in those aged 50 years or older. Notably, association between testosterone and brain volumetrics remained robust and independent of age
Conclusion: Baseline serum levels of testosterone and FSH are independently associated with structural brain metrics and clinical progression in MS. These findings underscore a potential modulatory role of sex hormones in MS evolution and warrant further investigations into hormone-based therapeutic strategies.

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P1603
From Neural Adaptation to Network Collapse: EEG Functional Connectivity Signatures of Cognitive Reserve in Multiple Sclerosis

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Introduction: MS is characterised by adaptive functional reorganisation of brain networks. However, as neural resources are depleted, this reorganisation becomes insufficient, leading to network collapse. Cognitive reserve (CR), shaped by intellectually enriching experiences, reflects the brain's adaptability to pathology. Yet, its electrophysiological correlates in people with MS (PwMS) remain underexplored.
Objectives/Aims: To investigate how CR is reflected in the functional brain organisation of PwMS using resting-state EEG (rsEEG).
Methods: Cognitive assessments and rsEEG recordings were obtained from 72 PwMS (13 males; 53 RRMS, 19 PMS; age: 41 ± 11.56 years, EDSS: 2.99 ± 1.54; disease duration: 9.88 ± 8.85 years) and 40 age- and sex-matched healthy controls (HC; 10 males; age: 39 ± 11.41 years). PwMS were grouped into high (CR_H) and low (CR_L) CR based on CR Index questionnaire scores. Local and global (average) functional connectivity was estimated in the delta, theta, alpha1, alpha2, and beta bands, using the Phase Lag Index (PLI). MS groups were compared on demographics and disease characteristics. CR_L, CR_H, and HC were compared on cognitive performance and global PLI (gPLI), with multiple comparisons corrections. Where gPLI differed by band, local PLIs were compared via permutation testing, controlling for sex and MS type where applicable.

Results: Relative to CR_H, CR_L comprised more males (p=0.006) and progressive cases (p=0.003). Compared to HC, CR_H showed reduced performance in processing speed (PS), attention and verbal fluency (VF), while preserving verbal (VM) and visuospatial memory (VSM), and CR (*adjusted-p*<0.05). In contrast, CR_L exhibited preserved VSM but declined VM, PS, attention, and phonemic VF. They also showed reduced semantic VF (SVF) and CR (*adjusted-p*<0.05), along with higher theta-band gPLI compared to both HC and CR_H (*adjusted-p*=0.039). Locally, CR_L demonstrated hyperconnectivity within and between the default mode (DMN) and somatosensory network (SMNs), and between DMN, SMN and the dorsal and ventral attention and visual networks.
Conclusion: Our findings suggest that high CR in PwMS is linked to preserved functional organisation, supporting memory retention despite disease burden. In contrast, low CR is associated with widespread hyperconnectivity—potentially reflecting inefficient compensatory mechanisms—which may precede or coincide with network collapse and cognitive decline. These electrophysiological markers highlight CR's critical role in modulating MS-related brain network integrity.

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P1604
Preliminary Results of Long-Term Home-Based Smartphone Monitoring in Multiple Sclerosis

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Introduction: Smartphone applications in MS address the limited ecological validity of clinical outcomes by enabling frequent real-life monitoring. To translate these tools for routine disease monitoring, it is critical to establish normative expectations for long-term use.
Objectives/Aims: Here, we present an overview of preliminary findings of long-term digitally measured outcomes.
Methods: We reassessed subjects of the APPS-MS cohort 5 years (5y-FU) after their initial baseline study visit (BL). Participants used the MS sherpa app (smartphone 2-Minute Walk Test (s2MWT) and smartphone SDMT (sSDMT)) and Neurokeys app (keystroke dynamic clusters for upper motor function (KD-MSC) and cognition (KD-CSC)) at the initial study visit and for 21 days at 5y-FU. Clinical assessment included an Expanded Disability Status Scale (EDSS), Timed 25-Foot Walk (T25FW), 9-Hole Peg Test (HPT), and oral Symbol Digit Modalities Test (SDMT) performed at BL and 5y-FU. We compared 1) the average of ten BL s2MWT and ten sSDMT trails, with the average of s2MWT and sSDMT trails at 5y-FU, and 2) two week median KD-MSC and KD-CSC aggregates at BL and 5y-FU. We used paired samples T-tests and Wilcoxon signed-rank sum tests.
Results: 83 of the 102 participants of the initial APPS-MS study completed the follow-up after 5.3y (SD:0.3). At BL there were 73.5% females, mean age was 47.6y (SD:10.4), and disease duration was 9.1y (IQR:5.0- 17.1). 60.2% had relapsing-remitting, 27.7% secondary-progressive, and 12.0% primary progressive MS. At BL median EDSS was 3.5 (IQR:2.5-4.0), SDMT 54.6 (SD:10.4), T25FW 4.7s (IQR:4.1-5.7), HPT 21.05s (IQR:19.35-23.26), s2MWT 138m (SD:38.1), sSDMT 49.8 (SD:7.9), KD-MSC 0.47s (SD:0.22), and KD-CSC 0.95s (SD:0.37). At 5y-FU, three participants converted to secondary progressive MS. At follow-up, the SDMT (57.3, SD:12.5, p=0.009), sSDMT (53.0, SD:8.8, p<0.001), and KD-CSC (1.10s, SD:0.47, p=0.035) were higher compared to baseline. The EDSS (3.5, IQR:2.5-6.0, p=0.301), T25FW (5.1s, IQR:4.5-6.3, p=0.088), HPT (20.42s, IQR:18.84-24.34, p=0.603), s2MWT (148m, SD:45.5, p=0.055), and KD-MSC (0.49s, SD:0.25, p=0.590) were not significantly different.
Conclusion: This study reports on group-level, clinically measured motor function and cognition, and provides an overview of long-term digitally acquired outcomes. Future research in this cohort should aim at anchoring smartphone-measured progression to clinical domains and atrophy on brain MRI.

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(payments to institution); adjudication committee of MS clinical trials of Immunic (payments to institution).; M.M. Schoonheim serves on the editorial board of Neurology, Multiple Sclerosis Journal and Frontiers in Neurology, receives research support from the Dutch MS Research Foundation, Eurostars-EUREKA, ARSEP, Amsterdam Neuroscience and ZonMW (Vidi grant, project number 09150172010056) and has served as a consultant for or received research support from Atara Biotherapeutics, Biogen, Celgene/Bristol Meyers Squibb, EIP, Sanofi, MedDay and Merck; E.M.M. Strijbis reports speaker relations with Merck and Novartis (all payments to institution).

P1605
Cortical excitability and cognitive impairment in individuals with Multiple Sclerosis (MS)

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Introduction: This study investigates cortical excitability and cognitive impairment in individuals with Multiple Sclerosis (MS) compared to matched healthy controls.
Objectives/Aims: Our aim is to explore their interrelationship and implications for disease pathology and management.
Methods: We assessed 44 individuals diagnosed with MS and a matched control group of 44 healthy participants. Cortical excitability was measured using transcranial magnetic stimulation (TMS), while cognitive performance was evaluated using standardized neuropsychological tests targeting memory, attention, and executive function. Demographic and clinical variables, including disease duration and disability scores, were analyzed to control for potential confounders.
Results: Participants with MS exhibited significantly altered cortical excitability parameters, including reduced motor threshold and increased intracortical facilitation, compared to healthy controls ($p < 0.05$). Cognitive assessments revealed deficits in attention, memory, and executive functioning among the MS group, with moderate to strong correlations observed between cortical excitability measures and cognitive performance ($r = 0.4–0.6$, $p < 0.01$). These relationships persisted after adjusting for age, education, and disease severity.
Conclusion: This study highlights the interplay between cortical excitability and cognitive impairment in individuals with MS, suggesting a potential neurophysiological basis for cognitive deficits in this population. These findings underscore the importance of integrating neurophysiological assessments into clinical evaluations and exploring interventions targeting cortical excitability to mitigate cognitive decline in MS.

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P1606
Unraveling Genetics and B-Cell Dynamics: FCGR3A-V158F Polymorphism Does Not Predict Rituximab Response in NMOSD

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Introduction: Rituximab (RTX), a monoclonal antibody targeting CD20, has shown potential in managing neuromyelitis optica spectrum disorders (NMOSD) by depleting B cells and reducing relapse rates. However, there is no established consensus on the optimal dosing regimen for RTX, and genetic factors, particularly the FCGR3A-V158F polymorphism, may influence treatment outcomes.
Objectives/Aims: This study aims to examine the effect of FCGR3A-V158F genotypes on the efficacy of RTX in European NMOSD patients receiving a uniform treatment regimen
Methods: A retrospective analysis was conducted involving twelve European NMOSD patients who underwent FCGR3A-V158F genotyping and were followed for at least five years.
The genotypes of FCGR3A-V158F were determined, and the treatment responses were assessed, including relapse rates, time to first relapse (TFR), B-cell depletion, and treatment retention.
Results: Among the analyzed patients, seven received standardized doses of Rituximab. Patients were assessed every six weeks for the total percentage of CD27 in peripheral blood over five years. A booster dose was administered if the percentage exceeded 0.05 during the first year or 0.1 in subsequent years. Among the FCGR3A-V158F genotypes, one patient displayed the FF genotype, four had the VF genotype, and two had the VV genotype. Regardless of genotype, no significant differences were observed throughout the five-year follow-up in the number of relapses, early relapses, progression of the Expanded Disability Status Scale (EDSS), or the number of Rituximab doses based on CD27 repopulation.
Conclusion: This small study indicates that there is no correlation between CD27 depletion and its subsequent repopulation concerning the various FCGR3A-V158F genotypes. It is advisable to employ standard-dose RTX therapy and vigilant monitoring of peripheral blood B-cell levels for these individuals to optimize treatment effectiveness.

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P1607
Transorbital sonography in multiple sclerosis patients: correlations with visual evoked potentials

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Introduction: The eye plays a crucial role in multiple sclerosis (MS): approximately 70% of MS patients experience optic neuritis during the relapsing-remitting phase, optic nerve has been proposed as the fifth topography to confirm dissemination in space in the updated MS diagnostic criteria and retinal changes are found to reflect global neuroaxonal degeneration. While research on assessing visual pathway involvement in MS is expanding, transorbital sonography (TOS) remains underexplored.
Objectives/Aims: This study aims to investigate the correlations between visual evoked potentials (VEPs), a well-established technique for evaluating optic pathway involvement, and TOS measurements in MS patients.
Methods: Adult MS patients without a history of other neurological disorders, psychiatric comorbidities, or ocular pathologies (other than optic neuritis) were recruited. Patients underwent full-field pattern reversal VEP testing using 30' and 15' checkerboard patterns. Latencies of the N75, P100, and N145 peaks, the duration of the N75-N145 complex and the amplitude of the P100 wave were analyzed. For TOS measurements, the optic nerve diameter (OND) was measured 3 mm from the retina, at a 90-degree angle relative to the optic nerve axis. In statistical analyses, each patient's eye was analyzed separately.
Results: 38 eyes of 19 relapsing-remitting MS patients were included. Thirty-one eyes had no history of MS-associated optic neuritis (MSNON), while 7 had (MSON). A significant negative correlation was found between OND and the N145 peak latency (p=0.010) and between OND and the duration of the N75-N145 complex (p=0.045) for 15' VEPs in MSNON eyes.
Conclusion: Despite the small sample size, the observed correlations suggest that TOS may be a valuable tool for assessing visual pathway involvement in MS. Larger studies are needed to confirm these findings and further explore the potential role of TOS in clinical practice.

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Imaging & Non-Imaging Biomarkers – Big data and bioinformatics

P1608
Associations of the plasma lipidome with multiple sclerosis susceptibility and severity: a two-sample Mendelian randomisation study

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Introduction: Recent evidence suggests that circulating metabolite levels may correlate with multiple sclerosis (MS) risk and severity, yet causal relationships remain unclear.
Objectives/Aims: Our study employs two-sample Mendelian randomization (MR) to investigate the causal effect of metabolic exposures on MS risk and severity.
Methods: Genetic instruments for 249 metabolites, predominantly lipids and lipoproteins, were obtained from a combined dataset of 599,249 European individuals from the UK and Estonian Biobanks. Outcome data were obtained from the IMSGC MS susceptibility GWAS and the IMSGC MS severity GWAS. MR analyses considered MS risk and severity as distinct outcomes. We utilized the inverse variance-weighted (IVW) multiplicative random-effects method, and sensitivity analyses, including heterogeneity testing, pleiotropy assessment, and MR-PRESSO. Multiple comparisons were adjusted for by applying the number of effective tests from the metabolite correlation matrix to the Bonferroni correction.
Results: No metabolic exposures demonstrated statistically significant evidence of a causal relationship with MS susceptibility. For MS severity, two traits showed suggestive associations – triglycerides in very-low-density lipoproteins (VLDL) (b = -.101, p = .013 cor.) and triglycerides in chylomicrons and extremely large VLDL (b = -.104, p = .040 cor.).
Conclusion: Our findings suggest that genetic predisposition to higher triglyceride content in VLDL may correlate with a lower severity of MS. These results do not align with existing observational data, which indicate that lipids in VLDL, particularly cholesterol, positively correlate with age-adjusted disability. We are undertaking further work to clarify this discordance, which may offer further insights into the contribution of the plasma lipidome to disability in MS.

Disclosure of interest: Jakub Nagrodzki: nothing to disclose. Ruth Dobson: received honoraria for speaking and/or traveling from Biogen, Esai, Merck, Teva, Janssen, and Sanofi. She served on advisory board of Roche, Biogen, Janssen, sandoz and Merck. She has received grant support from Biogen, Merck, Celgene, Barts Charity, the UK MS Society, NMSS, MRC, and the Home Family Charitable Trust. Benjamin Jacobs: nothing to disclose.

P1609
Association of smartphone-based step count monitoring and disability scales in patients with Multiple Sclerosis

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Introduction: Walking impairment is one of the major causes of disability in MS. Although widely used, the Expanded Disability Status Scale (EDSS) has limitations to detect subtle yet clinically significant changes in ambulatory function. Daily step count measured by wrist sensors has emerged as a promising tool for MS follow-up.
Objectives/Aims: We aimed to study the correlation between median daily step count (mDSC) obtained through smartphone and baseline disability scales in patients with MS, such as EDSS, 9-hole peg test (9HPT), timed 25-foot walk (T25FW) and Processing Speed Test CogEval® (PST) raw and Z-score.
Methods: Single-centre transversal study in patients with MS, excluding patients with an EDSS score of >6.5. We passively assessed the mDSC measured by an in-house smartphone application for two weeks and included patients with at least five valid days in such period (a valid day was defined as one in which participants took 128 steps or more). Correlations between mDSC and baseline disability measures were obtained with Spearman's rho and multivariable linear regression models (including age and mDSC).
Results: Of the 70 patients recruited, 64.3% were women, with a median age of 44.5 years old (IQR: 40.1-52.1) and a median EDSS score of 2.5 (IQR:1.5-4.5). Distribution by MS subtypes was: 84.3% relapsing-remitting MS, 12.9% secondary-progressive MS and 2.8% primary-progressive MS. Most patients (78.5%) were under disease-modifying treatments, of which 43.6% received high-efficacy therapies. mDSC showed a negative correlation with median EDSS score (-0.33, p=0.005), 9HPT (-0.30, p=0.01) and T25FW (-0.45, p=0.0001), while no significant correlation was found with cognitive scales (PST raw and Z-score). Linear regression models revealed that mDSC was independently associated with EDSS score, 9HPT and T25FW.
Conclusion: Step count measured through our smartphone correlated with motor baseline disability scales and could provide a useful assessment of ambulatory function.

Disclosure of interest: None

P1610
Real-World Gait Monitoring in MS: A Smart Insole Framework for Data-Driven Gait Quality Assessments

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Introduction: Gait patterns of persons with multiple sclerosis (PwMS) reveal important insights about their disability status, making spatiotemporal (ST) gait metrics valuable digital biomarkers for monitoring disease progression. However, their practical use is limited by time intervals between collections, technology (e.g., cost, capture volume), and the need for expert interpretation. A more cost-effective and user-friendly solution is required to evaluate real-world gait quality in PwMS.
Objectives/Aims: To demonstrate an instrumented shoe Insole Framework (IF) that identifies activities, detects gait events, and calculates ST metrics to produce a gait composite index (GCI; 0-100%) that holistically evaluates gait quality and assesses fatigue-related changes.
Methods: Nineteen healthy non-MS controls (HC) and 40 PwMS were recruited; 21 PwMS walked up to 15 minutes three times a week in free-living conditions; HC and 19 PwMS performed one day of in-lab testing (six- and 500-meter walks, stair navigation). All participants wore instrumented shoe insoles (pressure + inertial measurement units; 50 Hz; ReGo, Moticon, Germany) that streamed raw data to a smartphone application (Celestra Health Systems, Canada). Laboratory data were used to validate the gait detection algorithms, train a neural network (NN) to identify ambulatory activities (stand, walk, turn, stair ascend/descend), and train a support vector machine (SVM) to project gait data on a decision plane that classifies individuals as HC or PwMS, which is used to generate the GCI via z-scores. Spearman correlations compared the GCI to the free-living participants' disability metrics: expanded disability status scale (EDSS), 12-item multiple sclerosis walking scale (MSWS12), symbol digit modalities test (SDMT), nine-hole peg test (9HPT), and the timed 25-foot walk (T25FW). A linear mixed model tested for changes in GCI over 500 m.
Results: The NN identified activities with an accuracy of 94.6%. ST algorithms were validated against motion capture (average $ICC_{2,1} = 0.862$). The SVM recorded 90.3% accuracy and 92.8% F1 score. GCI correlations to EDSS, MSWS12, SDMT, 9HPT, and T25FW were -0.840, -0.817, 0.752, -0.666, and -0.792. When correlating EDSS to MSWS12, SDMT, 9HPT, and T25FW, Spearman Rho values were 0.835, -0.566, 0.600, and 0.797. Nine PwMS increased and 10 decreased their GCI over 500 m, resulting in a significant GCI group * distance interaction ($p < 0.001$); the average response was a GCI decrease ($p = 0.015$).
Conclusion: The IF can accurately identify ambulatory activities and gait events to assess gait quality in free-living environments. The resulting GCI strongly correlates with disability metrics and is, on average, 0.046 higher than the corresponding EDSS correlations. The IF can identify significant changes in gait quality decrease during prolonged walking. This innovative solution may be ideal for monitoring real-time disease progression in PwMS.

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Machine Learning-Generated Longitudinal Synthetic International Data in Multiple Sclerosis

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Introduction: Data scarcity and privacy concern impedes research requiring large datasets in neurology. Synthetic data holds the promise of facilitating research that requires significant analytical power. Longitudinal data in MS represents a significant challenge, because of the high complexity of this neurological condition.

Objectives/Aims: This study presents a dual generative framework to produce a synthetic MS data, assessing their utility in predictive modelling, and the credibility of the generated synthetic data.

Methods: We used the MSBase data to train two models: an autoencoder for cross-sectional data, which used clinico-demographic information from 77,215 patients, and a Long Short-Term Memory model for longitudinal data, which was trained on 261,939 patient sequences. The process was used to generate 2.8 million synthetic patient records.

Results: Synthetic cross-sectional data generated by the autoencoder showed a mean age at onset of 31.6 years (SD:10.5), a mean disease duration of 6.89 years, and a female prevalence of 70.54%, closely matching the real dataset. A Kolmogorov-Smirnov test for age at onset showed no significant difference (p=0.85, statistic=0.0022).The synthetic EDSS distribution (mean:2.95, SD:2.06) similarly approximated the real data. Spearman correlation analysis revealed preserved intra-variable relationships, with synthetic correlation coefficients (r=0.248–0.329) aligning well with those of the real dataset. LSTM-generated longitudinal data exhibited a mean follow-up duration of 8.9 years (95% CI:8.7–9.1), an annualized relapse rate of 0.19, and a treatment distribution of 13.2% Ocrelizumab across all visits in the synthetic predictions, closely matching the real data and demonstrating strong alignment with actual treatment patterns. Spearman correlation analysis confirmed preserved intra-variable relationships in the synthetic data, with correlation coefficients (r=0.28–0.95) consistent with those observed in the real data.

Conclusion: Dual autoencoder-LSTM approach is suitable for generation of cross-sectional and longitudinal synthetic data in multiple sclerosis. This solution has the potential to augment research requiring large and representative clinical datasets.

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P1612
Smartphone-Derived Gait Biomarkers in Prodromal Multiple Sclerosis: A Preliminary Analysis

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Introduction: Early detection of prodromal indicators in multiple sclerosis (MS) is critical for prompt intervention. Given the rising usage of smartphones, passively collected digital health data, which has demonstrated reliability across multiple studies, may offer insights into modest pre-diagnostic mobility changes. Thus, the purpose of this study was to investigate the differences in mobility-related metrics between healthy and MS patients that were obtained from iPhone Health app data retrospectively, with an emphasis on the time before diagnosis or relapse.
Objectives/Aims: To determine the predictive potential of iPhone Health app data for MS diagnosis or relapse and its correlation with neurological clinical scales, aiming to explore the utility of existing measurements and big data in assisting MS patients.
Methods: Data from the iPhone Health app was gathered retrospectively from two MS patients and ten healthy controls. A custom software (Python/SQL) was developed to automate data processing and organization into a database. Weekly aggregations were elaborated and used to examine mobility metrics like step count, walking asymmetry, step length, and double support time. Pearson's correlations and group comparisons were part of the statistical analysis, and the results were displayed for interpretation (Excel; Power BI; JASP)
Results: Results indicated significant differences in gait dynamics between groups. For all participants, walking stability exhibited a positive correlation with walking speed ($r = 0.183$, $p < .001$) and a negative correlation with double support time ($r = -0.526$, $p < .001$). As opposed to the weaker, more biomechanically typical correlations seen in healthy controls, the MS group exhibited markedly stronger correlations between stability and multiple gait parameters (e.g., negative with step length, $r = -0.290$, $p < .001$; negative with double support time, $r = -0.465$, $p < .001$). These discrepancies between the groups imply that MS alters normal gait dynamics, which may be a result of compensatory mechanisms or greater gait variability that stem from neurological impairments and disability.
Conclusion: Smartphone-derived health data shows promise for detecting potential early gait abnormalities in MS. Although limited by the small sample size and retrospective design, highlight significant alterations in gait dynamics with particularly the interplay between stability, double support time, and step length in individuals with MS. These may serve as early digital biomarkers of prodromal MS. Larger-scale prospective studies are being conducted to validate these preliminary findings and determine their clinical value

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P1613
Multimodal predictors of functional and cognitive decline in relapsing-remitting multiple sclerosis

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Introduction: The underlying mechanisms for disease progression in relapsing-remitting multiple sclerosis (MS) are complex and incompletely understood.
Objectives/Aims: Multivariate and multimodal investigations integrating demographic, clinical, multi-omics, and neuroimaging data provide opportunities for detailed analyses, aimed to define markers of disease progression.
Methods: We used data from a 12-year longitudinal cohort of 88 people with MS (pwMS), to test the predictive value of multi-omics, MRI, clinical examinations, self-reports on quality of life

(SF-36), demographics, and general health-related variables for future functional and cognitive disability. Progressive functional loss beyond an Expanded Disability Status Scale (EDSS) score ⩾4 was used to define a functional loss group (FLG). A cognitive decline group (CDG) was defined by a ⩾25% decrease from the maximum (cognitive) Paced Auditory Serial Addition Test (PASAT) score of 60. We used a multiverse approach to identify which baseline variables were most predictive for functional and cognitive loss group memberships, while minimizing analysis bias.
Results: We identified several factors predicting an increased risk of future FLG and CDG within 12 years after baseline, including a higher EDSS (0-10, median Odds Ratio per baseline unit increase [mOR_{FLG}=2.15±0.51; mOR_{CDG}=2.46±1.60]), PASAT score (1-60 [mOR_{FLG}=0.98±0.03; mOR_{CDG}=0.91±0.06]), number of previous relapses [mOR_{FLG}=1.56±0.26; mOR_{CDG}=1.44±0.60], lower serum vitamin A levels (umol/l [mOR_{FLG}=0.92±0.06; mOR_{CDG}=0.33±0.36]), as well as worse self-reported mental health (1-100 [mOR_{FLG}=0.96±0.02; mOR_{CDG}=0.91±0.09]) and physical functioning (1-100 [mOR_{FLG}=0.99±0.01; mOR_{CDG}=0.97±0.03]). At the same time, we observed analysis-choice induced variability.
Conclusion: Our results suggest that clinical assessments of physical function and cognition, self-reported mental health as well as physical functioning, and potentially vitamin A levels are the best predictors for risk-group stratifications of pwMS at baseline. Our study showcases a strategy to circumvent bias originating from analyses choices.

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P1614
Artificial Intelligence Driven Prediction of Cognition Using Estimated Structural and Functional Connectivity in Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS) is a chronic autoimmune disorder that causes ambulatory and cognitive impairment. Approximately 40-65% of MS patients suffer from varying levels of cognitive impairment. Advanced neuroimaging biomarkers such as structural and functional connectivity offer a valuable tool to identify patients who are more likely to develop cognitive impairment, enabling more personalized treatment plans to prevent or delay cognitive impairment. Our prior work demonstrated that estimated structural and functional connectomes (eSC and eFC) generated using multiple sclerosis (MS) lesion masks and artificial intelligence (AI) models can predict disability as effectively as SC and FC derived from diffusion and functional MRI in MS.
Objectives/Aims: The goal of this study was to assess the ability of eSC and eFC and artificial intelligence in predicting baseline and 4-year follow-up cognition in MS patients.
Methods: One hundred seventy-one MS patients (age: 42.67±10.41, 74% females) were included. The Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT), and Brief Visuospatial Memory Test (BVMT) were used to assess cognition. The Network Modification tool was performed to estimate SC, which was then used as an input to Krakencoder, an encoder-decoder model, to estimate FC. Ridge regression was performed to predict cognition using regional and pairwise eSC and eFC, along with demographics and clinical information as well as conventional MRI metrics. Baseline cognition was added to the models that were used to predict the follow-up cognition. Spearman's correlation (r) was used to assess the prediction accuracy.
Results: The highest accuracy was obtained when predicting follow-up SDMT using regional eSC or eFC (median r=0.58 for eSC and r=0.56 for eFC), which is similar to or exceeds performance reported in prior studies predicting cognition in MS patients or healthy controls. Decreased eSC and eFC in the cerebellum and increased eFC in the default mode network were associated with lower follow-up SDMT scores. Baseline SDMT, clinical subtype, and age were the most important non-connectome metrics in predicting follow-up SDMT. Among the pairwise models, the pairwise eFC outperformed the pairwise eSC in predicting the baseline and follow-up SDMT and BVMT.
Conclusion: Our findings demonstrate that eSC and eFC derived from clinically acquired MRI and AI models can effectively predict cognition. This work highlights the potential for using connectome mapping in the clinic to make personalized treatment plans aimed at preserving cognition in people with MS.

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P1615
Machine learning-based prediction of new neurological lesions in multiple sclerosis using routinely collected clinical and patient-reported data

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Introduction: MRI is the gold standard for detecting new neurological lesions in multiple sclerosis (MS), but its use is costly and logistically demanding. Identifying patients at low risk of new lesions could help optimize MRI scheduling.
Objectives/Aims: To develop a machine learning (ML) model capable of predicting the presence of new MRI-detected lesions in MS patients using clinical and patient-reported data, prioritizing sensitivity to minimize false negatives.
Methods: A cohort of 240 MS patients from a second-level hospital in Spain was followed prospectively over 18 months. Clinical data (CROs), PROMs (MSIS-29, HAQ, FSS, Neuro-QoL), and baseline variables were collected. Due to class imbalance (only 11 positive cases), we applied ADASYN oversampling. Classification models tested included Random Forest, Support Vector Machine (SVM), and XGBoost. Variables were selected based on feature importance from initial model iterations. The final models were evaluated for sensitivity and precision across PROMs, CROs, and combined (All-data) subsets.
Results: The PROMs-based Random Forest model achieved 64% overall accuracy with 100% sensitivity and 0 false negatives. The CROs-based model reached 69% accuracy, also with 100% sensitivity. The All-data model improved precision (72% accuracy), maintaining perfect sensitivity. The best feature combinations included MSIS-29, HAQ, disease evolution form, prior exacerbations, and spinal lesions at diagnosis. For CROs, relevant variables were recent exacerbations, gender, and initial MRI findings.
Conclusion: ML models can accurately identify patients at risk of developing new lesions using clinical and self-reported data. The PROMs-based model achieved perfect sensitivity, making it suitable for remote risk stratification. These tools may support MRI decision-making, reducing unnecessary imaging and associated healthcare costs without compromising patient safety.

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P1616
Identifying causal genes for multiple sclerosis and neuromyelitis optica via integrating multi-omics

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Introduction: Genome-wide association studies (GWAS) have been increasingly popular for identifying numerous loci associated with multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD).
Objectives/Aims: In this study, an integrative analytical pipeline was performed to efficiently transform genetic associations to identify causal genes as potential therapeutic targets for MS and NMOSD.
Methods: Utilizing the multidimensional high-throughput data generated, we integrated proteome-wide association studies (PWAS), transcriptome-wide association studies (TWAS), Mendelian randomization (MR) and Bayesian co-localization analysis to prioritize genes that contribute to MS and NMOSD through affecting their protein and mRNA abundance in brain and blood. A Protein-protein interaction (PPI) network was constructed to explore the interactions between the above identified genes and the targets for current MS and NMOSD medications.
Results: Simultaneously meeting the requirement of PWAS, TWAS, MR and Bayesian co-localization analysis, TSFM and TYMP were demonstrated to be causal for MS in brain and blood respectively. Additional potential causal genes for MS mainly included IFI30, TYMP, FAM213B, OGFOD2, TRAF3, ZC2HC1A, SCO2, MYO19, METTL21B, and CASQ1 in the brain and CD58, AHI1, CD37, MMEL1 and FCRL3 in the blood. Notably, TYMP was the only overlapped gene identified both in brain and blood. For NMOSD, SLC17A5 was identified as a causal in both the brain and blood, meeting the requirement of TWAS, MR and Bayesian co-localization analyses.
Conclusion: This study identifies TSFM and TYMP as causal genes for MS, influencing both protein and gene expression level, while SLC17A5 is implicated as a causal for NMOSD by influencing gene expression level. These findings provide a foundation for future animal studies and prioritize targets for immunotherapy.

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P1617
Intestinal bacteria at the onset of Multiple Sclerosis can predict disease worsening within one year

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Introduction: Dysbiosis of the gut microbiome has been linked to Multiple Sclerosis (MS). However, if the composition of gut bacteriome influence disease severity and progression remains unknown.
Objectives/Aims: This study aimed to determine whether specific taxa were associated with different MS- related clinical parameters.
Methods: Stool samples were collected from 53 MS patients at disease onset and used for metagenomic sequencing. Demographics (age, sex, BMI) and clinical parameters such as type of onset, Expanded Disability Score Scale (EDSS) score, presence or absence multifocal, spinal, and infratentorial lesions, gadolinium-enhancing lesions, low or high lesion load were collected at baselines. Exposure to DMT, worsening in EDSS, relapses, or new MRI lesions were also recorded during a 12-months follow-up.
Results: Gut bacteriome analysis revealed the differential abundant species (DAS), associated with clinical features. We identified specific taxa associated with number of lesions, presence of spinal cord lesions, gadolinium-enhancing lesions and infratentorial ones. Based on these data, we could develop a score that was used for patient clustering. This score was sufficient to stratify patients into two or more distinct clusters and to predict disease progression in our cohort. Interestingly, five species showed differential abundance between the cluster with a favorable outcome and the one with a worse outcome over the one-year follow-up period
Conclusion: Our data suggest that gut microbiome could be used as a novel prognostic biomarker at the onset of MS. Further studies, increasing the follow-up period and considering the effect of therapies, will allow us to identify an effectively predictive core microbiome.

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P1618
Understanding the significance of serum neurofilament light chain across MS phenotypes: preliminary findings from a data-driven clustering analysis using unsupervised machine learning

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Introduction: Multiple Sclerosis (MS) is characterized by marked heterogeneity and disease modifying therapies (DMT) variably target relapses, progression, and progression independent of relapse activity (PIRA). This variability is difficult to predict or quantify in clinical settings. Understanding the determinants of PIRA—especially as radiological disease control improves with highly effective therapies—is critical to addressing this clinical heterogeneity. There is a need for reliable, quantifiable biomarkers that correlate with disease progression and outcomes. Serum neurofilament light chain (sNfl) has emerged as a potential biomarker of both progression and inflammatory disease activity in MS. While sNfl dynamics have been studied in other neurodegenerative diseases, in MS, their specific significance and temporal evolution across MS phenotypes remains unclear.
Objectives/Aims: The primary objective of this study is to identify novel subgroups of people with MS using sNfL levels and PIRA status via unsupervised clustering. It is hypothesized that multiple distinct phenotypes can be identified. Secondary objectives are to identify clinical and radiological determinants of cluster membership and compare these data driven phenotypes with conventional MS phenotypes.
Methods: This is a retrospective observational cohort study. Participants include individuals aged 18–60 with any MS phenotype followed at the London Ontario MS Clinic, with at least one sNfl measurement, and temporally corresponding clinical assessment and MRI. Age, sex, disease duration, MS phenotype, DMT use, EDSS, timed 25-foot walk, and presence of PIRA or progression independent of relapse and magnetic resonance imaging (PIRMA) are recorded. They are compared between the clusters.
Results: A total of 163 people with MS met the inclusion criteria. Mean age is 46.7 years (10.2 SD); 122 were females. Median sNfl level was 1.34 (range 0.5-12.70). Time series k-means clustering was performed using the Scikit-learn package on Python. Using sNfl, PIRA status, and disease duration as input features, three distinct clusters were identified based on the elbow plot and a silhouette score of 0.61 (range: -1 to 1, where 1 indicates maximum separability).
Conclusion: Redefining MS progression phenotypes to account for both clinical and temporal variances is an important and timely approach, where artificial intelligence (AI) methods offer a novel framework for deciphering disease heterogeneity. The preliminary findings suggest that unsupervised clustering can identify distinct patient groups based on sNFL and progression markers, independent of traditional MS phenotype labels. Future work will focus on identifying predictors of cluster membership and examining their longitudinal trajectories, with the goal of improving individualized care and outcomes in MS.

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P1619
Deciphering the immunosuppressive role of monocytic myeloid-derived suppressor cells in MS lesions: a dual approach combining traditional versus AI-driven methods

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Introduction: Monocytic myeloid-derived suppressor cells (M-MDSCs) represent an important component of the regulatory mechanisms in immune-mediated diseases like MS. Our group has described the presence of M-MDSCs associated with high inflammatory areas of MS lesions. Interestingly, the density of M-MDSCs is higher in progressive MS patients with a milder clinical course according to the disease duration. Notably, the role of M-MDSCs in MS is also a matter of debate, as circulating M-MDSCs exhibit clear suppressive activity in relapsing-remitting MS patients, which is lost or reversed in progressive patients. Despite these findings in the peripheral blood, assessing the *in situ* activity of M-MDSCs in MS lesions remains controversial, due to the lack of direct functional assays in human tissue. However, indirect approaches are available to infer the immunosuppressive function of M-MDSCs, such as evaluating T cell apoptosis, their canonical target, as well as the presence of CD84, a described marker of their immunosuppressive activity.
Objectives/Aims: We aim to perform the morpho-functional evaluation of M-MDSC and its association with MS severity in demyelinating lesions using two different approaches
Methods: CNS samples from 17 MS patients with varying disease duration were used to detect M-MDSCs and T cells by immunohistochemistry. The identification of immunosuppressive M-MDSCs and apoptotic T cells in demyelinating lesions will be approached using two methods: a) conventional M-MDSC of quantification by manual counting, and their association to the presence of $TUNEL^+$ $CD3^+$ T cells; b) automated quantification of CD84 expression in M-MDSCs through an AI-based neural network.
Results: The density of apoptotic T cells determined by manual counting increased in MS patients with milder clinical courses. The immunosuppressive function of M-MDSCs (assessed by both methods) will be correlated with the disease progression in each MS patient.
Conclusion: Both technical approaches for cell quantification will help us to analyse the functional activity of M-MDSCs in human tissue, shedding light on the relevance of their activity in the severity of MS clinical course.

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P1620
Correlation Between T1 Hypointense Lesions and Brain tissue segmentation in Multiple Sclerosis: A Multimodal Analysis

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Introduction: T1 hypointense lesions ("black holes") in Multiple Sclerosis (MS) indicate irreversible axonal damage and correlate with disease progression. While brain volumetry is a well-established neurodegenerative biomarker, the relationship between hypointense lesion volume and cerebral volumetric measures remains insufficiently characterized, particularly across different demyelinating conditions. This study investigates the correlation between these biomarkers to improve differential diagnosis and monitoring of disease progression.
Objectives/Aims: This study investigates the correlation between these biomarkers to improve differential diagnosis and monitoring of disease progression.
Methods: This study investigates the correlation between these biomarkers to improve differential diagnosis and monitoring of disease progression.

Results: MRI data from 132 patients, including 109 with relapsing-remitting MS and 23 with other demyelinating diseases, were analyzed. The mean hypointense lesion volume was 2,218.39 mm³, and the mean left hemispheric white matter volume was 232,658 mm³. A negligible correlation between lesion volume and white matter volume was found (r=-0.0970, p=0.267). MS patients exhibited significantly higher lesion volumes compared to other demyelinating diseases (12.4±8.7 cm³ vs. 5.2±4.3 cm³, p<0.001). Thalamic atrophy was more prevalent in MS patients (38%) versus other diseases (5%) (p=0.002). Stratification by disease duration revealed stronger correlations in patients with disease duration >10 years (r=-0.29, p=0.035).
Conclusion: These findings suggest that T1 hypointense lesion volume and white matter volume are weakly correlated, with regional atrophy playing a role independent of global white matter measures. Thalamic atrophy appears to be a promising discriminative biomarker for MS. Future studies should incorporate machine learning and longitudinal analysis to better capture complex patterns and evolution over time.

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THERAPY – Immunomodulation/ Immunosuppression

P1621
Safety and Efficacy of Extended Versus Standard Interval Dosing of Natalizumab in Relapsing-Remitting Multiple Sclerosis: An Updated Systematic Review and Meta-Analysis

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Introduction: Natalizumab is a high-efficacy monoclonal antibody used in relapsing-remitting multiple sclerosis (RRMS), but standard interval dosing (SID) is associated with a substantial risk of progressive multifocal leukoencephalopathy (PML) in JC virus (JCV)-positive patients. Extended interval dosing (EID) has been proposed to reduce PML risk while preserving clinical efficacy. This study aims to synthesize updated evidence on the comparative safety and effectiveness of EID versus SID in RRMS.
Objectives/Aims: To systematically evaluate the safety and clinical efficacy of extended interval dosing (EID) compared to standard interval dosing (SID) of natalizumab in patients with relapsing-remitting multiple sclerosis (RRMS), integrating data from randomized and observational studies.
Methods: We conducted a PROSPERO-registered (CRD42024612558), PRISMA-compliant systematic review and meta-analysis of PubMed, EMBASE, and Cochrane Library through November 2024, comparing extended (>4 weeks) versus standard (≤4 weeks) natalizumab dosing in adult RRMS patients, assessing MRI activity, clinical relapses, and PML risk using pooled odds ratios under a random-effects model.
Results: A total of 21 studies were included. EID showed a non-significant trend toward fewer new/enlarging T2 lesions (OR 0.68; 95% CI: 0.37–1.24; $p = 0.09$; $I^2 = 66\%$). No significant differences were found in Gd+ lesion incidence (OR 1.31; 95% CI: 0.74–2.34; $p = 0.25$; $I^2 = 25\%$) or clinical relapses (OR 0.95; 95% CI: 0.73–1.24; $p = 0.69$; $I^2 = 27\%$). PML risk was similar (OR 1.09; 95% CI: 0.16–7.27; $p = 0.91$), though limited by low event rates.
Conclusion: Extended interval dosing of natalizumab up to 8 weeks appears to maintain efficacy while potentially reducing PML risk in RRMS. Despite trends favoring EID, findings are limited by heterogeneity and low PML event counts. Further prospective studies are warranted to define optimal individualized dosing strategies.

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P1622
Besides B cells, CD19 is expressed on a fraction of T cells and monocytes, which are concomitantly depleted by anti-CD19 inebilizumab

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Introduction: The B cell-depleting anti-CD19 antibody inebilizumab was recently approved for the treatment of neuromyelitis optica spectrum disease (NMOSD). Inebilizumab effectively depletes $CD19^+$ B cells, since CD19 is expressed from the pro-B cell up until the plasma cells stage of B cell development and is considered a lineage marker for B cells.
Objectives/Aims: This study is focused on the question if there are other immune cell populations that can be depleted by inebilizumab.
Methods: First, we analyzed if there are other cell populations such as T cells and monocytes, which express CD19. We

isolated human peripheral blood mononuclear cells (PBMCs) or cells from murine primary and secondary immune organs and examined them via flow cytometry. Next, we analyzed the phenotype, cytokine expression, and developmental state of $CD19^+$ monocytes and T cells using flow cytometry. Samples from healthy controls were compared with multiple sclerosis patients and naïve mice were compared to experimental autoimmune encephalomyelitis (EAE)-induced mice to examined a potential pathogenicity of those cells. PBMCs from inebilizumab-treated NMOSD patients were analyzed via flow cytometry to see if $CD19^+$ T cells and monocytes are also depleted.
Results: $CD19^+$ T cells and $CD19^+$ monocytes could be found in human and murine samples. In comparison, $CD19^+$ T cells show enhanced features of pathogenicity both in mice, as well as in patients with MS. In wild-type mice, $CD19^+$ T cells could be shown to expand during EAE. Both $CD19^+$ T cells and $CD19^+$ monocytes can be depleted by anti-CD19 inebilizumab therapy.
Conclusion: CD19 can not only be found on the surface of B cells, but also on monocytes and T cells. Therefore, the anti-CD19 antibody inebilizumab is not as B cell-specific as so far assumed. The additional depletion of proinflammatory $CD19^+$ T cells may substantially support the effectiveness of inebilizumab therapy.

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P1623
Differential Impact of Ozanimod on Lymphocyte Subsets in Patients with Early Relapsing Multiple Sclerosis in the ENLIGHTEN Study

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Introduction: The therapeutic effects of ozanimod, a selective sphingosine 1-phosphate receptor modulator, may involve reduced lymphocyte migration into the central nervous system.
Objectives/Aims: To evaluate subsets of circulating lymphocytes in patients enrolled in the ENLIGHTEN trial who received ozanimod for 1 year.
Methods: ENLIGHTEN (NCT04140305) is a phase 3b, multicentre, open-label study of ozanimod 0.92 mg in adults with early relapsing multiple sclerosis (RMS). Whole blood samples taken at baseline and year 1 were tested on a flow cytometry panel to characterise circulating lymphocyte subsets. Wilcoxon-Signed-Rank two-sided tests determined significant changes from baseline, and Mann-Whitney U one-sided tests determined significant changes between cell types.
Results: Of 162 patients with lymphocyte measures at both baseline and year 1, 79% were female, 86% were White, and 68% were treatment naive. Mean (standard deviation [SD]) age was 39.7 (10.4) years, years since MS onset was 4.0 (5.6), and number of relapses in the prior 12 months was 0.8 (0.7). Significant ($P<0.05$) decreases from baseline were observed in levels of all lymphocyte subtypes examined. Ozanimod had significantly less impact on levels of natural killer cells (median % change from baseline: -16.1%) compared with $CD19^+$ B cells (-86.0%) and $CD3^+$ T cells (-84.5%), $CD4^+$ T cells (median -94.4%), and $CD8^+$ T cells (-71.3%) (all $P<0.0001$); $CD8^+$ T cells were impacted less than $CD4^+$ T cells ($P<0.0001$). Ozanimod had less impact on $CD4^+$ effector memory T cells (median % decrease: -90.9%) than CD4+ central memory T cells (-94.4%; $P=0.021$) and less impact on $CD8^+$ effector memory T cells (-61.1%) than CD8+ central memory T cells (-81.3%) ($P<0.001$). Finally, ozanimod also had less impact on $CD4^+$ and $CD8^+$ terminally differentiated T cells (median % decrease -61.6 and -21.7% respectively) compared with naive CD4+ and CD8+ T cells (-97.5% and -78.3% respectively), and on regulatory B cells (-45.9%) and transitional B cells (-58.5%) compared with memory B cells (-91.0%) (all $P<0.0001$).
Conclusion: The differential effects of ozanimod on circulating levels of immune cells permit inhibition of inflammation while maintaining immune surveillance. These results expand upon earlier findings in patients with RMS and Crohn's disease, which illustrated that the effects of ozanimod on lymphocyte subsets occurs by 3 months and remains stable with further treatment.

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P1624
Baseline characteristics of the Determining the Effectiveness of earLy Intensive Versus Escalation approaches for the treatment of Relapsing-remitting MS (DELIVER-MS) trial cohort

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Introduction: There is growing support for high-efficacy Disease Modifying Therapy (DMT) in treatment-naive people with relapsing remitting multiple sclerosis (RRMS), stemming from observational, real-world studies suggesting more favorable long-term disability outcomes. However, for many reasons, an Escalation (ESC) approach to DMT remains a commonly preferred option. A randomized trial is needed to establish the comparative effectiveness and safety of early highly effective (EHT) and ESC.
Objectives/Aims: We describe characteristics of the baseline DELIVER-MS cohort.
Methods: DELIVER-MS (NCT03535298) is a pragmatic randomized controlled trial (RCT) with a parallel observational study (OBS) comparing the clinical and radiological outcomes of people with early RRMS according to whether they received ESC or EHT as their initial DMT algorithm. The primary outcome is brain volume loss from baseline to 36 months. Participants who declined the randomized study were asked to provide a reason, allowing more than one reason per participant. Groups were compared using univariable logistic regression for each characteristic, p-values were derived from corresponding Wald tests. Multivariable logistic regression was used to examine the adjusted associations between baseline characteristics and: 1) participation in the RCT vs. OBS study, and 2) selection of EHT vs. ESC (within the OBS cohort).
Results: 816 people with RRMS were enrolled (modified intent to treat population: 393 in RCT and 374 in OBS cohort). EHT and ESC groups in the RCT were well balanced for demographic and clinical characteristics. People declined to randomize due to preference for a particular DMT (85%), efficacy concerns (20%), safety concerns (9%). Those entering the RCT had a higher white matter fraction on brain MRI (0.360 [0.022] versus 0.356 [0.024], p=0.009) than those entering the OBS cohort and were significantly less likely to randomize during pre-vaccine era of the COVID-19 pandemic ($p<0.001$). Overall, 125 (33%) of those entering the observational study chose ESC and 249 (67%) chose EHT. Prescribing practice differed significantly between US and UK sites with greater EHT use in the US (63% vs 37%, $p<0.001$). Regarding DMT selection, patients choosing *ESC* often cited *safety concerns*, while those opting for *EHT* were more frequently motivated by *efficacy*. The other factors predicting EHT commencement in the OBS cohort was higher educational attainment ($p<0.001$).
Conclusion: Our data demonstrate ongoing clinical equipoise between Escalation and High Efficacy approaches and support the ongoing need for an RCT to address whether all people with MS require first-line high-efficacy DMT.

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P1625
Disease-modifying therapies change the cellular composition of deep cervical lymph nodes of patients with multiple sclerosis

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Introduction: We previously showed an altered lymphocyte compartment within the deep cervical lymph nodes (dcLNs) of patients with MS (pwMS) at the diagnostic phase, before immunotherapy, compared to healthy controls. Whether disease-modifying therapies (DMTs) change the cellular composition of dcLNs, where lymphocyte targeting of central nervous system is suggested to be initiated, has not been explored.

Objectives/Aims: To investigate the dcLN immune cell subsets by frequency distributions of pwMS before and after DMTs.
Methods: We used fine needle aspirations (FNAs) of dcLNs followed by single-cell RNA sequencing (scRNAseq). We studied five patients across three treatment groups: two receiving dimethyl fumarate, two on rituximab or ofatumumab (B-cell depleting), and one on natalizumab (leukocyte trafficking inhibitor). We compared scRNAseq data sampled pre-treatment and at a stable follow-up time point from the same individual.
Results: We observed significant differences in the cell type frequency distributions (Pearson's Chi-squared test, p-value $<$ 2.2e-16), and evaluated the adjusted Pearson residuals to find significant differences in specific cell type frequencies (residuals above $\pm$3.66, corresponding to Bonferroni corrected p-values $<$ 0.00013). B cell-depleting therapies rituximab and ofatumumab produced significant decreases in the proportions of memory B cells, naïve B cells, germinal center (GC) B cells and plasmablasts. At the same time, significant increases in T follicular helper (Tfh)-like cells, natural killer (NK)-like CD8, NK cells, effector CD4, monocytes, and T follicular regulatory (Tfr) cell proportions were seen. In contrast, natalizumab produced significant increases in GC B cells, memory B cells and GC Tfh within the dcLN. Decreases were observed in T regulatory (Treg) cells, plasmablasts, and naïve CD8s and CD4s, as well as NK-like CD8s. PwMS treated with dimethyl fumarate showed significant increases in naïve CD4, NK cells and naïve CD8 T cell populations, while decreases were observed in proportions of memory B cells, NK-like CD8s, effector CD4s, memory CD8s, GC B cells and Tfh cells.
Conclusion: Our study demonstrates intranodal effects of DMTs, where B cell depletion reaches the dcLNs, as has been shown for patients with neuromyelitis optica. Natalizumab, on the contrast, appears to amplify the alterations of the intranodal compartment present at the diagnostic phase, concordant with the mechanism of action.

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P1626
Rescue Cyclophosphamide Therapy for Severe and Refractory Multiple Sclerosis Relapses

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Introduction: While a wide range of high-efficacy disease modifying therapies are now available for the prevention of relapses in MS, treatment of acute relapses remains limited. Severe relapses are typically treated with high dose IV corticosteroids followed by plasma exchange. Patients who remain refractory to initial treatment lack universally accepted second-line options. Cyclophosphamide is a DNA alkylating and chemotherapeutic agent that is used in clinical practice for severe multiple sclerosis relapses refractory to initial therapy. Despite its clinical use, there are no conclusive data demonstrating its efficacy.
Objectives/Aims: This study aims to describe safety and efficacy of cyclophosphamide in a clinic-based cohort of MS patients where cyclophosphamide was used as rescue therapy.
Methods: We reviewed the UBC pharmacy cyclophosphamide distribution list to identify patients followed at the UBC MS clinic that received cyclophosphamide between June 2009 to June 2024 who fulfilled the 2017 McDonald diagnostic criteria for multiple sclerosis. Clinical response was determined based on the Expanded Disability Status Scale (EDSS) scores preceding cyclophosphamide treatment and at last follow-up within 12 months of completing cyclophosphamide treatment. Brain and spinal cord MRIs obtained prior to cyclophosphamide treatment and up to 12 months after completion of cyclophosphamide treatment were reviewed for identification of new T2 hyperintense lesions.
Results: The median age at initiation of cyclophosphamide treatment was 39 years (range 25-66). The median EDSS score prior to cyclophosphamide therapy was 6 (range 2.5-9). 13/23 patients had an improvement in EDSS, while 5/23 had a $\geqslant$3 EDSS numerical improvement. 0/23 patients had relapses within 1 year following completion of cyclophosphamide treatment. 2/23 patients had new T2 lesions within 1 year following completion of cyclophosphamide treatment, notably both in patients with highly active disease and remarkable recovery following cyclophosphamide. One case each of sinus infection, dental infection, and epididymitis were reported, all of which resolved with antibiotic treatment. No serious adverse events were reported.
Conclusion: In patients with relapsing MS with severe relapses who fail to respond to steroids and plasma exchange, cyclophosphamide treatment was associated with substantial improvements in some patients. Despite the availability of high efficacy disease modifying therapies, this cohort shows there is a role for cyclophosphamide in the context of severe attacks. Current practice for patients who remain refractory to steroids and plasma exchange involves either empiric treatment with an off-label therapy such as cyclophosphamide or rapidly initiating an approved disease-modifying therapy, often an anti-CD20 antibody. Future randomized-controlled studies may help better compare efficacy between both approaches.

Disclosure of interest: The authors declare no relevant disclosures.

P1627
The Efficacy and Safety of Sampeginterferon β-1a: Two-year study in Relapsing-Remitting Multiple Sclerosis Patients

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Introduction: Interferon beta (IFNβ) remains an important treatment option in relapsing-remitting MS (RRMS), but its adherence is limited by frequency of injections. PEGylation enhances IFNβ pharmacokinetics by extending half-life, reducing dosing, and improving bioavailability. Sampeginterferon β-1a (samPEG-IFNβ-1a) is an original pegylated recombinant IFNβ-1a conjugated to a linear 30 kDa mPEG. This was a two-year, international, multicenter, randomized, double-blind, placebo-controlled study (NCT02744222) to compare samPEG-IFNβ-1a and non-pegylated IFNβ-1a (Avonex®).
Objectives/Aims: To assess the efficacy and safety of 2 doses of samPEG-IFNβ-1a once every 2 weeks versus non-pegylated IFNβ-1a once weekly in RRMS.
Methods: Randomized patients with RRMS (aged 18-60 years, Expanded Disability Status Scale ⩽5.5) received samPEG-IFNβ-1a (180 or 240 μg), non-pegylated IFNβ-1a, or placebo (withdrawn at 20 weeks). SamPEG-IFNβ-1a treatment continued up to Week 100 at a 240 μg dose. Exclusions: primary/secondary progressive MS, prior IFNβ use. Primary endpoint: time to first relapse (TFR) at 52 weeks. Safety assessed through adverse events (AEs) and serious adverse events (SAEs). Secondary endpoints: annualized relapse rate (ARR) and MRI markers like new/enlarging T1Gd+ lesions, T2-weighted lesion count and volume.
Results: A total of 399 patients were randomized, and 340 patients received at least one dose of an active drug (N=113; N=114 for samPEG-IFNβ-1a at 180 μg and 240 μg respectively; N=113 non-pegylated IFNβ-1a). Both doses of samPEG-IFNβ-1a were superior to non-pegylated IFNβ-1a in reducing the risk of relapse in patients RRMS after 52 weeks. The hazard ratio for TFR was 0.54 (95% CI, 0.297 to 0.977; p=0.04) for the 180μg group and 0.39 (95% CI, 0.203 to 0.748; p=0.003) for the 240μg. Compared to non-pegylated IFNβ-1a (0.32), both doses of samPEG-IFNβ-1a significantly reduced ARR over the first year: 0.18 in the 180μg group (p=0.044) and 0.14 in the 240μg group (p=0.006). This effect was stable over the second year, with an ARR of 0.16 (95% CI 0.09 to 0.26) and 0.09 (95% CI 0.04 to 0.18) in the samPEG-IFNβ-1a 180μg and 240μg, respectively.
There was no negative dynamics of MRI markers in all treatment groups, with samPEG-IFNβ-1a showing greater improvement comparing to non-pegylated IFNβ-1a. The safety profile of samPEG-IFNβ-1a was consistent with the known of IFNβ therapy.
Conclusion: SamPEG-IFNβ-1a showed superior efficacy over non-pegylated IFNβ-1a with sustained benefits over two years of treatment.

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P1628
High risk of pneumonia in MS patients treated with antiCD20 mAbs: data from a real world cohort and correlation with lymphocyte subpopulations and immunoglobulin levels

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Introduction: Pneumonia has been rarely reported as an adverse event in the phase III clinical trials of ocrelizumab (OPERA study) and ofatumumab (ASCLEPIOS study). However, in our experience in a real world setting the frequency of pneumonia in Multiple Sclerosis (MS) patients treated with ocrelizumab/ofatumumab appears to be higher.
Objectives/Aims: In this study, we calculated the frequency of pneumonia in a cohort of MS patients treated with ocrelizumab

or ofatumumab, and we assessed the risk factors for pneumonia in this population.
Methods: The study included all MS patients in our center treated with anti CD20 monoclonal Antibodies (mAbs) and in which lymphocyte subpopulations and immunoglobulin (IgG, IgA, IgM) levels (tested every 6 months) were available. All pneumonia events in the last 2 years were recorded. Logistic regression models were used to assess the risk factors for pneumonia in this population, including as independent variables age, EDSS, duration of treatment, sex, smoking status, presence of cardiovascular comorbidities, presence of diabetes, overweight, mean CD4+ lymphocyte count, mean CD8+ lymphocyte count, mean CD19+ lymphocyte count, mean immunoglobulin levels.
Results: This study included 250 MS patients treated with anti CD20 mAb (157 ocrelizumab, 75 ofatumumab, 18 rituximab). Mean age was 41.6 years, median EDSS 4.0. Fifty out of 250 patients were treatment naive. Over the course of 2 years, 20 pneumonia events in a cohort of 250 patients were observed (9 SarsCov2-positive, 11 SarsCov2-negative). Sixteen out of 20 patients needed hospitalization (1 in an intensive care unit). All patients survived. In 4/20 patients, anti CD20 mAb treatment was interrupted after pneumonia. No difference in the risk of pneumonia was observed between different types of anti CD20 mAbs.
Immunoglobulin G levels were the only predictive variable for the risk of pneumonia in the multivariate analysis (OR 0.718, $p = 0.030$). In 6/20 patients with pneumonia, immunoglobulin G levels were under the lower laboratory reference limit.
Conclusion: We observed a relatively high frequency of pneumonia (20/250 over 2 years) in a real-world cohort of MS patients treated with anti CD20 mAbs, much higher than the frequency reported in phase III trials (1/894 in OPERA and 3/946 in ASCLEPIOS). Immunoglobulin G levels were the only predictive variable for the risk of pneumonia in this cohort.

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P1629
Post Hoc Analysis of rate and severity of infections and immunoglobulin Levels in Ocrelizumab-Treated Chilean Patients: Trends and Relation to Severe Infections

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Introduction: Ocrelizumab is a monoclonal antibody that targets CD20-positive B cells, and chronic therapy has been associated with hypogammaglobulinemia and increased risk of infections.
Objectives/Aims: To assess the rate of severe infections and to Analyze its association with immunoglobulin levels (IgG and IgM) In a cohort of Latin patients, who are underrepresented in pivotal trials.
Methods: A post hoc analysis included 378 patients treated with ocrelizumab from June 2018 to March 2025. All infections were reported as adverse events. Immunoglobulin levels were measured in a subset over five years. We evaluated these levels and assessed their relation to severe infections.
Results: Rate and severity of infections were assessed in patients who completed at least 1, 2, 4, and 5 years of follow-up. In Year 1, 31 patients had infections, including one severe case (COVID pneumonia, IgG not available). In Year 2, 26 patients experienced infections, with two severe cases (one COVID-related death and one pneumonia, IgG were not available in both patients). By Year 3, 39 patients had infections, with two being severe (Both COVID pneumonia, one patient had a IgG: 836 mg/dl, the other unknown). In Year 4, a total of 8 infections were reported, one severe case (COVID pneumonia, IgG not available, and in Year 5, 5 infections occurred, none severe.
IgG levels showed a consistent decline from an average of 1108 mg/dL in Year 1 to 886 mg/dL in Year 5. IgM levels also decreased from an average of 100 mg/dL in Year 1 to 52.7 mg/dL in Year 5. We did not find differences among clinical phenotypes. Throughout these years, there was no observed correlation between IgG levels and the incidence or severity of infections.
Conclusion: This analysis highlights a decline in immunoglobulin levels over five years in ocrelizumab-treated MS patients, although low immunoglobulin levels do not correlate consistently with severe infections, underscoring the need for comprehensive monitoring and tailored management strategies.

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P1630
Head to head comparison of B cell depletion with rituximab and ocrelizumab: efficacy, side effects, impact on immune cells and immunoglobulins

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Introduction: The principle of anti-CD20-based B-cell depletion is widely used in neuroimmunology. The parent compound rituximab continues to be used in a wide range of less well characterised antibody-mediated diseases. Ocrelizumab is used to treat relapsing forms of MS (RMS) and primary progressive MS (PPMS). In addition to the desired immunosuppression, there is an increased susceptibility to infection due the changes in the humoral and cellular immune response. Nevertheless, there is a paucity of head-to-head comparisons between the various substances.

Objectives/Aims: Our aim was to compare both substances with regard to paraclinical events and changes in immune cells and antibody titres over a period of several years.
Methods: 166 patients (139 RMS, 27 PPMS) treated with ocrelizumab and 52 patients treated with rituximab (including vasculitis, autoimmune encephalitis, neuromyelitis optica spectrum disease) were followed up for a median of 39 and 42 months respectively. During this period, clinical data (occurrence of relapses, infections, malignancies) were observed. The cellular immunity parameters (lymphocytes, granulocytes, basophils, eosinophils, natural killer cells, T cells, CD19+ B cells, CD4+ T cells and CD8+ T cells) were measured using flow cytometry on a semi-annual basis. In addition, the levels of immunoglobulins were measured.
Results: The patients in the rituximab group were older (mean ± SD: 53 ± 15 versus 46 ± 12) and had more comorbidities than those in the ocrelizumab group. There were no significant treatment-related changes in the T or NK cells in the group comparison. The median B-cell count was consistently 0 in both groups, but there were significantly more patients without complete B-cell depletion in the rituximab group. Despite this, there was treatment-related IgM hypogammaglobulinaemia in this group ($p = 0.005$), which was significantly more pronounced than in the ocrelizumab group. This effect could not be demonstrated for IgG.
Conclusion: Overall, B cell depletion was well tolerated and treatment adherence was high in both groups. There were few relevant changes in the immune cells. Over a period of more than 3 years, however, rituximab appears to lead to significantly greater IgM hypogammaglobulinaemia. It can be hypothesised that other, primarily IgM-producing B cells are affected here than under treatment with ocrelizumab. This may be helpful for future therapy selection.

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P1631
Head-to-head comparison of ocrelizumab and ofatumumab in B cell depletion and repletion kinetics in human CD20 transgenic mice

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Introduction: Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS). B cell-depleting monoclonal antibodies (mabs) have demonstrated significant efficacy in reducing inflammatory activity and slowing the progression of disability in MS. Ocrelizumab (OCR) and ofatumumab (OFA) are both anti-CD20 mabs approved for MS therapy. Despite differences in administration routes, dosing intervals, and dosages, both agents exhibit beneficial effects in MS treatment (Florou et al., 2020).
Objectives/Aims: This study aims to compare OCR and OFA with respect to their B cell depletion and repletion kinetics.
Methods: In the first experiment, we evaluated the B cell depletion capacity of OCR and OFA in human CD20 transgenic mice. The human therapeutic protocols for both agents, including administration routes, intervals, and dosages, were adapted to the respective mouse model. Three concentrations of either OCR or OFA were administered to human CD20 transgenic mice to simulate a treatment period of approximately 18 months in humans. Following treatment, B cell populations in the blood, bone marrow, inguinal and cervical lymph nodes, and spleen were analysed via flow cytometry.
Results: Our results demonstrated a dose-dependent depletion of B cells across all organs. Notably, OCR induced a more profound depletion of B cells in the bone marrow, lymph nodes, and spleen, whereas both mabs showed comparable effects in the blood. Further analysis of the remaining B cells and their phenotype is ongoing.
Conclusion: Overall, this study seeks to delineate differences between OCR and OFA, which could lead to more tailored and evidence-based treatment strategies for MS patients.
Florou, D., Katsara, M., Feehan, J., Dardiotis, E., Apostolopoulos, V., 2020. Anti-CD20 Agents for Multiple Sclerosis: Spotlight on Ocrelizumab and Ofatumumab. Brain Sci. 10, 758.

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P1632
Targeting senescent immune cells as a potential treatment for multiple sclerosis

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Introduction: The debut of multiple sclerosis (MS) at an older age is associated with an increased risk of developing primary progressive MS. In addition, the transition from relapsing-remitting (RR)MS to secondary progressive MS is more associated with aging than disease duration, suggesting that the accumulation of senescent immune cells may contribute to disability progression in older patients. Navitoclax, quercetin and dasatinib

are senolytic compounds that specifically target senescent cells and that also possess immunomodulatory properties, offering the potential to rejuvenate the aged immune system.
Objectives/Aims: To evaluate the therapeutic potential of these senolytic compounds as a possible therapy for elderly MS patients with progressive (P)MS.
Methods: We included untreated RRMS aged 18-35 years-old (n=4) and PMS over 50 years-old (n=5), and age and sex-matched healthy controls (HC). Peripheral blood mononuclear cells (PBMCs) were used to assess T cell functionality in RRMS and PMS patients and the effects of senolytic treatments on T cell function. Cells were treated with navitoclax (5 and 10μM), quercetin (50 and 100μM) and dasatinib (10 and 20μM). We evaluated: i) early activation by means of CD69 expression (18h stimulation); ii) late activation through CD25/CD69 expression (70h stimulation); iii) PBMC death upon activation; iv) proliferation using CFSE dilution; v) TCR signaling in enriched T cells through the detection of phosphorylated Erk1/2. T cells were activated with anti-CD3/CD28 antibodies. We also quantified the expression of senescence-associated β-galactosidase (SA β-gal) in T cells.
Results: T cells from PMS patients did not show altered T cell function compared to those from RRMS patients. Navitoclax had a more pronounced effect in PMS than RRMS in reducing early T cell activation, increasing cell death upon activation and decreasing TCR signaling. Quercetin also presented a stronger effect in PMS at reducing early T cell activation and promoting cell death. Dasatinib was also more effective in PMS than in RRMS, particularly in reducing late T cell activation and halting TCR signaling. Additionally, T cells from PMS patients showed higher expression of SA β-gal compared to RRMS, which may explain the greater efficacy of senolytic compounds in this group. We are currently including more patients and HC to confirm these preliminary results.
Conclusion: Senolytic compounds navitoclax, quercetin, and dasatinib showed preliminary potential beneficial effects in the context of progressive forms of MS.

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P1633
Baseline and early safety data following full recruitment of ChariotMS, the first DMT trial for people with advanced MS (EDSS 6.5-8.5)

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Introduction: Disease-modifying treatments (DMT) have transformed the management of people with MS (pwMS). However, those with an EDSS⩾6.5 are commonly excluded from DMT due to (i) focus on ambulation, (ii) the assumption that in advanced MS inflammation plays a negligible role, (iii) disregard for potentially length-dependent neuro-axonal CNS damage. Cladribine tablets (CladT) are licensed for people with active relapsing MS. Cladribine effectively depletes B cell subsets, particularly memory B cells, a likely key mechanism of disease control in pwMS.

Objectives/Aims: To report baseline characteristics and early safety data of pwMS participating in ChariotMS – **C**ladribine to **ha**lt dete**rio**ra**t**ion in people with advanced **m**ultiple **s**clerosis (NCT04695080).

Methods: UK-wide, randomised, double-blind, placebo-controlled trial to test efficacy, safety and cost-effectiveness of CladT in pwMS with EDSS 6.5-8.5. There is no upper age limit for enrolment. Primary outcome: nine-hole-peg-test speed at 104 weeks. Sample size N=200 to detect 15% treatment effect with 90% power at 5% significance, assuming 20% dropouts.

Results: Between July 2021 and December 2024, a total of 302 participants have been screened of which 204 were enrolled across 24 sites (59.8% female; median age 55 (range: 38-80) years. Median baseline EDSS: 7.0 (range: 6.5-8.5); 177/204 (87.0%) White, 4 (2%) Asian, 2 (1%) Black and 2 (1%) each mixed race/other). By the end of March 2025, 60/204 had completed all follow-up visits; 59 serious adverse events were recorded; 18 suspected unexpected serious adverse reactions (in nine participants). Both SAEs and SUSARs were mainly due to infections. 48 events of grade 3, and one case of grade 4, lymphopenia were recorded. Results of the primary endpoint analysis are expected in Q3 2027.

Conclusion: ChariotMS is the first DMT-trial focusing on pwMS at a level of disability that requires wheelchair assistance, and with no upper age limit. Full recruitment of the target population has been achieved within the expected age and disability distribution. Bearing in mind the study remains blinded, SAEs and SUSARs appear in keeping with this demographic of pwMS.

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P1634
Ultra-rapid elimination of B cells directly after intravenous infusion of anti-CD20 therapy

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Introduction: Ocrelizumab Versus Rituximab Off-Label at the Onset of Relapsing MS Disease (OVERLORD-MS) is a double-blinded interventional trial comparing the efficacy and safety of off-label rituximab to ocrelizumab. Anti-CD20 therapies are widespread in the treatment of MS, but pharmacodynamic aspects such as time to onset of effects have not been well established. Blood samples taken immediately before and after infusion were analysed to examine the direct effects of either drug on lymphocyte composition.
Objectives/Aims: The overall objective was to gain a deeper understanding of how anti-CD20 therapies affect B cells and other lymphocytes, with a primary focus on how rapidly the drug depletes B cells.
Methods: Whole blood samples were taken prior to first intravenous infusion (rituximab or ocrelizumab). Blood samples were also collected immediately after the medication was fully administered, approximately 4 hours after the start of infusion. The samples were fixed using proteomic stabilizer and promptly stored at -80°C. The samples were further processed for flow cytometry analysis. A six-marker panel was used to determine the lymphocyte composition, including the absolute cell counts. Depletion of B cells was measured by CD19 expression.
Results: The post-infusion samples demonstrated the immediate effect of anti-CD20 therapies in all patients. On average, CD19 positive cells accounted for 8.4% of lymphocytes prior to infusion. After infusion, CD19 positive cells were reduced to 0.4%. The overall lymphocyte composition was also affected between pre- and post-infusion samples. A relative increase in natural killer cells was observed. Additionally, in most patients, the CD4/CD8 ratio decreased after infusion.
Conclusion: Rituximab and ocrelizumab, displayed a complete elimination of B cells immediately after infusion, in all MS patients.

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P1635
The Economic Burden of Multiple Sclerosis: An Umbrella Review of Systematic Literature Reviews

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Introduction: Autoimmune diseases such as multiple sclerosis (MS) are currently managed with lifelong immunosuppressive and supportive therapies, which reduce inflammation but fail to address the root cause of disease.
Objectives/Aims: This umbrella review aims to synthesize evidence from existing systematic reviews to provide a comprehensive overview of the economic burden of MS.
Methods: A systematic umbrella review was conducted using Medline, Embase, and the Cochrane Library. Included studies were systematic literature reviews (SLRs) published in English with no date restrictions. No meta-analysis was performed. The protocol was registered in PROSPERO (code: CRD42024579643).
Results: Twenty-five SLRs were analyzed, with a primary focus on the economic burden of MS. Fifteen reviews applied a general approach, while ten reviews concentrated on certain therapies like disease-modifying drugs, informal care, rehabilitation. Sixteen reviews were cost-of-illness studies and investigated direct and indirect, medical and non-medical costs, while in four SLRs cost-effectiveness and economic evaluations were reviewed. Three reviews concentrated on the occupational

outcomes and socioeconomic consequences of MS, while two SLRs provided information both on costs and employment rates. The findings consistently demonstrated that MS has a high and multifaceted economic burden. Pharmacy costs were the main cost drivers, while relapses contributed significantly to hospitalization and productivity-related costs.
Conclusion: Our review showed that while the direct costs related to MS are well researched, further evidence is required to fully understand the indirect and intangible costs, along with their main drivers to capture the true burden faced by patients. There is a need for standardized approaches and further research to support informed policy and resource allocation, considering that cost-effectiveness results are specific to the local settings.

Disclosure of interest: Rok Hren: nothing to disclose

P1636
Disease-Modifying Therapies Use Patterns in Canadian Pediatric MS Centre

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Introduction: Approximately 10% of individuals with MS are diagnosed during childhood. Pediatric patients face unique barriers to accessing disease-modifying therapies (DMTs), including a lack of pediatric-specific clinical trials required for regulatory approval. This complicates drug access and insurance coverage compared to adults.
Objectives/Aims: This study assessed uptake and trends of DMT use for pediatric MS patients attending a comprehensive MS centre in Toronto, Canada.
Methods: Data were obtained from MS patients enrolled in a prospective registry (2002–2025) at the Hospital for Sick Children in Toronto, Canada. Demographic and clinical information was collected, including details on DMTs use, treatment start and stop dates, and the type of coverage used.
Results: 155 pediatric MS patients were included (106 females; mean age of diagnosis: 14.4years). The median time from diagnosis to DMT initiation was 2.3 months (IQR 1.3 – 4.4 months). For first-used therapy, 67.7% of patients were started on moderate-efficacy DMTs, 21.3% on high-efficacy DMTs, and 11.0% received no DMT. The most commonly prescribed first-used therapies were peginterferon beta-1a (18.1%) and dimethyl fumarate (16.8%). When considering only patients diagnosed ⩾2018 (n=90), 57.8% were on moderate efficacy DMTs, 32.2% on high-efficacy DMTs and 10% on no DMT for first-used therapy. Among all patients, 48.6% required switch in therapy. The median time to treatment switch from the initiation of the first DMTs was 12.1 months (IQR 6.6 – 22.3 months). Among those initially treated with moderate-efficacy DMTs, 56.2% required a switch in therapy, while 24.2% of those started on high-efficacy DMTs required a switch in therapy (p=0.001).
Conclusion: Although numerous studies have shown that early initiation of high-efficacy DMTs improves long-term outcomes in MS, access to these therapies remains limited in the pediatric population. This study highlights persistent challenges in ensuring timely and appropriate access to DMTs for pediatric MS patients within a public healthcare system.

Disclosure of interest: No disclosures

P1637
Association Between Immunoglobulin Level and Risk of Infections in Multiple Sclerosis Patients on Anti-CD20 Therapies

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Introduction: Hypogammaglobulinemia is a known side effect of treatment with anti-CD20 monoclonal antibodies, and it is associated with the risk of infections. Among the anti-CD20 monoclonal antibodies, Ocrelizumab (OCR) is used for highly active MS and Primary Progressive MS (PPMS) while Rituximab (RTX) is widely used as off-label treatment for secondary Progressive Multiple Sclerosis (SPMS) as well as for Neuromyelitis Optica Spectrum Disorder (NMOSD).
Objectives/Aims: The aim of this study was to assess the frequency of hypogammaglobulinemia in MS and NMOSD patients treated with OCR or RTX and its association with the occurrence of severe infections. Moreover, we aimed to identify predictors of hypogammaglobulinemia and of severe infections.
Methods: This retrospective multicenter study conducted among 3 centers (neuroimmunology and MS unit at Al-Azhar University Hospitals; Al-Hussein and Sayed Galal Hospitals and Cairo Fatemic Hospital). All patients diagnosed with MS according to the 2017 revised McDonald criteria, as well as patients diagnosed with an NMOSD according to the most recent criteria available at the time of disease onset with at least one year of treatment (at least 2 infusional cycles) and with an available baseline level of immunoglobulin (Ig) G and M were enrolled during routine clinical visits. Exclusion criteria were previous body irradiation/bone marrow transplantation and inherited immunoglobulin deficiencies.
Results: We included 455 patients who fulfilled inclusion criteria: 427 MS patients (195 RRMS, 180 SPMS, 52 PPMS) and 28 NMOSD patients. Of these, 247 were on OCR and 208 on or RTX. Mean follow-up duration was 26.71 months (25.41 on OCR and 32.38 on RTX, $p<0.001$). IgG hypogammaglobulinemia occurred in 20% and IgM hypogammaglobulinemia in 34% of patients. At multivariable analysis, the risk of IgG hypogammaglobulinemia was influenced by an older age (⩾50 years) (OR 1.64, 95%CI: 1.06-2.54, p=0.027), and by the number of treatment cycles (OR: 1.20, 95%CI: 1.09-1.33, $p<0.001$).Thirty-three patients on OCR (13.3%) and 35 patients on RTX (16.8%, $p<0.001$) relapsed during follow-up. Serious adverse events

(SAEs) other than infections recorded during follow-up were 9 neoplasms, 6 of which were malignant: 1 cervical cancer, 1 bladder cancer, 2 melanomas, 1 endometrial cancer, 1 breast cancer. A total of 25 severe infections occurred (100 person-years rate: 1.8), with a disease phenotype other than relapsing-remitting (OR 1.50, 95%CI: 1.02-2.20; p=0.039) and IgG hypogammaglobulinemia (OR 2.65, 95%CI: 1.15-6.12; p=0.022) increasing its risk.
Conclusion: IgG and IgM hypogammaglobulinemia occurred in a considerable proportion of patients. IgG hypogammaglobulinemia increased the risk of severe infections, which were, nevertheless, relatively infrequent. Our results highlight the importance of monitoring immunoglobulin levels during treatment with anti-CD20 agents, to personalize treatment strategies.

Disclosure of interest: "Elsayed Abed: nothing to disclose."

P1638
Correlation of ImmunoWELL JCV IgG and STRATIFY JCV DxSelect for PML risk stratification using the anti-JCV-AK indices

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Introduction: Multiple sclerosis (MS) is the most common chronic immune-mediated demyelinating disease of the central nervous system (CNS) in Europe and North America and is also known as the "disease of 1000 faces". Recent studies have also shown different MS phenotypes at the cellular level. Multiple Sclerosis can be seen as a continuum and due to the variability of disease courses, it requires a patient-adapted therapy. A distinction between three categories is made and there are now 17 disease-modifying therapies to choose from to treat MS effectively. One of the most potent disease modifying drug is Natalizumab. Two natalizumab-containing preparations (TYSABRI® and TYRUKO®) have been approved in Europe and the USA.
Objectives/Aims: Following the expiry of the patent for natalizumab (Tysabri, Biogen), the first biosimilar PB006 (TYRUKO®, Sandoz) has now been available since 2023 and, as the name biosimilar suggests, is not identical but very similar to the original preparation and can therefore be used without further safety concerns. Sandoz developed an equivalent test procedure to TYSABRI® to ensure the safety of therapy with the new biosimilar. The motivation and objective of this present work is to compare the two test systems regarding their sensitivity and specificity for the JC virus for risk stratification, to switch or readjust patients to the biosimilar without health disadvantages.
Methods: In this study, 493 serum samples from 496 multiple sclerosis patients were included and systematically tested by two independent laboratories. The results of ImmunoWELL JCV IgG from Sandoz were subsequently compared with the JCV antibody indices results of STRATIFY JCV DxSelect from Unilabs.
Results: The test had a sensitivity of 93% and a specificity of 73%, thus fulfilling the criteria for the two-sided confidence interval. 28.4% of patients were already undergoing highly effective therapy. Overall, the JC virus infection rate in this study population was 50.3% (248/493) [95% CI: 45.9% to 54.7%] and, as expected, showed a low negative rate in the already treated group.
Conclusion: The study demonstrates a high diagnostic accuracy of the ImmunoWELL JCV IgG test and leads to the conclusion, that it detects the JC virus equivalently to the STRATIFY DxSelect reference test in cases of infection.

Disclosure of interest: Lucie de Azevedo: nothing to disclose. U. Proschmann received speaker honoraria from Roche. K. Akgün received personal compensation from Novartis, Biogen Idec, Sanofi, Alexion, Celgene, and Roche for consulting service and speaker honoraria

P1639
Investigating the role of rituximab in preventing secondary autoimmunity after alemtuzumab therapy in multiple sclerosis

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Introduction: The anti-52 monoclonal antibody alemtuzumab is a highly effective therapy for relapsing-remitting MS. The common occurrence of autoimmune adverse events has limited the use of alemtuzumab. The RAMBLE trial aims to assess the effect of rituximab in reducing this risk. This is a preliminary analysis of lymphocyte repopulation.
Objectives/Aims: To elucidate the effect of the B-cell agent rituximab on lymphocyte subsets following alemtuzumab therapy in multiple sclerosis (MS).
Methods: The RAMBLE trial is a multicenter study in which small doses of rituximab/placebo are administered to people receiving alemtuzumab for MS. Participants received rituximab or placebo at a ratio of 2:1, on weeks 10 and 30 of both years one and two. Immunophenotyping studies by flow cytometry are conducted before and after each treatment cycle with alemtuzumab and rituximab to assess the immune reconstitution response.
Results: One participant in the rituximab arm exhibited a marked decline in CD19+ B cell count over time. At baseline, CD19+ cells comprised 25.8% of the lymphocyte total. Consistent with previous observations in alemtuzumab treatment, B cell counts declined sharply after the first dose of alemtuzumab, followed by a rapid reconstitution of CD19+ cells by week 9, accounting for 13% of the total lymphocyte count. This was followed by a substantial B cell depletion by week 26, consistent with the expected response to rituximab treatment, with CD19+ B cells representing 0.4% of total lymphocytes. Persistent B cell depletion was evident through week 50, in which CD19+ B cells comprised 0.5% of the total lymphocyte population.

Conclusion: These findings reflect sustained B cell depletion and slow repopulation consistent with the expected effect of the anti-CD20 agent rituximab following alemtuzumab therapy. Patient follow-up and data collection are still underway

Disclosure of interest: Sofia Jimenez Sanchez: has received grant funding from MS Australia (grant ID: 22-3-052)

P1640
Characteristics of patients starting ocrelizumab subcutaneous in Denmark, Germany, and the United Kingdom

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Introduction: The new subcutaneous administration of ocrelizumab (OCR SC) offers a convenient MS treatment option for people diagnosed with relapsing remitting, primary progressive, or secondary progressive MS with relapses (pwMS). OCR SC has recently been approved in Europe and insights into the real-world treatment with OCR SC are just emerging.
Objectives/Aims: This study aimed to describe the characteristics of pwMS who initiate OCR SC and the treatment patterns with OCR SC usage in Denmark, Germany, and the United Kingdom.
Methods: Retrospective cohort study of pwMS treated with OCR SC using data from the Danish MS Registry, the German NeuroTransData Registry, and the United Kingdom MS Registry, from time of OCR SC approval in 2024 (June in Denmark/Germany, July in United Kingdom) to February 2025. Patient characteristics at OCR SC start and prior disease-modifying therapies (DMT) were described by country.
Results: Overall, 659 pwMS initiated OCR SC (Denmark: 545, Germany: 79, United Kingdom: 35) with 80%, 77%, and 97% relapsing-remitting MS type, respectively. In Denmark, Germany, and the United Kingdom, the respective mean age (SD) was 45.6 (10.0), 48.5 (10.1), and 46.0 (8.7) years, with a mean disease duration from MS diagnosis to OCR SC start of 11.5 (7.8), 13.6 (8.9), and 10.2 (6.2) years. Expanded disability status scale score (EDSS) ranged from 3.1 in Denmark and the United Kingdom to 3.7 in Germany (respective SD 2.2, 2.1, 2.2). Mean (SD) crude relapse rate 1-year before OCR SC start was 0.05 (0.24), 0.09 (0.29), and 0.05 (0.23) in Denmark, Germany, and the United Kingdom. The proportion of treatment naïve OCR SC patients, defined as no prior DMT (and no prior OCR IV), was <4% in Denmark and Germany and 14.3% in the United Kingdom. Of those with prior DMTs, 87.7%, 88.6%, and 77.1% switched from OCR IV in Denmark, Germany, and the United Kingdom, and <2% from other anti-CD20s. In Germany among those switching from DMTs, 63% reported patient preference as a reason for switching (German data only).
Conclusion: In Denmark, Germany, and the United Kingdom, in the first months after market approval, the characteristics of people with MS who start ocrelizumab subcutaneous seem comparable across the countries, with a large proportion of individuals transitioning from intravenous ocrelizumab. A limitation of this study is its low sample size in Germany and the United Kingdom as well as a lack of follow-up over time.

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Heer are employees of Rewoso AG, a company which received funding from Roche for the conduct, management, and data analytics of this study. A. Ferro is an employee and shareholder of Roche Products, Ltd. J. Acosta is an employee and shareholder of F. Hoffman La-Roche. M. Magyari has served on scientific advisory boards for Merck, Neuraxpharm, Novartis and Sanofi, and has received honoraria for lecturing from Biogen, Bristol Myers Squibb, Merck, Genzyme, Novartis and Roche.

P1641
Study Design of Two Phase 1/2 Studies to Assess Safety and Efficacy of YTB323, an Autologous CD19-Directed CAR-T Cell Therapy, in Multiple Sclerosis

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Introduction: B-cells are critical in multiple sclerosis (MS) pathogenesis. Approved high-efficacy therapies (HETs) effectively reduce relapse rates and new magnetic resonance imaging (MRI) lesions. However, a high unmet need remains for people with relapsing MS (RMS) presenting breakthrough disease activity despite HET, and for those with progressive forms of MS, where treatment options are limited. YTB323 (rapcabtagene autoleucel) is an investigational, autologous CD19-directed chimeric antigen receptor-T cell therapy targeting a broad population of the B-cell lineage. We report the designs of two phase 1/2 studies for YTB323 in RMS with breakthrough disease activity during previous HET and non-active progressive MS (PMS), respectively.
Objectives/Aims: To assess the safety, efficacy and cellular kinetics of YTB323 in people with MS.
Methods: These are two ongoing, open-label, multicentre, non-confirmatory Phase 1/2 studies with an ascending single-dose design including 3 sentinel cohorts of 3 participants each, followed by an expansion cohort of up to 19 participants. The RMS study (NCT06617793) is enrolling ambulatory participants (Expanded Disability Status Scale [EDSS] $\leqslant$6.5) aged $\geqslant$18 to $\leqslant$60 years, RMS duration of $<$15 years and evidence of recent (within 1 year) breakthrough disease following $\geqslant$6 months on HET (natalizumab, alemtuzumab, anti-CD20s). Breakthrough disease is defined as one or more of 1) a confirmed clinical relapse or 2) persistent MRI activity. The non-active PMS study (NCT06675864) is enrolling participants aged $\geqslant$18 to $\leqslant$60 years with non-active secondary progressive MS or primary progressive MS, EDSS score $\geqslant$3 to $\leqslant$6.5, disease duration $<$15 years, no relapse in the previous year, no gadolinium-enhancing brain lesions at screening and evidence of disease progression of $\geqslant$0.5 points on the EDSS scale within the previous year. The primary endpoint in both trials is the incidence of adverse events and serious adverse events. Secondary endpoints include efficacy measures (changes from baseline in disability, MRI lesions, cognitive processing, fatigue) and the pharmacokinetics and cellular kinetics of YTB323.
Results: Both trials are actively recruiting. Safety data will be reviewed after each sentinel cohort before dosing of the next sentinel cohort. Approximately 28 participants will be treated with YTB323 on each trial. Following a 2-year core study, participants will be monitored for an additional 13 years.
Conclusion: These studies will provide the scientific evidence needed for further development of YTB323 in MS.

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P1642
The evolving role of the pharmacist in the MS team

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Introduction: The increase in disease modifying therapies (DMTs) has led to the increasing involvement of specialist pharmacists supporting MS teams. Their role at our centre has evolved over time from managing access to one new therapy to prescribing and monitoring of all DMTs and running pharmacist DMT clinics for those patients starting or switching therapy.
Objectives/Aims: To demonstrate the contribution a pharmacist can make by detailing the activities undertaken in clinic, how these have evolved over time and how they contribute to patient care. To show the impact of having a pharmacist clinic on the time taken to start treatment. To demonstrate patient satisfaction with a pharmacist clinic
Methods: Data was collected on the outcome of the pharmacist clinic between 2022 and 2025. Activities were grouped as either advice on first DMT, DMT switching, review of current therapy, family planning, infusion pre-assessment or other. Other activity included assessment of adverse drug reactions

(ADRs), infection risk, compliance, EDSS, obtaining consent to treatment and stopping treatment. Data was also collected on which treatments were commenced and which DMTs patients were switched from and to. A patient satisfaction questionnaire was also sent to a sample of patients reviewed in the clinic

Results: Clinic outcome data was obtained from September 2022 to February 2025. 714 patients were reviewed in 89 clinics with an average of 8 patients in each clinic. 48% (343) had a new DMT discussion, 24% (171) were given advice on switching therapy, 13% (92) had a review of current therapy, 7% (47) had family planning discussion, 7% (47) were for infusion pre assessment and 3% (20) were classed as other (described above). The majority of patients reviewed were started or escalated to a B cell therapy. Further data will be presented on treatment choice for new and switching patients.

Time to start treatment with ocrelizumab decreased from 4.2 months in 2022 to 1.7 months in 2024.

Patient satisfaction surveys rated the overall experience in the pharmacist clinic as very good or excellent. In particular scoring highly for 'feeling listened to' and 'explaining things clearly'.

Conclusion: The addition of a pharmacist to an MS team accesses expert advice which can enhance the skills of the wider MS team and release clinic capacity. A pharmacist clinic dedicated to DMT advice is welcomed by patients and improves time to DMT commencement.

Disclosure of interest: Participation in educational events, advisory boards and conferences sponsored by Roche, Novartis, Sanofi, Merck, Biogen & Neuraxpharm

P1643
Rituximab for the treatment of multiple sclerosis: A retrospective observational study of 50 cases from Morocco

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Introduction: Rituximab (RTX) showed to be effective and relatively safe in the treatment of relapsing-remitting and progressive forms of multiple sclerosis (MS), both in the phase II setting and in some observational studies.

Objectives/Aims: To investigate the effectiveness and safety of rituximab in MS.

Methods: We report a retrospective observational study to describe the effectiveness and safety of off-label rituximab in the treatment of a population of Moroccan MS patients including 50 relapsing-remitting (RRMS) and progressive multiple sclerosis (PMS) subjects.

Results: Our study showed that the RTX treatment was associated with the mean ARR decreasing by 0.72 at one year follow up. EDSS scores improved after 1 year of treatment with RTX by a score of 0.5-1.0 in 31 (62%) patients and remained stable in the second year of therapy. It should be emphasized that the mean reduction in EDSS was more significant in the RRMS subgroup compared to the PMS group (RRMS-25, SPMS-6, PPMS-0). EDSS score remained same in 12 patients (24%), of which 9 had RRMS and 3 SPMS. EDSS worsened after 2 years from RTX in 7 (14%) patients (5 SPMS, 2PPMS). Follow up MRI Brain with contrast at one year, show new T2 lesions in 6 patients (12%), with no enhancing lesions either old or new. Concerning safety issues in our patients, we observed a frequency of infusion associated reactions inferior to the data reported in other studies. Majority of patients (98%) tolerated RTX infusion well.

Conclusion: RTX could be an effective and safe treatment in RRMS. Some selected PMS patients could also benefit from this treatment.

Disclosure of interest: nothing to disclose

P1645
Tocilizumab therapy in two children with refractory MOGAD

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Introduction: Relapsing Myelin Oligdendrocyte Glycoprotein Associated Disease (MOGAD)has been reported in approximately 27-53% of the paediatric cohort with significant accrual of disability associated with relapse. Currently there are no standarised regimes for relapsing MOGAD. Conventional immunotherapies such as Azathioprine, MMF, IVIG and Rituximab have been used with variable effects on disease control and outcome.

IL-6 has been postulated to contribute to the pathogenesis of MOGAD, with Tocilizumab, a monoclonal antibody targeting IL-6, proving an effective option for refractory MOGAD among the adult population. There is currently very little data on the use of tocilizumab in the paediatric population.

Here we report two paediatric cases with refractory MOGAD who achieved disease remission following Tocilizumab initiation.

Objectives/Aims: To describe two paediatric cases of refractory MOGAD with inadequate response to monthly intravenous immunoglobulins, and failure of response to Rituximab

Methods: Patients with refractory MOGAD, treated with Tocilizumab, were included in in this study. We describe their clinical profile, treatment regimens, and clinical outcomes

Results: Case 1 presented aged 11 with unilateral optic neuritis. He had 5 relapses over 4 years, failing combination therapies of IVIG, MMF and Rituximab. He had significant steroid-related complications with vertebral fractures and adrenal insufficiency. IV tocilizumab was commenced monthly with concomittant IVIG following his 5th relapse. The patient is now relapse- free at 22 months post Tocilizumab initiation, and has weaned steroids completely.

Case 2 presented, aged 3 years, with leukodystrophic-like ADEM. She had 7 relapses over 10 years, failing combination

therapies of IVIG, MMF and Rituximab despite B cell depletion. IV tocilizumab was commenced monthly with IVIG. The patient is now relapse-free 20 months post Tocilizumab initiation.
Conclusion: Our study adds to the current evident that Tocilizumab can be effective and safe in paediatric patients with relapsing MOGAD who failed Rituximab therapy. There were no major adverse events associated with the use of Tocilizumab in either patient. Both patients were able to successfully wean steroid therapy

Disclosure of interest: Claire Thompson: Nothing to disclose

P1646
Positive therapeutic response to Anifrolumab (Saphnelo) in a pediatric patient with Aicardi-Goutières Syndrome and recurrent inflammatory attacks: a case report

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Introduction: Aicardi-Goutières Syndrome (AGS) is a rare genetic early-onset encephalopathy classified under type I interferonopathies. It typically presents in infancy with neuroinflammatory symptoms, intracranial calcifications, cerebrospinal fluid (CSF) lymphocytosis, and elevated type I interferon signaling. Treatment options are limited, and most patients do not respond well to standard immunosuppressive therapies, making management challenging. Anifrolumab, a monoclonal antibody that blocks the type I IFN receptor, has recently shown efficacy in adult systemic lupus erythematosus (SLE), making it a potential option for treating other interferon-driven diseases such as AGS.
Objectives/Aims: To describe a pediatric case of AGS with recurrent inflammatory flares unresponsive to conventional therapies, who demonstrated significant clinical and immunologic improvement following treatment with anifrolumab (Saphnelo).
Methods: We report on an 11-year-old female with a history of chronic anemia, hepatosplenomegaly, intracranial calcifications, developmental delay and seizures. Extensive immunologic, infectious, and genetic workup confirmed a strong type I interferon signature, in the context of a heterozygous CEBPE variant. Despite treatment with corticosteroids, tofacitinib, and IVIG, she continued to experience encephalopathy and systemic inflammation. During a hospitalization for worsening vision changes and neurologic symptoms, she received anifrolumab following minimal response to high-dose steroids and tocilizumab. Clinical outcomes were monitored using the CASE score and inflammatory markers.
Results: After minimal response to high-dose methylprednisolone, she was treated with tocilizumab with some response and anifrolumab (Saphnelo) with marked clinical improvement. Her CASE score improved from 14 to 4 over the course of 8 days while hospitalized. Repeat labs showed persistent but reduced interferon-related markers (CXCL9, CD169+ monocytes). She continues to receive multidisciplinary care for seizure management, behavioral symptoms, and hematologic monitoring.No adverse events were noted. The patient tolerated monthly infusions well and remained stable on a combination of tofacitinib and anifrolumab.
Conclusion: This case highlights the promising role of anifrolumab in pediatric AGS with recurrent inflammatory flares unresponsive to traditional immunosuppression. Type I interferonopathies should be suspected in cases of early-onset, treatment-refractory autoimmune disease. Targeted IFN blockade with anifrolumab offers a rational and potentially effective approach for long-term disease control in this population. This report supports further investigation into the safety and efficacy of IFN receptor antagonists in pediatric neuroinflammatory disorders.

Disclosure of interest: Dhanalakshmi Angappan: nothing to disclose; Michael Kruer: nothing to disclose

P1647
Eculizumab for Severe Acute Relapse in anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis opticaspectrum disorders (NMOSD): A Case Report

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Introduction: Eculizumab, a humanized monoclonal antibody that inhibits the conversion of C5 to C5a/b complement proteins, is approved as long-term immunotherapy for anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorders (NMOSD). Its mechanism of action suggests potential use in managing aggressive AQP4-Ab+NMOSD acute relapses unresponsive to conventional treatment.
Objectives/Aims: Describe the clinical course and therapeutic challenges in a severe anti-AQP4+ NMOSD relapse unresponsive to first-line therapies (high-dose steroids and PLEX)
Methods: Case report.
Results: We present the case of a 54-year-old male who experienced a one-month history of progressive numbness, lower limb weakness, sphincteric disfunction rapidly evolving to lodging. Neurologic examination revealed paraplegia with sensory loss at the D4 level and bilateral Babinski signs. His initial EDSS score was 9. MRI showed an extensive inflammatory lesion (from C6 to D10) occupying over 50% of the spinal cord area. Serum and cerebrospinal fluid were positive for AQP4-Ab and a diagnosis of AQP4-Ab+ NMOSD was made. The patient received methylprednisolone (1 g/day IV for five days) followed by five plasma exchange (PLEX) sessions, with no improvement. Two weeks after admission, eculizumab (900 mg IV weekly) was initiated, resulting in gradual improvement in numbness and strength; physical rehabilitation was promptly started. One month later, he could walk with a walker (EDSS 6.5) and follow-up MRI showed reduced swelling and

gadolinium enhancement in spinal cord lesions and six months later EDSS was 5.5 and MRI spinal cord lesion was restricted to D5-D8.
Conclusion: This case highlights the potential of eculizumab as adjunctive therapy for severe acute relapses in AQP4- Ab+ NMOSD, aiding recovery and minimizing disability. Further studies are warranted to establish its role in acute settings.

Disclosure of interest: Mario Rotolo: nothing to disclose

P1648
Tolebrutinib influences B cell and monocyte phenotype and function in treatment-naïve relapsing-remitting and progressive forms of multiple sclerosis

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Introduction: Bruton's tyrosine kinase (BTK) is expressed in B cells and monocytes, and regulates cytokine production (pro- and anti-inflammatory) and the expression of surface molecules involved in antigen presentation. Tolebrutinib, a BTK inhibitor, is in late-stage clinical trials for both relapsing-remitting multiple sclerosis (RRMS) and progressive MS (PMS). To date, studies investigating BTK inhibition in B cells have offered important insights into MS pathophysiology and provide a strong mechanistic rationale for targeting BTK in MS. Given monocytes are critical regulators of the immune response in MS and express BTK at comparable levels to B cells, investigations into the consequences of inhibiting BTK in monocytes of individuals with MS are warranted.
Objectives/Aims: Determine how tolebrutinib alters cell phenotype and function in MS patient-derived monocytes and B cells (RRMS and PMS) in both treatment-naïve and anti-CD20 treated individuals.
Methods: Cryopreserved peripheral blood mononuclear cells (PBMCs) were carefully thawed from age/sex matched healthy controls (HCs), RRMS (stable), RRMS (active), RRMS (anti-CD20), SPMS, and PPMS; all were treatment-naïve except for the anti-CD20 group (n=12-15/group). Cells were exposed to tolebrutinib (1μM; 24hrs) and subsequently stimulated with LPS and IFNγ overnight. Levels of BTK and pBTK were measured by ELISA. A 14-colour flow cytometry panel was used to assess surface expression of HLA, CD80, CD86, CD19, CD14, and CD16 in B cells and monocyte subsets. Cytokine expression (TNF, IL-6, IL-10, and IL-12p40) was measured *via* both ELISA and intracellular cytokine staining. qPCR was also used to measure expression of MS-relevant microRNAs that are known to influence lymphocyte and monocyte function.
Results: Tolebrutinib significantly decreased the inflammatory-mediated pBTK:BTK ratio in all patient groups. Within whole PBMCs, tolebrutinib significantly decreased TNF and increased IL-10 in HCs, PMS, RRMS (stable), and RRMS (anti-CD20). In RRMS (active) and SPMS patients, tolebrutinib significantly decreased TNF and IL-12 in $CD14^{+}CD16^{high}$ monocytes, while also decreasing CD80 and CD86 surface expression. Tolebrutinib also significantly influenced cytokine levels within CD19+ B cells and decreased expression of microRNAs associated with immune cell activation (e.g. mir-155-5p, mir-223-3p).
Conclusion: In B cells and activated monocytes derived from treatment-naïve RRMS and SPMS patients, tolebrutinib significantly increased IL-10 levels while decreasing TNF, IL-12, and the expression of co-stimulatory molecules and microRNAs involved in antigen presentation and effector function. These results suggest that tolebrutinib limits both innate and adaptive immune responses that are associated with relapse activity and disease progression in MS.

Disclosure of interest: Authors have nothing to disclose.

P1649
Design and Baseline characteristics of the real-world MAVENAGE study in relapsing MS patients older and younger than 50 years treated with cladribine tablets

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Introduction: Post-hoc analysis combining data from cladribine pivotal trials have been performed to evaluate the effect of age (⩽50 or >50 years) in efficacy and safety aspects. Also observational studies with cladribine are providing clinical information outside the boundaries of the clinical trials with respect to age but still is important to continue collecting data in a clinical setting to better support physicians treatment decisions

Objectives/Aims: We report the design and the results of the MAVENAGE study first interim analysis of baseline characteristics

Methods: MAVENAGE is an ongoing 2-year prospective observational study of cladribine in relapsing MS patients (pts) aged ⩽50 and >50 years recruited from 15 sites in Spain.Here we present the design and main inclusion criteria of study, including the first interim analysis of baseline characteristics, including clinical and MRI activity, and clinical outcomes assessments (COAs) on fatigue (5-item Modified Fatigue Impact Scale, MFIS-5), anxiety and depression (Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory II, BDI-II), cognitive function (Symbol Digit Modalities Test, SDMT), overall health (29-item MS Impact Scale, MSIS-29) and quality of life (MS International of Quality of Life, MusiQoL)

Results: From November 2024 to March 2025 (database lock), 41 pts were included: 22 ⩽50 years (mean age: 37.7±7.0) and 19 pts >50 years (59.2±5.6). Time since MS diagnosis to cladribine initiation (first cycle, year 1) was 3.6±4.8 years (pts ⩽50) and 11.8±7.2 years (pts >50). Ten pts ⩽50 (52.6%) and three pts >50 (16.7%) were treatment-naive. Mean number of previous MS treatments was 0.8±1.1 (pts ⩽50) and 1.4±0.9 (pts >50). EDSS was 1.5±0.6 (pts ⩽50) and 2.5±1.4 (pts >50), number of relapses in the previous year was 1.0±1.2 and 0.4±0.5, respectively, and Gd+ lesions were 0.3±0.5 (pts ⩽50) and 0.2±0.4 (pts >50). T2 lesion burden was mild (1-25 lesions) in 11 (78.6%) pts ⩽50 and moderate (25-50 lesions) in 7 (46.7%) pts >50. Baseline scores on all COAs were within normal ranges except for SDMT (47.1±8.9) in pts >50.

Conclusion: These preliminary data reinforce the use of cladribine tablets in a real-life setting for patients older and younger than 50 years. Final results will provide evidence on effectiveness, safety and patient-centered outcomes which may support better-informed treatment decisions.

Disclosure of interest: Jose E. Meca-Lallana has received honoraria as a consultant, as a chairman or lecturer in meetings and has participated in clinical trials and other research projects promoted by Alexion, Almirall, Biogen, Bristol-Myers-Squibb, Horizon, Johnson & Johnson, Merck, Neuraxpharm, Novartis, Roche, Sandoz, Sanofi and UCB. Sara Eichau received honoraria for speaking or consultant from Alexion, Amgen, Biogen Idec, BMS, Horizon, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme, Sandoz, Viatris, Neuraxpharm and Teva. Celia Oreja-Guevara received honoraria for speaking, consulting and serving on advisory boards from Alexion, Amgen, Biogen Idec, BMS, Horizon, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme, Sandoz, Viatris, Neuraxpharm and Teva. Virginia Meca has received honoraria for her participation in conferences, consulting services, clinical research, and travel support from Almirall, AstraZeneca, Biogen, Bristol Myers Squibb, Janssen, Merck, Merz, Neuraxpharm, Novartis, Sanofi-Genzyme, Sandoz, Wellspect and Roche. Gary Ciceron Alvarez Bravo has received honoraria for his participation in conferences, consulting services, clinical research, and travel support from Amgen, Biogen, Bristol Myers Squibb, Merck, Neuraxpharm, Novartis, Sanofi-Genzyme, and Roche. Lucienne Costa-Frossard has received honoraria for her participation in conferences, consulting services, clinical research, and travel support from Almirall, Amgen, AstraZeneca, Biogen, Bristol Myers Squibb, Janssen, Merck, Neuraxpharma, Novartis, Sanofi-Genzyme, and Roche. Ester Moral Torres received compensation for consulting services and speaking fees from Merck, Biogen, Novartis, Sanofi, Almirall, BMS, J&J, ROCHE, Amgen, Horizon, Astra-Zeneca, Neuraxpharm and Viatris. Jorge Millan-Pascual has received honoraria as a consultant, as lecturer in meetings and has participated in clinical trials and other research projects promoted by Biogen, Bristol-Myers-Squibb, Janssen, Merck, Novartis, Roche and Sanofi. Andrés Labiano: Nothing to disclose. María Isabel Sánchez Magro is employee of Merck, S.L.U., Madrid, Spain, an affiliate of Merck KGaA. Maria Luisa Martinez Ginés received compensation for consulting services and speaking fees from Merck, Biogen, Novartis, Sanofi, Almirall, BMS, J&J, ROCHE, Amgen, Horizon, Astra-Zeneca, Neuraxpharm and Viatris. Irene Moreno Torres: Nothing to disclose. Miguel Angel Hernández has received honoraria as speaker or consultant for Biogen, Merck, Roche, Almirall, Novartis, Neuraxpharm, Janssen and BMS. Eduardo Agüera Morales has received honoraria as speaker or consultant for Biogen, Merck, Roche, Almirall, Novartis, Neuraxpharm, Janssen and Ultragenyx. Ana María Alonso has received honoraria as speaker or consultant for Biogen, Merck, Roche, Almirall, Novartis, Neuraxpharm, Janssen and BMS. Mercedes Romera has received honoraria as speaker or consultant for Biogen, Merck, Roche, Almirall, Novartis, Neuraxpharm, Janssen, BMS y Teva. Luis Brieva Ruiz has received honoraria for her participation in conferences, consulting services, clinical research, and travel support from Bayer, Biogen, Roche, Merck, Novartis, Allmirall, BMS, Janssen y Sanofi

P1650
Susceptibility-weighted imaging changes in drug-associated progressive multifocal leukoencephalopathy - a case series

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Introduction: Progressive multifocal leukoencephalopathy (PML) is an opportunistic viral central nervous system demyelinating disease caused by JC polyomavirus (JCV). PML is seen in immunocompromised patients, as well as a treatment complication of immunomodulatory and immunosuppressive drugs like rituximab and natalizumab, and has a high mortality rate. On brain magnetic resonance imaging (MRI) of PML patients, the appearance of a hypointense juxtacortical band (HJB) on susceptibility-weighted imaging (SWI) at the periphery of PML lesions might represent lesion chronicity and could indicate long-term survival.
Objectives/Aims: This case series investigates the presence of HJBs or any other hypointense SWI changes related to PML lesions in a cohort of drug-associated PML patients and assess their impact on patient survival.
Methods: This retrospective study included six patients with a definite diagnosis of PML according to the American Academy of Neurology criteria. Four patients were treated with rituximab for lymphoma, one received several immunosuppressive treatments for multiple myeloma, and one MS patient was treated with natalizumab. Each patient had at least one brain MRI on a 3T MRI scanner including SWI. In the case of patients with only one brain 3T MRI with SWI, that MRI examination was done before the patient died. All brain MRI examinations were analysed by a senior neuroradiologist.
Results: Four patients had only supratentorial PML lesions, while two had only infratentorial PML lesions. HJBs were detected in a part of the supratentorial PML lesions, and there were no detectable HJBs in one patient with supratentorial PML lesions. No HJBs or any hypointense SWI changes were visible on the infratentorial PML lesions. Three patients with supratentorial PML lesions and two patients with infratentorial PML lesions died within a period of 6 months after PML diagnosis, while only one patient with supratentorial PML lesions and HJBs was a long-term survivor (47 months), who ultimately died of lymphoma.
Conclusion: HJB on SWI is detectable in a part of PML lesions, supratentorial PML lesions show the coexistence of PML lesions with or without HJBs and there are no HJBs or any hypointense SWI changes related to infratentorial PML lesions. No clear relation between the presence of HJBs or hypointense SWI changes was found concerning patient survival, therefore the value of SWI for monitoring and survival prognosis in drug-induced PML is questionable, and a case-by-case approach is suggested.

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P1651
Analysis of initial therapeutic management and reasons for treatment discontinuation in patients with multiple sclerosis at a national referral hospital in peru

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Introduction: Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating, and neurodegenerative disease of the central nervous system. Therapeutic management at our hospital is constrained by limited access to high-efficacy disease-modifying therapies (DMTs).
Objectives/Aims: This study aims to analyse the initial treatment approach and primary reasons for discontinuation of first-line therapy in MS patients at a national referral hospital in Peru.
Methods: A retrospective observational study was conducted, including outpatients and hospitalised MS patients under neurological care between 2020–2023.
Results: The study population comprised 198 patients, predominantly female (59.6%), with a mean age of 37 years (±13 SD). Phenotype distribution was: relapsing-remitting MS (RRMS, 50%), primary progressive MS (PPMS, 28.8%), and secondary progressive MS (SPMS, 21.2%). Acute relapse management involved intravenous methylprednisolone (90%). First-line maintenance therapies included interferon β (48.3%), prednisone with azathioprine (12.8%), remained untreated (10.5%), self-funded treatments (9.9%), azathioprine monotherapy (9.3%), mycophenolate monotherapy (3.5%), prednisone with mycophenolate (3.5%) and fingolimod (1.2%). RRMS patients received interferon β (64.6%), PPMS patients were treated with azathioprine-based regimens (64.3%), and SPMS patients received interferon β (61.4%). Reasons for discontinuation of initial therapy included disease progression (29.3%), adverse drug reactions (16.3%), unspecified causes (15.2%), loss to follow-up (12%), transition to privately funded treatments (6.6%), enrolment in clinical trials (5.4%), contraindications to available therapies (5.4%), and treatment refusal (4.3%). In RRMS, discontinuations were due to unspecified reasons (23.3%), loss to follow-up (16.3%), disease progression (11.6%), and adverse reactions (11.6%). In PPMS, discontinuations were due by disease progression (50%), loss to follow-up (18.2%), adverse reactions (9.1%), and enrolment in clinical trials (9.1%). In SPMS, discontinuations were due to disease progression (40.7%), adverse reactions (29.6%), and unspecified reasons (14.8%).
Conclusion: Findings reveal consistent use of methylprednisolone for acute relapses, while phenotype-driven maintenance therapies predominantly featured interferon β. Early treatment discontinuation was primarily driven by disease progression, highlighting systemic constraints in accessing high-efficacy therapies within Peru's healthcare framework.

Disclosure of interest: Diego Canales: nothing to disclose

P1652
Ten-Year Long-Term Efficacy of Fingolimod in Relapsing Multiple Sclerosis: Sustained Disease Control and Relapse Prevention in Long-Term Users

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Introduction: Fingolimod is a well-established oral disease-modifying therapy (DMT) for relapsing multiple sclerosis (MS). This study focuses on the long-term efficacy of fingolimod, evaluating patients who have been continuously treated with the therapy for at least ten years.
Objectives/Aims: The goal is to assess relapse rates, disease progression, and the overall stability of the disease in this unique cohort.
Methods: A total of 217 MS patients (62.2% female; mean age: 47.89 ± 9.24 years) who have been on fingolimod therapy for at least ten years were retrospectively analyzed. Key variables included age, age at disease onset, disease duration, annualized relapse rate (ARR), and disease progression. Statistical methods such as paired t-tests, Wilcoxon tests, Pearson correlation, and logistic regression were applied to the data.
Results: The mean ARR was 0.0378 ± 0.0686, with values ranging from 0 to 0.49, indicating sustained low relapse activity over the ten-year period. Of the patients, 87.1% (n = 189) remained clinically stable, while 11.5% (n = 25) experienced disease progression. There were no statistically significant differences between progression and non-progression groups in terms of age, age at disease onset, or disease duration. Additionally, 33 patients (15.2%) discontinued fingolimod during the follow-up, with 14 discontinuing due to lack of efficacy and 19 due to adverse effects or personal preferences.
Conclusion: Fingolimod continues to be highly effective in maintaining disease control and preventing relapses in patients who have been using it for at least ten years. The majority of patients remained stable, with a low relapse rate observed over the extended period. These results further support the long-term use of fingolimod as an effective therapeutic option for managing relapsing MS. Further research is needed to identify factors that influence disease progression and to optimize long-term treatment strategies for MS patients.

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P1653
Efficacy and safety of ocrelizumab in a real-world setting: a monocentric observational study

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Introduction: Ocrelizumab is a highly effective therapy approved for the treatment of Relapsing and Primary Progressive MS. Although 10-year data from randomized controlled trials support a favorable risk-benefit profile, real-world data remain limited. This observational study evaluates the long-term efficacy and safety of Ocrelizumab (OCR) in a monocentric cohort of people with MS (pwMS).
Objectives/Aims: This observational study evaluates the long-term efficacy and safety of Ocrelizumab (OCR) in a monocentric cohort of people with MS (pwMS).
Methods: We analyzed demographic and clinical data from pwMS followed up at the MS center of Tor Vergata University Hospital, Rome, receiving standard-dose OCR (600 mg) with at least 6 months of clinical follow-up. Predictors of disease reactivation (clinical relapses and new MRI lesions) and progression (EDSS) were explored. Rate of adverse events (infections, malignancies and other relevant medical conditions) was also assessed.
Results: We enrolled 223 pwMS treated with OCR (50.9% women; mean age±SD at OCR initiation 39.8±9.5 years; mean±SD disease duration 9.8 ± 7.8 years; median EDSS 3.0, range 0-8.0; 60.5% RMS). Their median follow-up was 44 months, range 6-97.
Over the follow-up period, 22 (9.9%) experienced ⩾1 relapse, 37 (16.6%) had radiological activity (new or enlarged T2 lesions, Gd+ lesions). We found no predictors of relapses and radiological activity. Progression[MOU1] independent from relapse and MRI activity (PIRMA) occurred in 52 (23.3%) patients, with baseline EDSS as the only predictor of PIRA (HR = 1.28, p=0.03). Forty-eight (21.5%) patients developed lymphopenia (Grade 1= 50%, Grade 2=48%, Grade 3=2%), that was associated with older age at OCR initiation (HR=1.05, p=0.006) and history of lymphocytopenia with prior therapies (HR=2.80, p=0.001), whereas naïve pwMS had a reduced risk (HR=0.29, p=0.015). One or more infection events were reported in 150/223 (67.5%) patients, yielding an infection event rate of 3.6 for 100 patient/years; 9 (4.0%) patients required hospitalization. We also recorded 4 cases of skin cancers.
Conclusion: This study provide insight on the risk-to-benefit profile of OCR in a real-world MS cohort. PwMS with greater baseline disability showed lower therapeutic response, reliably reflecting reduced efficacy on ongoing neurodegenerative processes. Increased incidence of lymphocytopenia in older PwMS suggests immunosenescence as a possible underlying mechanism.

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P1654
Impact of Early High-Dose Corticosteroids Treatment in Long-term Functional Outcome of Immune-mediated Myelopathies

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Introduction: High-dose intravenous methylprednisolone (HDIVM) in immune-mediated myelopathies (IMM) has shown benefits in deficit stabilization and recovery. Data is lacking regarding the timing of its introduction and long-term functional outcome.
Objectives/Aims: To identify impact of early HDIVM in the functional outcome of patients with IMM.
Methods: We included all adult patients admitted to our Neurology department diagnosed with a first acute or subacute IMM and treated with HDIVM, between 1st january 2007 and 31st december 2023, with a minimum one-year follow-up. We collected demographic and clinical data including motor, sensory and bowel/bladder function deficits classified Functional Systems Score (FSS) (at nadir and at 1-year follow-up). We grouped the patients in 2 categories: early treatment (ET) and late treatment (LT) (until 6 days and more than 6 days since symptoms onset to treatment, respectively). We compared their FSS-sum at admission, at 1-year follow-up and the magnitude of the recovery 1 year after admission.
Results: Sixty-two patients were included (mean 34.8 years ± 12.6, 58.1% female), 14 (22.6%) of them were submitted to early treatment. The median FSS-sum at admission in the ET group was 5 and in the LT 5 (p=0.259). The median FSS-sum at 1-year follow-up in the ET group was 1 and in the LT 1 (p=0.979). The median magnitude of recovery 1 year after admission in the ET group was 4 and in the LT 3.5 (p=0.176). Subpopulation analyses of the patients not diagnosed with MS (total: n=17; ET: n=4; LT: n=13) showed no statistically significant results, however, we observed higher median FSS-sum at admission and lower median FSS-sum at 1-year follow-up was present in the ET group.
Conclusion: Our retrospective analysis didn't demonstrate better functional outcomes with early methylprednisolone treatment in patients with IMM. These results can be explained by a predominance of MS diagnoses, which it is known that a relapsing-remitting pattern is the common phenotype in early stages of the disease. However, we highlight that the analysis of the subgroup of patients not diagnosed with MS showed a tendency for a better functional outcome at 1 year after the IMM. We postulate that in IMM not attributable to MS, an early immunosuppressive treatment may contribute to better outcomes, and multicentric studies of this subpopulation may elucidate this question.

Disclosure of interest: Leonardo Barbosa: nothing to disclosure

P1655
Low initial IgG levels predict hyper BAFF response, increased serum biomarkers of neuroaxonal damage and inflammation in patients with multiple sclerosis on ocrelizumab

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Introduction: Multiple sclerosis (MS) disease activity is currently monitored in clinical practice through physical exam and interval imaging. New, more dynamic and precise approaches for monitoring are emerging with the development of serum biomarker testing. Octave Biosciences Inc developed the first approved biomarker panel for evaluation of MS disease activity (MSDA panel). Many questions remain regarding dynamics of these biomarkers in MS patients. In particular, no studies have focused on investigating whether ocrelizumab causes alterations in the biomarker profile.
Objectives/Aims: We hypothesized that serum biomarker panel (Octave MSDA) is affected by disease modifying therapy with ocrelizumab and certain biomarkers may inform clinicians on best strategy for DMT management.
Methods: We analyzed retrospective data from 118 MSDA tests done on stable patients with multiple sclerosis at UCI who were either on no DMT or on ocrelizumab. Data on disease activity, history, symptoms, DMT history, laboratory, imaging, and biomarker data were included in the data set. Data was then analyzed and visualized using R.
Results: 1. We have demonstrated that an age-adjusted serum biomarker profile is affected by ocrelizumab. 2. One significant change that stood out by the magnitude of difference was BAFF level in ocrelizumab group. 3. BAFF strongly correlated with IGG levels in ocrelizumab patients. 4. Longitudinal analysis of IGG levels revealed that patients with lower historical trend for IGG had higher BAFF levels. 5. Increased BAFF levels in ocrelizumab, but not in no DMT group, correlated with increased serum markers of inflammation and neuroaxonal damage. 6. Analysis in infection frequency and co-morbid systemic autoimmune disease revealed further correlations with IGG and BAFF.
Conclusion: By examining serum biomarker profile in stable multiple sclerosis patients, we have uncovered a potential predictor of hypogammaglobulinemia in ocrelizumab patients

- BAFF. We further demonstrated a link between IGG, BAFF, inflammation and autoimmunity in patients receiving ocrelizumab therapy. These results may help guide initiation and duration of treatment with ocrelizumab. Further studies are warranted in the mechanistic role of BAFF in pathogenesis of iatrogenic hypogammaglobulinemia.

Disclosure of interest: Anastasia Chumakova: nothing to disclose

P1656
Cryptococcal meningitis developing secondary to fingolimod use: a case report

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Introduction: Fingolimod reduces the infiltration of autoreactive T and B lymphocytes into the central nervous system. Cryptococcal meningitis (CM) was an exceedingly rare condition, primarily affecting immunosuppressive patients.
Objectives/Aims: We present the case of an MS patient receiving fingolimod therapy, who developed cryptococcal meningitis, which progressed to disseminated cryptococcosis.
Methods: A 38-year-old female patient has been followed up with a diagnosis of MS for 6 years. The patient has been using fingolimod 0.5 mg/d for 5 years and has not come for a follow-up visit for the last 1 year. The patient was admitted with nausea, vomiting, headache and diplopia. Lymphocyte was 0.21 x 10^9/L. No diffusion restriction or contrast enhancement was observed on brain and spinal MRI. The patient was started on IVMP treatment. After 1 week, the patient's complaints increased. When Lymphocyte 0.9 x 10^9/L was detected, the patient's Fingolimod treatment was discontinued,plasmapheresis treatment was done No new lesions were seen on repeated Brain MRI. LP showed that the opening pressure was high, Protein: 177mg/dL, 45 Leukocytes/**µ**L. Cryptococcus latex agglutination antigen test was positive in CSF. Cryptococcus neoformans(CN) growth was seen in the CSF culture taken later. Amphotericin and Fluconazole treatment was started. Also she had pelvic pain and pelvic MRI was showed radiolucent area in the left iliac bone, revealing nodular lesions with lytic characteristics in both iliac bones. Biopsy from pelvic area was showed CN. After one-week severe papilledema was detected. Brain MRI showed meningeal enhancement in the supratentorial region and subcortical T2 hyperintense lesions.
Results: The MRI and clinical condition stabilized after completing antifungal and acetazolamide treatment in 2 months.
Conclusion: Fingolimod use increases the risk of cryptococcosis, especially CM. Clinicians should have a high suspicion for cryptococcal infection in MS patients on fingolimod, especially if decreased lymphocytes. Management requires a multidisciplinary approach.

Disclosure of interest: Author's name: nothing to disclose."

P1657
Long-term Efficacy and Safety of Divozilimab in Patients with Relapsing Multiple Sclerosis: Results of BCD-132-EXT Trial

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Introduction: Divozilimab (DIV) is an original humanized afucosylated anti-CD20 monoclonal antibody.
Objectives/Aims: To assess long-term efficacy and safety of DIV in patients with relapsing multiple sclerosis (RMS).
Methods: BCD-132-EXT was an open-label single-arm trial that enrolled 44 patients with RMS, who previously completed phase III MIRANTIBUS trial according to the Protocol. Patients received DIV 500 mg intravenous (i.v.) infusions every 24 weeks. Overall duration of therapy with DIV was 4 years, including BCD-132-EXT trial (2-years). Main efficacy endpoints included annualized relapse rate (ARR), proportion of relapse-free patients, confirmed disability progression over 3 months (CDP3mo) and MRI parameters such as contrast-enhancing T1 lesions (T1Gd+) and combined unique active (CUA) lesions (new T1Gd+ and new/enlarging T2-weighted lesions without double counting).
Results: The majority of patients had no relapses. The proportion of relapse-free patients over 4 year was 77.3% (34/44). The ARR (95% CI) decreased from 0.091 (0.034; 0.242) over the first year to 0.023 (0.003; 0.161) over the fourth year of treatment. Proportion of patients with no CDP3mo was 95.5% (42/44). At the time of completion of follow-up, the proportion of patients without T1Gd+ was 93.2% with the adjusted T1Gd+ number per scan of 0.011 (95% CI: 0.004; 0.035). The adjusted CUA per scan for the entire treatment period was 0.018 (95% CI: 0.006; 0.052). During the 4 years, treatment-related adverse events were observed in 59.1% (26/44). The most frequent (5% or more) reported treatment-related adverse events were decreased lymphocyte counts in 36.4% (16/44 patients), decreased leukocyte counts in 20.5% (9/44 patients), decreased neutrophil counts in 15.9% (7/44 patients), and infusion-related reactions in 11.4% (5/44 patients). There were no serious treatment-related adverse events.
Conclusion: Treatment with DIV for 4 years provides sustained long-term efficacy in patients with RMS. Safety profile of DIV was favorable and consistent with the previous studies.

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P1658
Exploring the inhibition of Myc as a novel therapeutic approach for multiple sclerosis

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Introduction: The protein encoded by the proto-oncogene myelocytomatosis (*MYC*) controls global gene expression and regulates a wide variety of cellular processes. Upon T and B cell activation, *MYC* is upregulated and controls the survival, proliferation and production of inflammatory mediators in these cell types. T and B cells have been identified as key players in the pathogenesis of multiple sclerosis (MS), therefore the inhibition of their function has been investigated as a therapeutic approach for MS. We hypothesized that Omomyc, a MYC inhibitor mini-protein with demonstrated therapeutic potential in cancer, may also effectively suppress immune response in MS.
Objectives/Aims: This study aimed to assess the potential of Omomyc to modulate the immune activation of T and B cells in MS.
Methods: Peripheral blood polymorphonuclear cells (PBMCs) from 10 untreated relapsing-remitting MS patients were cultured and activated in the presence of Omomyc (20 and 30 mM). Anti-CD3/CD28 stimulus was used to activate T cells in a TCR-dependent manner, and phorbol 12-myristate 13-acetate (PMA) and ionomycin as a TCR-independent stimulus. Activation at 24h was assessed by means of CD69 and CD25 expression, and the TCR-mediated proliferation was measured through CFSE dilution at 7 days. B cells were activated for 24h with anti-BCR and IL-4 in a BCR-dependent fashion, and with ODN through toll-like receptors (TLR). The frequency of activated B cells was determined by means of HLA-DR, CD80, CD86 and CD40 expression.
Results: Omomyc (20 and 30 mM) significantly reduced the TCR-mediated activation of CD4 (mean reduction respect to vehicle-treated cells: 27.50% and 35.14%, respectively) and CD8 T cells (mean reduction respect to vehicle-treated cells: 50.64% and 58.33%). In addition, it significantly reduced both CD4 (mean reduction respect to vehicle-treated cells: 6.24% and 16.71%) and CD8 (mean reduction respect to vehicle-treated cells: 5.06% and 19.90%) T cell proliferation in a concentration-dependent manner. Regarding B cells, treatment with Omomyc resulted in a significant reduction of all studied markers (HLA-DR, CD80, CD86 and CD40; $p<0.05$) when challenged not only with anti-BCR but also through TLRs, and in both cases the reduction of B cell activation was independent of the concentration of Omomyc used.
Conclusion: These results highlight the promising immunomodulatory effects of Omomyc through the modulation of immune function of both T and B cells, suggesting that MYC inhibition could be a potential therapeutic approach for MS.

Disclosure of interest: H Eixarch, C Espejo, S Casacuberta-Serra, M Beaulieu and L Soucek are inventors of a patent that protects the use of MYC inhibition as therapy for autoimmune diseases, licensed to Peptomyc SL. S Casacuberta-Serra, ME Beaulieu and L Soucek are employees and shareholders of Peptomyc SL. B Rodriguez-Acevedo has received speaking honoraria from Merck, and travel expenses and congress attendance support from Sanofi and Merck. Professor Montalban's institution has received compensation for lecture honoraria and travel expenses, participation in scientific meetings, clinical trial steering committee membership, or clinical advisory board participation in recent years from Abbvie, Actelion, Alexion, Astrazeneca, Autolus, Bial PD, Biogen, Bristol-Myers Squibb/Celgene, EMD Serono, Genzyme, Hoffmann-La Roche, Immunic Therapeutics, Indivi, Janssen Pharmaceuticals,Juvisé Pharmaceutical, Lilly, Medday, Medscape, Merck, Mylan-Viatris, Nervgen, Neuraxpharm, Novartis, Peervoice, Rewind Therapeutics, Samsung-Biosys, Sandoz, Sanofi-Genzyme, Teva Pharmaceutical, TG Therapeutics, Zenas Biopharma, Excemed, ECTRIMS, MSIF, and NMSS or any of their affiliates. I Boutitah, M Castillo and A Abellán have nothing to disclose. Funding sources: This work was supported by the "Agència de Gestió d'Ajuts Universitaris i de Recerca" (AGAUR) under the grant 2021SGR782, Generalitat de Catalunya, Spain.

P1659
A Markov Model Framework for Evaluating the Cost-Effectiveness of Preventative Immunotherapies in Neuromyelitis Optica Spectrum Disorder

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a relapsing autoimmune disease of the central nervous system associated with significant disability. New immunotherapies demonstrate strong efficacy for the prevention of relapse in NMOSD, but their high cost raises concern about long-term cost-effectiveness.
Objectives/Aims: Develop a Markov model to simulate the health states and transition probabilities of NMOSD, allowing for an incremental cost-effectiveness analysis of preventative immunotherapies.
Methods: We are constructing a Markov model using R Statistical Software to represent the health states of patients with aquaporin-4 immunoglobulin G antibody (AQP4-IgG) positive NMOSD living in the United States, including first attack, level of disability according to the Expanded Disability Status Scale (EDSS), relapse, drug-related adverse event, and death. The model will use a cycle length of 3 months over a lifetime horizon. Transition probabilities will be derived from published clinical trial data and real-world data. Drug costs, direct medical costs, and utility values associated with each health state will be obtained from national financial databases, health outcome data, and patient questionnaires. The analysis will be performed from a United States healthcare system perspective and societal perspective.
Results: Model development and validation are ongoing. Once finalized, it will be used to estimate the incremental cost-effectiveness ratios (ICERs) in cost per quality-adjusted life year (QALY) gained for eculizumab against ravulizumab, inebilizumab, satralizumab, rituximab, mycophenolate mofetil, and azathioprine for the prevention of relapse in NMOSD. One-way sensitivity analyses will evaluate how ICERs are impacted by variation in drug costs, relapse rates, and utility values.
Conclusion: The model will provide a framework for understanding the clinical and economic consequences of preventative immunotherapies in NMOSD and will lay the foundation for future policy and decision-making on fair drug pricing and patient access within the United States healthcare system. This represents an important step toward making highly effective treatments available to all people living with NMOSD.

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P1660
Design and baseline characteristics of IMPACT-MS, a single-center, nested case-control study investigating the immunological effects of ocrelizumab compared to immunomodulatory therapies in newly diagnosed, untreated, relapsing-onset MS

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Introduction: Ocrelizumab (OCR) efficiently depletes B cells and is approved for treatment of relapsing and primary progressive forms of MS. Elevated intrathecal synthesis of gamma globulin is a hallmark of MS and fulfils diagnostic criteria for "dissemination in time". Whether early intervention with OCR in newly diagnosed MS patients influences intrathecal gamma globulin production is unknown. IMPACT MS is a nested, case-control study, embedded within the UCSF ORIGINS observational cohort study that seeks to understand the immunological characteristics of untreated persons with relapsing onset MS (RMS) within 90 days of first relapse.
Objectives/Aims: To present the study design, baseline characteristics and preliminary results of IMPACT MS.
Methods: IMPACT MS is a single center, open-label, case-control study comparing the impact of OCR to immunomodulators on intrathecal gamma globulin synthesis in RMS. Eligibility criteria included age 18–50 years, high risk CIS or RMS, screening within 90 days of first clinical demyelinating event, no prior MS disease modifying therapy, no corticosteroids within 7 days of first ocrelizumab treatment, and EDSS < 4.0. Participants were treated with OCR for 3 years. CSF samples were collected at baseline, month 6 and at year 3. The primary outcome is persistence of elevated intrathecal gamma globulin synthesis at year 3. Secondary endpoints include: relapses, disability progression/improvement; patient reported outcomes, quantitative magnetic resonance imaging of the brain and spinal cord; serum markers of CNS injury; single cell CSF cellular phenotypes and clonal abundance; safety and tolerability.
Results: The trial enrolled 30 participants. Baseline mean ($\pm$SD) age was 33.4 ($\pm$8.7) years. 73% were women, 20% men and 7.0% were non-binary. 73.3% met 2017 International Panel criteria for RMS and 23.6% were classified as high-risk CIS. Median baseline EDSS was 2.0 (range 0-3.5). The mean ($\pm$SD) brain volume was 1123 $\pm$96 cm^3. The mean C2 spinal cord area was 83$\pm$7mm^2. The mean ($\pm$SD) T2 brain lesion volume was 2.4 $\pm$3.0 cm^3. 67% had more than 9 discrete brain lesions. The median (range, IQR) number of spinal cord lesions was 1 (0-9,

1, 4). 53% of participants had gadolinium-DPTA enhancing lesions. CSF-restricted OCBs were present in 90%. All participants were recruited within 90 days of symptom onset. The reference population consists of a cohort of UCSF ORIGINS participants matched for age, sex and disease duration who were treatment naïve at baseline but were treated with non-lymphodepleting immunomodulatory therapies. This study has 90% power to detect eradication of CSF-restricted OCBs in 30% of study participants.

Conclusion: On completion, this study will determine whether 3 years of treatment with OCR in newly diagnosed, untreated RMS/high risk CIS participants can eradicate OCBs. This study will also provide comprehensive immunophenotyping of the cerebrospinal fluid in these participants.

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P1662
Comparative Effectiveness of Rituximab in Treatment-Naïve vs Switch Patients with Multiple Sclerosis

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Introduction: Rituximab, an anti-CD20 monoclonal antibody, is increasingly used off-label for multiple sclerosis (MS).
Objectives/Aims: This study evaluates its efficacy and safety in treatment-naïve patients versus those switching from other disease-modifying therapies (DMTs) at Security Forces Hospital, Makkah (SFHM).
Methods: A retrospective cohort study analysed MS patients treated with rituximab at SFHM (January 2018–December 2024). Patients were categorized into treatment-naïve (no prior DMT) and switch (prior DMT) groups. Outcomes included annual relapse rate (ARR), Expanded Disability Status Scale (EDSS) progression, MRI activity (new/enhancing lesions), adverse events, and treatment discontinuation rates. Statistical analyses compared outcomes between groups.
Results: Among 34 patients (Naïve = 16, Switch = 18), rituximab demonstrated significant efficacy in reducing relapse rates and stabilizing disease activity. In the treatment-naïve group, all patients reported zero relapses post-rituximab, while the switch group also showed a marked reduction in relapses, with most patients reporting zero relapses after treatment. MRI activity remained stable in the majority of patients, with no new or enhancing lesions observed in follow-up scans for most cases. For example, one treatment-naïve patient with multiple enhancing lesions at baseline showed no enhancement in follow-up MRIs, and a switch patient with prior spinal cord lesions also demonstrated stable MRI activity post-treatment. EDSS scores remained stable or improved in most patients across both groups. One treatment-naïve patient improved from a baseline EDSS of 6 to a follow-up score of 5, while a switch patient improved from 3 to 2. Adverse events were minimal, with only one patient reporting a mild skin rash during infusion and another developing lymphopenia. No severe adverse events or treatment discontinuations were reported in the data.
Conclusion: Rituximab demonstrated high efficacy in reducing relapse rates and stabilizing MRI activity in both treatment-naïve and switch MS patients. The safety profile was favorable, with minimal adverse events reported. These findings suggest that rituximab is an effective treatment option for MS, regardless of prior DMT exposure. Further long-term studies are needed to confirm these results and optimize treatment strategies.

Disclosure of interest: nothing to disclose.

P1663
Zanubrutinib for Treatment of Patients with Recurrent Neuromyelitis Optica Spectrum Disorders

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory autoimmune disease of the central nervous system with high recurrence. Bruton's tyrosine kinase (BTK) regulates the development of B cells that are implicated in the pathogenesis of NMOSD. So BTK inhibitors might be a therapeutic candidate for patients with NMOSD.
Objectives/Aims: To assesse the therapeutic potential of the BTK inhibitor zanubrutinib in recurrent NMOSD patients.
Methods: This was a single-center, single-arm, open-label study enrolling patients with recurrent NMOSD in China. All patients had a history of at least two attacks in the 2 years before screening, with at least 1 of which occurred within 12 months before screening, and received 80mg zanubrutinib twice daily (at least 12 hours apart) for 48 weeks. The primary endpoint of this study was the relapse-free rate at 48 weeks. Secondary endpoints included changes in the EDSS score, the titer of the AQP4 antibody, IgG, IgM, and IgA, and the absolute value of lymphocyte subsets and other blood immune parameters. Adverse events were also recorded for safety assessment. The study was registered at ClinicalTrials.gov as NCT05356858.
Results: Five patients were enrolled, three of whom relapsed after rituximab treatment. All patients had no attack during the 48 weeks of treatment. Three of the five patients showed a decrease in EDSS score, while two of these patients' AQP4 antibody titers declined. Total B cell counts were slightly decreased in all patients. No serious adverse events occurred.
Conclusion: In this small study, zanubrutinib has the potential to be a safe and effective treatment for patients with recurrent NMOSD, especially for those who have failed B cell depletion therapy. A multicenter randomized controlled study with a larger sample is needed to further assess its safety and efficacy.

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THERAPY – Regenerative and neuroprotection trials

P1664
Twelve-week intermittent hypoxia intervention in multiple sclerosis – a phase II pilot trial

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Introduction: Improving neuronal energy metabolism might be a therapeutic strategy to mitigate neurodegeneration in multiple sclerosis (MS). Exposure to low oxygen concentrations at high altitudes leads to remarkable physiological adaptations of energy utilization. An intermittent hypoxia intervention may therefore provide a safe and feasible therapeutic approach to enhance neuronal resilience in people with MS (pwMS).
Objectives/Aims: Provide initial insights into the safety, feasibility and effects on clinical outcomes of a 12-week intermittent hypoxia intervention in pwMS.
Methods: This monocentric, single-arm, non-blinded, interventional phase IIa pilot trial included individuals with primarily progressive MS (18-60 years; EDSS ⩽ 6.5). Participants underwent a 12-week hypoxia intervention with 2-3 standardized 2-hour weekly sessions simulating altitudes up to 4,500 meters, with a minimal fraction of inspired oxygen of 11%. The primary outcome was the incidence of high-altitude sickness, assessed using the Lake Louise Score. Secondary outcomes included evaluations of disability measures, cognitive function, patient-reported outcomes, MRI progression, immune cell subpopulations in the blood, serum neurofilament light chain and serum metabolites.
Results: Twelve pwMS were enrolled in the study, of whom ten completed the intervention. None of the participants developed moderate or severe symptoms of high-altitude sickness. No systemic safety concerns or worsening of clinical or paraclinical markers were observed. Disability-related outcomes showed improvements in the 9-hole peg test of the dominant hand (adjusted change from Baseline (BL) at 12 weeks (W) -13.24, 95%-CI [-21.27;-5.21], P=0.001), the Timed 25-foot Walk Test (adjusted change from BL at 12W -1.86, 95%-CI [-2.85;-0.86], $P<0.001$) and the Symbol Digit Modalities Test (adjusted change from BL at 12W 0.29, 95%-CI [-0.03;0.56], P=0.028).
Conclusion: A 12-week regimen of intermittent hypoxia intervention is safe and well-tolerated in pwMS, with no evidence of high-altitude sickness, systemic adverse events or worsening of MS progression. This supports further investigation of this approach in larger clinical trials.

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P1665
N-acetyl-L-leucin has a neuroprotective effect on multiple sclerosis-specific human induced primary neurons

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Introduction: N-acetyl-L-leucine (NALL), an acetylated derivative of the amino acid leucine, has been demonstrated to reduce neuronal cell death and neuroinflammation in murine models. Beneficial effects in patients with lysosomal storage diseases Niemann-Pick Type C have led to recent FDA approval. However, the neuroprotective effects of NALL remain to be fully elucidated.
Objectives/Aims: To investigate neuroprotective effects of NALL in human induced primary neurons (iPNs) derived from MS donors.
Methods: To analyse neuroprotective effects, iPNs were treated with the microtubule destabilising reagent nocodazole (Noco 10 µM) or Noco/NALL co-treatment at concentrations of 1mM and 5mM for 6 hours, followed by fixation. Evaluation was performed by measuring neurite length using the ImageJ neuronJ plugin. In addition, iPNs were treated with 1mM and 5mM NALL for 24 hours for quantitative real time polymerase chain reaction (qPCR) analysis for oxidative stress markers (glutamate cysteine ligase – GCL; nuclear factor (erythroid-derived 2)-like 1 – NRF2; NAD(P)H quinone oxidoreductase 1 protein – NQO1; Glutathione reductase – GSR). Statistical analysis was performed using Kruskal-Wallis test.
Results: A significant increase in neurite length was observed in MS-specific iPNs treated with NALL and Noco simultaneously for 6 hours in comparison to Noco treatment alone (neurite length in µm (mean±SD): Noco: 44.37±11.00; p=<0.0001; 1mM: 71.69±19.92; p=0.0079; 5mM: 71.96±21.30; p=0.006; N=3; n=15 each N). qPCR analysis of oxidative stress targets indicated an upregulation of GCL expression after 24-hour 5mM NALL treatment (p=0.0283; N=3 in duplicates) compared to untreated control cells.
Conclusion: Our results show that iPNs co-treated with Noco and NALL exhibited a significant increase in neurite length compared to Noco treatment. This observation suggests a neuroprotective effect induced by NALL. Our qPCR analysis of

oxidative stress, specifically of GCL as a target for oxidative stress defence, indicates that iPNs treated with NALL have a higher cellular protective response against potential oxidative stress.

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P1666

Hsa-miR-219a-5p-enriched extracellular vesicles boost neuronal excitability: Unraveling their pro-active role in cortical neurons and human iPSC-derived motor neurons via multielectrode array

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Introduction: Neurodegenerative diseases such as Multiple Sclerosis represent a significant health challenge, affecting millions worldwide. These conditions are characterized by progressive neuronal and glial cell loss, along with selective dysfunction of neural networks in the central nervous system. Extracellular vesicles (EVs) have emerged as mediators of intercellular communication, playing key roles in myelination maintenance, neuroprotection and neuronal survival. Notably, our group and others have demonstrated that Hsa-miR-219a-5p-enriched EVs can enhance oligodendrocyte precursor cell differentiation into mature, myelinating oligodendrocytes which could provide neuroprotection while accelerating nerve conduction. However few is known about their impact on Neurons.

Objectives/Aims: To elucidate the impact of miR-219a-5p-enriched EVs from different cellular origin on complex neuronal network activity and function.

Methods: HEK 293T and SVG-p12 (astroglia-like) cells were transfected with either a plasmid containing the miR219a-5p sequence (219) or a control plasmid (PLKO), and their derived EVs were isolated by centrifugation at 20,000×g, yielding miR219a-5p-enriched EVs (219 EVs) and control EVs (PLKO EVs). ddPCR analysis confirmed significantly higher miR219a-5p expression in 219 EVs compared to PLKO EVs for both HEK 293T (FC: 19.55; $p<0.01$) and astroglial cells (FC: 9.97: $p<0.05$). These EVs were tested in primary rat cortical neurons using multielectrode array (MEA). Rat Neurons were plated on 24-well MEA plates. At 12-14 days post-seeding, cultures were incubated with 5×10^8 particles and their activity was recorded for 170 min. To validate these findings in a human cell model, the same experiment was performed using human iPSC-derived motor neurons as recipient cells. In this case, astroglial-derived EVs were additionally evaluated alongside HEK-293T-derived EVs to assess cell-type-dependent effects on neuronal activity.

Results: MEA recordings demonstrated significantly different neuronal activity patterns between 219 EV- and PLKO EV-treated cultures in both experimental models. In rat cortical neurons, 219 EVs produced a more pronounced stimulatory effect over time compared to control EVs ($p < 0.05$). Similarly, in human iPSC-derived motor neurons, 219 EVs from both HEK 293T ($p<0.0001$) and astroglial ($p<0.05$) cell sources consistently elicited higher neuronal firing rates over time relative to PLKO EV treatment.

Conclusion: The findings indicate that miR-219a-5p-enriched EVs significantly enhance neuronal activity in rodent and human cell models. This work represents a critical step toward the understanding of EV-mediated therapeutic applications for neural repair and protection.

Ongoing studies will assess axonal integrity (NfL), viability (LDH), and transcriptomic regulation (RNA-seq) to dissect the transcriptomic impact of miR-219a-5p-enriched EVs from distinct cellular sources on neuronal gene expression and signaling pathways.

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P1667
TGFα controls checkpoints in astrocytes and CNS infiltrating immune cells to promote resolution of autoimmune inflammation

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Introduction: After acute lesions in the central nervous system (CNS), the interaction of astrocytes, microglia, and infiltrating immune cells decides over lesion resolution or chronification. However, this CNS-intrinsic cross-talk is poorly characterized. In previous research, we have identified TGFa as a potential mediator of tissue protection and lesion resolution within the CNS, however, its cellular sources, target populations and therapeutic potential remain unidentified.
Objectives/Aims: We thus aimed at investigating the CNS-intrinsic production, cellular effects, and inflammation-mitigating properties of TGFa during autoimmune CNS inflammation.
Methods: We analyzed cerebrospinal fluid samples of Multiple Sclerosis (MS) patients and used the animal model of MS, experimental autoimmune encephalomyelitis (EAE), in combination with mechanistic *in vitro* studies, *in vivo* treatment paradigms, scRNA sequencing, CRISPR-Cas9 genetic perturbation models, and magnetic resonance imaging to evaluate the function and translational potential of TGFa in the CNS.
Results: We demonstrate that a mutual cross-talk between astrocytes, microglia, and CNS-infiltrating immune cells mediated by glia-derived TGFα drives recovery from acute CNS lesions. Indeed, TGFα is secreted in a highly regulated temporospatial manner by astrocytes and microglia at the peak of autoimmune neuroinflammation, contributing to recovery by decreasing infiltrating T cell cells, pro-inflammatory myeloid cells, oligodendrocyte loss, demyelination, axonal damage, and neuron loss during early and late disease stages. In a therapeutic approach, blood-brain barrier penetrating intranasal application of TGFα attenuates pro-inflammatory signaling in astrocytes and CNS infiltrating immune cells, while promoting neuronal survival and lesion resolution.
Conclusion: Together, we here identify TGFα as an important mediator of glial immune crosstalk and highlight its therapeutic potential to promote resolution of acute as well as late-stage autoimmune CNS inflammation.

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Therapy – Risk management and treatment De-escalation

P1668
Opportunistic Varicella Zoster Virus Infection among patients with Multiple Sclerosis and association with Disease Modifying Treatments: a monocentric study

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Introduction: Opportunistic infection by Varicella Zoster Virus (VZV) may occur in persons with Multiple Sclerosis (PwMS) treated with disease modifying drugs, as documented by the results of clinical trials. Nevertheless, limited data exist on the incidence and severity of clinical presentation in real life cohorts.
Objectives/Aims: To describe incidence and clinical features of VZV infections among PwMS followed up at the MS center of Tor Vergata University Hospital and association with exposure to DMTs.
Methods: Clinical charts of people with MS with at least one outpatient visit recorded at the MS center of Tor Vergata University hospital were interrogated searching for VZV infection record. Information on demographic and clinical characteristics of MS and VZV infection, as well as treatment history were collected.
Results: Among the 3.742 individuals with at least one visit recorded from 2003-2025, we found 59 records of VZV infection (2 chicken pox and 57 shingles) in 50 PwMS (Mean age 44.44 years +/- SD 11.17; F 70%, DD 19.34 +/- SD 30.92). 54/57 shingles had dermatomeric skin eruption presentation. 3/57 were complicated by eye involvement and uveitis. No death occurred. In 14/59 cases, the infections underwent spontaneous recovery, while in 45/59 cases therapy with antiviral drugs was necessary. Infections were observed in 14/59 cases on S1P modulators treated patients, in 12/59 on Natalizumab, in 8/59 on Dimethyl fumarate, in 5/59 on Glatiramer acetate, in 5/59 on Interferon b1a, in 5/59 on anti-CD20 monoclonal antibodies, in 3/59 on Cladribine, in 2/59 on Teriflunomide, and in 5/59 without any treatment. Forty out of 50 patients were vaccinated with Shingrix vaccines following the event.
Conclusion: In agreement with previous evidence, VZV primary infection or reactivation is a rare event usually with favourable outcome. In our study, the majority of the events occurred in patients treated with S1P modulators, NTZ and DMF. We can speculate that T cells peripheral or CNS depletion observed as an effect of these treatments may represent a risk factor for VZV opportunistic infections. Monitoring and preventive vaccination against VZV infections should be implemented particularly in these patients to prevent more serious complications.

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Novartis, Biogen. She is a sub-investigator in clinical trials for Biogen, Merck Serono, Roche, Sanofi, Novartis, Teva, Bristol Mayer Squibb; Marfia G.A. is an Advisory Board member of Almirall, Amgen, Alexion, Neuraxpharm, Sandoz, Sanofi Genzyme, Merck-Serono, Novartis, Roche and received honoraria for speaking or consultation fees from Almirall, Bayer Schering, Biogen, Merck Serono, Neuraxpharm, Novartis, Sanofi-Genzyme, Roche, Amgen, Alexion and BMS. She is the principal investigator in clinical trials for Biogen Idec, Merck Serono, Novartis, Roche, Sanofi-Genzyme, Merck Serono and BMS; Landi D. received travel funding from Biogen, Merck Serono, Sanofi, Teva, Bristol Myers Squibb, Mylan, Neuraxapharm, speaking or consultation fees from Sanofi, Merck Serono, Teva, Biogen, Roche, Novartis, Bristol Myers Squibb, Janssen, Alexion, Amgen.

P1669
Evaluating the Need of Routine Testing and Antibiotic Use in Patients Receiving Ocrelizumab

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Introduction: At Cambridge University Hospital (CUH), patients receiving ocrelizumab infusions routinely complete COVID-19, pregnancy, and urine dipstick testing beforehand. Patients with positive urine dipstick results but no urinary symptoms are often treated with antibiotics and have their ocrelizumab infusion on the same day. Routine testing may not always be clinically necessary, potentially causing delays, inappropriate antibiotic use, and reduced service efficiency.
Objectives/Aims: This review assessed the need of routine pre-infusion testing, the appropriateness of antibiotic prescribing based on urine dipstick results, and the potential to safely omit testing to improve service efficiency.
Methods: Patients who received ocrelizumab within the previous 12 months were identified from the service database. A total of 247 patients were included. COVID-19, pregnancy, and urine dipstick results, alongside antibiotic prescriptions, were reviewed retrospectively. Positive urine dipstick results were defined by nitrites or leucocytes $\geqslant 2+$. Urine culture results were analysed where available.
Results: A total of 247 patients with 481 infusion appointments were reviewed. All COVID-19 (439/439) and pregnancy tests (360/360) were negative. Nine per cent (44/475) of urine dipstick tests were positive, but 89% (39/44) were false positives with no confirmed infection. Only 1% (5/475) of patients had asymptomatic bacteriuria, and none developed symptomatic urinary tract infections. Despite this, 88% (42/44) of patients with positive dipstick results were prescribed antibiotics unnecessarily. Replacing routine testing with a five-minute screening questionnaire for approximately 650 ocrelizumab infusions each year could save around 270 hours, allowing 54 additional ocrelizumab infusions or 119 subcutaneous treatment slots annually.
Conclusion: Routine pre-infusion testing could be safely replaced with a screening questionnaire, with further tests performed in patients with specific risk factors. This would reduce inappropriate antibiotic prescribing and antimicrobial resistance risk, without compromising safety. Streamlining the process could save up to 270 hours annually at a single centre, improving patient flow and capacity. Across England, with 50% uptake, this could enable approximately 737 additional ocrelizumab infusions or 1,767 subcutaneous treatment slots each year.

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P1670
Long-term follow-up of multiple sclerosis patients treated with cladribine tablets as de-escalation strategy from anti-CD20

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Introduction: Prolonged treatment with anti-CD20 antibodies (antiCD20) leads to hypogammaglobulinemia and increased infection risk in MS. Treatment with cladribine (CLAD) is rarely associated with hypogammaglobulinemia
Objectives/Aims: To investigate changes in IgG and IgM serum concentration (sIgG/IgM) and the frequency of infections in MS patients switching from antiCD20 to CLAD.
Methods: Prospective, observational study including MS patients switched from antiCD20 to CLAD for hypogammaglobulinemia (sIgG/IgM reduction$>$10%) and/or infection risk. sIgG/IgM, frequency/severity/type of infections, and effectiveness paramenters (relapses, EDSS progression, new/enlarging T2 MRI lesions, changes in neurofilament light [NfL] and glial fibrillary acidic protein [GFAP] z-scores) were collected. Wilcoxon-matched pair test and linear mixed-effect models with time*treatment group interaction term were used.
Results: 14/44 MS patients [27 females, median age 46(36-55) years] switched to CLAD and 30 continued antiCD20 for 3.1 years. At baseline, disease duration, EDSS and antiCD20 exposure were greater in CLAD-group.

Baseline sIgG was 7.2(6.2-10.3) g/L in the CLAD-group and 9.0(7.8 to 10.5) g/L in the antiCD20-group. These remained stable over three years (median change: CLAD-group=-0.08[-0.73-0.88], p=0.944; antiCD20-group=-0.33[-1.28-0.47], p=0.142). There was a trend towards a minor reduction over time in sIgG in the CLAD-group (time*treatment group: β=0.04; p=0.093).
Baseline sIgM was 0.46 (0.36-0.57) g/L in the CLAD-group and 0.63 (0.49-0.87) g/L in the anti-CD20-group. sIgM remained stable over follow-up in the CLAD-group (median change=0.02 [-0.08-0.16], p=0.551), while decreased in the antiCD20-group (-0.12[-0.22-0.03], p<0.001). There was a significant time*treatment group interaction (β=0.10 p<0.001).
Thirty-seven adverse events occurred in the antiCD20-group and 18 in the CLAD-group, the most common being mild-moderate infections. Five (35.7%) patients in the CLAD-group and 4(12.9%) in the antiCD20-group had EDSS progression. No clinical relapses occurred. One (7.1%) patient in the CLAD-group had a new T2 spinal lesion; while in the antiCD20-group 1(3.2%) had a new brain T2 lesion, and 2(6.5%) new T2 spinal lesions. Data on NfL and GFAP will be presented.
Conclusion: Switching to CLAD from antiCD20 treatment due to increased infection risk and/or hypogammaglobulinemia was associated with a stabilization of sIgG and sIgM, a good safety profile, and maintained effectiveness towards MS focal inflammatory activity.

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P1671
Low natalizumab trough concentrations are associated with reduced seroconversion of the John Cunningham virus in natalizumab-treated patients with multiple sclerosis - Implications for personalized extended interval dosing to increase drug safety

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Introduction: Natalizumab is a highly effective drug for patients with relapsing-remitting multiple sclerosis (MS). A disadvantage of this treatment is the risk of progressive multifocal leukoencephalopathy (PML) in patients who are seropositive for the John Cunningham virus (JCV). JCV seroconversion rates increase under natalizumab treatment compared to non-natalizumab using controls.
Objectives/Aims: The aim of this study was to assess whether lower natalizumab trough concentrations are associated with reduced JCV seroconversion compared to higher natalizumab trough concentrations.
Methods: Two overlapping cohorts of patients treated with intravenous natalizumab in the Netherlands were combined for this study. JCV seroconversion was assessed during periods of high (⩾15 μg/mL) and low (<15 μg/mL) natalizumab trough concentrations. Low trough concentrations were mainly the result of trough concentration guided personalized extended interval dosing (EID). The seroconversion rates during high and low trough concentrations were compared using a generalized linear mixed model with a Poisson link function. Results of these analyses have already been published; however, for the ECTRIMS, additional analyses will be conducted to assess JCV seroconversion in subgroups.
Results: A total of 357 patients from 21 hospitals in the Netherlands were included. The annual seroconversion rate of

8.4% observed in patients during periods of high trough concentrations (n=226) was 2.32 times higher than the seroconversion rate of 4.8% in patients during periods of low trough concentrations (n=252) (95% CI = 1.32-4.08, p=0.0035).
Conclusion: The seroconversion rate observed in MS patients with low trough concentrations was substantially lower compared to those with high trough concentrations during natalizumab treatment. This emphasizes the importance of personalized EID, where intervals between infusions are prolonged to achieve lower natalizumab trough concentrations, to increase drug safety.

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P1672
Stopping disease-modifying therapies in multiple sclerosis: a retrospective case-control analysis

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Introduction: Currently, there is lack of evidence on the strategies for disease-modifying therapy (DMT) discontinuation in multiple sclerosis (MS) patients.
Objectives/Aims: The objective of this study is to evaluate confirmed disability progression (CDP) and evidence of disease activity-3 (EDA-3) after one year of DMT discontinuation compared with a control group.
Methods: Single-centre retrospective observational case-control study, including patients diagnosed with MS who had discontinued DMT and had a minimum follow-up of one year (June 2013-December 2024). Controls without DMT discontinuation were selected from a prospectively collected MS patients database by propensity score matching by age, sex, MS type and DMT. Controls exclusion criteria included less than one year follow-up and no clinical or radiological stability for at least 3 years. We classified patients according to VIAADISC scale. This scale predicts the risk of activity after DMT discontinuation according to age, and clinical and MRI data.
Results: After propensity score matching, 32 patients who discontinued DMT and 44 controls who did not discontinue DMT were included. No statistically significant differences were found between the two groups regarding age (median 54.2 vs 51.3 years), sex, MS phenotype, DMT, EDSS and VIAADISC score. After one year, there were no significant differences between the two groups in terms of CDP (OR 0.55, 0.07-2.85, p-value=0.69) and EDA-3 (OR 1.05, 0.37-2.92, p-value=0.6). There were no differences regarding new MRI lesions (p-value=0.18), although slightly more relapses in the control group were observed (p-value=0.04).
Conclusion: Discontinuation of DMT in selected MS patients showed no higher risk of disease activity and disability accumulation after one year.

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P1673
HPV Infections in Patients with Multiple Sclerosis: a monocentric study

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Introduction: People with Multiple Sclerosis (PwMS) treated with different Disease Modifying Therapies (DMTs) may experience an increased risk of Human Papilloma Virus (HPV) infection, as reported in Randomized Controlled Trials (RCTs). However, real world data are still lacking.
Objectives/Aims: To describe the prevalence of HPV infections among PwMS followed up at the MS center of Tor Vergata University Hospital in association with DMTs exposure, Disease Duration (DD), age and sex.
Methods: A retrospective study was conducted on clinical records of MS patients followed-up at Tor Vergata Hospital. We investigated the prevalence of HPV infection and collected demographic, clinical and DMT history data. Logistic regression and non-parametric statistical tests was performed.
Results: Among patients with at least one visit between 2003 and 2025, we identified 164 individuals (mean age 39.01 $\pm$ 9.75 years; female 98.78%, disease duration 7.51 $\pm$ 6.16 years) who underwent to HPV-DNA test or Pap test. Among them, 61 patients (37.19%) were positive for HPV-DNA test, and 28 out of 61 (45.9%) reported a high-risk HPV genotype (HR-HPV). HPV infection was observed in 9/18 patients receiving interferon beta-1a, 3/6 teriflunomide, 9/22 dimethyl fumarate, 11/28 S1P modulators, 12/26 natalizumab, 5/11 cladribine, 5/18 anti-CD20 monoclonal antibodies, and 7/35 untreated. HPV infection was associated with younger age ($p = 0.003$, odds ratio 0.943). No significant predictors of HPV infections were found considering disease duration, DMTs class, or sex.
Conclusion: In our cohort, we found a higher prevalence of HPV infection, particularly among younger patients and unrelated to DMTs exposure. Nevertheless, long standing treatment with immunosuppressants may heighten the risk of persistent infection and cancer. Our data highlight the need of proactive HPV screening and risk minimization by vaccination, as well as of specific counselling.

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P1674
Safety and Efficacy of De-Escalating Therapy from Rituximab to Cladribine in Multiple Sclerosis

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Introduction: B-cell depletion with Rituximab (RTX) is associated with reduced IgG levels, immunosuppression, risk of infections and malignancies and vaccination restrictions. Whereas, Cladribine is a weaker but effective immune reconstitution therapy. It has a prolonged action with lesser risk of infections and reduced treatment visits and monitoring burden. Switching from RTX to Cladribine may be advantageous.
Objectives/Aims: To report the safety and efficacy of de-escalation of therapy from RTX to Cladribine tablets in persons with multiple sclerosis (PwMS).
Methods: Cladribine was available for limited use as part of pre-licensing clinical trial in India. PwMS who were switched from RTX to Cladribine were closely monitored for blood parameters, infections and NEDA-3 status (Clinical features, Disability progression and MRI- done at baseline and after each year). Standard dose of Cladribine (year-1 and year-2) was initiated after verifying standard safety recommendations. Repopulation of CD-19 /CD-20 B cells and adequate IgG levels were ensured before switching
Results: Eleven PwMS receiving RTX (duration 1.5-7 years) were switched to Cladribine. Indications for RTX were poor

prognostic features for disability- high disease activity, high lesion load or infra-tentorial involvement. All had good response to RTX and maintained NEDA. The switch was considered due to severe infections (n=4), long duration on RTX (n=2) and patient preference for a relatively safer, easier, and possible permanent treatment (n=5). As of present, four PwMS have completed 30 months and seven have completed 14 months post Cladribine. All patients maintained NEDA-3 throughout. One patient had transient asymptomatic leukopenia; two patients had UTI requiring antibiotics. There were no hospitalisations. None of the patients reported fatigue or cognitive dysfunction.

Conclusion: De-escalation to Cladribine from RTX seems an effective and safe option in PwMS. Advantages of switch from B-cell therapies to Cladribine includes continued treatment efficacy, maintenance of NEDA status, lesser incidence of serious infections, ease of treatment burden with possibility of a permanent treatment. Our study is limited by its small numbers, short duration of observation and variable duration of RTX treatment prior to cladribine. Larger studies addressing these shortfalls can help develop treatment algorithms for PwMS on B-cell therapies.

Disclosure of interest: NOTHING TO DISCLOSE

P1675
Safety profile of siponimod in patients with secondary progressive multiple sclerosis: A retrospective real-world analysis

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Introduction: Siponimod is a selective sphingosine-1-phosphate receptor modulator approved for the treatment of secondary progressive multiple sclerosis (SPMS). Although its efficacy has been verified, the safety profile of siponimod requires further real-world investigation.

Objectives/Aims: This study aims to evaluate the incidence and severity of lymphopenia and other side effects in patients with SPMS treated with siponimod, as well as their impact on treatment continuation. Moreover, the study assesses the influence of previous disease-modifying therapy on lymphocyte levels.

Methods: The retrospective study included 225 patients with SPMS treated with siponimod at our center. Clinical and demographic data were collected from medical records. Lymphopenia levels were graded based on CTCAD criteria. The statistical analysis was performed using descriptive and analytical statistics.

Results: The mean age of the patients was 52.6±8.4 years, with 143 (63.6%) being female. The average EDSS was 5.6±0.95. The lymphocyte count dynamics were monitored in 175 patients, of whom 162 (92.6%) developed lymphopenia. Among them, 68 (42%) had grade 3 and 5 (3.1%) developed grade 4 lymphopenia. There was no significant influence of previous disease-modifying therapy on lymphocyte count ($p = 0.168$). Other common adverse effects included infections, elevated liver enzymes, and vertigo. Hypertension occurred less frequently, while isolated cases of macular edema and left bundle branch block were observed. No cases of skin malignancy, seizures, or opportunistic infections were noted. In 15 patients, the dose of siponimod was reduced, primarily due to persistent lymphopenia (86.7%). Overall, 18 patients discontinued siponimod treatment, most often due to the lack of motivation of the patient to continue therapy (33.3%).

Conclusion: Siponimod treatment in patients with SPMS is associated with a high incidence of lymphopenia and various other side effects. Regular monitoring of lymphocyte count, OCT of the macula, dermatological evaluation, and individualized risk assessment are essential for the safe and effective use of siponimod.

Disclosure of interest: Dušan Ristić: nothing to disclose

P1676
Is It Safe to Stop? A Systematic Review and Meta-analysis of Discontinuation Versus Continuation of Disease-Modifying Therapies in Multiple Sclerosis

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Introduction: The use of disease-modifying therapies (DMTs) in multiple sclerosis (MS) is increasing. Sustained disease stability over time while on DMTs has led to growing interest in whether treatment discontinuation may be appropriate in select patients, particularly given the cumulative burden, cost, and potential adverse effects associated with these drugs. However, the safety and clinical impact of stopping DMTs remain debated.

Objectives/Aims: This systematic review and meta-analysis aim to assess the outcomes of DMT discontinuation versus continuation in MS.

Methods: A systematic search was conducted across PubMed, Embase, Scopus, and Cochrane Library from inception to March 2025. We included randomized controlled trials and observational studies comparing outcomes between patients who discontinued DMTs and those who continued. Primary outcomes included relapse rate, MRI activity, confirmed Expanded Disability Status Scale (EDSS) progression, and the mean change of EDSS from baseline. Subgroup analyses were performed based on patient age and DMT efficacy (high-efficacy vs low/moderate or mixed therapies).

Results: A total of 8 studies including the DISCOMS and DOT-MS trials encompassing 2605 patients (970 discontinued DMTs; 1635 continued DMTs) met the inclusion criteria. Discontinuation of high efficacy DMTs was associated with a significantly higher risk of clinical relapse (RR = 4.32; 95% CI: 2.24 – 8.31; $p < 0.001$). However, no significant difference between discontinuation and continuation of low/moderate and mixed DMTs was found (RR = 0.87; 95% CI: 0.70 – 1.07; p = 0.18), (RR = 1.15; 95% CI: 0.79 – 1.69; P = 0.46), respectively. Higher rates of MRI activity were found in the discontinuation group; however, the results were not significant (RR = 3.76; 95% CI: 0.09 – 15.66; P = 0.07). Similarly, no significant difference was found between the two groups in terms of confirmed EDSS progression rate and the mean change of EDSS from baseline ($P > 0.05$).
Conclusion: Discontinuation of high-efficacy DMTs is associated with a significantly higher risk of relapse, while no significant difference was found for low/moderate or mixed efficacy DMTs. Younger patients are at higher risk of relapse compared to older patients. These findings suggest that discontinuation may be more feasible with lower-efficacy therapies and in older patients, though careful monitoring is necessary.

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P1677
DMT (disease modifying therapy) role in the ageing MS (multiple sclerosis) population: U

S. Neurologist Survey, Flavia nelson[1], Regina Berkovich[2], Samuel Hunter[3,4], Amy Perrin Ross[5], Daniel Bandari, MD[6], Daniel Kantor[7,8,9,10]
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Introduction: Despite evidence to the contrary, there is a push by some U.S. key opinion leaders for DMT discontinuation. DOT-MS was halted due to worsening of MS in DMT discontinuers. OFSEP also demonstrated more MS activity in DMT discontinuers. Despite DISCOMS's focus on a narrow, very carefully selected population enriched for those less likely to have activity, there was still an increase in disease activity; curiously, this was downplayed in DISCOMS's conclusions. Payors should not hide behind those conclusions due to the dangers of discontinuation.
Objectives/Aims: To assess U.S. neurologists' perspectives on DMT discontinuation in older PwMS (people with MS).
Methods: Members of the Medical Partnership 4 MS+ (MP4MS+), a group of >1,300 neurologists, were surveyed anonymously in 06/24 (after DISCOMS and OFSEP) and 02/25 (after DOT-MS) to explore attitudes towards DMT benefits in older patients, disability influence on treatment, risk of relapse after discontinuation, and criteria for considering discontinuation.
Results: A total of 176 (06/24) and 165 (02/25) responses were completed. 87.5% and 86.67% indicated that there is "really no [age] rule because patients are different." Notably, the proportion of respondents disagreeing that age plays a role increased significantly from 18.75% to 40%, suggesting DOT-MS influenced a shift towards individualized assessment over strict age cutoffs. The majority, 62.5 % and 66.67% felt that having high disability does not play a role in discontinuation because the "goal of treatment is preservation of function for as long as possible." A large majority, 87.5% and 86.67% agreed that PwMS relapse, even after long-term stability. When discontinuation due to stability was considered, there was a shift to requiring a longer interval of stability. At both time points, a majority do not tell their stable patients to discontinue – 23% and 27% of those respondents discuss it only after raised by the patient/care partner, consistent with patient-centered decision-making.
Conclusion: A large majority of neurologists support individualized assessment, over age-based rules in considering discontinuation after stability. Neurologists agree that disability level, age, and ambulation should not preclude DMT use. Avoidance of any type of disease activity in patients remains a principal goal, including in those who are "older." Clinical trial data and neurologist perspectives debunk oft-repeated myths: "MS Burns Out" and "MS after age X does not need treatment."

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P1678
Long-term serostatus dynamics in patients across different age groups who were anti-JCV antibody negative at baseline: Insights from an integrated TOUCH/Quest Dataset

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Introduction: Natalizumab (NTZ; TYSABRI®) is a highly effective treatment for people with MS (pwMS). It is associated with a rare but serious adverse event, progressive multifocal leukoencephalopathy (PML), which is caused by mutated pathogenic forms of the John Cunningham Virus (JCV). PwMS who are anti-JCV antibody (Ab) positive, indicating viral infection, have a higher risk of developing NTZ-associated PML than those who are negative. Although PML risk is low (0.07 per 1000) in anti-JCV Ab negative pwMS, they should be retested periodically as they are still at risk of JCV infection. In anti-JCV Ab positive pwMS, PML risk can be further stratified by treatment duration and prior immunosuppressant use. Although previous clinical studies have analyzed JCV serostatus dynamics, data were limited to 4 years and did not include age subgroups.
Objectives/Aims: To assess long-term dynamics of JCV serostatus across different age groups in patients who were anti-JCV Ab negative at baseline.
Methods: De-identified patient data from the TYSABRI Outreach: Unified Commitment to Health (TOUCH®) Prescribing Program database were matched with STRATIFY JCV® DxSelect™ Ab test results from Quest Diagnostics. Ab samples were analyzed between 01 Jun 2013 to 30 Nov 2023. Baseline anti-JCV Ab status was defined as the serostatus with the closest proximity of the first NTZ dose. Descriptive statistics were used. Kaplan-Meier analyses were conducted to estimate the probability of the first anti-JCV Ab positive test result occurring over time across different age groups.
Results: At baseline, 6770 patients were anti-JCV Ab negative, including 105, 5429, and 1236 who were <18, 18-50, and >50 years old, respectively. Of these baseline anti-JCV Ab negative patients, $\geqslant$78% remained negative over time irrespective of the age subgroup. The length of follow-up in the patients who remained anti-JCV Ab negative ranged from 0.01-8.84 years. The estimated probability of the first anti-JCV Ab positive test result at 8 years was 46% in the overall group, 37% in patients <18, 45% in patients 18-50, and 51% in patients >50. Additional descriptive analyses examining JCV serostatus and index value dynamics in those patients who had a serostatus change to anti-JCV Ab positive will be presented in the poster.
Conclusion: These findings extend previous analyses with results suggesting dynamics may be similar irrespective of age. They also reiterate the importance of long-term monitoring in anti-JCV Ab negative NTZ-treated pwMS.
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P1679
Rituximab treatment and infection risk in Norwegian multiple sclerosis patients

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Introduction: Rituximab treatment in multiple sclerosis (MS) is commonly administered every 6 months. Longer dose intervals seem to give the same efficacy. Whether extended dose intervals reduce infection risk, especially with increasing age, has not been thoroughly investigated.
Objectives/Aims: To investigate if infection risk is influenced by dose interval extension and age in MS-patients treated with rituximab.
Methods: We are conducting a nation-wide observational study linking compulsory national health registries. MS-patients were identified through the Norwegian Patient Registry (NPR) and the Norwegian MS registry. Rituximab treatment and hospital-treated infections were captured by the NPR. Further infections requiring prescription treatment or physician contact were captured by the Norwegian Prescription Database and the Norwegian Control and Payment of Health Reimbursements Database. Sociodemographic data were retrieved from Statistics Norway.
Data will be analysed using the Prentice, Williams and Peterson (PWP) gap time model to account for longitudinal design and recurrent outcome events. PWP models are adjusted for relevant explanatory variables.
Results: We identified 3410 rituximab treated MS-patients with a total of 13811 rituximab infusions between November 2010 and June 2022. During the study, 969 hospital-treated infections and a total of 15749 infections were recorded. We will present further results of statistical analysis investigating the effect of age and rituximab interval extension on infection risk in MS patients.
Conclusion: We will present data, which may help guide future rituximab treatment regimens in MS.

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P1680

Personalized dosing in MS: extended interval dosing of ocrelizumab, a real-world observational study

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Introduction: Ocrelizumab, administered every six months, has raised concerns about its impact on B-cell repopulation, immune function, and vaccine responsiveness. Adjusting the dosing schedule may help mitigate these risks without compromising efficacy.
Objectives/Aims: This study evaluates the safety and effectiveness of extended interval dosing (EID) of ocrelizumab in patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: We conducted a retrospective, single-centre observational study including RRMS patients who received at least one cycle of ocrelizumab. Per protocol, all patients initially received three cycles at six-month intervals, after which dosing intervals were individualized based on B-cell counts (>1%). Patients who received at least one extended dose were included in the safety and effectiveness analysis. Clinical, radiological and biological data were recorded. B-cell repopulation was monitored via blood tests every three months. Rapid B-cell repopulation was defined as CD19+ B-cell >1% of total lymphocytes at 6 months from last Ocrelizumab dose. Descriptive statistics and group comparison tests were used as appropriate.
Results: Of 84 patients treated with ocrelizumab, 60 received at least one EID dose and were included. Mean age at treatment initiation was 38.4 years (SD 11.3); 75% (n=45) were women. Median disease duration was 7 years (IQR 1.3–13), with a pre-treatment annualized relapse rate (ARR) of 0.67 (SD 0.66) and median EDSS of 2.5 (IQR 1.0–3.5). Fifteen patients (25%) were treatment-naïve. Median follow-up after treatment onset was 3 years (IQR 2–4), and median EID delay was 9 months (IQR 8–11). Rapid B-cell repopulation occurred in 4 patients before 6 months and in 6 patients between 6 and 9 months. During the EID period, only 2 of 60 patients (3.3%) developed new T2 lesions on brain MRI. Four relapses were recorded: one early (3 months after treatment onset), and three during the EID period (at 1, 10, and 13 months post-last infusion). ARR during standard dosing (0.02, SD 0.13) and EID (0.048, SD 0.22) did not significantly differ (p=0.16). EDSS remained stable between year 1 (median 2.0, range 1.0–3.0) and year 2 (median 2.0, range 0–3.0; p=0.096). No serious infections were reported during follow-up.
Conclusion: In this real-world cohort, extended interval dosing of ocrelizumab was not associated with increased clinical or radiological disease activity. These findings suggest that EID may be a safe and effective strategy for selected RRMS patients, though prospective studies directly comparing EID with standard six-month dosing are warrant.
Key-words: Personalized treatment, extended dosing, high efficacy treatment.

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P1681

Evaluation of Hepatitis B Virus Status in Patients Treated with Rituximab: A Retrospective Cohort Study

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Introduction: Rituximab, a monoclonal anti-CD20 antibody, is widely used in the treatment of autoimmune disorders such as multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). Despite its efficacy, rituximab poses a potential risk for hepatitis B virus (HBV) reactivation, particularly in patients with prior HBV exposure. Given the clinical significance of HBV reactivation and its potential complications, understanding the HBV status of patients undergoing rituximab therapy is crucial.
Objectives/Aims: This study aimed to evaluate the HBV status in patients treated with rituximab and assess the prevalence of past HBV exposure in this cohort.
Methods: Seventy-three patients who had received at least one cycle of rituximab for MS, NMOSD, or MOGAD were retrospectively analyzed. Data collection focused on demographic characteristics, disease-related factors, and HBV serological status. Patients were categorized based on HBV infection status into two groups: those with resolved HBV infection (anti-HBc IgG-positive but HBsAg-negative) and those without HBV infection (HBsAg-negative and anti-HBc IgG-negative).

Additionally, vaccination history was recorded to identify patients with vaccine-induced immunity.
Results: Among the 73 patients, 15 had MS, 52 had NMOSD, and 6 had MOGAD. The majority of NMOSD patients were female (78.8%), while females represented 53.4% of the MS group and 33.4% of the MOGAD group. The mean age at disease onset was 33.68 (±12.86) years, with a mean disease duration of 11.5 (±9.3) years. The average duration of rituximab treatment was 2.6 (±2.24) years. Notably, 36.5% of NMOSD patients were seropositive for AQP4-Ab.
Regarding HBV status, no patients tested positive for HBsAg, anti-HIV, or anti-HCV antibodies. Only one patient (1.3%) had resolved HBV infection, characterized by anti-HBc IgG and anti-HBs positivity. Among HBV-naïve patients, 19 had received HBV vaccination (anti-HBs-positive), while 53 had no history of HBV infection or vaccination (anti-HBs-negative). No cases of acute HBV infection, chronic HBV infection, or occult HBV carriers were identified in this cohort.
Conclusion: This study underscores the low prevalence of HBV infection in rituximab-treated patients with MS, NMOSD, and MOGAD. While our findings suggest a minimal risk of HBV reactivation in this population, routine HBV screening remains essential, especially in regions with higher HBV endemicity. Future prospective studies are needed to further evaluate the long-term safety of rituximab in patients with prior HBV exposure.

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P1682
Immunoglobulin-G dynamics and relation to antibiotic prescriptions in MS-patients treated with rituximab: a real-world cohort

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Introduction: Rituximab, a B-cell-depleting therapy, is widely used for multiple sclerosis (MS). While effective, long-term treatment may reduce immunoglobulin G (IgG) levels, potentially increasing infection risk.
Objectives/Aims: This study evaluates IgG dynamics and antibiotic use in MS patients receiving Rituximab in Örebro County, Sweden.
Methods: A retrospective cohort study was conducted on MS patients treated with Rituximab over a 10-year period. Patients included had at least two infusions and a follow-up of ⩾6 months after the last infusion. IgG levels and antibiotic prescriptions were registered longitudinally.
Results: A total of 213 patients (72% female, mean age 40.1 ± 10.6 years) were included, with a mean follow-up time of 44.8 ± 10.6 months. The mean IgG level at treatment initiation was 11.5 ± 2.4 g/L, declining to 10.4 ± 2.3 g/L after the last infusion, with a mean decrease of 1.1 ± 1.4 g/L. Hypogammaglobulinemia (IgG $<$ 6.7 g/L) occurred in 4% of patients. Serum IgG levels demonstrated a significant decline over the course of Rituximab treatment ($p < 0.001$). However, linear mixed modeling did not detect a statistically significant acceleration over time.
Antibiotic prescriptions were recorded in 63% of patients, with a mean of 2.5 ± 3.3 prescriptions per patient. The most common indications were urinary tract infections (29%) and respiratory tract infections (19%). No significant correlation was found between lower IgG levels and higher antibiotic use.
Conclusion: Rituximab treatment in MS was associated with a significant decline in IgG levels over time. However, the incidence of infections requiring antibiotics did not correlate with IgG decline, suggesting that most patients maintain sufficient immune function. These findings support the continued use of Rituximab in MS while highlighting the need for monitoring IgG levels during long-term treatment.

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P1683
Menstrual cycle disorders in women with multiple sclerosis receiving cladribine or anti-CD20 therapies: Insights from a single-centre cohort study

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Introduction: Cladribine tablets and anti-CD20 monoclonal antibodies, such as ocrelizumab and ofatumumab, are highly effective therapies for treating relapsing and active secondary progressive multiple sclerosis (MS) in adults. These treatments selectively target and deplete B lymphocytes, operating through different mechanisms. While both types of therapies are generally well-tolerated, it is crucial to address the significant lack of data regarding female-specific adverse events, particularly given that women comprise the majority of the MS population.
Objectives/Aims: We aimed to evaluate reports of abnormal uterine bleeding and other menstrual cycle irregularities in female MS patients during the first two years of cladribine and anti-CD20 treatment.
Methods: As part of the real-world cohort of 613 MS patients treated with cladribine, ocrelizumab, and ofatumumab at our tertiary center, women of reproductive age (18-45 years) reported their experiences related to the timing

of vaginal bleeding, the severity of menstrual symptoms, and lifestyle factors in a structured interview form. Responses to survey questions were analyzed, and associations between symptoms and therapy were examined.
Results: The anti-CD20 treatment group comprised 89 women. While the proportion of menstrual changes in the cladribine group was 50%, approximately 30% of the women treated with anti-CD20 antibodies reported menstrual changes. A differentiated presentation of the types of menstrual disorders and a comparison of the treatment groups is currently being prepared.
Conclusion: A higher magnitude of menstrual irregularities was associated with using cladribine in our real-world cohort of MS patients. Future monitoring of these adverse events is advised to understand better their incidence rate, pathophysiology, and long-term complications. These findings are important for treatment education prior to therapy.

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P1684
Evaluating the Consistency of CD19+ B-Cell Repopulation in People with MS Under Extended Interval Dosing of Ocrelizumab

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Introduction: Extended interval dosing (EID) of ocrelizumab is considered a way to reduce its infection-related side effects. There is no established method for determining the appropriate dosing schedule for EID. Some centres, including Nottingham, re-administer ocrelizumab when CD19+ B-cell counts reach 10/μL or more, referred to as CD19+ B-cell repopulation.
Objectives/Aims: To determine whether people with MS (pwMS) demonstrate a personalised pattern of CD19+ B-cell repopulation following ocrelizumab administration, which could reduce the burden of monitoring.
Methods: Nottingham adopted EID of ocrelizumab in 2020. Data on CD19+ B-cell counts and ocrelizumab administration were collected for pwMS in Nottingham who received ocrelizumab from 2019 to 2025. Intra-class correlation (ICC) was used to assess the consistency of the time from ocrelizumab administration until a CD19+ B-cell count of 10/μL or more was reached across repeated measurements within individuals.
Results: One hundred randomly selected pwMS (out of 270) with a mean (standard deviation; SD) age of 43 (11) years and 58% female were included. They had received a median (interquartile range) of 6 (4 – 8) intravenous infusions of ocrelizumab over a mean (SD) duration of 3.4 (1.3) years.
Among 88 pwMS who had two or more episodes of CD19+ B-cell counts of 10/μL or more, the ICC of the time from ocrelizumab administration to CD19+ B-cell repopulation was o.33.
Conclusion: CD19+ B-cell counts do not show a consistent duration to repopulation following ocrelizumab administration in order to reliably guide EID without CD19+ B-cell count monitoring. An updated analysis of the total population will be presented.

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P1685
Comparing STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCVTests in RRMS to Assess PML Risk

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Introduction: The risk of developing progressive multifocal leukoencephalopathy (PML), a rare but potentially fatal opportunistic infection of the central nervous system caused by the J.C. virus (JCV), remains a primary concern associated with natalizumab therapy in the clinical management of patients diagnosed with multiple sclerosis (MS).
Objectives/Aims: The main objective was to determine the comparability of these tests in classifying PML risk. Eligible patients were selected from a database, and all specimens for the STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV antibody tests were collected on the same day.
Methods: Patients were classified into three risk categories (low, intermediate, or high) based on threshold values for each test.This study compared two tests, STRATIFY JCV™ DxSelect™, and IMMUNOWELL™ JCV antibody tests, for assessing the risk of PML in patients diagnosed with relapsing-remitting multiple sclerosis (RRMS) who had received disease-modifying therapy (DMT) with branded natalizumab (Tysabri®).
Results: The analysis showed 85.5% agreement between the two tests for risk classification. Ten discordant cases were identified, mainly between intermediate- and high-risk categories.

Compared to STRATIFY JCV™ DxSelect™, IMMUNOWELL™ JCV antibody test tended to categorize more patients as higher risk. No significant association was found between discordance and prior use of immunosuppressant drugs and >24 doses of natalizumab. The agreement between tests, assessed with the weighted Cohen's Kappa coefficient, was substantial (κ=0.6222).
Conclusion: Compared to the STRATIFY JCV™ DxSelect™, the IMMUNOWELL™ JCV test tends to place more patients in higher risk categories. Further, longitudinal studies are needed to evaluate the clinical impact of these differences in PML risk assessment.

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P1686
A Longitudinal Study of John Cunningham Virus (JCV) Seroconversion among Multiple Sclerosis Patients Treated with Natalizumab: A Retrospective Analysis of Risk Factors

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Introduction: Natalizumab is regarded as an efficacious disease-modifying therapy (DMT) for the management of relapse-remitting multiple sclerosis (RRMS). However, it is limited by progressive multifocal leukoencephalopathy (PML) risk associated with John Cunningham virus (JCV) seropositivity.
Objectives/Aims: Herein, we aimed to investigate the seroconversion rate in initially JCV-negative RRMS patients receiving natalizumab.
Methods: This multicenter, retrospective cohort study included 103 JCV-seronegative RRMS patients initiating natalizumab between 2016-2025. JCV antibody index was measured semi-annually using a two-step ELISA. Seroconversion was defined as two consecutive positive results (AI ⩾0.4). Cox proportional hazards models assessed associations between seroconversion and possible covariates.
Results: 103 patients were enrolled. 90.3% of the patients were female with a mean age of 35.89 ± 8.95 and a mean disease duration of 5.64 ± 5.31 years at natalizumab initiation. Most patients (78.6%) had a history of DMT exposure, of which the foremost used was fingolimod (29.6%). Over 51.93 ± 21.01 months, 20 patients (19.4%) patients seroconverted, with a mean time to seroconversion of 40.9 ± 24.12 months. Previous DMT type (P=0.23), geographical province of residence (P=0.42), disease duration (P=0.29), and age at natalizumab initiation (P=0.30) showed no significant association with seroconversion. Conversely, male gender and patients undergoing an extended period of treatment with the standard interval dosing (SID) protocol exhibited a propensity towards a higher risk of seroconversion (HR=1.38, 95% CI 0.82–2.3, P=0.08) and (HR=1.07, 95% CI 0.62–1.9, P=0.05), respectively.
Conclusion: JCV seroconversion occurred in over one-fifth of initially seronegative patients within four years of natalizumab therapy, with male sex and longer time on SID regimen as independent risk factors. These findings underscore the need for vigilant JCV monitoring every 6 months, particularly in high-risk subgroups, to mitigate PML risk.

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P1687
JC virus index trajectory among patients treated with extended-interval dosing Natalizumab infusions

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Introduction: Prior studies have suggested that a rise in the JC virus index (JCVi) heralds the development of Progressive Multifocal Leukoencephalopathy in Multiple Sclerosis patients' (pwMS) treated with Natalizumab (NTZ). The extent to which this is counteracted by alternative dosing schemes (ie Extended Interval Dosing) is not fully understood.
Objectives/Aims: The aim of our study was to evaluate the evolution pattern of JCVi after switching to the Extended Interval Dosing in Multiple Sclerosis patients treated with NTZ.
Methods: Longitudinal retrospective single-centre study, reviewing digital patient charts and JCVi data extracted from the *Stratify JCV* platform from consecutive MS patients treated with NTZ between 2014-2024. Patients with < 1-year NTZ infusions or missing JCVi data were excluded. EID was defined as any >6 months period with an infusion interval between 5 and 7 weeks. In patients with standard interval dosing (SID), baseline JCVi and last recorded JCVi were documented, whereas in EID patients the first titre recorded >6 months after EID switch was additionally collected. Delta JCVi was dually defined as the subtraction of last recorded JCVi-baseline JCVi for SID patients and as postEID JCVi-last recorded SID JCVi for EID patients. DeltaJCV trajectory was further categorized

as positive vs negative-stable (ie JCVi increment vs reduction/stability) accordingly.
Results: 43 patients were included, 84% of which were female with a mean age at NTZ start of 37.1years (±8.02) and baseline EDSS 2.5 (min1-max6). 25.6% were JCV positive at baseline (n=11) with a median baseline JCVi 1.12 (min0.19-max3.64) and a seroconversion rate of 43.8% (n=14) at follow up. 20 patients (46,5%) were defined as EID. The proportion of negative delta JCV was significantly higher in the EID patient subgroup (DeltaJCV negative EID n=18/20 vs DeltaJCV negative SID n=13/23, p=0.015). A higher proportion of EID patients with Baseline JCVi>3 showed a positive DeltaJCV when compared to patients with baseline JCVi<3 (n=2/2 vs n=1/18, p=0.016).
Conclusion: In this cohort, we observed a predominantly negative DeltaJCV trajectory in the EID subgroup, possibly in keeping with an effective PML mitigation risk strategy. Nevertheless, at > 3 baseline JCVi range we observed incremental DeltaJCV in the EID subgroup, suggesting a possible limitation of this risk-mitigation strategy with potential therapeutic implications for pwMS.

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P1688
Absence of oligoclonal bands is not a useful biomarker for absence of early reactivation after discontinuation of first-line multiple sclerosis therapies

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Introduction: Stopping of first-line disease-modifying therapies (DMTs) can be considered in people with MS (pwMS) with long term stable disease. However, biomarkers predicting recurrent disease activity are limited. Unique cerebrospinal fluid (CSF) oligoclonal bands (OCBs) can disappear during disease course in some pwMS. We hypothesized that absence of OCB could serve as putative biomarker for absence of early recurrent MS activity after DMT cessation.
Objectives/Aims: To study the proportion of people with absence of CSF unique OCBS with long term stable disease and early recurrence of disease activity within year after discontinuation first-line DMT.
Methods: We included pwMS above 45 years of age, who had been clinically and radiologically stable for at least 5 years and were scheduled to discontinue their DMT as part of routine clinical care. These participants underwent a lumbar puncture prior to DMT discontinuation and were followed-up prospectively. DMTs included were interferon beta, glatiramer acetate, dimethyl fumarate and teriflunomide. For primary endpoint analysis, presence of OCBs at inclusion time was assessed. Recurrent disease activity was defined as clinical relapses or new T2/ gadolinium-enhancing MRI lesions at 1-year follow-up.
Results: Between January 2021 and April 2025, 18 participants were included, of which 6/18 (33.3%) lacked OCBs at time of inclusion. Comparing OCB+ and OCB- participants, median age was similar (58.9 years [IQR 54.4-63.4] vs 60.9 years [IQR 51.6-70.3], resp.), as were median VIAADISC-scores (1.0 vs 1.0, resp.) and IgG levels (0.051 [IQR 0.027-0.070] vs 0.032 [0.024-0.051], resp.). In 3/6 participants without OCB, a presence of OCBs was registered at time of an earlier lumbar puncture. Of 12/18 participants with a 1 year follow-up thus far, none experienced clinical relapses. One participant, who was negative for OCB, showed radiological activity. Rate of MS activity during prolonged follow-up is still being investigated, as is the predictive value of other CSF soluble biomarker and lymphocyte characteristics.
Conclusion: Preliminary results indicate that the majority of long-term stable pwMS on first-line DMTs continues to show persistent CSF OCBs. This suggests that assessment of CSF OCB is not useful as biomarker to predict low rate of early recurrent disease activity after DMT discontinuation.

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P1689
Anti-CD20-Associated Hypogammaglobulinemia in Neuroimmunological Disorders: Insights from a Single Center

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Introduction: Anti-CD20 therapies have revolutionized the treatment of neuroimmunological disorders by targeting B cells. Rituximab, used off-label for multiple sclerosis (MS) and

neuromyelitis optica spectrum disorder (NMOSD), was the first to demonstrate disease-modifying effects, followed by regulatory approvals of ocrelizumab, ofatumumab, and ublituximab for MS. However, these highly effective therapies are linked to hypogammaglobulinemia, raising concerns about their long-term safety and infection risk.

Objectives/Aims: Phase 1 of this study aimed to characterize the clinical and demographic profiles of patients on anti- CD20 therapies as well as to assess the prevalence and timing of hypogammaglobulinemia. Phase 2 will explore the clinical consequences of hypogammaglobulinemia, including infection risk and its associated factors.

Methods: We performed a retrospective chart review of 352 patients with central nervous system (CNS) inflammatory disorders treated with anti-CD20 therapies between 2017 and 2025. Data were collected using the Research Electronic Data Capture (REDCap) system. Time-to-event analysis was used to determine the onset of hypogammaglobulinemia.

Results: A total of 352 patients met eligibility criteria. Preliminary data were available for varying numbers of patients: demographics (n=225), clinical characteristics (n=154), and immunoglobulin (Ig) levels (n=130). The mean age of the cohort was 46 years (SD 11.2), with 69% female. 90% of patients had MS (138/154), with 65% of those having RRMS. The remaining 10% had other disorders, including NMOSD, MOGAD, or a non-specified CNS inflammatory disorder. The most frequently used anti-CD20 agent was ocrelizumab (60%), followed by ofatumumab (32%). Hypogammaglobulinemia (defined as IgG $<$600 mg/dL) was identified in 11% of patients (14/130), with 3% (4/130) falling below 400 mg/dL. Mean time to first detection of low IgG was 24 months (range 4-91). In contrast, mean time to first detection of low IgM levels was 22 months (range 1-120). IgM reductions to undetectable levels (defined as $<$20 mg/dL) occurred in 7% of patients.

Conclusion: Hypogammaglobulinemia developed in 11% of our patients on anti-CD20 therapies, typically emerging within 2 years of treatment. These findings underscore the need for regular monitoring of Ig levels in clinical practice to mitigate potential risks. Ongoing analyses will further explore the clinical consequences, including infection risk, and the efficacy of mitigation strategies once this complication arises. Overall, our data exhibited a broad range, reflecting heterogeneity in disease course, diagnostic delay, prior treatment exposure, and variable clinical documentation, which led to differing data availability across patients.

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P1690

Adherence to risk minimization measures for alemtuzumab use in multiple sclerosis: a drug utilisation study in four European countries

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Introduction: Additional risk minimisation measures were added to the EU SmPC for alemtuzumab in January 2020. These included: restricted indication; new contraindications; and newly required monitoring before, during, and after infusion.

Objectives/Aims: Primary objectives were to measure: 1a) proportion of newly treated patients with the revised indication; and 1b) proportion of courses without contraindications, per revised SmPC.

Secondary objectives were to measure: 2a) proportion of courses with cardiac monitoring, full blood count (FBC)/transaminases/creatinine, urinalysis testing and thyroid function testing 30 days prior to infusion; cardiac and platelet testing during infusion; and 2b) percentage adherence, at patient level, to long-term monitoring of FBC/transaminases/creatinine and urinalysis (monthly) and thyroid function (trimonthly), per revised SmPC.

Methods: This was a descriptive cohort study. Patients with multiple sclerosis (MS) and treated with alemtuzumab were included. Data sources included; administrative data from AIM-IMA (Belgian Social Security database), ReMuS (Czech MS registry), chart review data from three UK centres (Cardiff, Cambridge, Plymouth), and an ongoing cohort study in Germany (TREAT-MS). Study period was January 2020 to the data cut-off for each source (March 2022 - January 2024). Descriptive

proportions were calculated to address each objective, at either patient or course level.
Results: Objective 1a (indication): Using a 12-month assessment period, the revised indication was met in 100% (AIM-IMA), 66.7% (UK centres), 66.7% (ReMuS, increasing to 75.3% after manual checking), and 87.5% (TREAT-MS) of patients. With a 24-month assessment, UK adherence rose to 79.5%.
Objective 1b (contraindication): The majority of courses had no contraindication; 77.5% (AIM-IMA) - 97.8% (TREAT-MS).
Objective 2a (monitoring prior / during infusion): Approximately >70% of courses had prior heart rate [HR], blood pressure [BP] and FBC tests. Urinalysis and thyroid function testing were an exception in UK. During the infusion, ⩾80% of courses had HR and BP monitoring. Platelet testing on Day 3 or 5 of infusion was observed in 29%-51% courses.
Objective 2b (long-term monitoring): Adherence was approximately >50% for all tests, even in years 3-4 post-infusion, except for urinalysis and thyroid function testing in the UK.
Conclusion: There is concordance with the revised SmPC. Overall adherence to long-term monitoring was satisfactory, even considering the impact of COVID-19 on healthcare access. Low adherence, e.g. urinalysis in the UK, was qualitatively explained.

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Therapy – Measurement of treatment response

P1691
Evaluating MRI-Confirmed Relapses as a Novel Endpoint in Multiple Sclerosis Trials

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Introduction: In multiple sclerosis (MS) trials, relapses are defined based on clinical symptoms, without requiring radiological confirmation. However, recent findings suggest that a substantial proportion of events, termed acute clinical events with stable MRI (ACES), are not associated with a new T2 lesions or gadolinium-enhancing T1 lesions.
Objectives/Aims: We aimed to evaluate the advantages of using MRI-confirmed relapses as a novel endpoint in MS clinical trials by differentiating between relapses with active MRI (RAM) and ACES.
Methods: A meta-analytical approach was applied to 10 randomized controlled trials (RCTs) evaluating disease-modifying therapies (DMTs) in MS. Data from the French MS registry (OFSEP) were used to develop a logistic model predicting RAM vs. ACES probabilities based on patient characteristics and DMT. The model was applied to RCT aggregated data to estimate expected RAM and ACES probabilities in each treatment arm, and treatment effects on clinically defined relapses, RAM, and ACES were compared. The statistical power gain associated with the use of RAM as the primary outcome was evaluated under different scenarios.
Results: The estimated treatment effects were greater or equivalent when using RAM as the primary endpoint compared to clinically define relapses, with effect sizes up to twice as large in the OPERA trial. In contrast, ACES rates were stable across treatment arms. Using RAM as the primary outcome would theoretically reduce the required sample size or trial duration by ~37% to achieve equivalent statistical power assuming an ARR of 0.15 in the active arm and 0.30 in the control arm.
Conclusion: This study highlights the potential advantages of systematically seeking MRI confirmation of relapses to evaluate MRI-confirmed relapses (RAM) as the primary outcome in MS trials. By excluding ACES, which do not appear to be targeted by current DMTs, future trials could improve treatment effect estimation and reduce sample size requirements.

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P1692
Real-World Outcomes of Ocrelizumab and Ofatumumab Treatment in Pediatric Onset Multiple Sclerosis

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Introduction: Despite increasing evidence suggesting benefits of early initiation of high-efficacy disease-modifying therapies (DMT) in pediatric onset multiple sclerosis (POMS), options for approved therapies are severely lacking. Ocrelizumab and ofatumumab are B-cell depleting medications that are FDA-approved DMTs for adult onset multiple sclerosis (AOMS). Studies evaluating the safety and efficacy of similar B-cell depleting DMTs in children and adolescents are needed.
Objectives/Aims: Describe the reasons for initiation of, adverse effects from, and clinicoradiological relapse rates after treatment with ocrelizumab and ofatumumab in a single center cohort of POMS patients.
Methods: Retrospective chart review of patients evaluated at Children's National Hospital who fulfill 2017 McDonald criteria for relapsing-remitting multiple sclerosis (RRMS) and were treated with either ocrelizumab or ofatumumab between 2015 and 2025. Clinical, radiologic, and laboratory data were collected from the electronic medical record and analyzed with descriptive statistics.
Results: 44 patients were included, with mean age at diagnosis of 15 years (range 8-20 years). 35/44 (80%) patients were treated with ocrelizumab and 9/44 (20%) with ofatumumab. Ocrelizumab or ofatumumab were first choice therapies in 4/13 (31%) patients before 12/31/2021 and 20/31 (65%) after 1/1/2022. 20/44 (45%) patients were prescribed a previous DMT, and radiologic worsening or clinical relapse was the most common reason for switching to a B-cell depleting DMT (9/20, 45%). 6/44 (14%) patients experienced an infusion or injection site reaction, which were all mild and managed conservatively. No patients discontinued ocrelizumab or ofatumumab due to adverse effects. Only 1/44 (2%) had a clinical relapse occurring >3 months after ocrelizumab or ofatumumab initiation, and 4/44 (9%) had new or enlarged T2 hyperintense lesions after re-baseline MRI scans.
Conclusion: These results highlight the high efficacy and tolerability of ocrelizumab and ofatumumab in POMS. Just as in AOMS, both therapies warrant consideration as treatment options for POMS.

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P1693

Extended Rituximab INterval with concomitant oral steroids for maintenance treatment of aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder: E-RIN study

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Introduction: Rituximab (RTX) was approved in Japan in June 2022, based on the results of the RIN-1 study. The maintenance regimen of RTX is the same as in the RIN-1 study: every 6 months. However, the RIN-2 study, the open-label extension study, showed that the interval of RTX could be extended to about 9 months by B-cell monitoring. After the RIN-2 study ended in March 2019, most participants were treated with conventional oral steroids until new biologics are approved.
Objectives/Aims: To investigate the effect of oral steroids on the duration of rituximab efficacy by comparing the rituximab monotherapy and the rituximab therapy combined with immunosuppressants including oral steroids.
Methods: Participants of the RIN-2 study conducted in our hospital were retrospectively analyzed. Patient characteristics, number and timing of RTX administration, lymphocyte subsets of CD19 and CD20, and concomitant drugs such as prednisolone (PSL) and immunosuppressants, were extracted from the medical records. The B cell depletion time (BCDt) as the duration of the efficacy of RTX was defined as the time (days) from the first day of rituximab administration to the day when either CD19 or CD20 exceeded 1% in the lymphocyte subset test. Prior to the study, IRB approval was obtained at our hospital (UTA-06-10).
Results: Of 21 participants (20 women, 1 man), we analyzed the data of 17 patients, excluding 4 patients. The total number of RTX doses administered since the start of the RIN-2 study was 43 courses. All patients were taking PSL (2-20 mg) at the start of the RIN-2 study, but 14 patients (82%) had withdrawn after the first course, and 8 of 14 patients had treatment periods of RTX monotherapy: the total of 12 courses; their BCDt was 294±31 days. After the RIN-2 study, 14 patients (pts) took PSL (1 pt on 2mg, 1 pt on 4mg (in combination with tacrolimus(FK)), 12 pts on 5mg or more (1 pt with azathiopurin)), 2 pts with FK only (3mg), and 1 pt was untreated. The BCDt was 593±299 days in the PSL combination group and 311±39 days in the FK group. In the analysis of three PSL groups (0mg, 1-4mg, 5mg or more), a significant prolongation of the BCDt was observed in the group of 5mg or more. There were no relapses of neuromyelitis optica after the RIN-2 study.
Conclusion: The efficacy of RTX was significantly prolonged by taking oral steroids of more than 5 mg during RTX treatment. Although the side effects of long-term steroid use need to be considered, the combination of RTX and low-dose oral steroids may be a new form of rituximab therapy.

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P1694

Impact of Cladribine Tablets on GFAP Levels and Intrathecal Biomarkers in RMS: Results from the MAGNIFY-MS Study

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Introduction: Cladribine tablets (CladT), an immune reconstitution therapy, have demonstrated significant efficacy in reducing disease activity in people with relapsing MS (PwMS). Prior studies have reported reduction and disappearance of oligoclonal bands (OCBs) in CladT-treated PwMS, suggesting decreased intrathecal antibody production, as well as a reduction in neuroaxonal damage (neurofilament light [NfL] levels). The impact of CladT on glial fibrillary acidic protein (GFAP) and biomarkers of intrathecal activity has not been extensively studied.
Objectives/Aims: To evaluate the effects of CladT on neuroinflammation and intrathecal activity in serum and cerebrospinal fluid (CSF).
Methods: In the MAGNIFY-MS study (NCT03364036), biomarkers from participants treated with CladT were measured at baseline (BL), month (M)12 and M24. Serum GFAP (N=258) levels were assessed with single molecule array (SIMOA). C-X-C motif chemokine ligand 13 (CXCL-13) levels from matched serum and CSF samples (N=11) were quantified using the Meso Scale Discovery U-PLEX assay. Serum and CSF levels for kappa free light chains (KFLC) levels were determined using nephelometry. KFLC index (N=22) and immunoglobulin G (IgG) index (N=5) were calculated from CSF and serum IgG levels for participants with elevated KFLC and IgG values at BL.
Results: Mean (standard deviation [SD]) serum GFAP levels were reduced from 23.1 (11.4) at BL to 21.3 (9.8) at M12 and 21.0 (9.4) at M24, indicating reduced astrocyte damage and neuroinflammation. Mean (SD) KFLC index decreased from 62.20 (77.66) at BL to 37.08 (30.21) at M24. Similarly, mean (SD) IgG index decreased from 1.05 (0.31) at BL to 0.72 (0.11) at M24 suggesting reduced intrathecal immunoglobulin synthesis. CXCL-13 levels decreased from BL to M24 in both serum and CSF. Mean (SD) CXCL-13 index decreased from 76.49 (54.6) to 20.82 (13.2) at M24, reflecting reduced intrathecal B-cell recruitment and inflammatory activity. Descriptive data for clinical outcomes for PwMS with reduced biomarkers will be present at the congress.
Conclusion: These results provide evidence that CladT reduced serum and CSF biomarkers of neuroinflammation and intrathecal activity. Taken together with previously reported impact on OCBs and NfL these results highlight potential benefits of CladT on reducing neurodegeneration and neuroinflammation beyond its previously established clinical efficacy in relapsing MS.

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P1695
Different Definitions of Confirmed Disability Progression and Their Association With Brain Atrophy in Patients With Relapsing Multiple Sclerosis Treated With Ozanimod for up to 8 Years in the Phase 3 SUNBEAM/RADIANCE and Open-label DAYBREAK Studies

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Introduction: Confirmed disability progression (CDP) can be assessed based on various definitions. Brain atrophy is believed to be strongly associated with CDP.

Objectives/Aims: To report long-term CDP in patients with relapsing MS (RMS) treated with ozanimod based on various definitions and explore associations between CDP and brain atrophy.

Methods: Patients with RMS were treated with ozanimod 0.46 or 0.92 mg/d or interferon β-1a 30 μg/wk for 24 months in RADIANCE (NCT02047734) or ⩾12 months in SUNBEAM (NCT02294058); completers could enrol in an open-label extension trial (DAYBREAK–NCT02576717) of ozanimod 0.92 mg/d for up to an additional 6.5 years. Patients were pooled across studies and treatment arms (database lock: 7 April 2023). *CDP-6* was defined as a ⩾1-point increase from baseline in Expanded Disability Status Scale (EDSS) score, confirmed after 6 months. Progression independent of relapse activity (PIRA) was considered if CDP-6 onset occurred without relapse in the preceding observation period or >90 days after a relapse; for relapses with incomplete recovery, EDSS >90 days after relapse onset was reset as baseline to identify a possible next PIRA event. Patients who experienced relapse within the ±90-day window were categorised as having relapse-associated worsening (RAW). Sustained *EDSS (SEDSS)-6* was defined as reaching a score of 6 on EDSS sustained for 6 months. Event rates and atrophy rates in progressors vs non-progressors were analysed for each disability progression assessment.

Results: After approximately 6–8 years of ozanimod treatment (n=2256), 80.1% of patients were free of CDP-6, 9.9% experienced PIRA, 10.5% experienced RAW, and 3.9% had SEDSS-6. In 762 patients continuously treated with ozanimod 0.92 mg/d over approximately 8 years, 80.1% were free of CDP-6, 10.5% experienced PIRA, 9.7% experienced RAW, and 3.7% reached SEDSS-6. At month 84, in progressors vs non-progressors, mean whole brain atrophy rates were 2.4% vs 1.9%, 2.2% vs 2.0%, 2.6% vs 2.0%, and 2.8% vs 2.0%, and mean thalamic atrophy rates were 5.1% vs 4.1%, 4.1% vs 4.3%, 6.6% vs 4.1%, and 5.7% vs 4.3% for CDP-6, PIRA, RAW, and SEDSS-6, respectively; thus, the largest numerical differences in brain atrophy percentages between progressors and non-progressors were observed for RAW and thalamic volume.

Conclusion: After approximately 8 years of ozanimod treatment, less than 4% of patients reached SEDSS-6. Atrophy rates varied across CDP definitions, but all CDP definitions and RAW and PIRA were associated with whole brain and thalamic atrophy.

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P1696
Variability in treatment response to natalizumab versus fingolimod among children with multiple sclerosis

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Introduction: Understanding which children with multiple sclerosis (MS) derive most benefit from natalizumab when compared with fingolimod is essential for optimising their management.

Objectives/Aims: To evaluate the effectiveness of natalizumab versus fingolimod in children with relapsing-remitting MS, in relation to clinical and demographic characteristics.

Methods: Patients who commenced natalizumab or fingolimod before the age of 18 and remained on therapy for at least 3 months were identified from the French MS Registry, Italian MS Register, and the MSBase Registry. The primary outcome, time to first relapse, was analysed using an inverse probability treatment weighted Cox proportional hazards model under the per-protocol paradigm. A Bayesian additive regression trees model was used to estimate the conditional average treatment effect for each patient within a counterfactual framework. The estimated conditional average treatment effects were then analysed to identify potential treatment effect heterogeneity, quantified as the risk difference in the probability of a relapse between patients receiving natalizumab versus fingolimod, using a classification and regression trees model.

Results: A total of 324 patients were included (fingolimod: 80, natalizumab: 244). Patients treated with natalizumab had a 75% lower risk of a relapse compared to fingolimod (HR [95% CI]: 0.25 [0.14, 0.44]). We found that female children who were previously treated with interferon beta or mitoxantrone and had experienced a relapse within the previous 6 months benefitted from natalizumab most, with a risk difference of 32% (95% CI: -34%, -30%). In contrast, male children with no relapse in the previous 6 months showed the smallest risk difference, 18% in favour of natalizumab (95% CI: -21%, -13%).

Conclusion: In children with MS, natalizumab is superior to fingolimod at reducing the risk of relapse. The relative treatment response varies among children and is primarily driven by sex, recent relapse activity, and previous treatment.

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P1697
Systematic Screening for Anti-Natalizumab Antibodies in Multiple Sclerosis: Insights into Detection, Predictors, and Clinical Impact

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Introduction: Natalizumab (NZ) is a high-efficacy therapy for relapsing-remitting multiple sclerosis. As a monoclonal antibody, NZ carries a risk of immunogenicity, potentially reducing efficacy and causing allergic reactions. Detecting anti-natalizumab antibodies (ANZ) is therefore crucial, as their presence may influence treatment outcomes.

Objectives/Aims: To evaluate systematic ANZ screening in a real-world cohort and assess the predictive value of different testing indications.

Methods: This single-centre retrospective observational study included 182 patients treated with natalizumab. A total of 356 ANZ measurements were performed between 2018 and 2024 using enzyme immunoassay (EIA). Testing was carried out systematically at 6, 12, and 18 months after treatment initiation, and selectively when therapeutic failure or allergic reactions were suspected.

Results: The overall frequency of ANZ was 4.9% (9 patients). Five positive cases were identified through systematic screening (5/304), and four during testing prompted by suspected inefficacy (4/38). Testing indication was an independent predictor of ANZ positivity, with suspected treatment inefficacy significantly associated with ANZ presence (OR = 5.6, p = 0.029). Patients testing positive due to suspected inefficacy had a shorter disease duration than those without ANZ (p = 0.05). All positive tests occurred before the 13th natalizumab infusion. One case of delayed ANZ positivity was reported four months after a perfusion-related reaction.

Conclusion: Suspected treatment inefficacy was a stronger predictor of ANZ positivity than systematic screening. Delayed ANZ detection following a perfusion reaction suggests the need for extended monitoring. During the first 18 months of natalizumab treatment, close observation for infusion tolerance and potential disease reactivation (clinical relapse and/or MRI lesions) is advisable. ANZ testing should be considered in cases of clinical suspicion, with confirmation one month later before

adjusting treatment. A targeted screening approach may help identify patients at risk of reduced efficacy or adverse reactions, optimising therapeutic decisions.

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P1698
Real World Clinical Data of Persistence, Effectiveness and Safety of Ozanimod Treatment in RRMS Patients in Spain: Interim Analysis of the AppreZiate Study

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Introduction: The AppreZiate study is an observational, multicenter, ambispective study analyzing the persistence and effectiveness of Ozanimod treatment in patients with relapsing-remitting multiple sclerosis (RRMS) in clinical practice in Spain.
Objectives/Aims: To evaluate treatment persistence with Ozanimod at 12 months, to describe reasons for discontinuation, treatment effectiveness, incidence of adverse events (AEs), and sociodemographic and clinical characteristics.
Methods: Eligible patients were adults with RRMS of low to moderate activity who initiated Ozanimod treatment three months prior to study inclusion. Retrospective and prospective data were collected on clinical variables, neuroimaging, and self-administered questionnaires.
Results: 87 patients met inclusion criteria, with a safety sample of 96 patients. 65.5% women (57), 34.5% men (30). Mean age at RRMS symptom onset was 38.7 years (SD 10,29); ozanimod initiation occurred at a mean age of 43.5 years (SD 10,08). At ozanimod initiation, 96,7% (84) of patients were treatment-naïve and 3 patients had received some previous treatment (2 patients teriflunomide and 1 patient subcutaneous interferon β1b). Mean (SD) Expanded Disability Status Scale (EDSS) score was 1,45 (0,99). Mean (SD) Symbol Digit Modalities Test (SDMT) score was 47,41 (12,8). 61% of patients had SDMT scores >44. 3 out of 4 patients remained stable or improved SDMT (76,5%). Median ozanimod treatment duration follow-up at data of cutoff was 6.44 (5.32, 11.96) months. Whereas mean number of relapses in the year before ozanimod start was 0,69, the annualized relapse rate with ozanimod at 1 year was 0,16. From baseline to month 12, EDSS was stable (1,45 vs 1,42). No RAW was observed, and 5 patients (5.7%) had PIRA. At baseline mean number of lesions was 29.70. The mean lesion volume was 10.92 cm^3. 100% persistence at 3 months. 87.9% persistence at 12 months. 53 AEs were reported in 26 patients (27,1%). 31 AEs related to treatment were reported in 14 patients (14,6%). The most common (MedDRA preferred term in >5%) being lymphopenia (7,3%) as expected pharmacodynamic effects and infections (8,3%).
Conclusion: The intermediate analysis of the AppreZiate study suggests that ozanimod demonstrates to be an effective treatment showing high persistence rates, favorable safety profiles, and effectiveness in patients with RRMS with low to moderate activity. Further follow-up is ongoing to consolidate findings.

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P1699
Safety and tolerability of a modified ublituximab dosing regimen: Updates from the ENHANCE study

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Introduction: Ublituximab is a novel monoclonal antibody glycoengineered for enhanced antibody-dependent cellular cytotoxicity that is approved for relapsing multiple sclerosis (RMS). Ublituximab is dosed at 150 mg on Day 1, 450 mg on Day 15, and 450 mg on Week 24 and every 24 weeks thereafter. A modified dosing regimen that 1) consolidates Day 1 and Day 15 doses into a single 600 mg infusion and 2) shortens the duration of 450 mg doses from 1 hour to 30 minutes has the potential to improve patient convenience.

Objectives/Aims: To report updated data from ENHANCE on a modified ublituximab dosing regimen.

Methods: ENHANCE is a 48-week, Phase 3b multi-center study designed to investigate the efficacy and tolerability of a modified ublituximab dosing regimen in participants with RMS. B-cell-depleted ($<$10 cells/μL) participants who transitioned from prior anti-CD20 therapy received either 450 mg or 600 mg of ublituximab administered in 1–2 hours. Non-depleted ($\geqslant$10 cells/μL) participants received either 150 mg over 4 hours or 600 mg in 2–4 hours. The tolerability of a 30-minute 450 mg infusion is being assessed for all participants at Week 24.

Results: To date, 103 participants have received 600 mg ublituximab infusions on Day 1, of which 33 (32%) were B-cell depleted at baseline. The proportion of Depleted and Non-depleted participants experiencing infusion related reactions (IRRs) was 27.3% and 24.3%, respectively. IRRs were mild to moderate and all completely resolved.

At Week 24, 97 participants have received 30-minute 450 mg infusions with 92% completed without interruption or slowing, and a median 32-minute duration. The incidence of IRRs was 15%, which were primarily mild to moderate, all of which completely resolved.

Conclusion: In the ENHANCE study, a modified ublituximab dosing regimen consolidating the initial 150 mg and 450 mg doses into a single 600 mg infusion and administering 450 mg doses in 30 minutes demonstrated a safety profile that appeared consistent with that seen in the pivotal ULTIMATE I/II Phase 3 trials. The ENHANCE study has been amended to a randomized trial to evaluate the pharmacokinetics, safety, and efficacy of 600 mg doses compared to the approved dosing regimen. Enrollment in ENHANCE is ongoing and additional data will be presented.

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P1700
Lymphoplasmapheresis for steroid-refractory neuromyelitis optica spectrum disorder: A multicenter study in China

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Introduction: Lymphoplasmapheresis (LPE), an innovative hemopurification technique that integrates conventional plasma exchange (PE) with lymphopheresis, has demonstrated efficacy in various neuroimmune disorders by removing excessive or dysfunctional lymphocytes and pathological components from plasma.
Objectives/Aims: This study aimed to unveil the mechanisms of LPE and provide additional clinical evidence supporting its use in the acute treatment of steroid-refractory NMOSD.
Methods: This study included 105 acute-stage steroid-refractory NMOSD patients. The efficacy and potential mechanisms of LPE were clarified by monitoring severity scores, clinical laboratory parameters, immune cell subsets and cytokine levels.
Results: In the retrospective cohort, LPE proved effective for acute steroid-refractory NMOSD and non-inferior to PE. In the prospective cohort, LPE significantly decreased Expanded Disability Status Scale (EDSS) and Activities of Daily Living (ADL) scores ($P<0.05$). In both cohorts, erythrocytes, hemoglobin and platelets decreased. Notably, LPE significantly reduced the proportions of activated platelet-adherent monocytes, plasmablasts and memory B cells, while increasing that of naive $CD8^+$ T cell subsets ($P<0.001$). Additionally, LPE significantly reduced the levels of AQP4-Ab, fibrinogen, erythrocyte sedimentation rate, C-reactive protein, complements, immunoglobulin and proinflammatory cytokines ($P<0.05$).
Conclusion: LPE represents an promising treatment for AQP4-Ab^+ NMOSD patients, particularly those with an inadequate response to glucocorticoid therapy.

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P1701
GA Depot (long-acting IM glatiramer acetate) and its impact on EDSS in Relapsing forms of Multiple Sclerosis (RMS) and Primary Progressive Multiple Sclerosis (PPMS)

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Introduction: Multiple sclerosis (MS) is a chronic inflammatory, demyelinating disease characterized by neurological disability accumulation over time. The Expanded Disability Status Scale (EDSS) is widely used to assess disability worsening in both relapsing and progressive forms of MS. Glatiramer acetate (GA) Depot is a long-acting intramuscular (IM) formulation of GA administered once every 28 days
Objectives/Aims: To evaluate the impact of GA Depot on EDSS stability in patients with RMS and PPMS based on data from two clinical studies, including an analysis of early discontinued patients.
Methods: EDSS assessments were collected from two prospective GA Depot clinical studies:
An ongoing, up to three years, open-label, phase IIa study in PPMS patients (n=30).
A one-year, double-blind, placebo-controlled, pivotal phase III study in RMS patients (n=1,016 of which n=508 in the active arm).
An additional post hoc analysis assessed EDSS changes in patients who discontinued early across both studies.
Results: In the phase II PPMS study, the mean EDSS at baseline was 5.1, remaining stable at week 148 (mean= 4.9). In the phase III RMS study, the mean EDSS in the GA Depot group was 2.6 at baseline and 2.5 at the end of the one-year placebo-controlled period. The Mixed Model Repeated Measures (MMRM) analysis

of EDSS changes over time showed a small but statistically significant reduction in EDSS in the GA Depot group compared to placebo at Week 52 vs. baseline. A post hoc responder analysis indicated that 96.4% of GA Depot-treated patients had no EDSS increase at Week 52 versus 91.6% in the placebo group (p=0.0068), showing a higher proportion of stabilized patients with GA Depot. A subgroup analysis of early discontinued patients showed that EDSS remained unchanged from baseline to the last available assessment in both studies: in the PPMS study, early discontinued patients had a mean EDSS of 5.4 at baseline and 5.3 at their last assessment, while in the RMS study, early discontinued patients had a mean EDSS of 2.6 at both baseline and their last assessment.

Conclusion: GA Depot showed a stabilizing effect on EDSS in both RMS and PPMS patients, irrespective of baseline EDSS. These findings suggest the potential of GA Depot in slowing disability progression, reinforcing its role in MS management.

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P1703
Gut microbiota diversity is affected by glucocorticoid treatment in Multiple Sclerosis

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Introduction: Glucocorticoids (GCs) are a type of steroid commonly used to treat acute relapses in MS for their immunosuppressive and anti-inflammatory properties. Evidence of their effects on gut microbiota has been observed in several murine models of diseases, but studies in humans, and in MS, are lacking.

Objectives/Aims: This study aims to investigate gut microbiota composition in people with MS (pwMS) at the diagnosis that have received or not GCs.

Methods: Stool samples were collected from 22 GC-treated pwMS and 29 GC-untreated pwMS. DNA was extracted from stool samples, and shotgun metagenomic sequencing was performed. Reads obtained were aligned to human reference genomes HG38 and CHM13 for the removal of host DNA from the samples. Unmapped reads were assigned to Bacterial, Archaea and Eukarya taxa using Kraken and Bracken. Reads were normalized and assigned to taxa after the manual removal of the non-human taxa, based on literature. Then, a filtering based on OTUs relative abundance ($> 0.01\%$) was applied. Differential abundant species (DAS) were identified using Limma and Lefse programs.
Results: GCs treatment affected the alpha-diversity of Bacteria and Eukarya but not of Archea. Beta-diversity of all the domains were not statistically different between GC-treated and GC-untreated pwMS. We identified 28 DAS among Bacteria, 16 DAS among Archaea and 3 DAS among Eukarya; Bacteria of the orders of Bacillales and Mycobacteriales resulted increased in the GC-untreated group, while the archaeal order of Acidilobales resulted increased in GC-treated group. At family level, Peptostreptococcaceae, Turicibacteraceae, Oscillospiraceae, Lactobacillaceae and Pichiaceae families resulted increased in the GC-treated group, while Staphylococcaceae and Mycobacteriaceae in the untreated one.
Conclusion: Our findings indicate differences in gut microbiota composition between pwMS that received or not GCs at the diagnosis suggesting that GC may exert their antiflammatory effect through gut microbiota too. Further intra-subject comparison studies before and after GC-treatment could provide new insights both in terms of changes in microbial composition and in clarifying which the size and how long lasting the effect of GC on MS microbiota is.

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P1704
B-Lymphocyte kinetics and clinical outcomes of Ocrelizumab and Ofatumumab in Multiple Sclerosis

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Introduction: Anti-CD20 monoclonal antibodies like Ocrelizumab and Ofatumumab represent a key class of the disease-modifying therapies (DMTs) available for patients with multiple sclerosis (MS), mainly exerting effect through the depletion of B-cells. However, there are limited studies that directly compare Ocrelizumab and Ofatumumab's effects in B-cells and its clinical correlation.
Objectives/Aims: To compare the effect of Ocrelizumab and Ofatumumab on B- lymphocytes population and subpopulations over a 12-month period, along with possible clinical correlations.
Methods: All patients who had received either Ocrelizumab or Ofatumumab for MS treatment and with a follow-up of at least 12 months were included. Flow cytometry in peripheral blood was used to assess B-lymphocyte populations and subpopulations. The laboratory evaluations were conducted at baseline, at 6 months and at 12 months of treatment.
Results: A total of 156 patients with MS were selected. 93 patients received Ocrelizumab while the other 63 received Ofatumumab. At baseline, B-lymphocyte populations and subpopulations were similar between patients treated with Ocrelizumab and Ofatumumab. After 6 months, both groups maintained similar levels, except for a significant difference in Immature B-cell counts ($p = 0.004$). At 12 months, both total B-cell count and plasmablasts count were significantly lower in the Ofatumumab group ($p < 0{,}001$ and $p = 0{,}002$, respectively). Regarding clinical outcomes (EDSS progression and new relapses), during the 12-month period of treatment, no significant differences between the two groups were observed.
Conclusion: Our study reveals some differences on B-cell kinetics between the anti-CD20 treatments, as Ofatumumab patients have a significant lower total B-cell count compared to Ocrelizumab at 12-months. Other differences in subpopulations were found, such as in Immature B cell and Plasmablasts populations. Despite these immunologic variations, the clinical outcomes remained similar between the two groups. Therefore, the clinical significance of these immunological differences remains to be determined with longer longitudinal studies.

Disclosure of interest: Bruna Costa: nothing to disclose

P1705
GA-transition study: a real-world analysis of safety and efficacy in switching between two branded forms of Glatiramer Acetate

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Introduction: Glatiramer Acetate originator (GA) has long been used to treat relapsing-remitting multiple sclerosis (RRMS). Following its patent expiration in 2015, biosimilar versions such as Copemyl (CO) were introduced. The evaluation of their real-world comparability in terms of efficacy and safety is clinically relevant.

Objectives/Aims: To assess the real-world efficacy and safety of GA versus CO in MS patients treated consecutively with both.

Methods: Clinical and demographic data over four years (with ⩾2 years per treatment) were collected, including medical history, MRI activity, EDSS, relapses, and AEs. MRI activity under the two DMTs was compared within subjects using McNemar's test. ARR differences were assessed with the Wilcoxon signed-rank test and mean paired difference (95% CI). Time to 6-month confirmed EDSS progression was compared using a Cox model clustered by patient.

Results: Among 138 MS patients, the mean treatment durations were 96 (SD: 55.4) months for GA and 53 (SD: 15.2) months for CO. All received GA first, then CO. Most patients were female (70.3%) with a mean age of 43 years, 84.1% had at least one comorbidity and 27.5% were treated with a previous DMT. At GA start, 92.8% had RRMS; 5.1% converted to SPMS during CO.

At the start of GA, 92.8% of patients had RRMS, 2.9% had PPMS, and 4.3% had SPMS. During treatment with CO, seven RR patients (5.1%) progressed to SP form.

The mean within-patient difference in ARR between CO and GA was −0.009 (95% CI: −0.028 to 0.010). The Wilcoxon signed-rank test indicated no statistically significant difference between the two treatment periods ($p = 0.38$).

MRI activity numerically decreased after switching treatment: 9 patients had activity only before the switch, 3 showed new activity only after, without a statistically significant difference ($p = 0.15$).

6-month confirmed EDSS progression occurred in 6.0% of treatment periods with GA and 7.3% with CO. Over a median follow-up of 36.1 months, no significant difference in progression risk between groups was observed (HR 1.53, 95% CI 0.74–3.16, $p = 0.26$). The median time to 6-month confirmed EDSS progression was not reached during the follow-up period.

During treatment with GA, 17 AEs occurred in 16 patients, with 7 of them (41.2%) being certainly related to the treatment, and 2 serious AEs (SAEs) not related to the treatment. Fifteen AEs occurred in 14 patients during treatment with CO, with 4 of them (26.7%) certainly related to the treatment, and 4 SAEs not related to the treatment.

31 patients stopped CO after two years (mean 38.2 ± 15.7 months): 1 due to inactivity, 5 due to disease progression, 5 due to safety reason, 1 due to convenience, 15 due to needle fatigue. Teriflunomide was the most common alternative (61.3%).

Conclusion: CO appears to offer comparable clinical efficacy and safety to GA. These findings are consistent with the non-inferiority of CO compared to GA.

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P1706
The patient experience of autologous stem cell transplant for Multiple Sclerosis: a systematic review and qualitative study

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Introduction: Autologous haematopoietic stem cell transplant (HSCT) is an increasingly considered treatment option for people with highly active relapsing multiple sclerosis (MS) who are not adequately responding to disease-modifying therapies. To date, research has predominantly focused on disease-specific outcome measures, with limited research on the patient experience of the HSCT process and the impact of HSCT on patient-reported outcome measures.
Objectives/Aims: First, this research aimed to systematically review the literature that included patient-reported outcome measures, such as cognition, fatigue, mood, and quality of life, in the evaluation of HSCT for MS. Second, a qualitative study was conducted to explore the patient experience of undergoing HSCT for MS.
Methods: A systematic review was conducted of peer-reviewed studies which included at least one standardised patient-reported outcome measure pre- and post-HSCT. Qualitative research was carried out with 12 adults with MS who had undergone HSCT treatment. Online semi-structed interviews explored the experience of deciding on the treatment, the HSCT process itself, and the patient-reported outcomes following HSCT. Interviews were audio-recorded and transcribed verbatim. A thematic analysis approach was employed.
Results: Eleven studies were identified in the systematic review which included patient-reported outcome measures (quality of life, cognition, fatigue, and mood) in the evaluation of HSCT for MS. Long-term improvements in quality of life post-HSCT were identified. Arguments for interpreting these results with caution are presented based on risk of bias.
From qualitative research, three main themes were identified: (1) *Balancing hope and fear* explores the decision-making experience when considering HSCT as a treatment; (2) *Distinct emotional experience* highlights the unique challenges faced on all stages of the treatment journey; and (3) *Adjusting to outcomes* explores how participants make sense of the aftermath of the treatment, including managing the ongoing uncertainty of symptoms and complications arising from HSCT.
Conclusion: HSCT is a complex treatment, both physically and psychologically for MS patients. Further research is required to progress clinician and patient understanding of the impact of HSCT treatment on patient-reported outcomes. A comprehensive and holistic care pathway is required to support people with MS at all stages of the treatment process, to ensure patient-centred planning and care.

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P1707
Cladribine Tablets Show Low 4-Year PIRA Rates in MS: Insights from Pooled Analyses of CLARIFY-MS and MAGNIFY-MS Studies

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Introduction: People with multiple sclerosis (PwMS) acquire disability over time (confirmed disability accumulation [CDA]) via inflammatory (relapse-associated worsening [RAW]) and non-inflammatory (progression independent of relapse activity [PIRA]) neurodegenerative processes. The long-term effect of cladribine tablets (CladT) on PIRA has yet to be reported.
Objectives/Aims: To investigate the long-term effects of CladT on PIRA, RAW, and CDA in PwMS.
Methods: A pooled analysis was conducted from an integrated database including 4-year data from the CLARIFY-MS and MAGNIFY-MS Parent studies and their 2-year treatment-free Extension studies in PwMS treated with short-course CladT. Six-month confirmed PIRA, RAW, and CDA were investigated. **PIRA** was based on the Expanded Disability Status Scale (EDSS), and included 6-month confirmed disability progression (CDP). **RAW** included any CDP event that did not qualify as a PIRA event, and **CDA** included any PIRA or RAW event. **Composite (c)PIRA** included CDP, and 20% progression on either the timed 25-foot walk (T25FW) or 9-hole peg test. **cRAW** and **cCDA** were calculated using the cPIRA criteria. Time to first event was analysed by the non-parametric

Kaplan-Meier (KM) method. Subgroup analyses included age (⩽40 *vs* >40 years), and history of disease-modifying therapy (treatment-naïve [Tx-naïve] *vs* experienced (Tx-exp]).
Results: A total of 752 PwMS (CLARIFY-MS, n=482; MAGNIFY-MS, n=270) were included in the pooled analysis. Of these, 444 were aged ⩽40 years, and 251 were Tx-naïve. At Year 4, KM estimates for PIRA, RAW and CDA were 10.8%, 6.3% and 16.4%, respectively. KM-estimated rates of PIRA were higher in participants aged >40 years *vs* those ⩽40 years (15.4% *vs* 7.6%), but were similar between Tx-naïve *vs* Tx-exp (10.5% *vs* 11.0%) subgroups. The KM estimated probability of first PIRA event was 10.8%. In all participants, the cPIRA rate was 24.8%, cRAW rate was 8.7%, and cCDA rate was 30.6%. The greatest contributing factor to 6m-cPIRA was the T25FW (55.9% of PwMS with an event), with 6mCDP contributing 42.2%. cPIRA rates were higher in participants aged >40 years *vs* those ⩽40 years (33.4% *vs* 18.6%), but were similar between Tx-naïve *vs* Tx-exp (22.9% *vs* 25.7%) subgroups.
Conclusion: These findings demonstrate long-term control of inflammatory and non-inflammatory components of disease accumulation and disability in a large pool of PwMS treated with CladT. The vast majority of PwMS were free from PIRA at Year 4 overall, and in the ⩽40 vs >40 years subgroups.

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P1708
Short-term efficacy of ocrelizumab on new cortical lesions in patients with multiple sclerosis

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Introduction: Cortical lesions (CLs) are a common finding in multiple sclerosis (MS) but data regarding the impact of treatment on their evolution are lacking.
Objectives/Aims:
This study evaluates CLs status and new CLs accrual over 2-year follow-up in a cohort of patients treated with ocrelizumab (OCR), their correlation with neurological disability and with white matter lesions (WMLs) accrual.
Methods: 92 relapsing-remitting MS patients [62 (67%) women, mean (SD) age 39 (9.9) years, median (IQR) baseline EDSS 2.5 (2)] underwent clinical, neuropsychological assessment and brain 3T-MRI at baseline and two years after OCR start. CLs were manually segmented using Artificial Intelligence-Driven Imaging Reconstruction (AIDIR) sequences.
Results: At baseline, 22 patients (24%) had no CLs, 31 (34%) had 1 CL, 17 (19%) had 2 CLs, and 22 (24%) had>=3 CLs. Higher CLs number was associated with longer disease duration (r=0.2, p=0.06), lower SDMT (r=-0.22, p=0.07) and lower total brain volume (r=-0.32, p=0.002). 17 patients (19%) experienced WML accrual and 16 patients (17%) disability progression over follow-up, but none of them developed new CLs. We detected only one new CL at follow-up in a female patient (29 years-old, disease duration 2.9 years). This patient maintained NEDA-3 status, showed improved physical disability (EDSS 3.5 to 2.5) and no cognitive decline despite baseline SDMT impairment (z score -1.4 to -0.21).

Conclusion: In a cohort of patients treated with OCR only one new CL in a patient without concurrent WMLs accrual was detected. These data support OCR efficacy in minimizing lesion accrual and suggest distinct mechanisms underlying CLs and WMLs development in MS.

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P1710
Optimizing Methods for Long-term Follow-up Studies in Multiple Sclerosis

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Introduction: Long-term follow-up studies are essential for understanding disease progression in multiple sclerosis (MS). Locating participants years after study completion is a challenge. Limited research exists on how to re-engage previous participants in long-term follow-up studies.

Objectives/Aims: To describe the methods for locating SPRINT-MS trial participants up to a decade after original study completion.

Methods: SPRINT-MS was a Phase 2 trial that completed original participant follow-up between 2015-2017. All 255 original participants were eligible to enroll in a single-visit long-term follow-up study between 2024-2025. Only study sites had access to identifying information on participants. Study sites documented methods used to locate and contact each participant. Methods included electronic medical records (EMR), institutional databases, internet search engines, public obituary databases, state voting records, and patient-initiated contact.

Results: With >95% of the study data collected and analyzed, of 255 original participants, 7 (2.7%) could not be identified or found. For the remaining 248 (97.3%), most participants (n=226, 91.1%) were located using a single method, primarily the site's EMR (n=207, 91.6%) or institutional databases (n=14, 6.2%). For the 22 participants requiring more than one method (mean: 2.6 methods), 13 needed two (5.2%), 4 needed three (1.6%), and 5 needed four methods (2.0%), with EMR still most frequently used (n=21, 95.5%), supplemented by search engines (n=12, 54.5%) and public obituary databases (n=11, 50.0%). The median (IQR) time between original study completion and follow-up contact was 8.1 (7.8, 8.4) years overall. To date, the outreach resulted in 139 participants agreeing to enroll, while 44 declined participation, 40 did not respond to repeated contact attempts, and 25 were deceased.

Conclusion: Ninety-seven percent of the original SPRINT-MS participants were successfully located approximately 8 years after study completion. Although local EMR was the most

common method for locating participants, additional methods were necessary for some participants. The high rate of successful contact demonstrates the effectiveness of these methods, highlighting how research teams can locate and re-engage the vast majority of study participants even after an extended interval following original study completion.

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P1711
Evaluating the response categories of the Multiple Sclerosis Impact Scale-29: A Rasch Analysis

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Introduction: The Multiple Sclerosis Impact Scale (MSIS-29) is a patient reported outcome measure aiming at measuring physical (20 items) and psychological (9 items) impact of multiple sclerosis (MS). The original version with five response categories for each item was culturally adapted and translated into Norwegian (MSIS-29 NV), evaluated for measurement properties and published in 2010. This scale has since then been used in research and included in the Norwegian MS Registry and Biobank (NMSRB). The developers of the original MSIS-29 conducted a Rasch analysis on data from the UK (n=1725), leading to the removal of one response category, and are currently recommending all users to adopt to the revised scale.
Objectives/Aims: The aim of this study was to investigate whether a reduction of response categories was supported based on data from a Norwegian MS population.
Methods: All persons with MS that reported MSIS-29 NV in the NMSRB during 2023 (n=6137), were analyzed using the Rasch Partial Credit Model to determine whether any of the response categories were redundant. Separate analyses were done for the physical and psychological subscales.
Results: Except for one item (question 17), the order of rating scale category thresholds was as expected ($t1 < t2 < t3 < t4$). The Item Characteristic Curves showed, except again for question 17, that all five categorical responses had an area across the trait range where it was the most likely one to be chosen. This suggests that for each item (except for question 17), each categorical response contributes unique information to the scale.
Conclusion: Our comprehensive dataset provides no support for reducing the number of response categories, and therefore, we recommend that all five response categories be retained in the Norwegian version of MSIS-29.

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P1712
Assessment of short-term ocrelizumab treatment impact on regulatory immune cell subsets through intracellular cytokine measurement in patients with multiple sclerosis

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Introduction: Ocrelizumab, a CD20-targeting monoclonal antibody, is known to significantly alter peripheral blood immune cell subsets in patients with multiple sclerosis (MS). However, the impact of ocrelizumab on regulatory adaptive immune cell subsets with suppressive capacity has not been investigated.
Objectives/Aims: Our aim was to evaluate the interactions between ocrelizumab treatment and regulatory B- and T-cell subsets in MS patients.
Methods: Eight patients wih relapsing remitting MS (RRMS) and 8 healthy controls were included. Immunophenotyping and intracytoplasmic staining of peripheral blood B and T cells of healthy controls and RRMS patients before and 6-months after ocrelizumab treatment were performed using flow cytometry. Chemotaxis towards BAFF was evaluated under microscope and by flow cytometry. Flow cytometry data (FCS files) underwent scaling and transformation processes and unsupervised dimensionality reduction was performed using uniform manifold approximation and projection (UMAP).
Results: During the 6-month treatment period, naive B (CD19+CD5+) cell populations with anti-inflammatory cytokine production were significantly increased (IL-10; p=0.013, IL-35; p=0.039, TGFβ-1; p=0.0004). Additionally, follicular helper T cells (CD3+CD4+CXCR5+) exhibited elevated IL-21 levels at 6-months (p=0.035). B cells of ocrelizumab-treated patients showed trends towards exhibiting decreased BAFF-induced chemotaxis. NEDA (non-evidence of disease activity)-3 status was associated with increased CD3+CD4+CD25+CD127-TGFβ-1 positive regulatory T cell (p=0.024) and CD3+IL-10+ T cell (p=0.017) subset ratios.
Conclusion: Ocrelizumab modulates the immune system and treatment effcicacy at least partially through alteration of IL-10, IL-35 and TGFβ-1-expressing adaptive immune cell subset ratios and reduction of B cell chemotaxis.

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P1713
Dynamics of neurofilament light chain serum concentration after high-efficacy treatment initiation

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Introduction: The decrease of neurofilament light chain concentration in serum (sNfL) after initiation of disease-modifying treatment (DMT) mirrors the treatment-induced reduction of disease activity. The exact dynamics and the key factors which affect the DMT-associated decrease of sNfL over time are less known.
Objectives/Aims: To examine sNfL dynamics after HET initiation and identify factors which affect NfL decrease.
Methods: We measured sNfL concentrations at baseline, 3 and 6 months after high-efficacy treatment (HET) initiation in a cohort of relapsing MS (RMS) patients. Their sNfL levels and EDSS values were compared using paired t-tests. One-way ANOVAs and partial correlations controlling for age and BMI were used to test for association between further clinical variables and sNfL dynamics.
Results: A total of 54 patients with a mean age of 35y (95% CI 32.18 - 37.9y), of whom 75.9% were female, were included in the analysis. sNfL decreased from baseline to month 3 (20.1 pg/ml vs. 15.1 pg/ml, p=0.024) but remained stable between month 3 and month 6 (12.3 pg/ml vs. 13.2 pg/ml, p=0.544). EDSS didn't change significantly during the whole time period (1.83 vs. 1.86, p=0.652; 1.64 vs. 1.61, p=0.721).
RMS patients who have had their first manifestation of the disease within the last 12 months exhibited less pronounced sNfL reduction 6 months after HET initiation as compared to RMS patients with a longer disease duration (+3.4 pg/ml vs -10.4 pg/ml, p=0.030).
The presence of gadolinium-enhancing lesions (GEL) on initial MRI was associated with a stronger decline in sNfL levels 3 but not 6 months after baseline (-22.0 pg/ml vs. -3.7 pg/ml, p=0.019; -16 pg/ml vs. -6 pg/ml, p=0.520).
Gender, being on a low efficacy treatment (LET) vs. none before starting HET, baseline sNfL and EDSS values, annualized relapse rate, time since last relapse and number of prior DMTs did not affect sNfL dynamics.
Conclusion: Our data suggests that HET reduces sNfL levels mainly during the first 3 months and less in months 4-6 after HET start. During this time the sNfL concentration decline is more marked for patients exhibiting GEL and might be less pronounced for patients in the very early stages of the disease.

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P1714
Olfactory threshold as a complementary predictive marker to NEDA-3 for treatment monitoring in multiple sclerosis

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Introduction: No evidence of disease activity 3 (NEDA-3) is a composite endpoint used to monitor the response to disease-modifying therapy (DMT). Olfactory threshold (OT) is a widely accessible short-term marker of inflammatory activity in patients with multiple sclerosis (pwMS). However, the additional predictive value of integrating OT into NEDA-3 criteria remains unclear.
Objectives/Aims: To assess whether OT improves the predictive capacity of NEDA-3 regarding short- and medium-term disability progression in MS.
Methods: In an ongoing prospective observational study at the Medical University of Vienna, pwMS newly started on DMT received OT testing by Sniffin' Sticks before DMT start as well as after 3, 6 and 12 months in addition to baseline and 12-month MRI plus ⩾12 months of clinical follow-up. NEDA-3 vs. EDA-3 status was determined 12 months after DMT start. Increased OT indicating inflammatory activity was defined as OT scores ⩽ 6.5 at month 3, 6 or 12. The primary endpoint was time to inflammatory disease activity (relapse and/or new T2 lesions on MRI compared to baseline). We calculated Kaplan-Meier estimates and Cox regression analyses adjusting for sex, age, disease duration, previous DMT, current DMT category, and relapses within 1 year preceding baseline.
Results: A total of 113 patients were included (female: 75.2%, mean age: 34.8 [SD 8.5], high efficacy DMT: 70.8%), with 12.4% displaying inflammatory disease activity and 10.6% EDSS worsening during a median follow-up of 2.43 years (IQR, 1.55-3.23). Overall, 13.3% met EDA-3 criteria within the first year, associated with an increased risk for inflammatory disease activity (adjusted hazard ratio [aHR] 3.15, 95% CI 0.98-10.15,

p=0.055). When incorporating OT, 51 patients (45.1%) met the combined criteria (EDA-3+OT), but there was no significant association with the likelihood of inflammatory activity (aHR 1.63, 95% CI 0.54-4.88, p=0.384).
Conclusion: Short-term inflammatory activity, as indicated by OT, does not seem to provide additional predictive value for medium-term inflammatory activity when combined with NEDA-3. Further studies will aim to determine whether OT can have clinical utility by enhancing the identification of patients at risk.

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P1715
EDSS and age are associated with the risk of progression independent of relapse and MRI activity in natalizumab-treated Multiple Sclerosis patients

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Introduction: Clinical, biological and radiological data useful to predict and manage the Progression Independent of Relapse and MRI Activity (PIRMA) in multiple sclerosis are currently very limited.
Objectives/Aims: To identify prognostic factors of PIRMA in natalizumab (NTZ) treated RRMS patients.
Methods: RRMS patients who started NTZ in the period July 2007 to February 2017 were retrospectively investigated. Clinical and radiological data were collected every 6 months. Survival estimates for clinical relapses, radiological relapses, and PIRMA were analysed. Multiple logistic regression models were used to analyse the probability of developing PIRMA according to several factors at therapy initiation, including sex, age, disease duration, previous disease modifying therapies, reimbursement criterion and Expanded Disability Status Scale (EDSS).
Results: 288 patients (197 F, 91 M) with a mean age at baseline of 26.6±9.6 years and followed for a mean time (from the first infusion to the last follow-up or end of NTZ treatment) of 66.3±52.0 months. Among these, 129 (58%) discontinued NTZ for high JCV index. PIRMA was observed in 77 patients (27.8%) after a mean time of 34.5±30.6 months and was sustained in 85%. The probability of PIRMA-free condition at 24, 48, and 62 months was respectively 84.3%, 75% and 69.7%. Multivariate analysis (AUC 0.7525, p<0.0001) identified higher EDSS (β: 0.57, $p<0.0001$) and advanced age (β: 0.03, $p=0.02$) as independent factors associated with an increased probability of PIRMA. Thus, patients were grouped according to age (cut-off value: 42.5 years) and EDSS at baseline (cut-off value: 4.0) by means of ROC analysis, and a model to stratify patients for PIRMA prediction, setting three levels of risk, was developed, namely low (EDSS <4.0 and age <42.5 years), intermediate [EDSS <4.0 and age ⩾42.5 years (HR: 2.2; 95%CI: 0.92-5.26, $p<0.0239$)] and high risk [(EDSS ⩾4.0; HR 4.98; 95% CI: 2.86-8.67, $p<0.0001$)].
Conclusion: PIRMA was identified as the main driver of disability progression in RRMS treated with NTZ. PIRMA occurrence was predicted by age and EDSS at therapy initiation, stratifying patients into three different risk categories. The early treatment of younger patients with lower EDSS would be particularly effective in delaying (or preventing) PIRMA.

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P1716
Serum Neurofilament Light Chain and Glial Fibrillary Acidic Protein Remain Stable After Switching from Intravenous to Subcutaneous Natalizumab in RRMS

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Introduction: Subcutaneous natalizumab has demonstrated efficacy comparable to the intravenous formulation in controlling disease activity in relapsing remitting multiple sclerosis (MS), with the added benefit of easier and faster administration. However, no studies have assessed subclinical disease activity using serum neurofilament light chain (sNFL) or glial fibrillary acidic protein (GFAP). In clinical practice, many patients have transitioned from intravenous to subcutaneous natalizumab for greater treatment convenience.
Objectives/Aims: To compare sNfL and GFAP levels over 12 months after transitioning from intravenous to subcutaneous natalizumab in a real-life cohort of MS patients.
Methods: This prospective study included consecutive patients who switched from intravenous to subcutaneous natalizumab between April and October 2022. sNFL levels and GFAP were measured at baseline and after 6 and 12 months of subcutaneous treatment, alongside clinical and radiological assessments.
Results: A total of 23 patients were included (mean age 44 ± 10 years, 91% female). Median time since MS onset was 14 (IQR 14)

years, time on first disease-modifying therapy (DMT) 10 (IQR 8) years, and time on natalizumab 5 (IQR 4.6) years. Baseline annualized relapse rate (ARR) was 0.09 ± 0.2, relapse-free time (RFT) 4.0 (IQR 4.7) years, and EDSS 2.0 (IQR 2). Median sNFL levels were 7.7 (IQR 3.3) at baseline, 8.6 (IQR 3.4) at 6 months, and 9.0 (IQR 3.7) at 12 months, with no statistically significant difference (p=0.438). A repeated analysis using Z-score normalization confirmed these findings (p=0.401). Median GFAP levels were 87.7 (IQR 77.8) at baseline, 86.8 (IQR 81.8) at 6 months, and 90.2 (IQR 79.8) at 12 months, with no statistically significant difference (p=0.957). Over 12 months, ARR remained stable at 0.08 ± 0.3 (p=1), while RFT increased to 4.7 (IQR 4.8) years (p=0.001). No radiological activity was detected.
Conclusion: sNFL and GFAP levels, as well as clinical and radiological disease activity, remained stable in RRMS patients who transitioned from intravenous to subcutaneous natalizumab, supporting its comparable effectiveness in real-world practice.

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P1717
Reducing the Risk of PIRA in RRMS: The Value of High-Efficacy Disease-Modifying Therapies

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Introduction: Disability accumulation in multiple sclerosis (MS) may occur through relapse-associated worsening (RAW) and progression independent of relapse activity (PIRA). Disease-modifying therapies (DMTs) are intended to reduce relapse rates and delay long-term disability
Objectives/Aims: This study aims to assess the association between DMT efficacy and the development of PIRA in individuals with relapsing-remitting MS (RRMS).
Methods: This interim analysis is based on data from a prospective, real-world cohort managed at a tertiary MS center in Argentina, including patients who initiated DMTs between 2011 and 2019. Of 226 patients, 176 had data for inclusion in the analysis. A retrospective observational approach was employed, using a Cox proportional hazards model to evaluate the association between DMT efficacy and the occurrence of PIRA (binary outcome), adjusting for age at onset, disease duration, and number of treatment switches. DMTs were classified as high- (cladribine tables and monoclonal antibodies), moderate/low-efficacy (other treatments), and treatment switches were modelled as time-dependent covariates.
Results: Among the 176 patients, 55% were female, with a median age of 32 years (IQR 26–39) at the time of treatment initiation. The mean follow-up duration was 9 years (IQR 7–11). At baseline, 6.2% of patients were receiving high-efficacy disease-modifying therapies (DMTs), 37% moderate-efficacy, and 55.3% low-efficacy DMTs.
By the time of analysis, 43% of patients initially on moderate-efficacy DMTs and 74% of those on low-efficacy DMTs had switched treatment due to therapeutic failure. High-efficacy DMTs were associated with a significantly reduced risk of developing PIRA. In contrast, moderate- and low-efficacy DMTs were associated with an increased risk of PIRA (HR = 7.36, 95% CI 1.9–28, $p < 0.005$). Patients who failed their initial treatment and required a switch were also at increased risk of PIRA (HR = 2.56, 95% CI 1.5–4.3, $p < 0.001$).
Conclusion: Early initiation of high-efficacy DMTs may reduce the risk of PIRA in individuals with RRMS. Continued follow-up and analysis of the complete cohort are anticipated to validate these findings and enable more granular subgroup analyses.

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P1718
Six-Year Disease Trajectory in Multiple Sclerosis: A Pre- and Post-Ocrelizumab Treatment Analysis

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Introduction: Ocrelizumab, a humanized anti-CD20 monoclonal antibody, has been shown to effectively reduce disease activity and delay disability progression in both relapsing and progressive forms of multiple sclerosis (MS). This study aimed to evaluate the clinical trajectory of MS patients during the three years preceding and following the initiation of ocrelizumab therapy.
Objectives/Aims: This study aimed to evaluate the clinical trajectory of MS patients during the three years preceding and following the initiation of ocrelizumab therapy.
Methods: We conducted a retrospective analysis of 268 people with multiple sclerosis (pwMS) treated with ocrelizumab. Patients were stratified into relapsing-remitting MS (RRMS, n=138) and progressive MS (PMS; 111 secondary progressive MS, 19 primary progressive MS; total n=130) groups. Clinical outcomes were assessed by comparing annualized relapse rates (ARR) in the three years before and after treatment initiation. Expanded Disability Status Scale (EDSS) scores were recorded at three time points: three years before treatment, at the time of initiation, and three years post-initiation. In the post-treatment period, the proportion of patients achieving no evidence of disease activity (NEDA-3)—defined as the absence of clinical relapses, confirmed disability progression, and new or enlarging MRI lesions—was also evaluated.
Results: The mean age of the cohort was 53.2 years (SD = 12.1), with 63.4% female. The average age at MS onset was 30.8 years (SD = 10.2), and the mean disease duration was 22.3 years (SD = 8.8).
In the RRMS group, the ARR declined significantly from 0.35 (SD = 0.34) in the three years before treatment to 0.014 post-treatment ($p < .001$). EDSS scores remained stable (baseline: 3.57, SD = 1.76; year 3: 3.54, SD = 1.90; $p = .765$).
In the PMS group, the ARR decreased from 0.31 (SD = 0.35) to 0.0077 (SD = 0.05) after treatment ($p < .001$), with EDSS scores showing no significant change (baseline: 6.27, SD = 0.91; year 3: 6.36, SD = 0.91; $p = .080$).
Notably, NEDA-3 was achieved in 46.0% of RRMS patients and 54.6% of those with progressive MS over the three-year follow-up, highlighting the broad efficacy of ocrelizumab across different MS phenotypes.
Conclusion: This six-year observational window reveals that ocrelizumab substantially suppresses disease activity in both relapsing and progressive MS. The therapy was associated with a marked reduction in relapse rates and stabilization of disability over time. The achievement of NEDA-3 in a considerable proportion of patients, including those with progressive forms of MS, underscores the potential of ocrelizumab to effectively modify disease trajectory even in long-standing and advanced cases.

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P1719
Reading Between the Spinal Lines: Are Spinal Lesions Predictive of Suboptimal Cladribine Response in MS?

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Introduction: Cladribine, an oral immune reconstitution therapy for relapsing multiple sclerosis (MS), has demonstrated efficacy in clinical trials. Nonetheless, real-world data are limited, especially regarding how spinal cord lesions influence treatment success. In routine practice, spinal magnetic resonance imaging (MRI) is sometimes bypassed unless clinical suspicion is high, raising questions about potential under-detection of relevant disease activity. Understanding the broader real-world effects of cladribine, including any distinct impact of spinal lesions, can help optimise clinical decision-making.
Objectives/Aims: To characterise clinical and radiological outcomes of cladribine therapy in a single-centre, real-world cohort of patients with MS, and to explore whether baseline or pre-treatment spinal MRI findings might predict suboptimal response.
Methods: We retrospectively reviewed 73 patients with relapsing MS who initiated cladribine between 2019 and 2024. Data collected included prior disease-modifying therapies, relapse rates, and Expanded Disability Status Scale (EDSS) measurements from baseline to five years. Spinal MRI was not systematically performed; 42% of participants had baseline spinal imaging, and 34% underwent at least one follow-up spinal scan (⩾12 months). Using univariable and multivariable models (Cox and logistic), adjusted for age, disease duration, and prior therapies, we assessed factors associated with cladribine failure (relapse, radiological breakthrough, or early discontinuation) and EDSS progression.
Results: Univariable analyses revealed that a higher total spinal lesion count (hazard ratio [HR] 1.34, p=0.01) and ⩾1 gadolinium-enhancing (Gd+) spinal lesion in the year prior to treatment (HR 13.20, p=0.04) were linked to increased risk of treatment failure. However, these associations lost significance in adjusted models—likely reflecting the limited subset of patients with spinal imaging. Those displaying new spinal Gd+ lesions by year two or early relapses had a higher likelihood of EDSS deterioration, while other clinical and imaging variables were not consistently predictive.

Conclusion: These real-world data suggest that cladribine provides meaningful disease control for many patients, yet baseline or emerging spinal lesions may identify individuals at greater risk of suboptimal outcomes. Larger prospective studies with more comprehensive spinal MRI protocols are warranted to clarify whether routinely assessing the cord could better guide patient selection and long-term management.

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P1720
Serum neurofilaments (NfL s) levels like a predictor of activity in Cladibine patients in year 4 after starting treatment

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Introduction: Cladribine tablets is an induction therapy for the treatment of Multiple Sclerosis. One of its most important characteristics, durability of efficacy, has been established in clinical trials. There are doubts about the management in years 3 and 4 and the need of another curse of treatment. Serum neurofilament light chain could be a good prognostic factor to support decision making

Objectives/Aims: To describe the clinical evolution and Serum neurofilaments (NfL s) level in a cohort of ms patients in treatment with cladribine in years 3 and 4
Methods: Retrospective and observational study in a cohort of 93 MS patients treated with cladribine. We analyzed demographic data, disease activity (clinical and MRI) anf NfLs levels. We analyzed clinical evolution of patients with activity and its correlation with other prognosis factors. Serum NfL levels are analyzed using the Single Molecule Array (Simoa®) technique on the Quanterix SR-X equipment.
Results: In a cohort of 93 MS patients treated with cladribine,56 patients reached year 4 and we have the levels of NfLs in 27.
In this patients we observed NfLs levels above 10 pg/ml in year 4 in 3 patients. 2 of them presented clinical activity of the disease near this determination and MRI activity too. 1 patient didn,t present activity of the disease. 4 patients presented levels between 8-10 pg/ml without activity. We didn,t observe activity of the disease with normal levels of NfL. 2 patients presented progression of the disease with normal NfLs levels.
Conclusion: Serum NfL levels is a useful biomarker for monitoring activity of the disease. We could anticipate MS activity with a correct monitoring of NfL levels in Cladribine patients to avoid clinical and radiological activity and maybe plan re-treatment.

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P1721
Ublituximab as a Treatment Option for Relapsing Multiple Sclerosis Patients with Early B-Cell Repopulation on Ocrelizumab: Case Series

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Introduction: Anti-CD20 monoclonal antibodies, such as ocrelizumab and ublituximab, are FDA-approved for the treatment of relapsing MS (RMS). These medications primarily work by depleting B cells through a mechanism called antibody-dependent cellular cytotoxicity (ADCC). Ublituximab, which has a glycoengineered Fc region, demonstrates enhanced ADCC activity compared to other anti CD20-therapies. Early B-cell repopulation (EBR) has been observed between ocrelizumab infusions, but its occurrence with ublituximab has not been studied.
Objectives/Aims: To present a case series of three patients with RMS who tested positive for EBR and switched to ublituximab shortly after developing EBR on ocrelizumab.

Methods:EBR, defined as ⩾1% of CD19+ B cells of total lymphocytes, is tested every 6 months, approximately 4 weeks before the scheduled anti-CD20 infusion. This study evaluated the effect of transitioning to ublituximab on B-cell subsets, relapse frequency and MRI disease activity. Patient specific data, including white blood cell counts, age, sex, BMI (body mass index), BSA (body surface area), pretreatment therapy, and clinical outcomes were also analyzed.
Results: The mean age was 38 years (standard deviation [SD] 4.5) with disease onset at 30 years (SD 2.51). 67% were male. Median prior disease-modifying therapies were 2 (interquartile range [IQR] 2). Median BMI and BSA were 44 and 2.3, respectively. EBR was observed after a median of three treatment cycles (IQR 5) and 17 months (IQR 30) following initiation of ocrelizumab therapy. Two patients developed EBR after initial depletion, while one never achieved depletion. All responded to ublituximab achieving <1% CD19 expression within 6 months. None had relapses. One patient showed a new MRI lesion with EBR on ocrelizumab, which reduced in size after switching to ublituximab. B-cell depletion was maintained in all patients during the 6- and 12-month follow-up on ublituximab. EDSS (expanded disability status scale) progression occurred in the patient with a new lesion, while others had stable clinical outcomes.
Conclusion: All three patients demonstrated improved B-cell depletion and clinical stability following the transition, with one patient showing radiological improvement. Ublituximab may improve B-cell depletion when ocrelizumab fails to maintain it between 6-monthly infusions. Larger, diverse studies with extended follow-up are needed to validate these findings and to better understand the clinical significance of EBR.

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P1722
Unlocking Insights: Early Disability Trends, Biomarkers, and MRI Insights in MS Patients on Ofatumumab

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Introduction: Ofatumumab is a subcutaneous anti-CD20 therapy approved for relapsing multiple sclerosis (RMS). Understanding early outcomes and their relation to MRI findings, biomarkers, and immunological features is essential in real-world settings.
Objectives/Aims: This study describes the demographic and clinical characteristics of MS patients treated with ofatumumab, evaluates early disability outcomes (EDSS at 6 and 12 months), and examines their associations with diagnostic delay, spinal cord involvement, and serum neurofilament light chain (NFL) levels. We also explore the prognostic value of cerebrospinal fluid oligoclonal IgM bands and baseline MRI findings to identify early biomarkers and clinical factors predicting short-term progression in patients.
Methods: We conducted a retrospective study of 23 patients treated with ofatumumab at a single MS center, with 13 completing 12 months of follow-up.
Demographics: 85% female, mean age at treatment 33.0 years, clinical onset 32.0 years. Collected clinical data included EDSS scores at 6 and 12 months, serum NFL levels at baseline and 12 months, spinal cord lesions, and oligoclonal bands (IgG and IgM) in CSF. Correlation and subgroup analyses were performed.
Results: Disability outcomes show a mean EDSS of 1.0 at 12 months, with a strong correlation (r 0.76) between EDSS at 6 and 12 months. A moderate positive correlation exists between diagnostic delay and EDSS scores at 6 months ($r \approx 0.66$) and 12 months ($r \approx 0.55$). At 6 months, NFL positively correlated with EDSS ($r \approx 0.64$), indicating higher neurofilament levels relate to greater disability. At 12 months, NFL negatively correlated with relapse activity ($r \approx -0.50$), suggesting a neurodegenerative perspective.
Spinal cord lesions occurred in 85% of patients and were associated with a higher EDSS at 12 months (1.09 vs. 0.50).
IgM oligoclonal bands were present in 4 (31%), absent in 5 (38%), and not evaluated in 4 (31%).
No significant correlations were found between age and EDSS scores or NFL.
Conclusion: Most patients treated with ofatumumab experienced mild early disability, but those with spinal cord lesions and high NFL levels showed greater disability. Diagnostic delays impacted initial EDSS scores. A third of cases had IgM bands, indicating a need for larger sample investigations. These results underscore the value of early biomarker assessment and MRI phenotyping for personalized MS management.

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P1723
Influence of Baseline Scores, Education Level, and Sex on 8-point Change in Symbol Digit Modalities Test Scores in Patients With Early Relapsing Multiple Sclerosis: Year 1 Interim Analysis of the Ozanimod Open-Label ENLIGHTEN Study

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Introduction: Cognitive impairment can occur early in the disease course of relapsing multiple sclerosis (RMS) and may be influenced by education level and sex. The primary endpoint of the open-label ozanimod ENLIGHTEN study was to determine the proportion of patients with improved Symbol Digit Modalities Test (SDMT) scores, defined as an increase of ⩾ 4 points or 10% from baseline; however, an 8-point improvement may better represent individual-level cognitive processing speed changes.

Objectives/Aims: To explore the effects of baseline SDMT score, education level, and sex on 8-point SDMT improvement after 1 year of ozanimod treatment.

Methods: ENLIGHTEN (NCT04140305) is a multicenter, phase 3b, open-label study of ozanimod 0.92 mg in adults with early RMS (⩽1 disease-modifying therapy; Expanded Disability Status Scale score ⩽3.5; ⩽5 years since diagnosis; ⩽10 gadolinium-enhancing lesions). Improved or worsened SDMT scores were considered an increase or decrease of ⩾8 points from ENLIGHTEN baseline, respectively, while stable was a change <8 points. A multivariable logistic regression model assessed baseline SDMT scores, education level (college degree or higher vs no college degree), and sex (male vs female patients) as predictors of improved 8-point SDMT scores after 1 year of ozanimod treatment (data cutoff: 7 Feb 2024).

Results: For the 168 patients with baseline and year 1 SDMT data, baseline mean (SD) age was 39.9 (10.7), mean (SD) SDMT score was 53.2 (11.6), 101 (60.1) had a college degree or higher, and 132 (78.6%) were female patients. After 1 year of ozanimod treatment, 48 (28.6%), 106 (63.1%), and 14 (8.3%) patients had improved, stable, or worsened SDMT scores, respectively. Lower baseline SDMT scores were associated with increased 8-point improvement after 1 year of ozanimod treatment (odds ratio [95% CI] per 1-point SDMT score increase at baseline 0.96 [0.94–0.99]; $P = 0.008$). Education level and sex did not significantly affect the odds of 8-point improvement (odds ratio [95% CI] 0.67 [0.34–1.32]; $P = 0.243$, and 1.04 [0.47–2.29] $P = 0.925$, respectively).

Conclusion: After 1 year of ozanimod in ENLIGHTEN, most patients had improved or stable SDMT scores, with lower baseline SDMT scores, but not education level or sex, being associated with 8-point improvement on the SDMT. These interim findings support the use of ozanimod early in the treatment of patients with RMS.

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P1724
Nasal foralumab induces a regulatory immune response (TGFb) and decreases immune activation (B2M and STAT1) in non-active secondary progressive MS subjects within the first six months of treatment

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Introduction: In mouse EAE models, nasally administered anti-CD3 has been shown to mitigate disease. Nasal foralumab, a fully humanized anti-CD3, was administered to a cohort of non-active secondary progressive (na-SPMS) subjects, as part of an expanded access program. Participants received 50µg of foralumab nasally three days a week for two weeks, followed by a one week break from treatment. This three-week cycle was continued for at least six months.
Objectives/Aims: In this study, we aimed to investigate what effects a continuous six-month treatment course of nasal foralumab has on peripheral blood mononuclear cells (PBMCs) in patients with na-SPMS, and when those effects begin to occur.
Methods: Four subjects provided blood samples before first treatment (baseline), at three months (four treatment cycles), and at six months (eight treatment cycles) from which PBMCs were isolated and subjected to single-cell RNA sequencing (scRNA-seq).
Results: Changes in peripheral blood gene expression occurred as early as three months and affected antigen presentation, interferon responses and regulatory pathways on multiple cell types including Foxp3 Tregs, CD4 Tcm cells, CD8 Tem cells, CD14+ and CD16+ monocytes and B cells. There was a consistent decrease in the gene expression of B2M and an increase in TGFB1, as well as a reduction in STAT1 expression beginning at three months and sustained at six months.
Conclusion: These results demonstrate that nasally administered foralumab modulates immune response as early as three months following treatment start, with a sustained response at six months. Treated subjects had stable EDSS scores across the evaluation period, and no incidence of relapse.

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P1725
Cladribine treatment in Multiple Sclerosis — what comes after year four?

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Introduction: Cladribine is a short-course, immune reconstitution therapy approved for the treatment of patients with multiple sclerosis (MS). Treatment involves two courses over the first two years, followed by a drug-free period in years three and four. However, management beyond this four-year period remains uncertain.
Objectives/Aims: This study aims to evaluate the clinical course of patients treated with cladribine beyond year four and possible strategies for management.
Methods: We identified all patients who had received cladribine since 2018 and included those with a follow-up of more than four years. We subsequently collected demographic, clinical, laboratory, and radiological data and analysed the possible reasons for retreatment with cladribine or switching to another disease modifying therapy (DMT) after year four.
Results: 168 patients treated with cladribine were identified and 45 had more than 4 years of follow-up. 33 patients (73.3%) had no other DMT during the first 4-year course. After year 4, 19 patients (57.6%) had no reasons for retreatment or switching DMT, 13 (39.4%) had a new course of cladribine (10 of them at

year 5, 2 at year 6 and 1 at year 7) and 1 (3.0%) switched to another DMT (at year 5). The reason for retreatment was magnetic resonance imaging (MRI) activity in 7 patients (21.1%), increased levels of serum neurofilaments (sNfL) in 2 patients (6.1%), a proactive strategy in 2 patients (6.1%), a combination of increased sNfL and MRI activity in 1 (3.0%) and clinical worsening in 1 (3.0%).
The lymphocyte profile following cladribine retreatment was similar to the first and second course (mild to moderate lymphopenia) and no serious adverse events occurred.
Conclusion: After year four, a significant proportion of patients (39.4%) initiated a new course of cladribine tablets. The reason was mainly due to subclinical evidence of disease activity (MRI activity or increased sNfL).

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P1726
T-Lymphocyte kinetics and clinical outcomes of anti-CD20 antibodies (Ocrelizumab vs Ofatumumab) in Multiple Sclerosis

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Introduction: Although CD20 expression is primarily related to B-lymphocytes, some T-lymphocytes also expresses CD20. Anti-CD20 therapies like ocrelizumab and ofatumumab are used for multiple sclerosis (MS) treatment and their mechanism of action is primarily related to depletion of CD20+ cells. However, it is still uncertain whether these two antibodies have different impact in CD20+ T-lymphocytes.
Objectives/Aims: To compare ocrelizumab and ofatumumab effects on CD20+ T-lymphocyte levels and subpopulations over 12 months in MS patients and explore possible clinical correlations.
Methods: We identified all patients who had received either ocrelizumab or ofatumumab for MS treatment and subsequently collected demographic, clinical and laboratory data of these patients. We used flow cytometry in the peripheral blood to count T-cells and its CD20+ subpopulations, namely CD4+CD20+, CD8+CD20+ and gamma delta (γδ) CD20+ cells at baseline, at 6 and at 12 months of treatment.
Results: We included 156 patients with MS, treated with ocrelizumab (n=93) or ofatumumab (n=63). After 6 and 12 months, there was a global and significant reduction across all subpopulations of CD20+ T-lymphocytes. However, when comparing patients treated with ocrelizumab and ofatumumab there were no significant differences in CD20+ T-cell count and in all CD20+ T-cell subpopulations except for CD4+CD20+ at 12 months (median 0,00 ± interquartile range 1,09 *vs* 0,71 ± 1,38; p = 0,043, respectively).
Regarding EDSS progression, relapse occurrence and infectious complications, no significant differences between the two treatment groups were found.
In the whole sample, we did not find any statistically significant differences regarding the CD20+ T-cell subpopulations counts after 6 or 12 months of treatment and infectious complications, EDSS progression or new relapses.
Conclusion: In our study, both anti-CD20 treatments decreased CD20+ T-cell counts in the peripheral blood but had a slight difference on the CD4+CD20+ lymphocyte subpopulation. However, no between-treatment difference in clinical outcomes was found.

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P1727
Longitudinal analysis of gut microbiota changes over one year in multiple sclerosis patients undergoing cladribine treatment

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Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative disorder influenced by a combination of genetic predisposition and environmental triggers. One key environmental factor is the gut microbiota, which has been shown to contribute to the immune dysregulation characteristic of the disease. While therapies can impact immune function, their specific effects on the gut microbiota, and whether these changes influence treatment outcomes, remain poorly understood.
Objectives/Aims: This study aims to explore how the gut microbiota is altered in individuals with MS undergoing treatment with cladribine.
Methods: 24 MS subjects starting treatment with cladribine were clinically evaluated. For each subject, stool samples and demographic, clinical, diet and lifestyle data were collected.
Stool samples were prospectively collected before (T0), three (T3), and twelve (T12) months after starting cladribine treatment. DNA was extracted from stool samples, and shotgun

metagenomic sequencing was performed. Reads were aligned with the BWA algorithm against the human genome (hg38 and CHM13) for host contaminant removal. Taxonomic classification was performed with Kraken2. Reads were normalized and assigned to taxa after the manual removal of the non-human taxa, based on literature. Then, a filtering based on OTUs relative abundance (> 0.01%) was applied. Differential abundant species (DAS) were identified using Limma and Lefse programs.

Results: The 10 most abundant species were identified, along with alpha and beta diversity. Additionally, the DAS were obtained between T3 vs T0 and T12 vs T0. Among them, the DAS identified only between T3 and T0 pointed out a transient modulation of the microbiota, while the DAS found only between T12 and T0 established the late gut microbial asset obtained after a year of cladribine treatment.

Conclusion: Overall, our results indicate that cladribine moderately influences the gut microbiota, with changes emerging as early as three months after the start of treatment and continuing throughout the following year. To better understand the potential clinical relevance of these microbiota shifts, further analyses will be carried out, taking into account clinical data as well as dietary and lifestyle factors.

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P1728

Risk of progression independent of relapse activity (PIRA) over five years among different regimes of disease modifying treatments in people with relapsing multiple sclerosis

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Introduction: Current disease modifying treatments (DMT) prevent relapse-associated worsening (RAW) in MS, uncovering the underneath progression independent of relapse activity (PIRA). To date, RAW is the real target of DMTs, while studies investigating effects of treatments on PIRA are lacking.

Objectives/Aims: To investigate DMTs efficacy on PIRA, we compared the risk of reaching the first substained (fs)PIRA and RAW events among different regimens of DMTs over a period of 5 years in people with relapsing MS (pwRMS).

Methods: pwRMS with at least a five-years long follow-up for one DMT and one visit in the last 12 months were included in the study. Risk of reaching the fsPIRA and fsRAW, time to EDSS 6.0 and conversion to secondary progression (SP), were estimated using multivariable Cox proportional hazards models.

Results: We studied 339 pwRMS (DMTs: ocrelizumab=92, natalizumab=129, platform =81, fingolimod=37). FsPIRA was found in 122 patients (20 Ocrelizumab, 38 natalizumab, 15 fingolimod and 38 platform). Compared to platforms DMTs, ocrelizumab has the lowest risk of fsPIRA (HR 0.14 [0.077-0.26]; p<0.0001), followed by natalizumab (HR 0.32 [0.19-0.54]; p<0.0001) and fingolimod (HR 0.41 [0.21-0.78]; p=0.007). Ocrelizumab was also the most effective DMT to reduce the risk of reaching EDSS 6 (HR 0.24 [0.08-0.7], p=0.001) and SP conversion (HR 0.21 [0.08-0.5], p=0.001) versus natalizumab (HR 0.53 [0.26-2.08]; p=0.08 and HR 0.29 [0.1-0.7]; p=0.01), and fingolimod (HR 0.9 [0.3-2.4]; p=0.9 and HR 0.66 [0.28-1.56]; p=0.34).

Conclusion: high efficacy DMTs are consistently more effective for the prevention of PIRA compared to platform DMTs. In our cohort, Ocrelizumab showed the greatest efficacy, closely followed by natalizumab, in protecting from reaching fsPIRA, SP and EDSS 6.

Disclosure of interest: All the authors have nothing to disclose

P1729

A Comparative Analysis of Efficacy, Safety, and MRI Outcomes of Anti-CD 20 monoclonal antibodies in Relapsing-Remitting and primary progressive Multiple Sclerosis: A Systematic Review and Network Meta-Analysis

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Introduction: Multiple sclerosis (MS) is a chronic, immune-mediated disorder of the central nervous system characterized by inflammation, demyelination, and neurodegeneration. Anti-CD20 monoclonal antibodies, such as ocrelizumab, rituximab, and ofatumumab, have emerged as pivotal treatments that target B cells, a key driver of MS pathology.
Objectives/Aims: To compare the efficacy and safety of Anti-CD20 monoclonal antibodies in relapsing remitting and primary progressive multiple sclerosis using network meta-analysis.
Methods: An electronic search was conducted to retrieve all] to retrieve all randomized controlled trials that reported the efficacy and safety of using Anti-CD20 antibodies in treating primary progressive or relapsing remitting multiple sclerosis. This review was prospectively registered with Prospero [CRD420251021195].
Results: The analysis assessed the efficacy of multiple sclerosis treatments by examining relapse rates, gadolinium-enhancing lesions, new T2 lesions, and T2 lesion volume changes. Among the treatments, ofatumumab demonstrated the most significant reduction in relapse rates, with a mean difference (MD) of -0.36 and an SUCRA score of 25.3%, indicating its superior efficacy compared to other active treatments. Rituximab and ocrelizumab were also effective, with mean differences of -0.3 (SUCRA = 37.2%) and -0.27 for 600 mg (SUCRA = 41.02%) and -0.23 for 2000 mg (SUCRA = 49.35%), respectively. For new T2 lesions, Ofatumumab doses of 60 mg and 30 mg emerged as the most effective, with MD values of -2.0 and -2.1 and SUCRA scores of 64.52% and 60.6%, respectively. However, lower doses, such as 3 mg and 60 mg administered every four weeks, demonstrated comparatively reduced efficacy (MD values of -2.5 and -2.9; SUCRA scores of 45.24% and 28.28%). In contrast, ocrelizumab 2000 mg delivered the greatest reduction in T2 lesion volume (MD = -464.1; SUCRA = 37.1%).
Conclusion: The findings emphasize the differing effectiveness of multiple sclerosis treatments across various clinical and radiological measures. Ocrelizumab and rituximab demonstrated significant success in lowering relapse rates and gadolinium-enhancing lesions, whereas ofatumumab showed potential in reducing new T2 lesions. However, the unexpected increase in the T2 lesion volume associated with ofatumumab requires further research. These results highlight the need to personalize treatment decisions based on the unique characteristics and goals of each patient.

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P1730
External validation of a multiple sclerosis treatment decision score (MS-TDS) using data of the ProVal-MS cohort study

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Introduction: Using a treatment decision score (TDS) for relapsing-remitting multiple sclerosis (RRMS) is an emerging way to personalize and objectify the treatment decision process. These scores aim to support patients and clinicians in choosing whether to start a disease-modifying treatment (DMT) based on individual disease characteristics and preferences by integrating key clinical data and patient-specific factors. External validation means testing the MS-TDS on a new, independent dataset for an unbiased assessment of performance and generalizability.

Objectives/Aims: To provide an external validation of the MS-TDS (Hapfelmeier et al., 2023, doi: 10.1177/17562864231161892), a recently developed tool for treatment decision, in the prospective multicentre ProVal-MS study of persons with early RRMS and clinically isolated syndrome (CIS) (study Nr. DRKS00014034). The MS-TDS predicts the occurrence of at least one new or enlarging T2 lesion (T2L) within six to 24 months after a new MS diagnosis considering two alternatives: No treatment versus receiving a platform treatment.
Methods: The MS-TDS was calibrated and its prognostic ability was assessed using the Area Under the Receiver Operating Characteristic Curve (AUROC) and the Brier score. Inverse probability treatment weights (IPTWs) and Decision Curve Analysis (DCA) were employed to quantify unbiased treatment effects and the net benefit in a counterfactual framework by comparing MS-TDS based treatment recommendations to actually employed treatment decisions.
Results: A total of 271 untreated individuals with CIS or RRMS from the ProVal-MS study were included in the analysis as recruited from March 2019 to June 2022 in five German academic centres specialized in the treatment of MS. Of these, 202 (78.2%) subjects received platform medication, while 59 (21.8%) were not treated. The AUROC was 0.561 (95% CI 0.492 – 0.630). Counterfactual analyses showed a 7.7% reduction in the probability of T2 lesion occurrence when the MS-TDS is used. Also, DCA demonstrated an improvement in net benefit when using the MS-TDS compared to decisions made by the experienced treating physicians.
Conclusion: The validation of the MS-TDS showed modest predictive properties to guide treatment decisions. Despite this, the MS-TDS may be recommended as a complementary tool for physicians in treatment decision-making to reduce the probability of new T2 lesions following a first treatment decision. It is implemented in a Shiny app, an interactive web application built with R.

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P1731
Impact of Anti-CD20 vs Other Disease-Modifying Therapies on Serum Neurofilament Light Chain in MS Patients

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Introduction: Neurofilament light chain (NfL) is a cytoskeleton protein released in response to axonal damage. It is a biomarker of disease activity in Multiple Sclerosis (MS) and increases in the setting of focal inflammatory activity. Various disease-modifying therapies (DMT) are successful in decreasing serum NfL levels.
Objectives/Aims: To compare the effect of anti-CD20 therapy on serum NfL levels to other MS DMT.
Methods: A comprehensive literature search and analysis of PubMed, Google Scholar, and Scopus were conducted from January 1, 2000, to March 10, 2025. We included studies that compared serum NfL levels in people with MS (PwMS) treated with anti-CD20 therapy (Ocrelizumab [OCR], Rituximab [RTX], Ublituximab [UTX], and Ofatumumab [OFA]) and another DMT in MS. A meta-analysis was conducted (Cochrane RevMan) and the effect size (standardized mean difference) was computed.
Results: We identified a total of five studies that compared serum NfL levels in people with Multiple Sclerosis treated with anti-CD20 therapy (OCR n = 3, OFA n = 2) and other DMT. Four studies were randomized controlled trials, and one was a retrospective observational study.
No studies were available for UTX or RTX. OCR was compared to natalizumab and interferon beta 1A, and OFA was compared to teriflunomide. 1,453 individuals received anti-CD20 medications, while 1,413 patients received other DMT (teriflunomide n= 699, natalizumab n=13, and interferon beta 1A n= 701). The majority of included patients had relapsing-remitting MS, with 3.67% having progressive MS. The overall mean difference favors anti-CD20 over other DMT (MD -2.51. 95% CI -2.87 to -2.14), $P<0.001$).
Conclusion: Anti-CD20 therapy leads to higher decreases in serum NfL levels compared to other MS DMT.

Disclosure of interest: nothing to disclose

THERAPY – Real world evidence

P1732
Real-World Clinical Effectiveness and Safety of Ozanimod for Relapsing-Remitting Multiple Sclerosis in Germany: An Interim Analysis of the Prospective, Noninterventional OzEAN Study

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Introduction: Ozanimod was approved in 2020 for treatment of adults with relapsing forms of multiple sclerosis in the US and relapsing-remitting multiple sclerosis (RRMS) in the EU.
Objectives/Aims: This interim analysis of the prospective OzEAN study (NCT05335031) describes patients prescribed ozanimod in clinical practice and reports real-world evidence of effectiveness and safety.
Methods: Adults with confirmed RRMS at 64 sites in Germany enroled from March 2021–March 2024. The decision to prescribe ozanimod was independent from and preceded inclusion in the study. Baseline characteristics, reasons for ozanimod use, and approximate 2-year (y) clinical effectiveness and safety are reported (data cutoff: 25 Feb 2025).
Results: The 397 enroled patients (275 women, 122 men) had a mean age of 40.2 (standard deviation [SD] 11.4) years at baseline. They were diagnosed with RRMS a mean (SD) of 5.9 (6.9; n=391) years before ozanimod initiation. At ozanimod initiation, 35% of patients were treatment naive. Pretreated patients commonly initiated ozanimod after insufficient effectiveness (31% overall [n=123/397]) or adverse events (AEs; 18% overall [n=73/397]) on prior therapy. Median (interquartile range) ozanimod treatment duration at data cutoff was 30.0 (21.0, 38.1) months. Whereas mean (SD) number of relapses in the year before baseline was 0.83 (0.76; n=377), the annualised relapse rate after approximately 2 years of ozanimod treatment was 0.08. During 2 years of ozanimod use, 85% of patients remained relapse-free. After 2 years of ozanimod treatment, EDSS was stable or decreased in 61% and increased in 39% of patients, and SDMT scores were >44 in 87%, stable or improved by ⩾4 points in 90%, and worsened by ⩾4 points in 10% of patients. At least one treatment-emergent AE (TEAE) was reported in 299 (75%) patients. Serious TEAEs occurred in 33 (8%) patients. About 9% of patients discontinued ozanimod due to TEAEs. As of the data cutoff, no deaths were reported.
Conclusion: In this interim analysis of the real-world OzEAN study, ozanimod treatment was associated with a low relapse rate, stable disability, and stable/improved cognitive processing speed after approximately 2 years of treatment. The overall safety profile of ozanimod was consistent with the phase 3 clinical trials, except for a slightly higher rate of TEAEs leading to treatment discontinuation, consistent with other real-world studies of disease-modifying therapies.

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P1733
Disease-modifying therapy of multiple sclerosis: a 29-year longitudinal study based on The Danish Multiple Sclerosis Registry

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Introduction: The availability of disease-modifying therapies (DMTs) for multiple sclerosis (MS) has increased considerably in Denmark since the first DMT became available in 1996, from one DMT in 1996 to more than 20 in 2024.

Objectives/Aims: To investigate how the increased availability of DMTs has influenced treatment delay (from onset to first treatment) and choice of DMT efficacy.

Methods: Using data from the nationwide Danish Multiple Sclerosis Registry (DMSR), we identified all individuals diagnosed with relapsing-remitting MS (RRMS) between 1.1.1996 and 31.12.2023, and this population's DMTs between 1.1.1996 and 31.12.2024. We analyzed the annual treatment delay, frequencies and proportion of patients who initiated or were in ongoing DMT.

Results: We identified 14,360 individuals in the DMSR with RRMS of whom 90% had initiated a DMT by 31.12.2024. The number of annual DMT initiations increased from 24 in 1996 to 1,073 in 2024, peaking in 2014 with 2,530 initiations. Moderate efficacy DMTs were the preferred choice as initial drug for newly diagnosed patients until 2022, when the proportion reached 50%. In 2024, this proportion was 27%. At 1.7.2000, 624 patients were on DMT (no high efficacy). By 1.7.2024 over 9,500 were on DMT (63% high efficacy). For patients diagnosed in 1996, 26% have never received DMT, for those who have, the median treatment delay was 85 months (interquartile range (IQR): 109). For patients diagnosed in 2023, 4% have not received DMT, the median treatment delay was 11 months (IQR: 38). The shortest treatment delay was found for those diagnosed in 2021 (median: 8 months, IQR: 30).

Conclusion: The number of DMTs, initiated or ongoing, has increased significantly since 1996. A more significant proportion of the RRMS-population now initiates DMT sooner after onset and diagnosis, more often on high efficacy DMT. Only a limited number of recently diagnosed patients never initiate DMT.

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P1734
Sex-Specific Differences in Fingolimod Efficacy and Discontinuation Risk in Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) disproportionately affects women, with sex-specific factors influencing disease progression and treatment responses. While fingolimod (FTY),

a sphingosine-1-phosphate (S1P) receptor modulator, effectively reduces relapses in relapsing-remitting MS, sex-specific differences in efficacy and safety remain underexplored. Biological sex might influence treatment outcomes and the frequency and severity of disease reactivation after FTY discontinuation. This is a critical knowledge gap in personalized treatment strategies.
Objectives/Aims: We aimed to assess (1) sex-specific differences in FTY efficacy and the role of S1P in modifying treatment outcomes and (2) sex-related disparities in disease reactivation risk following FTY cessation with a multimodal (human data/samples and EAE models), multi-domain approach.
Methods: Efficacy: we analyzed reporting odds ratios (rOR) for relapses in pharmacovigilance data from EudraVigilance, and we compared serum S1P and hormone levels in FTY treated men/women with MS. We also analyzed disease activity in male and female mice with myelin oligodendrocyte glycoprotein 35-55 induced experimental autoimmune encephalomyelitis (EAE) under FTY and/or S1P.
Safety: we analyzed EudraVigilance registry to quantify sex-specific risks of disease reactivation. We also examined S1PR1 expression on CD4 cells from FTY-treated patients. In EAE, disease severity post-FTY cessation in both sexes and S1PR1 expression on T cell were assessed.
Results: Efficacy: Female FTY-treated patients reported more relapses (rOR 1.20, $p<0.001$). Serum S1P levels were higher in males ($p=0.05$). In the EAE model, FTY was more effective in males ($p<0.01$), but S1P supplementation improved outcomes in both sexes ($p<0.01$).
Safety: Women more frequently reported disease reactivation post-FTY (rOR 2.00, $p<0.001$). In the EAE model, females showed more severe post-FTY disease activation ($p<0.001$) with increased S1PR1 expression on infiltrating CD3+ T cells ($p<0.0001$).
Conclusion: Our findings highlight sex-based differences in FTY efficacy and post-cessation reactivation risk, emphasizing the need for sex-specific MS treatment strategies. S1P supplementation may improve outcomes, particularly in women.

Disclosure of interest: MM, SM, AK and IM have no COI related to this work. AC has received speakers'/board honoraria from Actelion (Janssen/J&J), Alexion, Almirall, Bayer, Biogen, Celgene (BMS), Genzyme, Merck KGaA (Darmstadt, Germany), Novartis, Roche, and Teva, all for hospital research funds. He received research support from Biogen, CSL Behring, Genzyme, and UCB, the European Union, and the Swiss National Foundation. He serves as associate editor of the European Journal of Neurology, on the editorial board for Clinical and Translational Neuroscience and as topic editor for the Journal of International Medical Research. MP received research support from the Swiss MS Society. RH received speaker/advisor honorary from Merck, Novartis, Roche, Biogen, Alexion, Sanofi, Bristol-Myers Squibb, and Almirall. He received research support within the last 5 years from Roche, Merck, Sanofi, Biogen, and Bristol-Myers Squibb. He also received research grants from the Swiss MS Society.

P1735
Time is Brain, Cord, and Eyes in MOGAD: The Power of Early PLEX!

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Introduction: Myelin oligodendrocyte glycoprotein-associated disease (MOGAD) is a heterogeneous neuroimmunological disease. Relapses are primarily treated using corticosteroids, with a subset of refractory cases treated with plasma exchange (PLEX). However, the response to PLEX and the optimal timing of its initiation remain uncertain as compared to other disorders.
Objectives/Aims: This study evaluated the impact of PLEX and it's time to initiation on clinical outcomes, as measured by the Expanded Disability Status Scale (EDSS).
Methods: All consecutive patients of MOGAD requiring PLEX from January 2019 to July 2023 at a tertiary care centre were included. Inclusion criteria were ages 10-60 with a positive anti-MOG antibody test and use of PLEX due to inadequate steroid response. Exclusion criteria were pseudo-relapse and denial of consent. The primary outcome was the percentage improvement in EDSS at 90 days. Secondary outcomes included the proportion of responders (defined as >33% EDSS improvement) and those with a good response (66-100% improvement).
Results: Among 38 patients with MOGAD, the mean percentage improvement in EDSS was 37.73% ± 28.24% at 90 days. Overall, 60.53% of patients responded to plasmapheresis, with 15.8% achieving a good response. A significant negative correlation was found between the delay in PLEX and the percentage improvement in EDSS ($p = 0.020$). Complications occurred in only 7.9% of patients.
Conclusion: PLEX is effective and safe in MOGAD, but delaying its initiation is associated with reduced clinical improvement, highlighting the importance of early intervention.

Disclosure of interest: B.P, R.B, M.B.S, M.V.P, V.V.Y, R.R, A.G, M.T, A.K.S and A.D.U report no disclosures.

P1736
Real-World Insights on Ofatumumab in Australian RMS Patients: MSBase Registry Analysis

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Introduction: The study includes the latest findings from the MSBase Registry on the real-world Australian experience with Ofatumumab (OFA) in the treatment of relapsing multiple sclerosis (RMS). Here, we report the latest patient demographics, disease characteristics, and prior therapy history, providing valuable insights into the clinical efficacy and treatment persistence of OFA in both treatment-naive patients and those who have switched from prior therapies.

Objectives/Aims: To continue to characterize the use of OFA in Australia through an evaluation of patient demographics, baseline characteristics and prior therapy of patients initiating OFA as recorded in MSBase. In addition, evaluations of clinical efficacy included annual relapse rate and estimates of time to first clinical event.

Methods: This is the second analysis of a retrospective, secondary use of data study from the MSBase Registry, describing the baseline characteristics of RMS patients in Australia initiated on OFA treatment. Analyses included demographics, expanded disability status scale (EDSS) and treatment history with disease-modifying therapies (DMTs). Kaplan Meier estimates were calculated for persistence, time to EDSS milestone and confirmed disability worsening.

Results: As of 1st March 2025, MSBase has included 605 Australian patients who received at least one dose of ofatumumab, with a median age of 42.25 (35.86, 50.73) years and 76.7% female. The median disease duration was 8.75 (3.21, 16.43) years, and 22.3% of the participants were treatment-naive. The most common previous DMTs included ocrelizumab (26.9%) and natalizumab (16.4%). The annualized relapse rate (ARR) during the follow-up period was significantly reduced to 0.05 (0.04, 0.07) compared to 0.34 (0.29, 0.40) in the year prior to starting ofatumumab ($p<0.0001$). Additionally, the change in EDSS from baseline indicated stable disability scores with median change 0 (-0.5, 0), 0 (-0.5, 0.5) and 0 (-0.5, 0.5) at 12, 18 and 24 months respectively. Kaplan Meier estimates calculated treatment persistence at 96.6% [0.9441, 0.9795] at one year and 93.3% [0.8999, 0.9553] at two years follow-up.

Conclusion: The second analysis of the real-world data from the MSBase registry provides further insight into the Australian experience of relapsing MS patients initiated on OFA, with a high treatment persistence and stable disability over 24 months on treatment.

Disclosure of interest: HB received institutional (Monash University) funding from Biogen, Roche, Merck, Alexion and Novartis; has carried out contracted research for Novartis, Merck, Roche and Biogen; has taken part in speakers' bureaus for Biogen, Novartis, Roche and Merck; has received personal compensation from Oxford Health Policy Forum for the Brain Health Steering Committee. AvdW served on advisory boards and receives unrestricted research grants from Novartis, Biogen, Merck and Roche She has received speaker's honoraria and travel support from Novartis, Roche, and Merck. She receives grant support from the National Health and Medical Research Council of Australia and MS Research Australia. TS received compensation from servicing on steering committees and advisory boards from Biogen. AK received speaker honoraria and scientific advisory board fees from Bayer, BioCSL, Biogen, Genzyme, Innate Immunotherapeutics, Merck, Novartis, Sanofi, Sanofi-Aventis, and Teva. JLS has received travel compensation from Novartis, Biogen, Roche and Merck. Her institution receives the honoraria for talks and advisory board commitment as well as research grants from Biogen, Merck, Roche and Novartis. NAJ is a PI on commercial MS studies sponsored by Novartis, Roche, Biogen and Sanofi. He has received speaker's honoraria from Merck. He has had conference travel and registration reimbursement; and consultancy fees from Novartis. MB served on scientific advisory boards for Biogen, Novartis and Genzyme and has received conference travel support from Biogen and Novartis. He serves on steering committees for trials conducted by Novartis. His institution has received research support from Biogen, Merck and Novartis. MS has no relevant disclosure. WC has received travel assistance and honoraria for participation in industry sponsored meetings from and provided advice to, Bayer Schering Pharma, Biogen-Idec, Novartis, Roche, Genzyme, Sanofi-Aventis, CSL, Teva, Merck and Cellgene. SH has received consulting fees and speaker honoraria from Biogen, Novartis, Roche, Merck, and has received grants for her Institution from Biogen, Merck, Novartis, and Roche. PM received speakers fees and travel grants from Novartis, Biogen, T'évalua, Sanofi. MFP received travel compensation from Merck. TK served on scientific advisory boards or as a consultant for MS International Federation and World Health Organisation, Therapeutic Goods Administration, BMS, Roche, Janssen, Genzyme, Novartis, Merck and Biogen, received conference travel support and/or speaker honoraria from WebMD Global, Merck, Sandoz, Novartis, Biogen, Roche, Eisai, Genzyme, Teva and BioCSL and received research or educational event support from Biogen, Novartis, Genzyme, Roche, Celgene and Merck. RM or his institution have received remuneration for his speaking engagements, advisory board

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P1737
Factors influencing AI-clinician disagreement in disease-modifying therapy selection for Relapsing-Remitting Multiple Sclerosis

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Introduction: The therapeutic landscape for relapsing-remitting multiple sclerosis (RRMS) has expanded, making treatment selection complex and influenced by clinical and patient factors. Artificial intelligence (AI) models may aid clinicians, but their alignment with real-world decisions remains unclear.
Objectives/Aims: This study evaluates the agreement between an AI-based treatment selection model using ChatGPT-4o and clinician-assigned disease-modifying therapies (DMTs) and identifies factors influencing disagreement.
Methods: We included RRMS patients who started a DMT between January 2015 and February 2023 at Montichiari Hospital, Brescia, Italy. Data included age, gender, disease duration, Expanded Disability Status Scale (EDSS), annualized relapse rate (ARR) in the previous year, number of previous DMTs, last DMT received, and MRI activity at treatment choice. ChatGPT-4o assigned a DMT based on these parameters, and the prescribed DMT by the clinician was used as the comparator. Disagreement was defined as any difference in therapy choice or discordance in first- vs. second-line therapy. Logistic regression identified factors associated with disagreement.
Results: A total of 799 patients (median age: 42 years, range: 18–73; 72.1% females; median EDSS: 2; naïve: 44.9%; ARR: 0.5 ± 0.79; median years from onset: 9, IQR: 3–16) were included. ChatGPT-4o and clinicians agreed in 89.4% of cases when distinguishing first- vs. second-line therapies, while overall disagreement on therapy choice was 83.7%. The AI frequently assigned Teriflunomide (n=340 vs. 113), while clinicians preferred Glatiramer Acetate (n=118), Interferon beta (n=76), or Ocrelizumab (n=47). Disagreement was more likely with higher EDSS ($p=0.012$) and less likely with higher ARR ($p<0.001$), longer disease duration ($p<0.001$), recent treatment initiation ($p=0.005$), and male sex ($p=0.022$). Disagreement in first- vs. second-line therapy was less likely with longer disease duration ($p=0.043$), recent treatment initiation ($p<0.001$), and higher EDSS ($p=0.033$), while higher ARR ($p<0.001$) increased disagreement.
Conclusion: ChatGPT-4o-based treatment selection aligned well with clinicians for first- vs. second-line classification but differed in specific drug choices. Disease duration, relapses, and EDSS influenced disagreement, highlighting differences between structured clinical reasoning and real-world prescribing. AI models may support decision-making but require refinement for better clinical alignment.

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P1738
Efficacy and safety of cladribine tablets in the treatment of relapsing – remitting multiple sclerosis in older patients with more advanced disease: a 4-year multicenter, real world observational study in a Polish cohort

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Introduction: Cladribine tablets (CladT) is an immune reconstitution therapy approved for the treatment of relapsing-remitting multiple sclerosis (RRMS), whose efficacy and safety have been confirmed in clinical trials and real-world evidence studies.

Objectives/Aims: To evaluate the clinical efficacy and tolerability of CladT in patients with RRMS over 45 years of age.
Methods: This observational study was conducted across 10 MS clinical centers in Poland and included patients with RRMS who initiated treatment with CladT between December 2019 and November 2023. Patients were divided into two subgroups: age ⩽45 years and >45 years.
Results: 187 patients ⩽45 years (77% female, mean age 33,8 years) and 43 subjects >45 years (81%female, mean age 54,6 years) were included. Patients >45 years had longer mean disease duration (13,6 years vs 8,2 years) and higher mean baseline Expanded Disability Status Scale (EDSS) score (3,79 vs 2,42). The annualized relapse rate before treatment initiation in both groups was 1.42. Most patients in both groups had previously received one or two disease-modifying therapies. There were no significant differences between subgroups in proportion of relapse-free patients across years 1 to 4. In the ⩽45-year subgroup, the proportion of relapse-free patients increased from 14% (26/187) at baseline to 76% (113/148) in year 1, 81% (73/90) in year 2, and 77% (40/52) in year 3 with no relapses in year 4 (4/4). In the ⩾45-year subgroup, the proportion increased from 14% (6/43) at baseline to 79% (26/33) in year 1, 86% (18/21) in year 2 and 67% (6/9) in year 3 with no relapses in year 4 (2/2). Moreover, no statistically significant differences were observed between the ⩽45 and >45 age subgroups in the proportion of patients with stable or improved EDSS scores: year 1 – 88% (128/146) vs 77% (24/31), p=0.16; year 2 – 83% (73/88) vs 69% (11/16), p=0.21; year 3 – 75% (36/48) vs 67% (6/9), p=0.61; and year 4 – 83% (5/6) vs 100% (3/3), p=0.35. Remarkably, adverse event (AE) rates were comparable between age groups throughout the study. During the first 2 years of treatment, 15% of AEs were recorded in the group ⩽45 years and 24% of AEs in the group >45 years (p=0.19) and in the 3rd year 5% and 11%, respectively (p=0.55).
Conclusion: The study showed that the safety and efficacy of CladT were comparable between younger patients and older patients with more advanced disease. This confirmed the benefit of CladT treatment also in patients with late treatment initiation and greater disease progression.

Disclosure of interest: Adam Stępień: In relation to the content of the publication: served as a lecturer and an expert at advisory boards for Allergan, Amgen, Bayer, Novartis, Biogen, Merck, Polpharma, Roche, Teva, and Eli Lilly. Aleksandra Pogoda-Wesołowska: Workshops, conferences attendance, article and lectures for Merck, Novartis, Roche, BMS, Biogen. Marcin Wnuk: Received lecture fees and sponsored participation in conferences from the following companies: Bayer, Biogen, Merck, Novartis, Roche, Sanofi-Genzyme and Teva. MW also received consultation fees from the following companies: Amgen, Biogen, Merck, Novartis and Roche. MW received grants from the National Centre for Research and Development (no. SZPITALE-JEDNOIMIENNE/18/2020) and Medical Research Agency (no. 2020/ABM/01/00006)". Monika Marona: Monika Marona received compensation for preparing training sessions, workshops, and financial support related to participation in scientific conferences from: Biogen, Roche, Novartis, and Merck. Elżbieta Tokarz-Kupczyk: Lectures sponsored by pharmaceutical companies delivered during workshops, conferences and Round Table meetings. Cooperation in this area with companies: Biogen Poland, Roche Polska, Novartis Poland, Bristol Myers Squibb, Merck, Janssen-Cilag Polska. Participation in the ECTRIMS conference sponsored by Merck and participation in the XXV Congress of the Polish Neurological Society sponsored by Bristol Myers Squibb. Konrad Rejdak: Received speaking honoraria and travel expenses for participation in scientific meetings and participated in advisory boards in the past years with Bayer, Biogen, Merck Healthcare KGaA, Darmstadt, Germany, Novartis, Roche, Sanofi-Genzyme, and Teva Pharmaceutical. Anna Jamroz-Wiśniewska: Received honoraria for lectures and took part in conferences organized by pharmaceutical companies: Bayer, Biogen, BMS, Merck, Novartis, Roche, Sandoz, Teva. Monika Adamczyk-Sowa: Received compensation for speaking and consulting services from Biogen, Bayer, Novartis, Roche, Merck, Teva, Sanofi-Genzyme and BMS. None of the consulting agreements are relevant to the submitted work. Katarzyna Kubicka-Bączyk: Received compensation for preparing training sessions, workshops, and financial support related to participation in scientific conferences from: Biogen, Roche, Novartis, and Merck. Iwona Kurkowska-Jastrzębska: Speaker honoraria from a company for lectures (not directly connected to above publication). Alina Kułakowska: Received compensation for speaking and consulting services from Biogen, Bayer, Novartis, Roche, Merck, Teva, and Sanofi-Genzyme. Waldemar Brola: Discloses being involved in scientific advisory boards for Biogen, Roche, Novartis, and Merck and receiving honoraria for lecturing from Biogen, Merck, Novartis, Sanofi Genzyme, and Roche Halina Bartosik-Psujek: Received advisory board and/or speaker honoraria from Biogen, BMS, Novartis, Merck, Roche and support for congress participation from Novartis. The other authors declare no conflict of interest.

P1739
Adverse events in patients with multiple sclerosis on Rituximab versus biosimilar in a large racial-ethnically diverse community cohort

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Introduction: Rituximab is widely used in multiple sclerosis (MS) with proven efficacy, yet data comparing rituximab-abbs (biosimilar) to originator rituximab remain limited in diverse populations.
Objectives/Aims: To assess post-infusion adverse event risks of rituximab versus rituximab-abbs in MS patients.
Methods: This study included patients with multiple sclerosis (MS) from a large integrated healthcare system receiving ⩾1 infusion of rituximab or rituximab-abbs (biosimilar) between 1

January 2012 and 30 June 2022, typically every 6 months. Adverse events (AEs) post-infusion were assessed: emergency department visits or steroid use within 7 days, or abnormal immunoglobulin G (IgG) levels, CD19 counts, or serious infection admissions within 6 months. Generalised estimating equation models with repeated measures evaluated medication type effects on AEs, adjusting for confounders.
Results: Of 2308 MS patients (age 63.9 years, 74.1% female), over 6479 rituximab and 7508 rituximab-abbs infusions, rituximab was associated with higher rates of emergency department visits (1.9% vs 1.4%), steroid use (1.0% vs 0.3%), abnormal white blood cell counts (0.9% vs 0.4%), and infections (1.8% vs 1.2%) within 6 months, while rituximab-abbs had higher incidence of hypogammaglobulinemia (1.3% vs 0.3%). CD19 cells ⩾25 were higher with rituximab (16.8% vs 3.4%). Multivariable models showed lower AE odds with rituximab-abbs (OR 0.40, 95% CI 0.34-0.47).
Conclusion: In this diverse MS cohort, rituximab-abbs had lower odds of adverse events (OR 0.40, 95% CI 0.34-0.47) than rituximab, with fewer emergency visits, steroid use, and infections, suggesting better tolerability despite higher incidence of hypogammaglobulinemia. Rituximab had higher acute adverse events but less hypogammaglobulinemia. Further analysis is needed to assess efficacy.

Disclosure of interest: Mark Waheed, DO: Nothing to disclose

P1740
The Imapct of Ocrelizumab and Ofatumumab on Immunoglobulin Levels and the Risk of Infection

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Introduction: Anti CD20 therapies are effective in reducing relapses, new MRI lesion formation, and disability progression although patients are possibly at a higher risk of infection. The Providence Anti B Cell Registry was established to monitor long-term treatment and safety outcomes using real-world data from a community-based MS center. Because hypogammaglobulinemia has been linked to some of these therapies, the FDA recommends monitoring these levels at the start, during, and after stopping these therapies.
Objectives/Aims: The objective was to determine a relationship between the risk of infections based on age and immunoglobulin (IgG and IgM) levels.
Methods: MS patients with ⩾ 1 IgM/IgG value and received ⩾2 doses of ocrelizumab (OCR) or ofatumumab (OFA) were included. IgG/IgM levels were obtained every 6 monhs. Infections were recorded at each visit from baseline. Generalized estimating equation was used and odds ratios (OR) and 95% confidence intervals (CI) were reported, to examine the relationships between treatment, age at treatment start, IgM/IgG and infections.
Results: Between 2017 and 2024, 237 patients were enrolled: 75.5% were female; mean age was 48.4 (SD 12.0) and the median disease duration at treatment initiation was 9.00 (3 – 16) years. In the OCR cohort (n=209, 88.2%), mean age at OCR start was 48.0 (SD 11.6), 27.3% were age > 55 and median treatment duration was 54.5 months (IQR 31.5-69.5). In the OFA cohort (n=28, 11.8%) the mean age at OFA start was 51.9 (14.2), 53.6% were age > 55 and median treatment duration was 21.9 months (IQR 12.0-30.0). There was no significant difference in the risk of infections between the two therapies, OR 0.78 (95% CI 0.48—1.3, p=.33). Infections were not more common in patients 55 and older, OR 1.1 (95% CI 0.76—1.5, p=.73). Hospitalization due to infection occurred in 30 (12.7%) patients with no significant difference based on age, p=.22. IgM <= 45 g/dL or IgG <= 680 g/dL were not associated with an increased likelihood of infections.
Conclusion: There was no difference in the risk of infection between OCR and OFA. We did not observe age as a risk factor for infection in this cohort. Furthermore, neither baseline nor follow up IgM or IgG levels were associated with infections in this registry.

Disclosure of interest: KS - consulting and/or research support - Biogen, BMS, EMD Serono, Genzyme, and Genentech. HM, TS, CC - nothing to disclose.

P1741
Evaluating Clinical Outcomes and Tolerability in Patients 55 years and older in the Providence Health System who have started Cladribine

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Introduction: Cladribine was approved in the US in 2019 for the treatment of relapsing forms of multiple sclerosis (RMS). As the population ages, there is a pressing need to reassess treatment strategies to mitigate the risks associated with older age. Cladribine potentially could serve as a transitional therapy with the eventual goal of discontinuation of disease modifying therapy (DMT).
Objectives/Aims: We evaluated the utilization, efficacy, and safety of cladribine in RMS patients in a western US healthcare system.
Methods: Retrospective chart review was performed for patients 18 years of age or older with RMS who had taken at least one course of cladribine between March 2019 and April 2024. Patient demographics and clinical characteristics, cladribine utilization, safety, tolerability, and efficacy data were collected through review of electronic medical record.
Results: Of the 267 patients reviewed, 107 were 55 and older. In this older cohort, 72.9% were female; median age was 63.0 [58.4, 67.2]; ARR 12 months prior to cladribine initiation was 0.05 (0.21) with a median baseline EDSS of 3.0 [2.0. 6.0]. The most common DMTs prior to switching were interferon or glatiramer acetate, 25.2%, anti-CD20 agent 25.2%, and fumarate 16.8%. In the study follow up period (median16.0 [7.0, 28.0] months), the ARR while on cladribine was 0.00; the median EDSS at Year 2 (n=38) was 3.0 [2.5, 6.1]. Median time to first MRI after starting cladribine was 9.0 [5.0, 11.0] months; 96.2% of the patients were radiographically stable. New T2 lesions were seen in 3 patients, and there were no enhancing lesions. Three patients switched to another DMT with median time from

start of cladribine to new DMT, 35.0 [19.0, 35.0] months. Three deaths occurred during the follow up period: motorcycle collision, COVID-19 infection, and idiopathic pulmonary fibrosis. One patient discontinued due to lymphopenia, and two patients discontinued due to non-lymphopenic adverse events, frequent upper respiratory infections and B-cell lymphoma.
Conclusion: None of the patients 55 and older had a relapse after starting cladribine, and 96.2% had a stable MRI with no enhancing lesions. EDSS was stable at Year 2. One death was possibly related to cladribine, COVID-19 infection, and only one person did not complete course 2 due to prolonged lymphopenia. In this older cohort, cladribine appears to be well tolerated and effective.

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P1742
Treatment satisfaction of SPMS patients in Germany switching to siponimod from low efficacy therapies or fingolimod

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Introduction: About 60% of patients with relapsing remitting multiple sclerosis (RRMS) will convert to secondary progressive MS (SPMS) within 20 years. The selective sphingosine-1-phosphate receptor modulator siponimod is approved for the treatment of active SPMS in the EU. The AMASIA study investigates patients with active SPMS who are treated with siponimod in a real-world setting.
Objectives/Aims: This analysis aims to evaluate the effect of prior treatments on the treatment satisfaction of SPMS patients who switched to siponimod.
Methods: In this multi-center non-interventional study in Germany, 670 siponimod-treated active SPMS patients were followed for up to 3 years. Visits could be documented every 6 months. Demographic data were assessed at baseline and Treatment Satisfaction Questionnaire for Medication (TSQM) was used to assess patient's satisfaction throughout the observational period. We analyzed the effect of siponimod on TSQM subscales by last treatment before study enrollment: 1) fingolimod (FTY; n=82), 2) interferone/glatirameracetate (IFN/GA; n=144) and 3) dimethylfumarate (DMF; n=78).
Results: Overall demographic and baseline characteristics were balanced between subgroups (age range: 52.2 to 56.3 years; disease duration: 16.5 to 19.8 years; EDSS: 5.1 to 5.2). The TSQM global satisfaction score is highest throughout the study in the FTY subgroup (baseline (BL): 65.7, month 36: 72.4), and lowest in patients who switched from DMF (BL: 56.0, month 36: 68.1). This group, however, presented with the largest change during the study with an increase of 12.1 in global satisfaction. Similarly, in the effectiveness score the DMF subgroup showed an increase of 14.5. The largest increase in convenience score was detected in the IFN/GA subgroup (16.8), whereas the switch from fingolimod to siponimod did not change patients' assessment of convenience (BL 85.2, month 36: 85.2).
Conclusion: Previous medication influences treatment satisfaction as evaluated by the TSQM. Patients switching to siponimod from interferone, glatiramer acetate, or dimethyl fumarate exhibit lower levels of satisfaction compared to those switching from fingolimod. However, from baseline to 36 months of siponimod treatment, there is a notable increase in satisfaction in patients previously treated with IFN/GA and DMF. Overall, despite prolonged disease duration and previous treatments these patients demonstrate a high level of treatment satisfaction with siponimod over a period of up to three years.

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P1743
Effectiveness and Safety of Cladribine Tablets in Relapsing MS Patients Stratified by Age: A Retrospective Study from Kuwait

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Introduction: Age is often a factor influencing the choice of disease-modifying therapies (DMTs) for patients with multiple sclerosis (MS), especially with concerns about safety and long-term efficacy in older populations. However, real-world evidence on the age-related response to newer oral therapies such as cladribine remains limited.
Objectives/Aims: To evaluate the effectiveness and safety of cladribine tablets in patients with relapsing MS, stratified by age, in a Kuwaiti clinical setting.
Methods: We conducted a retrospective chart review of 207 relapsing MS patients treated with cladribine tablets at a major MS center in Kuwait. Patients were stratified into two cohorts based on age at treatment initiation: ⩾45 years (n=31) and <45 years (n=176). Key clinical parameters assessed included annualized relapse rate (ARR), Expanded Disability Status Scale (EDSS), proportion of relapse-free patients, and EDSS worsening over an average follow-up of approximately 2.3 years. Safety was evaluated through adverse event reporting.
Results: Baseline differences between groups were significant: older patients had a longer disease duration (12.00 ± 8.42 vs. 4.78 ± 5.23 years), higher prior DMT exposure (1.35 ± 1.20 vs. 0.76 ± 0.86), and higher baseline EDSS (1.74 ± 1.16 vs. 1.10 ± 0.87), all $p<0.001$. Despite these differences, treatment with cladribine tablets resulted in similar clinical outcomes. ARR was significantly reduced in both groups (from 0.37 to 0.013 in ⩾45; from 0.345 to 0.025 in <45). The proportion of relapse-free patients was identical at 96.8% in both cohorts. EDSS remained stable with minimal mean changes, and EDSS worsening was reported in 10% of older and 1% of younger patients. No serious adverse events were reported in either group. Only one patient in the <45 group experienced grade 3 lymphopenia.
Conclusion: This real-world retrospective study suggests that cladribine tablets are effective and well-tolerated in patients with relapsing MS regardless of age. Older patients experienced similar relapse control and disability stabilization compared to younger counterparts, despite higher baseline disease burden. These findings support the consideration of cladribine as a treatment option across age groups in appropriately selected MS patients.

Disclosure of interest: nothing to disclose

P1744
Real World Data on Ofatumumab Comparing First-Switch and Late-Switch Multiple Sclerosis Patients

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Introduction: The early initiation of high-efficacy therapies for relapsing multiple sclerosis (RMS) has been shown to enhance clinical outcomes in comparison to escalation from low-efficacy treatments. This real-world study aims to characterize patient populations switching to ofatumumab based on the reasons for therapy switch and to investigate clinical parameters comparing first-switch and late-switch ofatumumab patients.
Objectives/Aims: Ofatumumab is a fully humanized subcutaneous anti-CD20 monoclonal antibody that targets and depletes CD20+ B- and T-cells. In the pivotal trials, it significantly reduced inflammatory activity, annual relapse rates, and disability progression in relapsing multiple sclerosis (RMS) patients compared to teriflunomide. However, there is limited real-world evidence data of patients switching from other therapies to ofatumumab
Methods: KAIROS is a multicenter non-interventional study with around 300 patients at 40 sites in Germany. RMS patients receiving ofatumumab previously treated with another EU-approved disease modifying therapy (DMT) are eligible for enrollment. Data, including EDSS, MRI parameters and relapses are gathered through questionnaires and an electronic case report form.
Results: We present results of an interim analysis, which includes clinical and safety data of the full study population with an average treatment time of 321.7 days. We show a positive benefit/risk profile of Ofatumumab in a real-world-setting, including stable IgG-Values of patients after switching to Ofatumumab. A comparison of first-switch (37%) and late-switch (63%, >1 previous DMT) shows differences in clinical parameters including relapses. On Average, patients with only 1 previous DMT were slightly younger (39 vs 41 years), had a lower EDSS (2.33 vs. 2.66) at baseline and a lower annualized relapse rate compared to patients with >1 previous DMT.
Conclusion: The results complement findings from clinical trials and highlight the value of early initiation of ofatumumab in patients with RMS. Safety data from this real-world cohort further confirm the favorable benefit/risk profile of ofatumumab, consistent with the pivotal ASCLEPIOS I and II studies. These findings reinforce the importance of early treatment intervention and provide robust evidence supporting the use of ofatumumab in clinical practice.

Disclosure of interest: Josef Redolfi: Employee of Novartis Pharma GmbH

P1745
Low risk of progression independent of relapse activity in people with relapsing multiple sclerosis during the two years following cladribine treatment

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Introduction: Responsiveness to Cladribine has been highlighted in high disease activity patients with relapsing multiple sclerosis (pwMS). However, no data are available about the effects of cladribine on progression independent of relapse activity (PIRA) events after the two years of treatment.
Objectives/Aims: The main objective of this study was to estimate the risk of reaching the first PIRA event confirmed at six months and sustained for all the observation period in the two years following the completion of two cycles of cladribine.
Methods: pwRMS who completed the two cycles of cladribine and with a subsequent follow-up of at least 24 months were included in the study. Risk of reaching the first PIRA was estimated using multivariable Cox proportional hazards models.
Results: we included 83 pwRMS who received cladribine between 2019 and 2022 at three MS centers and without other DMTs during the two years following the completion of cladribine. First PIRA event was found in 12 patients (n=14.5%). PwMS having PIRA were older (41 [36-48] vs 32 [26-42], p=0.002), had a higher baseline EDSS (4.5 [3-6] vs 1.5 [1-2], p<0.0001) and less frequently had received cladribine as first DMT (18 [25.4%] vs 1 [8.3%], p=0.2). During the two years of follow-up, people with higher baseline EDSS had the highest risk of PIRA (HR 1.9 [1.4-2.8]; p<0.0001), while no other significant difference was observed as associated to sex, age at cladribine starting and number of previous DMTs.
Conclusion: cladribine appeared to be effective in reducing risk of PIRA in most patients. However, some pwMS (14.5% of them) experienced disability accumulation through PIRA. Early recognition (or identification) of these patients is of particular relevance since they could benefit from rapid initiation of a different high efficacy DMT.

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P1746
Eculizumab for the acute attack of neuromyelitis optica spectrum disorder

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is a debilitating disease frequently resulting in permanent vision loss and motor paralysis.
Objectives/Aims: To evaluate the effectiveness and safety of eculizumab in treating acute attacks of NMOSD.
Methods: This was an observational study conducted within a prospectively followed NMOSD registry cohort at Huashan Hospital. Between October 2023 and February 2025, patients receiving eculizumab within 30 days of attack onset were included. Eculizumab was administered 900 mg weekly for four consecutive weeks, with an observation period extending to eight weeks. Primary outcomes included visual acuity and visual field for optic neuritis (ON) and muscle strength (assessed by the Medical Research Council [MRC] scale) for longitudinally extensive transverse myelitis (LETM). Serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (sGFAP) were monitored.
Results: Nine patients (seven with ON, two with LETM) were enrolled. Following eculizumab treatment, six of the seven patients with ON achieved significant improvements in visual acuity and visual fields, with five recovering to near-normal vision or their pre-attack status. Visual field mean deviation significantly improved from −22.4 dB (range −32.8 to −4.8) to −2.0 dB (range −30.7 to 1.4) ($p = 0.008$) within 8 weeks. Among LETM patients, one regained substantial lower limb strength (MRC grade 0 to 3 proximally, 4 distally), while the other showed improved distal strength (MRC grade 0 to 3) at week 8. Serum sGFAP decreased sharply from 278.0 (range 48.0 to 26,360.0) pg/mL to 130 (range 50.0 to 617.0) pg/mL ($p = 0.027$) within two weeks of treatment, whereas sNfL levels exhibited a transient increase, peaking at week 4 before stabilizing. Patients with LETM developed urinary tract infections, and one developed *Klebsiella pneumoniae* pneumonia; all infections were effectively managed.
Conclusion: Eculizumab was well-tolerated and demonstrated efficacy in reducing disability during acute NMOSD attacks.

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P1747
Ozanimod Reduces axonal Damage and CNS-restricted and peripheral blood inflammation in RRMS: Soluble Biomarkers Analysis from AppreZiate RWE Study (NCT05811416)

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Introduction: Ozanimod's efficacy in treating relapsing-remitting multiple sclerosis (RRMS) may be reflected by changes in specific soluble biomarkers indicative of axonal damage and immune function.
Objectives/Aims: This study aims to assess the impact of ozanimod on these biomarkers over six months of treatment.
Methods: Observational, multicenter, ambispective study in Spain in patients with mild to moderate RRMS treated with ozanimod (NCT05811416). As an exploratory objective, patients were monitored for changes in markers of axonal damage (serum neurofilament light chains (sNfL), of astrogliosis (serum gliofibrilar acid protein,sGFAP) and serum pro (IL-17, IFN-gamma, IL-1, IL-6) and anti (IL-10, IL-35) inflammatory cytokines at baseline and after 6 months.
Results: 32 treatment-naive patients with biomarker data available were included in the analysis. Mean age at RRMS symptom onset was 40,39 years (SD 10,27), at diagnosis 42.16 years (SD 10.73) and ozanimod initiation occurred at 45.88 years (SD 7.63). Mean (SD) number of relapses in the year before baseline was 0,66. Mean (SD) Expanded Disability Status Scale (EDSS) score was 1,61 (1,07). We observed a significant decrease of sNfL values (p=0.04) mainly due to those with baseline values higher than 10 pg/ml (p=0.0007). In the same line, patients with high sGFAP values at baseline experienced a clear decrease (p=0.0004) thus sGFAP values diminished from 91.6 (40.2) to 79.9 (31.3), indicating potential neuroprotection and reduced astroglial activation. After six months of treatment, we also detected a clear reduction of IL-17 levels in patients with high baseline values (p=0.005) thus suggesting a decrease in Th17-mediated pro-inflammatory activity. An increase of IL-35 was also observed in patients with low baseline levels (p=0.0003), indicating an enhanced anti-inflammatory response. IFN-gamma, IL-1, IL-6, and IL-10 levels remained stable, showing no significant changes during follow-up at the 6-month mark.
Conclusion: These results show that ozanimod treatment is associated with reduced levels of sNfL suggesting neuroprotective effects. It also induces a reduction of serum GFAP and Il-17 values thus suggesting a down-regulation of innate and adaptive inflammation. Finally, it associates with an increase in IL-35 levels indicate that ozanimod exerts significant immunomodulatory functions, promoting a shift towards an anti-inflammatory profile. These findings support the potential of ozanimod in mitigating autoimmune inflammation in RRMS patients.

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P1748
Five-Year Real-World Outcomes of Fingolimod in Multiple Sclerosis: Long-Term Effectiveness and Treatment Continuation Patterns

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Introduction: Long-term real-world data on fingolimod therapy are essential to evaluate its sustained clinical benefit and tolerability in patients with multiple sclerosis (MS).
Objectives/Aims: This study aimed to assess five-year treatment outcomes, reasons for discontinuation, and predictors of disease progression.
Methods: This retrospective cohort study included 989 patients who initiated fingolimod therapy in or before 2019. Demographic, clinical, and treatment-related data were analyzed. Expanded Disability Status Scale (EDSS), annualized relapse rate (ARR), and treatment persistence were evaluated over a five-year period. Statistical analyses included paired-samples t-tests, Wilcoxon signed-rank tests, chi-square tests, and correlation analyses.
Results: Among the 693 patients who completed at least five years of therapy, the mean age was 44.91 $\pm$ 10.43 years and 69.3% were female. Mean age at disease onset was 27.72 $\pm$ 8.80 years, mean disease duration was 17.19 $\pm$ 7.23 years, and mean treatment duration was 7.50 $\pm$ 2.22 years. Baseline EDSS (2.09 $\pm$ 1.85) showed a modest but statistically significant improvement at year five (1.86 $\pm$ 1.98; $p < .001$). EDSS improvement was observed in 32.9% of patients, while 13.3% showed worsening. Mean ARR was 0.0736 $\pm$ 0.20. Annual effectiveness rates declined gradually from 94.6% in year one to 79.1% in year five. Treatment persistence decreased to 65.7% by the fifth year. Among 123 patients with known

discontinuation reasons, 64.2% cited lack of efficacy. Male patients were more likely to discontinue due to inefficacy than females (OR = 2.76; 95% CI: 1.13–6.71; p = 0.023). No significant associations were found between EDSS worsening and age, disease duration, or treatment duration.
Conclusion: In this large real-world cohort, fingolimod was associated with low relapse rates and overall clinical stability over a minimum of five years. While many patients remained on therapy for extended periods—a notable outcome in long-term MS management—treatment persistence gradually declined. Discontinuation due to inefficacy emerged as a key reason for stopping therapy, particularly among male patients. These findings support the value of fingolimod in selected patients, while underlining the need for individualized treatment strategies over time.

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P1749
Real-world clinical outcomes with eculizumab and ravulizumab in anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD): results from the global NMO SPOTLIGHT Registry

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Introduction: The Alexion complement component 5 inhibitor therapies eculizumab and ravulizumab (ALXN-C5ITs) are approved in multiple countries for adults with AQP4-Ab+ NMOSD. The global NMO SPOTLIGHT Registry (NCT05966467) collects ALXN-C5IT real-world safety and clinical effectiveness data in adults aged ⩾18yrs with AQP4-Ab+ NMOSD.
Objectives/Aims: To describe the characteristics and clinical outcomes of Registry patients with AQP4-Ab+ NMOSD treated with ALXN-C5ITs in real-world clinical practice.
Methods: Adults with AQP4-Ab+ NMOSD receiving ALXN-C5ITs were enrolled in the Registry starting August 2023. Demographics, number and characteristics of relapses 1yr prior to and after initiating ALXN-C5IT, meningococcal infections, and vaccination data were collected. An NMOSD relapse was defined as a new onset/worsening of neurologic symptoms for >24hrs requiring acute standard-of-care treatment preceded by ⩾30d of clinical stability. Data were summarised for all patients, including patients who switched from rituximab (RTX).
Results: As of 14Oct2024, 56 adults were enrolled in the Registry and available for analysis (female, 89.3%; White, 35.7%; Black, 33.9%; median age at diagnosis, 46.5yrs [interquartile range (IQR), 33.5-56.5]). Median (IQR) duration of exposure to eculizumab (n=52) and ravulizumab (n=12) was 42.5 (22.2-54.3) mo and 5.3 (4.0-14.1) mo, respectively. In the 1yr prior to ALXN-C5IT, 21 (37.5%) patients had 28 relapses (annualised relapse rate [ARR]: 0.50 [95% CI: 0.33-0.72]); 4/21 (19.0%) patients had >1 relapse. While on ALXN-C5IT, 3 (5.4%) patients had relapses (ARR: 0.02 [95% CI: 0.00-0.05]); no patients had >1 relapse. Among patients who switched from RTX to ALXN-C5IT (n=15; median time from last RTX discontinuation date to ALXN-C5IT initiation=141.5d, meningococcal vaccination=112d), 6 (40.0%) had 7 relapses in the 1yr prior to ALXN-C5IT initiation (ARR: 0.47 [95% CI: 0.19-0.96]); none experienced a relapse while on ALXN-C5IT. In the 1yr prior to ALXN-C5IT through Registry enrolment, 52 (92.9%) patients received ⩾1 meningococcal vaccination. No receipt of a meningococcal or other vaccination in the 4wks prior to relapse was reported; no meningococcal infections were reported.
Conclusion: Consistent with clinical trial and real-world data previously reported on ALXN-C5ITs among patients with AQP4-Ab+ NMOSD, these results demonstrate the strong clinical benefit of eculizumab and ravulizumab in relapse prevention. No new safety signals were detected; no meningococcal infections were reported.

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P1750

Two-year outcomes in MultipleMS, a prospective observational study in new onset Multiple Sclerosis across 7 European countries

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Introduction: A range of disease-modifying therapies (DMTs) are available for multiple sclerosis (MS). However, treatment approaches vary due to insufficient information on how treatment outcomes in real-world practices can be optimized.

Objectives/Aims: The H2020-funded MultipleMS project aims to develop personalized medicine approaches in MS. The objective here is to report two-year outcomes stratified by DMT classes in the prospective observational MultipleMS study.

Methods: From 2018 to 2020, 509 persons newly diagnosed with MS were recruited across 7 European countries (Belgium, n=32; Denmark, n=50; Germany, n=86; Italy, n=218; Norway, n=29; Spain, n=25; Sweden, n=69) with structured annual clinical follow-up, magnetic resonance imaging and collection of bio samples. DMT groups were defined as: (1) injectable, (2) oral platform, (3) highly effective therapies (fingolimod, cladribine, natalizumab, alemtuzumab), (4) B cell-depleting (BCDT), and (5) untreated. Annualized relapse rates (ARR), change in T2 lesion volumes and serum neurofilament light chain (z-score transformed sNfL) at 2 years were primary outcomes, with treatment persistence as a secondary outcome. An intention-to-treat approach was employed, with regression models used to adjust for baseline differences, as outlined in the final presentation.

Results: Median age at baseline was 33 years (interquartile range, IQR, 28-41), with a median disease duration of 8 months (IQR 3-26). The disease course at the time of inclusion was as follows; clinically isolated syndrome 6.5%, relapsing-remitting MS 88.8%, progressive MS 4.5%. Females comprised 63.9% (325) and median Expanded Disability Status Scale (EDSS) at inclusion was 1.5 (IQR 1-2). Mean sNfL z-scores normalized from 1.25 at baseline to 0.06 at 2 years with no significant differences observed between the DMT groups. Mean ARR at 2 years was 0.13, ranging from 0.04 (BCDT) to 0.22 (injectable). Proportions remaining on their first DMT were the following: 56% injectables, 70% oral platform, 61% highly effective therapies, 90% BCDT, and 47% untreated group. Mean T2 lesion volume changes will be included in the final presentation.

Conclusion: Substantial differences between DMT classes were observed with respect to relapse rates and treatment persistence, but not sNfL z-scores. Findings suggest that structured monitoring in real-world practice may facilitate earlier treatment escalation, if needed. Longer follow-up is required to assess potential differences in disability outcomes.

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P1751
Efficacy and safety of Ozanimod in real-world clinical practice: An observational study of a spanish patient cohort

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Introduction: Ozanimod modulates sphingosine-1-phosphate receptors, selectively targeting subtypes 2 and 5. Approved in 2022 for active relapsing multiple sclerosis (RMS), its efficacy and safety have been evaluated in phase III randomized controlled trials (SUNBEAM and RADIANCE) against INF β-1a.

Objectives/Aims: To evaluate the real-world efficacy and safety of ozanimod in a Spanish cohort.
Methods: A multicenter observational study across 13 public hospitals in Madrid and Ávila, including patients who initiated ozanimod based on routine clinical practice criteria through March 2025. We collected demographic, clinical, radiological, safety, and persistence data.
Results: We included 157 patients (58% female), a mean age of 44,6 years (±8,34), and a mean MS duration at the onset of Ozanimod of 10,6 years (±11,65). Mean follow-up was 38,5 months. 147 patients (94%) had RMS. Baseline EDSS was 1.83 (±1.23). Cardiovascular disease and diabetes were present in 1.9% of cases. 3.8% of patients had a cancer history, but only one experienced an oncological event during treatment. Fifty-five (35%) were treatment-naïve. 39.1% had relapses in the year prior to starting ozanimod. Prior disease-modifying therapy (DMT) included interferons (21.5%), glatiramer acetate (9.8%), and dimethyl fumarate (29.4%). Reasons for switching were inefficacy (30%) and adverse effects (30%). At baseline, 49.3% had moderate lesion load (>20 T2/FLAIR lesions); 81% had no gadolinium-enhancing (GD) T1 lesions. Spinal cord involvement was present in 50%. GDT1-positive patients were more likely to discontinue treatment (p=0,02). Low basal lesion load reduced discontinuation risk, though not significantly. Seven patients relapsed after starting ozanimod. At 1-year MRI follow-up (n=96 patients): 88% had no new T2/FLAIR lesions, 97% had no new GDT1 lesions. At 2-years (n=23) MRI follow-up 91% had no new T2/FLAIR lesions and 100% no new GDT1 lesions. EDSS remained stable in 91. Only 19 patients (12%) discontinued ozanimod, mainly due to lymphopenia (26%) and inefficacy 21.3%. Three patients experienced an early relapse but subsequently remained stable, with no treatment discontinuation. No rebound effect observed. Among discontinuations, 77% switched to an anti-CD20 therapy. Lymphopenia occurred in 86% of patients, however, only 3 experienced grade 4. Mean baseline lymphocyte count dropped from 1732.03 μL (±346.37) at baseline to 682.6 μL (±331.11) at 6 months. Sixteen had respiratory infections; HSV and VZV infections occurred in four and two patients, respectively. One severe respiratory infection was reported. Liver profile abnormalities were seen in four patients (2.5%), with one persistent case. No pregnancies or macular edema reported.
Conclusion: Ozanimod shows good safety, tolerability, and efficacy in real-world patients with moderately active RMS, consistent with pivotal trial results.

Disclosure of interest: All the authors hav nothing to disclose in this study

P1752
Impact of Prior Fingolimod Treatment on Cladribine Efficacy in Relapsing–Remitting Multiple Sclerosis: A Retrospective Analysis

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Introduction: Treatment response in relapsing–remitting multiple sclerosis (RRMS) may be influenced by prior disease-modifying therapy (DMT) exposure. Switching from fingolimod to cladribine may result in suboptimal disease control.
Objectives/Aims: To evaluate the impact of prior fingolimod use on clinical and MRI outcomes in people with RRMS treated with cladribine.
Methods: We retrospectively analyzed 206 patients with RRMS treated with cladribine, grouped as: (1) prior fingolimod (n = 46), (2) treatment-naïve (n = 77), and (3) prior DMTs other than fingolimod (n = 83; interferon-β, glatiramer acetate, teriflunomide, or dimethyl fumarate). Baseline demographics, MRI activity (new/enlarging T2 or gadolinium-enhancing lesions), and the need to initiate a new therapy post-cladribine were recorded. Statistical analyses included t-tests, chi-square tests, and logistic regression for treatment switch odds.
Results: Sex distribution and baseline EDSS were similar across groups. Treatment-naïve patients were younger ($p = 0.045$) and had shorter disease duration ($p < 0.001$). After a mean follow-up of 29.5 ± 4.9 months, patients previously on fingolimod had significantly more relapses ($p = 0.002$) and higher MRI activity compared to both treatment-naïve ($p = 0.002$) and other DMT groups ($p = 0.027$). Treatment switching occurred in 22.7% of the fingolimod group, vs. 6.6% and 10.5% in the treatment-naïve and other DMT groups, respectively. Compared to the fingolimod group, the odds of requiring a treatment switch were 4.2 times lower in the treatment-naïve group (OR = 0.24, $p = 0.02$) and 2.5 times lower in the other DMT group (OR = 0.40, $p = 0.05$).
Conclusion: Prior fingolimod exposure is associated with increased disease reactivation and a greater need for treatment change after cladribine. These findings underscore the importance of DMT sequencing to improve long-term outcomes in RRMS.

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P1753
Real-world Evaluation of the Efficacy and Safety of Ofatumumab as a Second-line Therapy in Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease

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Introduction: Ofatumumab has emerged as a promising therapeutic option for patients with refractory myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD). Refractory MOGAD is typically defined as a highly relapsing course (⩾2 attacks within one year) or failure to respond to two or more immunosuppressive therapies. However, the efficacy and safety of ofatumumab in the treatment of MOGAD remained unclear.
Objectives/Aims: To evaluate the safety and efficacy of Ofatumumab (OFA), a fully humanized anti-CD20 monoclonal antibody in patients with MOGAD.
Methods: We conducted a single-center, retrospective, observational study involving 22 patients with MOGAD treated with ofatumumab. Annualized relapse rate (ARR), Expanded Disability Status Scale (EDSS) scores, MOG-IgG titers and adverse events were collected and analyzed retrospectively.
Results: Twenty-two patients received ofatumumab for a median duration of 12 months (range 6-33). Among them, 16 patients (72.73%) were classified as having refractory MOGAD. Following initiation of ofatumumab, 20 patients (90.91%) remained relapse-free. The ARR significantly decreased from 1.05 (0-6) to 0 (0-1.33) ($p < 0.0001$), accompanied by an improvement in EDSS scores, which declined from 1 (0-8) to 0 (0-7) (p=0.0078). In a subgroup analysis of patients with refractory MOGAD, ARR was further reduced from 1.52 (0.17–4.8) prior to treatment to 0 (0–1.33) following ofatumumab administration (p =0.0002). Adverse events were reported in 12 patients (54.55%), including one case of a serious adverse event that occurred after the first dose.
Conclusion: Ofatumumab showed favorable efficacy in reducing relapse rate and disability in patients with refractory MOGAD. However, careful and continuous safety monitoring remains essential during treatment.

Disclosure of interest: Yuxin Fan, Lei Zhou, Wenjuan Huang, Hongmei Tan, Zhouzhou Wang, Jingzi Zhangbao and Chao Quan: Nothing to disclose

P1754
Lymphocyte recovery after Fingolimod discontinuation in people with Multiple Sclerosis

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Introduction: Fingolimod is a sphingosine 1-phosphate receptor modulator that prevents the release of T and B lymphocytes from lymph nodes, leading to lymphopenia. In some cases, sustained lymphopenia persists after fingolimod discontinuation, which may delay the initiation of subsequent disease-modifying therapies and potentially increase the risk of multiple sclerosis (MS) reactivation.
Objectives/Aims: This study aimed to identify factors associated with the time to lymphocyte recovery following fingolimod discontinuation and its impact on MRI activity.
Methods: This retrospective observational study included patients with relapsing-remitting MS (RRMS) from our MS unit who received fingolimod between 2005 and 2025 and discontinued it for any reason. The time to lymphocyte recovery following fingolimod withdrawal was analyzed in relation to various factors, including age at treatment discontinuation, treatment duration, lymphocyte counts at treatment initiation, and before and after treatment discontinuation. MRI activity, including new T2 lesions or gadolinium-enhancing lesions, at 3 and 12 months was also analyzed following fingolimod cessation.
Results: The cohort included 103 RRMS patients, 69.9% of whom were women. The mean age at fingolimod initiation was 41.18 (SD 10.83), with a median treatment duration of 3.74 (IQR 2.95) years. The median lymphocyte count, measured 17.5 days (IQR 54) before discontinuation, was 0.47 (IQR 0.36) $\times$ 109/L. The proportion of patients who took ⩾60 days to recover above 1.0 x 109/L was 59.2% (95%CI 49.7%-68-7%), ⩾90 days 30.1%, and ⩾120 days 17.5%. Kaplan-Meier survival analysis revealed that patients with a lymphocyte count below 0.47 $\times$ 109/L before discontinuing fingolimod took significantly longer to recover, with a median recovery time of 73 days (95% CI 57.44-88.57) compared to 61 days (95% CI 56.79-65.21) in patients with higher limphocyte counts ($p = 0.036$). In MRI performed 87 (IQR 74.50) days after discontinuation, 37.6% patients showed new T2 and/or gadolinium enhancing lesions. In MRI performed 414 (IQR 134) days after cessation, 11.7% patients exhibited activity. No association between MRI activity and the lymphocyte counts was observed.
Conclusion: Severe lymphopenia in patients on fingolimod may delay lymphocyte recovery and subsequent treatments, highlighting the importance of identifying the optimal timing

for discontinuing fingolimod and the most appropriate next disease-modifying therapy.

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P1755
Adherence, Safety, and Efficacy of Inebilizumab in Chinese Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD): A Multicenter Retrospective Study

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Introduction: Inebilizumab, the first globally approved CD19-targeted B-cell-depleting agent for NMOSD, demonstrated efficacy in significantly reducing relapse risk in the N-MOmentum trial. Evidence on adherence, treatment response, long-term safety in Chinese populations, particularly real-world practice data, remains scarce.
Objectives/Aims: To retrospectively analyse the real-world efficacy, safety of inebilizumab in Chinese NMOSD patients.
Methods: This multicenter, retrospective cohort study included AQP4-IgG seropositivity NMOSD patients treated with inebilizumab across 5 Chinese centers. Data collected included demographics, clinical features, dosing regimens, annualized relapse rate (ARR), Expanded Disability Status Scale (EDSS) scores, AQP4-IgG titers, and adverse events (AEs).
Results: A total of 61 patients received inebilizumab treatment. Within six months post-treatment, 4/61 patients (6.6%) changed to other treatment. Among the 42 patients who received treatment for over six months, none altered their regimen by the last follow-up. AEs occurred in 41/61 patients (67.2%), primarily infections (24/61, 39.3%), infusion reactions (27/61, 44.3%), pruritus (14/61, 23.0%), and cutaneous warts (14/61, 23.0%). One severe AE (severe pain) was reported (1/61, 2.4%). At six months post-treatment, significant reductions were observed in IgG ($p=0.011$), IgA ($p<0.001$), and IgM ($p<0.001$) levels. CD20+ B-cell counts markedly decreased from 274.2 ± 194.8/μL to 5.7 ± 13.5/μL after treatment ($p<0.001$). After a median follow-up of 13.5 (range: 6–28) months, 40/42 (95.2%) remained relapse-free. The baseline mean ARR decreased from 0.473 to 0.088 (82.3% reduction, $p<0.001$). The median EDSS score decreased from 3.5 (range: 1.5–7) to 3 (range: 1–7) ($p=0.035$). AQP4-IgG titers decreased in 25/39 patients (64.1%) and none showed an increase.
Conclusion: Real-world data confirm that inebilizumab significantly reduces relapse rates and EDSS score, and demonstrates high treatment adherence in Chinese NMOSD patients, with a manageable safety profile.

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P1756
Clinical Effectiveness and Safety of ofatumumab for PwMS Treated at least 12 Months in the Swedish post-market surveillance study "Immunomodulation and Multiple Sclerosis Epidemiology 12" (IMSE 12)

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Introduction Ofatumumab is a human CD20 monoclonal antibody targeting B-cells and a small population of CD20+ T-cells. The treatment is administered once a month (after initial dosing) with subcutaneous injections for persons with MS (PwMS) with relapsing MS (RMS). Ofatumumab is included in the Swedish post-market surveillance study "Immunomodulation and Multiple Sclerosis Epidemiology 12" (IMSE 12).
Objectives/Aims: To assess effectiveness and safety of ofatumumab with focus on 12 months treatment outcomes.
Methods: Data on Extended Disability Status Scale (EDSS), MS Severity Scale (MSSS), Symbol Digit Modalities Test (SDMT), MS Impact Scale (MSIS-29), relapses and Adverse Events (AEs) were collected from the nationwide Swedish Neuro Registry (NeuroReg). Effectiveness measures and relapse rates were assessed using Wilcoxon Signed Rank Test. All reported AEs were collected from the Swedish Medical Products Agency (MPA).
Results: 188 ofatumumab treated PwMS have been included in IMSE 12 since March 2021. 38% of PwMS had switched from rituximab (age 38.9 ± 10.4, duration (months) since diagnosis (DSD) 107.2 ± 74.5), 25% from natalizumab (age 40.6 ± 10.3, DSD 77.6 ± 76.6), 12% had been treatment naïve/no treatment registered prior start with ofatumumab (age 45.2 ± 12.0, DSD 2.6 ± 4.5) and 25% from other treatments (age 42.2 ± 10.6, DSD 129.2 ± 77.3).
15 PwMS discontinued treatment due to AEs (n=9; 5 unspecified, 2 headaches and 2 infections), other reasons (n=4) and pregnancy (n=2). 9 AEs were reported to the MPA (7 serious, 2 non-serious) from 4 individuals.
107 PwMS have been treated with ofatumumab for ⩾12 months. The ⩾12month cohort demonstrated a non-significant trend for improvement in mean EDSS, MSSS and SDMT score compared with baseline (EDSS; 2.6 ± 2.5 to 2.5 ± 2.6, p=0.478, MSSS; 3.7 ± 3.1 to 3.5 ± 3.0, p=0.394 SDMT; 55.7 ± 11.5 to 56.0 ± 11.1, p=0.491). The mean annual relapse rate (ARR) decreased significantly (p=0.005) during first year of treatment (0.03 ± 0.22) compared to the ARR (0.10 ± 0.30) one-year prior treatment initiation. The number of PwMS with new T2 lesions decreased significantly (p=0.04) from 6 PwMS the first treatment year with new T2 lesions to none the second treatment year.
Conclusion: PwMS treated for ⩾12 months display clinical stability. Significant improvements were seen in both ARR and the proportion of patients with new T2 lesions. Longer observation times will be needed to assess the effectiveness and identify potential AEs of ofatumumab.

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P1757
Ocrelizumab (OCR) stabilizes and even improves fatigue in the majority of patients with relapsing MS after 24 months: Key findings from the second interim analysis of the observational study MoOzaRt

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Introduction: Fatigue is considered the most common and one of the most debilitating symptoms in multiple sclerosis being observed in 75-90% of MS patients. In the Phase IIIb Casting-Liberto study less patients with relapsing remitting multiple sclerosis (RRMS) treated with OCR experienced severe fatigue over the 4-year study period. However, real world data on the short- and long-term impact of OCR on fatigue in patients with relapsing forms of MS (RMS) is still limited.
Objectives/Aims: MoOzaRt aims to assess the impact of OCR on patient-reported persistent (trait) and transient (state) fatigue around infusions and on factors that may influence fatigue in RMS patients receiving OCR.
Methods: The ongoing, non-interventional MoOzaRt study (ISRCTN55332718) recruited 272 RMS patients treated for the first time with OCR in Germany and Switzerland. The primary combined endpoint is a clinically meaningful reduction in trait

fatigue (⩾9 points) or stabilization from baseline (range ±8 points), measured by the Fatigue Scale for Motor and Cognitive Functions (FSMC) total score over 24 months. Secondary endpoints include state fatigue (Visual Analogue Scale), Expanded Disability Status Scale (EDSS), Patient Reported Outcomes (PROs) and safety.

Results: The 2nd interim analysis (data cut-off Mar 27, 2025, snapshot) included a total of 214 patients (69.9% female, mean age 38.3, SD 10.7 years, mean EDSS score 2.38, SD 1.47), of which 80 patients entered the analysis after a follow-up of at least 24 months. FSMC total scores remained stable or were reduced in 88.8% of patients over 24 months-follow-up. Of those, 33.8% displayed even a clinically meaningful improvement. At month 24, clinically meaningful reduction was also shown in 22.1% (n=68) patients and the proportion of patients with no fatigue in the cognitive FSMC score compared to baseline (44.1% vs. 37.5%) increased. In the motor score, the proportion of patients with severe fatigue decreased (45% vs 37.7%). Further analyses will be performed, studying the influence of age, gender, EDSS and other factors such as sport on trait fatigue.

Conclusion: The 2nd interim analysis of the MoOzaRt study showed stable and even improved FSMC total scores in a very high proportion of RMS patients treated with OCR for 24 months. Further analyses including VAS and assessments of mental and physical activity will specify the long-term impact of OCR on fatigue and provide insights into potential correlations and interactions with self-rated behavioural data (PROs) in RMS patients.

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P1758
Real-World Outcomes in Patients with Relapsing Multiple Sclerosis with Cladribine Tablets in a large Spanish cohort

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Introduction: While numerous studies have highlighted the efficacy of cladribine over a four-year period, there is a scarcity of research examining outcomes beyond this timeframe. Real-world studies are crucial for evaluating its long-term effectiveness and safety in diverse patient populations.

Objectives/Aims: To assess the long-term safety and effectiveness outcomes of cladribine tablets (CladT) in patients with Multiple Sclerosis (MS) in a real-world setting.

Methods: A descriptive retrospective observational study with RMS patients treated with CladT was conducted between October 2018 and March 2025. This analysis compromises demographic, clinical and radiological data, including but not limited to the number of relapses and Gd+ and T2 lesions identified on MRI. Additionally, reasons for treatment discontinuation and re-treatment with CladT were also collected.

Results: A total of 144 patients (pts) were included in this analysis. 116 pts (80.56%) were women. The average age was 42.6 years (SD=10.84). The mean baseline EDSS score was 2.08 (SD=1.4) before CladT. Regarding the use of previous DMTs: 42 pts (29,17%) were naïve and 102 pts (70,83%) had switched from other DMTs (22.5% injectables, 46.08% oral platforms, 31.32% high efficacy DMTs). A total of 97 pts (67.36%) showed comorbidities, with the most significant being dyslipidemia (31.96%), migraine (26.80%) and hypertension (15.46%).

Prior to initiating CladT, the mean ARR for the previous year was 0.63 (SD = 0.71), with a decrease compared to baseline of 79.56% in the first year (ARR: 0.13), 86.03% in the second year (ARR: 0.09), 80.59% in the third year (ARR: 0.12), 74.77% in the fourth year (ARR: 0.16), and 93.93% in the fifth year (ARR: 0.04).

At baseline, almost 80% of the population had at least one T2 lesion on MRI. After four years of complete follow-up, 73% pts were free from T2 lesions and 89% from T1 Gd+ lesions. 12 pts switched to HE-DMT during their follow-up, while 1 pts discontinued treatment due to a diagnosis of Raynaud's Syndrome. A total of 68 pts completed the two courses (year 1 and 2) with only 3 requiring an additional course of CladT in the third year. Furthermore, 6 patients have been re-treated with CladT in year 5 due to disease activity and/or poor prognostic factors.

Regarding safety, the treatment was generally well tolerated by most patients, though there were few cases reported of fatigue and herpes zoster no disseminated.

Conclusion: This study demonstrated high long-term effectiveness and safety of CladT treatment, especially when used in early phases of the disease.

Disclosure of interest: Miguel Ángel Hernández has received honorarium as speaker or consultant for Biogen, Merck, Roche, Almirall, Novartis, Neuraxpharm, Janssen and BMS. Rossana Abreu has nothing to disclose. Claudia Villar Van den Weygaert has received honorarium as speaker from BMS, Novartis, Sanofi, Merck, Neuraxpharm and Roche. Yessica Contreras has received honorarium as speaker from Novartis, Merck. Carlos Solé has received honorarium as speaker from Neuraxpharm. Hugo Hernández Tost has nothing to disclose. Pilar Diaz has received honorarium as speaker from Biogen, Novartis, Sanofi, Merck, Neuraxpharm and Roche. Jennifer Rodríguez has received honorarium as speaker from Neuraxpharm and Merck through an EM expert course. Luisa Díaz has received honorarium as speaker from Merck.

P1759
Comparative Analysis of Ofatumumab versus Low-Medium Efficacy Disease Modifying Therapies in Multiple Sclerosis: Serum Neurofilament Light and Three-Year Clinical Outcomes

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Introduction: Ofatumumab was shown to be highly effective in treating relapsing remitting MS (RRMS) in pivotal trials and more real-world data comparing its efficacy to other disease modifying therapies (DMTs) is needed. Serum neurofilament light (sNfL) is an emerging biomarker that has been shown to correlate with inflammatory activity in MS.
Objectives/Aims: To determine disability progression and NEDA-3 (No Evidence of Disease Activity) rates in patients with RRMS treated with ofatumumab compared to low-medium efficacy DMTs.
To compare sNfL levels across treatment groups and assess the predictive value of a single baseline sNfL.
Methods: Patients receiving ofatumumab were allocated to treatment group 1. The low-medium efficacy treatment group (group 2) included patients receiving BRACE therapies, teriflunomide, dimethyl fumarate, siponimod, fingolimod and cladribine. All patients had a single sNfL test at year one of the study and thereafter underwent six monthly assessment of disease activity using three parameter 'no evidence of disease activity' criteria (NEDA-3); 1) no clinical relapse 2) no confirmed disability progression 3) no new or enlarging T2 lesions on brain MRI.
Results: Thirty-four patients treated with ofatumumab (group 1) and 31 with low-medium efficacy DMTs (group 2) were included. Mean ages were 44.8 (±11.3) years and 50.5 (±14.3) years for group 1 and 2 respectively. Median follow up was 2.6 years (2.2-3.0). NEDA-3 during follow up was significantly higher in the ofatumumab group at 91.2% compared to 73.0% in group 2 (p=.037). Although serial EDSS' did not significantly differ between groups, there was a significant interaction between time and treatment group (p=0.023) indicating that EDSS step-change over time significantly differed. Mean sNfL in group 1 was 11.2 (±9.5) pg/ml and 14.4 (±17.7) pg/ml in group 2, a non-significant difference (p=0.6). Receiver operating characteristic analysis found a weak ability for a single sNfL result to predict disease activity during follow up (area=0.45).
Conclusion: This real-world study demonstrates significantly higher NEDA-3 rates with ofatumumab compared to low-medium efficacy DMTs in RRMS patients. Although baseline sNfL levels were lower in the ofatumumab group, this difference did not reach statistical significance, and further research with a larger sample size is warranted. Additionally, a single baseline sNfL measurement was not a reliable predictor of clinical outcomes over the 2.6-year follow-up period, which may also be related to a small study population.

Disclosure of interest: Nothing to disclose

P1760
Cladribine as Exit Strategy from Natalizumab: A Monocentric Experience

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Introduction: Discontinuation of natalizumab (NTZ) is associated with high risk of disease activity rebound, primarily due to timely α4β1 integrin saturation decline and rapid lymphocytes transmigration into the central nervous system. Several studies investigated DMTs for risk mitigation, but no definite sequencing algorithm has been defined.
Objectives/Aims: This study aims to evaluate CLAD efficacy as an exit strategy from NTZ, exploiting its rapid depleting effect on peripheral autoreactive B and T lymphocytes to prevent disease activity rebound and its safety profile.
Methods: A retrospective observational study was conducted in RRMS patients starting CLAD after NTZ discontinuation and with at least 3 months follow-up after CLAD initiation followed up at the MS Center of Tor Vergata University Hospital, Rome. Clinical and radiological activity, lymphocyte counts, and adverse events were collected to assess the efficacy and safety of this switching strategy.
Results: We enrolled 22 RRMS patients (17 women, median age 44.5 (27-69) years, disease duration 13.5 (7-42) years, baseline EDSS 1.0 (0.0-4.0), follow-up 29 (3-73) months, NTZ infusions 50 (15-161)). Discontinuation was due to high PML risk in 21/24, patient's choice and antiNTZ neutralizing antibodies in n=2 and n=1 respectively. Mean NTZ washout period was 29 ± 4.65 days and no clinical relapses occurred during this interval. One of 22 patients experienced a clinical relapse within 3 months after initiating CLAD, but no relapses occurred at 6 months (n=20) or 12 months (n=19). ARR in the 12-months after starting CLAD was not statistically different from ARR in the 12 months preNTZ interruption (ARR=0.05 and ARR=0.04 respectively, p=0.95). New T2 lesions were found in 3/20 asymptomatic patients at the first MRI (mean 5 ± 3.36 months) and in 2/19 patients at the second MRI (mean 14 ± 5.84 months). At 12 months, median EDSS was unchanged=1(0-5.5).
Grade 3 lymphocytopenia occurred in 1/20 patients during year 1; no grade 4 events occurred. The most common adverse events were hair loss n=2, mild upper n=1 and lower respiratory tract infections n=1, candidiasis n=1 and Sars-Cov2 infection n=1. No serious adverse events or PML cases were reported.
Conclusion: A prompt switch to CLAD within about 4 weeks of NTZ discontinuation effectively prevented rebound activity, with no relapses during the washout period. Disease stability was maintained over time, and the treatment showed a favorable safety profile. These findings support CLAD as a compelling exit strategy after NTZ.

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P1761
Treatment with intermittent negative pressure for MS-related spasticity and pain - A new digital platform for patient consultation, engagement and follow-up

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Introduction: Treatment with intermittent negative pressure can improve spasticity and spasticity-related symptoms in people with multiple sclerosis (MS). FlowOx 2.0 is a medical device used to apply intermittent negative pressure to the lower limb and has received marketing approval in Europe for managing spasticity-related symptoms in people with MS.
Objectives/Aims: FlowOx 2.0 has recently been introduced into the Scandinavian market, using a new digital platform.
Methods: The digital platform educates patients, guides potential users to an online consultation, facilitates the consultation by requesting patients to provide clinical information prior to consultation, and thereby minimizing consultation time. During treatment, patients are invited to report user experiences, treatment efficacy, and adverse events through to the digital platform.
Results: After the introduction of the FlowOx 2.0 for MS symptoms in Denmark in November 2024, 143 subjects have created a profile on the digital platform. Of the first 100 subjects who signed up, 77 went on to book a video consultation with a clinical specialist. So far, 59 subjects have completed the video consultation, and 57/59 (97%) have started treatment with FlowOx. In total, 50 subjects have received treatment for 6 weeks. Data on user experiences and treatment efficacy will be released for post-marked surveillance purposes when 100 subjects have been treated for 6 weeks. Reports on adverse events are continuously being reviewed, and actions are taken accordingly.
Conclusion: The use of a new digital platform for patient consultation, engagement, and follow-up works well for people with MS, who constitute a relatively young patient population, and generates valuable post marked surveillance data on user experiences, treatment efficacy and safety.

Disclosure of interest: Iacob Mathiesen, Claus Kjærsgaard and Henrik Hoel are shareholders and employees of Otivio AS

P1762
Clinical Effectiveness of Cladribine Tablets for PwMS Switching from Natalizumab, antiCD20 treatment or "other"; data from the Swedish post-market surveillance study "Immunomodulation and Multiple Sclerosis Epidemiology 10" (IMSE 10)

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Introduction: Cladribine is a deoxyadenosine analogue prodrug targeting proliferating B- and T-lymphocytes. Cladribine tablets (CladT) are administered in two courses, 12 months apart, for persons with MS (PwMS) with relapsing MS (RMS). AntiCD20 (aCD20) and Natalizumab (NTZ) are the two most used MS drugs in Sweden. The effects of switching from these drugs to CladT needs further investigations to understand the impact on the clinical effectiveness of such a switch.
CladT is included in the Swedish post-market surveillance study "Immunomodulation and Multiple Sclerosis Epidemiology 10" (IMSE 10).
Objectives/Aims: To assess the effectiveness of CladT with focus on PwMS treated with NTZ or aCD20 prior to CladT.

Methods: The cohort was divided into 3 groups based on treatment prior to CladT; NTZ, aCD20 and other. Data on Extended Disability Status Scale (EDSS), relapses and lesions were collected from the Swedish Neuro Registry. Wilcoxon Signed Rank Test and the McNemar's statistical tests were used.
Results: A total of 459 CladT exposed PwMS have been included in IMSE 10. 82 PwMS were treated with NTZ prior to CladT and 87 with aCD20. The remaining 290 PwMS defined as other included 142 treatment naïve, 48 with dimethyl fumarate and 23 with missing data on prior treatment.
Mean EDSS values did not change significantly for the three groups over the 3-year follow-up period.
The ARR decreased significantly from 1 year prior to TS compared to the first and third year with CladT for all three groups (NTZ: 0.26 to 0.03 (yr1)/0.03(yr2)/0(yr3), aCD20: 0.16 to 0.05(yr1)/0.08(yr3),other:0.38to0.08(yr1)/0.03(yr2)/0.01(yr3)). However, the aCD20 group had a significantly lower ARR the year prior to TS than the other two groups resulting in a non-significant decrease during the second follow-up year. The remaining two groups had significant decreases in ARR all three years.
The proportion of PwMS with new T2 lesions during CladT treatment dropped from 12% the first treatment year to 3% the following two years. This decrease was greater for PwMS previously treated with NTZ or other than aCD20. However, none of these differences were significant.
Conclusion: CladT was generally effective for the cohort as a whole. When the cohort was divided by previous treatment data showed greater improvements for PwMS previously treated with NTZ or other than aCD20. However, it is important to note that patients switching from aCD20 had a different profile with a higher initial EDSS level, lower ARR and fewer lesions than the remaining two groups.

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P1763
Anti-CD20 disease modifying therapy for multiple sclerosis: safety and efficacy data from Kenya

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Introduction: Access to disease modifying therapies (DMTs) for multiple sclerosis (MS) is limited in resource-poor countries. In Kenya, we have only five DMTs to choose from that are regularly available, of which rituximab and ocreluzimab (anti-CD20 therapies, anti-CD20t) are the only ones available for highly active disease. Rituximab is more widely available due to its diverse indications for treatment outside of MS.
Objectives/Aims: We have the largest documented MS cohort from the East African region, and began using anti-CD20t in 2016; we report here our experience to date.
Methods: We conducted a retrospective cross-sectional chart review of patients with MS prescribed anti-CD20t since 2016 at our tertiary regional referral neurology centre in Nairobi.
Results: We identified 62 patients: 85.5% (53/62) were female, median ages of onset and diagnosis 31 and 33.5 years respectively. The most common presentations were sensori-motor deficit, optic neuritis and ataxia. The majority [69.4% (43/62)] had documented relapsing-remitting MS, with 11.3% (7/62) having progressive MS. A significant minority [22.6% (14/62)] were recommended anti-CD20t but did not end up having the treatment due to various factors including affordability. Of the remainder, 60.4% (29/48) were on rituximab of which 41.4% (12/29) eventually converted to ocrelizumab [total 60.4% (29/48)]. Cumulative relapses in the year preceding and year after anti-CD20t was 7 and 2 respectively. Safety concerns occurred in a minority [8.3% (4/48) had infections, of which there was one fatality from COVID-19].
Conclusion: Out study shows that anti-CD20t are safe and effective in our population, although there still remain financial and access barriers to some patients with MS in our region. There is need to effect the World Health Organisation essential medicines list 2023 to improve access to DMTs such as anti-CD20t.

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Cladribine Tablets Real-World Clinical and Safety Outcomes in a Relapsing Multiple Sclerosis Cohort Including Older Individuals and Transitioning from an anti-CD20

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Introduction: Real-world evidence (RWE) generated from routine patient care complements the data from randomized controlled studies. The efficacy and safety of cladribine tablets (CladT) were ascertained in the CLARITY trial. RWE enriches and improves the understanding of this therapeutic approach, especially in subgroups not previously systematically studied.
Objectives/Aims: To report demographics, and clinical, paraclinical, and safety outcomes of CladT in a large real-world cohort of people with relapsing multiple sclerosis (pwRMS).
Methods: This is a single-center, retrospective study, of pwRMS age ⩾18 years treated with at least 1 course of CladT from August 2019 to May 2024 at the Oklahoma Medical Research Foundation in the US. Data were descriptively analyzed for the entire cohort (n=305) and for subgroups of patients ⩾50 years (n=183) and those transitioning from an anti-CD20 treatment (n=54). The analysis includes demographics, treatment history, annualized relapse rate (ARR), MRI activity, lymphocyte dynamics, grade of lymphopenia, EDSS, RFNL thickness, and T25FW.
Results: Baseline data (mean) for: all patients, 50 years or older, and anti-CD20 switches in that order include age 52(±11.2), 59.6(±6.2), 52.9(±11.2); disease duration 14.3(±8.1), 17(±8.6), 14.1(±8.2); ARR 0.08, 0.04, 0.06; EDSS 2.8(±2.1), 3.2(±2.1), 3.5(±2.5); T1 Gd+ brain lesions 1.9(±2.1), 2.6(±2.8), 1.2(0.4). Follow up data for all groups stratified by years 1-5 for each parameter includes: ARR (0-0.02), percentage relapse free (98.5-100), EDSS (2.6-3.4), percentage with worsening MRI activity (0-50), percentage with worsening T25FW (0-25), and RNFL values. Brain MRI activity was present in 22.9% of subjects by year 3. EDSS was stable or improved in 88.1% and showed a nominal improvement in all studied groups. Lymphocyte count dynamics, grades of lymphopenia, and adverse events were consistent with those from the randomized clinical trial data and will be presented.
Conclusion: CladT clinical and safety outcomes in a large RWE cohort showed persistence of a low ARR and no disease progression over the follow up period, and did not identify new safety concerns. Outcomes for pwRMS over the age of 50 and those transitioning from an anti-CD20 medication did not differ from the general cohort.

Disclosure of interest: GP has received speaker honoraria and/or consulting fees from Alexion, Biogen Idec, Celgene/BMS, EMD Serono, Horizon/Amgen, Novartis, Roche/Genentech, Sanofi-Genzyme and TG Therapeutics; received research support (to the institution) from Abbvie, Adamas, Alkermes, Biogen Idec, EMD Serono, NewView, Novartis, Roche/Genentech, Sanofi-Genzyme and TG Therapeutics; and is on the advisory board for Progentec Diagnostics and Cadenza Bio. CB has received fees as an advisory board participant with EMD Serono, TG Therapeutics, Sanofi, Genentech, Biogen. She also has received fees as a speaker for EMD Serono, and TG Therapeutics. JS has received fees as a speaker or consultant from Amgen, Biogen, Novartis, Sanofi, TG Therapeutics and EMD Serono. AS, MD, and CFP have no disclosures.

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Two-Year Real-World Single-Centre Experience with Ofatumumab: Data from Slovenia

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Introduction: Ofatumumab (OMB), a subcutaneous anti-CD20 monoclonal antibody, is indicated for the treatment of adult patients with active relapsing multiple sclerosis (RMS). Real-world evidence provides valuable insights into the effectiveness and safety of treatments in everyday healthcare settings. We present data from our experience with OMB at the University Medical Centre (UMC) Ljubljana, Slovenia, where it has been in use since June 2021.
Objectives/Aims: The aim of this study was to evaluate the effectiveness and safety of OMB in patients with RMS in real-world clinical settings, with a focus on treatment outcomes, relapse rates, and adverse events.
Methods: We retrospectively analysed clinical data from 140 patients with RMS treated with OMB. The data collected included demographics, prior treatments, and the effectiveness and safety profile of OMB. Finally, reasons for treatment cessation were analysed.
Results: Mean follow-up time was 2.28 (1.0-3.7) years. 74% of patients were female with a mean age of 39.9 (18.3-69.1) and a mean disease duration of 5.9 years (0.1-34.8) which is comparable to other studies. 43.6% of patients were treatment naïve and the most common previous treatments were dimethyl fumarate (30.7%), glatiramer acetate (12.1%) and teriflunomide (4.3%). In the first year of treatment (n=129), annualised relapse rate (ARR) was 0.06, representing a 90% reduction compared to the pre-treatment ARR of 0.64. In the second year of treatment (n=67), the ARR dropped to 0.00 from 0.73. In the first year 48.5% of patients had stable Expanded Disability Status Scale (EDSS), 30.7% showed improvement and 20.8% had EDSS progression; in the second year, these values were 59.7%, 16.4%, and 23.9%, respectively. After two years (n=71), 36.6% had stable EDSS, 38.0% improved, and 25.4% progressed. NEDA-3 was achieved by 58.9% of patients in the first year (n=90), 78.8% in the second year (n=33), and 61.3% after two years (n=31). Adverse events, most commonly injection-site reactions, were reported by 40 patients. Serious events included febrile neutropenia and serious infections such as

Fournier's gangrene. Thirteen patients discontinued the treatment after an average of 1.29 years due to disease activity or adverse events.
Conclusion: OMB shows high efficacy, on par with other high-efficacy treatment options. It is well-tolerated and exhibits a favourable safety profile in real-world clinical settings.

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P1766
Evolution of anti-CD20 therapeutic strategies and impact on long-term disability in multiple sclerosis: a real-word mono-centric study in a French University Hospital

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Introduction: Emerging evidence supports the benefits of early high-efficacy therapies (HET) in relapsing-remitting MS (RR-MS).
Objectives/Aims: The aim of this study was to analyse real-world evolution of anti-CD20 prescription strategies at the Bordeaux University Hospital and their impact on clinical disability.
Methods: This is a retrospective monocentric study conducted using the local EDMUS database. RR-MS patients treated with anti-CD20 and followed for at least two years were included and separated into 2 groups depending on anti-CD20 initiation date: before or since January 2021. Demographic, clinical and radiological data at anti-CD20 onset were compared between the two groups. Clinical disability was measured using the EDSS score at last follow-up (LFU).
Results: 319 patients met ongoing diagnostic criteria for RR-MS and were treated with anti-CD20 (Rituximab, Ocrelizumab or Ofatumumab) for at least 2 years: 159 initiated anti-CD20 before January 2021 (group 1) and 160 from January 2021 (group 2). Age at disease onset, time to first disease modifying treatment (DMT) and to first anti-CD20 (8,8 years in group 1 and 9,3 years in group 2) were similar in both groups. Early intensive treatment strategy (compared to escalation strategy) was used equally in both groups (30% of patients in group 1 and 34% in group 2). However, at anti CD20 onset, in group 2, median EDSS (2 vs 2.5 p=0.007) and annualized relapse rate (ARR) were lower than in group 1 (0.8 vs 1.8 $p<0.001$); though new T2 lesions were more frequent (45% vs 24% of patients, $p<0.001$). In group 2, patients received on average 1.6 other disease modifying treatment (DMT) before anti-CD20 compared to 2.1 DMT in group 1 (p=0.034), with notably, less frequent S1P-receptor inhibitors use (21% vs 40%, $p<0.001$).
After adjusting for sex, age, EDSS and time to first DMT, ARR and MRI activity at anti-CD20 onset and follow-up duration, ARR (0.006 vs 0.9, p=0.007) and median EDSS at LFU (2 vs 2.5, p=0.01) were lower in group 2.
Conclusion: This study demonstrates a shift towards earlier anti-CD20 use in our MS-care specialized unit, associated with improved clinical outcomes.

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P1767
Treatment Patterns and Annualised Relapse Rate in Patients With Multiple Sclerosis Who Escalate Versus Continue Disease-Modifying Therapies Following Relapse: A Retrospective Cohort Study

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Introduction: After relapse on a platform disease-modifying therapy (pDMT), multiple sclerosis (MS) treatment (tx) guidelines recommend switch to a pDMT with a different mechanism of action or, preferably, escalation to high-efficacy therapy (HET). Real-world (RW) data on tx patterns and outcomes after relapse on a pDMT are scarce.
Objectives/Aims: To describe RW tx patterns after relapse on a pDMT and compare subsequent relapse rates in patients (pts) who continue pDMT vs. escalate to HET.
Methods: A retrospective cohort study was performed using Optum Clinformatics claims data (3/2016-7/2024) in a base sample of adults with MS with an initial claim for a pDMT from 3/2017; ⩾1 relapse after ⩾3 months (mo) on pDMT; and ⩾12mo continuous enrolment (CE) before pDMT initiation and after initial relapse. Relapse was defined as IP stay with primary MS dx or OP/emergency visit with MS dx with a claim

for high-dose oral corticosteroid, IV methylprednisolone (excluding ±5d of DMT infusion), corticotropin, or plasma exchange within 7d. Proportions of pts continuing pDMT and escalating to HET and time to escalation were described in 12mo after initial relapse. In the base sample, a prevalent new user design will be adopted to compare annualized relapse rates (ARR) in sub-cohorts who continue a pDMT vs. escalate to HET after relapse, matched using propensity scores conditional on time of tx after relapse to balance pt characteristics.
Results: 753 eligible pts (mean [range] age: 54 [18-85]; 80% female) relapsed on pDMT between 2017-2023, with median (Q1, Q3) time from pDMT initiation to relapse of 9 (5-17) mo. Most common pDMTs were teriflunomide (30%), dimethyl fumarate (29%), and glatiramer acetate (21%). Within 12mo of relapse, 19% of pts escalated to HET (16% parenteral, 3% oral). Most pts (68%) remained on initial pDMT, while 6% switched to a different pDMT and 7% had no subsequent DMT claim. Among pts escalating to HET, median (Q1, Q3) time to escalation following relapse was 3.5 (1.4, 6.2) mo overall, 3.3 (1.4, 5.9) for parenteral and 4.5 (3.0, 9.3) for oral HET. Analyses comparing ARR in sub-cohorts are ongoing.
Conclusion: In RW settings, most pts continue pDMT after relapse, and pts who escalate to HET have delayed switching. Further investigations are being conducted to compare subsequent relapse rates in pts who remain on a pDMT or escalate to HET following a relapse.

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A Cross-Sectional Study to Assess the Effectiveness and Safety of Ofatumumab in Patients with Relapsing Multiple Sclerosis in Clinical Practice: the CRONOS-MS Study

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Introduction: Ofatumumab is a fully human anti-CD20 monoclonal antibody approved for relapsing MS. Real-world data on ofatumumab use is still limited.
Objectives/Aims: To assess the effectiveness, safety, adherence and patient profile of patients receiving subcutaneous ofatumumab in clinical practice.
Methods: This cross-sectional study, conducted across 32 centers in Spain, included patients receiving ofatumumab for at least 12 months or who discontinued ofatumumab after receiving at least one dose with a minimum monitoring of 12 months.
Results: A total of 310 patients were analyzed (68.4% female; mean age: 42.2 years). Mean (standard deviation; SD) time from diagnosis was 8.4 (8.1) years. The mean (95% confidence intervals, CI) number of relapses 12 months before ofatumumab

initiation was 0.66 (0.58-0.74). The mean (SD) Expanded Disability Status Scale (EDSS) at baseline was 2.1 (1.4). Most patients (65.7%) were previously treated, with a mean (SD) of 2.0 (1.3) prior disease-modifying treatments (DMT; 56.8% with moderate-efficacy DMTs, 43.2% with high-efficacy DMTs). After 12 months, ofatumumab decreased the annualized relapse rate (ARR) by 92% to 0.055 (95% CI, 0.036-0.085; $p<0.0001$). Stratification by prior DMT showed a 93% reduction in the ARR in treatment-naïve patients (0.069 [0.037-0.128]; $p<0.0001$) and a 90% reduction in previously treated (0.048 [0.027-0.087]; $p<0.0001$). Patients previously treated with high-efficacy DMTs had an ARR reduction of 83.3% (0.068 [0.030-0.154]; $p<0.0001$) and those who had received moderate-efficacy showed an ARR reduction of 93.3% (0.036 [0.015-0.084]; $p<0.0001$). The EDSS remained stable ($p=0.896$) at month 12. Only one out of 134 patients with available magnetic resonance imaging (MRI) measures had gadolinium-enhancing T1 lesions. At month 12, 139 out of 158 patients (88%) did not present new/enlarging T2 lesions. One hundred ninety-seven (63.6%) patients reported adverse events (AEs) but only seven serious AEs were reported in five patients. The total number of AEs was 550, and 267 were considered unrelated to ofatumumab. Most patients (97.7%) received all monthly doses. Only 2.6% of patients discontinued treatment.

Conclusion: In a real-world clinical setting, ofatumumab demonstrated to be effective in decreasing relapses regardless of the presence and type of prior treatment, particularly in naïve patients and those previously treated with moderate efficacy therapies. The safety profile of ofatumumab was consistent with findings from clinical trials. The adherence to ofatumumab was high.

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Why the Disease-Modifying Therapy Transition? Investigating the Reasons and Clinical Consequences in Multiple Sclerosis

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Introduction: Over 20 disease-modifying therapies (DMT) are approved by the U.S. Food and Drug Administration for people with multiple sclerosis. Transitioning from one DMT to another may result from medical (e.g., disease worsening, safety), tolerability (e.g., side effects), or non-medical reasons (e.g., cost, adherence). Understanding these transition reasons and their clinical implications can improve personalized MS management.

Objectives/Aims: To characterize reasons for DMT transitions, evaluate transition patterns across racial/ethnic groups, and assess associated clinical and radiological outcomes.

Methods: We retrospectively analyzed medical records from an MS specialty clinic (January 2010–October 2022), including adults with relapsing-remitting MS with $\geqslant 1$ DMT transition. Transition reasons were categorized as medical, non-medical, or tolerability-related. Transition patterns and delays were compared between matched cohorts of European ancestry (EA) and Non-European ancestry (Non-EA), adjusting for social determinants of health (SDoH). Effects of transitions on subsequent

DMT initiation, MRI activity, acute clinical relapse/hospitalizations, and disease worsening (physician/patient-reported) were analyzed using regression and survival methods.
Results: A total of 1,134 individuals (889 females; 623 Black/African American; mean age at symptom onset=33.6 years (y) (standard deviation=11.1y)) were studied. No significant difference in DMT transition timing between EA and Non-EA groups emerged after adjusting for SDoH (Hazard Ratio (HR)=1.11, p=0.05), although Hispanic individuals had an increased risk of DMT transition compared to Non-Hispanics (HR=1.39, p=0.02). Individuals with non-medical transitions were significantly less likely to immediately initiate subsequent DMT compared to those with medical (HR=0.45, p<0.0001) or tolerability-related transitions (HR=0.53, p=0.002). Transitions due to side effects (tolerability-related) were most common, and each additional tolerability-related transition per patient reduced the risk of acute clinical relapse by 22% (p=0.007). Conversely, each additional medical-related transition per patient substantially increased the odds of physician-reported (4.69-fold, p<0.0001) and patient-reported disease worsening (4.48-fold, p<0.0001).
Conclusion: DMT transitions are prevalent, and their reasons differentially impact health outcomes and treatment management. Proactively addressing specific treatment concerns may improve transition efficiency, patient satisfaction, and disease control.

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P1770
Exploring the differences between treated and never treated PwMS in the German MS Register

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Introduction: Disease-modifying therapies (DMTs) are prescribed to reduce the frequency and severity of relapses, and to slow disease progression in patients with MS (PwMS). However, some PwMS never receive DMTs, although the vast majority of PwMS in Germany are covered by health insurance.
Objectives/Aims: We aimed to 1) ascertain the proportion and characteristics of PwMS who have never received any DMT (nevDMT) and 2) to compare one-year annualised relapse rates (ARRs) of currently treated PwMS (currDMT), nevDMT and currently untreated PwMS who discontinued their previous DMT (pastDMT).
Methods: Data from the German MS Register from 2000 to 02/2025 were included, encompassing clinical and demographic variables. Inclusion criteria were confirmed MS diagnosis and documented diagnosis date. A cluster analysis was conducted for the nevDMT group, exploring subgroups by age/disease duration.
Results: The total study population (n=23,437) consisted of 0.7% nevDMT (n=167), 82.5% currDMT (n=19,338), and 16.7% pastDMT (n=3,925). The nevDMT group showed a slightly lower median EDSS score (2 [interquartile range: 3.5] vs. 2.5 [2.5] vs. 4 [4.5]), shorter median disease duration since diagnosis (6.2 [17.6] vs. 15.7 [14.3] vs. 10.9 [12.2] years) and higher age at onset (34.9 [14.9] vs. 30.5 [14.8] vs. 31.8 [15.6] years) than the currDMT and the pastDMT groups. The comparison of the three groups regarding the ARR revealed no significant differences (nevDMT: 13.1%, currDMT: 12.9%, pastDMT: 14.0%).
Cluster analysis revealed two subgroups within the nevDMT group: late continuously untreated patients (UN: n=93) and early still DMT-naïve patients (EN: n=74). The median disease duration since diagnoses was 17.4 (16.4) years in the UN and 0.22 (1.0) years in the EN group. Furthermore the UN group was considerably older at MS onset (median: 38.1 [17.8] vs. 32.5

[9.4] years) and at the last visit (62 [11.7] vs. 34.9 [11.4] years), diagnosed at an older median age (42.1 [18.7] vs. 34.2 [11.0] years) and showed a higher median EDSS score (4 [4.0] vs. 1.5 [1.4]) than the EN group. Additionally, the UN group is characterised by less relapse activity (ARR: 8% vs. 18%), less employment (full- or part-time: 26.9% vs. 72.1%), and a more frequent chronic progressive disease course (PPMS: 17.2% vs. 8.1%; SPMS: 32.3% vs. 0.0%) compared to the EN group.
Conclusion: These findings highlight the variability within the nevDMT population and underscore the need for further research to understand the predictors and implications of DMT treatment decisions.

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P1771
Cladribine Our Clinical Experience with Immune Reconstitution

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Introduction: Cladribine is a disease-modifying treatment (DMT) for active relapsing-remitting multiple sclerosis (RRMS). It is administered orally in two annual courses, with sustained effects due to its immune reconstitution mechanism of action.
Objectives/Aims: This study aims to analyze the proportion of patients who maintained or improved the Expanded Disability Status Scale (EDSS) control and those requiring additional management in treatment or safety terms.
Methods: We evaluated 39 RRMS patients treated with cladribine at *Hospital Universitari Arnau de Vilanova de Lleida* in 2018–2024 period. Demographic data, efficacy, and safety outcomes were analyzed using statistical methods with IBM SPSS 30.0.0.
Results: The mean age of patients with multiple sclerosis (pwMS) was 33.83, with a female predominance (3:1). Of the cohort, 51.28% were treatment-naïve. A reduction in annualized relapse rate (ARR) was observed in 93.5% of patients, while 51.4% showed improvement in the Expanded Disability Status Scale (EDSS). Additionaly, the 64% did not require retreatment or change in DMT. A third cycle was administered in four cases. In 10 pwMS (25.6%), the DMT was switched due to lack of efficacy. Only two patients experienced mild adverse events (AEs). Among the eight patients aged ⩾50, no AEs were recorded and only one required a treatment switch rituximab (RTX) due to (*progression independent of relapse activity*) PIRA. Among 18 pwMS between 5 and 6 years of follow-up, 50% did not require retreatment or DMT change. In contrast, three pwMS received a third cycle and in six required a treatment switch due to therapeutic failure.
Conclusion: Cladribine showed a favourable safety profile, including in patients ⩾50 years and those who received a third cycle. At five years, 50% did not require further treatment.

Disclosure of interest: nothing to disclose

P1772
Clinical and Cognitive Outcomes in Ocrelizumab-Treated MSPatients: Insights into the Wearing-Off Phenomenon

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Introduction: Ocrelizumab (OCR) has proven effective in altering the disease trajectory of multiple sclerosis (MS) patients. However, many patients experience a preinfusion "wearing-off phenomenon" (WoP) characterized by a resurgence of MS symptoms.
Objectives/Aims: This study aimed to investigate the relationships between WoP and various clinical, functional, and cognitive parameters and to compare demographic and radiological data between patients with and without WoP.
Methods: This prospective study was conducted across two MS centers and included 84 MS patients aged 18–70 years who had received at least two OCR doses. Clinical disability was assessed via the Expanded Disability Status Scale (EDSS), whereas cognitive function was evaluated via the Symbol Digit Modalities Test (SDMT). The functional outcomes were measured via the nine-hole peg test (9HPT) and the 25-Foot Walk Test (25FWT). Immunoglobulin G (IgG) levels were monitored, and radiological activity was tracked through MRI.
Results: Among the 84 patients, 58.3% experienced WoP, predominantly starting more than four weeks before their scheduled infusion. Patients with WoP had significantly shorter disease durations, lower IgG levels, and more gadolinium-enhancing lesions than did those without WoP ($p<0.05$). Preinfusion 25FWT times were significantly longer in the WoP group ($p = 0.025$), although cognitive and functional assessments postinfusion were not significantly different between the groups.
Conclusion: WoP is a prevalent phenomenon among OCR-treated MS patients, characterized by transient functional impairments, particularly in motor performance, that resolve postinfusion. Its association with shorter disease duration, lower IgG levels, and increased radiological activity underscores the need for personalized treatment approaches. While standardized dosing schedules are effective for many, optimizing infusion intervals based on patient-specific clinical and immunological

factors may enhance outcomes and mitigate symptom recurrence in OCR therapy for MS.

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P1773
Treatment Continuation With Cladribine Tablets Beyond Year 4: Analysis of Longitudinal Prescription Data From Germany

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Introduction: Currently, there are few reports on the clinical management of multiple sclerosis (MS) in Year (Y)5 and Y6 after initiating treatment with cladribine tablets (CladT), including continuing CladT treatment. Real-world insights on the characteristics of people with highly active relapsing MS (PwMS) who continue/discontinue therapy can help inform clinical decision making.
Objectives/Aims: To describe treatment patterns and characteristics of PwMS in Germany who reached Y5 and Y6.
Methods: Descriptive analysis of retrospective, longitudinal, prescription data from IQVIA LRx database in Germany was performed using datasets available in two timeframes: long-term panel (previous disease-modifying therapy [DMT] use) and trust center panel (Y5 and Y6 population sizing and profiling), with CladT treatment (3.5 mg/kg cumulative dose over 2 years) initiated between Sep 2017 and Dec 2018. Observation period: from 1st CladT prescription until end of Y5 and Y6 with an additional ⩾6 months' follow-up. Three cohorts were analysed: continuing CladT treatment in Y5, no CladT treatment in Y5, and switching to another DMT (at any time after CladT initiation). Furthermore, the PwMS who continued CladT treatment in Y5 were grouped by also receiving CladT treatment in Y6 or not.
Results: In a cohort of 1642 PwMS initiating CladT within the index period (primarily used as a first or second line of treatment [each ~40%]), 65.8% (n=1080) did not receive further CladT treatment, 16.9% (n=278) continued CladT treatment in Y5, and 17.3% (n=284) switched to another DMT. A total of 1350 PwMS (82.2%) completed the full 2-year CladT treatment course. Among the PwMS who received CladT treatment in Y5 (n=278), 62.7% (n=174) were eligible for a prescription in Y6, of whom 66.7% (n=116) received such a prescription.
Conclusion: The majority of PwMS (82.2%) successfully completed the full CladT treatment course and 65.8% of PwMS did not continue treatment beyond Y4. Among the 16.9% of PwMS who received additional treatment in Y5, most were also eligible for a second dose in Y6. These data further inform disease management with CladT into Y5 and Y6.

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P1774
Longitudinal Impact of Fingolimod on Disease Course in Multiple Sclerosis: A Three-Year Pre- and Post-Treatment Analysis

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Introduction: Fingolimod is a widely used oral disease-modifying therapy (DMT) for multiple sclerosis (MS), known for reducing relapse rates and delaying disease progression.
Objectives/Aims: This study aimed to assess the clinical impact of fingolimod by comparing disease activity and progression over three years before and after treatment initiation.
Methods: A retrospective analysis was conducted on 657 MS patients treated with fingolimod, including 596 with relapsing MS and 61 with secondary progressive MS. Key clinical measures, including Expanded Disability Status Scale (EDSS) scores, annualized relapse rate (ARR), and no evidence of disease activity (NEDA-3) status, were assessed at three time points: three years before fingolimod initiation, at treatment initiation, and three years post-treatment.
Results: Among relapsing MS patients (mean age 45.0 ± 10.2; 69.5% female), ARR significantly declined from 0.34 before treatment to 0.08 after three years of fingolimod therapy, while mean EDSS remained stable (1.48 pre-treatment, 1.48 at initiation, 1.43 post-treatment). Notably, 69.6% of patients achieved NEDA-3. Patients who attained NEDA-3 were older (45.64 vs. 43.55 years, p=0.021), had longer disease duration (5.84 vs. 5.09 years, p=0.005), and a lower baseline EDSS (1.22 vs. 2.07, $p<0.001$) compared to NEDA-3-negative individuals.
In secondary progressive MS patients (mean age 50.2 ± 10.9; 65.6% female), EDSS scores increased from 5.12 pre-treatment to 6.10 post-treatment over the six-year period, indicating ongoing disability progression. However, ARR decreased from 0.61 to 0.27. Only 16.4% of these patients achieved NEDA-3, and those who did had significantly higher baseline EDSS scores

(6.11 vs. 4.94, p=0.002). No significant differences in age or disease duration were observed between NEDA-3-positive and NEDA-3-negative patients.
Conclusion: Fingolimod demonstrated strong efficacy in reducing relapse rates and maintaining overall clinical stability in relapsing MS patients, with a substantial proportion achieving NEDA-3. In secondary progressive MS, while ARR declined, disability progression remained evident, underscoring the need for more effective treatment options for this patient subgroup. These findings reinforce fingolimod's long-term disease-modifying effects in relapsing MS and provide valuable insights into patient characteristics associated with better treatment outcomes.

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P1775
Effectiveness and safety of ofatumumab in treatment-naive and oral DMT-switched multiple sclerosis patients: a multicenter observational study in China

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Introduction: Ofatumumab, a fully humanized anti-CD20 monoclonal antibody, is a highly effective disease modifying therapy (DMT) approved for the treatment of relapsing multiple sclerosis (RMS) in China. Real-world data are necessary to investigate the factors for switching from oral DMTs and to assess the effectiveness and safety of ofatumumab in the Chinese MS population.
Objectives/Aims: We conducted a multicenter observational study to evaluate the effectiveness and safety of ofatumumab in RMS patients who were either treatment-naïve or had switched from oral DMTs, including siponimod, fingolimod, teriflunomide and dimethyl fumarate.
Methods: Medical records at three tertiary hospitals were collected between December 2021 and March 2025. Clinical relapses, MRI activity, confirmed disease progression, and adverse events were reviewed.
Results: Treatment-naïve and switched data were obtained for 38 (68.4% women, mean age 30.29 years, median disease duration 2.31±4.08 years, median follow-up 13.5±3.74 months) and 59 (83.1% women, mean age 26.85 years, median disease duration 5.30±4.17 years, median follow-up 21.71±7.63 months) patients, respectively. Among treatment-naïve patients, the annualized relapse rate (ARR) at the final follow-up decreased from 0.11 ± 0.24 to 0.05 ± 0.22 ($p = 0.284$), while the Expanded Disability Status Scale (EDSS) score at month 12 after treatment dropped from 2.59 ± 1.46 to 1.74 ± 1.40 ($p < 0.001$). For patients switched from oral DMT, the mean reasons for transitioning were disease progression (22.9%), clinical relapse (23.7%), MRI activity (25.4%) and adverse reaction (6.8%). After switching, ARR and EDSS score at month 12 reduced from 0.37 ± 0.43 to 0.05 ± 0.17, and from 3.02±1.76 to 2.31±1.89 (both $P<0.001$), respectively. And no significant increase in T1 Gd-enhancing lesions or new/enlarged T2 lesions identified. No obvious clinical relapses, EDSS worsening, and MRI activity were observed in either treatment-naïve or switched MS patient. During follow-up, no serious adverse events were reported.
Conclusion: This real-world study revealed a significant decrease in disease activity and progression among MS patients treated with ofatumumab, including treatment-naïve and oral DMTs-switched patients, while maintaining a well-tolerated safety profile.

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P1776
Efficacy and safety of Ofatumumab in real-world clinical practice: multicenter study

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Introduction: Ofatumumab was commercialized in Spain in November 2022 for adults with relapsing forms of multiple sclerosis (MS).
Objectives/Aims: The main goal was to analyze the efficacy and safety in MS patients treated with ofatumumab in real-world clinical practice.
Methods: Retrospective multicentre cohort study included patients treated with Ofatumumab using data from the EMCAM (Multiple Sclerosis Study group of Madrid) cohort.
Results: A total of 394 patients were included. 29% were naive. 64% were female. The mean age was 41.2 (15-68).
18.6% of patients switched to ofatumumab due to relapse, 31% due to radiological activity and 15.7% for both reasons. 34.7% switched for other reasons such as safety concerns or adverse events (AE).
3.5% patients have discontinued treatment.
Prior to starting treatment, the annualized relapse rate (ARR) was 0.57. After one year of ofatumumab therapy, the ARR dropped significantly to 0.01. Regarding radiological activity, gadolinium-enhancing lesions decreased from 0.7 before treatment to 0.04
Baseline IgG and IgM levels were 10.42 (4.33-17.2) and 1.23 (0.11-5.37) G/L respectively. After twelve months IgG levels had decreased to 10.0 (4-17.7) and IgM to 0.88 (0.14-4.58) G/L.
Adverse events were reported by 44% of patients following the first dose, with flu-like symptoms occurring in 68% of these cases. All reported symptoms were mild .
Conclusion: Ofatumumab was well-tolerated, with no moderate or severe adverse events. After one year, we observed a significant reduction in both ARR and Gd+ lesions, supporting its efficacy and safety in treating relapsing multiple sclerosis.

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P1777
Real-world data sources for the collection of safety events: the experience of the Italian Multiple Sclerosis and Related Disorders Register

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Introduction: Recently, MS real-world data sources have gained increasing attention in pharmacovigilance, since the evidence derived from these data can fill the knowledge gap on the most serious risks to disease-modifying treatments (DMTs), namely infections and malignancies. In this scenario, the "Italian Multiple Sclerosis and Related Disorders Register" (RISM) can play a crucial role.
Objectives/Aims: To characterise the safety profile of subjects under DMTs and recorded in RISM, focusing on the occurrence of adverse events of interest (infections and malignancies).
Methods: Safety events and all the relevant data to characterise the study cohort were extracted from the RISM database from

01 January 2016 to 28 February 2025. Inclusion criteria to select the subjects included: Clinically Isolated Syndrome/MS diagnosis, age ⩾ 18, and presence of the first DMT during the study period. Descriptive statistics were used to describe the study population and the occurrence of clinical events, focusing on malignancies and infections.
Results: In the study period, 24,909 subjects started the first DMT. The majority of subjects were female (65.8%), while the mean age at disease onset and diagnosis was 34.6 (±11.7) and 37.2 (±12.2) respectively. 4,950 clinical events were reported for 3,580 subjects (14.4%), of whom 1,443 (5.8%) experienced more than one event. Of the 4,950 events, 2,162 were classified under the SOC name "infections and infestations", the majority were related to COVID-19 (74.6%), followed by herpes zoster (5.55%) and urinary tract infections (0.97%). Among the 242 reported as "neoplasms benign, malignant and unspecified", the most frequent were breast cancer (12.81%), malignant melanoma (7.02%), and basal cell carcinoma (6.20%).
Conclusion: Healthcare data collected in RISM can provide a holistic view for the evaluation of DMT safety in the long period and can answer relevant questions on drug policies and public health.

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P1778
The real-world effectiveness and safety of cyclophosphamide in progressive multiple sclerosis: A single-centre retrospective cohort study

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Introduction: Therapeutic options for people with progressive multiple sclerosis (PMS) remain limited, with currently approved disease-modifying treatments applicable to only a subset of this population. Cyclophosphamide (CYC) is often used off-label, yet real-world data on its safety and effectiveness remain scarce.
Objectives/Aims: This study evaluated CYC's long-term effectiveness and safety in a real-world cohort of people with PMS.
Methods: This single-centre, retrospective cohort study included all patients with primary (PPMS) or secondary PMS (SPMS) who received at least one treatment cycle of intravenous CYC at Noorderhart, Rehabilitation and MS Centre in Pelt, Belgium. A treatment cycle consisted of four to six CYC infusions. Follow-up included maintenance therapy following CYC treatment. Effectiveness was assessed using the expanded disability status scale and neurologist-reported clinical stability. Safety was evaluated based on adverse event reporting. Kaplan-Meier analysis was used to estimate progression-free survival over time.
Results: A total of 169 patients (median age 60 [IQR 53–68]; 93 female, 76 male; 45 PPMS, 124 SPMS) were included. Most patients (72.8%) received a single cycle of CYC treatment, while 23.1% underwent two cycles, and 4.1% received three cycles. Over a median follow-up of 7.6 years [range 1.3–14.3], 27.2% of patients remained stable or improved during the observation period. Clinical stability or improvement was observed in 78.7% (± 3.2 SD) of patients at one year, 55.1% (± 3.9 SD) at three years, and 26.2% (± 3.7 SD) at five years following initiation of the first treatment cycle. No significant differences in outcomes were observed based on MS subtype, prior treatment exposure, or number of CYC cycles. Adverse events occurred in 48.5% of patients, most frequently nausea (16.0%), fatigue (15.4%), and urinary tract infections (12.4%).
Conclusion: CYC was associated with clinical stability or improvement in a substantial proportion of PMS patients in a real-world setting. The treatment was generally well tolerated, with a manageable safety profile. These findings support the potential utility of CYC as a therapeutic option for people with PMS and underscore the need for further prospective studies.

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P1779
The impact of early initiation of ofatumumab therapy on inhibition of relapse activity and disability progression in patients with relapsing - remitting multiple sclerosis based on data from real world evidence study in Poland

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Introduction: Ofatumumab (OFA) is an anti-CD20 monoclonal antibody approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). Its high efficacy in inhibiting disease activity and progression has been demonstrated in clinical studies and confirmed by reports from real-world evidence (RWE).
Objectives/Aims: Evaluation of the efficacy and safety of OFA based on data from the first year of a multicenter observational study in Poland.
Methods: The study retrospectively analyzed data from RRMS patients treated with OFA between May 2022 and August 2024 from 6 multiple sclerosis centers in Poland. Patients were divided into two groups: naïve and switch patients.
Results: Initially, 310 patients (66% women) were included in the switch group with a mean age of 38,54±9,57 years and mean disease duration 9,28±5.82 years. The naïve group consisted of 107 patients (67% women) with a mean age of 33,45±9,62 years and mean disease duration 3.13±3.06 years. From the previously treated group, patients with treatment ineffectiveness were selected. Switch patients, especially with ineffectiveness, had a statistically significantly higher mean Expanded Disability Status Scale (EDSS) score (2,28±1,19 and 2.32±1.20 respectively) compared to untreated patients (1,76±1,15) ($p < 0.001$). However, naïve patients showed higher disease activity in terms of annualized relapse rate (ARR) (1.15 ±0.48 vs 0.46±0.62 and 0.66±0.49 respectively; $p < 0.001$). After one year of OFA therapy, a statistically significant reduction in ARR ($p < 0.001$) was achieved in all groups with the highest reduction in naïve group (1,21 +- 0,45 vs 0.09 +- 0.35 ; $p < 0.001$). Moreover, no progression of EDSS was observed in any of the groups (untreated - 1.65 ±1.19, treated - 2.28±1.34 and those with ineffectiveness - 2.25±1.32). No grade 3 and 4 lymphopenia or new adverse events were reported.
Conclusion: The results of the presented study confirmed the efficacy and safety of OFA in the one-year observation of RWE study. Moreover, the validity of the choice of highly effective treatment in naïve patients was indicated. OFA therapy was proven to inhibit disease progression and significantly reduce relapse activity in all groups, but this was most pronounced in patients included de novo, despite their highest disease activity at baseline. The study was limited by the relatively short follow-up resulting. Therefore, further data collection is needed, which is being continued in our centers and next results will be presented.

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P1780
Cladribine in Patients Aged Over 50 with Multiple Sclerosis: A Real-World Case Series of 29 Patients

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Introduction: Treatment of multiple sclerosis (MS) in patients over 50 poses unique challenges due to immunosenescence, comorbidities, and longer disease duration. Cladribine, an oral immune reconstitution therapy, may offer an effective and well-tolerated option in this population.
Objectives/Aims: To evaluate the clinical experience, safety, and effectiveness of cladribine in patients over 50 years old with relapsing MS in a real-world setting.
Methods: We conducted a retrospective review of 29 MS patients aged ⩾50 years (mean age 56.9, range 50–68; 9 males, 20 females) treated with cladribine in a tertiary center. No patients were treatment-naïve. The median disease duration was 16 years (range 1–38). Median baseline Expanded Disability Status Scale (EDSS) was 2.5. Treatment history included dimethyl fumarate (n=13), teriflunomide (n=6), interferon-glatiramer (n=8), and ocrelizumab (n=1). The most frequent reasons for switching to cladribine were clinical activity (n=14), MRI activity (n=8), adverse events (n=9), and progression (n=8).
Results: Twenty-five patients initiated treatment; 16 have completed both cycles as scheduled, while the remaining are within the follow-up period and scheduled for the second cycle. Median follow-up was 32 months (range 1–63). MRI follow-up was available for 20 patients, all of whom showed no disease activity, and EDSS remained stable in all 20. Three relapses occurred, prompting treatment changes in two cases. One patient was lost to follow-up. Two mild herpes zoster infections were reported without sequelae. No other significant infections occurred. Two patients experienced delayed second-year dosing due to lymphopenia, but both were successfully administered the second cycle once lymphocyte counts recovered. Lymphocyte monitoring showed mild (Grade 1–2) transient lymphopenia, with rare Grade 3 events and no Grade 4 cases. By month 24, 85% of patients had recovered normal lymphocyte levels, supporting the favorable hematologic safety profile of cladribine. No third cycle was required.
Conclusion: Cladribine appears to be a safe and effective treatment option in MS patients over 50 years of age, even in those with long-standing disease and prior treatment failures. Real-world data support its use as a high-efficacy therapy with a favorable safety profile in this demographic.

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P1781
Real world data of cladribine effectiveness: Data from MS Belgrade treatment cohort with up to 5 year follow-up

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Introduction: Cladribine real world data regarding safety and efficacy is still being collected regarding cladribine treatment due to its recent approval for treatment of relapsing-remitting MS.
Objectives/Aims: to evaluate the effectiveness of cladribine in a real-world setting.
Methods: Data on cladribine effectiveness and treatment response predictors in 306 patients with MS followed at Belgrade tertiary MS center are presented. Data was prospectively collected of patients with RRMS who had regularly attended MS outpatient clinic at the Neurology Clinic, University Clinical Center of Serbia and are part of the Serbian national MS treatment Registry. Clinical and magnetic resonance imaging (MRI) data were collected by following the local medication monitoring plan and hospital guidelines.
Results Mean age at cladribine initiation was 37 ± 10.6 years, and there was a significant female sex predominance (78%). Mean duration of MS before cladribine treatment initiation was 5 years. 35% of patients were treatment naive, while 65% were switching from previous therapies. Follow up median was 23 (IQR 15-31) months, range 0 to 61 months. Baseline EDSS score was 2.0, and was stable during the follow-up period. Annualized relapse rate (ARR) was 1.07 at the year before treatment initiation, whilst the ARR was 0.1 with a 90.5% of risk reduction after first year of treatment. No evidence of disease activity (NEDA3) was demonstrated in 86% of patients after first year of treatment, whilst the second through fourth year showed 89%, 80.3% and 74% NEDA3 respectively. Treatment naive patients had better chance for treatment resposnse in comparison to treatment experienced patients with an odds ratio of 2.68 (CI 0.88-8.15).
Conclusion: Real world data confirms high effectiveness of cladribine, especially in treatment naïve patients with MS. Cladribine might be more effective when placed as an earlier choice along the treatment algorithm.

Disclosure of interest: nothing to disclose

P1782
The Comparative Effectiveness of Rituximab and Ocrelizumab in Relapsing-Remitting Multiple Sclerosis: A Real-World StudyThe Comparative Effectiveness of Rituximab and Ocrelizumab in Relapsing-Remitting Multiple Sclerosis: A Real-World Study

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Introduction: Ocrelizumab (OCR), a humanized anti-CD20 monoclonal antibody, is approved for relapsing-remitting multiple sclerosis (RRMS). Rituximab (RTX), another anti-CD20 agent, is used off-label as a high-efficacy option. Despite wide-

spread use, head-to-head randomized trials are lacking, and real-world comparative data remain limited.
Objectives/Aims: To compare the effectiveness and safety of RTX versus OCR in a real-world cohort of RRMS patients using data from the MENACTRIMS registry.
Methods: This registry-based, retrospective, multicenter study included RRMS patients from 7 Middle Eastern countries treated with RTX or OCR and followed for ⩾12 months. Primary outcomes included annualized relapse rate (ARR), confirmed disability progression/improvement, and magnetic resonance imaging (MRI) activity. Descriptive statistics and logistic regression adjusting for age disease duration, sex, baseline Expanded Disability Status Score (EDSS), number of relapses in the previous year, and number of disease-modifying therapies prior to switching were used to describe and compare the sample groups.
Results: A total of 1,277 RRMS patients were included, with 776 receiving RTX and 501 OCR. Patients treated with RTX had a significantly higher baseline EDSS and longer disease duration. The crude ARR was significantly higher in the RTX group compared to OCR (0.127 vs. 0.078, p=0.004), but this difference was not statistically significant after adjustment for baseline differences (adjusted rate ratio [RR] 0.79, 95% CI 0.62–1.02, p=0.267). MRI analysis showed a significantly lower proportion of patients with new T2 lesions in the OCR group (3.1% vs. 45.2%, adjusted OR 38, 95% CI 2.76–533, p=0.007). Rates of enhancing lesions were numerically lower with OCR, though statistical comparison was limited due to absence of events. The overall rate of adverse events was comparable between the two groups (7.8% OCR vs. 5.5% RTX, p=0.110), but RTX was associated with a significantly higher rate of treatment discontinuation due to AEs (7.0% vs. 2.4%, p<0.001). Data on confirmed disability progression will be presented at the congress.
Conclusion: In this large real-world cohort, RTX and OCR showed similar effectiveness in reducing relapses. OCR was associated with significantly lower MRI activity and fewer treatment discontinuations due to AEs. These findings provide real-world evidence supporting the comparable efficacy and tolerability of both anti-CD20 therapies in RRMS management.

Disclosure of interest: All authors have nothing to disclose.

P1783
The use of mobility aids in patients with multiple sclerosis

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Introduction: Despite the imunotherapy can MS lead to progression of neurological disability.
Objectives/Aims: The aim of our questionnaire survey was to map patients' experiences of mobility aids in order to provide more targeted advice and interventions by occupational therapists.
Methods: For the purposes of the study a questionnaire was created regarding the use of compensatory aids and the experience with their use. This questionnaire was supplemented with a standardized questionnaire assessing fatigue (Fatigue Severity Scale-FSS) and the degree of neurological disability (Patient Determimed Disease Scale-PDDS) and questions on demographic characteristics of the respondents.
Results: A total of 225 respondents responded, with 161 respondents (71.5%) using mobility aids. The mean duration of use of mobility aids was 6.8 years, median 3 years (min 0.1-40 years). MS patients using mobility aids were significantly older (p>0.000), with longer disease duration (p=0.001), more likely to no longer work (p>0.000), and have significantly higher pathological fatigue (p=0.001). For 21% of respondents it was difficult to admit the necessity of using an aid, most respondents also did not have the professional advice of an occupational therapist to select a suitable aid. Only 35% of respondents believed that they did not need professional advice, the rest would have liked this option.
Conclusion: Our questionnaire survey points out that a large number of patients with MS did not have the possibility of individual professional consultation of suitable compensatory aids with an occupational therapist. As the users of the aids are more often elderly with significant pathological fatigue, it might be advisable to consider offering a similar form of consultation in the future, also at a distance. A professional consultation could also help patients to accept more easily the fact that they need to use an aid.

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P1784
Patient satisfaction and neurofilament light chain levels in persons with MS following subcutaneous ocrelizumab in the prospective SurfSubQ study: baseline data

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Introduction: OCR SC may improve patient satisfaction in pwRMS/pwPPMS. Patient-reported outcomes (PROs) are important for long-term therapy adherence and success. sNfL is a useful biomarker for MS disease activity. Yet, prospective PROs and longitudinal real-world evidence (RWE) on changes

in sNfL and serum glial fibrillary acidic protein (sGFAP) levels with OCR are limited.
Objectives/Aims: To determine patient satisfaction of subcutaneous (SC) ocrelizumab (OCR) and changes in serum neurofilament light chain (sNfL) in a prospective real-world population of persons with relapsing or primary progressive MS (pwRMS/pwPPMS) with OCR SC.
Methods:
SurfSubQ (ML45551, NCT06780150) is an active, prospective, non-interventional study in Germany and Switzerland recruiting up to 349 pwRMS/pwPPMS to be treated with first-time OCR SC over 12 months (920 mg every 6 months; initial treatment or switch). Here we show data from 51 participants at baseline, while data from 100 participants will be presented. PRO-collection included the Therapy Administration Satisfaction Questionnaire SC (TASQ-SC) and Treatment Satisfaction Questionnaire for Medication. sNfL and sGFAP levels were assessed using the Roche Elecsys electrochemiluminescence immunoassay. Absolute sNfL levels were corrected for age and body mass index (BMI) using the Simoa® NF-LightTM assay-based healthy controls reference database converted to the Elecsys assay. Physician-rated usefulness of sNfL for management of pwRMS/pwPPMS was assessed using the General NfL survey.
Results: Among the participants (n=51), 70.6% were very satisfied and 21.6% were satisfied with OCR SC based on the TASQ-SC. Mean (standard deviation; SD) age (n=49) was 45.3 (11.3) years, 36.7% were male, and 80.4% and 19.6% had RMS and PPMS (n=46), with a mean (SD) time since MS diagnosis of 10.3 (8.4) years, and last prior MS therapy of intravenous OCR (65.2%) and other disease-modifying therapies (26.1%); 8.7% were treatment naïve. Mean (SD) Expanded Disability Status Scale score (n=34) was 2.9 (2.0). Mean (SD) sNfL levels (n=41) were 1.2 (1.5) pg/mL, reflecting a Z-score of 0.27 (1.35), i.e. 60.6th age- and BMI-adjusted percentile. Of 11 physicians, 72.7% found the NfL parameter useful for the daily management of pwRMS/pwPPMS.
Conclusion: SurfSubQ is the first prospective study providing RWE in pwRMS/pwPPMS treated with OCR SC on PROs and changes in sNfL using the Roche Elecsys assay. These data show high patient satisfaction with OCR SC, and physicians found NFL a useful biomarker for their daily management of pwMS.

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P1785
Long-Term Effects of Ocrelizumab on Motor and Cognitive Functions in Progressive Multiple Sclerosis: A Three-Year Follow-Up Study

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Introduction: Ocrelizumab has been shown to delay disability progression and improve fatigue, quality of life, and cognitive function in relapsing-remitting multiple sclerosis. However, evidence regarding its long-term effects on physical and cognitive functions in progressive MS remains limited.
Objectives/Aims: To evaluate the long-term effects of ocrelizumab on extremity function and cognitive performance in individuals with progressive MS (pwPMS) over a three-year period.
Methods: This retrospective cohort study included patients diagnosed with primary or nonactive secondary progressive MS. Upper and lower extremity function, cognitive performance, and disability status were assessed at treatment initiation and after three years of continuous ocrelizumab therapy. Fine motor skills of the upper limbs were evaluated using the Nine-Hole Peg Test (9HPT), while lower limb performance was assessed with the Timed 25-Foot Walk (T25FW). Cognitive functions were examined using the Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT), and Brief Visuospatial Memory Test (BVMT). The Expanded Disability Status Scale (EDSS) was used to monitor disability progression.
Results: Thirty individuals with progressive MS receiving ocrelizumab were included in the study. The mean baseline EDSS

score was 5.52±1.68. While EDSS scores remained stable over the follow-up period, significant improvements were observed in verbal and visuospatial memory. Specifically, CVLT and BVMT scores improved significantly. No statistically significant changes were detected in SDMT, 9HPT, or T25FW performance.
Conclusion: Ocrelizumab was associated with preserved motor performance and stable disability levels over three years in patients with progressive MS. In addition, notable improvements in cognitive domains such as verbal and visuospatial memory suggest that ocrelizumab may exert beneficial effects beyond physical disability. These findings support its potential as a disease-modifying treatment with cognitive protective benefits in progressive MS.

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P1786
What prognostic factors drive treatment decision by the neurologists? Study on prognostic factors of naïve patients from 2 ms centers

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Introduction: Treatment choice between Monoclonal Antibodies (MAbs) or other Disease-modifying treatments (NoMAbs) in MS seems to be driven by the presence of baseline poor prognostic factors (BPF). However, some BPFs may have a stronger relevance than others in the neurologist's mindset. On the other hand, treatment choice may have implications for the evolution of people with MS (pwMS).
Objectives/Aims: To identify which BPFs are associated with being prescribed MAbs versus NoMAbs and compare disease activity in both groups.
Methods: We included pwMS diagnosed between 2021 and 2024 who were prescribed an approved DMT from two MS referral centers. BPFs (based on a modified version of the Rotstein/Moltalban review) and activity were compared between MAbs and NoMAbs groups.
Results: We included 206 pwMS (86.9% Relapsing-Remitting MS, 9.7% Clinically Isolated Syndrome, 3.4% Radiologically Isolated Syndrome). Female-to-male ratio was 2.38:1. Mean age was 36.37 years (95% CI: 34.88 – 37.86). Onset EDSS was 1.7 (95% CI: 1.5-1.9). 49.5% were prescribed MAbs.
Univariate analysis showed that pluri-symptomatic relapse at onset, MRI brain load ⩾20, spinal cord lesions ⩾2, black holes, atrophy, infratentorial lesions, ⩾2 gadolinium-enhancing lesions (⩾2Gd+), lipid-specific IgM oligoclonal bands (lsIgMOCB), and serum neurofilament light chain levels ⩾10 pg/ml were significantly associated with being prescribed MAbs. EDSS ⩾2 and annual relapse rate ⩾2 approached significance (p=0.067). In the multivariate analysis (n=132), pluri-symptomatic onset (OR 2.16), lsIgMOCB (OR 1.71), black holes (OR 1.17) and ⩾2Gd+ (OR 1.02) were significantly associated with being prescribed MAbs.
21 pwMS (10.2%) had activity after DMT start (13 clinical, 8 radiological). Activity was significantly lower in the MAbs group compared to NoMAbs (OR = 11.18, 95% CI: 2.52–49.66, $p < 0.001$). 12/19 (63.15%) of NoMAbs group with activity were switched to MAbs.
Conclusion: Relapse characteristics at onset, MRI parameters and biomarkers were the main factors driving the prescription of MAbs in our centers. There was a low rate of active patients, and although having worse prognosis at onset, pwMS receiving MAbs had significantly lower activity.

Disclosure of interest: All authors: nothing to disclose.

P1787
Viral Seroprevalence and Risk of Reactivation in MS Patients Treated with Ocrelizumab: A Real-World Cohort Study

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Introduction: Ocrelizumab, a humanized monoclonal antibody targeting CD20-positive B cells, has demonstrated efficacy in reducing disease activity in both relapsing and primary progressive multiple sclerosis (MS). Despite its clinical benefits, the immunosuppressive nature of ocrelizumab raises concerns regarding infectious complications, particularly the reactivation of hepatitis B virus (HBV). While cases of HBV reactivation have been reported in patients receiving ocrelizumab without antiviral prophylaxis, data on the potential impact of ocrelizumab on hepatitis A (HAV), hepatitis C (HCV), and human immunodeficiency virus (HIV) infections remain limited.
Objectives/Aims: This study aimed to investigate the prevalence of HBV, HAV, HCV, and HIV markers in patients with MS undergoing ocrelizumab therapy and to evaluate the incidence of viral reactivation in this population.
Methods: Patients receiving ocrelizumab therapy were retrospectively evaluated. Demographic, clinical, and laboratory data were collected, including MS subtype, disease duration, disability status, and viral serologies. Patients with positive serological markers were monitored annually, and antiviral prophylaxis was administered when indicated.
Results: A total of 273 MS patients treated with ocrelizumab were included in the analysis. The majority were women, and relapsing-remitting MS was the most common subtype, followed by secondary progressive and primary progressive MS. The average age at treatment initiation was in the mid-forties,

with a mean disease duration exceeding 16 years. Initial disability scores indicated moderate impairment, with no significant progression observed during ocrelizumab treatment. Clinical relapse activity was also markedly suppressed.
In terms of viral serologies, anti-HBs positivity was detected in 7.0% of patients, while 4.4% had positive anti-HAV results. HBsAg was identified in 1.5% of patients, and 0.4% tested positive for anti-HBc total. All patients with HBV markers received antiviral prophylaxis, and no reactivation was observed during follow-up. Additionally, one patient tested positive for anti-HCV and another for anti-HIV. The HIV-positive patient received antiretroviral therapy prior to ocrelizumab initiation, and no viral complications were reported during treatment.
Conclusion: This study emphasizes the importance of routine viral screening and individualized prophylactic strategies in MS patients receiving ocrelizumab. With proper monitoring and appropriate antiviral measures, ocrelizumab can be administered safely even in patients with positive viral serologies. These findings support the feasibility of maintaining effective MS control while minimizing infectious risks in this vulnerable population.

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P1788
Trends in disease-modifying therapy use in patients with multiple sclerosis using a population-based cohort study in Colombia

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Introduction: Numerous disease-modifying therapies (DMTs) have been approved for multiple sclerosis (MS) over the past two decades. However, limited research has examined how these approvals have affected prescribing patterns in Colombian patients with unique healthcare needs and challenges.
Objectives/Aims: We aimed to describe changes in DMT use by comparing initial and subsequent prescriptions in Colombian patients with MS.
Methods: A retrospective, comprehensive register-based study was conducted among individuals diagnosed with MS at two specialized MS care units in Bogotá, Colombia, from May 2016 to October 2024. DMT initiation and conclusion dates were systematically documented for each patient. We describe basic clinical and demographic characteristics of both cohorts, as well as the average number of DMTs received, the specific DMTs used after each treatment switch, and the relative frequency of DMTs over time, both individually and according to efficacy classification.
Results: Of the 1028 patients, 658 (64%) were from the HUN, and 370 (36%) were from Cayre multiple sclerosis center. 704 (68.5%) were women, with a mean (SD) age of 45.9 (13.1) years and a median (IQR) EDSS at the first evaluation of 1.5 (0.0 -3,5) and a last evaluation of 2.0 (1.0 - 4.0). 92 (8.9%) had PMS. The disease mean duration (SD) was 13.0 years (1.13). 942 (78%) received treatment at any point. The mean number (SD) of disease-modifying therapies (DMTs) received was 1.71 (0.92). The most frequent DMT first used were interferons in 36% of the cases, followed by fingolimod (16%) and natalizumab (12%) and a shift has operated from low to high efficacy therapies (HTE) over time.
Conclusion: This study provides a detailed analysis of the trends in the utilization of disease-modifying therapies DMT within the Colombian population. It emphasizes the significant rise in the adoption of these highly effective treatments in recent years. The analysis illustrates the transformative impact of newer DMT, highlighting an important evolution in treatment practices within Colombia's healthcare system.

Disclosure of interest: A Casallas-Vanegas is currently an ECTRIMS clinical fellowship awardee for 2024-2025 and receives support from ECTRIMS. In 2022 she was awarded with a grant from the European Charcot Foundation for MSM program. She has also received speaking honoraria from Roche, Novartis, Biogen, Merck, and Sanofi. S. Lema-Restrepo has nothing to disclose. L.E.A.-R has received travel expenses in the past three years for scientific meetings from Roche and Biogen-Idec; compensation for consulting services or participation on advisory boards from Amgen and Sanofi; lecture fees from Biogen-Idec, Merck, and Biopas; and research support from Roche. J.C Carrillo-Martínez has received honorariums from Atheneum advisory. He has also received travel expenses for scientific meetings and symposium by Merck, Gilead and GlaxoSmithKleine. T.R.Gómez has received travel expenses for scientific meetings from Roche, Merck, and Novartis. compensation for consulting services or participation on advisory boards from Amgen. L.L.-R was a 2022–2023 ECTRIMS nursing fellow; in the past three years has received travel expenses for scientific meetings from Merck and Roche. M.I Reyes.has received compensation for consulting services on advisory boards from Novartis, Merck, Biogen, Amgen; lecture fees from Novartis, Amgen, Merck, Biogen and travel expenses from Novartis. M.Reyes He has received speaking honoraria from Roche, Novartis, Biogen, Merck, and Sanofi. J.J Flores. Has nothing to disclose. J.P. Barrera. Has nothing to disclose. A.V. Navas. .has received compensation for lecture fees from Novartis, Biogen and Sanofi. L.N. Flórez has nothing to disclose. C. A. Navas. He has has received speaking honoraria from Roche, Novartis, AstraZaneca and Amgen. S.C.-R was a 2019-2020 ECTRIMS

clinical fellow; in the past three years he has received travel expenses for scientific meetings from Roche, Merck, and Genzyme; compensation for consulting services or participation on advisory boards from Amgen, Merck, Biogen-Idec, Sanofi and Novartis; lecture fees from Novartis, Merck, Sanofi, Janssen, Lumex pharma and Biogen-Idec; and research support from Biogen-Idec and Novartis.

P1789
Effectiveness of Cladribine in a real world setting from a Latin-American Country

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Introduction: Real world evidence of MS treatments is scarce in countries with a low prevalence of MS.
Objectives/Aims: Describe the effectiveness of cladribine for the treatment of relapsing MS in centers from Colombia.
Methods: Retrospective cohort observational study, carried out in 4 MS centers from the main cities in Colombia. We included patients exposed to at least one dose of cladribine and with at least one follow-up visit. We calculated the post-treatment annualized relapse rate (ARR) and 95% credible intervals (95%CI) using the ARR reported in the pivotal trial as parameters for estimating a prior distribution, and estimated survival estimates to the first relapse after treatment onset. Disability was analyzed as survival estimates to the first events of confirmed disability worsening (CDW), improvement (CDI) and progression independent of relapse activity (PIRA). We also estimated time to the first MRI activity (new T2 or enhancing lesions) and to the use of another DMT. ARR was described for the whole cohort and pre-specified subgroups: treatment naïve vs. experienced and high ($>$1 relapses) vs. low ($\leqslant$1 relapses) disease activity in the year before cladribine.
Results: A total of 99 MS patients (80.8% from Bogotá and 19.2% from Medellín) ever exposed to Cladribine were included. Seventy-two (72.73 %) were women with mean (SD) age at cladribine exposure of 38.1 (9.4) years. 64 complete cycles of cladribine were administered. During a total follow-up of 208 patient-years, 20 relapses, ten CDW, six CDI, and eight PIRA events were observed, after a median of 13.3, 13.4, 19, and 13.4 months, respectively. Thirteen patients had one, 2 had two, and 1 had three relapses. The annualized relapse rate (95%CI) after treatment onset was 0.13 (0.11 - 0.15). Forty-one and 4 patients were in the treatment naïve and highly active MS subgroups, respectively, and ARR (95%CI) was 0.14 (0.12 - 0.17) in both subgroups. Twenty-seven patients experienced MRI activity and 10 patients switched DMT after a median of 8.5 and 26.5 months, respectively.
Conclusion: Cladribine is effective for treating MS in the real-world clinical practice from our country.

Disclosure of interest: S.C.-R was a 2019-2020 ECTRIMS clinical fellow; in the past three years he has received travel expenses for scientific meetings from Roche, Merck, and Genzyme; compensation for consulting services or participation on advisory boards from Amgen, Merck, Biogen-Idec, Sanofi and Novartis; lecture fees from Novartis, Merck, Sanofi, Janssen, Lumex pharma and Biogen-Idec; and research support from Biogen-Idec and Novartis. M.I.Z was a 2015–2016 ECTRIMS clinical fellow; in the past three years has received travel expenses for scientific meetings from Merck, Sanofi, and Roche; compensation for consulting services or participation on advisory boards from Merck, Biogen-Idec, and Roche; lecture fees from Novartis, Merck,Roche and Biogen-Idec. A.C.-V. is currently an ECTRIMS clinical fellowship awardee for 2024-2025 and receives support from ECTRIMS. In 2022 she was awarded with a grant from the European Charcot Foundation for MSM program. She has also received speaking honoraria from Roche, Novartis, Biogen, Merck, and Sanofi. M.I.R.-M has received compensation for consulting services on advisory boards from Novartis, Merck, Biogen, Amgen; lecture fees from Novartis, Amgen, Merck, Biogen and travel expenses from Novartis. C.R has received honoraria for participation in the development and delivery of lectures from Merck, Novartis and Sanofi. T.R has received travel expenses in the past three years for scientific meetings from Roche, Merck and Novartis; Compensation for consulting services or participation on advisory boards from Amgen. A.N has received travel expenses for scientific meetings from Roche, Merck, Genzyme, Novartis, Biogen ; compensation for consulting services or participation on advisory boards from Amgen, Merck, Roche, lecture fees from Biopas. J.C.C.-M has received honoria from Atheneum advisory. He has also received travel expenses for scientific meetings and symposiums by Merck, Gilead and GlaxoSmithKleine. L.L.-R was a 2022–2023 ECTRIMS nursing fellow; in the past three years has received travel expenses for scientific meetings from Merck and Roche. L.E.A.-V has received travel expenses in the past three years for scientific meetings from Roche and Biogen-Idec; compensation for consulting services or participation on advisory boards from Amgen and Sanofi; lecture fees from Biogen-Idec, Merck, and Biopas; and research support from Roche.

P1790
Real-world clinical and patient reported outcomes of ofatumumab in relapsing MS: Interim Analysis from EAFToS Part II

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Introduction The EAFToS part II study investigates the utilization of ofatumumab (OFA) in Australian patients with relapsing multiple sclerosis (RMS).
Objectives/Aims: This analysis aims to elucidate the impact of OFA on patient-reported outcomes (PROs) in relation to clinical outcomes and baseline (BL) demographics. The study leverages the MSGo registry and integrates data from various real-world sources to comprehensively understand OFA's efficacy and safety profile.
Methods: The primary endpoint of this non-interventional, longitudinal sub-study, which used data extensively, was adherence. Adherence is defined as the proportion of doses not completed within 3 days of the expected date during initiation and the first 3 months of maintenance. Additionally, PROs and changes in clinical outcomes are evaluated.
Results: This interim analysis of 100 patients was completed using a data cut-off of 24/July/24. The patients were mostly female (73%) and aged 31-40 years (37%). The mean (SD) BL EDSS score was 1.43 (1.43), with a mean time since diagnosis of 5.69 years (7.73). The most common prior DMTs were ocrelizumab (14%) and natalizumab (13%), whilst 31% had received no prior therapy. High adherence to initiation doses 2 and 3 was observed (proportion: 0.967 (95% CI: 0.908-0.993). The proportion of maintenance doses 2 and 3 administered within 28±14 days showed adherence of 1.000 (95% CI: 0.960-1.000). The treatment satisfaction scores (mean Treatment Satisfaction Questionnaire for Medication) at BL and 6 months were: global satisfaction, 68.52 vs 72.37; effectiveness, 67.44 vs 70.18; side effects, 78.78 vs 82.80; convenience, 87.92 vs 87.15. EQ5D and fatigue scores remained stable over 6 months. The change in EDSS from BL to 12 months was -0.13 (-0.49, 0.24). There was a correlation of -0.32 between adherence to treatment and the number of relapses at 12 months.
Conclusion: This initial analysis provides insights into the Australian OFA patient cohort with respect to baseline characteristics, clinical outcomes, and patient-reported outcomes. The final analysis will evaluate PROs related to clinical outcomes up to 18 months on treatment, enhancing the understanding of real-world experiences for OFA patients.

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P1791
Administration time and societal impact of four different second-line MS treatments; comparing mode and location of administration

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Introduction: Relapsing-remitting multiple sclerosis (RRMS) is the most common form of MS, affecting approximately 85% of patients. Second-line disease-modifying treatments (DMTs) vary in their modes of administration, with some allowing for home-based treatment.
Objectives/Aims: The study compares the societal burden of second-line DMTs for adults with RRMS in the Netherlands by assessing administration time for patients and healthcare professionals (HCPs), caregiver impact, productivity losses, patient preferences, and total administration costs.
Methods: An observational, non-interventional study was conducted in four hospitals and one private clinic. Patients received either hospital-based intravenous (IV) ocrelizumab or IV natalizumab, or home-based subcutaneous (SC) ofatumumab or oral cladribine. Time measurements for hospital-based treatments were collected using case report forms and facility records. Home-based treatment administration time, caregiver time, treatment preferences, and productivity losses were measured through patient questionnaires.
Results: With approximately 90% of data collected (n=110; 40 ocrelizumab, 32 natalizumab, 7 cladribine, 31 ofatumumab), substantial differences in administration time were observed. Mean administration time was 194 minutes (SD 57) for ocrelizumab, 68 minutes (SD 10) for natalizumab, 3 minutes (SD 3) for ofatumumab, and 1 minute (SD 1) for cladribine. Administration-related HCP time was 27 minutes (SD 12) for

ocrelizumab and 17 minutes (SD 13) for natalizumab. Home-based administrations were performed by patients or their caregivers. Informal care was rare for home-based treatments, while 34% of patients receiving natalizumab and 68% of patients receiving ocrelizumab were accompanied by an informal caregiver. Similarly, home-based treatments rarely led to absence from work, whereas, of patients with a paid job, 35% receiving natalizumab and 60% receiving ocrelizumab reported sick leave. In general patients preferred the mode and location of administration they were currently receiving. However, some patients receiving hospital-based treatments would prefer home-based treatments, while no patients receiving home-based treatments would prefer hospital-based treatment. Cost comparisons were not yet available.
Conclusion: The study highlights important differences in administration time for patient and HCP, reliance on informal care and productivity losses between hospital-based second-line MS treatments and home-based treatments, in favor of home-based treatments.

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P1792
Inebilizumab in the Management of Overlapping NMOSD and Anti-NMDAR Encephalitis: A Case Report

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Introduction: Neuromyelitis optica spectrum disorder (NMOSD) and anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis are distinct autoimmune syndromes mediated by aquaporin-4 Immunoglobulin G (AQP4-IgG) and NMDAR-IgG, respectively. Although rare cases of their co-occurrence have been reported, the underlying immunological interactions and optimal therapeutic strategies remain undefined, particularly regarding B-cell depletion therapies, remain unclear.
Objectives/Aims: To present a case of a 19-year-old female with sequential NMOSD and anti-NMDAR encephalitis treated with inebilizumab.
Methods: We analyzed clinical data, including demographics, examinations, neuroimaging, serological/cerebrospinal fluid (CSF) findings, treatment regimens, and therapeutic responses.
Results: A 19-year-old female initially presented with intractable nausea and vomiting at age 12. Magnetic resonance imaging (MRI) revealed abnormal signals in the pons and medulla oblongata, extending to the C2 vertebral level of the spinal cord. Despite negative AQP4-IgG in serum and CSF, NMOSD was suspected. Symptoms resolved after methylprednisolone pulse therapy. At age 14, she relapsed with drowsiness and new MRI lesions in the left hippocampus, midbrain, pons, and bilateral cerebellar peduncles. Remission was achieved with repeat steroid therapy and mycophenolate mofetil prophylaxis. At age 19, she developed acute psychiatric symptoms, cognitive decline, orofacial dyskinesia, altered consciousness, and central hypoventilation. Repeat MRI showed no abnormalities, but serum tested positive for AQP4-IgG (1:320), and CSF tested positive for both AQP4-IgG (1:10) and NMDAR-IgG (1:10). Despite treatment with methylprednisolone pulse therapy, plasma exchange, and intravenous immunoglobulin (IVIG), She showed minimal improvement and remained dependent on mechanical ventilation (mRS is 5). Given the central role of B cells in multiple autoimmune diseases, including anti-NMDAR encephalitis, and the efficacy of CD19-targeted monoclonal antibodies in NMOSD. Inebilizumab was administered. Complete neurological recovery (mRS is 0) was achieved, with sustained remission over a six-month follow-up.
Conclusion: This case demonstrates the successful use of inebilizumab, a B-cell depletion therapy, in managing overlapping NMOSD and anti-NMDAR encephalitis. The sustained remission achieved highlights its potential in treating complex autoimmune overlaps.

Disclosure of interest: Yue Huang: nothing to disclose. Qi Meng: nothing to disclose.

P1793
A Real-World Study on Persistence of Ofatumumab in Canada: the CAPES study

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Introduction: Canada has one of the highest prevalence rates of MS globally, with over 90,000 Canadians affected. An important component of successful disease control in MS is treatment persistence, defined as the time a patient remains on a therapy.
Objectives/Aims: This study evaluates patient persistence to ofatumumab in a real-world Canadian setting.
Methods: This observational, non-interventional, real-world study utilized de-identified aggregate data from 5,448 patients prescribed ofatumumab. Data were collected through the Go Program, the Patient Support Program (PSP) in Canada, from its inception in April 2021 to May 2024. Patients were followed from initiation of ofatumumab until discontinuation, the end of the study period, or departure from the PSP.

Results: Patient persistence to ofatumumab remained high over the three-year study period, with persistence rates over 92% at three years post-index. Data will be reported across demographic and clinical history characteristics, as well as reasons for discontinuation.
Conclusion: The findings from this Canadian real-world study indicate that persistence to ofatumumab remained high over a three-year period. These high persistence rates and low discontinuation rates complement data from randomized controlled trials.

Disclosure of interest: Employee of Novartis Pharmaceuticals Canada

P1794
Evaluating Cognitive Outcomes in Multiple Sclerosis: Real-World Impact of Ozanimod on Processing Speed Using BICAMS

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Introduction: Cognitive dysfunction represents a major burden in multiple sclerosis (MS). The impact on cognitive outcomes of ozanimod in real-world settings remains to be fully elucidated.
Objectives/Aims: To evaluate longitudinally cognitive performance in a cohort of patients with MS undergoing therapy with ozanimod.
Methods: In this single-center observational study, we evaluated cognitive performance in 67 patients with MS (74.6% female) receiving ozanimod (mean treatment duration 17.7 ± 3.0 months). Cognitive assessment was performed using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, comprising Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), and Brief Visuospatial Memory Test-Revised (BVMT-R) collected at different time points
Results: Analysis suggested significant improvement in SDMT z-scores (mean improvement 0.337, SD 0.638; Cohen's $d = 0.42$, $p = 0.0111$). Baseline SDMT z-score emerged as the sole significant predictor of cognitive change (coefficient − 0.345, $p < 0.001$), accounting for 32.4% of variance. CVLT-II and BVMT-R scores remained stable across time points.
Conclusion: This real-world study suggests that ozanimod treatment is associated with significant improvement in information processing speed, independent of traditional prognostic factors. These findings complement existing clinical trial data and warrant further investigation through larger, multicenter studies with extended follow-up periods to validate these cognitive benefits.

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P1795
Experience with ofatumumab in real clinical practice

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Introduction Ofatumumab is a fully human antiCD20 monoclonal antibody approved for thetreatment of adult patients with relapsing forms of multiple sclerosis. In two phase III trials (ASCLEPIOS I and II), ofatumumab was more effective than teriflunomide in reducing the annualized relapse rate, as well as reducing MRI-detected lesion activity and limiting worsening of disability. Data about it use in clinical practice are limited.
Objectives/Aims: To describe "real-world" experience of the use of ofatumumab in a multicenter cohort,
focusing on:

- Annualized relapse rate (ARR)
- Expanded Disability Status Scale (EDSS) score change
- Radiological parameters
- Adverse events (AE)

Methods: This is a multicenter retrospective observational study. A total of 171 RRMS patients(64% female) from 9 university centers in the Northeast of Spain who received first dose of ofatumumab were included. Mean of follow-up was 0.9±0.6 (median 0.8) years. In this work, the results of the 79 patients who have completed a minimum of 1 year of follow-up are shown.
Statistical Analysis: Exploratory analysis (mean, standard deviation, median, range) over baseline and prospective data was performed. Wilcoxon signed-rank test was performed to check the differences between ARR and EDSS over follow-up times.
Stuart Maxwell test was performed to check the evolution of gadolinium-enhancing T1 lesions.
Results: At 12 months of follow-up, ofatumumab significantly reduced the ARR from 0.69±0.57 to 0.03±0.16 (p<0.001) (n 78) (RR -96%), and the EDSS score decreased from 2.25±1.18 to 2.09±1.35 (p<0.05) (n 76) (RR -7%); 94.7% (n 76) not showed clinical activity, and 72.5% (n 51) achieved NEDA3 status. Only one severe injection-related systemic reaction was reported. Serious infections occurred in 3 patients.
Conclusion: In our experience in clinical practice, ofatumumab has demonstrated to be highly effective in reducing ARR. Effect

on disability is more moderate. No concerns about safety had arisen.

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P1796
Long-term effectiveness and safety of ocrelizumab: a single centre real-world study

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Introduction: Ocrelizumab (OCR) is a recombinant humanized anti-CD20 monoclonal antibody approved as a high efficacy treatment (HET) for the treatment of MS. Long-term studies about effectiveness and tolerability of OCR in clinical practice remain scanty.
Objectives/Aims: This retrospective monocentric study evaluated the effectiveness and safety of OCR in relapsing multiple sclerosis (RMS) and primary progressive MS (PPMS) and identified predictors of treatment response.
Methods: We included 260 RMS and 73 PPMS patients treated with OCR for ⩾1 year at our MS Center until May 2024.
Results: Median follow-up was 3.90 years for RMS and 4.23 years for PPMS. Within 2 years from treatment initiation, annualized relapse rate (ARR) decreased from 0.412 to 0.014 and was maintained low throughout follow-up in RMS, with no relapses in PPMS. MRI activity significantly declined and was maintained in both groups ($p<0.0001$). After 3 years, CDP-free survival was high in relapsing-remitting MS (>97%) and lower in secondary progressive MS (48.9%) and PPMS (57.2%). Predictors of OCR inefficacy included higher baseline EDSS, older age and longer disease duration in RMS; male sex, older age and prior lower-efficacy treatments in PPMS. Adverse events were in line with previous clinical studies, with hypogammaglobulinemia and recurrent infections being the most frequent.
Conclusion: We confirm OCR sustained efficacy in controlling inflammatory disease activity, with greater impact in RMS, with a favourable safety profile. Early treatment initiation is crucial to prevent irreversible disability accumulation.

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P1797
Clinical Predictors of Therapeutic Response to Highly Effective Therapies in Argentine Patients with Relapsing-Remitting Multiple Sclerosis

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Introduction: Multiple treatment options are available for patients with relapsing-remitting multiple sclerosis (RRMS). Highly effective therapies (HETs) are often considered for individuals with a poorer prognosis. However, clinical predictors of treatment response remain poorly defined.
Objectives/Aims: To identify potential clinical and radiological predictors of treatment response in patients with RRMS after two years of HET.
Methods: Retrospective study included RRMS patients aged ⩾18 years from the Argentine RelevarEM Registry who received at least two years of HET (natalizumab, alemtuzumab, cladribine, or ocrelizumab). Treatment response was defined as: absence of relapses, no new gadolinium-enhancing (Gd+) T1 lesions, and no confirmed disability progression over two years. A composite outcome combining these three measures was also evaluated. Logistic regression analyses assessed ten independent variables related to demographic, clinical, and radiological characteristics at diagnosis and HET initiation.
Results: A total of 218 patients were included (66.5% female; mean age 38.3 ± 10.6 years). At diagnosis, mean age was 30.9 ± 9.8 years, with a median EDSS of 2.5 ± 1.5. At HET initiation, mean age was 34.3 ± 10.5 years and EDSS was 3.3 ± 1.9; 86.2% had experienced at least one relapse, and 78% had Gd+ T1 lesions on MRI.
After two years of HET:

- 12.1% experienced at least one relapse, significantly associated with prior relapse history ($p < 0.01$).
- 17.3% developed new Gd+ T1 lesions, less likely in patients who received HET as first-line therapy ($p < 0.05$).
- 12.3% showed disability progression, which was inversely associated with prior relapse activity, lesion burden on baseline MRI, and use of HET as first-line therapy ($p < 0.05$).

In the composite outcome analysis, initiation of HET as a first-line treatment showed a significant protective effect ($p < 0.01$).
Conclusion: This study suggests that certain baseline clinical and radiological characteristics may influence treatment response to HET in RRMS.This study suggests that, initiating HET as a first-line therapy was associated with a significantly better outcome across multiple response domains, including relapse rate, MRI activity, and disability progression. These findings support the early use of HET in appropriate patients to potentially modify the long-term disease trajectory and improve clinical outcomes.

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P1798
Impact of BMI on Hematopoietic Stem Cell Transplant Outcomes in Multiple Sclerosis Patients

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disorder affecting the central nervous system, characterized by inflammation, demyelination, and neuronal degeneration. Its complex etiology involves genetic, environmental, and lifestyle factors, with emerging research highlighting the importance of nutritional status, particularly body mass index (BMI), in disease progression. While BMI has been linked to other neurodegenerative conditions, its specific impact on MS remains unclear.
Objectives/Aims: This study aims to analyze the association between patients' BMI and the response of hematopoietic stem cell transplantation (HSCT) and their disease progression, measured by changes in the Expanded Disability Status Scale (EDSS) 12 months posttransplant. The goal is to determine

whether BMI influences treatment response and to identify potential predictors of outcomes in MS patients undergoing HSCT.
Methods: The analysis included 449 MS patients who underwent autologous HSCT between May 2015 and June 2023 at the Centro de Hematología y Medicina Interna de Puebla, Clinica Ruiz in Puebla, México. Patients were classified by BMI: underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), and obese (>30), with further subclassifications. Eligibility criteria included a Karnofsky performance status above 70% and an EDSS score of 8 or below prior to treatment. Follow-up assessments were conducted at one year using patient-reported EDSS scores. The primary endpoint was defined as stabilization or improvement in the EDSS scores after one year.
Results: Of the 449 patients, 96 had primary progressive MS, 142 secondary progressive MS, and 211 relapsing-remitting MS. Statistical analysis revealed no significant differences in age, weight, height, or EDSS changes based on BMI categories. However, a significant correlation ($p = 0.019$) indicated that higher BMI was associated with a lower likelihood of responding positively to HSCT, either stabilization or decrease of the EDSS score. This highlights the need to consider factors like diet, physical activity, and overall health in future research.
Conclusion: The study suggests a complex relationship between BMI and MS progression, particularly in the context of HSCT. While no significant differences in disease progression across BMI categories were found, the correlation between higher BMI and reduced treatment response prompts further exploration. Understanding these relationships may lead to more personalized treatment strategies and improved outcomes for MS patients. Future research should focus on clarifying these mechanisms and developing guidelines for integrating BMI considerations into patient care.

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P1799
The effect of theoretical and experiential education on practitioners' attitudes towards prescribing exercise in MS

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Introduction: Persons with MS have indicated that healthcare professionals are their preferred source of information on exercise.
Objectives/Aims: Using implementation study design we aimed to determine the effect of an online theoretical and experiential education programme on practitioners' attitudes towards prescribing exercise to persons with multiple sclerosis (MS).
Methods: Physiotherapists and exercise physiologists participated. They received online training and support to deliver a 16-week programme to persons with MS. Data on practitioners' self-confidence (PSC) and professional quality of life (ProQOL) were collected at baseline (week 0) and post-programme (weeks 1, 17, 52). Implementation data were collected post-programme using a TDF-based questionnaire and questions on behaviour change strategies and programme satisfaction. PSC, ProQOL, and TDF data were analysed using an imputation model for missing data. Effect-size estimates from generalised linear mixed models determined the magnitude of change for each outcome measure.
Results: Of 40 practitioners (20 physiotherapy and 20 exercise physiology) who provided baseline data, 24 completed the theoretical programme, and 16 completed the experiential programme. Self-confidence improved significantly ($|\beta s| \geqslant 1.208$, $SEs \geqslant 0.223$, $|ts| \geqslant 5.403$, $ps < 0.001$), with large effect sizes (percentage 234.5%-511.0%). Some TDF-based domains improved, such as beliefs about skills to prescribe. The 15 practitioners who completed all surveys expressed high satisfaction after the programme. The number of practitioners implementing behaviour change strategies increased from 11 to 15.
Conclusion: An online education programme for MS care improved practitioners' self-confidence and beliefs about physical activity, but high attrition suggests healthcare system barriers.

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P1800
Adverse events with Diroximel Fumarate versus Dimethyl Fumarate in Multiple Sclerosis: A Real-World Study

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Introduction: Diroximel fumarate (DRF) was approved for the treatment of MS to reduce the adverse events caused by dimethyl fumarate (DMF).

Objectives/Aims: The objective of this study was to evaluate and compare the adverse events associated with DRF versus DMF in a real-world clinical setting.
Methods: This was a retrospective observational study including patients with relapsing-remitting MS (RRMS) diagnosed according to the McDonald criteria, followed in our MS unit and treated with DRF or DMF between Novembre 2015 and March 2025. The lymphocyte count during the first 24 months of treatment and the occurrence of flushing, gastrointestinal (GI) side effects, or skin rash at any moment during treatment were assessed.
Results: The cohort included 165 RRMS patients, 74.5% were women and their median EDSS score was 2.0 (IQR 1.5). Of them, 129 received DMF and 36 DRF. The mean age at DMF initiation was 42.46 (SD 9.67) years and 50.97 (SD 10.97) years at DRF, $p<0.001$. The median follow-up time was 2.96 years (IQR 4.16) for DMF vs 0.83 years (IQR 1.16) for DRF, $p<0.001$. Baseline lymphocyte count was lower in the DRF group, 1.65 (IQR 0.56) vs 1.98 (IQR 1.0) in the DMF, p=0.013. This difference persisted after the first month of treatment (p=0.022), but no significant differences in the lymphocyte counts were observed at months 3, 6, 12, or 24. Similarly, there were no differences in the proportion of patients developing moderate ($<0.8x10^9$/L) or severe ($<0.5x10^9$/L) lymphopenia.
The multivariable analysis did not identify any predictors of treatment discontinuation due to lymphopenia, including age at treatment initiation, baseline lymphocyte count, lymphocyte levels at months 3, 6, and 12, or treatment duration.
Flushing was significantly more frequent with DMF, reported by 96 patients (75.6%) at any time, compared to 16 patients (44.4%) with DRF ($p < 0.001$). However, only two DMF patients discontinued treatment due to flushing. No significant differences were observed in the prevalence of gastrointestinal (GI) adverse events or skin rash between the groups. GI symptoms led to treatment discontinuation in 4 patients receiving DMF and 2 patients receiving DRF. Skin rash resulted in treatment suspension in 3 DMF patients and in 1 DRF patient.
Conclusion: Diroximel fumarate appeared to be a well-tolerated alternative to dimethyl fumarate, with a lower incidence of flushing and a similar safety profile in terms of lymphocyte counts, gastrointestinal effects and skin rash.

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P1801
Staying on Track: 22 Years of Natalizumab in the Real World

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Introduction: Natalizumab, introduced in 2002 during the original AFFIRM trial, was the first high-efficacy disease-modifying treatment (HE-DMT) for relapsing multiple sclerosis (MS). Despite the advent of new therapies, it remains one of the most potent options.
Objectives/Aims: To evaluate the long-term effectiveness and feasibility of continuous natalizumab treatment in patients who participated in the AFFIRM trial in Czechia.
Methods: This retrospective study utilized real-world data from the Czech ReMuS MS registry. Follow-up continued until the end of 2024. Patients with ⩾18 years of follow-up and sufficient

data were included and divided into two groups based on their treatment status: continuous natalizumab (CN) or discontinued (DN).
Descriptive analyses were performed to compare demographic and clinical characteristics (Expanded Disability Status Scale (EDSS), Annual Relapse Rate (ARR) after Tysabri initiation), and the incidence of Progressive Multifocal Leukoencephalopathy (PML). Additionally, a linear mixed-effects model was used to assess EDSS trajectories over time.
Results: Out of 159 original AFFIRM patients, 120 were identified, and 72 with sufficient data were included. Seventeen patients remained on natalizumab (CN), while 55 discontinued (DN). After discontinuation, 75.2% of patients switched to other HE-DMTs—mainly fingolimod (44%)—while 24.8% transitioned to platform DMTs or remained untreated. The most common reason for discontinuation was a rising anti-JCV index. A total of 4 patients developed PML (in the years 2009, 2012, 2013, and 2018; the duration on natalizumab at the time of PML was 7.3, 9.8, 7.1, and 11.9 years).
Descriptive statistics showed no significant differences between the two groups in terms of sex, age at natalizumab initiation, total follow-up, ARR, or baseline EDSS (2.4 for CN, 1.97 for DN). A significant difference was found in the latest EDSS values: CN group had an EDSS of 2.76 (SD 1.47) with a time-on-natalizumab of 21.04 years (SD 3.1), while the DN group had an EDSS of 4.24 (SD 1.92) with a time-on-natalizumab of 12.3 years (SD 6.0). The linear mixed-effects model indicated that the CN group had an approximately 25% slower EDSS progression rate compared to the DN group (0.03 vs. 0.10 points per year).
Conclusion: Long-term natalizumab treatment was associated with slower disability progression and fewer relapses, supporting its sustained effectiveness and feasibility in real-world care. Three out of four cases of PML occurred before the implementation of regular safety monitoring.

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P1802
Real-World Efficacy and Safety of Anti-CD20 Therapies in Multiple Sclerosis: A Single-Center Cohort from Brazil

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Introduction: Anti-CD20 monoclonal antibodies, including rituximab, ocrelizumab, and ofatumumab, have transformed the management of multiple sclerosis (MS) by targeting B cells to reduce disease activity. Despite a shared mechanism, differences in pharmacokinetics and safety profiles, such as infusion-related reactions, are observed. This study evaluates their efficacy, safety, and tolerability in a real-world, single-center MS cohort.
Objectives/Aims: To assess clinical outcomes, as well as safety profiles, in MS patients treated with anti-CD20 monoclonal antibodies at a single center.
Methods: A retrospective analysis was performed at Hospital Israelita Albert Einstein in São Paulo, Brazil, involving patients diagnosed with MS treated with anti-CD20 therapies (rituximab, ocrelizumab, or ofatumumab) from January 2007 to December 2024. Data collected included disease activity post-treatment initiation, Expanded Disability Status Scale (EDSS) progression, 25-Foot Walk Test (25FWT) performance, IgG levels, serum neurofilament light chain (sNFL) levels, and adverse events.
Results: Data from 180 MS patients (mean age 41.4 years, 64.4% female; 75.2% RRMS, 18.1% SPMS, 6.7% PPMS) showed 77.7% receiving ocrelizumab, 20% ofatumumab, and 3.8% rituximab. Adverse events affected 14.7% on ocrelizumab and 8.6% on ofatumumab, mainly infections, with three ocrelizumab cases of febrile neutropenia. Infusion reactions occurred in 25% of ocrelizumab-treated patients (none severe), while hypogammaglobulinemia was observed in 18.2% on ocrelizumab and 6.3% on ofatumumab. Disease activity was observed in 11.4% of patients on ofatumumab and 4.4% on ocrelizumab. First-line anti-CD20 users had lower EDSS (p=0.012) and greater sNFL reduction (p=0.009). A correlation was found between baseline sNFL levels and final EDSS (p=0.001). No significant differences in EDSS, 25-foot walk test, or sNFL were observed across drugs.

Conclusion: Anti-CD20 therapies reduced disease activity, in our observation more frequently with ocrelizumab. Naive patients were linked to better disability and axonal damage outcomes. Safety profiles showed manageable infections, infusion reactions, and hypogammaglobulinemia, consistent with prior studies. Baseline sNFL levels predicted final disability, supporting its prognostic value. These findings reinforce the efficacy of anti-CD20 therapies and the need for early initiation of high-efficacy drugs.

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P1803
Treatment continuation with cladribine tablets (CladT) beyond year 4 – second interim analysis of the CLIP-5 study

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Introduction: CLIP-5 is a non-interventional study conducted in Germany, in patients with relapsing multiple sclerosis (RMS) who received the full dosage of cladribine tablets (CladT) according to SmPC in year 1 and 2 and are continuing CladT therapy in year 5. Effectiveness and safety data are collected over 24 months (M).
Objectives/Aims: To assess reasons for treatment continuation with CladT in year 5, as well as lymphocyte counts and treatment emergent adverse event (TEAE) reports 18 months after treatment continuation.
Methods: Data cut-off for the second interim analysis took place on 19.12.2024 when at least 30 patients (out of 71 study participants) completed M18 visit after treatment continuation. Endpoints are presented as frequencies and percentages.
Results: The full analysis set includes 70 eligible patients with all documented visits up to M18. The safety analysis set includes 71 patients.
In 49 of 70 (70.0%) patients, treatment continuation with CladT was timeline triggered, without specific signs of disease reactivation.
At the treatment continuation baseline, 88.7% of 71 patients had lymphocyte counts ⩾1 x109/L, 5 patients (7%) <1-0.8 x109/L, 2 patients (2.8%) <0.8-0.5 x109/L and 1 patient (1.4%) had grade 3 lymphopenia (<0.5 – 0.2 x109/L). 18 months after treatment continuation, lymphocyte counts are available for 32 (45,1%) patients: 7 had ⩾1 x 109/L, 7 had <1 – 0.8 x109/L; 12 had <0.8 – 0.5 x109/L and 6 patients had <0.5 – 0.2 x109/L (grade 3) lymphocytes. For 28 out of these 32 patients CladT dosage in year 6 is documented.
Related TEAEs were reported for 26 (36,6%) patients: 21 (29,6%) lymphopenia, 5 (7%) infections, 3 (4,2%) skin disorders, 2 (2,8%) gastrointestinal disorders, 2 (2,8%) headache and 1 (1,4%) fatigue. Serious related TEAEs were reported for 2 (2,8%) patients: 1 lymphopenia (Grade 3) and 1 urosepsis. No progressive multifocal leukoencephalopathy (PML) was reported.
By M18, 59 of 70 (84.3%) patients were relapse-free.
Median EDSS remained stable at 2.0 over the 5,5 years of observation time (from first CladT intake).
Conclusion: The decision to continue with CladT therapy beyond year 4, was made by most of the patients on a timeline basis and not due to clinical or paraclinical symptoms. Treatment continuation has not induced new safety signals. Lymphopenia has been detected in line with the mechanism of action. Based on available lymphocyte counts 18 months after treatment continuation, no grade 4 lymphopenia (<0.2 x 10^9/L) has been reported.

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P1804
Clinical effectiveness of Cladribine Tablets for patients with few vs many treatments prior CladT initiation in the CLADCOMS study -CLADribine tablets long-term Control Of MS – a post-marketing investigator driven study

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Introduction: Cladribine is a deoxyadenosine analogue prodrug that induces immune reconstitution by selectively targeting B- and T-lymphocytes. Cladribine tablets (CladT) are administered in two courses, 12 months apart, for persons with MS (PwMS) with relapsing multiple sclerosis (RMS). Post-marketing surveillance is important for evaluation of long-term safety and effectiveness in a real-world setting. CLADCOMS (CLADribine tablets long-term Control Of MS) is a post-marketing investigator driven study.
Objectives/Aims: To assess effectiveness of CladT at 36 months follow up with the focus on the number of treatments prior to CladT initiation
Methods: CLADCOMS includes patients with RMS from eight academic neurology clinics in Sweden who started CladT treatment after 23rd of March 2018. PwMS being treatment naïve or exposed to one DMT prior to CladT were compared to PwMS exposed to two or more DMTs prior to CladT start. Data are prospectively registered in the Swedish Neuroregistry using highly structured annual follow-ups. Descriptive data, relapses and MRI activity were obtained from the registry. All statistics were performed using Wilcoxon Signed Rank Test
Results: By March 2025, a total of 147 PwMS had a treatment duration with CladT of at least 36 months. In this cohort 74 PwMS had 0-1 DMTs ("low" subgroup) prior to CladT initiation and, 73 PwMS had 2 or more DMTs ("high" subgroup) prior to CladT. In the "low" subgroup, 66% were treatment-naïve and 11% had been exposed to natalizumab. In the "high" subgroup, the mean number of prior treatments was 4 which included anti-CD20 (29%) and natalizumab (29%).
The proportion of PwMS being relapse-free in the group with 0-1 DMT prior was 70% over 36 months of treatment compared to 36% the year before CladT initiation (p=0.005). The proportion of PwMS with new T2 lesions significantly (p=0.05) decreased from 11% during the first treatment year to 5% during the third year.
In the group with ⩾2 DMTs prior CladT, there was no significant difference in the proportion of PwMS being free of relapses in the year prior to treatment start (81%) and third treatment year (84%). There was a non-significant decrease in MRI lesion activity during the first treatment year (7%) and third treatment year (2%).
Conclusion: CladT treatment showed an improvement in clinical effectiveness after 36 months in the subgroup of PwMS with 0-1 prior treatments, where both relapse activity and MRI lesion activity decreased significantly. For the group with ⩾2 DMTs prior CladT the signs of residual inflammatory disease activity remained stable during the entire treatment period.

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P1805
Differences between treatment-naïve and non-naïve patients treated with cladribine

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Introduction: The effects of disease-modifying treatments can leave an immunological footprint. There is limited information on whether this may affect patients with multiple sclerosis treated with cladribine.
Objectives/Aims: To study whether there are differences between patients treated with cladribine depending on whether they are naïve or non-naïve.
Methods: A retrospective, single-centre study of all patients who received cladribine at our centre, according to the Hospital Pharmacy records. Demographic characteristics, comorbidities, prior therapies, treatment response, and safety were analysed.
Results: A total of 78 patients were included, of whom 69.23% were women, and the average age at the start of treatment was 42.06±12.47 years. 92.03% of the cases were diagnosed with RR-MS, five cases with SP-MS, and one with RIS. 26.92% of patients were treatment-naïve, with a median of 1.5 (IQR 0-2) prior therapies, with interferons being the most frequently used treatment. No differences were found between groups in terms of sex or comorbidities. Statistically significant differences were observed regarding relapses in the year prior to treatment, clinical relapses during the first year and after the fourth year, as well as radiological activity prior to treatment and from the third year, all being more frequent in the naïve patients. Additionally, the baseline EDSS was significantly lower in the naïve group, but no differences were found in subsequent values. Lymphopenia was more frequent in non-naïve patients. No differences in safety (infections, neoplastic, dermatological, or digestive alterations) were observed between the two groups.

Conclusion: Cladribine demonstrates a robust safety profile, both as a first-line therapy and as a subsequent therapy in patients with multiple sclerosis.

Disclosure of interest: Nothing to disclose

P1806
Baseline Data from the FILAXOS Study: Real-World Impact of Serum Neurofilament Light Chain on Management of RMS Patients

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Introduction: Neurofilament light chain (NfL) is released after neuroaxonal damage and elevated NfL levels can detect RMS disease activity even before radiologically or clinically apparent. High efficacy DMTs such as ofatumumab effectively reduce (sub-)clinical disease activity, also shown by reduction of sNfL levels in clinical studies. Measuring sNfL as an objective and easily accessible real-time marker for subclinical disease activity has the potential to support optimized individual treatment decisions in clinical routine.
Objectives/Aims: The presented study (FILAXOS) will evaluate real world health outcomes in RMS patients switching to ofatumumab or maintaining current treatment with low efficacy DMT drugs after elevated sNfL level.
Methods: FILAXOS is a prospective, multicenter, observational, non-interventional study (NIS) involving MS patients in Germany with routine sNfL assessments. The study aims to collect data from 900 patients whose NfL levels were measured prior to entering the study. Based on the NfL level the decision was made to either switch to ofatumumab treatment or continue current therapy with either dimethyl fumarate/diroximel fumarate, glatiramer acetate, interferon beta or teriflunomide. Real-world data is collected for up to 24 months per patient, including disease activity parameters, MRI scans, patient-reported outcomes, and resource utilization questionnaires. Additionally, medical history of patients will be collected including disease duration, EDSS, relapses and prior treatment.
Results: The study started in September 2024. Currently a baseline visit is documented for 141 patients at 35 sites. Patients are on average 47 (+/- 12,6) years old and present with a mean NfL-value of 10 pg/ml (+/- 6,4) at baseline. 84,1 % of patients are perceived as stable independent of their NfL value at baseline. Consequently, 88,7 % remained on their current DMT with the start of the study and only 11,3 % were switched to ofatumumab.
The average disease duration among the patients was recorded at 13,6 years, with a standard deviation of 9,7 years. During the last 12 months prior to the baseline visit, the patients experienced an average of 0,2 relapses (+/- 0,5). Additionally, the mean Expanded Disability Status Scale (EDSS) score at baseline was 2,9 (+/- 2,6).
Conclusion: These baseline data provide initial insights into MS patients in Germany who are being treated with low efficacy DMT and have undergone NfL measurements. The majority of patients remain on their low efficacy DMT upon entering the study. The course of the study will show how the therapeutic decision impacts NfL value and patient outcomes.

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P1807
Ofatumumab observational study in Portuguese Multiple Sclerosis patients (PETROS) – demographic and clinical characteristics of early- and late-treatment cohorts

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Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative autoimmune disease of the CNS. With several high efficacy therapies (HETs), such as Ofatumumab, it has been debated whether an early HET treatment approach could improve disease prognosis.
Objectives/Aims: The study primary objective is to assess the effectiveness of Ofatumumab in two cohorts (early and late treatment) on clinical parameters of MS (NEDA-3 12-24 months) in routine medical care setting in Portugal. The secondary objectives include assessing the demographic and clinical characteristics, other effectiveness measures, patient-reported outcomes, treatment satisfaction, persistence, and safety of Ofatumumab in routine medical care settings. This interim analysis provides a demographic and clinical overview of the included population.
Methods: This non-interventional, multi-center, observational study in Portugal compares the effectiveness of Ofatumumab treatment between MS patients who began treatment within 3

years of diagnosis (early-cohort) and those who started more than 3 years after diagnosis (late-cohort). The study includes adult patients with Relapsing MS who initiated Ofatumumab up to 12 months prior to inclusion or at study inclusion. Patients previously on HET are excluded. Data is collected at three routine visits over 24 months. This interim analysis provides a demographic and clinical overview of the included population.
Results: 178 patients from 11 sites were included, with 86 (48.3%) in the early-cohort and 92 (51.7%) in the late-cohort. Data from visit 1 was collected retrospectively in 64.6% of patients. The overall mean age was 41.6 years (SD 10.5) and 70.8% were female. Employment rates were 75.1% globally, 83.5% in the early-cohort, and 67.4% in the late-cohort (p=0.003). Overall mean age at diagnosis was 35.0 years (SD 10.6), 37.9 years (SD 11.1) for the early-cohort and 32.2 years (SD 9.2) for the late-cohort (p=0.001). Median time since MS diagnosis was 0.3 years (IQR 0.5) for the early-cohort and 10.2 years (IQR 9.0) for the late-cohort ($p<0.001$). In the early-cohort, 76.7% were naïve patients. At Ofatumumab initiation, the mean EDSS score was 2.0 (SD 1.1) in the early-cohort and 2.3 (SD 1.3) in the late-cohort (p=0.081). In the year prior to initiation, the relapse rate was 72.6% for the early-cohort and 45.1% for the late-cohort (p=0.002).
Conclusion: This interim analysis highlights significant demographic and clinical differences between early and late-cohort MS patients treated with Ofatumumab in Portugal. The comparison between early-and late-cohort patients reveals significant differences in age at diagnosis and relapse rates prior to treatment initiation. These aspects must be considered when assessing treatment effectiveness.

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P1808
Long-Term Outcomes of Cladribine Tablets in Multiple Sclerosis: Treatment Completion, Persistence, and Subsequent Therapy Transitions in Southeast Europe

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Introduction: Long-term data on treatment with cladribine tablets in individuals with multiple sclerosis (pwMS) are scarce.
Objectives/Aims: To evaluate treatment completion rates, persistence, the administration of a third course of cladribine tablets, and the switching to other disease-modifying therapies (DMTs) among pwMS treated with cladribine tablets at MS centers in Southeast Europe.
Methods: We conducted a retrospective, observational, multicenter, and multinational study involving 195 pwMS who began cladribine tablets. The average follow-up period was 4.06 ± 1.17 years.
Results: Among the participants, 184 (94.4%) completed both courses of cladribine tablets, while 7 (3.6%) were lost to follow-up. Four (2.1%) switched to another DMT due to disease activity before receiving the second course. Over the follow-up period, 132 (67.7%) did not require any additional treatment after completing both courses. Eighteen (9.2%) received a third course of cladribine tablets, while 40 (20.5%) switched to another DMT, with two of these switches occurring after the third course. The median time to the third course was significantly longer (3.18 years [IQR 2.20–3.91]) compared to the median time to switch (2.27 years [IQR 1.79–3.13]) from the administration of the second course (p=0.009). Multivariate logistic regression analysis identified prior DMT use as the only significant predictor for requiring a third course of cladribine tablets and/or switching to another DMT (exp(B) 2.513, 95% CI 1.073–5.886, p=0.034).
Conclusion: A significant number of individuals with pwMS who are treated with cladribine tablets remain free from treatment for more than four years. In certain cases, a third course of cladribine tablets may prove beneficial.

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P1809
Safety and experiences with the natalizumab biosimilar in multiple sclerosis treatment

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Introduction: In 2023, the natalizumab biosimilar Tyruko was approved for patients with relapsing remitting multiple sclerosis (MS). In patients treated with Tyruko, a new test is used to detect antibodies against the John Cunningham virus (JCV): the ImmunoWELL assay. Approval studies showed similar pharmacokinetics, pharmacodynamics, and safety between the two natalizumab brands, as well as comparable performance between the ImmunoWELL and reference JCV assay (STRATIFY).
Objectives/Aims: To evaluate experiences of patients who switched from Tysabri to Tyruko, and to assess natalizumab serum concentrations and the performance of the ImmunoWELL assay in a real-world patient cohort.
Methods: Patients treated with intravenous natalizumab completed questionnaires and had trough concentrations measured at two time points: during Tysabri treatment and during subsequent Tyruko treatment. Patients were aware of the brand switch. The questionnaires assessed the impact of MS symptoms, treatment satisfaction including effectiveness, impact of side effects, convenience and overall satisfaction, wearing-off symptoms, and whether patients experienced any additional side effects or differences with Tyruko compared to Tysabri. JCV test results were analyzed both cross-sectionally, by comparing results from the STRATIFY and ImmunoWELL assay, and longitudinally, by evaluating consecutive ImmunoWELL results.
Results: Among 83 patients, no differences were observed in the impact of MS symptoms, perceived effectiveness, impact of side effects, or convenience between treatment with Tysabri and Tyruko. However, the overall satisfaction was significantly lower during treatment with Tyruko ($Z = -2.71$, 95% CI = 0.00004–10.81). Fifteen percent reported to experience more side effects or other differences with Tyruko compared to Tysabri. The occurrence of wearing-off symptoms and trough concentrations were similar during both treatments. The ImmunoWELL assay results differed significantly from those of the STRATIFY assay ($\chi^2(1) = 29.03$), with more positive test results and higher index values compared to the STRATIFY assay (median difference 0.17). Index values and results of the ImmunoWELL assay remained consistent over time.
Conclusion: While most patients perceived Tyruko as similar to Tysabri, some reported more side effects. However, this may be due to a nocebo effect, as this study was not blinded. Additionally, discrepancies in JCV results between the new ImmunoWELL assay and the STRATIFY assay complicate the clinical use of Tyruko.

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P1810
The rise of the CD20's: is this the beginning of the end for Traditional MS Therapies?

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Introduction: Since Disease Modifying Therapy (DMT) was licensed in the UK, there has been a steady growth in the number of DMT's available for people with MS.
The newer therapies, particularly the anti CD20's, have a higher efficacy at reducing relapses, and reduce rate of progression, means Neurologist are prescribing more DMTs than before. This has resulted in a shift of prescribing and cost implications within the MS landscape.
Objectives/Aims: Review collected data on prescribing trends of DMT's within South East Kent
Methods: A retrospective review of prescribing records held at East Kent Hospitals University Foundation Trust (EKHUFT) MS service from 2009-2025, in a fully funded health care system. All patients receiving treatment during this timeframe were included. Costings have been obtained through the latest publication of British National Formulary (BNF), although, this may differ from the agreement cost between National Health Service England (NHSE) and the Pharmaceutical companies.
Results: Catchment population 760,000 (approx), the regional prevalence 250/100,000 with an average 54 new diagnosis per year.
Total number of MS patients under the care of EKHUFT MS team 1900,
RRMS 878, receiving DMT 624
SPMS 389, receiving DMT 29
PPMS 264, receiving DMT 25
Since 2009 DMT prescribing has increased 380%, the East Kent MS team are prescribing CD20 medication to 38% of patients receiving DMT's with the majority being treatment naïve.
The increase in prescribing of newer medications has impacted upon cost to the NHS, costs in 2009 being £1,435,021.00 compared to 2025 of £10,327,461.00, with 50% of the spend being associated with CD20 medications.
Conclusion: Patients receiving CD20 medication have increased significantly since its inception in 2019 with 38% of the DMT caseload receiving CD20 medications, although this has

increased the overall spend significantly, the frequency of treatments switch from CD20's is minimal with a reduced monitoring burden.

Disclosure of interest: Bethan Tredwell: Nothing to disclose Clare Langham: Nothing to disclose

P1811
Validation of the MS-SATQ: Assessing Patient Attitude Towards Switching from IV to SC Monoclonal Antibody Therapy in MS

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Introduction: With the introduction of subcutaneous (SC) biosimilars, people with multiple sclerosis (pwMS) have gained a more flexible treatment option compared to intravenous (IV) therapies. Despite clinical guidance, patient attitude towards switching from IV to SC plays a key role in shared decision-making. However, no validated patient-reported outcome (PRO) currently exists to assess attitudes towards this transition.
Objectives/Aims: To validate a questionnaire measuring the attitude of pwMS towards switching from IV to SC monoclonal antibody therapy.
Methods: A cross-sectional study was conducted at the MS Center in Bari between September 2024 and January 2025. PwMS receiving IV monoclonal antibody treatment completed the MS-SATQ (MS Switching Attitude Questionnaire), a 12-item instrument evaluating ease of use, convenience, psychological acceptance, side effects, and adherence. Additional tools included the MSIS-29 for physical and mental impact and the TSQM-14 for treatment satisfaction. Reliability was assessed using Cronbach's alpha. Construct validity was tested through exploratory and confirmatory factor analyses (EFA/CFA), using the Bartlett test, KMO, CFI, TLI, SRMR, and RMSEA.
Results: A total of 179 patients participated (83.8% female; 62% aged 19–39). Key factors influencing a favorable attitude towards SC therapy included ease of administration, comfort, adherence, and nursing support. The MS-SATQ showed excellent reliability (Cronbach's $\alpha = 0.922$) and good construct validity. Mental well-being (MSIS-29) positively correlated with switching attitude ($\rho = 0.208$, $p = 0.005$), while concern about side effects (TSQM) showed a negative correlation ($\rho = -0.147$, $p = 0.050$).
Conclusion: The MS-SATQ is a reliable, valid tool to assess attitudes toward switching to SC therapy. Patient-centered approaches are essential to support informed treatment choices.

Disclosure of interest: Author's name: nothing to disclose.

P1812
First Latin American report of real-world direct and indirect cost of disease modifying treatments administrate by intravenous infusion in relapsing-remitting multiple sclerosis

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Introduction: While several studies have evaluated the costs associated with disease-modifying treatments (DMTs) for relapsing-remitting multiple sclerosis (RRMS) in general, little is known in Argentina and LATAM regarding the direct and indirect comparative costs associated with infused DMTs (IV-DMT) for MS.
Objectives/Aims: to determine and compare the first-year annual real-world cost of IV-DMT [ocrelizumab (OCR), alemtuzumab (ATZ) and natalizumab (NTZ)] in RRMS patients from Argentina.
Methods: A non-interventional study was conducted including 134 adult patients who initiated IV-DMTs between August 2018 and August 2020 (patient identification period). An ad-hoc questionnaire was used to fully describe the patients' resources utilization and costs of care. Cost by each patient, both direct (healthcare and non-healthcare) and indirect costs, were determined by multiplication of resource use and unit costs. Costs were estimated in Argentine pesos from December 2022 and converted to US dollars ($) [exchange rate: $1=AR$172.9]. The three health subsectors (public, social security, and private) were also included.
Results: 134 patients were included, 9 presented missing data. Mean age was 35.6 ± 10.8 years, mean disease duration 8.9 ± 6.7 years, mean EDSS 2 ± 2.5. Most frequent IV-DMTs was NTZ (53.7%), followed by OCR (31.3%) and ATZ (14.9%). In overall, total costs (direct costs + indirect costs) per patient in the 1st year was $62.831 ± $14.813. Stratified by DMT were $85.293 ± $2.934 for ATZ, $56.140 ± $13.935 for NTZ and $62.867 ± $7.602 for OCR. Main component of the total cost was the DMT (85%), follow by the cost associated with the hospital outpatient infusion (9.44%). Neither stratification by gender nor by EDSS score showed significant differences in total cost.
Conclusion: The first-year annual costs were $62.832 (±14.813). This total cost is 4.5 times higher than the GDP per

capita of Argentina, highlighting the significant financial burden of this treatment relative to the national economic context. This study shows for the first time real comparative annual costs associated with the administration of all IV-DMT in Argentina.

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P1813
Evaluation of the Efficacy and Safety of Sattralizumab in a Pregnant NMOSD Patient with AQP4/MOG-IgG Dual Seropositive: A Case Report

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Introduction: Neuromyelitis optica spectrum (NMOSD) is a chronic autoimmune neuroinflammatory disease, tipically characterized by the presence of AQP4-IgG, MOG-IgG, or both being negative. The coexistence of AQP4-IgG and MOG-IgG dual positivity in a single patient is exceedingly rare, with an incidence rate of less than 1%.
Objectives/Aims: This case report aims to present the clinical course of a 34-year-old woman with both AQP4-IgG and MOG-IgG seropositive, who successfully completed pregancy preparation, pregancy and parturition while continuing teatment with satralizumab monotherapy. This report highlights the efficacy and safety of satralizumab in managing NMOSD during pregnancy.
Methods: We collected and analyzed the clinical data of the patient, focusing on the efficacy and safety of satralizumab monotherapy throughtuot the entire pregancy period.
Results: This patient, a 34-year-old female, initially presented with decreased visual acuity in the right eye and was diagnosed with NMOSD for both AQP4(tier 1:100) and MOG (tier 1:32) seropositive. Traditional treatment of corticosteroids and mycophenolate mofetil led to gradual recovery of vision and stabilization of her overall condition. One year later, she expressed the desire to conceive, we transitioned her treatment to satralizumab monotherapy with her consent, given the elevated IL-6 levels associated with both NMSOD and MOGAD and the favorable safety profile of satralizumab in preganancy. Three months later, after five doses of satralizumab, the patient successfully conceived. Throughout her preanancy, all routine and prenatal assessments of the fetus were within normal limits and she matintained stable vision without relapse. Notably, AQP4-IgG became seronegative, and MOG-IgG titers remained stable at 1:32 without increase. On 7th April, she gave birth to a female infant with an Apgar score of 10, weighing 2450g, via normal vaginal parturition at 37 weeks and 2 days of gestation. A tatal of 14 doses of satralizumab were administered throughtout the entire fertility course as the sole treatment.
Conclusion: The coexistence of AQP4 and MOG antibodies in a patient with optic neuritis is an extremely rare and complex clinical scenario. When fertility is desired, the selection of therapeutic agents must be meticulously balanced between efficacy and safety. In such cases, satralizumab may serve as a viable option, offering promising effecacy and safety data.

Disclosure of interest: Author's name: nothing to disclose.

P1814
Subcutaneous administration of Natalizumab in relapsing-remitting multiple sclerosis: experience from a tertiary center

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Introduction: Recent studies have shown non-inferiority of subcutaneous Natalizumab (SC-NTZ) compared to its intravenous administration in relapsing-remitting MS (RRMS), offering a more convenient administration method.
Objectives/Aims: We aim to evaluate the efficacy of SC-NTZ in naïve RRMS patients and those previously treated with the intravenous formulation.
Methods: Retrospective observational study of RRMS patients treated with Natalizumab.
Results: We included 31 patients treated with SC-NTZ, mostly females (83.9%), with a mean age of 40,26±12,25 years. The average time from diagnosis was 9,65±6,5 years, with 6,52±4,63 years on Natalizumab and 2,11±0,80 years on subcutaneous administration. The 300mg SC-NTZ dose was administered every 4 weeks (80.6%) and every 6 weeks (19.4%).
From the 31 patients, 23 transitioned from intravenous to subcutaneous form. No significant differences in mean EDSS were observed before and after the switch (2,39 vs. 2,28, p=0,36). The average number of new demyelinating lesions decreased from 0,9±0,29 to 0 and relapses dropped from 0,13±0,06 to 0.
In the 8 patients who started subcutaneous therapy de novo, no significant differences were observed in mean EDSS (1.69 vs. 1.25, p=0.33). New lesions decreased from 0.33±0.52 to 0 and relapses decreased from 0.75±0.7 to 0.
Four patients switch to Ocrelizumab due to JCV seroconversion. No patients required therapeutic rescue due to disease exacerbation.
Conclusion: SC-NTZ demonstrated efficacy comparable to intravenous form, with no clinical or imaging deterioration in patients who switch or started subcutaneous treatment de novo. Future studies are needed to determine if subcutaneous dosage should match the intravenous form or be adjusted.

Disclosure of interest: Nothing to disclose

P1815
Cladribine in Multiple Sclerosis: A Retrospective Comparison of Efficacy and Safety in Patients Above and Below 45 Years of Age

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Introduction: In older patients, multiple sclerosis (MS) treatment is challenging due to comorbidities and infection risk. Cladribine's intermittent dosing and durable effect may benefit those over 45. However, more data are needed on its long-term safety in this group.
Objectives/Aims: To evaluate the efficacy, safety, and tolerability of cladribine in MS patients aged ⩾45 years, compared with those aged <45 years.
Methods: A retrospective study was performed based on medical records of patients treated with cladribine at Unidade Local de Saúde São João between 2023-2025. Patients were divided into two age-based cohorts (<45 (group 1) and ⩾45 (group 2) years). Primary outcomes included changes in disability progression measured by EDSS and incidence of serious adverse events. Secondary outcomes included MRI lesion activity, treatment discontinuation, tolerability, immune response, and time to first relapse.
Results: A total of 49 patients were included, with 17 in group 1 and 32 in the group 2. The median age in group 1 was 31 years old and in group 2 was 49 years old. Both groups exhibited a higher prevalence of female participants, with 21 patients in group 1 (65.6%) and 14 patients (82.4%) in group 2. No statistically significant differences in EDSS progression were observed at 1, 2, 3, or 4 years. Five (15,6%) patients in group 1 showed disease progression while on treatment with cladribine, as did four (23,5%) patients in group 2. Three patients (9,4%) in group 1 and two (11,8%) in group 2 experienced adverse effects, all of which were mild. No patient discontinued treatment due to adverse effects.
Conclusion: Cladribine appears to be an effective and well-tolerated treatment for MS in patients over 45 years of age, with comparable clinical and radiological outcomes to younger patients. These findings support its continued use in older populations. Further prospective studies are warranted.

Disclosure of interest: Teresa Durães: nothing to disclose

P1816
Early Morbimortality in Autologous Hematopoietic Cell Transplantation Performed on Outpatient Basis in Persons with Autoimmune Diseases: Experience in 1700 Patients

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Introduction: Autologous hematopoietic cell transplantation (aHCT) has been recognized as a viable therapeutic approach in patients with autoimmune diseases as it purportedly "resets" the immune response by abrogating autoreactive immune cells, among other effects. Multiple sclerosis (MS) appears to derive benefit from aHCT.
Objectives/Aims: Analyze the salient features of early post-aHCT complications when performed in the outpatient setting in 1700 patients with MS treated in the Mexico HSCT program. The primary endpoints were early morbi-mortality-free survival (MFS) and overall survival (OS), whereas secondary endpoints entailed hospital admissions, neutropenic fever, MS flare-up, development of pneumothorax, hyponatremia and myocarditis.
Methods: Persons with autoimmune diseases autografted in the HCT-Mexico program from June 2015 to August 2024, were included. The transplant started on an outpatient basis in all cases, following the "Mexican Method" conditioning regimen consisting of intravenous (I.V.) cyclophosphamide (200 mg/Kg, total dose, divided equally in four doses: days -11, -10, -2 and -1), filgrastim, MESNA, and rituximab (1000 mg). The prophylactic treatment consisted of oral cotrimoxazole, acyclovir, itraconazole, ondansetron, I.V. dexamethasone (4 mg on days -11, -10, -2 and -1), and oral dexamethasone (0.5 mg days -9, -8. -7, 0, +1 and +2).
Results: 1,700 consecutive aHCT recipients were analyzed: 1,667 with MS, 29 with CIDP and 4 with other autoimmune diseases. 1,643 procedures (96.6%) were fully performed in the outpatient setting. Two patients died due to septicemia during the neutropenic nadir; the causative agents were Klebsiella pneumoniae and Aeromonas veronii; one patient died due to pulmonary embolism. A central catheter was surgically placed in 1,632 cases (96%). In 12 patients (0.7%), a pneumothorax developed during the insertion and was resolved with a chest tube. 129 (7.58%) patients developed neutropenic fever for more than 48 hours; in all instances, an oral quinolone was added to the treatment, and 40 required to be admitted to the hospital to receive I.V. antibiotics (carbapenems). 21 (1.23%) patients developed hyponatremia and 2 were admitted for I.V. sodium correction. 45 patients (2.64%) had a MS flare-up which warranted steroid treatment; 2 were admitted to the hospital. One patient developed reversible acute myocarditis and was also admitted to the hospital (0.05%). The 30-day OS of the cohort was 99.8%, and the 30-day early MFS was 87.7%. The 30-day MFS has increased from 94.9% in the first 5 years to 98.2% in the last 5 years ($p = 0.0002$).
Conclusion: Following the "Mexican Method" in cases of autoimmune diseases is a safe procedure and could be conducted on outpatient basis. The 28-day mortality was 0.17%, whereas the 28-day morbidity was 3.3%. The rate of early complications

decreased over time, most likely reflecting a learning curve effect.

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P1817
Real-World Symptom Reporting and Treatment Trends in Brisa: A German Digital Health App for MS Patients

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Introduction: Digital companion apps like Brisa, tailored for MS patients, can aid the patient journey by collecting longitudinal data on real-world experiences of MS patients.
Objectives/Aims: This study aimed to describe Brisa users' demographics, health characteristics, treatment preferences, user activity, symptom reporting, and longitudinal symptom trends.
Methods: This retrospective analysis included Brisa users registered between August 6, 2021, and March 23, 2025, aged ⩾18 years, reporting category 1, 2, or 3 medication use (based on DGN guidelines), with no medication switching history. Users diagnosed within 0–1 years at registration were identified to approximate newly diagnosed cases. User activity was proxied by any screen activity. Symptoms were rated on a 1–5 smiley scale (1 = poor, 5 = excellent).
Results: Of 8,230 consenting users, 4,100 met the inclusion criteria. The majority were aged 36-45 (31.0%), female (80.8%), and diagnosed with relapsing-remitting MS (77.5%). Most had been diagnosed for 2-5 years (37.6%) and were on category 1 (43.2%) or category 3 medication (41.7%).
Category 1 medication was used by 43.2%, category 2 by 15.1%, and category 3 by 41.7%, with ocrelizumab being the most common category 3 medication (53.2%). The use of category 3 medications among newly diagnosed users increased significantly from 2023 (χ^2, $p < 0.0001$).
User activity decreased over time; 99.0% used the app within the first 3 months post-registration, dropping to 11.3% after 3 years. Users on category 3 medications were more likely to remain active after 2-3 years (category 1 vs. category 3: χ^2, $p < 0.001$; category 1 vs. category 2: χ^2, $p < 0.05$).
78.0% of users reported on at least one symptom. Most frequently, users reported on fatigue (61.0%), concentration disorders (52.8%), tingling (49.4%), forgetfulness (47.0%), and numbness (40.5%). Population-level mean symptom scores remained stable, with minor changes over three years. Among users reporting symptoms for at least two years, fatigue scores increased from 2.74 (year 1) to 2.91 (>2 years; paired *t* test, $p < 0.05$), and forgetfulness decreased from 3.42 (year 1) to 3.31 (>1-2 years; paired *t* test, $p < 0.05$).
Conclusion: A shift towards higher efficacy treatments in newly diagnosed users was observed, while symptom scores remained largely stable across medication categories. These findings highlight the potential of digital health tools for tracking treatment patterns and symptom progression, providing key insights for enhancing MS care.

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P1818
Satralizumab for the treatment of neuromyelitis optica spectrum disorders: a single center real life experience

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Introduction: Neuromyelitis optica spectrum disorders (NMOSD) is a rare inflammatory central nervous system disease which has historically been treated with rituximab (RTX). A better understanding of the pathogenesis of NMOSD has led to the recent introduction of new well-targeted preventive immunotherapies. Among them satralizumab is a an anti-IL6 receptor monoclonal antibody approved for AQP4 antibody positive patients switching from RTX for inefficacy or adverse events.
Objectives/Aims: To report our real-life single center experience.
Methods: We retrospectively collected data from all patients receiving satralizumab for NMOSD at our center. Demographic, clinical and radiological information was obtained
Results: 8 NMOSD patients (7 females) were enrolled. Median age at satralizumab initiation was 50,8 years (range: 30,7-71,8),

median disease duration was 15,4 years (range: 9,1-30,7), median EDSS was 4 (2-6,5). Last therapy before satralizumab was tocilizumab in 5/8 patients and rituximab in 3/8 patients. Among patients previously treated with tocilizumab 3/5 had been treated with rituximab and 2/5 had been treated with autologous haematopoietic stem cells transplantation. In patients treated with tocilizumab (off-label), reason for switch to satralizumab was shift to in label drug, in one patient switching from rituximab motivation for switch was inefficacy and in the other two patients switching from rituximab motivation for shift was safety (hypogammaglobulinemia with recurrent infections). Over a median follow-up in satralizumab of 1,9 years (0,27-2,19) all patients remained clinically stable with a median EDSS of 4 (2-6,5) and no radiological disease activity was observed. For patients switching from tocilizumab the global follow-up in anti-IL6 receptor monoclonal antibody was of 9,5 years (3,3-11).

The drug was well tolerated with retention rate of 100%. The only adverse events were transient liver enzymes increase, mild neutropenia, mild-moderate infections.

Conclusion: In conclusion in our small experience, satralizumab has proven to be effective and safe for the treatment of patients with NMOSD. Among our patients 5/8 had been treated with anti IL-6 receptor monoclonal antibody (tocilizumab followed by satralizumab) for a long period of time with sustained efficacy and safety. More data are needed to confirm these findings.

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P1819

The impact of subcutaneous administration of natalizumab on its efficacy in real world conditions – Pharmacokinetics and pharmacodynamics of natalizumab during intravenous to subcutaneous switch

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Introduction: Natalizumab (NAT) is a highly effective immune modulating drug in the treatment of relapsing-remitting multiple sclerosis (RRMS).

Since its approval in 2006 NAT has been administered by intravenous (iv) infusion. In 2021, subcutaneous (sc) injection of NAT was approved as a more time-efficient and patient-friendly alternative. Current studies primarily compare pharmacokinetics (PK) and pharmacodynamics (PD) between different administration cohorts.

Objectives/Aims: This single-center study focuses on changes in serum NAT levels and very late antigen-4 (VLA-4) saturation in MS patients switching from iv to sc administration under real-world conditions, including varying medical appointments.

Methods: 54 patients were enrolled, including those with standard dose interval (SDI) and those with extended dose interval (EDI, 6-week-interval). Blood samples were collected at maximum three-month intervals, at least 8 months before and 12 months after switching the administration route. Serum NAT levels and drug neutralizing antibodies (dnAB) were measured using a HL60-cell based FACS assay. VLA-4 saturation levels of peripheral blood mononuclear cells were assessed by FACS analysis detecting CD49d and cell-bound IgG_4.

Testing for dnAB was performed in case of particular serum level changes.

Results: Shifts of PK and PD induced by switching from iv to sc administration were heterogeneous. 41 patients (75.9%) showed a decrease in serum NAT levels, averaging about 69.5% of iv NAT levels, upon sc administration. In 13 patients (24.1%) increased serum levels were detected. One patient with EDI showed a 99.67% decrease in serum NAT levels after switching to sc administration, though no clinical effects were observed in terms of EDSS or relapse rate.

No patients developed dnAB.

Conclusion: A trend toward reduced VLA-4 saturation and serum NAT levels was observed following the switch from iv to sc administration. Clinical parameters concerning EDSS and relapse rate appear unaffected as well as the development of neutralizing antibodies.

Due to the high variability of serum NAT levels and VLA-4 saturation levels no clear prediction about individual performance of NAT sc can be made. A longer study period is necessary to better evaluate the long term impact of NAT sc on disease activity.

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P1820

Long-term effects of treatment with cladribine tablets on cognition and treatment satisfaction in people with relapsing multiple sclerosis: 4-year results from the non-interventional CLADQoL study

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Introduction: CLADQoL (CLADribine tablets – evaluation of Quality of Life) was a non-interventional, multicenter study in Germany and Austria including people with highly active relapsing multiple sclerosis (pwRMS) treated with cladribine tablets (CladT) and focusing on quality of life (QoL).
Objectives/Aims: To evaluate changes in cognitive functioning (CF) and treatment satisfaction (TS) over 4 years upon treatment initiation with CladT.
Methods: Changes in CF were assessed by a change in the Symbol Digit Modalities Test (SDMT) from baseline (BL) to Month (M) 24 and M48 using at least 4- or 8-points difference. Additionally, SDMT scores were standardized (Z-scores) according to age and level of education, and used for assessment of cognitive impairment (none, tendency, marginal, impaired). In addition, changes in TS were assessed by the Treatment Satisfaction Questionnaire for Medication (TSQM) Version 1.4 from BL to M6, M18 and M48.
Results: Overall, 305 patients (70.8% female; mean ±SD age 38.1 ± 9.9 years; disease duration 8.3 ± 7.3 years; 95.4% RRMS; median EDSS 2.0) were included in the analysis. 85.6% of patients received prior MS medications.
SDMT performance improved (with ⩾ 4-points) or was stable in 77.6% (n=97) participants at M24, and 72.9% (n=78) at M48. 8-point improvement or stability was observed in 88% (n=110) at M24, and 76.6% (n=82) at M48. The proportion of participants with no cognitive impairment (based on Z-scores) increased from 45.6% (n=99) at BL to 58.7% (n=84) at M24, and maintained until M48 with 53.5% (n=61).
The cognitive impairment was slightly reduced until M24 as seen by slight decrease in proportion of participants with clinically noticeable status (Z-score ⩽ -1.65) from 20.5% (n=44) at BL to 13.3% (n=19) at M24.
Steady increase in overall TS measured as Global Satisfaction Score from TSQM V1.4 was observed through M6 and M18, with mean ±SD change from BL to M18 reaching 9.5 ±26.54 and Cohen`s effect size (ES) of 0.36. By M48, mean ±SD change from BL was 8.3 ±29.80.
The mean annualized relapse rate was low: 0.03 or 0.04 during 24 or 48 months, respectively. No new safety concerns were detected in terms of rate, profile and severity of adverse events.
Limitation: high rate of missing data
Conclusion: The CLADQoL study demonstrated sustained benefits of CladT treatment on cognition and treatment satisfaction, 4 years after the initial dose of CladT.

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P1821

Patient-Reported Outcomes Following the Switch to Subcutaneous Ocrelizumab in South West Wales

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Introduction: Ocrelizumab is an anti-CD20 therapy licensed for the treatment of relapsing remitting and primary progressive

multiple sclerosis (MS). Ocrelizumab has been available in the UK since 2018, administered as an intravenous (IV) infusion. The subcutaneous (SC) formulation, administered as a single 920mg dose every 6 months, offers the advantage of administration over 10 minutes, compared to 2 to 3.5 hours for the IV infusion, potentially improving infusion suite capacity by reducing treatment time. A new marketing authorisation was granted on July 2024 in the UK. However, patient-reported outcomes following the switch to SC remain sparse.

Objectives/Aims: To obtain patient feedback from people living with MS in South West Wales who switched from IV to SC ocrelizumab.

Methods: We conducted a service review of people with MS who were treated with IV ocrelizumab and had switched to the SC formulation to determine their satisfaction with the switch and any side effects. These patients were contacted by phone to fill out a Microsoft Form.

Results: Between 01/09/2024 and 01/04/2025, 162 number patients received ocrelizumab of whom 81 patients chose to switch to SC. 74.1% (60) were female, the mean age was 43.4 years (range: 24–65). The average time on IV ocrelizumab before switching to SC ocrelizumab was 1248.5 days (SD = 691.9), with an average of 6.01 IV ocrelizumab doses (SD=3.33). Patients had all received at least 1 dose of SC ocrelizumab before being contacted (mean:1.02 doses, range:1-2). 48/81 patients responded to the questionnaire.

Overall satisfaction with the SC formulation was positive, 39/48 were "very satisfied" or "satisfied", 4 "neutral", 5 "dissatisfied" or "very dissatisfied". The majority of patients found the subcutaneous formulation more convenient (46/48 responded "much more convenient" or "slightly more convenient). 36/48 patients experienced side effects, including local redness, swelling and pain, of which 14 were rated as "mild", 18 as "moderate" and 4 as "severe". 40/48 said they would prefer to continue the SC formulation, 6 said they would prefer to switch back.

Conclusion: Half of patients established on ocrelizumab, choose to switch to SC dosing within the first 6 months. 81% were satisfied with the switch with only 6% of patients switching back to IV, predominantly related to local injection reactions. Introduction of SC dosing has been well tolerated and appreciated by the majority of patients. It has eased access to the service, freeing capacity and allowing quicker treatment of new patients.

Disclosure of interest: Charles-Henry Her: Received honoraria and travel expenses from Roche and Merck. Received travel expenses from Argenx. Served on an advisory board for Roche and Merck; Alexandra Strong: received honorariaRoche, Biogen, Eisai, HCRW REC Committee; Dr. Marguerite Hill has contributed to advisory boards for Argenx and UCB pharma. She has accepted hospitality from Argenx, UCB, Janssen-Cilag and Merck; Dr. Gillian Ingram has received honorariam, speakers fees and travel expenses from Biogen, Jazz Pharmacuiticals, Merck, Novartis and Roche; Dr. Owen R Pearson: Received honoraria and travel expenses from Biogen, Bayer, Genzyme, Merck, Novartis, Roche, Sanofi and Teva and served on advisory boards/ acted as a speaker for Biogen, Bristol Myers Squibb, Janssen-Cilag, Merck, Neuraxpharm, Novartis, Roche and Sanofi.

P1822

Real-world experience with second-generation S1P receptor modulators in relapsing multiple sclerosis: a prospective observational study

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Introduction: Second-generation sphingosine-1-phosphate (S1P) receptor modulators (Ponesimod and Ozanimod) are approved for relapsing multiple sclerosis (RMS) with evidence of clinical or radiological activity. Real-world data on their use, safety, and effectiveness remain limited.

Objectives/Aims: To describe the clinical characteristics, safety profile and treatment outcomes of RMS patients treated with S1P drugs in routine clinical practice.

Methods: Prospective observational study including RMS patients initiating these treatments between September 2022 and April 2025. Demographic and disease-related data, changes in scales (EDSS, SDMT, T25FW, 9PHT, PROs) and lymphocyte counts were collected.

Results: Thirty patients were included (60% male, mean age 44.7 years, mean EDSS 1.9, mean disease duration 12 years [0–33]). Fifteen received Ponesimod and fifteen Ozanimod. Median number of prior treatments was 1 (0-3); 56% showed radiological activity and 0.46 relapses in the previous year. Six patients discontinued treatment (three due to maintained lymphopenia, three by personal choice).

Mean lymphocyte count decreased by 51% at 1 month in Ponesimod group (baseline: 1200/mm³), with slight recovery at 6 months (43%), 12 months (40%) and 24 months (29%). In Ozanimod group, reductions were also sustained (51%, 67%, 55% and 48/% at each timepoint, respectively, from baseline 1490/ mm³).

After 12 months, 13 Ponesimod-treated patients were relapse-free, with a slight EDSS improvement (−0.19) and 1 patient had mild MRI activity. At year 2 (n=9), no relapses o new lesions were detected, with a mild improvement in EDSS (-0.39). Among 13 Ozanimod-treated patients after 1 year, one mild relapse and mild EDSS worsening (0.25) occurred, without MRI progression.

At 12 months, worsening in SDMT, fatigue (FSMC) and quality of life (EQ-5D-3L) was observed in a subset of patients (8 Ponesimod, 4 Ozanimod).

Conclusion: Ponesimod and Ozanimod showed expected lymphopenia while maintaining clinical-radiological stability. Patient-reported outcomes were generally stable, with fatigue and SDMT worsening observed in a number of cases.

Disclosure of interest: L. Garcia-Vasco received honoraria as a speaker from Merck, BMS and Novartis; and received support for attending meetings and congresses from BMS, Horizon, Janssen, Novartis and Sanofi. I. Gómez-Estévez received travel support or honoraria for conferences from Bristol Myers Squibb,

Janssen, Merck, Novartis and Viatris. C. Oreja-Guevara received honoraria for speaking, consulting and serving on advisory boards from Alexion, Amgen, Biogen Idec, BMS, Horizon, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme, Sandoz, Viatris, Neuraxpharm and Teva. L. Aguilera-Carretero, M. García-Rama and C- Bullón-Sánchez have nothing to disclose.

P1823
Real-world clinical practice data on the effectiveness and tolerability of Ofatumumab

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Introduction: Fatigue results in disability in patients with multiple sclerosis (MS). Real - world evidence on the role of highly effective disease-modifying treatments (DMTs) on fatigue is lacking.
Objectives/Aims: To evaluate the effectiveness and tolerability of Ofatumumab and to analyse the evolution of disability and fatigue.
Methods: A retrospective observational study was conducted on patients with multiple sclerosis (MS) treated with Ofatumumab between December 2022 and January 2025. Demographic, clinical, and radiological variables were assessed during follow-up, including Expanded Disability Status Scale (EDSS), Modified Fatigue Impact Scale (MFIS), and variables of effectiveness and tolerability/safety.
Results: We included 127 patients with MS: 120 (94.5%) with relapsing-remitting MS and 7 (5.5%) with secondary-progressive MS. Mean baseline age was 39.4±9.9 years. Most patients switched to ofatumumab due to ineffectiveness of previous treatments (69/114, 60.5%). There were no discontinuations after a mean follow-up of 14±7.6 months. Only 2/80 (2.5%) showed new MRI lesions after 6-month follow-up, and 9/65 (13.8%) showed EDSS worsening at 12-month follow-up; 6/9 (66.7%) due to Progression Independent of Relapse Activity (PIRA), 2/9 (22.2%) due to Relapse-Associated Worsening (RAW), and 1/9 (11.1%) due to postpartum. Adverse events occurred in 63/108 (58.33%), mostly after the first dose 46/63 (73.02%).The most common was flu-like syndrome 64/51 (79.7%). No significant differences were found in EDSS at baseline (n=126, 3.18±1.74), 6-month follow-up (n=102, 3.16±1.81) and 12-month follow-up (n=65, 3.10±1.80; p=0.084). Significant differences were found in MFIS at month 6 (n=75, 36.54±24.44) and month 12 (n=49, 36.38±23.64) compared to baseline (n=95, 40.69±20.27; p=0.019). However, differences were not found among groups.
Conclusion: Ofatumumab was effective and showed good tolerability and safety data. Improvement in fatigue is reported at 6 and 12 months of follow-up. Although promising, this should be further investigated in the future.

Disclosure of interest: Author's Adelaida Cuenca Relinque: nothing to disclose.

P1824
Impact of natalizumab on cognitive, functional, social, and psychological outcomes in people with MS: results from the prospective multicentre real-world TYPIFI study

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Introduction: Patient-reported outcomes and quality of life measures are increasingly recognized as essential since they provide a more thorough overall insight on the consequences of multiple sclerosis (MS).
Objectives/Aims: To evaluate the effect of natalizumab, on cognitive, functional, social, and psychological outcomes in people with MS (pwMS).
Methods: This was a 48-month prospective, observational study including relapsing-remitting MS (RRMS) pwMS from nine Portuguese centres. Participants were aged 18-55 years, with EDSS ⩽3.0 and were starting natalizumab as first or second disease modifying treatment. Data on demographics, clinical characteristics, and treatment were collected. Cognitive function, fatigue, psychological well-being, and social/functional impact were assessed using validated instruments. A

p-value of <0.05 was considered statistically significant in all analyses.

Results: Sixty patients were included (80.0% females; mean age of 31.9±8.1 years). PwMS had RRMS for a mean of 4.3±5.6 years; baseline EDSS was 1.8±0.7; annualized relapse rate was 1.32. At 12-month, 97.8% achieved clinical no evidence of disease activity (NEDA3), which remained high throughout the study. PwMS performed better at the Symbol Digit Modalities Test at 36-month vs baseline (median±IQR: 57.5±16.5 vs 45.0±12.5; p=0.01). Fatigue levels decreased significantly over the first three years. The MS impact scale score showed a significant improvement at 12 and 18-months. While on natalizumab, the impact of MS on work productivity and activity was small, with an improvement of the percentage of time worked at 48 months, 100.0%, versus 86.1% at baseline (p=0.022). At 49 months, 68.8%of patients were working/studying compared to 62.5% at baseline ($p>0.05$). Additionally, depressive symptoms (Beck Depression Inventory-II) significantly decreased at 24 months vs baseline (median±IQR: 4.5±7.5 vs 8.5±3.2; p=0.011).

Conclusion: This real-world study adds evidence on natalizumab long-term effectiveness not only in disease control but also in improving important patient-centered outcomes that should be considered when making treatment decisions in routine clinical practice.

Disclosure of interest: PA participated in advisory board and gave consultancy to Biogen, Novartis, Merck, Roche, Sanofi; participated as investigator in clinical trials sponsored by Novartis, Merck, and Biogen. CCN participated in advisory board from Biogen, Novartis and Merck and participated as investigator in clinical trials sponsored by Roche, Novartis and Merck. AM received honoraria from Merck, Biogen and Bristol Meyers Squibb. JS received honoraria from Merck, Roche and Biogen. AT participated in advisory board from Roche, Novartis and Merck and participated as investigator in clinical trials sponsored by Roche and Novartis. JC participated in advisory board and gave consultancy to Biogen, Bristol MyersSquibb, Novartis, Merck, Roche, Sanofi and Sandoz; participated as investigator in clinical trials sponsored by Roche, Novartis, Merck, Bristol Myers Squibb and Sanofi. FC, MJS, RG, AS, CF, CS and SP have nothing to disclose.

P1825
Profile of patients over 50 years old treated with cladribine: our real-world experience

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Introduction: In recent years, cladribine is positioning itself as an alternative for patients over 50 years old. In this study, we present our real-life results in this age group.

Objectives/Aims: To describe the phenotype of patients over fifty years of age treated with cladribine.

Methods: A retrospective, single-centre study of all patients over fifty who received cladribine at our institution, according to Hospital Pharmacy records. Demographic characteristics, comorbidities, prior therapies, treatment response, and safety were analysed.

Results: Of 78 patients treated with cladribine, 21 were over 50, with a median age of 55.48 years (IQR 52.91–60.95) and a female predominance (76.19%). The most common comorbidities were hypertension and dyslipidaemia. A total of 23.81% of patients were treatment-naïve. Median number of prior disease-modifying therapies was 2 (IQR 1–3), with interferons being the most frequently used. The main reason for switching to cladribine was lack of efficacy. The median baseline EDSS was 4 (IQR 2.5–5). Only seven patients completed both cycles, with a median follow-up of 9.76 months (IQR 5.59–20.93). Cladribine was initiated in 61.90% of patients during 2024–2025. In the year prior to treatment, 42.85% experienced clinical relapses and 42.85% had radiological activity, which decreased to 4.76% and 9.52%, respectively, in the first year. The median EDSS improved by 0.5 points during follow-up. Six patients (28.57%) developed Grade I or higher lymphopenia. Statistically significant differences were found in comorbidities, EDSS, and prior DMTs compared to the younger cohort.

Conclusion: Cladribine prescriptions for patients over 50 have increased. This age group shows more comorbidities and baseline disability compared to younger patients. Multicentre studies are needed to guide therapeutic decisions and ensure a proper risk-benefit balance.

Disclosure of interest: Nothing to disclose

P1827
Biologic Switching Within One Year Following an Attack in Neuromyelitis Optica Spectrum Disorder (NMOSD): A Retrospective Study

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Introduction: Relapse risk is highest within the first year after an attack of neuromyelitis optica spectrum disorder (NMOSD), highlighting the importance of early relapse prevention. Targeted biologic therapies have significantly reduced relapse rates, but differences in therapeutic onset among agents require careful consideration when switching treatments. However, data on switching biologics within one year of an attack remain limited.

Objectives/Aims: To evaluate the safety and outcomes of biologic switching within one year after an NMOSD attack, focusing on relapse prevention and treatment strategies.
Methods: We retrospectively reviewed NMOSD patients followed at St. Marianna University School of Medicine who had switched biologics by March 2025. Cases with switching within one year of an attack were included. Clinical data included patient background, biologics used, oral prednisolone (PSL) dosage at switching, presence of pre-treatment, and relapse occurrence after switching.
Results: Among 13 patients with 20 biologic switches, 6 switches in 6 patients occurred within one year of an attack. One patient switched from eculizumab to ravulizumab, and two from rituximab to inebilizumab (within-class switches), all without relapse or pre-treatment. Three patients switched from complement inhibitors to inebilizumab. One received plasma exchange prior to switching and had no relapse. Of the two who did not receive pre-treatment, one relapsed while on 15 mg/day PSL and had a history of seven relapses, while the other, in the post-initial attack phase and on no PSL, remained relapse-free.
Conclusion: Switching from complement inhibitors within one year of an NMOSD attack requires caution due to underlying disease activity and drug mechanisms. In high-activity cases, pre-treatment such as plasma exchange may support safer transitions between therapies.

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P1828
The AIMS project - How Artificial Intelligence can help people understand systematic reviews on complementary therapies for Multiple Sclerosis

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Introduction The AIMS-Project investigates how Artificial Intelligence (AI) can support people in understanding systematic reviews on complementary therapies for Multiple Sclerosis (MS). AIMS is a citizen science project led by a core team comprising a citizen partner and researchers.
Objectives/Aims: To explore how AI, in particular Large Language Models (LLMs), can support people living with MS

(PwMS) to better understand systematic review abstracts, and to identify the key needs, wishes, concerns, and questions regarding the use of AI to translate scientific content into plain, accessible language.

Methods: This project employs participatory research approaches. It is informed by the evidence and gap map on complementary therapies for PwMS, available at: https://digital-health-space.ch/en/gap-map-english. A series of co-creative workshops will be conducted with stakeholders including PwMS, health care professionals, researchers, AI experts, etc., to foster dialogue and gather insights into the usability and trustworthiness of AI-generated content. If a workshop at ECTRIMS is not feasible, we are open to present our findings as an oral presentation or poster.

Results: Preliminary observations by our citizen partner Birgit Bauer (Data Saves Lives, Germany), who lives with MS and is an international expert in patient communication, show that PwMS are generally open to using digital tools such as LLMs. However, there is a notable knowledge gap regarding effective use and critical evaluation of these tools, underscoring the need for enhanced digital health and data literacy.

Conclusion: People with MS need support, information, and digital literacy to make informed decisions with their health professionals. AI tool scan supports this process. The AIMS project promotes co-creation and empowerment, and the proposed session aims to advance the understanding and application of AI in patient education.

Disclosure of interest: Birgit Bauer: nothing to disclose

P1829
TRUSTED: Trials and Registries Unified Sign-up Tool for Equitable Discoveries

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Introduction: MS registries can answer countless questions about the condition, its investigation and treatment. Yet, amongst 150,000 people living with MS in the UK, <1% are consented to MSBase and <5% have the minimum clinical dataset in the UK MS Register.

Trials of new drugs typically take years to recruit despite strong appetite from people with MS.

Many registries and trials recruit ungeneralisable populations, worsening healthcare inequalities.

Objectives/Aims: To transform registries and trials by empowering people with MS to participate instead of relying on busy clinicians. Here, we present pilot data from the first 4 hospital sites.

Methods: We built an ethically approved national sign-up tool, TRUSTED (www.trusted.org.uk). By completing this single form (online or paper), people with any neuroimmunological condition can consent to MSBase, the UK MS Register, locally approved observational studies, a trial eligibility checker and a new national inequalities study (RIGHT-MS).

To pilot TRUSTED, all people with MS under the care of Cambridge, Ipswich, Frimley and Wexham hospitals were invited to participate.

Results: From the 4 pilot sites, 1372/3224 people (42%) participated including 1366 joining MSBase (doubling the entire UK cohort; previously 0 participants at these sites) and 1070 new participants joining UK MS Register (previously 1112 participants at these sites).

1368 people joined the TRUSTED trial eligibility checker, which increased the consent rate of an ongoing remyelination study by 71% and enabled prioritised recruitment of under-served groups.

1370 people completed the RIGHT-MS inequalities study including participants from 61/65 NIHR-defined under-served groups (see Soares-Regua et al, ECTRIMS 2025).

Conclusion: We built a national research sign-up tool, TRUSTED, which has now empowered more than 3,000 people with MS from 9 sites to participate in research, including tripling the UK's contribution to MSBase.

We invite new sites – and all UK people with MS - to join TRUSTED by visiting www.trusted.org.uk

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P1830
Observational study in clinical practice to compare Ocrelizumab vs Ofatumumab in relapsing multiple sclerosis: 2 years follow up

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Introduction: Ocrelizumab and Ofatumumab share the same target CD20+ cells,there are some differences between them: the epitope to which they bind on the CD20+ lymphocyte, route of administration and dose. There are doubts about if that imply differences in effectiveness or safety. In a previous study we analyze the effectiveness of both drugs and compare them in two cohorts of Relapsing MS.We didn,t find differences between them.

Objectives/Aims: To analyze the cohort with two years of follow up.We evaluate: clinical and radiological effectiveness, CD19+ lymphocyte subpopulations levels, safety, tolerability and differences in the profile of use of the drug.

Methods: Single-center retrospective non-interventional longitudinal analytical observational study. We created through multivariate analysis,two similar groups of patients of Ocrelizumab and ofatumumab,to be able to homogenize them and make an adequate comparison. For the selection of these patients, the following baseline variables will be taken into account:Age, relapses, EDSS, T2 load on MRI, number of Gd+ lesions in MRI and duration of MS

Results: We Analyze123 patients treated with Ocrelizumab and 28 treated with Ofatumumab. After adjustment, both groups of 28 patients are balanced: moderate/high T2 lesions, basal relapse rate (Ocrelizumab 1,08 vs Ofatumumab 0,85), 29-25% naïve patients, EDSS 2.3 in both groups and 6.8-5.2 years of disease evolution. After 2 years of treatment rate relapses decreased in both groups: year 1 Ocrelizumab 0,11vsOfatumumab 0,15;year2 Ocrelizumab 0,03vs ofatumumab 0).Regarding MRI:Ocrelizumab: T2 lesions year 1 0,15, year 2 0 without Gd+lesions; Ofatumumab: T2 lesions year 1:0,3, year 2:0, Gd+ year 1: 0,07 year2:0.

Six patients switch the treatment in the first year in Ofatumumab group, 2 of them due to lack of efficacy. None patient switch treatment in ocrelizumab group.

We observed in mean of CD19+ cells: Ocrelizumab year1: 8,26, year 2: 3,98; Ofatumumab year 1 0,75 year 2 0,4. We have a bias in this determination:we measured CD19+ cells before each ocrelizumab dose, and at a random moment in Ofatumumab. EDSS keep stable.

Conclusion: Both treatments were effective, reducing the relapse rate and MRI lesions in the first 2 years. We observed more drop out in Ofatumumab group. We dindnt observe a clear correlation between Cd19+ levels and relapses, but we need more data. After observing CD19+ dynamic we conclude probably will be necessary adjust in each patient the time of Ocrelizumab administration. Both drugs were safe.

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P1831
Effect of a therapeutic patient education program on treatment adherence over time

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Introduction: The effectiveness of disease-modifying therapies used in multiple sclerosis relies on good adherence. Numerous tools, based on knowledge of the disease, have been created to improve the management of MS patients. Most show a positive effect on quality of life, anxiety and the ability to make informed decisions. This study evaluates the interest of a multidisciplinary therapeutic education program (TEP) conducted by a MS network on treatment adherence in relapsing-remitting (RRMS) and secondary progressive (SPMS) patients.
Objectives/Aims: The aim of the study was to evaluate the impact of a TEP program administered by a nurse, a social worker and a psychologist, in the 3 months preceding or in the month following the start of the treatment, on compliance, by comparing patients who participated to a TEP and no participation.
Methods: We analyzed retrospectively treatment-naive MS patients who started a 1st-line treatment between 2001 and 2011. The program offers several workshops on learning about the disease, communicating better with those around you, managing emotions, fatigue or stress, advices on diet and information on social rights. Therapeutic education on the chosen treatment completes this information. Only the fisrt workshop and the therapeutic education were mandatory. Data were analyzed using pvalue software.
Results: N=264 patients were included in the study: 95 patients received TEP and 169 did not. At 6 months of treatment, the percentage of treatment discontinuation was significantely lower for patients who had received TEP vs those who had not (19% vs 81% $p<0.05$). There was no significant difference at 12, 18 or 24 months). The impact of TEP was tested on the reasons for discontinuation of treatment (intolerance and inefficiency) and no significant difference was found, although a positive trend was observed.
Conclusion: The use of a multidisciplinary therapeutic education program in multiple sclerosis reduces the risk of treatment discontinuation at 6 months

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P1832
Patterns of initial disease modifying therapy selection over 25 years at a multiple sclerosis referral center

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Introduction: Over twenty disease modifying therapies (DMT) have been approved in MS, but investigations into patterns of real-world use as first-line therapy are limited.
Objectives/Aims: To describe the patterns of initial DMT use in a tertiary MS center over 25 years from 1998 to 2023.
Methods: We retrospectively collected electronic health records from a large academic MS referral center. The inclusion criteria were ⩾2 occurrences of ICD-9/10 G35 (MS) or consented participation in MS research studies. We applied a large language model (llama3.3, 70.6B model) on office visit notes to systematically extract initial DMT and associated start year. The investigated DMTs included 18 approved and 1 off-label (rituximab) therapies and were classified into 3 classes: platform injectable (interferons and glatiramer acetate), oral (S1P receptor modulators, fumarates, cladribine, and teriflunomide), and high-efficacy monoclonal therapies (alemtuzumab, natalizumab, and B-cell depleters). Lastly, we obtained the normalized frequency between 1998 and 2023. The proportions of 3 classes were analyzed using the Cochran-Armitage test for trend in proportions.
Results: Of the 9767 eligible patients, 1728 were excluded due to limited data; 628 were never on DMT; 482 started DMT <1998 or >2023. 6929 patients were analyzed. The mean (standard deviation [SD]) age at the initiation of first DMT was 39.5 (11.3) years and 72% were female. The median (interquartile range) annual number of patients analyzed was 263 (201- 325).
In 1998, all DMTs were the platform injectables (100%). In 2015, DMT proportions included 44% platform injectables, 46% oral, and 11% high-efficacy monoclonal therapies. In 2023, the proportions changed to 1% platform injectables, 14% oral, and 86% high-efficacy monoclonal antibodies. The Cochran-Armitage test showed significant trend in proportions ($p<0.001$).
Conclusion: Three distinct periods of DMT use were identified, one with preponderance of injectables, followed by a period of oral therapies, and finally monoclonal antibodies. The highly effective monoclonal therapies have become the most common first-line DMT in MS, and an escalating approach was uncommon at our tertiary care center in 2023.

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P1833

Real world clinical experience from ENABLE, the first Phase 4 observational study for patients with relapsing multiple sclerosis initiating ublituximab

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Introduction: Ublituximab (UBL) demonstrated significant reduction in MS disease activity vs. teriflunomide in two Phase 3 studies- ULTIMATE I and II. ENABLE (NCT06433752) is the first prospective phase 4 observational study to assess the real-world efficacy, tolerability and safety in patients treated with ublituximab.

Objectives/Aims: To evaluate the real-world clinical experience of patients with relapsing MS treated with ublituximab.

Methods: The analysis included 177 participants enrolled in ENABLE from the start of study (July 2024) until the data cut of February 2025. This real-world cohort was used to summarize the baseline demographics, disease history, prior disease-modifying therapy (DMT) use, and clinical outcomes on ublituximab. Patient enrollment is ongoing with a goal of at least 500 participants.

Results: The patient demographics of the real-world cohort constitutes a slightly older population (mean age 42.8 years vs 35.4 years in ULTIMATE) with a higher proportion of female participants (72.9% vs. 62.9% in ULTIMATE). Black/African American population represents 19.8% and Hispanic/Latino population represents 16.9% of enrollees. Participants also had longer disease duration since onset of MS symptoms (10.7 years vs. 7.4 years), were relapse-free (44.1%) or had one relapse (28.8%) in the 2 years prior to screening. The majority of participants did not have Gadolinium (Gd)-enhancing lesions (57.1%) or new/enlarging T2 hyperintense Lesions compared to previous scan (45.2%) at baseline. Although 31.1% were treatment naïve at study start, the majority of participants (65.5%) switched to ublituximab from a prior DMT. Among those switching to ublituximab, 42.2% were from anti-CD20 therapy, 20% from natalizumab, 9.5% from fumarates, 7.7% from other oral therapies, 5.2% from teriflunomide, 5.1% from platform therapies, and 3.4% from alemtuzumab. Over 67% of participants switched due to inadequate efficacy on prior DMT. Additional results on real-world efficacy and safety will be presented.

Conclusion: The real-world cohort from ENABLE represents a slightly older, and more diverse MS population with longer disease duration compared to ULTIMATE I and II. The real-world data from this cohort may aid clinical decision making for patients either initiating ublituximab or transitioning from a prior MS therapy.

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P1834
Safety of Glatiramer Acetate in Real-World People with MS: Insights from the Italian Multiple Sclerosis and Related Disorders Register

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Introduction: Glatiramer acetate (GA) is a widely used disease-modifying therapy for MS, with over 20 years of proven efficacy and safety. After its patent expired in 2015, equivalent glatiramoids (Copemyl/CopemylTri) were introduced in 2017 in Italy. Data from the Italian Multiple Sclerosis and Related Disorders Register have been extracted.
Objectives/Aims: This retrospective analysis aimed to evaluate the safety profiles in a real-world setting of Copaxone (COPAX), and Copemyl/CopemylTri (COPEM) in people with MS (pwMS).
Methods: PwMS with ⩾1 COPAX or COPEM claim between 01/01/2017 and 31/12/2024 were included. Demographic, clinical data, and clinical events, were analysed using descriptive statistics, Wilcoxon rank-sum test, and Pearson's chi-square test.
Results: 1040 pwMS treated with COPAX and 1324 with COPEM were identified. The mean follow-up was 36.4 (±26.3) months for COPAX and 33.4 (±21.0) months for COPEM. In the COPAX group, 34.4% discontinued treatment after an average of 27.0 months (mainly due to intolerance, patient choice/benefit, adverse events, and MRI activity). In the COPEM group, 22.7% discontinued after 23.7 months for the same reasons. The COPEM group was significantly older (49.3 vs. 43.9 years, $p<0.001$), had a longer disease duration at treatment initiation (14.0 vs. 8.9 years, $p<0.001$), and a higher proportion of males (29.6% vs. 24.7%, $p=0.008$). The frequency of at-least-one clinical event was similar (11.0% for COPAX and 12.2% for COPEM, $p=0.338$). A total of 54 treatment-related adverse events were reported (16 in COPAX, 38 in COPEM). None of these events was classified as severe. The frequency of at–least-one treatment-related adverse event was similar between groups (13.2% in COPAX and 19.1% in COPEM, $p=0.189$) with the most common being "general disorders/conditions related to site of administration" (31.3% and 42.1%, COPAX vs COPEM) and "skin/subcutaneous tissue disorders" (25.0% and 31.6%, COPAX vs COPEM).
Conclusion: In a real-world setting, these preliminary results found no significant differences in the safety profiles of pwMS treated with the different GA formulations.

Disclosure of interest: Ponzio M, Lepore V, Mosconi P, Dettorre A, Salivetto M, Paletta P, Guerra T, Iaffaldano P: nothing to disclose with respect to the content of the current study

P1835
The State of MS Care in Texas: a claims-based analysis of existing disparities in a diverse state

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Introduction: Despite significant diagnostic and therapeutic advances in MS, access to MS care and treatments is not equally distributed. Texas is one of the most racially and ethnically diverse states in the US, with 14% of the population living below poverty level and 17.9% foreign-born. Additionally, over half of Texas counties are considered medically underserved.
Objectives/Aims: To determine the prevalence and incidence of MS, time-to-first disease-modifying therapy (DMT), and rates of DMT utilization in Texas.
Methods: This retrospective cohort analysis used the Texas All-Payers Database (TX-APCD), a large administrative database containing medical, pharmacy and dental claims collected from private and public payers. Adult (age> 18) people with MS (pwMS) were identified in 2022 using a previously validated algorithm. Newly diagnosed pwMS had no DMT or claim with ICD-10 code for MS in the 3 years prior to initial MS diagnosis. The prevalence and incidence of MS were determined and stratified by age, sex, insurance coverage, geography, and rurality. Rates of DMT utilization and time-to-first DMT were compared across age groups and insurance types.
Results: A total of 21,260 people with MS were identified from a reported population of 7,598,885 insured adult Texans. Of those, 1,024 were newly diagnosed. The prevalence of MS was highest in age groups 55-64 and 65-74, with 14% of pwMS living in rural areas. DMT utilization was 33.9% overall and highest in age group 18-34 (55.8%). In pwMS with new diagnosis in 2022, only 222/1024 initiated a treatment that year. For those who started DMT, median time from first diagnosis code to DMT was 40 days, with shorter times for those on Medicare compared to commercial insurance, and for those living in urban areas compared to rural areas. In the incident group, 75% of new DMT initiations were with high efficacy therapy.
Conclusion: These real-world data from the TX-APCD show that a significant portion of pwMS in Texas do not receive DMT. Low rates of DMT utilization were seen in newly diagnosed patients, and even in younger cohorts. Despite overall low DMT uptake, high-efficacy DMT were preferentially used in new DMT users.

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P1836
Non-Inferiority of Rituximab Vs Ocrelizumab in Treating Patients with Relapse-Remitting Study: An Iranian Three-Year Real-World Experience

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Introduction: Anti-CD20 monoclonal antibodies are regarded as a secure and efficacious disease-modifying therapy (DMT) for the management of relapse-remitting multiple sclerosis (RRMS).
Objectives/Aims: Herein, we aimed to compare the efficacy of OCR and RTX in treating RRMS patients over a three-year follow-up.
Methods: Between 2018-2023, RRMS patients prescribed OCR or RTX at the Imam Hossein MS Center in Tehran, Iran, were identified. Clinician-reported data were retrospectively collected.
Results: 150 patients (OCR=90, RTX=60) were enrolled. 77.3% of the patients were female with a mean age of 38.46 ± 9.50 and a mean disease duration of 8.55 ± 4.86. Most patients (79.3%) had a history of DMT exposure, of which the foremost used was fingolimod. In terms of demographic and MS-related characteristics, no significant difference was observed between the two groups ($P>0.05$). Over a mean follow up of 42.13 ± 15.07 months, no significant difference was observed between the two groups in confirmed disability worsening (1.11% vs. 6.66%) (P=0.06) and clinical relapse (1.13% vs. 3.33%) (P=0.34). 27 patients (18%) manifested secondary hypogammaglobinemia (SHG), predominantly during the third year of treatment, which did not exhibit a significant difference between the two groups (P=0.60). SHG was mainly asymptomatic, with only three patients (11.11%) necessitating intravenous immunoglobulin replacement therapy. Twelve patients (8%) also developed non-infectious adverse events leading to DMT discontinuation in one patient treated with ocrelizumab.
Conclusion: Our preliminary results revealed a comparable efficacy of RTX vs. OCR in RRMS patients, with a similar tolerability profile.

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P1837
Ublituximab use in a Real-World Setting: Rapid CD19+ B-Cell Depletion and Comprehensive Clinical Evaluation Beyond EDSS

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Introduction: Ublituximab is a chimeric glycoengineered monoclonal antibody (mAb) that targets a unique epitope on the CD20 antigen and has a great antibody-dependent cellular cytotoxicity. Moreover, given the rapidity of B-cell depletion, it is possible that it has a faster onset of action than other anti-CD20 Abs.
Objectives/Aims: The aim of this study was to characterize the immunophenotype at initial infusion, assess the rapidity of B-cell depletion, and provide a comprehensive evaluation of efficacy outcomes beyond Expanded Disability Status Scale-EDSS, integrating cognitive assessment, patient-reported outcomes, and upper limb function evaluation.
Methods: A monocentric, real-world Italian experience of patients treated with Ublituximab at the MS center of Foggia, Italy from December 2024. Blood samples were obtained before and at the end of the first split infusion (PRE/POST T0), after 7 days (T1), after the second split dose (14 days) (POST T2) and after two months (T4). Demographic, clinical and immunophenotype data were collected, together with patients reported outcomes (PROs), The Brief International Cognitive Assessment for Multiple Sclerosis, the 9-Hole Peg Test (9HPT), Timed 25-Foot Walk (T25FW), Lower Extremity Functional Scale (LEFS), Arm Function in Multiple Sclerosis Questionnaire – Short Form (AMSQ-SF), Multiple Sclerosis Quality of Life-54 (MSQoL-54), Multiple Sclerosis Impact Scale (MSIS-29) and EQ-5D-5L questionnaires. These data were collected at baseline, before Ublituximab initiation and will be re-administered at the 6-month follow-up after the first infusion.
Results: Nine patients started therapy with Ublituximab (44.4% female), age 49 (Q1-Q3: 46-56), mean BMI 27.1±2.3, and median baseline EDSS of 3.5 (Q1-Q3: 3.0-5.0).
Pre-infusion (T0) mean absolute lymphocyte count was $2.0\pm0.8\times10^3/\mu L$ and mean CD19+ B-cell count was 276±115.8 cells/μL. Immediately post-infusion (T0), mean absolute lymphocyte count decreased to $0.18\pm0.05\times10^3/\mu L$ and mean CD19+ B-cell count to 9.2±8.0 cells/μL. At T1, mean absolute lymphocyte count was $1.7\pm0.7\times10^3/\mu L$ and mean CD19+ B-cell count was 0.4±0.5 cells/μL. At T2, mean absolute lymphocyte count was $1.5\pm0.5\times10^3/\mu L$ and mean CD19+ B-cell count was 0.5±1.0 cells/μL. At T4, mean absolute lymphocyte count was $1.3\pm0.6\times10^3/\mu L$ and mean CD19+ B-cell count was 0.5±0.6 cells/μL.
At baseline, Mean Z-SDMT score was -0.6±1.2. Mean time to complete the 9HPT was 27.8±7.5 seconds for the dominant hand and 30.7±8.0 seconds for the non-dominant hand. Mean T25FW score was 31.4±19.1 seconds (median: 21.8; Q1-Q3: 19.1-44). Mean LEFS score was 37.9±23.6 (median: 33;

Q1-Q3: 20.5-62). Mean AMSQ-SF score was 23.9±16.7 (median: 16; Q1-Q3: 11-34.5).
Conclusion: This study provides the first Italian real-world experience with Ublituximab, including immunological profiling of CD19+ B-cell depletion following the initial infusion. Moreover further validation in larger cohorts is warranted.

Disclosure of interest: All the authors have nothing to disclose related to the submitted abstract

P1838
Preliminary Experience of Inebilizumab in Treating Neuromyelitis Optica Spectrum Disorder Comorbid with Primary Sjögren's Syndrome: A Single-Center Prospective Real-World Study

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Introduction: The comorbidity rate of Neuromyelitis Optica Spectrum Disorder (NMOSD) and Primary Sjögren's Syndrome (pSS) is as high as 15% to 30%. Patients with this comorbidity often exhibit adverse clinical features such as high relapse rates and rapid progression of disability. This study is the first to prospectively evaluate the efficacy and safety of inebilizumab (INEB) in a real-world cohort of patients with NMOSD-pSS comorbidity.
Objectives/Aims: To assess the efficacy and safety of INEB in Chinese AQP4-positive NMOSD patients with comorbid pSS.
Methods: Patients with NMOSD and pSS who were treated with INEB from June 2024 to February 2025 were recruited. The diagnosis of pSS was based on the 2016 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for pSS. The primary outcome was the annualized relapse rate (ARR). Secondary outcomes included the Expanded Disability Status Scale (EDSS), Modified Rankin Scale (mRS), and EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), as well as the occurrence of adverse events (AEs).
Results: Five female patients were enrolled, with a median age at onset of 32 years (range: 24-72 years) and a median follow-up duration of 6 months (range: 1.4-8.3 months). Two patients initiated INEB directly after their first attack, two patients received INEB after relapse following conventional immunotherapy, and one patient switched to INEB due to adverse reactions from other treatments. Attack types comprised optic neuritis in 3 patients, optic neuritis with myelitis in 1 patient, and myelitis in 1 patient. Before treatment, the ARR was 0.5. As of March 30, 2025, none of the five patients had relapsed. The median EDSS score decreased from 2 (range: 1-4) to 1 (range: 1-4), $p>0.05$. The median ESSDAI score decreased from 4 (range: 2-5) to 3 (range: 2-4), $p>0.05$. The median mRS score decreased from 2 (range: 1-4) to 1 (range: 1-2), $p>0.05$. No adverse reactions were observed in any of the five patients.
Conclusion: INEB lowered relapse rates in NMOSD-pSS patients without significant adverse reactions, with trends toward improved mRS, EDSS, and ESSDAI scores, though not statistically significant. Larger studies with extended follow-up are needed to confirm INEB's long-term efficacy and safety in this patient population.

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P1839
The DEPERSONALIZED Indication in Multiple Sclerosis is a New Approach to Therapeutic Decision

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Introduction: Disease-modifying therapies(DMTs)have significantly impacted multiple sclerosis (MS) by reducing inflammation and slowing disability progression. Early treatment with high-efficacy drugs (HET) and personalized indications (PI) can keep some patients free of MS activity, making HETs the best choice based on disease degree and activity.
Objectives/Aims: Establish % change of pharmaceutical formula by health providers in our patient population during 12/2022 to 07/2024 for both switch and naïve.
Methods: Demographic data of the population under study are analyzed. Groups n(%) were established according to accession: Group 1(G1) suggested DMT granted; Group2 (G2) another DMT than suggested; Group 3(G3) is still awaiting approval. Depersonalized indication is defined as access to drugs suggested by the payer and not by medical criteria
Results: n=62 total; G1n=18(29%); G2n=24(38.8%); G3n=20(32,2%) G2: HET to HET lowest cost n13 (54.1%); HET at S1Pn=6(25%); change between S1P n=3(12.5%); Exchange/delivery iRegular n=2(8.4%). Payers: Nation=1; IOMA=2; PAMI=3; OS=14; Private insurance=4 G3 Payers n = Public Healthcare System 11; Institute of Medical Assistance Work(IOMA) 4; OS 4; Private insurance1
Conclusion: IP in MS evidence supports early use of HET. However, cost and individual payer status lead to the ID. 54.1% of patients who accessed treatment received another lower-cost formulation and 32.2% are untreated. The results show that 38.8% received a different treatment from what was suggested. The current "depersonalized indication" needs evaluation to determine its impact on MS progression, and guidelines should

be established to avoid patient risks and increased Public Health expenses.

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THERAPY – Symptom managment and rehabilitation

P1840
From 0 to >5800 screened: How we developed and implemented a new digitised cognitive screening pathway in six UK MS clinics

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Introduction: Cognitive problems are highly prevalent amongst people with MS. However, in the UK, as part of standard clinical care in National Health Service (NHS), people with MS are not routinely offered cognitive screening. This is partly due to staffing issues and costs associated with the purchase and use of cognitive screening tests.
Objectives/Aims: To overcome these issues, we aimed to develop, norm, and validate a new screening battery (based on the Stroop test, Symbol Digit Modalities Test, and subjective ratings of mood, cognition, and fatigue) and embed this within a newly created clinical pathway.
Methods: Both the tests and the pathway were co-developed with stakeholders (people with MS, families/carers, clinicians, and service commissioners). Using the Consolidated Framework for Implementation Research as a guiding principle, we were able to determine the barriers and facilitators to deliver this clinical pathway. The initial pathway was pilot tested and iteratively developed further to develop a blueprint of the pathway that can be adapted to different NHS services.
Results: We have successfully delivered this service in 6 NHS MS clinics around England and Wales where it has now become part of their usual care, and have screened >5800 people with MS, thus enabling services to triage patients to appropriate types of treatments. In this presentation, I will explain the co-development process, the barriers and facilitators to implementing this clinical pathway.
Conclusion: Embracing a co-development philosophy and using an iterative Plan-Do-Fail-Evaluate-Retry cycle, we have successfully developed and implemented a cognitive screening programme in NHS MS clinics. Knowledge of implementation science enabled us to proactively work through some of the challenges to deliver a sustainable, stakeholder-approved cognitive screening pathway.
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P1841
The effects of probiotics supplementation on fatigue in relapsing-remitting multiple sclerosis; a randomized double-blinded placebo-controlled trial

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disease where symptoms like cognitive impairment and fatigue affect quality of life. The gut microbiome alterations may influence its pathogenesis by modulating inflammation and oxidative stress and through the gut-brain axis.
Objectives/Aims: This RCT aimed to evaluate probiotics supplementation effects on fatigue in RRMS patients with Expanded Disability Status Scale (EDSS)<4.
Methods:
In this parallel, randomized, double-blind, placebo-controlled trial, the intervention group received probiotics supplementation (Lactocare®) twice daily for four-moths, while the placebo group received starch-filled capsules. Fatigue and its related factors, was assessed using the Comprehensive Fatigue Assessment Scale for MS Patients (MS-CFAB), which evaluates the patient-reported general health summary (including VAS for fatigue, pain, depression, stress, anxiety, sleep problems, poor nutrition, and walking problems), as well as Social, mental and physical fatigue, pain impact, sleep, mood, stress, anxiety, nutrition, motility, environment, and fatigue management indices. Assessments were conducted at baseline and after four months.
Results: Out of 90 randomized patients, 60 completed the trial. Probiotic supplementation did not show significant effects on fatigue or overall health (p-values>0.05 for all of the CFAB-MS scale, including the VAS for general health summary and fatigue-related indices); however, significant improvements were observed in the placebo group for stress ($p = 0.01$), and anxiety ($p = 0.01$), while probiotic supplementation led to a significant change in the nutrition index ($p = 0.02$). Intragroup improvements were observed in both the probiotics and placebo groups, but these changes were not clinically significant.
Conclusion: Supplementation with a multi-strain probiotic product for four months did not result in significant improvements in fatigue in RRMS patients.

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P1842
Feasibility of implementing a small-changes approach to healthy eating among adults with MS

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Introduction: An increasing body of evidence supports an association between dietary intake and MS outcomes, and innovative on-line programs may help people with MS (pMS) improve their diet. Small change approaches in which participants focus on small, incremental, behavioral goals rather than follow specific diet prescriptions, have shown promise for long-term behavior change in the general population, but have not been widely studied among pMS.
Objectives/Aims: The purpose of this study was to assess the feasibility of implementing a 4- week small change diet program for pMS delivered via virtual group meetings.
Methods: English-speaking pMS were recruited through a US non-profit MS organization. The program included four 75-minute meetings offering education and behavioral support from registered dietitians and a psychologist. We assessed sleep quality, fatigue, and pain at baseline, end of the program, and 3 months post-program. Feasibility measures were analyzed with descriptive statistics and qualitative feedback. Repeated measures ANOVA were used to explore changes over time and effect size. Given the exploratory nature of the analyses, baseline data were compared between completers and non-completers. Longitudinal analyses included completers only.
Results: 48 participants (77% white, 100% female) completed baseline surveys. Mean (SD) participant age was 58.1 (8.26) years and mean age at diagnosis was 39.4 (9.1) years. 11 (23%) participants completed surveys at all 3 timepoints and 15 (31%) completed 2 timepoints. Mean fatigue scores decreased from 43.7 (15.1) at baseline to 33.4 (15.4) at the end of the program and continued at 33.5 (13.8) at 3 months post-program. Sleep quality and pain did not change. 14 participants reported they liked the 4-week duration of the program, while 3 noted it was too short to help them change their diet behaviors. The group setting and interactive discussions were the most noted strengths of the program, and wanting a more prescriptive diet plan was the most common weakness.
Conclusion: A small changes dietary program delivered in a group online setting may help reduce fatigue, however interventions that combine diet prescriptions with small changes may be needed to increase feasibility of long-term retention.

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P1843
Home-based balance exercise can improve balance in people with multiple sclerosis

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Introduction: Balance disorders and mobility impairments are a common problem in people with multiple sclerosis (MS). Increasingly, the effect of remote exercise has been investigated, particularly since the COVID-19 pandemic, when rehabilitation services were limited. Balance training provided in the patient's

home environment could increase accessibility to exercise and help improve mobility and balance in individuals with MS.
Objectives/Aims: The aim of the study is to evaluate the effectiveness of balance training on balance and functional mobility.
Methods: Patients with MS who experienced subjective balance disorders and had an Expanded Disability Status Scale (EDSS) ranged from 2.0-6.5 were selected for the study. The selected participants were divided into two groups (control, experimental group). The 12-week intervention consisted of remote individual balance exercises with supervision for the experimental group. The control group was without intervention. At the baseline and after the intervention, participants in both groups were assessed using a series of questionnaires (Multiple Sclerosis Walking Scale-12 – MSWS-12, Modified Fatigue Impact Scale – MFIS, Activity-specific Balance Confidence Scale – ABC Scale, Falls Efficacy Scale-International – FES-I) and functional tests (Timed Up and Go – TUG, TUG Cognitive, One-Leg Stance, Berg Balance Scale – BBS).
Results: A total of 40 individuals with MS participated in the study. The experimental group (n = 20, 4 men) and the control group (n = 20, 5 men) were comparable in age, disease duration and level of neurological disability with median EDSS of 5.0. When comparing the two groups, there was a statistically significant improvement in the experimental group in balance (One-Leg Stance p = 0.02, BBS p= 0.01), subjectively perceived gait (MSWS-12 p = 0.004) and fatigue (MFIS p = 0.03) after the intervention.
Conclusion: Remote balance training with supervision is safe, feasible, and appears to lead to improvements in balance parameters.

Disclosure of interest: Grosserova Barbora: nothing to disclose. Novotna Klara: nothing to disclose.

P1844
"Impact of a strength training program with elastic bands on fatigue and walking in people with multiple sclerosis: A randomized controlled pilot study with 12-week follow-up."

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Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative disease that affects motor function, fatigue, and quality of life. Physical activity, particularly strength training, shows potential benefits, but evidence on accessible, low-cost programs like resistance bands remains limited.
Objectives/Aims: To evaluate the effects of a strength training program using elastic bands on fatigue and walking in people with MS.
Methods: A 12-week randomized controlled trial was conducted with 21 participants (16 women, 5 men; mean age 41) diagnosed with MS, recruited from the "Asociación Tinerfeña de Esclerosis Múltiple". Participants were randomly assigned to an intervention group (n = 12) performing elastic band strength training, or a control group (n = 9) with no specific intervention. The program included four progressive lower limb exercises (rugby squat, clamshells, hip flexions and lateral lunges) with varying band resistance, performed twice weekly in the first month and three times weekly in the following two months. Fatigue was assessed with the Modificated Fatigue Impact Scale (MFIS), subjective walking impact with Twelve Item MS Walking Scale (MSWS-12), and objective walking capacity with the Timed 25-Foot Walk test (T25FW). Measurements were taken at baseline, 1, 2, and 3 months.
Results: For the variables of interest (MFIS, TF25W, and MSWS-12), no significant differences were observed between the groups at baseline ($p > 0.05$). No differences were found between the groups on the fatigue scale at 3 months. However, regarding ambulatory capacity, both the objective test (TF25W) and the subjective measure (MSWS-12) showed significant differences after 3 months of intervention. In the case of the TF25W test, significant differences were already evident at 8 weeks.
Conclusion: This pilot study suggests that strength training with elastic bands may improve walking in people with MS, as shown by objective and subjective measures after 12 weeks, with early benefits over walking ability according to the TF25W test at 8 weeks. No significant changes were found in perceived fatigue. These findings support the potential of accessible, low-cost exercise interventions in MS rehabilitation and underscore the need for larger trials to confirm these results.

Disclosure of interest: Cristina Casanova, Laura de Armsas and Fernando Hernández-Abad: nothing to disclose.

P1845
A clinical audit of pre-existing longitudinal body mass index data highlighting weight changes in a paediatric demyelinating cohort

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Introduction: Symptoms and treatments associated with paediatric acquired relapsing demyelinating syndromes (RDS) present challenges to managing weight. However, data on growth patterns in paediatric RDS remain limited. Understanding these trajectories is essential to inform targeted interventions that support long-term health and wellbeing.

Objectives/Aims: To review and report pre-existing longitudinal height and weight trajectories from clinical records of RDS patients from two tertiary UK centres.
Methods: We conducted a longitudinal retrospective clinical audit (2009–2019) of children aged 5–17 with demyelinating conditions from two UK tertiary centres. Pseudo-anonymized patient records were identified by clinical teams and included body mass index (BMI), Expanded Disability Status Score (EDSS), fatigue/pain status, and steroid use. BMI z-scores were calculated using the World Health Organization (WHO) growth charts. Descriptive analyses were performed, and longitudinal trajectories were assessed for patients with ⩾2 assessments over >1 month. (Ethical approval (DREC: 0420_01)).
Results: At baseline (n=60) 53% were overweight or obese, while 5% were thin or severely thin. Most patients had minimal disability, 70% had an EDSS or 0-1, and 8% had EDSS ⩾5. Longitudinal (n=53, median 5 assessments over 18 months) showed 47% maintained their BMI z-score band. BMI increased in 23% and decreased in 17% of patients. Height remained stable in 79% of patients, with 19% showing a decline in height z-score; 60% of whom were receiving steroids.
Conclusion: Most children were overweight or obese, however, weight and height trajectories were diverse, with notable changes within short timeframes. Weight gain was more common in those with NMOSD/ADEM and steroid use, though not exclusively. Interestingly, a reduction in height trajectory was observed in 19% of patients. These highlight the need to consider weight management strategies when supporting children with RDS.

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P1846
Tailored follow-up for persons with multiple sclerosis to optimize physical functions, health and employment: a prospective single-blinded randomized controlled trial

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Introduction: People with multiple sclerosis (PwMS) have complex challenges involving sensorymotor functions, low levels of physical activity and unemployment when disability is mild to moderate. There is a scarcity of evidence regarding proactive comprehensive interventions concurrently addressing function, health and work in pwMS This study explores effects of a new, comprehensive, cross-sectional intervention; CoreDIST addressing these challenges.
Objectives/Aims: The aim of this study is to investigate effects of a comprehensive intervention, CoreDISTparticipation on barriers for work, physical activity, physical functions, fatigue, and HRQoL for employed pwMS.
Methods: An assessor-blinded prospective multicenter randomized controlled including 115 pwMS (Expanded disability status scale (EDSS) 0-4) randomly allocated to CoreDISTparticipation (n=57) or standard care (n=58). The CoreDISTparticipation intervention includes 1) Information videos; hospital outpatient physiotherapist assessment; meeting with employment consultant. 2) Municipality; Small group physiotherapy for 6 weeks; one indoor CoreDIST-balance training and one outdoor CoreDIST-balance and high-intensity interval training. 3) 6 weeks of digitally supported independent training x2 weekly.
Assessments at baseline, weeks 9, 16 and 52. Primary outcomes: Multiple Sclerosis Work Difficulties Questionnaire-23 (MSWDQ-23) and ActiGraph wGT3x-BT monitors. Secondary outcomes: Trunk Impairment Scale-modified Norwegian Version (TIS-modNV), Mini-Balance Evaluation Systems Test, AccuGait Optimized force platform, Six-minute walk-test, Multiple Sclerosis Walking Scale-12, Multiple sclerosis Impact Scale-29 (MSIS-29) and Fatigue Severity Scale. The statistical analyses included descriptive statistics and repeated measures mixed models.
Results: The sample includes 86 women and 29 men, mean age 46.9 (9,3) years, mean years since diagnosis 9.72 (8.42). 60.5% reported full-time employment. Assessments at baseline, weeks 6 and 16 has been conducted successfylly. The 52-week retest will be completed by August 2025.
Overall effects at week 16 were significant, in favour of the intervention group for the MSWDQ-23 (p=0.002), for MSIS-29 (p=0.006) and for TIS-modNV (p=0.047). Effects regarding physical activity data and force platform measurements have not been calculated but will be presented along with overall effects at 52 weeks for the full sample.
Conclusion: The preliminary results at 16 weeks indicate that it is useful to direct focus toward physical function and work adaptation for employed pwMS.

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P1847
Empowering yet challenging: managing multiple sclerosis in the workplace – an interview study

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Introduction: Having a chronic disease such as multiple sclerosis (MS) may pose challenges for affected individuals in their working life. Given its progressive nature and wide range of symptoms, living with MS requires ongoing adaptation, adding an extra layer of complexity in balancing professional responsibilities. In addition to work accommodations and support, individuals may develop their own strategies to manage their condition at work.
Objectives/Aims: To explore the experiences of people with MS (PwMS) in managing MS in the workplace, focusing on the strategies they employ to facilitate their work lives and the challenges they navigate.
Methods: Semi-structured individual interviews were held with 16 working PwMS in Sweden. Interviews were analysed using reflexive thematic analysis.
Results: Three main themes were identified that highlight strategies for managing MS. The first theme, 'Adapting to MS', included statements on how critical self-reflection led to strategies more aligned with health needs and understanding the best practices and pitfalls of managing a chronic disease. The second, 'Taking responsibility in the workplace', described the participants' commitment to protecting their health at work, and the efforts made to create an environment more conducive to their condition. Finally, 'Approaching sustainability' included reports on making sustainable choices in relation to their work life, both in the short and long term.
Conclusion: This study provides insights into the experiences of those living and working with MS. The results demonstrate the active agency in managing their condition. The PwMS employed various strategies, concentrating on adapting to MS mentally and practically, taking an active stance for their health, and making choices based not only on their current health status but also on potential future circumstances.

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P1848
Beyond SMART: evaluating goal setting in a neuropsychological rehabilitation trial in multiple sclerosis

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Introduction: Goal setting in neuropsychological rehabilitation (NPR) provides a collaborative framework that helps motivate patients, tailor interventions, track progress, and evaluate NPR effectiveness clinically and academically. Development of specific, measurable, achievable, relevant, time-bound (SMART) goals can increase self-efficacy and is a holistic approach to measuring NPR attainment through incorporation of patient's individual values and motivations.
Objectives/Aims: This study evaluated goals set collaboratively between clinicians and participants, and their applicability to SMART criteria, as part of mid-trial monitoring on the NEuRoMS rehabilitation trial which aims to evaluate a brief NPR for people with multiple sclerosis.
Methods: In total, goals of 50 participants were rated by two independent raters at two separate time points (first timepoint n=30, second timepoint n=20), with a third reviewer to resolve discrepancies. Inter-rater reliability was calculated using Intraclass correlations (ICC) across raters, time-points, and blinding criteria (neuropsychological difficulty and short- or long-term goal). Goals were rated on a traffic-light criteria, based on SMART principles and application to NPR; (1) red if neuropsychological difficulty was not explicit or the goal was unrelated to neuropsychology, (2) amber if there was an element of SMART principles missing, and (3) green if the goal adhered to all the SMART principles.
Results: In total, 134 goals were rated. Of these, 16 were rated as Green (12%), 111 as Amber (83%) and 7 as Red (5%) under blinded conditions. When unblinded, 132 were rated as Green (98%). At the first time-point, ICC was 0.86 ($p<.001$) for

blinded goals, and 0.76 ($p<.001$) for unblinded, both indicating a good agreement. For the second time-point, ICC was 0.86 ($p<.001$) for blinded goals, indicating a good agreement. However, ICC was -0.06 ($p=.575$) for unblinded, indicating poor agreement due to unbalanced category use and limited rating variability, with only one disagreement and the remaining goals rated as Green.

Conclusion: From the results, the criteria for goal setting were refined, as illustrated by the rating system, and disseminated via a training refresher session to the clinical teams in the NPR trial. Training materials were updated to reflect the updated criteria. The criteria developed can be used to enhance SMART goal development in NPR, particularly applicability to neuropsychological difficulties, and heighten accuracy in using goals as an outcome measure of attainment in NPR.

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P1849
Impact of Ankle Muscle Strength and Voluntary Activation on Walking Performance in Multiple Sclerosis

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Introduction: Lower limb strength deficits are a significant barrier to functional independence in individuals with multiple sclerosis (PwMS). Focusing on ankle joint dorsiflexion and plantar flexion, we investigated whether strength and voluntary activation of ankle joint muscles in the less (LE) and more affected (MO) legs was associated with walking performance in people with MS.

Objectives/Aims: This study aimed to examine the relationship between ankle muscle strength, voluntary activation, and walking performance in PwMS, focusing on both the more and less affected legs.

Methods: Twenty adults with MS ($n = 12$ females, age 51 ± 11 yrs, Patient-Determined Disease Steps (PDDS) 1.5 ± 1.46) performed maximal isometric ankle dorsiflexion and plantarflexion trials for each leg. Strength measures included maximal voluntary contraction force (MVC) and rate of force development (e.g. 0-50 ms following onset of contraction). Voluntary activation was assessed during dorsiflexion using surface electromyography (EMG) and the twitch interpolation technique. Walking performance was assessed via the 6-Minute Walk Test (6MWT) in meters. Pearson's correlations were used to evaluate associations between these measures of strength, voluntary activation and walking performance.

Results: In the MO leg, both dorsiflexion and plantarflexion MVC force showed a strong positive correlation with 6MWT distance ($r = 0.64$, $p < 0.01$; $r = 0.61$, $p < 0.01$). RFD for dorsi- and plantarflexion also showed strong correlations ($r = 0.64$, $p < 0.01$; $r = 0.48$, $p < 0.05$). Voluntary activation measures demonstrated moderate positive associations with 6MWT distance (dorsiflexor, twitch interpolation technique; $r=0.46$, $p=0.05$). In the LE leg, plantar MVC also demonstrated a significant positive association with walking performance ($r = 0.51$, $p = 0.03$), while the associations between dorsiflexion parameters and walking performance were weaker. No other significant correlations were observed.

Conclusion: The present findings emphasize that both maximal and early force production, particularly in the more affected leg, are key factors associated with physical functional capacity, assessed as walking performance, in adult PwMS. Although voluntary activation measures contributed modestly, strength metrics were most strongly linked to 6-minute walking distance. Targeting force-generating capacity in the most affected limb (i.e. exhibiting the greatest impairment in strength parameters) may present a means to preserve or even enhance physical functional capacity in PwMS.

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P1850
Evaluating the Impact of Prolonged-Release Fampridine on Mobility Goals in Multiple Sclerosis Using Goal Attainment Scaling

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Introduction: MS is a neurodegenerative condition affecting mobility, with gait impairments reducing life quality. Prolonged-release (PR) Fampridine, a potassium channel blocker, improves walking speed in MS. Its role in achieving patient-centred goals remains unexplored.

Objectives/Aims: To evaluate the impact of PR-Fampridine on personalised mobility goals using Goal Attainment Scaling (GAS).
Methods: This prospective cohort study included patients from the MS walking clinic at National Hospital for Neurology and Neurosugery. Mobility goals were set using GAS before starting PR-Fampridine. Responders were defined as achieving ⩾20% improvement in the Timed 25-Foot Walk (T25FW). GAS and T25FW were measured at: baseline, 2 weeks, 3 months, 6-9 months, beyond a year. Self-reported walking disability was assessed using the 12-item MS Walking Scale (MSWS-12) at: baseline, 2 weeks, 3 months. Statistical analyses included: paired t-tests, ANOVA, correlation tests.
Results: 31 participants showed significant improvements in GAS scores at 2 weeks, 3 months and beyond a year against baseline ($p < 0.0001$). Improvements in T25FW and MSWS-12 were observed at 2 weeks, with no significant change after. No significant correlation was found between T25FW and GAS or MSWS-12.
Conclusion: PR-Fampridine improves patient-centred mobility goals, measured by GAS, with sustained benefits beyond a year. The lack of correlation between T25FW and GAS suggests PR-Fampridine may benefit patients beyond walking speed improvements. Future studies could utilise GAS to measure improvements in participants' performance in a progressive condition with an intervention.

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P1851
Central autonomic network connectivity: abnormalities in multiple sclerosis and aerobic training effects

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Introduction: Autonomic dysfunction is common in multiple sclerosis (MS); however, functional abnormalities of the central autonomic network (CAN) have not yet been investigated in this disease.
Objectives/Aims: To explore resting state (RS) functional connectivity (FC) of the CAN in MS and its potential modification after aerobic training (AT).
Methods: A total of 75 MS patients (38 relapsing-remitting [RR] and 37 progressive [P]) underwent 3T RS functional MRI at baseline and after two (RRMS) or three months (PMS) of AT. Sixty-seven matched healthy controls (HC) served as baseline RS FC reference. Seed-based RS FC analysis used core CAN modulatory regions: left/right ventromedial pre-frontal cortex (vmPFC), mid-cingulate cortex (MCC), amygdala, hypothalamus, anterior and posterior insula.
Results: Compared to HC and PPMS patients (conjunction analysis, $p<0.001$), RRMS patients were characterized by increased RS FC of the left hypothalamus with the cerebellum. In PMS, compared to RRMS and HC (conjunction analysis, $p<0.001$), we found increased RS FC of the bilateral insula and amygdala with ipsilateral deep grey matter nuclei, of the vmPFC with posterior cingulate cortex and angular gyrus, and of the MCC with the cerebellum. PMS were also characterized by decreased RS FC of the bilateral insula with cerebellum, and of the MCC with insula. After AT, decreased hypothalamic network RS FC in RRMS was observed, while no changes were detected in PMS.
Conclusion: CAN dysregulation is present in MS, with distinct RS FC abnormalities characterizing RRMS and PMS patients. AT may be insufficient to modulate CAN RS FC in progressive patients.

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P1852
Understanding the training needs in Europe for designing high-quality neuropsychology and vocational rehabilitation trials in multiple sclerosis

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Introduction: Designing high-quality randomised controlled trials (RCTs) in neuropsychological (NPR) and vocational rehabilitation (VR) interventions for multiple sclerosis (MS) poses methodological challenges. Addressing these challenges is crucial for building evidence on the effectiveness of these interventions.
Objectives/Aims: To identify the barriers to designing high-quality randomised controlled trials (RCTs) for NPR and VR in MS and explore the training needs of clinicians and researchers.
Methods: An online survey was distributed among European MS researchers and clinicians. The survey explored trial design challenges, resource constraints, and training gaps. Data were analysed descriptively to assess common barriers and support needs.
Results: Fifty participants from nine countries (Italy, the UK, Norway, Belgium, Spain, Denmark, Switzerland, Finland, and Ireland) completed the survey. Respondents worked in a wide range of settings, including MS rehabilitation centres (30%), general hospitals with specialist MS clinics (26%), non-MS specific rehabilitation clinics (18%), university settings (8%), MS clinics (8%), and other settings (10%).
Key barriers included difficulties in selecting appropriate outcomes, defining inclusion/exclusion criteria, and minimising bias in these complex interventions. Resource constraints, such as limited funding and access to trial methodology expertise, further impeded high-quality RCT design. While half of the respondents stated using reporting guidelines (e.g., CONSORT, TIDieR), these were perceived as inadequate for rehabilitation research and failed to support researchers in designing these studies. Training gaps were evident, with many respondents relying on peer-reviewed literature or informal support. The majority expressed a strong interest in structured training opportunities, including workshops and collaborative platforms.
Conclusion: This study underscores the urgent need for improved training and methodological guidance in designing RCTs for NPR and VR in MS. Addressing these gaps through structured education and collaboration may enhance trial quality, strengthen evidence for rehabilitation interventions, and ultimately improve patient outcomes.

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P1853
Art Therapy and Psychosocial Well-being in People with Multiple Sclerosis

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Introduction: Multiple sclerosis (MS) has been shown to impact quality of life and is associated with mental health conditions such as depression and anxiety, which may exacerbate fatigue. Art therapy has emerged as a promising intervention for enhancing emotional well-being in neurological conditions; however, its application in people with MS remains limited.
Objectives/Aims: To evaluate the effect of a visual art therapy intervention on quality of life, fatigue, self-esteem, and depression in people with MS.
Methods: A quasi-experimental design was utilised to assess the impact of a ten-session art therapy programme. The following instruments were employed to evaluate the variables of interest: quality of life (Multiple Sclerosis Quality of Life-54, MSQOL-54), fatigue (Modified Fatigue Impact Scale – MFSI), self-esteem (Rosenberg Self-Esteem Scale), and depression (Beck Depression Inventory – BDI-IA). Paired t-tests were conducted to analyse pre- and post-intervention changes in scores for each variable.
Results: Twenty-one individuals diagnosed with MS participated in this study. Statistically significant improvements ($p < 0.05$) were observed in self-esteem ($p=0.007$), depression ($p=0.003$), and the physical health ($p=0.021$) and mental health ($p=0.046$) dimensions of quality of life. No significant changes were found in fatigue scores following the intervention.
Conclusion: The findings suggest that art therapy may positively influence the reduction of depressive symptoms, enhance

self-esteem, and improve perceived quality of life in individuals with MS. It is recommended that art therapy be considered as a complementary approach to support the psychosocial and overall well-being of this population.

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P1854
MODAFIMS: study protocol of an open-label, single-center clinical trial to evaluate predictors of response to MODAFinil in the treatment of cognitive deficits in patients with Multiple Sclerosis

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Introduction: Cognitive impairment (CI) is a common symptom among persons with multiple sclerosis (pwMS), with substantial detrimental effects on their activities of daily living and quality of life (QoL). Currently, there are no commercially authorized therapeutic options available for the treatment of CI in pwMS. We propose that modafinil, a drug approved for treating excessive sleepiness associated with narcolepsy, may be a promising candidate for the treatment of CI.
Objectives/Aims: Our primary objective is to evaluate the effect of modafinil on cognitive deficits in adult pwMS and identify predictors of response using resting-state (rs) and Go/No-Go task functional Magnetic Resonance Imaging (fMRI).
Methods: This study will involve 64 eligible pwMS that will be enrolled to receive modafinil at a dose 200 mg (2 tablets of 100 mg) once per day, in the morning, for 12 weeks. PwMS will undergo fMRI pre- and post-12 weeks of modafinil treatment, and features that best differentiate between responders and non-responders will be selected. These patient groups will be determined based on the improvement rate in the Symbol Digit Modalities Test (SDMT), which will be evaluated at screening and at the end of treatment. At the same time, we will evaluate the individual changes in fMRI features between baseline and 12 weeks. For a more comprehensive analysis, we will also evaluate patient-reported outcomes (PROs), changes in fatigue using the Modified Fatigue Impact Scale (MFIS), safety outcomes, and an extensive battery of neuropsychological tests.
Results: Recruitment started in September 2024; so far 27 patients were included (35 screened), aged between 28 to 64 years old (median 50), with an EDSS between 1 to 6,5 (median 3,5) and SDMT scores from 4 to 54 (median 31). 18 patients already completed the trial. Enrollment is predicted to end in June 2025.
Conclusion: If successful, it could provide a promising therapeutic option in selected patients with cognitive impairment, particularly with processing speed information deficits. Our aim is to identify, at baseline, the fMRI characteristics/markers that predict which patients will achieve SDMT improvement upon continuous modafinil treatment.
The trial was registered May 17th, 2024, version 1.1 at EU Clinical Trials Register with the EU CT Number: 2022-501414-53-00.

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Results: Participants (mean age: 36.33 ± 15.04 years) included 5 females and 1 male. The cooling vest had no significant effect on 6MWT distance ($p > 0.05$) but may have influenced MoCA scores and PVT performance ($p < 0.05$). Patients reported feeling lighter after the intervention. Due to the small sample size, results should be interpreted with caution.
Conclusion: Findings suggest that cooling vests may improve cognitive and vigilance performance in MS patients while providing a sense of relief. The use of a cooling vest appears to be effective in tasks requiring vigilance and cognition in hot conditions. However, as a pilot study with a small sample, further research with larger cohorts is needed for definitive conclusions.

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P1856
The effects of cooling vest intervention on physical, cognitive, and psychomotor vigilance performance in patients with multiple sclerosis: a pilot study

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Introduction: Multiple sclerosis (MS) is a chronic neurological disease affecting physical, cognitive, and vigilance functions. Many patients experience symptom worsening due to temperature sensitivity, but evidence on the acute effects of body cooling is limited.
Objectives/Aims: This pilot study aimed to investigate the effects of cooling vest use on physical, cognitive, and psychomotor vigilance performance in MS patients to inform future research.
Methods: The study used a crossover design. MS patients were assessed in two conditions in a randomized order: with a cooling jacket and under normal conditions. There was a minimum 2-week interval between assessments. Evaluations included the 6-Minute Walk Test (6MWT), Psychomotor Vigilance Test (PVT), and Montreal Cognitive Assessment (MoCA). Differences were analyzed using the Wilcoxon signed-rank test.

P1859
Relationship Between Absenteeism From Work/ Study and the Type of Medication Used for Multiple Sclerosis

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Introduction: With the advancement of treatment options for Multiple Sclerosis (MS), several routes of medication administration are now available. Studies have identified that oral formulations are preferred by MS patients, positively impacting quality of life, treatment adherence, and patient satisfaction (Martínez et al., 2020). Given that MS predominantly affects a younger population, the type of treatment may often interfere with patients' professional and academic activities.
Objectives/Aims: To evaluate the relationship between absenteeism from work or study and the type of medication used in the treatment of MS.
Methods: A brazilian nationwide online survey was conducted in Brazil with the participation of 464 individuals diagnosed with MS, including 368 women and 96 men. Of these, 76.6% (369) had the relapsing-remitting form of the disease. A chi-square test was used to assess the relationship between the need to miss work or school and the type of medication currently used

by the patient (infusional, injectable, or oral). p-values < 0.001 were considered statistically significant.
Results: The average age of the respondents was 37.94 years (ranging from 17 to 71 years), with most having been diagnosed with MS for approximately four years. Regarding current medication administration routes, 61.4% (219) of patients were using intravenous medications, 12.9% (33) were using injectable treatments (subcutaneous or intramuscular), and 17.1% (156) were on oral medications. In this study, 14 patients (8.9%) reported not using any medication for MS. Among the 284 individuals who were currently employed or engaged in academic activities, the average number of days missed per month due to MS treatment was 2.8. When analyzed by treatment type, patients receiving infusional therapy reported missing approximately 3.86 days/month, compared to 1.57 days/month for those on oral therapy and 0.77 days/month for those using injectable treatments.
Conclusion: The route of administration of MS medications has a direct impact on treatment adherence and on patients' professional and academic lives. This study found that injectable and oral therapies are associated with lower levels of absenteeism when compared to infusional therapies. These findings suggest that the choice of treatment route may significantly affect patients' educational development and work-related responsibilities.

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P1860
Association Between Discomfort With Medication Use and Route Preference for Multiple Sclerosis Treatment: A Brazilian Cohort

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Introduction: Multiple Sclerosis (MS), as a progressive disease of the central nervous system, currently has no definitive cure. However, various oral, injectable, and infusion medications are available, each associated with potential adverse events (AEs). These AEs require a careful selection of treatment based on the individual's clinical history and condition. Furthermore, previous experience with adverse effects may influence a patient's preference regarding the route of administration.
Objectives/Aims: To evaluate the association between previous adverse effects and patients' preferred route of administration for MS treatment.
Methods: An online questionnaire was administered in Brazil with the participation of 464 individuals diagnosed with MS, including 368 women and 96 men. Among them, 76.6% (369) had the relapsing-remitting form of the disease. A chi-square test was used to assess the relationship between discomfort experienced when using infusion or injectable treatment and the preferred route of administration for MS treatment. p-values < 0.001 were considered statistically significant.
Results: The average age of participants was 37 years, with the majority having been diagnosed with MS for four years. Regarding the current route of medication administration, 61.4% (219) of patients were using intravenous medications, 12.9% (33) were on injectable treatments (subcutaneous or intramuscular), and 17.1% (156) were taking oral medications. In this study, 14 patients (8.9%) reported not using any medication for MS. Among those receiving infusion or injectable treatments, 26% reported experiencing discomfort associated with the therapy. Of these, 55.2% expressed a preference for oral administration, and 48.7% still preferred the infusion route ($p < 0.001$).
Conclusion: The route of administration of MS therapies directly impacts treatment adherence and patients' quality of life. Individuals who reported discomfort with infusion or injectable therapies tend to prefer alternative routes, such as oral administration. This is an important factor to consider in drug formulation and prescription, as treatment adherence can be significantly influenced by the level of discomfort associated with specific administration methods.

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P1861
Challenges in building a Multidisciplinary Multiple Sclerosis Center: Integrating Neuroimmunology and Rehabilitation – Initial Experiences and Opportunities

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Introduction: Multiple sclerosis (MS) requires comprehensive, multidisciplinary care to address its complex and evolving manifestations. In Israel, with an estimated 8,700 MS patients (2021), Clalit Health Services—the nation's largest healthcare provider—launched a dedicated MS center at Beilinson Hospital. This initiative integrates the hospital's well-established Neuroimmunology Unit (NeU) with a newly developed, state-of-the-art Rehabilitation Department.
Objectives/Aims: To describe the establishment, operational model, initial clinical experiences, emerging challenges and opportunities in creating an integrated MS center within a major Israeli hospital.
Methods: A multidisciplinary framework was established, incorporating Neurology, Physical Medicine & Rehabilitation specialist (PM&R), Physiotherapy (PT), and Occupational Therapy (OT). To assess patient needs and preferences, a screening questionnaire was distributed to NeU patients (1,000 sent, 644 responses), 71.5% were female, average age was 44.75 years. Pilot multidisciplinary clinics (MDCs) were conducted to

evaluate patients and determine optimal rehabilitation pathways. An ICF (International Classification of Functioning, Disability and Health)-based rehabilitation approach was developed, incorporating international models and offering diverse interventions, including inpatient, day hospital, home-based telerehabilitation, and hybrid models.

Results: Survey results demonstrated strong patient interest, with 75% preferring care in a multidisciplinary center over community-based services. Existing community therapy recommendations included PT (62%) and OT (28%). In the initial six MDCs, 15 patients underwent comprehensive assessment, leading to treatment recommendations including day hospital rehabilitation (n=5), inpatient rehabilitation (n=2), telerehabilitation (n=1), and targeted outpatient PT/OT interventions (n=7). At submission, one patient had begun rehabilitation, with additional three admissions planned in the upcoming days.

Conclusion: Early findings confirm the feasibility and strong demand for an integrated MS center combining neuroimmunology and rehabilitation. Key challenges include optimizing interdepartmental collaboration, resource allocation, and patient pathway efficiency. However, this model presents significant opportunities to enhance access to specialized, holistic MS care, improve patient outcomes, facilitate interdisciplinary communication, and establish a foundation for future research—representing a potentially transformative approach within Israel's largest healthcare provider.

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P1862
Effects of mindfulness-based interventions on quality of life in people with Multiple Sclerosis

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Introduction: Mindfulness-based interventions (MBI) hold significant promise in improving mental health, fatigue and overall Quality of life (QoL) in people with Multiple Sclerosis (pwMS).

Objectives/Aims: We aimed to evaluate the impact of MBI in pwMS using the Multiple Sclerosis Quality of Life-54 (MSQOL-54), the Beck Depression Inventory-II (BDI-II), the Fatigue Severity Scale (FSS) and the Five facet mindfulness questionnaire (FFMQ). We furthermore sought for correlations between the FFMQ and patients' demographic and clinical variables.

Methods: MBI sessions were conducted over 8 weeks by a trained mindfulness instructor either in-person or on-line. A control "wait-list" group read a book on mindfulness. Questionnaires were collected before and shortly after sessions and after six months from completion.

Results: A total of 24 patients (20F, 4M, mean age 53 years) completed MBI sessions: 14 in-person (six of which previously included in the "wait-list" group) and 10 online.

There were no statistically significant improvements in any of the questionnaires in the overall cohort or in the control group. However, within the online group, which had a longer disease duration (22 vs 9 years, p=0.003) and higher disability (EDSS 5.2 vs 2.2, p=0.012), the MSQOL-54 mental health composite score and the BDI-II scores showed improvement shortly after MBI (69.3 vs 48.4, p=0.007 and 8.9 vs 15.8, p=0.057, respectively), though this was not sustained at six months. At six months, the MSQOL-54 physical health composite score was significantly higher compared to baseline (109.8, vs 58.5 p=0.033).

Among the whole cohort, FFMQ scores at baseline were higher in patients with progressive MS (142 vs 119 p=0.036, correlated with EDSS (rho=0.612, p=0.006). and inversely correlated with BDI-II scores (rho=-0.511, p=0.012).

Conclusion: These preliminary results on a small patient sample show that MBI provided, at least a short-term, improvement in mental health QoL in pwMS with higher EDSS, which correlated with baseline FFMQ scores.

Disclosure of interest: Nothing to disclose

P1863
Comparing the Effectiveness of Supervised vs Web-Based Exercise Programs in People with Severe Multiple Sclerosis

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Introduction: As the Expanded Disability Status Scale (EDSS) score increases in people with multiple sclerosis (PwMS), clinical signs and symptoms become more severe and frequent. For this population, accessing physiotherapy and rehabilitation becomes increasingly challenging due to higher levels of disability, need for a caregiver, and transportation difficulties. In such cases, treatment programs can be implemented at home, either with a physiotherapist or via telerehabilitation.

Objectives/Aims: The aim of this study was to investigate and compare the effectiveness of home-based supervised and web-based exercise programs in people with severe MS.

Methods: Twenty participants were included in the study (Supervised Group: 9 female, 1 male; mean age:50.4±8.98 years; EDSS: 5,95±0,36; Web-based Group: 8 female, 2 male;

mean age: 47.60±12.78 years; EDSS: 6.10±0.39). Walking endurance was assessed using the 2-Minute Walk Test (2MWT), lower extremity muscle strength with the 5 Times Sit-to-Stand Test (5TSTS), fatigue level with the Fatigue Severity Scale (FSS), fall efficacy with the Modified Falls Efficacy Scale (MFES) and quality of life with the Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL). The program, consisting of aerobic, strengthening, and balance exercises, was administered twice a week for 8 weeks. The supervised group performed the exercises at home under the supervision of a physiotherapist, while the web-based group followed video-guided sessions via the website 'https://www.telenororehab.com/'.

Results: The demographic and clinical characteristics of the participants were similar at baseline. Intra-group analysis revealed that both groups showed significant improvements in all outcome measures ($p<0.05$). However, inter-group comparisons indicated no significant differences between the groups in any of the assessments ($p>0.05$).

Conclusion: As a result of this study, exercise training was found to be effective in improving clinical symptoms in people with severe MS. Furthermore, web-based exercise training appears to be a viable alternative for those who have difficulty accessing conventional rehabilitation services.

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P1864
Investigation of the Effects of Video-Based Exercise on Biomarkers, Motor, Cognitive Function and Quality of Life in Individuals with Multiple Sclerosis

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Introduction: Video-based exercise approaches (VBEA), which have recently been increasingly used as a rehabilitation option, have an important place in the MS rehabilitation process. Effects of exercise protocols consisting of games to improve coordination, strength, balance and endurance on cognitive parameters have been shown in MS. However, the effect of VBEA on biomarkers such as BDNF, GFAP and NFL, which are associated with cognition and disease progression, has not been investigated in MS.

Objectives/Aims: The aim of this study was to compare the effects of VBEA consisting of games that specifically improve cognitive function and VBEA, including aerobic exercise activities on BDNF, NFL, GFAP, motor, cognitive function and quality of life in individuals with MS.

Methods: Thirty-three patients with MS (average age: 48.09±23.39 years; duration of disease:11.03±7.23, EDSS score: 1.34±1.47) were randomly divided into three groups as cognitive activities-VBEA, aerobic activities-VBEA and control group (CG). The VBEA performed exercises including aerobic or specifically cognitive activities, while the control group performed conventional exercises for 8 weeks. Biomarkers (BDNF, NFL, GFAP), motor (Timed 25 foot walk test and 30sn sit to stand test), cognitive function (California Verbal Learning Test II (CVLT II)) and quality of life (Multiple Sclerosis International Quality of Life (MUSIQOL)) were evaluated at baseline and after 8 weeks of training.

Results: NFL and GFAP were significantly decreased in the cognitive activities-VBEA group after training than other groups ($p<0.05$). CVLT II was reduced in both VBEA groups ($p<0.05$). BDNF decreased in the aerobic exercise group ($p=0.03$), although there was no significant change between the groups ($p>0.05$). Timed 25 foot walk test was significantly decreased in all groups after training ($p<0.05$).

Conclusion: Cognitive activities-VBEA plays a potential role in reducing blood NFL and GFAP levels. VBEA affects biomarkers and cognitive function.

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P1865
Effects of Oral Magnesium Supplementation on Cognition, Mood, and Fatigue in Patients with Relapsing-Remitting Multiple Sclerosis: A Triple-Blind Randomized Controlled Trial

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Introduction: Cognitive impairment, fatigue, and mood disturbances are common and disabling in relapsing-remitting multiple sclerosis (RRMS). Oxidative stress and neuroinflammation have been proposed as contributing factors. Magnesium, with antioxidant and neuroprotective properties, may help modulate these symptoms.

Objectives/Aims: This study evaluated the effect of oral magnesium supplementation on cognitive performance, mood, fatigue, and related serum biomarkers in RRMS.

Methods: In this triple-blind randomized controlled trial, 60 RRMS patients were enrolled and randomly assigned to two groups. One group (n = 30) received magnesium oxide 250 mg three times daily, and the other (n = 30) received a matched placebo, both for 90 days. Cognitive function (MACFIMS), mood

(Beck Anxiety Inventory, Beck Depression Inventory), and fatigue (Fatigue Severity Scale) were assessed at baseline and after 3 months. Serum magnesium, superoxide dismutase (SOD), brain-derived neurotrophic factor (BDNF), and interleukin-6 (IL-6) were also measured. Inclusion criteria included age 18–55, RRMS diagnosis, ability to walk ⩾100 meters unaided, education above high school, and at least one month since last relapse or corticosteroid use. Pregnant or breastfeeding women were excluded.

Results: Of the 60 participants, 45 patients (22 placebo, 23 magnesium) completed the trial per protocol. Baseline characteristics were comparable. After 90 days, the magnesium group showed significant improvement in depression scores (BDI: $p = 0.009$), while the placebo group did not ($p = 0.718$). Anxiety scores (BAI) improved marginally in the magnesium group ($p = 0.055$), but not in the placebo group ($p = 0.387$). Fatigue scores (FSS) did not significantly change in either group.

Significant cognitive improvements in the magnesium group were observed in verbal learning (CVLT-II: $p = 0.003$), long-delay recall (CVLT-LD: $p = 0.029$), and processing speed (SDMT: $p = 0.008$). Serum levels of magnesium, IL-6, BDNF, and SOD showed no significant changes in either group.

Between-group comparisons revealed a statistically significant reduction in anxiety scores (BAI) in the magnesium group, whereas anxiety slightly increased in the placebo group ($p = 0.049$). No other between-group differences were significant.

Conclusion: Magnesium supplementation for 90 days led to significant improvements in depression and select cognitive domains in RRMS, with a notable reduction in anxiety compared to placebo. These findings suggest a potential role for magnesium as an adjunctive treatment targeting mood and cognition in MS.

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P1866
Investigating the Relationship Between Interoception, Physical Activity, and Emotional State in Individuals with Multiple Sclerosis

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Introduction: It has been suggested that interoceptive awareness may be related to physical activity level and mood; however, studies examining this relationship in detail in individuals with MS are quite limited.

Objectives/Aims: This study was conducted to investigate the relationship between interoception, physical activity, and affective state in individuals with Multiple Sclerosis (MS).

Methods: The study included 44 participants aged between 20-60 years, with an Expanded Disability Status Scale (EDSS) scores ranging ⩽ 5.5, who had not experienced a relapse in the last 3 months and had been diagnosed with MS by a neurologist. Comprehensive physical and cognitive assessments were conducted for all participants. Initially, demographic information was collected. Physical activity was assessed self-reported by using the Godin Leisure-Time Exercise Questionnaire and objectively assessed using the SenseWear activity monitor over a week period. Perceived fatigue was assessed using the Modified Fatigue Impact Scale and the Fatigue Severity Scale, while measured fatigue was evaluated with 6-Minute-Walk Test. Interoception was measured using the Interoceptive Sensory Scale. Anxiety was assessed with the Hamilton Anxiety Rating Scale, depression with Hamilton Depression Rating Scale, and alexithymia with the Toronto Alexithymia Scale.

Results: The average age of the participants was 45.27 ± 8.53 years, the average Body Mass Index (BMI) was 24.49 ± 4.77, and the average disease duration was 13.8 ± 6.28 years. Analysis of the relationship between interoception and demographic information revealed a statistically significant positive low correlation with disease duration ($r=0.298$ and $p<0.005$). No statistically significant relationships were found between interoception and both objectively and subjectively measured physical activity ($p>0.005$). Examination of the relationships between interoception and fatigue revealed a statistically significant positive good correlation with the Fatigue Impact Scale ($r=0.679$ and $p<0.005$) and a positive moderate correlation with the Fatigue Severity Scale ($r=0.412$ and $p<0.005$). No statistically significant relationships were found between interoception and measured fatigue,anxiety, depression, or alexithymia ($p>0.005$).

Conclusion: The findings of this study demonstrate that interoception influences perceived fatigue.The data suggest that interoception may indirectly affect physical activity, thereby highlighting the importance of considering interoception in both evaluation and treatment within clinical practice.

Disclosure of interest: ENDER AYVAT: nothing to disclose. FİRÜZE AYGÜN: nothing to disclose.

P1867
The impact of combination of flax (Linum usitatissimum) and black seed (Nigella sativa) hydroalcoholic extracts on fatigue in RRMS patients; a parallel randomized double-blind placebo-controlled clinical trial

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Introduction: The chronic autoimmune disease known as multiple sclerosis (MS) disrupts nerve conduction and demyelinates axons, resulting in a wide range of symptoms. One of the symptoms that people suffer the most is fatigue.
Objectives/Aims: Our goal was to assess how hydroalcoholic extracts of flax (Linum usitatissimum) in combination with black seed (Nigella sativa) affected MS patients' fatigue.
Methods: Patients having a confirmed diagnosis of relapsing-remitting multiple sclerosis (RRMS) according to the McDonald 2017 criteria with fatigue complaints were enrolled in this randomised controlled clinical study (RCT). Combination of Hydro-alcoholic extracts of Nigella sativa and flaxseed administered for three months (twice daily). Patients completed the Comprehensive Fatigue Assessment Battery for Multiple Sclerosis (CFAB-MS) questionnaire to gauge their level of fatigue and related factors twice during the study: first at baseline and then 3 months later. CFAB-MS includes VAS for General summary of health. SPSS software, version 23, was used for statistical analysis.
Results: As a result, 35 of the 50 randomised individuals in this study finished the trial. Of these, 18 were in the placebo group and 17 were in the therapeutic group. Thirty (85.7%) of the participants were female, and their average age was 34.11 years (SD = 9.10). Nigella sativa and flaxseed hydro-alcoholic extracts did not significantly enhance the following indicators: physical, mental, and social fatigue; pain; sleep issues; stress; mood; anxiety and worry; nutrition; mobility; and environment (p-values$>$0.05). Regarding the general summary of health, only patients' nutritional status as determined by the VAS was significantly affected by their ingestion of flaxseed and Nigella sativa.
Conclusion: When compared to a placebo, this RCT revealed that hydro-alcoholic extracts of Nigella sativa and flaxseed did not significantly enhance the status of fatigue and its related factors in RRMS patients.

Disclosure of interest: Reza Mosaddeghi-Heris: nothing to disclose.

P1868
Developing a fidelity assessment tool for a brief neuropsychological rehabilitation intervention for people with multiple sclerosis

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Introduction: Neuropsychological rehabilitation (NPR) is a "complex intervention", meaning that there are multiple components that constitute the intervention that need to work together to effect positive outcomes. Ensuring that NPR is implemented with fidelity is crucial for maintaining the validity of outcomes, minimising errors, ensuring consistency and preserving the intervention's theoretical framework. Variations in implementation fidelity across sites, over time and among therapists can adversely impact trial outcomes and increase the risk of false negatives (type II errors) and incorrect conclusions about the intervention's effectiveness (type III errors).
Objectives/Aims: We aimed to develop tools for assessing the fidelity of delivery of a brief NPR intervention for people with multiple sclerosis (MS) with mild to moderate cognitive problems, and assess the feasibility of its use in a multicentre randomised controlled trial.
Methods: A fidelity checklist informed by the Conceptual Framework for Implementation Fidelity was developed drawing on the intervention framework. Data were mapped onto the key intervention elements, including content, coverage, frequency and duration, with a focus on facilitation strategies, quality of delivery and participant responsiveness. The intervention record forms, audio/video recordings and case notes of the intervention sessions were used to complete the checklist to identify intervention deviations. A codebook was also developed to code the recordings for audio/video analysis of intervention delivery.
Results: Time-sampling of 28 recorded sessions (1211 minutes; 8 participants), using the fidelity checklist, showed that 88% of time coded was spent discussing intervention-specific content; the rest of the time was spent discussing other topics unrelated to cognitive problems, and included social chat/rapport building. The intervention content categories discussed most frequently were goal setting and progress on goals (27% of time) and discussing cognition and cognitive problems experienced (17% of time), which were core intervention components.
Conclusion: Therapists delivered the intervention with fidelity. The checklist developed and refined in this research can be used to evaluate the fidelity of the delivery of the NPR for people with MS in a definitive trial as part of the process evaluation. This fidelity checklist can be adapted for other similar complex interventions.

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P1869

Sunlight-enhanced Exercise Training as a Neuroimmune Modulator in MS: Effects of Outdoor vs Home-based Pilates training on Vitamin D and the Kynurenine Pathway

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Introduction: Lifestyle interventions, including structured exercise training and sunlight exposure, are increasingly recognized as modifiable factors in multiple sclerosis (MS) management. The kynurenine pathway (KYNP) is a key metabolic route linked to neuroinflammation and neurodegeneration in MS.
Objectives/Aims: This study aimed to investigate whether outdoor Pilates training under sunlight induces greater modulation of KYNP markers and serum vitamin D (vitD) levels compared to identical home-based training.
Methods: In this three-arm randomized controlled trial, 44 women with relapsing-remitting MS (RRMS) were allocated to outdoor Pilates training (OPT, n=15), home-based Pilates training (HPT, n=15), or a control group (CON, n=14). Both intervention groups completed standardized Pilates training via instructional video, three times per week for eight weeks. Serum levels of vitD, kynurenine (KYN), kynurenic acid (KA), quinolinic acid (QA), and the QA/KA ratio were assessed at baseline and post-intervention.
Results: Both OPT and HPT significantly increased KA and decreased KYN, QA, and QA/KA ratios ($p<0.05$), reflecting a shift towards a more neuroprotective KYNP profile. The OPT group showed a significantly higher increase in serum vitD (+78.4%, $p<0.001$) compared to HPT (+9.6%, $p<0.05$) and CON. Changes in vitD were strongly correlated with increases in KA ($r=0.577$, $p<0.001$) and reductions in QA ($r=-0.570$, $p<0.001$) and QA/KA ratio ($r=-0.521$, $p<0.001$).
Conclusion: These findings suggest that Pilates training promotes neuroimmune modulation in MS, with outdoor, sunlight-enhanced Pilates training offering superior biological effects via vitamin D–mediated pathways. Integrating environmental exposures such as sunlight into exercise training may enhance the efficacy of non-pharmacological MS interventions.

Disclosure of interest: Faranak Balaghi Inaloo: nothing to disclose

P1870

A Remote, Quantitative Assessment of Pelvic Floor Muscle Function in Women with Multiple Sclerosis: Pilot Data

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Introduction: Bladder dysfunction (BD) affects over 80% of people with multiple sclerosis (MS) and often results from pelvic floor muscle (PFM) impairment. Pelvic health physical therapy (PHPT) is the recommended first-line treatment due to its lack of drug interactions and side effects. Challenges to in-person PFM evaluations include travel, time, and cultural barriers. Remotely assessed PFM function could improve BD monitoring and real-time treatment response for both clinical care and research.
Objectives/Aims: To evaluate a device that promotes pelvic floor exercises as a tool for remotely assessing PFM function in women with MS, as part of a broader program to validate wearables for bladder dysfunction in MS.
Methods: Female adults with MS and BD were referred to PHPT (N=20) enhanced by a PFM training device (Perifit®). At baseline, PFM strength was assessed by a physical therapist using manual muscle testing (MMT) and an endurance check. Participants were then provided with Perifit®—a Bluetooth-connected, intravaginal tool that supports PFM training (Kegel exercises) via app-based games. Participants completed a specific game within one week of the MMT, designed to assess endurance, speed, control, and strength. Spearman correlations examined relationships between game metrics and MMT. LASSO regression identified top predictors of MMT, which were then included in a linear regression model.
Results: Data are available for the first 18 participants, with mean age 55 years (SD: 12), median disease duration 21 years (IQR: 11–26), and mild-to-moderate patient-reported EDSS (median 3.0, range 2.0–5.5). Mean MMT reflected fair strength (3-/5; range 1–5-/5), and mean endurance was 6.6 s (SD = 3.6). Device use was feasible, with an average of 107 games played over 3 months (SD:112, range ~ 353). Endurance, speed, and control all showed moderate correlations with MMT (Spearman r=0.48–0.55, $p<0.05$). When predicting MMT, LASSO selected endurance, control, and strength. Compared to the standard maximum likelihood model (generalized $R^2 = 0.314$), the LASSO model had a slightly lower R^2 (0.291) but better model fit (AICc and BIC). In both models, strength was significantly associated with MMT ($p = 0.018$ in Maximum Likelihood; $p = 0.026$ in LASSO).
Conclusion: These pilot data support the potential of neurotechnology to remotely assess key PFM domains in women with MS, outside the burdens of in-clinic evaluation. Initial analyses highlight the role of combined game metrics in predicting MMT,

with strength showing the strongest effect. Longitudinal validation in larger cohorts is planned.

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P1871
Streamlining CoachMS: A Structured Approach to Accelerate Program Implementation

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Introduction: The CoachMS program aims to provide structured coaching and education for healthcare professionals (HCPs) and people with multiple sclerosis (PwMS), fostering a collaborative learning environment. However, planning and implementing such a program requires significant coordination, involving scheduling, training, stakeholder engagement, and evaluation. A streamlined approach can accelerate program deployment while ensuring quality and effectiveness.
Objectives/Aims: To develop an efficient, structured framework to optimize the planning and implementation of the CoachMS education program, reducing time and administrative burden.
Methods: A structured roadmap was developed, incorporating milestone tracking, stakeholder engagement, and streamlined workflows. Key components included defining training schedules, identifying and recruiting HCPs and PwMS, leveraging industry collaborations, and utilizing validated evaluation tools. Meetings were held biweekly to assess progress, with responsibilities assigned to specific team members. A centralized tracking system was used to monitor completed tasks and pending actions.
Results: The structured framework significantly decreased planning and execution time by ensuring clear timelines, accountability, and systematic tracking of progress. Key milestones such as the identification of HCP trainees, development of training modules, and stakeholder engagement were achieved efficiently. The integration of a milestone-based tracking system provided real-time updates, preventing bottlenecks in implementation.
Conclusion: Implementing a structured approach to planning and executing the CoachMS program has accelerated the process, improved efficiency and reduced administrative delays. This model can serve as a replicable framework for developing similar education and coaching programs in healthcare, ultimately enhancing professional and patient engagement.

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P1872
Investigating Adverse Event Reporting in Rehabilitation Randomised Controlled Trials for People with Multiple Sclerosis

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Introduction: Multiple Sclerosis (MS) is a neurodegenerative disorder of the central nervous system, affecting an estimated 2.8 million people worldwide. MS leads to a progressive loss of neuronal function, resulting in various symptoms that impact daily life. Rehabilitation interventions aim to alleviate and/or manage these symptoms, optimise function and improve quality of life. Understanding the benefits and adverse effects (harms) of an intervention is important to inform clinical decision-making. The collection and reporting of such adverse events (AEs; defined by the World Health Organisation as 'any untoward medical occurrence that may present during treatment'), are an important aspect of trial design. Yet, guidelines used for this purpose are insufficiently detailed and the methodologies currently in practice, lacking.
Objectives/Aims: Objective: To conduct a systematic review of MS rehabilitation randomised controlled trials (RCTs) to

summarize the methods used to collect, classify, and report AEs, and identify limitations, thereof.
Methods: Methods: 15 databases were electronically searched in January 2025. Included studies were RCTs of MS rehabilitation interventions (January 2022 to January 2025). Abstracts and full texts were independently screened and selected for inclusion by two reviewers. Thematic analysis will be used to synthesize the results.
Results: Results: 1073 records were identified, of which 195 records were automatically excluded due to duplication. 878 records were screened at the title and abstract level. 736 records were excluded due to irrelevancy, 24 records due to unavailability, and 26 records due to duplication. 92 records are currently being full text screened and are anticipated to be included and data extracted. Results will be available by summer 2025.
Conclusion: This systematic review will provide insights into how AE methodology is currently implemented in MS rehabilitation RCTs. It will complement other work to be undertaken as part of a PhD studentship (Qualitative study, Delphi study), with the intended aim of strengthening the integrity and reliability of AE reporting in MS rehabilitation trials.
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P1873
Exploring the potential effects of resistance training on corticospinal excitability in persons with multiple sclerosis

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Introduction: CNS function is impaired in persons with multiple sclerosis (pwMS), and this has deleterious effects on motor function. While exercise and resistance training (RT), in particular, have beneficial effects on both voluntary strength and CNS function, limited knowledge exists for pwMS.
Objectives/Aims: The purpose of the present study was to evaluate the effects of 10 weeks of RT vs. control on (1) corticospinal excitability for the tibialis anterior muscle and (2) walking capacity in pwMS.
Methods: This preliminary dataset included n=16 pwMS (n=10 females, age 50±13 yrs, Patient-Determined Disease Steps (PDDS) 1.5±1.55 [range 0 to 4], time since diagnosis 6±9 yrs). Participants were randomized to progressive RT (n=7; 25 sessions within 10 weeks, high-loading and high-intensity, emphasis on lower extremity exercises) or control (n=9; continuation of habitual lifestyle). The primary outcome was corticospinal excitability measured as the amplitude of resting motor-evoked potentials (MEPs) using transcranial magnetic stimulation and normalized to the amplitude of the compound muscle action potential (CMAP). This was assessed for the tibialis anterior muscle of both legs (termed less and more affected side, respectively). The secondary outcome was walking capacity, represented by the 6-minute walking test distance (6MWT).
Results: At baseline, no differences were observed between RT and control in MEP amplitudes (neither for the less or more affected side) or in 6MWT. Following the 10-week intervention period, between-group changes were observed in tibialis anterior MEP amplitudes of the less affected side (increment: 0.088 [0.021;0.155], RT remained, control decreased) and of the more affected side (decrement: -0.163 [-0.236;-0.089], RT decreased, control remained). Also, a trend towards between-group changes was observed in 6MWT performance (increment: 20 [-14;54] m, RT improved, control remained).
Conclusion: Whereas RT appeared to elicit a noticeable improvement in walking capacity, these preliminary data are somewhat puzzling regarding the effects of resistance training on corticospinal excitability in pwMS. Of note, these findings are based on a limited sample size due to the ongoing nature of the project. It is anticipated that the findings relating to corticospinal excitability may change upon reaching the target sample size (n = 54).

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P1874
Can the Sense of Support Be Influenced by the Type of Medication Used in Multiple Sclerosis?

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Introduction: Multiple Sclerosis (MS) primarily affects individuals of working age and may present with mild symptoms

and minimal disability in some, while others experience disease progression and increasing disability over time. Coping with social stigma and receiving emotional support are significant challenges faced by young people with MS in academic and professional environments.

Objectives/Aims: To assess the correlation between feelings of support experienced by individuals with MS and the type of medication used in their treatment.

Methods: A Brazilian online survey was conducted with the participation of 464 individuals diagnosed with MS, including 368 women and 96 men. Among them, 369 had the relapsing-remitting form, 19 had secondary progressive MS, 8 had primary progressive MS, and 71 were unsure of their MS type. A chi-square test was used to assess the relationship between the type of medication used and the perception of stigma and emotional support in the workplace. p-values < 0.001 were considered statistically significant.

Results: The average age of participants was 37.87 years, and the average time since diagnosis was approximately 4 years (48.14 months). In terms of current treatment, 61.4% (219) were using intravenous medications, 12.9% (33) injectable (subcutaneous or intramuscular), and 17.1% (156) oral medications. In this study, 14 patients (8.9%) reported not using any medication for MS. Approximately 47% of participants had hidden their MS diagnosis due to fear of losing their job or a personal relationship. However, 71% reported feeling supported by family and friends. When analyzing the type of medication and feelings of support, 84.6% (OR = 3.25; 95% CI: 1.96–5.38) of those using oral medications reported feeling supported, compared to 57.6% of those not undergoing any treatment.

Conclusion: With the ongoing advancement in MS treatments, multiple administration routes are now available. This study observed that patients using oral medications reported a greater sense of support, while those not receiving any treatment were more likely to feel unsupported. These findings suggest that the choice of treatment may have psychosocial implications and could influence patients' perception of support in their social environments.

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RIMS – Outcomes and digital biomarkers to measure rehabilitation treatment effect in Multiple Sclerosis

P1876
Beyond walking speed: advanced kinematic analysis of lower limb joints can provide useful information to characterize changes in gait of people with Multiple Sclerosis

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Introduction: Speed (alone or in combination with other key spatio-temporal parameters such as step length and cadence) still represents the most widespread outcome employed to characterize the progression of gait dysfunctions, as well as the effectiveness of rehabilitative and pharmacologic treatments targeted on ambulation in people with Multiple Sclerosis (pwMS). However, while easy to measure, it lacks insight into gait quality, including joint mobility, coordination, and symmetry. Spatio-temporal parameters are also unable to highlight key altered gait cycle phases post-treatment.
Objectives/Aims: This study retrospectively analyzes three research projects at the Multiple Sclerosis Center of Sardinia (Cagliari, Italy), involving 96 pwMS undergoing integrated rehabilitative and/or pharmacologic treatments. Specifically, 20 participated in a 6-month Adapted Physical Activity (APA) program, 23 received combined rehabilitation and cannabinoid treatment for generalized spasticity, and 18 with focal ankle spasticity were treated with botulinum toxin (BT). The aim was to assess whether gait speed changes were accompanied by clinically meaningful kinematic variations.
Methods: Participants underwent 3D Gait Analysis to evaluate spatio-temporal parameters of gait as well as hip, knee, and ankle kinematics. Statistical parametric mapping (SPM), inter and intra-limb cyclograms, and the Gait Profile Score (GPS) identified gait cycle modifications post-treatment, quantified deviations from normal gait and characterize coordination.
Results: Participants in the APA program improved gait speed due to increase in cadence and stride length, while GPS remains practically unaltered. However, improvements in knee-ankle and hip-knee coordination were found and SPM detected increased knee flexion and ankle plantar-flexion at late stance. PwMS treated with rehab/cannabinoids improved gait speed, but GPS and SPM did not find any significant difference in kinematics during the gait cycle and hip-knee coordination slightly improved. Finally, in those treated with BT, no significant changes were observed in any of the parameters investigated.
Conclusion: Gait interventions should ensure that speed improvements align with enhanced joint mobility, coordination and symmetry, aspects that can be effectively assessed using easy-to use IMU-based motion capture systems.

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P1877
An engineered 9-Hole Peg Test for automated hand dexterity assessment in multiple sclerosis

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Introduction: The 9-Hole Peg Test (9HPT) is the gold standard for assessing upper limb function in people with multiple sclerosis (PwMS), with total time to insert and remove nine pegs recorded manually, making it operator-dependent.
Objectives/Aims: We propose a novel sensor-equipped 9HPT that automatically detects peg insertion and removal, eliminating operator bias and enabling the measurement of additional temporal parameters, such as insertion/removal times and inter-peg intervals, for a more detailed assessment of hand dexterity.
Methods: In this pilot study, we enrolled 10 PwMS (age = 56.6±5.8 y, disease duration = 18.1±11.9 y, median Expanded Disability Status Scale score = 3) and 10 healthy controls (HC) (age = 51.4±8.0 y) to assess the feasibility of this platform. All participants, right-handed, performed the test twice with their right (RH) and left (LH) hands. Results from the system, managed via a tablet app, were compared to manual stopwatch recordings by a single expert assessor, and derived parameters were compared between groups.
Results: Notably, both operator and participants found the system acceptable and comparable to the conventional test. A strong correlation was found between total execution times measured by both methods (RH: $r=0.99$, $p<0.001$; LH: $r=0.96$, $p<0.001$), indicating measurements reproducibility. Additionally, the engineered 9HPT provided temporal metrics unavailable through manual measurement. PwMS exhibited longer execution times than HC (RH: total: 21.95±4.21 vs. 18.14±1.57 s, $p=0.01$; insertion: 13.88±2.28 vs. 11.92±1.05 s, $p=0.02$; removal: 6.76±1.84 vs. 5.22±0.65 s, $p=0.02$; LH: total: 23.53±3.62 vs. 18.99±1.65 s, $p=0.002$; insertion: 14.96±1.95 vs. 12.77±1.34 s, $p=0.009$; removal: 7.09±1.71 vs. 5.18±0.60 s, $p=0.004$). PwMS also showed a longer interval between the insertion and removal phases (RH: 1.31±0.38 vs. 1.01±0.17 s, $p=0.03$; LH: 1.48±0.57 vs. 1.04±0.16 s, $p=0.03$) and longer inter-peg intervals with the LH (LH: insertion: 1.26±0.15 vs. 1.10±0.14 s, $p=0.02$; removal: 0.71±0.15 vs. 0.53±0.06 s, $p=0.003$). These findings suggest that PwMS need more time to plan the single finger movements.
Conclusion: We propose this engineered 9HPT as a new tool for assessing upper limb function in PwMS and plan to expand data collection in healthy individuals across age groups to establish normative values for evaluating hand dexterity in PwMS. This system could also offer insights into peg insertion order, potentially assessing cognitive aspects of motor planning, which are currently unexplored.

Disclosure of interest: The authors declare that they have nothing to disclose

P1878
Development of a telemonitoring system for assessing mobility and cognitive load during activity of daily living for People with Multiple Sclerosis

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Introduction: People with multiple sclerosis (PwMS) often experience difficulties performing Activities of Daily Living (ADLs). In current clinical practice, ADLs performance is typically assessed by occupational therapists using observation-based tools, which often lack sensitivity to mild impairments and subtle changes over time. Recent advancements in wearable sensor technologies and artificial intelligence (AI) offer promising opportunities to remotely monitor motor and cognitive function in real-life settings, enabling more objective and continuous assessments.
Objectives/Aims: This pilot study aims to evaluate the usability and acceptability of AI-MOKa—a telemonitoring system integrating wearable sensors and AI algorithms—and to collect preliminary metrics (pupil dilatation, gaze tracking, number of steps, weight distribution shift) in healthy subjects (HS). The system is designed to assess mobility and cognitive functions during ADLs in PwMS.
Methods: HS performed a coffee preparation task, extracted from the Assessment of Motor and Process Skills (AMPS), while wearing Tobii sensorized glasses for gaze tracking and pupil dilation analysis, and Sensing Tex sensorized insoles to assess gait and balance. AI-based algorithms processed the data to automatically detect the work areas (living room, cutlery drawer, coffee area, stock, shelf) marked with QR codes, identify task phases and object interactions, and extract metrics related to gait, balance, and cognitive load. Usability was evaluated through ad hoc questionnaires.
Results: Four HS (4 males, mean age = 38.0 ± 16.4 years) completed the task. The AI-MOKa system successfully identified working areas, objects, and task phases, showing that participants' movements were predominantly confined to the coffee preparation zone. Pupil diameter trends suggested that coffee machine manipulation and coffee serving were the most cognitively demanding subtasks. Preliminary motor metrics included: total number of steps (159.0 ± 60.3), steps during the serving phase (13.8 ± 8.8), number of weight distribution shifts between left and right foot in the coffee area (66.3 ± 45.7), and distribution shifts rate (10.6 ± 6.9 shifts/minute). Participants rated the system as comfortable, non-intrusive, and highly usable, with strong ecological validity.
Conclusion: This study introduces a novel technological approach for assessing motor and cognitive performances during ADLs in real-life settings, enabling more objective, accurate and continuous monitoring and evaluation.

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P1879
Different rehabilitative protocols of the upper limbs in progressive multiple sclerosis treated with anti CD20 monoclonal antibodies

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Introduction In progressive MS, both inflammation and degeneration occur, with inflammation potentially contributing to degeneration. Anti-CD-20 monoclonal antibodies reduce inflammation, and this study investigates whether patients with controlled inflammation may have a higher potential to benefit from rehabilitation (ClinicalTrials.gov ID: NCT06894940).
Objectives/Aims: This study aimed to assess the efficacy of different physiotherapeutic interventions on upper limb function in progressive MS patients treated with anti-B monoclonal antibodies.
Methods: Seventy-nine progressive MS patients treated with anti-B monoclonal antibodies for at least six months (3 ⩽

Expanded Disability Status Scale ⩽ 7, Mini-Mental State Examination ⩾ 24) were randomized into three groups: intensive task-oriented therapy with (A) or without (B) virtual reality, and passive mobilization (C). All received general rehabilitation. Upper limb performance was assessed using the Nine-Hole Peg Test (9HPT), Action Research Arm Test (ARAT), Hand Test System (HTS), and MRI at baseline (T0), after 8 weeks (T1), and at 3-month follow-up (T2).
Results: The primary endpoint was 9HPT, but no significant differences were observed between T0, T1, and T2. In the right arm, ARAT analysis showed significant differences between T2 and T0 (p=0.0029), with a trend for Group A vs C (p=0.059) and a significant difference for Group B vs C (p=0.010). In all patients treated with the three protocols, a significant reduction in HTS parameters was observed between T1 and T0, and in some assessments, also between T2 and T0 (right T1: p=0.21; T2: p=0.027, left T1: p=0.001, A vs C p=0.034, B vs C p=0.016; T2: p=0.34). No new MS lesions were observed at T1 and T2 in any subject. No significant differences were found in repeated measures analysis. Voxel-Based Morphometry (VBM) analysis revealed no significant differences within or between groups across the entire cortex.
Conclusion: The study demonstrated effective rehabilitation, with no significant improvement in 9HPT, which lacks sensitivity to small changes. The Hand Test System (HTS), offering personalized values, may better detect subtle changes in hand function. Gains were observed in ARAT scores, with sustained effects from task-oriented therapy and virtual reality (up to 3 months). Passive mobilization showed limited effectiveness. No changes in brain volumes were noted, but motor function and quality of life improved.
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P1880
Effectiveness of an Evidence-Based Online MRI Education Tool for People with Multiple Sclerosis: A Randomised Controlled Trial

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Introduction: Magnetic resonance imaging (MRI) is critical for managing multiple sclerosis (MS), but its complexity limits informed decision-making. To address knowledge gaps, we developed "Understanding MRI in MS" (UMIMS), an interactive evidence-based patient information (EBPI) tool.
Objectives/Aims: This study investigated whether UMIMS improves MRI-related risk knowledge and supports shared decision-making (SDM) among people with MS (pwMS).
Methods: In this double-blind, randomised controlled trial, 120 individuals with relapsing-remitting MS or clinically isolated syndrome were assigned to either the UMIMS intervention or a control website. The primary endpoint was the change in MRI-specific risk knowledge after two weeks, measured via the MRI-RIKNO 2.0 questionnaire (maximum score: 22). Secondary endpoints included MRI-related emotions, autonomy preferences, perceived SDM, and quality of life.
Results: MRI risk-knowledge increased significantly more in the UMIMS group (mean change: +4.00; SD 3.27–4.72) than in controls (+2.77; SD 2.06–3.48; p = 0.019). Feelings of competence improved in both groups, with a steeper increase observed in the control group. MRI-related anxiety and perceived control remained stable and did not differ between groups. Both groups reported high baseline levels of autonomy and SDM regarding MRI and treatment decisions, which remained unchanged throughout the study.
Conclusion: UMIMS significantly enhances MRI-specific risk-knowledge in pwMS. Despite no additional effect on MRI-related emotions or SDM behaviours, the tool may facilitate informed appraisal of MRI findings and support patient engagement in disease management.

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P1881
Reliability and Validity of the Turkish Version of the Arm Function in Multiple Sclerosis Questionnaire (AMSQ)

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Introduction: Upper extremity dysfunction is common in persons with multiple sclerosis (pwMS) and significantly impacts daily activities such as dressing and eating. However, it is often under-assessed, as clinical attention tends to focus on mobility issues. The Arm Function in Multiple Sclerosis Questionnaire (AMSQ) is a disease-specific patient-reported outcome measure (PROM) that captures patients' perceptions of upper limb function. Validating the Turkish version of the AMSQ allows its use in clinical and research settings in Türkiye, providing a patient-centred tool to complement objective assessments.
Objectives/Aims: This study aimed to examine the reliability and validity of the Turkish version of the AMSQ in pwMS.
Methods: The AMSQ was translated and culturally adapted into Turkish under the supervision of an expert committee to ensure linguistic accuracy and cultural relevance. A total of 230 pwMS were included. To assess reliability, internal consistency was measured using Cronbach's alpha, and test-retest reliability was evaluated with intraclass correlation coefficients (ICCs). Construct validity was examined using exploratory factor analysis. For convergent and known-group validity, the AMSQ was compared with the Manual Ability Measure-36 (MAM-36), Multiple Sclerosis International Quality of Life Questionnaire (MusiQoL) and its activities of daily living (ADL) subscale, 9-Hole Peg Test (9HPT), Coin Rotation Task (CRT), Jamar handgrip dynamometer, Patient-Determined Disease Steps (PDSS), Expanded Disability Status Scale (EDSS), and Modified Ashworth Scale (MAS).
Results: The mean age of participants was 40.3 years (SD=11.3), and 70% were female. Most had relapsing-remitting MS (80%), with a mean EDSS score of 2.9 (SD=2.3). Internal consistency of the AMSQ was excellent (α=0.98), and test-retest reliability was high (ICC=0.96). Factor analysis supported a single-factor structure explaining 62.4% of the variance. High correlations were found with MAM-36 (ρ = -0.91) and the MusiQoL ADL subscale (ρ = -0.72), and moderate correlations with 9HPT, CRT, handgrip strength, and the MusiQoL. Known-group validity was supported by significantly higher AMSQ scores in participants with upper limb spasticity ($p<0.001$).
Conclusion: The Turkish version of the AMSQ is a reliable and valid tool for evaluating upper extremity function in pwMS. It helps identify patient-reported upper limb limitations. Its use in rehabilitation can support personalised treatment planning, improve patient engagement, and track therapy outcomes. It also holds potential as an outcome measure in clinical trials targeting upper limb function in pwMS.

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P1882
Spatio-Temporal Variability During Gait with Cognitive Dual-Task as a Physical Biomarker in People with Multiple Sclerosis

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Introduction: Balance and gait impairment are common symptoms in multiple sclerosis and increase the disability level of people with multiple sclerosis (pwMS). However, balance and gait impairment in pwMS is challenging to measure and define because its presentation varies widely. Therefore, examining parameter variability during a task involving dynamic balance and locomotion, such as gait, may assist the clinician in identifying pwMS with balance and gait impairment.
Objectives/Aims: This study aimed to examine whether the spatio-temporal variability during gait with a cognitive dual-task could be used as a physical biomarker for balance and gait impairment in pwMS.
Methods: This cross-sectional study included 25 pwMS. Demographic information about the participants was recorded. Disability level was assessed with the Expanded Disability Status Scale (EDSS). BTS® G-walk gait analysis system was used for gait analysis, Biodex® Biosway Balance Analysis System was used for balance assessment, the 6-minute walk test (6MWT) was used for functional walking capacity assessment, and the timed up and go (TUG) test was used for mobility skill assessment. Each participant walked the 10-meter path 6 times. As a cognitive dual task, the participant were asked to count backwards by subtracting 7 from the given number during gait. For the calculation of spatio-temporal variability, coefficients of variation for gait cycle duration, stride length, step length, and first double support period duration of 6 gait repetitions were calculated.
Results: Participants' EDSS scores were a minimum of 1 and a maximum of 4. There was a negative relationship between TUG duration and variability of step length (p=0.02, r: 0.45) and the first double support time (p=0.006, r: 0.53). There was a negative relationship between 6MWT distance and variability of step length (p=0.03, r=0.43). There was a negative relationship between postural stability and variability of gait cycle time (p=0.03, r=0.41), stride length (p=0.04, r=0.41), step length ($p<0.001$, r=0.65), and first double support time (p=0.001, r=0.62). Also, there was a negative relationship between stability limits and variability of gait cycle duration (p=0.006, r=0.52) and the first double support time (p=0.007, r=0.52).
Conclusion: A moderate relationship was found between the variability of spatio-temporal parameters during gait with a cognitive dual-task and physical parameters of pwMS. Therefore, consistent with our hypothesis, spatio-temporal variability during gait with a cognitive dual-task is a usable

parameter in the evaluation of balance, walking capacity, and mobility skills of pwMS. It may be a good tool for rapid assessment of balance and gait in pwMS. Thus, clinicians can use spatio-temporal variability of gait both to demonstrate the effects of rehabilitation treatment and to determine balance and gait disorders in pwMS.

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P1883
Neurophysiological and interoceptive correlates of physical fatigability in early multiple sclerosis

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Introduction: People with multiple sclerosis (PwMS) often experience reduced physical endurance, even in the early stages of the disease. The interplay between fatigue, fatigability, and underlying mechanisms such as cortical excitability, inhibition, and interoception remains poorly understood.
Objectives/Aims: To investigate the relationship between fatigue, fatigability, cortical excitability/inhibition, and interoception in PwMS with minimal disability.
Methods: Sixteen PwMS (9F; age: 41.8±8.1; EDSS: 1.95±0.94) and twenty matched healthy controls (HC) performed a 6-minute walking test (6MWT) to assess endurance. A Visual Analog Scale (VAS) was used to quantify fatigue, and the Pittsburgh Fatigability Scale for physical (PFS_{phy}) and cognitive (PFS_{cog}) fatigability. Transcranial magnetic stimulation at 105–155% of the active motor threshold during a 10% maximal voluntary contraction of the first dorsal interosseus was used to build two recruitment curves (RC); one for Motor Evoked Potential amplitude (RC_{MEP}) and another for contralateral Silent Period duration (RC_{cSP}). Slope of RC_{MEP} and area under RC_{cSP} were considered as outcome variables. Additionally, a Heartbeat Tracking Task (HTT) was used to assess interoceptive accuracy, where participants silently counted their heartbeats without taking their pulse. Depending on data distribution, group comparisons were conducted using parametric or non-parametric tests, and correlations were assessed with Pearson or Spearman coefficients.
Results: PwMS walked shorter distances ($p=0.001$) and reported higher physical fatigability ($p<0.01$) compared to HC. In PwMS only, 6MWT performance significantly correlated with VAS ($r=-0.58$), PFS_{phy} ($r=-0.72$), and PFS_{cog} ($r=-0.55$). Lower RC_{MEP} slope was associated with higher PFS_{phy} ($r=-0.59$) and PFS_{cog} ($r=-0.60$), while greater area under RC_{cSP} correlated with higher PFS_{phy} ($r=-0.53$) and worse interoceptive accuracy ($r=-0.81$).
Conclusion: In PwMS with minimal disability, physical fatigability is strongly associated with walking endurance. This limitation appears to be linked to reduced cortical excitability and prolonged inhibition. Interoception may serve as a relevant outcome for evaluating rehabilitative interventions to improve endurance and reduce fatigability in PwMS.

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P1884
The effectiveness of combining a home-based Digital motor Telerehabilitation program with conventional therapy in Progressive Multiple Sclerosis: a multicentre, randomized controlled trial

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Introduction: The rehabilitative management of progressive forms of multiple sclerosis (MS) remains a complex challenge due to a limited understanding of their pathophysiology and the scarcity of effective rehabilitative strategies.
Objectives/Aims: This study primarily aims to evaluate the effectiveness of combining a home-based digital telerehabilitation program with conventional in-hospital rehabilitation on mobility, compared to in-hospital rehabilitation alone, in patients with SPMS or PPMS. Secondary objectives include assessing the effects on other motor, cognitive and psychological functions, fatigue, pain, perceived clinical change, quality of life, and cost-effectiveness.
Methods: This is a multicenter, randomized, controlled, single-blind study [NCT06485115], funded by the Italian Multiple Sclerosis Foundation (grant no. 2023/R-Multi/010), aiming to enroll 78 participants with SPMS or PPMS, randomized into two groups. The experimental group (EG) follows a 12-week home-based digital telerehabilitation program in addition to 10 in-hospital rehabilitation sessions (1 hour/day, 3 days/week). The control group (CG) receives only in-hospital rehabilitation. Validated tools are used to assess functional mobility (primary outcome), as well as motor and cognitive functions, quality of life, fatigue and pain, cost-effectiveness, and user experience with the technology. Blinded evaluations are conducted at baseline (T0), after in-hospital rehabilitation (T1), and at 12 (T2) and 24 weeks (T3).

Results: A total of 26 participants were enrolled (EG=15, CG=11; mean age: 57.4 ± 10.6 years; 14 F, 12 M; median EDSS: 5). Of these, 36% were employed, 32% retired; 14% reported emergency department visits and 7% had prolonged hospitalizations in the six months prior. Assistive devices were used by 30% of participants (mean cost: €151.70 ± 98.9), and average medication expenditure was €220.06 (±300.01); 21% had made home modifications. No significant differences were found in the primary outcome (TUG) at T1 (p=0.601) or T2 (p=0.730). Secondary outcomes also showed no significant differences at T1 (p>0.05), except for the B-IPQ (p=0.043). At T2 (n=9), no significant differences emerged for TUG, 10MWT, NHPT, PASAT, or T25FW. User acceptability of the technology was high, with a mean TSQ-WT score of 3.28 out of 4 (SD: 1.46), and a positive perception of the in-home rehabilitation experience (mean score: 7.33 out of 10; SD: 1.46).
Conclusion: Preliminary data indicate high acceptability of the technology, as reflected in satisfaction questionnaires, and suggest that digital telerehabilitation may represent a sustainable and well-tolerated option for the ongoing support of rehabilitation in people with progressive MS. Further analysis on the full sample will be essential to assess the potential long-term clinical impact and cost-effectiveness of this approach.

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P1885
Construct validity of a revised short falls efficacy scale for ambulatory and non-ambulatory people with MS

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Introduction: Fall self-efficacy is a recommended outcome measure of concern of falling to be used in all fall preventions interventions. To meet the need for a measure applicable for both ambulatory and non-ambulatory people with MS (PwMS) we revised the Short Falls Efficacy Scale-International (Short FES-I) by changing the wording in three of its seven items.
Objectives/Aims: To evaluate construct validity of a Revised Short FES-I (R Short FES-I).
Methods: Construct validity was evaluated by hypotheses testing. A priori hypotheses on expected relationships with questionnaires measuring similar and dissimilar constructs and a between-group difference were tested by Pearson's correlation analyses and an independent t-test, respectively. Baseline data from 165 ambulatory and 60 non-ambulatory PwMS participating in our ongoing *Fewer Falls* study were used. We hypothesised that R Short FES-I would have high positive correlations (r=0.7-0.9) with Short FES-I, FES-I and Spinal Cord Injury-Falls Concern Scale (SCI-FCS); moderate positive correlations (r=0.5-0.7) with Fatigue Severity Scale (FSS) and MS Impact Scale (MSIS-29) physical subscale; low positive correlations (r=0.3-0.5) with MSIS-29 psychological subscale and Hospital Anxiety and Depression (HAD) subscales; and negligible negative correlation (0 to -0.3) with Mini Montreal Cognitive Assessment Scale (Mini MoCA). In addition, a significant difference was expected between 108 participants classified as frequent fallers (>2 falls previous 6 months) and 117 non-frequent fallers. Frequent fallers were expected to have more concern of falling and thereby a higher mean R Short FES-I score.
Results: Seven of nine correlation hypotheses were supported, namely the correlations with FES-I (r=0.90), SCI-FCS (r=0.85), HADS depression subscale (r=0.34), MSIS-29 physical (r=0.68) and psychological (r=0.47) subscales and Mini MoCA (r= -0.09). However, the correlation between R Short FES-I and Short FES-I (r=0.93) was higher than expected, and correlations with FSS (r=0.38) and HAD anxiety subscale (r=0.20) were lower than expected. The between-group hypothesis was supported. The mean (95%) difference was 1.5 (95% CI 0.5-2,6), p=0.005.
Conclusion: These findings provide evidence of construct validity for a new concern of falling measure suitable for both ambulatory and non-ambulatory PwMS. However, further psychometric studies are recommended.

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P1886
Calcium Levels are Related to Muscle Activity and Functionality in Patients with Multiple Sclerosis

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Introduction: Calcium plays a crucial role in muscle contraction by regulating the interaction between actin and myosin, the proteins responsible for generating muscle force. Upon the transmission of a nerve signal to a muscle, calcium ions are released from the sarcoplasmic reticulum into the muscle cell, thereby initiating the contraction process. The relationship between muscle contractions and mineral levels is worthy of note. Mineral deficiencies, particularly in calcium, can have a deleterious effect on muscle function and mobility in patients with Multiple Sclerosis (MS).
Objectives/Aims: The aim of the study is to investigate relationships between muscle contractions and mobility, functional capacity, mineral levels in patients with MS.
Methods: Fifty-one patients with MS (38F/13M; 40.17± 12.32/ years) whose Expanded Disability Status Scale (EDSS) score <5 were included in this study. Superficial electromyographic measurements were performed with Myoplus 2 Neurotrac® device for bilateral m. vastus lateralis and m. rectus femoris. The mobility was assessed with Timed-up and go (TUG) test, functional capacity was assessed with 2 Minute Walk Test (2 MWT). Blood sample of patients was analysed for Calcium (Ca+2) in the laboratory.
Results: While there was a positive significant relationship between Ca level and right Vastus lateralis muscle work average level (r=0.308, p=0.028) there was a negative relationship between EDSS (r=-0.169, p=0.235), TUG (r=-0.195, p=0.170) and positive relationship between right and left rectus femoris (r=0.254, p=0.073; r=0.191, p=0.179), left vastus lateralis muscle work average level (r=0.266, p=0.060).
Conclusion: Low calcium levels in people with MS can affect the vastus lateralis muscle work and can also have a negative impact on disability, mobility and functional capacity. Considering essential role of calcium for effective muscle contraction, early and regular screen of calcium levels may prevent from the deteriorated muscle function and disability in patients with MS.

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P1887
Evaluating effectiveness of inpatient rehabilitation services at a national MS Rehabilitation Center in Norway

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Introduction: Rehabilitation for people with MS (PwMS) aims to improve symptom management, activity levels, and quality of life (QoL). Despite positive effects of rehabilitation, systematic evaluation in clinical practice is often lacking. Comprehensive assessment should cover multiple dimensions, including QoL, physical and cognitive function, fatigue, and other symptoms. Individual goal-setting is recommended. No internationally recognized questionnaire pack exists for routine use.
Objectives/Aims: To (1) develop a questionnaire package to evaluate rehabilitation outcomes; (2) evaluate the inpatient rehabilitation services at a national MS rehabilitation center in Norway; (3) provide recommendations to optimize the service.
Methods: Phase 1 identified what PwMS perceive as good rehabilitation outcomes and their opinion on assessment frequency. Based on their feedback and literature review, a questionnaire pack was developed. In Phase 2, this package was used to evaluate the services at admission (T1), discharge (T2), and six weeks post-discharge (T3).
Results: Two focus group interviews (n=11) showed diverse factors considered important for successful rehabilitation. Participants emphasized a balanced approach, sufficient time to experience change, and regular follow-up. Flexibility in data collection methods, including digital tools, was highlighted.
The developed questionnaire pack included measures of symptom burden (SINTEF-Hakadals questionnaire), self-efficacy (General Perceived Self-Efficacy Scale), acceptance of MS (MS Acceptance Questionnaire), physical and psychological impact (Multiple Sclerosis Impact Scale-29), individual goal achievement, and overall health status (EQ5D-5L).
Of 118 patients invited, 103 (87.2%) participated. The average age was 49.8 years (SD=12, range 26-77), with 69.9% women (n=72). At admission, participants reported an average of 11.9 symptoms, indicating complex needs. A general reduction in symptom burden was observed from T1 to T2 and T3. Significant improvements were observed in symptom burden, self-efficacy, and quality of life from T1 to T2 and T3.
Conclusion: Inpatient rehabilitation significantly improved symptom burden, function, and quality of life for PwMS. Most participants showed positive progress during their stay, with benefits persisting after six weeks. However, some regression was observed, highlighting the need for further follow-up. Continuous follow-up is necessary to maintain rehabilitation gains.

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P1888
Effects of Different Exercise Modalities on Distinct Serum Kynurenine Pathway Patterns in MS: A Secondary Analysis of Four Randomized Controlled Trials

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Introduction: Kynurenine pathway (KP) metabolites (kynurenines) are tryptophan derivatives with neuroactive properties that partially resemble molecular mechanisms of neuroaxonal damage in MS. We recently identified two distinct serum KP patterns in 353 persons with MS using exploratory factor analysis (EFA): an inflammation-driven neurotoxic pattern (*NeuroTox*) and a neuroprotective pattern (*NeuroPro*). Exercise provokes acute changes in concentrations of individual kynurenines in persons with MS.
Objectives/Aims: To assess exercise-induced changes in the KP patterns, *NeuroTox* and *NeuroPro*, in persons with MS.
Methods: In this secondary analysis, we examine the effects of different exercise modalities on *NeuroTox* and *NeuroPro* in four subgroups of our discovery cohort (EMSES, NCT03322761; EXBRAIN, NCT02661555; HIITMS, NCT04356248; FunTraiMS, DRKS00017091). *NeuroTox* and *NeuroPro* will be investigated in linear mixed model follow-up analyses from baseline to 3, 10, or 24 weeks of intervention. EFA will be repeated for kynurenine concentrations post-intervention to study temporal stability of *NeuroTox* and *NeuroPro*. Sensitivity analyses will be performed to assess changes in these KP patterns as a function of participant characteristics, such as age or baseline fitness.
Results: We investigate participants from the EMSES (n= 56, 73% female, 38.1 ± 9.6 years, EDSS 1.63 ± 1.00), EXBRAIN (n= 75, 56% female, 45.2 ± 9.4 years, EDSS 2.73 ± 1.47), HIITMS (n= 100, 69% female, 50.2 ± 9.5 years, EDSS 4.67 ± 1.29), and FunTraiMS cohorts (n= 20, 80% female, 36.1 ± 5.3 years, EDSS 1.55 ± 1.06). Data are currently being analyzed. We hypothesize (1) an exercise-induced reduction in *NeuroTox* and/or increase in *NeuroPro*, (2) while the two-factor solution and factor loading structure of EFA remain stable.
Conclusion: This study offers a comprehensive perspective on exercise-induced changes in the KP metabolome. Findings may inform future studies investigating changes in KP patterns as a molecular mechanism underpinning the beneficial effects of exercise in MS.

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P1889
Effect of functional proprioceptive stimulation on balance in moderate multiple sclerosis: a randomized controlled pilot and feasibility study

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Introduction: Mobility difficulties, especially balance impairment and increased risk of falls, are more common in moderate multiple sclerosis (MS) due to complex neuromuscular disability. The Vibramoove device may offer a novel approach by using proprioceptive stimulation to improve balance control and stimulate neuroplasticity.
Objectives/Aims: To assess feasibility of implementing Vibramoove device in outpatient rehabilitation and its potential effect on balance.
Methods: This was a randomized controlled pilot and feasibility study. Two-hundred fifty-nine patients from the MS Centre of the University Hospital Ostrava, with a history of outpatient rehabilitation (in the last three years), were screened to meet the inclusion criteria (EDSS 5.0-6.5); 57 of them (22%) were eligible. During the recruitment period (10patients/month), we approached 25 patients, of whom 5 (20%) declined to participate (unwilling to commute, not have enough time, excluded due to psychiatric comorbidity, and ischemic disease of the lower extremity). Twenty patients with moderate MS (EDSS 5-6.5, 56% females, age 49,7±10,9 years) were randomly allocated to either an experimental group (balance exercises using the Vibramoove device, protocol MODE 1, 3x/week, 6 sessions of 30minutes) or a control group (education in the same home balance exercises). Feasibility assessments focused on process, resources, management, and scientific domain. Clinical outcomes were measured by posturography (limits of stability (LoS)) and clinical balance test (Timed Up and Go (TUG)).
Results: Finally, both groups didn't differ in the baseline assessment. All patients improved in the monitored parameters of LoS. The experimental group showed a significant improvement in Endpoint Excursion Back *($p<0,05$)*. The control group showed a significant improvement in TUG *($p<0,05$)* but without minimal clinically important difference.
Conclusion: The Vibramoove device is well tolerated by patients in balance training – the adherence and retention rates

were 100%. Minor adverse events were observed during therapy; the level of vibration intensity protocol needed to be adapted to the body constitution. We recommend including patients with ischemic disease of the lower extremities in the exclusion criteria due to intolerance. The effectiveness of the Vibramoove device on balance in patients with moderate MS over a short period (2 weeks) has not been shown to be superior to exercise alone, but further research with larger sample sizes and over a longer follow-up period is needed to establish the true clinical value of Vibramoove for balance in MS.

Disclosure of interest: All authors have nothing to disclose.

P1890
Invisible symptoms in Multiple Sclerosis: quantify alterations in body perception to boost rehabilitation

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Introduction: Our body is an object of perception, we sense its shape, weight, temperature, and experience it as our own. These perceptions (BP) rely on neural body representations, shaped by a continuous brain-body exchange of multisensory signals. Disruptions due to neural damage or sensorimotor deficits can alter BP, affecting rehabilitation and quality of life. While BP alterations are documented post-stroke, their role in Multiple Sclerosis (MS) remains largely unexplored.
Objectives/Aims: This study aims to explore the presence and frequency of BP alterations in people with Multiple Sclerosis (PwMS). We will also investigate how sensory, motor, and cognitive deficits potentially contribute to these alterations, to inform future rehabilitative strategies.
Methods: We assessed BP in 31 individuals with relapsing-remitting MS using the Affected Limb Perception Questionnaire (ALPQ), a newly developed digital tool adapted for MS. PwMS were in early (⩽5 years post-diagnosis) and stable (⩾6 months since last relapse) disease phases.
Results: While recruitment is ongoing, preliminary analyses (N=31) showed frequent BP alterations in upper (UL, 61% of PwMS reporting at least 1 alteration) and lower limbs (LL, 84%), particularly in perceived temperature (UL: 35.48%; LL: 51.61%), weight (UL: 29.03%; LL: 58.06%), and involuntary movements (UL: 35.48%; LL: 51.61%).
Conclusion: To date, this is the first study to report a broad range of BP alterations in both UL and LL in PwMS. To identify the underlying factors influencing BP, we will model sensory, motor, and cognitive scores obtained through clinical assessments against ALPQ responses. The high and early presence of BP disturbances raise new questions about their role in disease progression and clinical phenotypes. This opens new opportunities for interventions, as tailored rehabilitative strategies directly targeting BP via multisensory stimulation.

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P1891
Tracking Walking Capacity in people with Multiple Sclerosis without disability: 3-Year Follow-Up of Objective and Subjective Gait Measures

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Introduction: This study aimed to investigate longitudinal changes in walking performance over a three-year period in individuals with multiple sclerosis (pwMS) exhibiting no or mild disability.
Objectives/Aims: A cohort of 321 pwMS (32.3 ± 9.8 years, 75% females, median EDSS 1.0) was followed for three years. Walking performance was assessed using the Timed 25-Foot Walk Test (T25FW), Six-Spot Step Test (SSST), 2-Minute Walk Test (2MWT), Timed Up and Go (TUG) test, and the Multiple Sclerosis Walking Scale-12 (MSWS-12). Leisure-time exercise behaviour was assessed using the Godin Leisure-time Exercise Questionnaire.
Methods: A cohort of 321 pwMS (32.3 ± 9.8 years, 75% females, median EDSS 1.0) was followed for three years. Walking performance was assessed using the Timed 25-Foot Walk Test (T25FW), Six-Spot Step Test (SSST), 2-Minute Walk Test (2MWT), Timed Up and Go (TUG) test, and the Multiple Sclerosis Walking Scale-12 (MSWS-12). Leisure-time exercise behaviour was assessed using the Godin Leisure-time Exercise Questionnaire.
Results: No significant changes in walking performance were observed over the three-year period. The median T25FW duration remained stable (4.8 s to 4.7 s, $p = 0.3$), and similarly, the SSST time did not show significant change (7.7 s to 7.2 s, $p = 0.517$). No significant change was observed in the 2MWT distance (171 m to 174 m, $p = 0.178$) or TUG time (6.8 s to 6.9 s, $p = 0.831$). Self-reported walking disability (MSWS-12) and leisure-time physical activity also remained unchanged ($p = 0.692$ and $p = 0.394$, respectively).

Conclusion: This study demonstrated that pwMS with no or minimal disability maintain stable walking performance over a three-year period. This stability may reflect functional reserve and lifestyle factors, allowing preservation of mobility despite disease progression. Future research should include more complex gait analyses and consider additional lifestyle factors.

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P1892
The effect of Pilates exercise in the form of telerehabilitation on the quality of life in people with MS

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Introduction: Quality of life in people with MS is often reduced and it is therefore important to monitor the possible effect of different form of exercise and telerehabilitation.
Objectives/Aims: Our aim was therefore to compare the effect of group and individually guided online Pilates exercises.
Methods: A total of 22 people completed the 12-week online Pilates group programme while 29 people had Pilates sessions in an individual form. Both forms of telerehabilitation were led by a physiotherapist. Participants' disability rates ranged from 1 to 6 EDSS and mean age was 48,5 y (SD 10,8). Quality of life was assessed using a standardized MSQoL-54 questionnaire completed online before and after the telerehabilitation program.
Results: There was no significant improvement in quality of life in the group form of telerehabilitation. In the individual form of telerehabilitation, a significant improvement in total physical health ($p<0.000$), pain ($p=0.007$), overal QoL ($p=0.018$) and sex function ($p=0.011$).
However, the results may be influenced by the fact that fewer participants in the group form of telerehabilitation (n=16) completed the full questionnaire.
Conclusion: Pilates exercise in the form of telerehabilitation can have a positive effect on the quality of life of people with MS. It seems that individual contact with a therapist is important for sufficient adherence and a positive effect of telerehabilitation on quality of life.

Disclosure of interest: All authors: nothing to disclose

P1893
Identifying health-related quality of life domains to develop an item bank for multidimensional computerized adaptive testing in Multiple Sclerosis: results from a literature review and a qualitative study

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Introduction: MS has a significant impact on individuals' health-related quality of life (HRQoL). Ideally, HRQoL assessment tools for MS should be tailored to individual patients, enhancing measurement efficiency by ensuring that each item contributes meaningfully. Multidimensional Computer Adaptive Testing (MCAT) offers a promising solution by improving HRQoL evaluation. The initial step in developing an MCAT involves creating a comprehensive item bank that addresses all relevant HRQoL domains.
Objectives/Aims: This process entails: 1) reviewing the literature and existing questionnaires (Action 1); and 2) confirming key HRQoL domains and integrating additional relevant ones (Action 2; focus of the current study).
Methods: Findings from the literature review were discussed in four focus group meetings (FGMs) with key stakeholders, including people with MS (PwMS) and healthcare professionals (HPs). Participants were purposefully selected from diverse geographic areas in Italy, with variation in gender, education, and (for PwMS) disease severity. FGMs were audio-recorded, transcribed, and analysed using content analysis by two independent researchers.
Results: Qualitative data collected during the four FGMs were analysed and organized into two overarching themes: 1) HRQoL Domains; 2) HRQoL Mediators. The HRQoL Domains theme is composed of five subthemes: 1.1 Physical Domain; 1.2 Psychological Domain; 1.3 Social Domain; 1.4 Work Domain; 1.5 Financial Domain. The HRQoL Mediators theme is composed of five subthemes: 2.1 Personal Factors; 2.2 Health-Related Factors; 2.3 Life-Related Factors; 2.4 Relational Factors; 2.5 Contextual Factors. The FGM results confirmed the HRQoL domains found in existing literature, while identifying two additional domains (Work and Financial) and providing further detail within each domain.
Conclusion: This study identifies key HRQoL domains for inclusion in the item bank, some of which are not well-represented in the literature. These findings will inform the development of an item bank tailored to PwMS, while also highlighting potential HRQoL mediators useful in developing further intervention targeting the promotion of HRQoL in PwMS.

Disclosure of interest: All the authors have nothing to disclose.

RIMS – Motor and cognitive reserve in MS: how we can improve it with physical activity and rehab

P1894
A Comparative Analysis of the Utilisation of Upper and Lower Extremity Functions in Mental Chronometry Tests

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Introduction: Mental chronometry tests, including upper and lower extremity functions, evaluate the temporal congruence component of motor imagery.
Objectives/Aims: This study aimed to compare the utilisation of upper and lower extremity functions in mental chronometry tests.
Methods: The study included 73 ambulatory individuals with multiple sclerosis (MS), all right-handed, with EDSS scores between 0 and 4.5, without cognitive impairments. The Box and Block Test (BBT) and the Timed Up and Go Test (TUG) were administered as mental chronometry tests. After administering these tests, execution function times, motor imagery times, and mental chronometry ratios were compared.
Results: A significant difference was observed in execution function times between the most and least affected extremities in the BBT ($p=0.001$). Similarly, motor imagery times in the BBT were significantly different between the most and least affected extremities ($p=0.007$). However, no significant difference was found in the mental chronometry ratio between the most and least affected extremities ($p=0.698$). Comparisons between upper and lower extremity tests revealed that the mental chronometry ratio was significantly higher for the BBT than for the TUG test in both the most affected and least affected extremities ($p=0.001$).
Conclusion: Individuals with MS demonstrated superior performance in mental chronometry tests assessing upper extremity function compared to those evaluating lower extremity function. Additionally, mental chronometry ratios remained consistent between the most and least affected extremities. These findings suggest that greater reliance on upper extremity functions in daily activities may enhance motor imagery capabilities. Consideration of these differences is crucial when selecting mental imagery tests based on upper or lower extremity performance.

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P1895
Impact of Chronic Pain on Cognitive Reserve in Multiple Sclerosis

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Introduction: Chronic pain in people with multiple sclerosis is associated with worse mental health and cognitive impairment, which can be both a cause and a consequence of brain structure and function alterations, such as maladaptive plasticity and dysregulation of the antinociceptive system. Cognitive reserve, which reflects the efficiency of internal brain connections, is a protective factor in multiple sclerosis (MS), potentially mitigating cognitive decline and reducing the risk of mental health disorders.
Objectives/Aims: The current study explored the impact of chronic pain on psychosocial factors, mental health, and cognition in people with MS (pwMS).
Methods: This cross-sectional study involved a total of 131 pwMS. The PainDETECT Questionnaire (PD-Q) was used to differentiate between nociceptive and neuropathic pain. The scores $\leqslant 12$ were considered as the presence of musculoskeletal pain, >12 as neuropathic pain, and zero as non-presence of pain. The Brief International Cognitive Assessment in Multiple Sclerosis (BICAMS) battery includes three subtests: Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), and Brief Visuospatial Memory Test-Revised (BVMT-R) was used to assess cognitive functions. Cognitive reserve level was assessed using the Cognitive Reserve Index Questionnaire (CRIq). Information such as Expanded Disability Status Scale (EDSS), disease duration and age of the participants were also recorded.
Results: The 131 participants included in the study were divided into three groups: 49 without pain (NP), 60 with Musculoskeletal Pain (MSP) and 22 with Neuropathic Pain (NP). There was no difference between the groups regarding age, disease duration and EDSS scores ($p>0.05$). There were no significant differences between groups regarding CRIq-education, CRIq-leisure time activities, CRIq-total score, and all three subtests of the BICAMS battery ($p>0.05$). However, there was a significant difference regarding CRIq-working activity. As a result of post-hoc analysis, there was a difference between MSP (95.73 ± 8.56) and without pain (100.24 ± 12.17) groups for CRIq-working activity.
Conclusion: This study suggests that while chronic pain in pwMS does not significantly impact overall cognitive reserve or cognitive performance as measured by the BICAMS battery, it may influence specific aspects of cognitive reserve, particularly work-related cognitive activities. The observed differences in CRIq-working activity between pwMS with musculoskeletal pain and those without pain highlight the potential role of pain in shaping cognitive engagement in occupational settings. Further research is needed to explore the mechanisms underlying this association and to develop targeted interventions to support cognitive function in pwMS experiencing chronic pain.

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P1896
The Effect of Cognitive Fatigue on the Vividness Components of Mental Imagery in Individuals with MS

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Introduction: Cognitive fatigue is a psychobiological condition affecting approximately 46% of individuals diagnosed with multiple sclerosis (MS). Among various strategies to cope with fatigue, mental imagery (MI) training is frequently utilized. However, the specific impact of cognitive fatigue on the distinct components of mental imagery remains largely unexplored.
Objectives/Aims: The objective of this study was to investigate the effect of cognitive fatigue on the vividness components of mental imagery in individuals with multiple sclerosis (MS). Specifically, the study aimed to assess the differential impact of cognitive fatigue on the kinesthetic, internal visual, and external visual imagery components.
Methods: Thirty-six individuals with MS (EDSS 1–4) participated in this study and were randomly allocated to either an experimental or a control group. mental imagery ability was assessed using the Kinesthetic and Visual Imagery Questionnaire (KVIQ) and the Movement Imagery Questionnaire (MIQ). The experimental group underwent a cognitive fatigue-inducing protocol comprising the Trail Making Test, the Brief International Cognitive Assessment for MS (BICAMS), the Paced Auditory Serial Addition Test (PASAT), and verbal fluency assessments, which included the Controlled Word Association Test and a category test. Following fatigue induction, the mental imagery assessments were repeated. The control group underwent the same assessments without any intervention.
Results: No significant change was observed in the KVIQ scores of the experimental group ($p > 0.05$). However, the MIQ revealed significant reductions in kinesthetic, internal visual, and external visual imagery components following cognitive fatigue induction ($p < 0.05$). Between-group comparisons showed a significant difference in KVIQ scores ($p < 0.05$). Although baseline MIQ scores were comparable, the experimental group exhibited more pronounced impairments across all subcomponents, with the exception of external visual imagery ($p < 0.05$).
Conclusion: This study demonstrates that cognitive fatigue selectively disrupts kinesthetic and internal visual components of mental imagery, potentially compromising the effectiveness of imagery-based rehabilitation. These findings underscore the importance of addressing cognitive fatigue in the design and implementation of mental imagery interventions for individuals with MS. Furthermore, individual variability in fatigue severity may significantly influence mental imagery performance and rehabilitation outcomes.

Keywords: Multiple Sclerosis, Cognitive Fatigue,Mental Imagery

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P1897
Early validation of a robot-based motor cognitive dual task assessment for Multiple Sclerosis

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Introduction: Cognitive and motor impairments are common in people with MS (pwMS), often occurring simultaneously and contributing to reduced functional independence. In pwMS, the simultaneous execution of motor and cognitive tasks often leads to performance deterioration, underscoring the clinical importance of integrated tools for assessment and training in dual-task conditions. Traditional cognitive evaluations, while validated, do not reflect real-world, multitask scenarios. Also, few rehabilitation devices target these skills simultaneously, and among these none focus on motor cognitive dual tasks in dynamic balance conditions
Objectives/Aims: This study wants to compare the on-screen cognitive assessments embedded on a medical robotic device with established classical pen-and-paper versions in healthy subjects, as a foundational step toward its application in pwMS.
Methods: 30 subjects completed a battery of cognitive tasks, such as the Trail Making Test (TMT), version A and the Bell Cancellation Test, both in traditional paper format and on the screen of the medical device while standing on its robotic platform. Outcome measures included completion time, number of errors/missed bells. Agreement between the two modalities was evaluated using correlation analysis and Bland-Altman plots. Also, Wilcoxon signed-rank test was used to assess differences between classical and digital versions of the tests.
Results: Relatively strong and moderate correlations were observed between digital and paper-based assessments (respectively TMT A: $r = 0.53$, $p < 0.01$; BELL: $r = 0.35$, $p = 0.045$). Bland-Altman analysis demonstrated good agreement, confirming that the digital versions reliably replicate the traditional formats. Wilcoxon test showed that the digital and paper versions of the Bell Test were comparable ($z = 280.0$, $p = 0.77$). Differently, the two versions of the TMT significantly differed ($z = 119.0$, $p < 0.05$), with faster completion times observed for the digital version, consistent with findings in literature on healthy controls.
Conclusion: These results demonstrated that the cognitive tests on the robotic device reflect the validated cognitive assessments, supporting their reliability. Given the relevance of dual-task deficits in MS, this system, which integrates validated

cognitive tests within a robotic platform designed for balance training for both standing and sitting, across static and dynamic conditions, offers strong potential for comprehensive assessment and personalized rehabilitation of pwMS.

Disclosure of interest: Elisa Misley has nothing to disclose. Maura Casadio has nothing to disclose. Tommaso Falchi Delitala is currently working at Movendo Technology. Valeria Falzarano is currently working at Movendo Technology. Giorgia Marchesi is currently working at Movendo Technology

P1898
The Effect of Cognitive Dual-Task on Fine Motor Performance: A Comparative Analysis in Individuals with Multiple Sclerosis and Radiologically Isolated Syndrome

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Introduction: Although individuals with radiologically isolated syndrome (RIS) are traditionally defined as asymptomatic, recent findings suggest that they do not entirely share the same characteristics as healthy individuals. Most notably, it has been demonstrated that motor performance is also affected in individuals with RIS. Upper extremity dysfunction is a significant issue that can impact activities of daily living in both multiple sclerosis (MS) and RIS.
Objectives/Aims: The aim of this study was to investigate the effect of cognitive dual-task on fine motor skills in individuals with MS and RIS.
Methods: Fine motor skills were assessed in 16 individuals with MS, 12 individuals with RIS, and 17 healthy controls (HCs) under both single-task (ST) and cognitive dual-task (CDT) conditions. The Purdue Pegboard Test (PPBT) was utilised to evaluate fine motor skills. In the CDT condition, PPBT performance was combined with a cognitive task involving phonemic word list generation task. Following the assessments, the dual-task cost (DTC) was calculated for each group.
Results: MS, RIS, and HC groups did not show a significant difference in fine motor performance under the ST condition ($p=0,112$). However, under the CDT condition, the MS group performed significantly worse than the HC group ($p=0,001$). While all three groups exhibited a significant performance decline in CDT compared to ST ($p<0,001$ *for MS group,* $p<0,001$ *for RIS group,* $p=0,040$ *for HC group*), this decline was greater in the MS and RIS groups than in the HCs ($p=0,006$, $p=0,037$; *respectively*). The degree of performance decline (DTC) was similar between the MS and RIS groups ($p=0,443$).
Conclusion: This study highlights that individuals with RIS, who are assumed to be clinically asymptomatic, may in fact exhibit clinical signs similar to those observed in individuals with MS. Therefore, a comprehensive assessment should be conducted, and individuals with RIS should be considered for rehabilitation programs that specifically target dual-task performance. Addressing dual-task impairments in RIS may help mitigate their impact on daily activities and improve overall functional outcomes.

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P1899
The Minnesota Manual Dexterity Test: A Reliable and Valid Measurement Tool in Multiple Sclerosis

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Introduction: Current literature has shown that upper extremity disorders are strongly associated with activities of daily living such as dressing, self-care, and bathing, thus affecting the independence and quality of life in people with Multiple Sclerosis (PwMS). Therefore, unilaterally and bilaterally assessing upper extremity function and manual dexterity is crucial in rehabilitation for patients and healthcare professionals.
Objectives/Aims: This study aimed to investigate the reliability and validity of using the Minnesota Manual Dexterity Test (MMDT) for PwMS.
Methods: Sixty ambulatory PwMS participated in this study. The concurrent validity of MMDT was determined by investigating its relationship with the Nine-hole peg test (9-HPT), the Jebsen Hand Function Test (JHFT), and the ABILHAND scale. The MMDT was repeated after 1 week to determine test-retest reliability.
Results: The MMDT showed excellent test-retest reliability (intraclass correlation coefficient 0.912-0.996). MMDT subtests showed fair to moderate positive correlations with 9-HPT and the JHFT scores (correlation coefficients ranged from 0.382 to 0.748, $p \leqslant 0.004$). Additionally, the subtests showed fair to moderate negative correlations with the ABILHAND scale (correlation coefficients ranged from -0.290 to -0.594, $p \leqslant 0.03$).
Conclusion: The MMDT has advantages such as evaluating bilateral hand functions, hand-eye coordination, and gross motor skills that are not found in many other manual dexterity assessment tools. The MMDT is reliable and valid for assessing manual dexterity in PwMS.

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P1900
Dual-Task Decoupling: A Sensitive Measure for Fall Risk Discrimination in Multiple Sclerosis Clinical Populations

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Introduction: Falling is a common problem in patients with Multiple Sclerosis (PwMS) and it is very important to recognise patients who fall in the early period in order to develop preventive approaches. Dual-task skills reflecting the daily living skills of PwMS need to be addressed in terms of fall discrimination.
Objectives/Aims: The objective of this study was to evaluate the efficacy of dual tasks involving upper and lower extremity, in conjunction with methods of assessing perspectives on dual task skills, with regard to discriminating falls in PwMS.
Methods: The study was conducted at Hacettepe University, Faculty of Physical Therapy and Rehabilitation. The Timed Up and Go Test (TUG) and Nine-Hole Peg Test (9HPT) were utilised for single-task assessments. The dual-task assessments included a motor task (carrying a cup) and cognitive tasks (phonetic, semantic, and subtraction tasks from series 3 and 7). Falls were prospectively recorded over three months using a falls diary. Fear of falling was assessed with the Falls Efficacy Scale-International (FES-I) and the impact of dual-task performance on daily activities was evaluated using the Dual-task Impact on Daily-living Activities (DIDA-Q). The predictive value for falls was analysed through Receiver Operating Characteristic (ROC) curve analysis.
Results: The study included 36 patients (mean EDSS: 3.36±1.17, mean age: 44.8±9.8), of whom 75% (n=27) were female and 25% (n=9) were male. According to the results of the ROC analysis, TUG+semantic task (Cut-off value=12.33; AUC=0.674; sensitivity=0.64; specificity=0.78), TUG+serial 7 subtraction (Cut-off value=11.97; AUC=0.616; sensitivity=0.70; specificity=0.57), 9DPT+semantic task (Cut-off value=39.46; AUC=0.662; sensitivity=0.58; specificity=0.89), 9DPT+serial 7 subtraction (Cut-off value=40.5; AUC=0.664; sensitivity=0.64; specificity=0.63), FES-I (Cut-off value=24; AUC=0.647; sensitivity=0.76; specificity=0.52), DIDA-Q (Cut-off value=23; AUC=0.657; sensitivity=0.64; specificity=0.68) was found.
Conclusion: According to the preliminary findings, in addition to the semantic and serial 7 subtraction task in all tests, the patient's perspective on dual task performance and fear of falling data moderately discriminate fall risk. It is not a sufficient stand-alone measure for fall risk prediction, so it is recommended that this assessment be included as part of a comprehensive falls screening programme.

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P1901
Analysis of aerobic capacity and its relation to stair negotiation time in patients with multiple sclerosis

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Introduction: Multiple sclerosis affects the patient's level of functioning. Aerobic capacity, which is important component of physical fitness, can also be affected. The extent of difference in aerobic capacity between patients with higher functional status and healthy population, and its relationship to stair negotiation time, has not been yet investigated in detail.
Objectives/Aims: To assess aerobic capacity of patients with relapsing-remitting multiple sclerosis with higher functional status and to determine its relationship to stair negotiation time.
Methods: The multiple sclerosis group consisted of 20 patients with a diagnosis of relapsing-remitting multiple sclerosis (⩽ 3 according to Expanded Disability Status Scale, EDSS), whereas a control group consisted of 20 healthy subjects. To assess the value of aerobic capacity, we performed a single-stage submaximal walking test on a treadmill. We used a timed stair test on a 12-step staircase to evaluate subjects' functional ability. We also assessed rate of perceived exertion with 15-stage Borg scale during the tests.
Results: The estimated aerobic capacity, stair negotiation time and ratings of perceived exertion were not significantly different between the groups. Heart rate at the end of the aerobic capacity test showed tendency ($p = 0.073$) of being higher in the patient group. A negative linear relationship between aerobic capacity and stair negotiation time ($r = -0,49$; $p < 0,05$) was observed only in the patient group.
Conclusion: Aerobic capacity of patients was comparable to the capacity of healthy subjects. The moderate negative association between aerobic capacity and stair negotiation time pinpoints the importance of the cardiorespiratory capacity for performing daily activities in this patient population. We assume that stronger association between the two variables would have emerge in both groups, if a longer and more strenuous test protocol was used to assess stair negotiation time.

Disclosure of interest: "Saša Alagić: nothing to disclose."

P1902
Is There a Relationship Between Upper Extremity Motor Function and Fall History in Multiple Sclerosis?

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Introduction: Electromyography tests have shown that the upper extremity functions may affect gait stability. Furthermore, it is suggested that locomotor activity is produced in spinal neuronal networks and that the central pattern generators affect the upper extremity motor neurons via ascending propriospinal pathways. In conclusion, the current findings support the possibility that the upper extremity and locomotor skills may be related. However, the relationships between falls, which are a

serious problem after the deterioration of locomotor skills in people with Multiple Sclerosis (PwMS), and the upper extremity function have not been examined before.
Objectives/Aims: We planned this study to bring attention to the upper extremity motor function impairments in PwMS and to investigate the relationship of upper extremity motor function dysfunction with fall history.
Methods: This cross-sectional study included 56 PwMS [Expanded Disability Status Scale (EDSS) score 1 to 6.5] Upper extremity motor functions were measured with the Nine-hole peg test (9-HPT) and the Jebsen Hand Function Test (JHFT). Information about fall history was recorded by asking the question "Have you fallen unexpectedly to the ground, floor, or a lower level in the last year, and how many?"
Results: Both hand 9-HPT and JHFT scores demonstrated significant moderately positive correlations with the number of falls (r:0.502-0.659, $p<0.05$). Additionally, significant low to moderate positive correlations were found between the scores and the EDSS ambulation score and disease duration (r:0.269-0.655, $p<0.05$).
Conclusion: The upper extremity motor function in PwMS is associated with increased incidence of falls, disease duration, and functional loss; therefore, it should be considered in clinical

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P1903
Markerless Motion Capture Technology for Remote Rehabilitation in Multiple Sclerosis: Accuracy Evaluation and Prototype Development

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Introduction: MS is a progressive disease that frequently causes significant impairments, affecting both personal and social life. Rehabilitation is helpful in reducing disability, focusing on maintaining functional progress and promoting social reintegration. However, standard in-clinic rehabilitation sessions may not be sufficient, as continuous physical activity is essential for preserving improvements and preventing further decline. In this context, promoting a continuum of care is crucial. Recent technological advances, in particular markerless systems, offer promising solutions that balance cost, accuracy, and usability for remote monitoring.
Objectives/Aims: This work aims to i) quantify the accuracy of a markerless system, compared to a gold standard marker-based one; ii) present a human-machine interface based on markerless pose estimation algorithms to support remote rehabilitation.
Methods: 10 subjects performed full-body exercises while their movements were recorded with an RGB-D camera and a marker-based motion capture system. Performance parameters such as ranges of motion were extracted. To evaluate the accuracy of the markerless system, mean errors were calculated for upper limb, lower limb, and trunk movements.
Results: Our approach achieved errors of $2.5\pm0.7°$ for lower limb, $3.6\pm0.9°$ for upper limb, and $2.3\pm0.4°$ for trunk, with no significant differences between the systems (ANOVA's *system* factor: $p>0.3$). These findings highlight that markerless systems can achieve clinically reasonable accuracy, supporting their application in remote rehabilitation interfaces. We developed a prototype that incorporates an RGB-D camera (OAK-D), which allows real-time 3D motion tracking using on-device neural network processing. Using BlazePose model, we extracted 2D body keypoints and estimated their 3D coordinates through depth sensor integration. A graphical interface presents interactive games that require targeted movements. During gameplay, both qualitative and quantitative metrics are computed in real-time to monitor performance.
Conclusion: Markerless motion capture technologies can be effective tools for home rehabilitation. They are ideal for long-term monitoring and patient engagement outside clinical settings, as they can provide accurate, real-time feedback without requiring complicated set-up. By providing continuous care and personalized guidance, these systems can promote patient autonomy, improve adherence to therapeutic routines and support the maintenance of functional abilities in people with MS.

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P1904
Effect of Analytic Group Therapy on cognition in Multiple Sclerosis patients

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Introduction: Multiple sclerosis (MS) is an autoimmune disease that most affects young adults. Previous studies have shown

that MS patients often experience psychological problems, including depression, anxiety, cognitive dysfunction, which severely impacts their quality of life and commutations with other. Additionally, psychological group therapy has been demonstrated to decrease anxiety and depression in MS patients in previous research.
Objectives/Aims: This study aimed to evaluate the impact of analytic group therapy on improving cognitive dysfunction in patients with multiple sclerosis.
Methods: This quasi-experimental study included a follow-up with a control group. Nine female MS patients, aged 30-50 years, participated in the group therapy after an initial evaluation with a therapist. Only patients without severe psychiatric or physical conditions were included. A separate control group of nine patients was also studied. Cognitive function was assessed using the MACFIMS test through pre- and post-tests. Each therapy session lasted 90 minutes and followed an analytic group therapy approach. During these sessions, participants engaged in free discussion, guided and managed by the analytic psychotherapist, who provided interventions as needed. Data get in SPSS and analyzed.
Results: The results showed a significant improvement in cognitive function, as measured by the MACFIMS test (COWAT, BVMT, JLO), when comparing pre-test and post-test scores (p-value <0.05): Mean COWAT post-test score: 9.11, compared to pre-test score: 2.11 (p-value: 0.031): Mean BVMT post-test score: 2, compared to pre-test score: 0.11 (p-value: 0.008): Mean JLO post-test score: 1.89, compared to pre-test score: -1.67 (p-value: 0.031)
Conclusion: Analytic group therapy can be a helpful way to improve cognitive function in people with multiple sclerosis. We believe adding this type of therapy to treatment plans could support their cognitive health and lead to a better quality of life.

Disclosure of interest: Kindly find enclosed the abstract entitled "Effect of Analytic Group Therapy on Cognition in Multiple Sclerosis Patients "which I am submitting for ECTRIMS2025. The material is original and has not been submitted for publication elsewhere while under consideration. All authors have contributed significantly, and that all authors are in agreement with the content of the abstract. Considering some sanction issues, we also declare that all authors have only academic positions and these positions are non-governmental. Moreover, we could not pay any APC or publication fee due to US sanctions. We hope this, would not affect our chance to publish our paper in your valuable journal. While I hope, you will give favorable consideration to this abstract and find that acceptable for "ECTRIMS2025", I remain. Yours sincerely,

P1905
Prediction of maximum walking distance in patients with Multiple Sclerosis

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Introduction: In patient with MS (pwMS), walking distance reflects disease severity and treatment response, but subjective estimation may be unreliable due to clinical constraints.
Objectives/Aims: The aim of the study was to develop a predictive mathematical model to estimate the maximum walking distance in pwMS by using data on muscle strength, muscle endurance, fatigue, and balance.
Methods: 80 MS patients were included in the study. The patients were mobilized until they declared that they would not walk any further, and the maximum walking distance was determined. One week after the walking distance was determined, the patients were evaluated using the EDSS (Expanded Disability Status Scale), Six-Minute Walk Test (6MWT), muscle strength and muscle endurance assessments, Fatigue Severity Scale (FSS), and Community Balance and Mobility Scale (CB&MS). The relationships between maximum walking distance and the assessment criteria were analyzed using Pearson correlation analysis. For model, the stepwise method of multiple linear regression was employed using data.
Results: A significant and strong correlation was found between maximum walking distance and CB&MS (r=0.757), FSS (r= -0.670), knee extension endurance (r= 0.735), and ankle plantar flexion strength (r= 0.646). Additionally, a multiple regression analysis conducted on the data generated the model that accounts for 77.8% of the variance in walking distance.
Conclusion: As a result of the study, a mathematical model was developed that predicts walking distance in MS patients with an accuracy of 77.8%, based on knee extension endurance, CB&MS, FSS, and strength of ankle plantar flexion values.

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P1906
The relationship between subjective and objective maximum walking distance and muscle strength in ms: an observational cross-sectional study

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Introduction: In MS, lower extremity weakness is linked to walking distance; however, it remains unclear whether subjective or objective measures better reflect this relationship.
Objectives/Aims: This study aimed to explore the relationship between walking distances and lower extremity muscle strength in MS.
Methods: The study involved 80 people with all forms of MS. Subjective walking distance was measured by asking patients how far they could walk before fatigue. Objective walking distance was assessed by encouraging participants to walk as far as possible without resting. Lower extremity muscle strength (hip, knee and ankle muscles) was evaluated by hand dynamometer.

The relationship between subjective-objective walking distance and lower extremity muscle strength was analyzed.
Results: Subjective walking distance showed moderate positive correlations with hip extensors, knee flexors and extensors, and ankle plantar flexors ($r = 0.510$, $p = 0.001$, $r = 0.422$, $p = 0.001$, $r = 0.466$, $p = 0.001$, $r = 0.420$, $p = 0.001$). Objective walking distance was significantly associated with multiple lower limb muscle groups, including hip flexors, extensors, and abductors; knee flexors and extensors; and ankle plantar and dorsiflexors ($r = 0.506$, $p = 0.001$, $r = 0.573$, $p = 0.001$, $r = 0.573$, $p = 0.001$, $r = 0.536$, $p = 0.001$, $r = 0.582$, $p = 0.001$, $r = 0.560$, $p = 0.001$, $r = 0.432$, $p = 0.001$). Notably, subjective distance was most associated with hip extensor strength, whereas objective distance correlated more with knee extensor strength.
Conclusion: The study showed that objective maximum walking distance had a stronger correlation with lower extremity muscle strength than subjective distance. This suggests that subjective distance might be affected by unmeasured factors. Subjective distance was more associated with hip extensors, while objective distance correlated more strongly with knee extensors.

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P1907
"How can we help?" A needs assessment to inform the development of an exercise intervention involving persons with multiple sclerosis with severe mobility impairments

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Introduction: Exercise can improve physical and mental health in persons with MS (PwMS). Evidence-based exercise recommendations for PwMS have been established, but PwMS with severe impairments are under-represented in exercise research.
Objectives/Aims: To conduct a needs assessment to inform the design of a pragmatic, person-centered exercise intervention involving PwMS with severe mobility impairments.
Methods: A team of researchers and clinicians with expertise in MS, exercise, health behavior change, and implementation science, and two community members with a lived experience of MS used the Behavior Change Wheel (BCW) to identify what PwMS with a severe disability need to exercise regularly. Starting from a thematic analysis of semi-structured interviews we conducted with PwMS with an EDSS $\geqslant 6$, we held two virtual meetings and followed a 3-step process to: 1) understand the behavior; 2) identify intervention options; and 3) identify content and implementation options. The intervention will be informed by the Capability, Opportunity, Motivation (COM-B) model and the affordability, practicability, effectiveness and cost-effectiveness, acceptability, side effects/safety, and equity (APEASE) criteria.
Results: BEHAVIOR. PwMS need to exercise to maintain their physical abilities. INTERVENTION OPTIONS. We identified specific needs in terms of capability (physical: multiple shorts bouts of exercise throughout the day; psychological: receiving resources to increase knowledge on exercise for PwMS), opportunity (physical: option to exercise at home; social: peer-support), and motivation (automatic: feeling exercise as a pleasure; reflective: confidence in the ability to exercise). Communication and service provision are the most appropriate categories for promoting exercise among PwMS with severe impairments. CONTENT AND IMPLEMENTATION. PwMS need an individualized exercise prescription supported by physical activity counseling with a tailored delivery of behavior change techniques.
Conclusion: PwMS with severe mobility impairments need a tailored, detailed exercise prescription that considers MS-related factors and individual preferences to engage in and adhere to exercise programs.

Disclosure of interest: Matteo Ponzano, Luca Beratto, Lara Bressy, Giampaolo Brichetto, Daniela Gaballo, Valeria Romano, and Anna Mulasso have nothing to disclose

RIMS – Supporting mental health in MS: empowerment – resilience – physical activity to support mental health

P1908
Experiences and Emotional Insights of Caregivers of People with MS: A Thematic Analysis

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Introduction: Relatives and friends play a crucial role in addressing the physical, psychological, social, and economic needs of people with MS (PwMS). The Italian Multiple Sclerosis Society (AISM) offers a helpline service that provides information and support for both PwMS and their caregivers.
Objectives/Aims: The present study aims to analyse the themes emerging from caregivers' communications (emails) to the helpline service, in order to gain a comprehensive understanding of their expectations and experiences.
Methods: An inductive Thematic Analysis (TA) following Braun and Clarke's approach was conducted within a social constructionist framework to identify core themes. This qualitative method was chosen to effectively explore the complexity and nuances of caregivers' experiences and emotions. Emails were analysed using the qualitative research software Dedoose.

Results: The emails written by 300 caregivers, 60.3% females, and 39.7% males, were analysed. The majority were spouses/partners (30%), followed by parents (24.7%), other relatives (21.3%), sons/daughters (18.3%), and close friends (5.7%). The coding process resulted in the generation of 550 codes, which were assigned to a total of 1,051 excerpts. The thematic analysis identified six key themes: 1) In the Heart of Conflict: Between Desire to Help and the Need to Protect Themselves (6.0% of the excerpts); 2) From Struggles to Strength: Coping, Support, and Hope (12.3% of the excerpts); 3) Fighting Alone: Indignation and Perceived Indifference (12.8% of the excerpts); 4) Seeking Clarity: Indignation, Doubts, and Quest for Answers (16.1% of the excerpts); 5) The Burden of Bureaucracy: Questions Without Clear Answers (17.0% of the excerpts); and 6) Enduring the Weight of Uncertainty: the Struggles and Desperation of Families (35.8% of the excerpts).
Conclusion: The findings of this study will guide the improvement of the AISM helpline service and the development of tailored interventions to better support family caregivers of PwMS.

Disclosure of interest: All authors have nothing to disclose.

P1909
Barriers to Peer Support Engagement in People with Multiple Sclerosis: Qualitative Findings from a Mixed-Methods Survey

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Introduction: People living with multiple sclerosis (PwMS) not only experience physical challenges but could also be at risk of lower psychological wellbeing and social isolation. Support from peers with MS through their shared lived experience may improve these outcomes; however, not all PwMS avail of peer support opportunities
Objectives/Aims: This study aimed to explore barriers to peer support among PwMS living in Ireland, as part of a broader mixed-methods study examining peer support need and engagement in this cohort.
Methods: A cross-sectional online survey co-designed with a public and patient involvement panel of seven PwMS was deployed in February 2024. Open-text responses were gathered from PwMS living in Ireland regarding the causes preventing or limiting their engagement with peer support, including barriers specific to accessing such support either in-person and online. Recruitment was facilitated through the mailing lists and online channels of a national MS organisation. Content analysis was employed to analyse the data.
Results: 218 PwMS participated. The majority (65%) had relapsing-remitting MS. Participants provided barriers preventing PS engagement (n=120, 55%), and specific reasons for having not previously engaged with in-person (n=71) or online (n=56) peer support. There were similarities across all three barrier categories, which were thematically merged. Three themes (and their sub-themes) were identified: 1) low access (limited accessibility, poor preference alignment, or difficulty accessing existing supports), 2) unsupportive peers and peer support (from negative interactions or difficulty connecting with peers), and 3) personal engagement barriers (poor health, inhibiting attitudes or no skills, or low perceived need for peer support).
Conclusion: Having limited access to peer support poses a significant barrier to engagement among PwMS, while available opportunities might not meet their needs or expectations. These findings have implications for existing and planned supports targeting this cohort, particularly in the Irish context.

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P1910
Systematic Review of the impact of Multiple Sclerosis on parenting

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Introduction: The average age of onset of MS is between 20 and 40 years. Many people living with MS also become parents during this period of life. The experience of being a parent can be significantly impacted by a complex interaction of varied and unpredictable MS symptoms. However, despite both its valued role and identified challenges for people with MS, research on the experience of parenting with MS and the development of appropriate supports has been neglected.
Objectives/Aims: This systematic review synthesises quantitative, qualitative, and mixed-method evidence to answer the following research questions: Does having MS affect the parenting role? If so, how is parenting affected by MS?
Methods: Systematic searches were conducted across five databases. The Johanna Briggs Institute guidance for mixed-method systematic reviews was followed during review question formation, data synthesis and extraction, and reporting results. The final review included 22 studies that met the inclusion criteria. Overall, 2,466 parents with MS participated in the studies included.
Results: Synthesised findings indicated that MS significantly impacts parenting, predominantly, negatively. Parents with MS encounter substantial daily challenges due to fatigue, limited mobility, and cognitive difficulties. Four main themes emerged from the data synthesis: Risk and protective factors related to parenting with MS; Impact of parental MS on parenting activities and daily family life; Emotional and mental health impact of MS on parents and their views of relationships within the family; Managing and coping as a parent with MS.
Conclusion: The findings from this systematic review point to a need for the development of bespoke interventions designed to support parents with MS. The systematic review identified specific factors and support mechanisms that could contribute to such interventions for parents with MS, including mental health

interventions, social support networks, and psychoeducation around family communication about MS diagnosis and its impact.

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P1911
Educational Module on Advance Healthcare Directives (AHDs), or Living Will, within the Neurorehabilitation Program at the Multiple Sclerosis Center of Catalonia (Cemcat): a preliminary report

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Introduction: The AHD allows individuals to document their healthcare preferences in case of medical complexity when they are no longer able to communicate. This is especially important for individuals with neurodegenerative conditions such as multiple sclerosis (MS). Completing an AHD ensures patient autonomy, respects their choices for care, and provides clarity for family members in critical decision-making situations.
Objectives/Aims: The objective of this study is to describe the role of social work within the neurorehabilitation program at Cemcat, focusing on promoting patients autonomy through the facilitation of the AHD.
Methods: In early 2023, the social worker at Cemcat implemented a module aimed at supporting individuals with MS and other neurodegenerative diseases in completing their AHD. Patients enrolled in our Neurorehabilitation program were informed and invited to attend informative sessions, either online or in person. The content of the sessions was organized into four key phases: (1) Patient autonomy and rights, (2) Components of the AHD, (3) Legal procedures, and (4) Completion and signature by healthcare professionals.. Following legislative changes in late 2024, the process was significantly streamlined, allowing easier signing by any healthcare professional. This reform aimed to enhance accessibility and support, empowering individuals to make informed healthcare decisions in advance.
Results: Of the 584 patients assessed for the neurorehabilitation program at Cemcat (2023-2024), 61 (10.4%) showed interest in the AHD. Of these, 81.9% were women, 32 received individual counselling, and 29 attended a online group session. By discharge, 3 patients had formalized their AHD.
Conclusion: Providing information, guidance, and support regarding AHD, fosters patient reflection on their values and wishes and promotes motivation to complete the document. The new legislation simplifies the process potentially enhance accessibility and accelerating implementation by streamlining procedural requirements.

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P1912
Well -being and Quality of life in Multiple Sclerosis: From an Animal Model to Clinical Practice

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Introduction: In preclinical research, an *Enriched Environment* (EE) is defined as the combined implementation of physical exercise (PE), cognitive stimulation (CS), and social interaction (SI). Our group previously demonstrated the histopathological, molecular, and cognitive benefits of EE in an animal model of chronic focal cortical pathology of multiple sclerosis (MS) (Silva et al., 2020, PMID: 31669283).
Objectives/Aims: To analyse the implementation of the three components of EE in a cohort of patients with MS from Latin America and to correlate with clinical and demographic variables, and quality of life.
Methods: A multicentre, cross-sectional study including people with MS (pwMS) followed at referral MD centres in Argentina. Participants completed the MS International Quality of Life Questionnaire (MusiQoL), validated in Spanish, and an ad-hoc survey assessing engagement in PE, CS, and SI, as well as access and perceived barriers. Clinical and demographic data were also collected
Results: A total of 211 pwMS were included; 66.4% (n=140) were female; 88.2% (n=186) were relapsing–remitting forms, mean age 40.3 ± 12.3 years, mean EDSS 1.8 ± 1.7, and mean disease duration 6.7 ± 4.9 years. Overall, 94.3% (n=199) were receiving disease-modifying treatments (DMTs); cladribine and ocrelizumab

being the most frequently used (27%, n=57 and 20.9%, n=44, respectively). Therapeutic failure to at least one DMT occurred in 29.9% (n=63). Regarding EE components: 77.3% (n=163) engaged in PE (51.7% aerobic, 10% anaerobic, and 15.6% both); 41.2% (n=87) participated in formal physical rehabilitation programmes Notably, 52.1% (n=110) were not engaging in PE at the time of MS diagnosis, and in 86.7% (n=183), PE was prescribed by a neurologist at diagnosis. In terms of CS, 58.3% (n=123) engaged informally, and 13.7% (n=29) formally through structured cognitive rehabilitation programmes. Prior to diagnosis, 75.4% (n=159) had not engaged in CS, and in 52.1% (n=110), CS was recommended at diagnosis. For SI, 93.8% (n=198) reported active engagement. Taken together, 16.1% (n=34) engaged in one activity, 29.4% (n=62) in two, and 50.7% (n=107) in all three (PE, CS, and SI). Moreover, 58.8% (n=124) believed that PE, CS, and SI were as important as DMTs in managing their MS. In the multiple linear regression analysis, higher EDSS scores ($\beta = -2.47$; $p = 0.001$) and not engaging in physical activity prior to MS diagnosis ($\beta = -5.48$; $p = 0.007$) were significantly associated with lower quality of life. In contrast, current physical activity ($\beta = 9.25$; $p = 0.002$) and greater social interaction ($\beta = 14.86$; $p = 0.001$) were positively associated with higher MusiQoL; adjusted $R^2 = 0.247$.

Conclusion: Physical activity and social engagement were strongly associated with better quality of life in pwMS, supporting the inclusion of lifestyle strategies in MS care

Disclosure of interest: No conflicts of interest from any author for this work.

P1913
Cognitive Difficulties, Coping Strategies and Barriers to Participation in Cognitive Rehabilitation in People with Multiple Sclerosis: A Qualitative Study Across Different Disability Levels

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Introduction: Cognitive impairment in people with Multiple Sclerosis (pwMS) varies across disability levels, affecting the type of challenges, coping strategies, and barriers to rehabilitation. Understanding these differences is crucial for developing personalized interventions that improve rehabilitation participation and outcomes.

Objectives/Aims: This study aimed to explore the cognitive challenges, coping strategies, and barriers to rehabilitation participation among pwMS with varying levels of disability.

Methods: A qualitative design was employed using semi-structured interviews with 32 pwMS, selected based on their Expanded Disability Status Scale (EDSS) scores: mild (0–3.5), moderate (4–5.5), and severe ($\geqslant$6). Participants were recruited through purposive sampling. Semi-structured interviews captured their cognitive difficulties, coping strategies and barriers to rehabilitation, with data analyzed through qualitative analysis using MAXQDA software.

Results: Of the 32 participants, 20 (63%) were female, with a mean age of 32.3 $\pm$ 10.0 years and a mean EDSS score of 4.52 $\pm$ 1.61. Participants were included based on their disability levels: 12 with mild disability, 10 with moderate disability, and 10 with severe disability. Participants with mild disability reported attention deficits and reduced work performance, coping by using reminders like calendars and alarms. Barriers to rehabilitation included lack of awareness and time constraints. Those with moderate disability experienced mental fatigue and poor concentration, managing these by breaking tasks into smaller steps and taking regular breaks. Barriers included struggling with sudden exhaustion and focusing more on physical rehabilitation. Participants with severe disability faced significant cognitive impairments, such as memory loss and word-finding difficulties, relying on caregivers for reminders and daily task support. Logistical barriers, such as limited service access and mobility restrictions, led many to prefer home-based or telerehabilitation.

Conclusion: The cognitive challenges and barriers identified across different disability levels in pwMS highlight the need for personalized rehabilitation approaches. Addressing logistical barriers and offering flexible options like home-based or telerehabilitation may increase participation and enhance rehabilitation outcomes for pwMS at all disability levels.

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P1914
Supporting families affected by MS: Exploring the lasting impact of Digesting Science on children and parents

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Introduction: Approximately 26000 children and young people (CYP) in the UK have a parent with MS. For these CYP, a lack

of accessible, age-appropriate information enabling open communication about their parent's condition can lead to uncertainty, worry and emotional strain. This may impact their mental wellbeing and wider family relationships. Parents with MS have significant anxiety around talking to their families, especially CYP, about their MS. Digesting Science is a structured interactive educational event that aims to engage CYP in science, to communicate health information and support families to have conversations about MS. Over 100 events have run internationally since 2013.

Objectives/Aims: We use creative methods to engage CYP in research, and present the topics that arose in interviews with them and their parents with MS. This provides valuable insights into how Digesting Science has supported families affected by MS.

Methods: We conducted photo elicitation interviews with CYP. They were asked to take 5-10 photos that related to their experience of Digesting Science and things that might have changed for their family since attending. The photographs were then used in lieu of a topic guide, with the photos guiding the interview to explore their experience and the impact of Digesting Science. We then conducted semi-structured qualitative interviews with parents with MS using a topic guide developed with patient collaborators to understand parents' experiences of attending the event with their family and what knowledge and skills they had gained and retained.

Results: Parents with MS discussed feeling empowered with knowledge to understand their own condition better and developed language and skills to explain MS to their CYP and other family member without fear and anxiety. CYP discussed how the event was a fun way to gain knowledge of MS and understand their parents' condition; understanding more about MS empowered them to feel like they could ask questions without it being scary. Importantly parents and CYP who attended an event up to 7 years ago still remembered and used the knowledge and skills they had been empowered with to make sense of symptoms and talk about MS.

Conclusion: Whilst prior to attending a Digesting Science event, families found it difficult to have conversations about MS, the event equipped them with the knowledge, language, and skills, to begin having conversations. This effect was retained up to 7 years after attending an event.

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P1915
State of the art of vocational rehabilitation interventions for people with multiple sclerosis: a systematic scoping review

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Introduction: Vocational Rehabilitation (VR) is an effective intervention to ensure access to work and keep job position for people with disabilities. However, evidence of vocational interventions for people with Multiple Sclerosis (pwMS) is poor.

Objectives/Aims: We conducted a systematic scoping review to frame the state of the art of VR for pwMS and identify VR interventions characteristics and methodology used to demonstrate their effectiveness.

Methods: According to Joanna Briggs Institute guideline, we systematically consulted the following electronic databases until the 6 of October 2024: PubMed (N=442), SCOPUS (N=1133), CHINAL (N=274), PsychInfo (N=220), clinical trial.gov (N=118), google scholar (N=103), Pedro (N=27), OT seeker (N=6). After duplicate removes, two reviewers independently screened 1575 articles, reading the articles' title and abstract. Next, 276 full-text of relevant articles selected were inspected and evaluated based on eligibility criteria by two independent reviewers.

Results: A total of 22 articles were included, involving 16,693 pwMS between 1996 and 2024. Most of the studies were conducted in Europe (N=11, 50%) and USA (N=7, 32%) and the most part were protocol of interventions (N=5, 23%), observational studies (N=4, 18%), pilot (N=3, 14%), and clinical trial studies (N=3, 14%). Studies were related to interventions aimed at: job retention (N=8, 37%), job retentions and improve work abilities (N=3, 14%), provide support in access, return and retention of job position (N=3, 14%) or focused on job seeking (N=2, 9%). Rehabilitation was the most common intervention delivered (N=7, 30%) together with a combination of rehabilitation, educational and work accommodations interventions (N=6, 26%). A significant number of studies provided educational online

packages (N=5, 21%) or educational programs (N=4, 17%) and the remain studies were VR agencies related interventions (N=2, 9%). 13 articles reported a positive effect of interventions.
Conclusion: Several steps have been taken to implement VR interventions, but randomized-controlled clinical trials are required to assess the efficacy of VR interventions for pwMS.

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P1917
Participatory research into the experiences of ethnically minoritised people with MS

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Introduction: Recent studies indicate that people from South Asian and Black British ethnic backgrounds have higher odds of developing multiple sclerosis (MS) at a younger age than people of White ethnicity. Despite this, their experiences remain under-researched.
Objectives/Aims: To explore the healthcare experiences of Black British and South Asian people with MS in London, Leeds and Bradford, focusing on identifying barriers to accessing healthcare, support services, and reliable information.
Methods: Using participatory research to amplify the voices of seldom-heard groups, we worked with six Black British and South Asian people with MS as peer researchers to speak with people with MS about their healthcare experiences. The peer researchers and participants were recruited through the MS service in Leeds, London and Bradford. They received bespoke research training, conducted semi-structured online interviews

and focus groups with 31 participants until data saturation was reached. Interviews and focus groups were analysed through participatory thematic analysis, with peer researchers actively contributing using their lived experience.
Results: Our analysis revealed that the healthcare experiences of Black British and South Asian people with MS are shaped by intersecting factors of age, gender, culture and education that lead to structural inequities. Barriers such as postcode lottery create disparities in diagnosis and service access, while access to reliable information was affected by myths and misconceptions about MS amongst these communities and also healthcare professionals . Gendered expectations further influenced coping strategies, with women often burdened by caring roles and men feeling pressured to mask symptoms. Community support, faith, and alternative care networks play a critical role in managing MS, sometimes filling gaps left by formal healthcare services.
Conclusion: Uncovering the experiences of Black British and South Asian people with MS can help inform co-design of interventions tailored to ethnically minoritised patients. Addressing inequities is crucial to improving healthcare access, patient experiences, and health outcomes for these communities.

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P1918
Probing LLM Capability to Support Empathic Communication in Multiple Sclerosis

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Introduction: Communicating a diagnosis of MS or the apperance of other clinical signs of the disease is a crucial moment with significant psychological implications for the patient, requiring particular attention to mental health and the physician–patient relationship.
Objectives/Aims: In this study, we explore the use of the COSTAR method to design prompts for large language models (LLMs), aimed at supporting neurologists in their dialogue with people with MS (pwMS), particularly in communicating the diagnosis empathetically and personally.
Methods: We performed a literature scan and selected common questions posed by pwMS to their doctors. These questions were used to prompt ChatGPT (GPT-4 model) using a structured format, such as "How would you reply to a patient with Multiple Sclerosis asking [question]?" The initial LLM responses were clear but lacked depth. We then enhanced the prompts with details figuring out a set of fictiuos patient's emotional and psychological profiles using the Big Five Personality Test (B5PT) and the Hamilton Anxiety Scale (HAS). However, the LLM responses did not reflect these prompted values. To improve the chatbot replies, we adopted the COSTAR methodology, which structures prompts by including: 1) Context, 2) Objectives, 3) Structure, 4) Tone, 5) Audience, and 6) Response. We also augmented the chatbot uploading the Italian clinical guidelines for MS, reformatted to fit the COSTAR structure. This approach allowed for the generation of more empathetic, clinically accurate, and personalized responses.
Results: The main result of our study shows that the COSTAR methodology significantly enhances the LLM's ability to produce responses that consider both clinical and psychological aspects of the patient's profile. A sample COSTAR-compliant prompt included detailed patient characteristics such as age, education, and emotional profile, guiding the LLM to deliver a more tailored and empathetic response.
Conclusion: Preliminary results suggest that when appropriately designed, LLMs can be valuable tools to improve communication during complex diagnosis delivery. The use of structured prompts, along with patient profiling and clinical guidelines, can lead to more effective, empathetic, and accurate communication, potentially improving the overall quality of care.
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P1919
Need to Cancel Commitments Due to Multiple Sclerosis Treatment: An Impact on Quality of Life

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Introduction: Patients with multiple sclerosis (MS) experience impairments that significantly impact their quality of life (QoL). In addition to mental health challenges, QoL can be indirectly assessed through changes in daily routine caused by treatment. Due to the wide range of symptoms resulting from neuronal damage in both the brain and spinal cord, MS considerably reduces patients' functional capacity and independence, leading to a lower QoL compared to the general population (Papuć & Stelmasiak, 2012).
Objectives/Aims: To assess the influence of the route of administration used in MS treatment on the need to cancel personal or professional commitments.
Methods: A nationwide online questionnaire in Brazil was conducted with 464 individuals diagnosed with MS, including 368 women and 96 men. Of these, 369 had the relapsing-remitting form, 19 had secondary progressive MS, 8 had primary progressive MS, and 71 were unaware of their MS subtype. The chi-square test was used to evaluate the relationship between the type of medication used and the need to cancel commitments due to treatment. p-values < 0.001 were considered statistically significant.
Results: Among the respondents, 77.5% had the relapsing-remitting form of MS. The average age was 37.87 years, and the average time since diagnosis was approximately four years (48.14 months). Regarding the current route of treatment, 61.4% (219) were receiving intravenous medications, 12.9% (33) were on injectable treatments (subcutaneous or intramuscular), and 17.1% (156) were taking oral medications. In this study, 14 individuals (8.9%) reported not using any MS medication. Among all respondents, 60% indicated having to cancel commitments due to their treatment. Among patients receiving infusion therapy, 80% (OR = 3.27; 95% CI: 2.10–5.10) reported canceling commitments due to medication use, compared to 73% of those on injectable therapies and 57.4% (OR = 0.49; 95% CI: 0.32–0.75) of those on oral treatments.
Conclusion: With the advancement of MS treatments, multiple routes of medication administration are currently available. Evaluating the need to cancel commitments due to treatment allows for an indirect assessment of its negative impact on quality of life. This study found that patients undergoing infusion therapy are 3.27 times more likely to cancel commitments compared to those not receiving such treatment. The choice of medication and its route of administration should aim to minimize interference with patients' daily routines, thereby preventing reductions in quality of life due to disease management.

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