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Disparities in treatment rates of paediatric end-stage renal disease across Europe: insights from the ESPN/ERA-EDTA registry

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ABSTRACT

Background. Considerable disparities exist in the provision of paediatric renal replacement therapy (RRT) across Europe. This study aims to determine whether these disparities arise from geographical differences in the occurrence of renal disease, or whether country-level access-to-care factors may be responsible.

Methods. Incidence was defined as the number of new patients aged 0–14 years starting RRT per year, between 2007 and 2011, per million children (pmc), and was extracted from the ESPN/ERA-EDTA registry database for 35 European countries. Country-level indicators on macroeconomics, perinatal care and physical access to treatment were collected through an online survey and from the World Bank database. The estimated effect is presented per 1SD increase for each indicator.

Results. The incidence of paediatric RRT in Europe was 5.4 cases pmc. Incidence decreased from Western to Eastern Europe (−1.91 pmc/1321 km, $P < 0.0001$), and increased from Southern to Northern Europe (0.93 pmc/838 km, $P = 0.002$). Regional differences in the occurrence of specific renal diseases were marginal. Higher RRT treatment rates were found in wealthier countries (2.47 pmc/€10 378 GDP per capita, $P < 0.0001$), among those that tend to spend more on healthcare (1.45 pmc/1.7% public health expenditure, $P < 0.0001$), and among countries where patients pay less out-of-pocket for healthcare (−1.29 pmc/11.7% out-of-pocket health expenditure, $P < 0.0001$). Country neonatal mortality was inversely related with incidence in the youngest patients (ages 0–4, −1.1 pmc/2.1 deaths per 1000 births, $P = 0.10$). Countries with a higher incidence had a lower average age at RRT start, which was fully explained by country GDP per capita.

Conclusions. Inequalities exist in the provision of paediatric RRT throughout Europe, most of which are explained by differences in country macroeconomics, which limit the provision of treatment particularly in the youngest patients. This poses a challenge for healthcare policy makers in their aim to ensure universal and equal access to high-quality healthcare services across Europe.

Keywords: disparities, paediatric nephrology, public health, renal replacement therapy

INTRODUCTION

End-stage renal disease (ESRD) in children is a rare and life-threatening disorder, which requires complex and expensive renal replacement therapy (RRT), i.e. dialysis or renal transplantation, to sustain life. All European Union Member states have made commitments towards universal access to high-quality health services; however, inequalities persist in the provision of paediatric RRT, with considerable differences in treatment rates between countries [1]. These disparities may exemplify inequalities in the provision of specialized care in Europe for other rare disorders that are complex and costly to treat [2].

In adults, the geographic variation in RRT rates has been explained, to some extent, by the percentage of elderly and the prevalence of diabetes and hypertension in the general population [3–6]. Factors influencing access to treatment, such as the adequacy of renal service supply, travel times, the number of private for-profit centres, macroeconomics, and access to RRT for older and more comorbid patients, also play a role in explaining the variation of RRT incidence in adults [7–9].

It is difficult to extrapolate previous findings from the adult to the paediatric RRT population, as ESRD is much rarer in children forming only 1% of the total RRT population. In addition, children are generally treated in public (mostly academic) facilities, and often have a higher priority to care over adults, for example via the paediatric prioritization of donor kidneys [10]. Conversely, as nearly all cases of paediatric ESRD have at least some genetic origin, differences in treatment rates across Europe could partly be explained by geographical differences in genetic background.

As little is known about the causes underlying international variation in paediatric RRT rates, in the present paper we aim to describe the geographic variation in paediatric RRT incidence across Europe, and to determine whether this variation arises from geographical differences in the genetic susceptibility to certain renal diseases [e.g. congenital nephrotic syndrome of the Finnish-type (CNF) in Finland], and to what extent non-medical country-level factors affect access to care.

MATERIALS AND METHODS

Paediatric RRT incidence

The European Society for Paediatric Nephrology/European Renal Association-European Dialysis and Transplantation Association (ESPN/ERA-EDTA) Registry collects data on paediatric RRT. This population-based registry covers a general population of almost 130 million children from 37 European countries [1]. Most countries report information collected from paediatric treatment centres only. As older children may be treated in treatment centres for adult patients, we limited ourselves to children aged 0–14 years. All countries provided data for the years 2007–2011, except for Moldova and Bosnia & Herzegovina (2011 only), Albania, Germany, Malta, Ukraine (2010 onwards) and Montenegro (2009 only). Germany reported only on transplant patients, and pre-emptive transplant patients were not initially reported by Italy. As this will have led to an underestimation of the RRT incidence in Germany and Italy, these countries were excluded from all analyses. Turkey was excluded as the national treatment coverage is unknown. Our outcome measure, paediatric RRT incidence, was defined as the number of new paediatric patients starting RRT per year, between 2007 and 2011 (or otherwise available), per million children, as obtained from the Eurostat database for each corresponding year. RRT incidence rates were standardized for age using the EU-27 for the year 2010 as reference population [11].

Geographical distribution of RRT incidence

To describe the geographic variation in RRT incidence across Europe, we explored geographical gradients in RRT incidence by modelling country RRT incidence against the country's longitude (from West to East) and latitude (from South to North). Longitude and latitude were determined by calculating the spatial centroid of each country using ArcGIS software [12]. Longitude was corrected for latitude and *vice versa* to isolate the effect of each direction. As the geographical location of the centre of Russia could highly affect the geographic gradient results due to the extreme Eastern position, combined with a higher population density in the West compared with the East of Russia, coordinates were based on the position of Moscow.

Geographical distribution of renal disease

To determine whether the variation in RRT incidence arises from geographical differences in the genetic susceptibility to certain renal diseases, we examined differences in the occurrence of causes of renal failure by European region. To achieve the statistical power necessary to detect geographical differences, genetically similar countries were aggregated to the regions East, West, South and North following the regional division of Europe as described by Ralph and Coop [13] (as listed in Supplementary data, Appendix I). In their paper, the authors describe the genetic geography of Europe, creating regional divisions of Europe based on the geographic location and correlations in the pattern of genome-wide data from 2257 Europeans. As the countries Belarus (East), Moldova (East), Lithuania (East), Malta (South) and Iceland (North) were not included in their study, we allocated them based on geographic location alone. Causes of renal failure were classified into 10 primary renal disease (PRD) groups according to the ERA-EDTA coding system for children [14]. We compared observed and expected percentages by PRD group and region using the χ^2 test. The χ^2 contribution of each table cell was used to determine, per region, which PRD groups occurred disproportionately more or less frequently compared with the rest of Europe, including correction for multiple testing using false discovery rate (FDR) adjusted P-values [15].

Country access-to-care indicators

We constructed a conceptual framework to illustrate how potential country-level factors may influence access to paediatric RRT in Europe (Supplementary data, Appendix II), based on a review of the literature and consultation with paediatric

nephrologists from the 37 European countries. Country indicators were extracted from the World Bank Database for each country and averaged for the corresponding years that RRT incidence data were collected (Table 1) [16]. Information regarding the number of paediatric RRT centres and reimbursement policies was collected through an online survey to a paediatric nephrologist in each of the 37 European countries between November and December 2013 (Supplementary data, Appendix III). Reminders were sent in the case of non-response. The response rate was 70%. Information on the proportion of diagnosed congenital anomalies of the kidney and urinary tract (CAKUT) cases resulting in termination of pregnancy was obtained from the EUROSCAN project for congenital malformations registries in 10 European countries (Supplementary data, Appendix IV) [17].

Statistical analyses

Linear regression models were used to explore the associations between country indicators and paediatric RRT incidence. Multivariate models were adjusted for macroeconomic factors. All regression analyses were weighted with the inverse standard error of the RRT incidence rate, which gives larger countries with a larger number of cases more influence on the regression slope. To allow for comparison of effect size across continuous indicators, we presented the estimated effect for a 1SD increase for each indicator [18]. Join-point regression was applied to identify any significant changes in the linear regression slope, allowing us to identify potential non-linearity (including floor and ceiling effects) in the relationship between continuous indicators and RRT incidence [19].

RESULTS

Geographic variation of RRT incidence

The overall age-adjusted incidence rate of paediatric RRT between 2007 and 2011 for 34 countries in Europe was 5.4 per million children (pmc) and varied markedly between countries, as illustrated by Figure 1. RRT incidence was lowest in Eastern Europe (3.6 pmc), followed by Southern (7.2 pmc), Western (7.8 pmc) and Northern Europe (8.1 pmc). The geographical variation in RRT incidence was demonstrated by a strong gradient decreasing from West to East (−1.91 pmc/SD increase in longitude, 1321 km, $P < 0.0001$), and increasing from South to North (0.93 pmc/SD increase in latitude, 838 km, $P = 0.002$).

Geographic variation of renal disease

Using RRT incidence as a proxy for disease occurrence, we explored whether regional differences in the distribution of renal diseases could explain the variation in RRT incidence (Figure 2a and b). Relative to the total number of cases, in

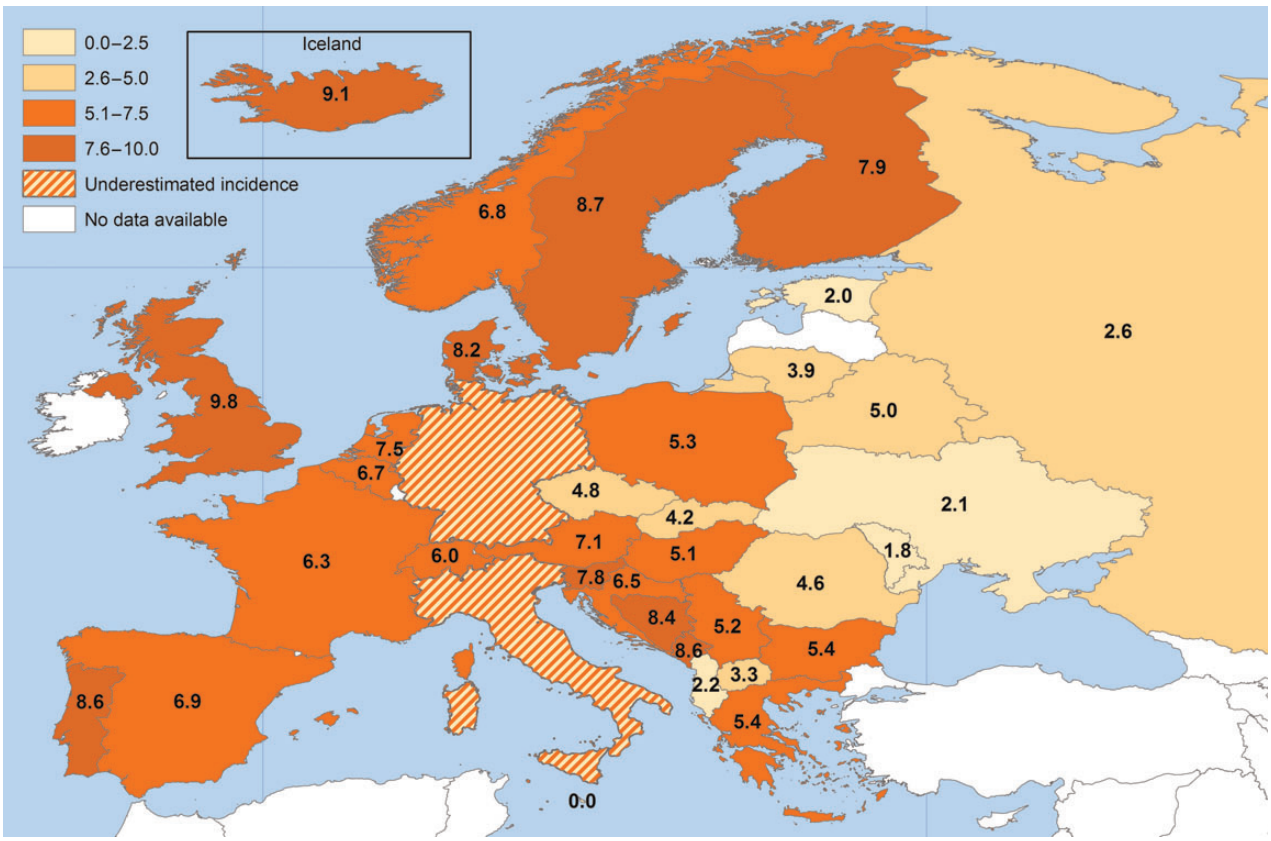

FIGURE 1: Paediatric RRT incidence per country for the period 2007–2011. Data from Germany are based on transplantation patients only and transplantation patients are not included from Italy. Therefore, the numbers are an underestimation of the true incidence and were not mapped.

Eastern Europe there was a significantly lower incidence of RRT for hereditary nephropathies (−1.7%, P = 0.0001, FDR P = 0.03) and haemolytic-uraemic syndrome (0.4%, P = .003, FDR P = 0.03), both of which remained statistically significant after adjustment for multiple testing, and a higher incidence of RRT for cystic kidney disease (2.8%, P = 0.03, FDR P = 0.14). Furthermore, there was a relatively high proportion of patients with hereditary nephropathies, mainly CNF, in Northern (8.6%, P = 0.01, FDR P = 0.07) and Western Europe (1.9%, P = 0.05, FDR P = 0.19). Finally, there was a relatively high incidence of patients with haemolytic-uraemic syndrome in Southern Europe (3.0%, P = 0.01, FDR P = 0.07). There were no further significant differences in PRD group distribution across European regions (Table 2).

Macroeconomics

RRT incidence increased with 2.47 pmc for every SD increase in GDP per capita (95% CI 1.68–3.26, P < 0.0001; Figure 3c). In countries spending <7.5% of national GDP on public health, RRT incidence increased with 2.48 pmc for every SD increase of public health expenditure (95% CI 2.19–2.77, P < 0.0001), but this effect was absent in countries spending >7.5% of GDP on public health (P = 0.26, Figure 3d). There was an inverse association between out-of-pocket health

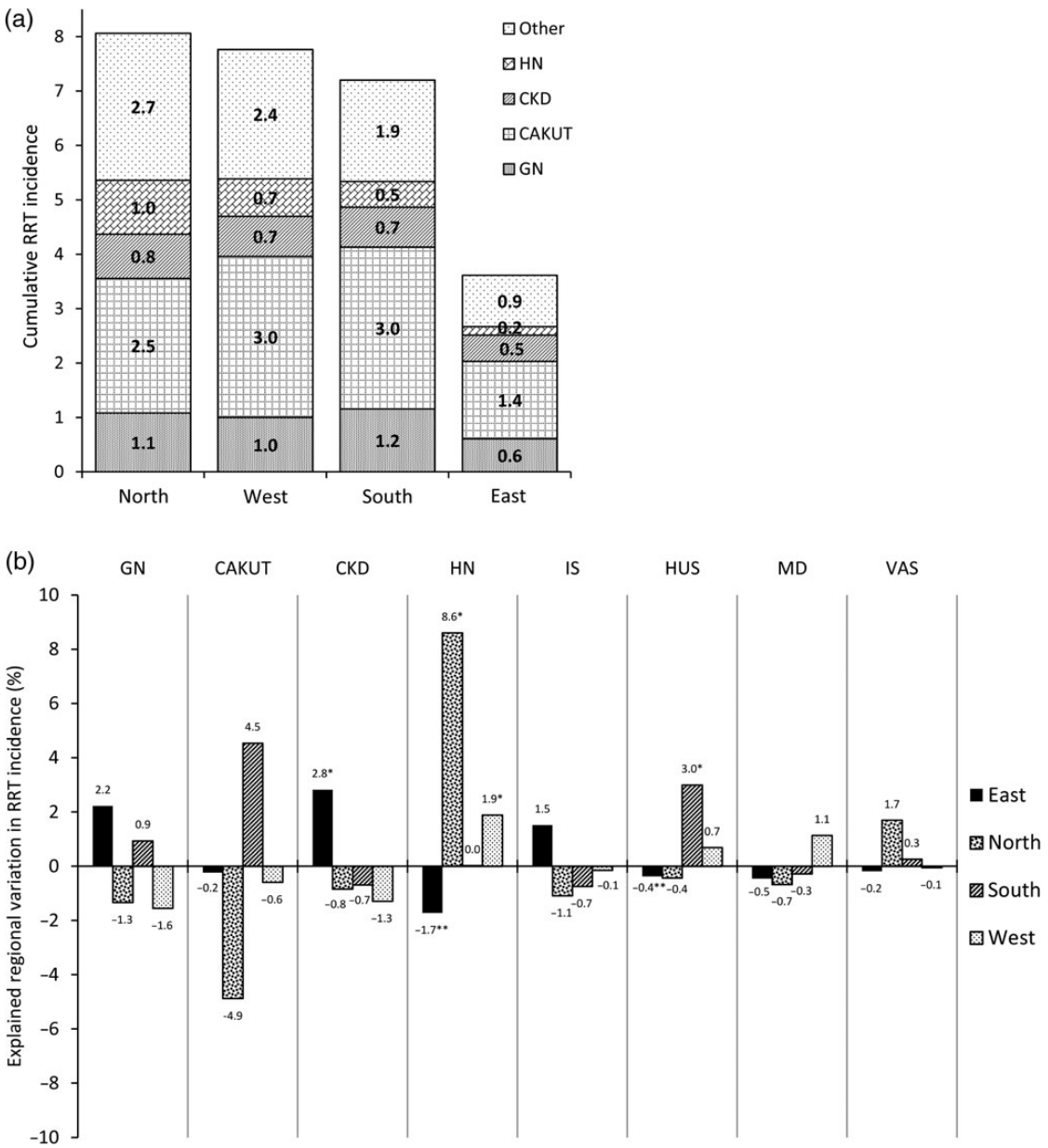

FIGURE 2: (**a**) The geographical distribution of renal disease divided across European regions. The cumulative incidence is presented for the largest PRD groups. GN, glomerulonephritis; CAKUT, congenital anomalies of the kidney and urinary tract; HN, hereditary nephropathies; CKD, cystic kidney disease. (**b**) The geographical distribution of renal disease across Europe. GN, glomerulonephritis; CAKUT, congenital anomalies of the kidney and urinary tract; CKD, cystic kidney disease; HN, hereditary nephropathies; IS, ischaemic renal failure; HUS, haemolytic-uraemic syndrome; MD, metabolic disorders; VAS, vasculitis. * P-value < 0.05. **Significant after FDR adjustment for multiple testing.

Table 1. Description of country-level indicators

Country indicator	Description
GDP per capita[a]	Gross domestic product (GDP) per capita, expressed as purchasing power parity (PPP) in Euros, is a measure for country wealth. The PPP method allows for the international comparison of economies.
Public health expenditure[a]	Public health expenditure is expressed as the percentage of national GDP that a government spends on healthcare.
Out-of-pocket health expenditure[a]	Out-of-pocket health expenditure is the proportion of private health expenditure borne directly by the patient where insurance does not cover the full cost of the healthcare.
Neonatal mortality rate[a]	An indicator of the quality of paediatric healthcare systems, expressed as the number of neonates dying before reaching 28 days of age, per 1000 live births.
CAKUT termination rate[b]	The proportion of CAKUT cases terminated during pregnancy.
Prenatal screening[c]	Availability of a prenatal ultrasound screening (at 18–22 weeks) to examine the fetus for the presence of abnormalities.
Density of centres providing paediatric RRT[c]	The number of centres providing paediatric RRT, expressed per million children (ages 0–14).
Paediatric population density[a]	The number of children (ages 0–14) per km^2.
Rural population[a]	The percentage of rural population.
Paved roads[a]	The percentage of paved roads.
Capability to treat neonates[c]	The capability to provide RRT to neonates (<28 days).
Reimbursement of treatment[c]	Reimbursement of paediatric RRT treatment, defined as >90% reimbursement of treatment costs for HD, PD and Tx.
Reimbursement of travel costs[c]	Reimbursement of travel costs, defined as >90% reimbursement of travel costs.

Sources: [a]World Bank Database, [b]Wiesel *et al.* [17], and [c]Survey.

expenditure and RRT incidence, with incidence decreasing by 1.83 pmc for every SD increase in out-of-pocket health expenditure (95% CI −2.27 to −1.38, P < 0.0001). All factors remained significant after adjustment for GDP (Table 3).

Perinatal care

Country neonatal mortality, as a proxy for the access to and quality of paediatric care, was negatively correlated with RRT incidence (−1.82 pmc for each SD, 95% CI −2.46 to −1.28, P < 0.0001, Figure 3e). This effect was explained by country macroeconomics, as after adjustment for GDP per capita and public health expenditure, the estimate was reduced to −0.43 pmc (95% CI −1.13 to 0.27, P = 0.22). In countries with a neonatal mortality of <6.7/1000 births, RRT incidence declined by 2.2 pmc/SD increase (95% CI −1.64 to −0.47, P = 0.001), while there was a floor effect in countries with a neonatal mortality rate >6.7/1000 births (P = 0.26).

All countries, except for Montenegro and Moldavia, reported it was possible to provide RRT to neonates. According to the questionnaire, ultrasound screening in the second trimester to examine the fetus for the presence of structural abnormalities was available to all women in all but one country. We identified an inverse relationship between RRT incidence and the proportion of pregnancies diagnosed with CAKUT that were terminated, with incidence declining by 1.79 pmc for every SD increase in termination rate (95% CI −3.34 to −0.24, P = 0.03, Figure 3f). However, this association was lost after excluding the Ukraine as an influential outlier (0.15 pmc, 95% CI −2.12 to 1.80, P = 0.86).

Physical access to treatment

In total, there were 153 centres providing one or more modes of paediatric RRT spread across 29 countries where this information was available, representing an overall density of 2.4 centres pmc. All countries were able to provide both haemodialysis (HD) and peritoneal dialysis (PD). There was no association between the number of (modality-specific) centres pmc and (modality-specific) RRT incidence, even after correcting for country GDP per capita and public health expenditure (Table 3).

As country indicators for the average distance to a treatment centre and patient travel time, we explored the relationships between RRT incidence, the general paediatric population density, the percentage of rural population, the percentage of paved roads, and the quality of trade and transport-related infrastructure. Countries with a denser paediatric population had higher RRT incidence rates (4.08 pmc for every SD increase in density, 95% CI 2.74–6.10, P < 0.0001), also after correcting for country GDP per capita. RRT incidence tended to be lower in countries with a higher percentage of rural population (−1.02 pmc/SD increase in rural population, 95% CI −2.22 to 0.19, P = 0.10), but this was reversed after correcting for country GDP per capita (1.17 pmc/SD increase in rural population, 95% CI 0.07–2.28, P = 0.04). The quality of trade and transport-related infrastructure was associated with RRT incidence, increasing by 1.94 pmc for every SD increase in infrastructure score (95% CI 1.63–2.25, P < 0.0001); however, we were unable to adjust for GDP per capita due to collinearity ($r = 0.89$). The percentage of paved roads was not associated with RRT incidence (P = 0.68 after adjustment for GDP per capita).

RRT treatment costs were reimbursed for all modalities in 26 responding countries, except for Bulgaria and Moldova, where none was reimbursed. Patient costs for travelling to RRT centres were reimbursed in 20 of the 29 responding countries, and were not associated with RRT incidence (P = 0.49).

Sensitivity analyses by patient age

We performed sensitivity analyses to establish whether the associations between country-level indicators and RRT incidence were explained by country differences in patient age distribution. RRT incidence varied more between countries in patient ages 0–4 (IQR 2.9–8.8) compared to ages 5–9 (IQR 3.1–5.6) and 10–14 (IQR 4.1–7.8) years. Countries with a higher RRT incidence were treating children at a younger age (IQR for all countries 7.1–8.8), with RRT starting age decreasing by 0.66 years for every SD increase in incidence (1SD = 2.43 pmc, P = 0.0002). This effect was largely explained by country GDP per capita (P = 0.26 after adjustment). Regarding macroeconomics, national GDP had a stronger effect on the RRT incidence in the youngest patients (ages 0–4, 3.33 pmc/SD, P < 0.0001), and to a lesser extent in the older patients (ages 5–14, 1.91 pmc/SD, P <

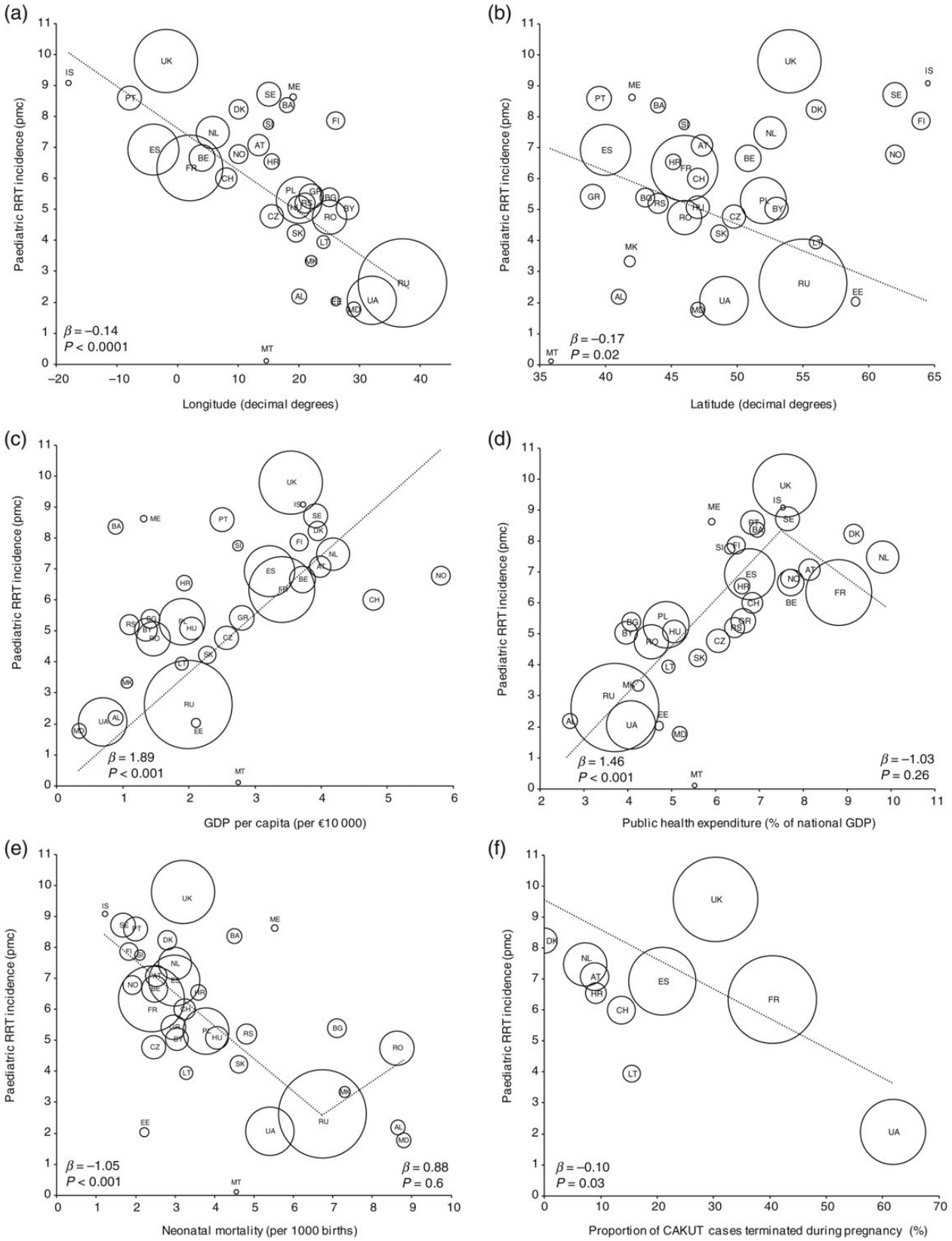

FIGURE 3: Bubble plots displaying the univariate association between country RRT incidence and (**a**) longitude, (**b**) latitude, (**c**) GDP per capita, (**d**) public health expenditure, (**e**) neonatal mortality and (**f**) proportion of CAKUT cases terminated during pregnancy, including the corresponding weighted (join-point) regression lines. The bubble sizes reflect the size of the countries paediatric (patient) population and the countries influence on the regression line. Country abbreviations were expressed by ISO2 country codes.

Table 2. Summary of incidence, macroeconomic, perinatal care, access to treatment and reimbursement characteristics of countries

	Mean (SD)	Number of countries (%)
Incidence (pmc)		
All	5.4 (2.6)	34 (100)
Ages 0–4	5.2 (5.9)	34 (100)
Ages 5–9	4.2 (3.3)	34 (100)
Ages 10–14	6.8 (3.9)	34 (100)
Western Europe	7.8 (1.5)	5 (15)
Eastern Europe	3.6 (2.4)	21 (62)
Southern Europe	7.2 (1.2)	3 (9)
Northern Europe	8.1 (0.9)	5 (15)
Age at start RRT (years)	7.8 (5.0)	34 (100)
Macroeconomics		
GDP per capita (per €10 000)	2.5 (1.3)	34 (100)
Public health expenditure (% of GDP)	6.1 (1.7)	34 (100)
Out-of-pocket expenditure (% of total health expenditure)	25 (11.9)	34 (100)
Perinatal care		
Prenatal screening (% yes)	96	26 (76)
Proportion of CAKUT cases terminated during pregnancy (%)	20.8 (18.7)	10 (29)
Neonatal mortality (per 1000 births)	4.0 (2.1)	34 (100)
Access to treatment		
Paediatric population density (children per km^2)[a]	22.1 (35.2)	34 (100)
Rural population (%)	29.8 (13.8)	34 (100)
Centres providing paediatric RRT (pmc)	2.4 (6.2)	26 (76)
Capability to treat neonates (% yes)	92	25 (74)
Paved roads (%)	76.5 (24.3)	29 (85)
Quality of trade and transport-related infrastructure (scale 1–5)	2.9 (0.6)	34 (100)
HD reimbursement (% yes)	92	26 (76)
PD reimbursement (% yes)	92	26 (76)
Tx reimbursement (% yes)	92	26 (76)
Travel cost reimbursement (% yes)	69	29 (85)

[a]Because of the skewed distribution, the log-transformation of paediatric population density was used in all analyses.

0.0001). Similar increases in effect were observed for public health expenditure and out-of-pocket health expenditure for the youngest patient group. In addition, there was a trend in the association between neonatal mortality and RRT incidence in the youngest patient group after adjustment for GDP per capita (−1.84 pmc/SD, 95% CI −2.8 to −0.9, P = 0.0003) and public health expenditure (−1.1 pmc/SD, 95% CI −2.4 to 0.25, P = 0.10), but was no longer present in the older age groups.

DISCUSSION

In Europe, there are considerable disparities in paediatric RRT treatment rates between countries, demonstrated by a decreasing gradient in RRT incidence from West to East and from North to South. These disparities were largely explained by country differences in macroeconomics, mainly affecting access to care in the youngest patients.

Geographical differences in the occurrence of specific renal diseases played a marginal role in explaining the variation in treatment rates. We found that the incidence of RRT for hereditary nephropathies, including CNF, which constitutes ∼7% of the total European paediatric patient population [20], varied most between European regions. Regional variation in other disease groups was less pronounced, showing only negligible differences in disease incidence, suggesting that international variation in treatment rates is predominantly determined by other factors than geographical differences in disease occurrence.

In adults, disparities in country macroeconomics have also been shown to explain a large portion of the international variation in RRT rates [8, 9]. In children, a non-population-based study has shown the influence of country wealth on paediatric PD prevalence [21], and Harambat *et al.* have shown how the percentage of children living with a functioning graft is affected by country wealth [10]. Here, we show for the first time that disparities in country wealth and healthcare financing strongly affect RRT rates across the full spectrum of European paediatric RRT patients, finding higher treatment rates in wealthier countries, which tend to spend more on healthcare, and where patients bear less out-of-pocket health expenditures. This relationship is understandable given the complexity and cost involved in the provision of renal care to children by a multi-professional paediatric team, and suggests that the need for paediatric RRT is not being met by governments burdened with financial constraints [22–24]. Moreover, the effect of country macroeconomics was strongest in the youngest patients, suggesting that financial constraints particularly hamper access to treatment in infants, who are the most challenging and resource intensive to treat [25]. Encouragingly, we identified a ceiling effect in countries spending >7.5% of GDP on healthcare, suggesting that RRT for all children with ESRD is attainable with healthcare spending around this margin.

Neonatal mortality has previously been used as a marker of health and care during pregnancy and delivery, and may reflect the effectiveness of health systems in the very young, as well as various socio-economic factors [26–28]. We found an inverse trend between neonatal mortality and RRT incidence in the youngest patients, after adjustment for GDP and health expenditure, suggesting that the effectiveness of a country's paediatric health–care system is affecting access to RRT. In addition, it may also reflect country differences in obstetric policies and the physicians' willingness to treat very young children with severe comorbidities. As neonatal dialysis constitutes <5% of the European RRT population, we do not consider neonatal mortality as a direct competing risk for RRT [29].

Congenital urinary tract abnormalities account for 15–20% of all birth defects and are associated with a high perinatal mortality rate of around 15–30%, mostly due to the termination of pregnancies and pulmonary hypoplasia [30, 31]. Increases in pregnancy terminations have previously been associated with declines in the prevalence of congenital anomalies among live-born infants [32]. Here, we show that countries with a high proportion of CAKUT cases terminated during pregnancy tend to have lower RRT incidence rates, indicating the degree to which terminations of pregnancy may affect live-birth CAKUT occurrence [33], although this association should be interpreted with caution given the small sample size of 10 countries and the loss of significance and effect after excluding the Ukraine.

Table 3. Associations between paediatric RRT incidence and country-level indicators

	Univariate		Adjusted for macroeconomics	
	Effect estimate (95% CI)	P-value	Effect estimate (95% CI)	P-value
Macroeconomics				
GDP per capita in € (per SD = €10 378 increase)	2.47 (1.68–3.26)	<0.0001	–	–
Public health expenditure as percentage of GDP (per SD = 1.7% increase)	1.71 (1.34–2.08)	<0.0001	1.45 (0.83–2.07)[a]	<0.0001
Out-of-pocket expenditure as % of total health expenditure (per SD = 12% increase)	−1.83 (−2.27 to −1.38	<0.0001	−1.29 (−1.91 to −0.67)[a]	<0.0001
Perinatal care				
Neonatal mortality (per SD = 2.1 deaths in 1000 births increase)	−1.82 (−2.46 to −1.28)	<0.0001	−0.43 (−1.13 to 0.27)[b]	0.22
Proportion of CAKUT cases terminated during pregnancy (per SD = per 19% increase)	−1.79 (−3.34 to −0.24)	0.03	−0.15 (−2.12 to 1.80)[c]	0.86
Access to treatment				
Population density in children per km^2 (per SD = 35.2 children per km^2 increase)	4.08 (2.74–6.10)	<0.0001	2.73 (1.99–3.77)[a]	<0.0001
Percentage of rural population (per SD = 14% increase)	−1.02 (−2.22 to 0.19)	0.11	1.17 (0.07–2.28)[a]	0.04
Percentage of paved roads (per SD = 24% increase)	0.28 (−0.68 to 1.23)	0.56	−0.13 (−0.75 to 0.49)[a]	0.68
Reimbursement of travel costs (yes versus no)	−1.16 (−4.61 to 2.28)	0.49	−0.66 (−2.32 to 0.99)[b]	0.78
Centres providing paediatric RRT (per SD = 6.2 centres pmc increase)	−0.76 (−1.92 to 0.39)	0.14	−0.46 (−1.42 to 0.48)[b]	0.32
Centres providing paediatric HD (per SD = 6.1 centres pmc increase)[d]	−0.52 (−1.08 to 0.05)	0.06	−0.43 (−1.02 to 0.16)[b]	0.11
Centres providing paediatric PD (per SD = 4.2 centres pmc increase)[d]	0.24 (−0.32 to 0.81)	0.38	0.13 (−0.45 to 0.72)[b]	0.64

The effect estimate is expressed as incidence pmc per SD increase.
[a]Adjusting for GDP per capita.
[b]Adjusting for GDP per capita and public health expenditure.
[c]Excluding Ukraine as an outlier.
[d]Modality specific incidence was used as the dependent variable.

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We found conflicting results regarding physical access to paediatric RRT. On the one hand, we found higher RRT rates in countries with a high paediatric population density, and lower incidence rates in more rural countries, suggesting that health services are physically more accessible in densely populated and urbanized countries, as patients may expect to face lower travel times and costs compared with more dispersed and rural countries [34]. On the other hand, we found no association between RRT incidence and the density of RRT centres, nor with the percentage of paved roads. This may be due to several reasons: (i) the availability of paediatric renal care throughout Europe has improved substantially over the past decades, especially for the youngest patients [23, 35], which is supported by our survey results, which show that currently all European countries are able to provide at least one modality of paediatric dialysis; (ii) most children are treated initially with PD, which takes place at home [36]; and (iii) parents are likely willing to travel relatively long distances to bridge a short pre-dialysis period before transplantation.

The present study has several limitations. Inherent to the observational nature of the study, there is likely to be residual confounding in these associations, which limits us in our ability to infer causality. The explanatory factors collected via the survey reflect the situation in each country as of 2013, whilst the country incidence rate was calculated over the period of 2007–2011. Some of the collected indicators may vary over time and this may therefore have influenced the accuracy of our results. In addition, we do not have full coverage of the entire study period for all countries, which may impact the reliability of our incidence estimates, although we have attempted to correct for this by weighting our analyses. Aggregation of countries to regions was necessary to provide the statistical power needed to detect differences in the geographical distribution of renal disease. However, although this may reflect the genetic background of these regions, differences between individual countries may be lost. Furthermore, due to underestimated RRT incidence rates in Italy and Germany, and unknown national coverage in Turkey, it was necessary to exclude the three large countries from all analyses, shrinking the relatively small sample size of European countries, which may have influenced the width of our confidence intervals.

In conclusion, significant inequalities persist in the provision of paediatric RRT throughout Europe, most of which are explained by differences in country macroeconomics that appear to limit the provision of paediatric RRT particularly in the youngest patients, which are notably challenging to treat. Considering the austerity-driven cuts in healthcare budgets experienced by most European countries over the past few years, this poses a challenge for healthcare policy makers in their aim to ensure universal and equal access to high-quality healthcare across Europe.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

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CONFLICT OF INTERESTS STATEMENT

None declared.

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