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Comment on: Conventional and biologic disease-modifying anti-rheumatic drugs for osteoarthritis: a meta-analysis of randomized controlled trials

SIR, We read with interest the recent article by Persson *et al.* [1]. The intention of the authors was to investigate the efficacy of DMARDs in patients with symptomatic OA. According to the results of this study, neither conventional nor biologic DMARDS were superior to placebo for pain relief. The pain associated with OA has a complex pathophysiology and there is a poor correlation between pain intensity in OA and the degree of joint degeneration. Peripheral and central sensitization contribute to creating the OA pain experience. Patients with OA can suffer from nociceptive, inflammatory, neuropathic pain or mixed-type pain [2, 3]. Also, French *et al.* [4] reported that 23% of patients with knee or hip OA may have a significant contribution of neuropathic pain. Eleven randomized controlled trials with a total of 1205 participants with clinically and radiographically confirmed OA were included in this meta-analysis. But patients were not evaluated in terms of the pain type in any of these studies and patients with neuropathic pain were not excluded from these studies [1]. A number of screening tools and questionnaires, such as PainDETECT and DN4 (Douleur Neuropathique en 4 Questions), can be used to described the location, intensity, frequency and quality of pain to indicate how likely it is to be neuropathic [5]. Identifying pain types in OA patients is important because they have distinct neurobiological mechanisms and treatment approaches.

In conclusion, the results of this study, consisting of a heterogeneous population, should be interpreted with caution. Negative results of this meta-analysis could be caused by the heterogeneity of patients rather than the ineffectiveness of the drugs. We believe that there is a need for well-designed prospective studies of the effects of DMARDs on pain relief in OA patients without neuropathic features.

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Comment on: Conventional and biologic disease-modifying anti-rheumatic drugs for osteoarthritis: a meta-analysis of randomized controlled trials: reply

SIR, We are grateful to Drs Tecer and Kucuk for their interest and comment on our recent publication on DMARDs for OA. [1, 2]

We agree with the current view that identifying distinct phenotypes in OA, which have different responses to mechanistically diverse treatments, is an important aim in optimizing the management of people with OA. In relation to DMARDs, the major endo-phenotypic variable of interest is the presence of joint inflammation [3]. The epitome of OA driven by inflammation is erosive hand OA. We therefore conducted a subgroup analysis of individuals with erosive hand OA and did not find a difference between DMARDs and placebo for this phenotype. Although limited by a small sample size ($n = 193$), the findings were markedly homogeneous (I^2 = 0.0%, P value 0.846). This suggests that inflammation in OA is different from that in RA.

Certainly, it is widely accepted that some individuals with OA report neuropathic-like pain. Its prevalence in people with knee OA varies by population, but generally affects a minority of individuals [4]. In our location in the East Midlands, UK, the prevalence of neuropathic-like pain in community-derived people with chronic knee pain is 14% [5]. Unfortunately, we were unable to examine people with neuropathic-like pain separately in our meta-analysis as this was not measured or reported for the trials. However, it is unlikely that the presence of this type of pain, estimated to affect 23% of study populations [4], would explain the lack of efficacy of DMARDs for pain relief in OA. In fact, similar rates of neuropathic-like pain have been reported in RA and other inflammatory arthritides [6] for which DMARDs are commonly used. Therefore, the reasons why DMARDs are effective for

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