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ORIGINAL ARTICLE

European chronic kidney disease registries for children not on kidney replacement therapy: tools for improving health systems and patient-centred outcomes

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ABSTRACT

Chronic kidney disease (CKD) in children, from birth to late adolescence, is a unique and highly challenging condition that requires epidemiological research and large-scale, prospective cohort studies. Since its first launch in 2007, the European Society for Paediatric Nephrology/European Renal Association (ESPN/ERA) Registry has collected data on patients on kidney replacement therapy (KRT). However, slowing the progression of CKD is of particular importance and thus the possibility to extend the current registry dataset to include patients in CKD stages 4–5 should be a priority.

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A survey was sent to the national representatives within the ESPN/ERA Registry to collect information on whether they are running CKD registries. All the representatives from the 38 European countries involved in the ESPN/ERA Registry participated in the survey. Eight existing CKD registries have been identified. General characteristics of the national registry and detailed data on anthropometry, laboratory tests and medications at baseline and at follow-up were collected. Results provided by this survey are highly promising regarding the establishment of an ESPN CKD registry linked to the ESPN/ERA KRT registry and subsequently linking it to the ERA Registry with the same patient identifier, which would allow us to monitor disease progression in childhood and beyond. It is our belief that through such linkages, gaps in patient follow-up will be eliminated and patient-centred outcomes may be improved.

Keywords: children, chronic kidney disease, Europe, kidney replacement therapy, registry

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INTRODUCTION

Disease registries are a tool for tracking the clinical care and outcomes of a defined patient population. They are mainly established to improve the quality of patient care and to guide physicians and health authorities by providing a basis for their decision making [1–3]. To accomplish this, they collect information regarding patient and disease characteristics, results of diagnostic tests, treatment options and prognosis. By summarizing these data in annual reports and in scientific publications, they may have a significant impact on patient care. Some of the registries may provide global benchmarking of patient outcomes and make it possible to perform observational studies on important clinical issues [4].

Many national and international organizations have been regularly collecting data on paediatric patients on kidney replacement therapy (KRT) [2–7]. In contrast, there are only a few experiences with data on children with advanced chronic kidney disease (CKD) not on dialysis in North America [8, 9]. A European paediatric CKD registry linked to a KRT registry is of particular importance to provide the full disease process of children from CKD diagnosis to outcome. It could provide not only insights about kidney disease progression rates and patterns, but also a chance to identify predictors for progression and early and effective management of modifiable risk factors in terms of preventive or protective strategies to slow down the progression. Based on many subjects, the development of prediction models based on artificial intelligence for disease progression or reaching end-stage kidney disease (ESKD) could also be a possible future prospect. North American paediatric patients undergoing KRT as well as those with CKD have been registered in the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) database [8]. The US Renal Data System has also been collecting paediatric KRT and CKD data [9]. However, these databases include a selection of patients and are not population based. Several paediatric nephrology societies from European countries have provided data on early stages of CKD showing an incidence of ≈11–12 per million of the age-related population (pmarp) for CKD stages 3–5 and 8 pmarp for CKD stages 4–5 [10]. Recently the UK Renal Registry reported the prevalence of stages 4, 5 and 5D CKD among UK children [11]. The authors found, at the end of 2019, a total of 1031 children <16 years of age with advanced CKD, resulting in a prevalence of 81.2 pmarp. All this information was derived from time-limited surveys, often in a selected cohort of children with access to specialist care. We are not aware of national registries that systematically and longitudinally collect information on paediatric non-dialysis-dependent CKD patients across Europe.

One of the eight prioritized research topics highlighted by the Nephrology and Public Policy Committee proposition was 'to review the feasibility and relevance of the development of CKD Stages 4–5 registries based on on-going experiences at the national level and explore if and how these can be brought together for quality assurance and research at the European level'. The European Renal Association (ERA) Registry attempts to stimulate such registries to use the same terminology, i.e. collect similar data and use the same definitions so that valid comparisons can be made in the future [12]. To this end, a recent publication of the ERA Registry reported the status of CKD registries in Europe in relation to their data collection on patients not on KRT [13]. There were six existing CKD registries and one in preparation reporting data on adults, but information on the existence of paediatric-specific CKD registries remains largely unknown. We therefore aimed to investigate and report the status of CKD registries in Europe in relation to their data collection on paediatric patients not on KRT. We believe that data collected by these registries may be useful for collaborative research on paediatric CKD trajectories and patient outcomes.

MATERIALS AND METHODS

A survey was sent to the national representatives within the European Society for Paediatric Nephrology (ESPN)/ERA Registry to collect information about whether they are running CKD registries. The survey consisted of three main parts: general characteristics, data collection at baseline and data collection at follow-up. There were eight questions, including owner, financial supporter, establishment year, objective(s), data collection and reporting policy, any link with a KRT registry and CKD stage as inclusion criteria in the general characteristics part of the survey. At baseline (i.e. entry into the CKD registry) and follow-up visits, the data collection was mainly related to medications and laboratory test results. Additionally, information included demographic and anthropometric data, feeding route and comorbidity status. Patient outcome was also queried.

RESULTS

All the representatives from the 38 European countries involved in the ESPN/ERA Registry participated in the survey. Eight existing paediatric CKD registries have been identified. Details are listed in Table 1. Specifically, CKD registries were nationwide in four countries (Portugal, Serbia, Norway and Spain) and regional in four countries (Czech Republic, Bulgaria, Ireland and Lithuania). The owners of the registries are departments of paediatric nephrology in four countries and national societies in four countries. If there was any financial support, these were the Ministry of Health in two countries and the national society in one country. In five countries the registry was established and running without any financial support. One country started

Table 1: General characteristics of CKD registries.

Characteristics	Portugal	Serbia	Czech Republic	Norway	Spain	Lithuania	Bulgaria	Ireland
Owner	National Paediatric Nephrology Society	National Paediatric Nephrology Society	Department of Paediatrics, Dialysis Unit, University Hospital Prague	National Nephrology Society	National Paediatric Nephrology Society	Paediatric Centre, Vilnius University Hospital	Department of Paediatric Nephrology, University Paediatric Hospital, Sofia	Department of Paediatric Nephrology, Children's Health Ireland
Financial support source (payer organization)	None	Ministry of Science	None	Ministry of Health	National Paediatric Nephrology Society	None	None	Health Services Executive
Participating centre identification	All 5 centres	4 centres—Belgrade, New Belgrade, Novi Sad, Niš	1 centre—Department of Paediatrics, Dialysis Unit, Prague	27 centres	75 centres	1 centre—Vilnius	1 centre—Sofia	Dublin
Year of start	2021	2000	2000	2016	2007	2009	1986	2015
Objectives								
Epidemiological research	+	+	+	+	+	−	+	−
Clinical research	+	+	+	+	+	+	+	+
Health economics research	−	−	−	−	−	−		−
Quality improvement through benchmarking	+	−	−	+	−	−		+
Healthcare planning	+	+	−	+	+	−		+
Obligatory data collection	+	+	+	+	−	−	+	+
Publication of annual reports	+	−	+	+	−	−	−	+
Linked with a kidney replacement therapy registry	−	−	+	+	+	+	+	−
CKD stage	3–5	2–5	5	5	2–5	2–5	Unknown	2–5

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Table 2: Data collection at baseline.

Characteristics	Portugal	Serbia	Czech Republic	Norway	Spain	Lithuania	Bulgaria	Ireland
Ethnicity	+	−	+	−	+	−	+	+
Underlying cause of CKD	+	+	+	+	+	+	+	+
Date of first paediatric nephrology visit	+	−	+	+	+	−	+	+
Comorbidity	+	−	+	+	+	−	+	+
Anthropometry (including birthweight/height)	+	+	+	+	+	−	+	+
Blood pressure	+	+	+	+	+	−	+	+
Feeding (oral, nasogastric tube, gastrostomy)	−	−	+	−	+	−	+	+
Medications								
Renin–angiotensin system blockers	+	+	+	+	+	−	+	+
Beta-blockers	+	+	+	−	−	−	+	+
Calcium channel blockers	+	+	+	−	−	−	+	+
Diuretics	+	+	+	−	−	−	+	+
Erythropoiesis-stimulating agents	+	+	+	+	+	−	+	+
Iron	+	+	+	−	+	−	+	+
Ketoanalogues	−	+	+	−	−	−	+	−
Phosphate binders	+	+	+	+	+	−	+	+
Protein intake recommendation	−	−	+	−	−	−	+	+
Statins	−	−	+	+	+	−	+	+
Active vitamin D analogues	+	+	+	+	+	−	+	+
25-hydroxyvitamin D supplementation	+	+	+	−	+	−	+	+
Calcium supplementation	+	+	+	−	+	−	+	+
Sodium, potassium supplementation	−	+	+	−	+	−	+	+
Growth hormone	+	+	+	−	+	−	+	+
Laboratory tests								
Sodium	−	−	+	−	+	+	+	+
Potassium	−	−	+	+	+	+	+	+
Bicarbonate	+	−	+	+	+	+	+	+
Calcium	+	+	+	+	+	+	+	+
Phosphate	+	+	+	+	+	+	+	+
Alkaline phosphatase	−	+	+	−	−	+	+	+
Uric acid	+	−	+	−	+	−	+	+
Urea	+	−	+	+	+	+	+	+
Creatinine	+	+	+	+	+	+	+	+
Cholesterol	+	−	+	+	−	+	+	+
Triglycerides	+	−	+	+	−	+	+	+
HDL cholesterol	+	+	+	+	+	+	+	+
Iron	+	+	+	−	+	+	+	+
Transferrin saturation	+	+	+	−	+	+	+	−
Ferritin	+	+	+	−	+	−	+	+
Albumin	+	−	+	+	−	−	+	+
C-reactive protein	−	−	+	−	−	−	+	+
Parathyroid hormone	+	+	+	+	+	+	+	+
eGFR	+	+	+	+	+	+	+	+
Proteinuria (24-hour or spot urine protein:creatinine ratio)	+	+	+	+	+	−	−	+

data collection in 1986, two in 2000, two after 2005 and three from 2015 onwards.

All countries reported that clinical research is the main purpose of the CKD registry, while it was reported as epidemiological research in six countries, healthcare planning in five and quality improvement through benchmarking in three. Four countries have been collecting data on CKD stages 2–5, one on stages 3–5 and two on CKD stage 5 only. Obligatory data collection, publication of annual reports and a link to a KRT registry were valid for five countries.

All registries have been collecting basic patient characteristics at baseline, including demographics, anthropometry (including birthweight and height) and blood pressure (BP), except in Lithuania, while comorbidity has been reported in six and feeding routes in four countries. Anthropometry and BP were registered at follow-up in all eight registries. Additionally, all registries gathered baseline (Table 2) and follow-up (Table 3) data on estimated glomerular filtration rate (eGFR), while six and seven registries collected data on proteinuria (at baseline and at follow-up, respectively), either based on 24-hour urine or spot urine protein:creatinine ratio.

Medications used in the management of CKD complications and most laboratory tests were determined at baseline (Table 2) and during follow-up (Table 3) visits in all registries, except for baseline visits in Lithuania.

Laboratory parameters, including complete blood count, serum biochemistry, bicarbonate, iron status and proteinuria, were evaluated in most registries. However, some of these parameters were not collected in all registries: C-reactive protein was not asked in five registries; proteinuria in two; sodium,

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Table 3: Data collection at follow-up.

Characteristics	Portugal	Serbia	Czech Republic	Norway	Spain	Lithuania	Bulgaria	Ireland
New comorbidity	+	−	+	+	−	+	Unknown	+
Anthropometry	+	+	+	+	+	+	Unknown	+
Blood pressure	+	+	+	+	+	+	Unknown	+
Feeding (oral, nasogastric tube, gastrostomy)	−	−	+	−	+	−	Unknown	+
Medications								
Renin–angiotensin system blockers	+	+	+	+	+	+	+	+
Beta-blockers	+	+	+	−	−	+	+	+
Calcium channel blockers	+	+	+	−	−	+	+	+
Diuretics	+	+	+	−	−	+	+	+
Erythropoiesis-stimulating agents	+	+	+	+	+	+	+	+
Iron	+	+	+	−	+	+	+	+
Ketoanalogues	−	+	+	−	−	−	+	+
Phosphate binders	+	+	+	+	+	+	+	+
Protein intake recommendation	−	−	+	−	−	−	+	+
Statins	−	−	+	+	+	−	+	+
Active vitamin D analogues	+	+	+	+	+	+	+	+
25-hydroxyvitamin D supplementation	+	+	+	−	+	+	+	+
Calcium supplementation	+	+	+	−	+	+	+	+
Sodium, potassium supplementation	−	+	+	−	+	+	+	+
Growth hormone	+	+	+	−	+	+	+	+
Laboratory tests								
Sodium	−	−	+	−	+	+	+	+
Potassium	−	−	+	+	+	+	+	+
Bicarbonate	+	−	+	+	+	+	+	+
Calcium	+	+	+	+	+	+	+	+
Phosphate	+	+	+	+	+	+	+	+
Alkaline phosphatase	−	+	+	−	−	−	+	+
Uric acid	+	−	+	−	+	+	+	+
Urea	+	−	+	+	+	+	+	+
Creatinine	+	+	+	+	+	+	+	+
Cholesterol	+	−	+	+	−	+	+	+
Triglycerides	+	−	+	+	−	+	+	+
HDL cholesterol	+	+	+	+	+	+	+	+
Iron	+	+	+	−	+	+	+	+
Transferrin saturation	+	+	+	−	+	+	+	−
Ferritin	+	+	+	−	+	−	+	+
Albumin	+	−	+	+	−	−	+	+
C-reactive protein	−	−	+	−	−	−	+	+
Parathyroid hormone	+	+	+	+	+	+	+	+
eGFR	+	+	+	+	+	+	+	+
Proteinuria (24-hour or spot urine protein:creatinine ratio	+	+	+	+	+	−	+	+
Outcome								
Partial recovery of renal function	+	+	+	+	+	+	+	+
Stable disease	−	+	+	+	+	+	+	+
CKD progression	−	+	+	+	+	+	+	+
Dialysis	+	+	+	+	+	+	+	+
Transplant waiting list	−	+	+	+	−	+	+	+
Transplantation	+	+	+	+	+	+	+	+
Death	+	+	+	+	+	+	+	+
Cause of death	+	+	+	+	−	+	+	+

albumin and alkaline phosphatase in two; and potassium, uric acid, lipids, transferrin saturation and ferritin in two.

Outcomes studied in all eight registries included (partial) recovery of kidney function, dialysis, kidney transplantation and death. All registries, except Spain, collected causes of death. CKD progression and stable kidney disease were not recorded in Portugal. Being on the transplant waiting list was recorded in all but two registries (Spain and Portugal).

DISCUSSION

ESKD in children from birth to late adolescence is a unique and highly challenging condition that requires epidemiological research and large-scale, prospective cohort studies. In contrast to the increasing availability of information pertaining to the care of children with CKD from large-scale observational and interventional studies, information on the incidence and prevalence of paediatric CKD is currently limited, imprecise and flawed by methodological differences between the various data sources.

Since the launch of the ESPN/ERA Registry for paediatric KRT in 2007, the number of countries providing individual patient data to the registry has increased and now 38 countries are participating, covering a general population of >100 million children ≤15 years of age. In recent years the ESPN/ERA Registry has successfully provided epidemiological data on incidence,

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prevalence, patient characteristics, KRT modalities and mortality in paediatric ESKD, along with relevant insights on cardiovascular risk, anaemia, nutrition and growth and dialysis and transplantation outcomes [14–16]. Additionally, the registry has released annual reports including overall European data and country-specific data, allowing comparisons of the outcome parameters as a feedback tool to improve the quality of care in children on KRT [17].

The ESPN/ERA Registry collects data on patients with CKD stage 5D or kidney transplantation only, but CKD is stratified into five categories from early CKD to ESKD and slowing the progression of CKD is of particular importance. Therefore the extension of the present national and regional registry datasets to include patients in CKD stages 4–5 at the national level should be a priority. If a patient's entire history of CKD stages from disease onset in childhood to transition to adult care is available and transfer dates and details between different KRTs are evident, the full disease spectrum could be visible and therefore reliable trajectory studies and outcome predictions will be accessible for clinicians and stakeholders. Thus the following topics could be covered by a European CKD registry for children with advanced CKD but not on KRT: epidemiology of different causes of CKD and their changes over time; temporal trends of CKD burden; CKD progression in relation to the new aspects of pharmacological nephroprotection; prevalence of CKD complications by CKD stage; potential application of recent formulas to estimate GFR in the paediatric age group; medication burden and compliance by age.

Today, no European paediatric CKD registry exists. In adults, only six European countries (Belgium, Czech Republic, France, Norway, Romania and Sweden) have engaged in routine data collection of patients with CKD stages 4–5, and Finland is preparing to do so. The current inventory has raised awareness of the existence of eight European countries collecting paediatric CKD data on a national or regional basis. This is highly promising in view of establishing a collective European paediatric CKD registry. Establishing an ESPN CKD registry linked to the ESPN/ERA KRT registry and subsequently linking it to the ERA Registry with the same patient identifier would allow us to monitor disease progression in childhood and beyond. By such linkages, gaps in patient follow-up will be eliminated and a continuum of CKD lifespan for each patient can be obtained to improve both health system and patient-centred outcomes.

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AUTHORS' CONTRIBUTIONS

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DATA AVAILABILITY STATEMENT

The data underlying this article are available in the article itself.

CONFLICT OF INTEREST STATEMENT

None declared.

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