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ORIGINAL ARTICLE

# Trends in the epidemiology of paediatric kidney transplantation in Europe between 2010 and 2021: an ESPN/ERA Registry study

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## ABSTRACT

**Background.** Kidney transplantation (KT) is the preferred treatment for paediatric patients with kidney failure, but information on trends in paediatric KT in Europe is lacking. We aimed to report on time trends in paediatric (0–17 years) KT rates and recipient characteristics in Europe between 2010 and 2021.

**Methods .** Thirty-one countries contributing data from 2010 to 2021 on paediatric KT to the European Society for Paediatric Nephrology/European Renal Association Registry were included. We reported trends in KT rates [per million age-related population (pmarp)], overall and by patient subgroup for Europe, and at macro-economic and country-specific levels. We also reported clinical variables in the first year post-KT. The 2020–21 period was analysed separately to account for the COVID-19 pandemic.

**Results .** The paediatric KT rate was stable at ≈5 pmarp between 2010 and 2019, and about one-fourth were pre-emptive KTs. In 2020–21 the KT rate was 5.6 pmarp. In low–, middle– and high–gross domestic product (GDP) countries, KT rates (pmarp) were 2.1, 6.1 and 7.6, respectively, and increased in low-GDP countries by 4.1% per year from 2010 to 2019, mainly in the youngest recipients. The proportion of pre-emptive KT increased only in middle-GDP countries. Low-GDP countries showed a higher prevalence of short stature while high-GDP countries showed more overweight/obese, hypertensive and anaemic patients.

**Conclusions .** The rate of paediatric KT in Europe has remained stable, with differences between GDP groups. Low-GDP countries had the lowest KT rates, but with an increasing trend over time. Opportunities to further increase access to paediatric KT should be explored.

**Keywords:** epidemiology, Europe, kidney transplantation, paediatrics, trends

## KEY LEARNING POINTS

**What was known:**

- Kidney transplantation (KT) is the preferred treatment modality for paediatric patients in need of kidney replacement therapy (KRT), leading to better growth, psychosocial development and quality of life, as well as longer life expectancy, and being more cost-effective than dialysis.
- In Europe, there are inequalities among countries in access to paediatric KT, which may be related to various factors such as macro-economics, KRT selection procedures, transplantation policies, donation rates and KT practices.
- KT rates in adult patients from Europe increased between 2010 and 2018, with large variations between countries. However, information on time trends in paediatric KT rates in Europe is lacking.

**This study adds:**

- Between 2010 and 2019, the overall rate of paediatric (age 0–17 years) KT in Europe remained stable at ≈5 per million age-related population (pmarp). However, there were differences by gross domestic product (GDP) level: rates were 2.1 pmarp in low-, 6.1 pmarp in middle- and 7.6 pmarp in high-GDP countries. Approximately one in four kidney transplants was performed pre-emptively and the proportion of pre-emptive KTs increased only in the middle-GDP group.
- Between 2010 and 2019, KT rates in low-GDP countries increased by 4.1% per year, mainly among very young children and among recipients of living donor kidney transplants.
- The COVID-19 pandemic was not found to have a substantial impact on the overall paediatric KT rate in Europe, which was 5.6 pmarp in 2020–2021. However, in middle- and high-GDP countries, deceased donor KT rates seemed to decrease and the time on dialysis before KT increased slightly.

**Potential impact:**

- This study provides an overview of trends in paediatric KT in nearly all European countries, suggesting an improvement in access to paediatric KT in low-GDP countries.
- The findings of this study may support policymakers and the medical community in identifying barriers and opportunities to further increase access to paediatric KT overall and also pre-emptive KT.

## INTRODUCTION

Kidney transplantation (KT) is the preferred treatment modality for paediatric patients who need kidney replacement therapy (KRT) [1–3], resulting in better psychosocial development and quality of life and longer life expectancy, while being more cost-effective than dialysis [1, 2, 4, 5]. Although only about one-fifth of the European children with kidney failure receive pre-emptive KT, the majority will receive a graft during childhood. By 31 December 2021, 73% of prevalent paediatric KRT patients in Europe (age <15 years) had a functioning kidney transplant [6, 7].

Country disparities in access to paediatric KT and recipient characteristics persist, possibly caused by macro-economic factors, KRT selection procedures and transplantation policies and practices [1, 5, 8, 9]. Well-resourced countries are usually able to accept more complex cases for KRT, including younger patients and those with more comorbidities [5, 9]. Furthermore, KRT care differences may have an impact on patients' clinical variables, such as growth and haemoglobin levels and are associated with quality of life and graft and patient survival [10, 11]. Although several studies have shown differences in paediatric KT practices [1, 5, 9], and the European Society for Paediatric Nephrology (ESPN)/European Renal Association (ERA) Registry published annual reports on the epidemiology of paediatric dialysis and KT [6, 7, 12, 13], information on time trends in European paediatric KT is lacking [8]. Comprehensive epidemiological data on such trends and geographical variations can help in determining whether efforts to improve paediatric KRT care have been successful, highlighting potential areas for improvement [1, 5].

The aim of this ESPN/ERA Registry study was to investigate trends in the epidemiology of paediatric KT (age 0–17 years) in Europe in the period 2010–19. Additionally, we evaluated the trends of paediatric KT during the COVID-19 pandemic (2020–21). Specifically, we aimed to provide details on trends in KT rates and clinical variables at macro-economic and country-specific levels.

## MATERIALS AND METHODS

### Data sources

Data were extracted from the ESPN/ERA Registry, a population-based registry that annually collects information on individual paediatric KRT patients from renal registries in Europe [12]. Thirty-one countries contributing data on patients ages 0–17 years who received a kidney transplant, including retransplantations, between 1 January 2010 and 31 December 2021 were included, covering on average 86% of the general European paediatric population (Supplementary Table S1). In The Netherlands, there was (almost) no underreporting of (pre-emptive) KT in 2010–16, but some underreporting exists for overall KT in 2017–19 (ranging from 14% to 32%) and for pre-emptive KT in 2017–21 (ranging from 25% to 43%).

Participating European countries were categorized into low–, middle– and high–gross domestic product (GDP) groups based on tertiles of average GDP between 2010 and 2021 obtained from the World Bank database (Supplementary Table S1) [14].

## Statistical analyses

Patient characteristics were described across periods, for Europe and by GDP group and presented as numbers (percentages). Primary renal diseases (PRDs) were grouped according to ERA Registry codes adapted for children [13]. Due to its low frequency, ischaemic kidney failure, haemolytic uraemic syndrome (HUS), metabolic diseases, vasculitis, miscellaneous and 'other' causes were combined into the category 'other' [13]. For countries that reported comorbidities (22 of 31), we hypothesized that comorbidities were absent if this information was missing [9]. Chi-squared tests were used to assess statistically significant differences in patient characteristics between GDP groups and time periods (2010–14 and 2015–19). To account for the potential impact of the COVID-19 pandemic on paediatric KT rates, the pandemic years (2020–21) were analysed separately.

KT rates were expressed per million age-related population (pmarp) and calculated by dividing the number of KTs in a year by the general population ages 0–17 years and multiplied by one million. General population counts were obtained from the Eurostat database [15]. Annual rates were calculated for all KTs performed in Europe, by country, and GDP group and stratified by age at KT, sex, PRD and donor type. Due to low annual paediatric KT rates per country, these were averaged and expressed per period (2010–14, 2015–19 and 2020–21) to obtain more stable estimates.

Time trends in KT rates were evaluated using the Joinpoint regression program, which estimates the annual percent change (APC) of a variable and allows the detection of time points at which the slope of the regression line changes significantly. It was therefore possible to identify statistically significant changes in KT rates over the study period. A detailed explanation of this method can be found elsewhere [16]. To avoid the potential impact of the COVID-19 pandemic, APC calculations were performed for the period 2010–19 [17]. The 10 data points included in the analyses allowed for the detection of a maximum of one joinpoint [18].

Several clinical variables, measured multiple times during the first year post-transplant, were described across periods, overall and by GDP group. These variables, reported as proportions [95% confidence interval (CI)], were short stature, overweight/obesity, hypertension, anaemia and hyperparathyroidism. Definitions of each clinical variable are provided in Supplementary Table S2. Generalised estimating equation models were used to correct for the correlation of multiple measurements at different time intervals in the same patient. Further details of this methodology can be found elsewhere [19].

Statistical tests were two-tailed and differences were considered statistically significant for $P$-values $<.05$. Data analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and Joinpoint 4.2.0.2 (2015; National Cancer Institute, Calverton, MD, USA).

# RESULTS

## Patient population

In Europe, the majority of paediatric kidney transplant recipients (KTRs) were male (59.5%), with congenital anomalies of the kidney and urinary tract (CAKUT) (36.0%), transplanted during adolescence (13–17 years; 40.3%). One-quarter of patients received a pre-emptive kidney transplant and one-third had comorbidities (Table 1). In low-GDP countries, compared with middle- and high-GDP groups, fewer patients received a kidney transplant at a very young age (0–5 years), were transplanted pre-emptively or had comorbidities (Table 2).

## Trends in KT

### Total KT in Europe and by GDP group

The annual paediatric KT rate was stable between 2010 and 2019: 4.9 pmarp in 2010–14 and 5.1 pmarp in 2015–19 [APC 0.1 (95% CI −1.1 to 1.2)]. Between 2010 and 2019 there was considerable variation between countries in KT rates, ranging from 1.1 pmarp in Romania to 9.5 pmarp in Finland and Sweden (Table 3, Fig. 1). The low-GDP group had the lowest KT rate; however, it increased significantly over time from 1.9 pmarp in 2010–14 to 2.4 pmarp in 2015–19 [APC 4.1 (95% CI 1.6 to 6.7)] (Table 3, Fig. 1). The average KT rate was stable in the middle- (6.1 pmarp both in 2010–14 and 2015–19) and high- (7.6 and 7.5 pmarp in 2010–14 and 2015–19, respectively) GDP groups.

### Pre-emptive KT in Europe and by GDP group

Of all the KTs performed (including retransplantation) between 2010 and 2019, the average overall proportion of pre-emptive KTs was 23.5%. In low-, middle- and high-GDP groups it was, respectively, 13.6%, 19.9% and 28.6% (Table 3). Between 2010 and 2019 the overall proportion of pre-emptive KTs remained stable but increased in the middle-GDP group (Supplementary Table S3).

## Trends in KT by patient subgroup

### Age at KT

KT rates were lowest among children ages 0–5 years (3.4 pmarp in both 2010–14 and 2015–19) and highest among adolescents (13–17 years; 7.0 pmarp in 2010–14 and 7.8 pmarp in 2015–19). There were no significant time trends in KT rates by age group, except in the low-GDP group. Despite the lowest KT rates among 0- to 5-year-olds, it increased on average by 9.3% per year (95% CI 4.5 to 14.4), from 0.9 pmarp in 2010–14 to 1.5 pmarp in 2015–19 (Fig. 2, Supplementary Table S3).

### Sex

Overall, the KT rate in 2010–19 in males (5.8 pmarp) was higher compared with females (4.2 pmarp) and there were no temporal trends by sex (Fig. 3). In low-GDP countries, we observed an increase in the rate of KT for males, with an average of 4.5% per year (95% CI 0.3 to 8.9), and a similar (non-significant) increase for females [APC 3.8 (95% CI −1.3 to 9.2)] (Supplementary Table S3).

### PRD

Overall, trends in KT rates by PRD group were stable (Fig. 4). In the high-GDP group there was a decrease in paediatric KTRs with 'other' PRD [APC −4.9 (95% CI −7.7 to −2.0)] and an increase in cystic kidney disease [APC: 3.6 (95% CI 1.6 to 5.6)].

### Donor type

Overall, there was a slight (non-significant) increase in the rate of living donor KTs between 2010 and 2019 [APC 1.5 (95% CI −0.6 to 3.7)] and the rate of deceased donor KTs remained stable [APC

**Table 1: Characteristics of paediatric KTRs overall and stratified by time period of KT.**

| Characteristics | Period of kidney transplantation 2010–19 | 2010–14 | 2015–19 | 2020–21[a] | P-value (2010–14 versus 2015–19) |
|---|---|---|---|---|---|
| Patients, *n* (%) | 6611 (100.0) | 3212 (48.6) | 3399 (51.4) | 1167 | |
| Age at kidney transplantation (years), *n* (%) | | | | | |
| 0–5 | 1554 (23.5) | 744 (23.2) | 810 (23.8) | 250 (21.4) | 0.539 |
| 6–12 | 2393 (36.2) | 1184 (36.9) | 1209 (35.6) | 424 (36.3) | |
| 13–17 | 2664 (40.3) | 1284 (40.0) | 1380 (40.6) | 493 (42.3) | |
| Age at kidney transplantation (years), median (IQR) | 11.5 (6.3–15.0) | 11.5 (6.2–15.0) | 11.4 (6.5–15.1) | 11.7 (6.8–15.3) | |
| Males, *n* (%) | 3930 (59.5) | 1891 (58.9) | 2039 (60.0) | 716 (61.4) | 0.348 |
| Age at KRT start (years), *n* (%) | | | | | |
| 0–5 | 2183 (33.0) | 1049 (32.7) | 1134 (33.4) | 408 (35.0) | 0.229 |
| 6–12 | 2457 (37.2) | 1221 (38.0) | 1236 (36.4) | 434 (37.2) | |
| 13–17 | 1962 (29.7) | 940 (29.3) | 1022 (30.1) | 322 (27.6) | |
| Unknown | 9 (0.1) | 2 (0.1) | 7 (0.2) | 3 (0.3) | |
| Primary renal disease[b], *n* (%) | | | | | |
| Glomerulonephritis | 1037 (15.7) | 499 (15.5) | 538 (15.8) | 179 (15.4) | **0.002** |
| CAKUT | 2377 (36.0) | 1158 (36.1) | 1219 (35.9) | 396 (33.9) | |
| Cystic kidney disease | 874 (13.2) | 405 (12.6) | 469 (13.8) | 159 (13.6) | |
| Hereditary nephropathy | 437 (6.6) | 198 (6.2) | 239 (7.0) | 72 (6.2) | |
| Other | 1255 (19.0) | 598 (18.6) | 657 (19.3) | 224 (19.2) | |
| Unknown | 631 (9.5) | 354 (11.0) | 277 (8.2) | 137 (11.7) | |
| Initial treatment modality[c], *n* (%) | | | | | |
| Haemodialysis | 2194 (36.4) | 1037 (35.0) | 1157 (37.7) | 368 (36.9) | **0.019** |
| Peritoneal dialysis | 2240 (37.1) | 1146 (38.7) | 1094 (35.6) | 378 (37.9) | |
| KT | 1487 (24.7) | 715 (24.2) | 772 (25.1) | 236 (23.7) | |
| Unknown | 111 (1.8) | 63 (2.1) | 48 (1.6) | 16 (1.6) | |
| Comorbidities, *n* (%)[d] | | | | | |
| Yes | 1513 (33.0) | 723 (31.8) | 790 (34.2) | 273 (34.8) | 0.078 |
| No | 3074 (67.0) | 1554 (68.3) | 1520 (65.8) | 511 (65.2) | |
| Time on dialysis before first KT (months)[c,e], *n* (%) | | | | | |
| 0 | 1492 (24.8) | 718 (24.3) | 774 (25.3) | 236 (23.7) | 0.341 |
| >0–6 | 921 (15.3) | 458 (15.5) | 463 (15.1) | 114 (11.5) | |
| >6–12 | 998 (16.6) | 500 (16.9) | 498 (16.3) | 137 (13.8) | |
| >12–24 | 1255 (20.8) | 640 (21.6) | 615 (20.1) | 217 (21.8) | |
| >24 | 1359 (22.6) | 644 (21.8) | 715 (23.3) | 291 (29.3) | |
| Kidney donor type, *n* (%) | | | | | |
| Deceased | 3745 (56.7) | 1859 (57.9) | 1886 (55.5) | 573 (49.1) | **<0.001** |
| Living | 2348 (35.5) | 1064 (33.1) | 1284 (37.8) | 386 (33.1) | |
| Unknown | 518 (7.8) | 289 (9.0) | 229 (6.7) | 208 (17.8) | |

Significant values in bold.
[a]Data from Russia are not included in the period 2020–21.
[b]The PRD category 'other' includes ischaemic kidney failure, haemolytic uraemic syndrome, metabolic diseases, vasculitis, miscellaneous and others.
[c]Türkiye presents an overestimation of pre-emptive KT and therefore underestimation of the true time on dialysis before first KT, hence it was excluded from this analysis.
[d]Countries that did not report data on comorbidities between 2010 and 2019 were excluded from this analysis (Austria, Denmark, Finland, France, Iceland, The Netherlands, Romania, Sweden and Ukraine). The following comorbidity categories were included: cardiovascular disease, chronic inflammatory disease, chronic intestinal disease, liver disease, multiple malformative syndrome, malignancy, neurological disorders, chronic pulmonary disease, systemic disease, preterm birth, developmental delay, chromosomal anomaly and diabetes mellitus.
[e]There were seven patients with unknown time on dialysis before the first KT between 2010 and 2019 due to unknown date of KRT start.

−1.1 (95% CI −3.1 to 1.0)] (Supplementary Fig. S1). When stratifying by GDP group, the increase in the living donor KT rate was only significant in the low-GDP group [APC 6.6 (95% CI 2.0 to 11.5)].

## Growth, body mass index (BMI), anaemia and hyperparathyroidism

Between 2010 and 2019, during the first year post-transplant, almost half of all patients had short stature [43.1% (95% CI 41.5 to 44.7)], approximately one-third were overweight/obese [32.8% (95% CI 31.2 to 34.5)] or hypertensive [33.1% (95% CI 31.6 to 34.7)], 16.7% had anaemia (95% CI 15.6 to 17.9) and 53.1% (95% CI 50.5 to 55.6) had hyperparathyroidism (Table 4). The proportion of patients with short stature decreased slightly between periods, while the prevalence of anaemia increased (Table 4). There were more paediatric KTRs with short stature in the low-GDP group [54.3% (95% CI 51.0 to 57.7)]. In the high-GDP group, higher proportions of patients were overweight/obese [35.2% (95% CI 32.8 to 37.7)], hypertensive [35.5% (95% CI 33.5 to 37.6)] and anaemic [18.4% (95% CI 17.0 to 19.8)] (Table 5).

**Table 2: Characteristics of paediatric KTRs stratified by GDP group between 2010 and 2019.**

| Characteristics | GDP group Low | Middle | High | P-value[c] |
|---|---|---|---|---|
| Patients who received a kidney transplant (% of all prevalent KRT patients)[a] | 45.5 | 71.5 | 78.8 | N/A |
| Patients, n (%)[b] | 1517 (23.0) | 1565 (23.7) | 3529 (53.4) | |
| Age at KT (years), *n* (%) | | | | |
| 0–5 | 288 (19.0) | 317 (20.3) | 949 (26.9) | **<0.001** |
| 6–12 | 613 (40.4) | 609 (38.9) | 1171 (33.12) | |
| 13–17 | 616 (40.6) | 639 (40.8) | 1409 (39.9) | |
| Age at KT (years), median (IQR) | 11.9 (7.9–14.7) | 11.6 (6.9–15.0) | 11.4 (5.6–15.4) | |
| Males, *n* (%) | 876 (57.8) | 922 (59.0) | 2132 (60.4) | 0.187 |
| Age at KRT start (years), *n* (%) | | | | |
| 0–5 | 414 (27.3) | 489 (31.3) | 1280 (36.3) | **<0.001** |
| 6–12 | 694 (45.8) | 623 (39.8) | 1140 (32.3) | |
| 13–17 | 406 (26.8) | 447 (28.6) | 1109 (31.4) | |
| Unknown | 3 (0.2) | 6 (0.4) | 0 (0.0) | |
| Primary renal disease[d], *n* (%) | | | | |
| Glomerulonephritis | 245 (16.2) | 282 (18.0) | 510 (14.5) | **<0.001** |
| CAKUT | 526 (34.7) | 507 (32.4) | 1344 (38.1) | |
| Cystic kidney disease | 217 (14.3) | 215 (13.7) | 442 (12.5) | |
| Hereditary nephropathy | 47 (3.1) | 99 (6.3) | 291 (8.3) | |
| Other | 304 (20.0) | 343 (21.9) | 608 (17.2) | |
| Unknown | 178 (11.7) | 119 (7.6) | 334 (9.5) | |
| Initial treatment modality[e], *n* (%) | | | | |
| Haemodialysis | 432 (46.1) | 526 (33.6) | 1236 (35.0) | **<0.001** |
| Peritoneal dialysis | 363 (38.7) | 689 (44.0) | 1188 (33.7) | |
| Kidney transplantation | 135 (14.4) | 340 (21.7) | 1012 (28.7) | |
| Unknown | 8 (0.9) | 10 (0.6) | 93 (2.6) | |
| Comorbidities[f], *n* (%) | | | | |
| Yes | 210 (16.0) | 739 (47.2) | 564 (33.1) | **<0.001** |
| No | 1107 (84.1) | 826 (52.8) | 1141 (66.9) | |
| Time on dialysis before first KT (months)[e,g], *n* (%) | | | | |
| 0 | 136 (14.5) | 341 (21.9) | 1015 (28.8) | **<0.001** |
| >0–6 | 208 (22.2) | 237 (15.2) | 476 (13.5) | |
| >6–12 | 174 (18.6) | 269 (17.3) | 555 (15.7) | |
| >12–24 | 196 (20.9) | 323 (20.7) | 736 (20.9) | |
| >24 | 223 (23.8) | 389 (25.0) | 747 (21.2) | |
| Kidney donor type, *n* (%) | | | | |
| Deceased | 661 (43.6) | 1058 (67.6) | 2026 (57.4) | **<0.001** |
| Living | 706 (46.5) | 238 (15.2) | 1404 (39.8) | |
| Unknown | 150 (9.9) | 269 (17.2) | 99 (2.8) | |

Significant values in bold.

[a]The percentages in this row correspond to the average proportion in 2010–19 of prevalent KRT patients (including dialysis) with a functioning kidney transplant by the end of the year in each GDP group.

[b]The percentages in this row correspond to the proportion of KTRs in each GDP group from the total number of KTRs in Europe.

[c]P-values comparing GDP groups.

[d]The PRD category 'other' includes ischaemic kidney failure, haemolytic uraemic syndrome, metabolic diseases, vasculitis, miscellaneous and others.

[e]Turkey presents an overestimation of pre-emptive KT and therefore an underestimation of the true time on dialysis before first KT, hence it was excluded from this analysis.

[f]Countries that did not report data on comorbidities between 2010 and 2019 were excluded from this analysis (Austria, Denmark, Finland, France, Iceland, The Netherlands, Romania, Sweden and Ukraine). The following comorbidity categories were included: cardiovascular disease, chronic inflammatory disease, chronic intestinal disease, liver disease, multiple malformative syndrome, malignancy, neurological disorders, chronic pulmonary disease, systemic disease, preterm birth, developmental delay, chromosomal anomaly and diabetes mellitus.

[g]There were seven patients with unknown time on dialysis before the first KT between 2010 and 2019 due to unknown date of KRT start.

### COVID-19 period (2020–21)

Paediatric KT rates remained stable in 2020–21 but the middle- and high-GDP groups showed a slight non-significant decrease (Table 3). Additionally, time on dialysis increased slightly, 51.1% of the KTRs in 2020–21 received ≥12 months of pretransplant dialysis, compared with 43.4% of patients transplanted in 2010–19 (Table 1).

## DISCUSSION

In Europe, overall paediatric KT rates and pre-emptive KT rates have remained stable over the last decade. There were considerable differences between countries and GDP groups. The lowest rate was observed in the low-GDP group, but with an annual increase of 4.1%, which was not observed in the middle- and high-GDP countries.

**Table 3: KT rates (pmarp) and proportion of pre-emptive KTs in 0- to 17-year-olds, by country and time period.**

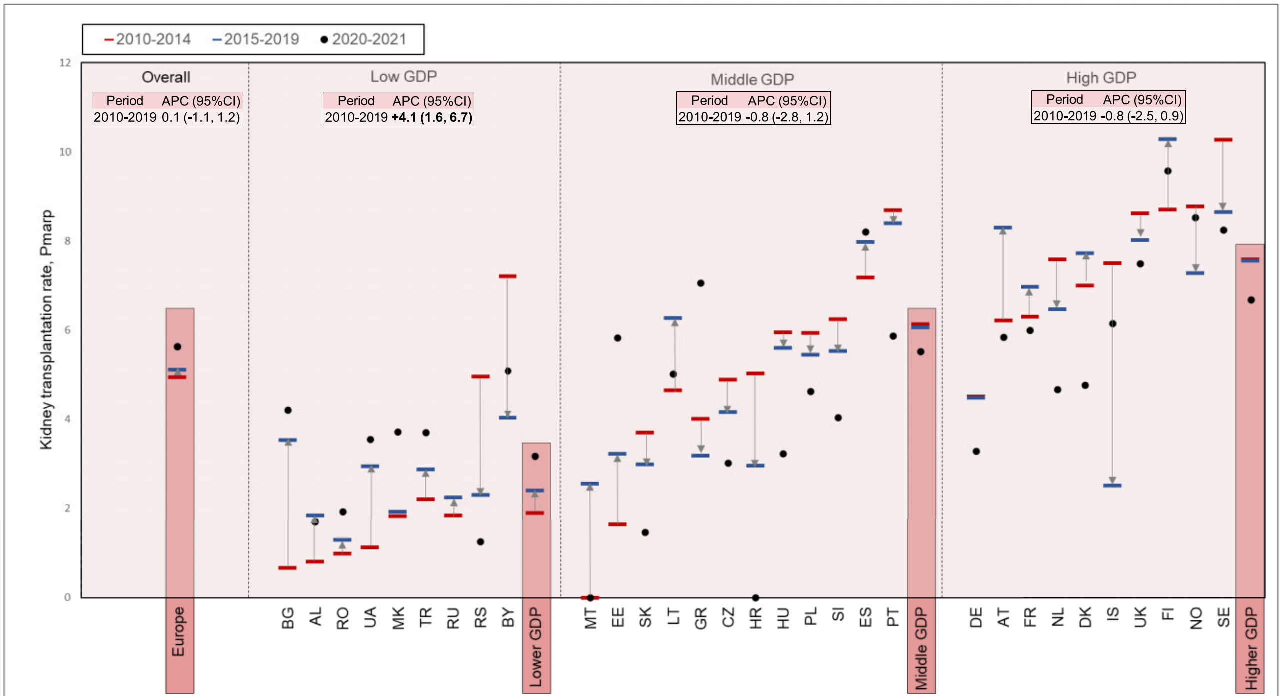
| | KT (pre-emptive KT) | | | |
|---|---|---|---|---|
| Country | 2010–2014 | 2015–2019 | 2020–2021[a] | Average 2010–2019 |
| Low GDP | | | | |
| Albania | 0.8 (0.0) | 1.8 (0.0) | 1.7 (0.0) | 1.3 (0.0) |
| Belarus | 7.2 (3.3) | 4.0 (2.2) | 5.1 (19.6) | 5.6 (2.7) |
| Bulgaria | 0.7 (0.0) | 3.5 (30.2) | 4.2 (60.0) | 2.1 (15.1) |
| North Macedonia | 1.8 (0.0) | 1.9 (30.0) | 3.7 (25.0) | 1.9 (15.0) |
| Republic of Serbia | 5.0 (14.5) | 2.3 (10.0) | 1.3 (0.0) | 3.6 (12.3) |
| Romania | 1.0 (10.0) | 1.3 (10.0) | 1.9 (0.0) | 1.1 (10.0) |
| Russia | 1.8 (16.8) | 2.3 (15.4) | N/A | 2.0 (16.1) |
| Ukraine | 1.1 (2.5) | 2.9 (18.1) | 3.5 (10.7) | 2.0 (10.3) |
| Türkiye | 2.2 (76.5) | 2.9 (58.8) | 3.7 (18.6) | 2.5 (67.6) |
| Total[b] | 1.9 (12.1) | 2.4 (15.2) | 3.2 (15.7) | 2.1 (13.6) |
| Middle GDP | | | | |
| Croatia | 5.0 (16.7) | 3.0 (5.0) | 0.0 (0.0) | 4.0 (10.8) |
| Czech Republic | 4.9 (10.6) | 4.2 (18.2) | 3.0 (0.0) | 4.5 (14.4) |
| Estonia | 1.6 (10.0) | 3.2 (20.0) | 5.8 (0.0) | 2.4 (15.0) |
| Greece | 4.0 (16.5) | 3.2 (16.7) | 7.0 (12.4) | 3.6 (16.6) |
| Hungary | 6.0 (15.4) | 5.6 (8.9) | 3.2 (36.7) | 5.8 (12.2) |
| Lithuania | 4.6 (0.0) | 6.3 (35.0) | 5.0 (12.5) | 5.5 (17.5) |
| Malta | 0.0 (0.0) | 2.6 (20.0) | 0.0 (0.0) | 1.3 (10.0) |
| Poland | 5.9 (12.1) | 5.4 (13.8) | 4.6 (10.5) | 5.7 (12.9) |
| Portugal | 8.7 (12.8) | 8.4 (27.2) | 5.9 (22.0) | 8.5 (20.0) |
| Slovakia | 3.7 (6.7) | 3.0 (5.0) | 1.5 (75.0) | 3.3 (5.8) |
| Slovenia | 6.2 (0.0) | 5.5 (0.0) | 4.0 (0.0) | 5.9 (0.0) |
| Spain | 7.2 (24.4) | 8.0 (33.0) | 8.2 (35.7) | 7.6 (28.7) |
| Total | 6.1 (16.8) | 6.1 (22.9) | 5.5 (24.6) | 6.1 (19.9) |
| High GDP | | | | |
| Austria | 6.2 (24.6) | 8.3 (35.8) | 5.8 (39.6) | 7.2 (30.2) |
| Denmark | 7.0 (38.9) | 7.7 (45.4) | 4.8 (32.1) | 7.4 (42.2) |
| Finland | 8.7 (6.5) | 10.3 (21.7) | 9.6 (35.9) | 9.5 (14.1) |
| France | 6.3 (25.7) | 7.0 (22.3) | 6.0 (11.4) | 6.6 (24.0) |
| Germany | 4.5 (23.5) | 4.5 (19.4) | 3.3 (18.9) | 4.5 (21.4) |
| Iceland | 7.5 (20.0) | 2.5 (0.0) | 6.1 (0.0) | 5.0 (10.0) |
| Norway | 8.8 (33.6) | 7.3 (69.0) | 8.5 (30.7) | 8.0 (51.3) |
| Sweden | 10.3 (34.1) | 8.7 (28.5) | 8.2 (41.9) | 9.5 (31.3) |
| The Netherlands[c] | 7.6 (34.6) | 6.5 (46.3) | 4.7 (38.5) | 7.0 (40.5) |
| UK | 8.6 (30.9) | 8.0 (25.6) | 7.5 (25.0) | 8.3 (28.3) |
| Total[b] | 7.6 (29.2) | 7.5 (28.0) | 6.7 (23.3) | 7.6 (28.6) |
| Total overall[b] | 4.9 (22.8) | 5.1 (24.2) | 5.6 (22.7) | 5.0 (23.5) |

[a]Data from Russia are not included in the period of 2020–21.
[b]Data from the German transplantation registry are not based on all the transplantation centres in the country. The incidence in Türkiye is an underestimation of the true incidence. Therefore Germany and Türkiye were excluded from the overall estimates.
[c]In The Netherlands, there was (almost) no underreporting of (pre-emptive) KT in 2010–16, but some underreporting exists for overall KT in 2017–19 (ranging from 14% to 32%) and for pre-emptive KT in 2017–2021 (ranging from 25% to 43%).

## Trends in KT

Similar to the USA and Australia [17, 20], European rates of paediatric KT have been stable over the last decade, with approximately one-third of children with kidney failure still on dialysis in 2019 [5, 21]. To identify the reasons for the stable KT rates in Europe it is important to investigate why a proportion of patients did not receive a kidney transplant and whether these reasons vary by GDP group. It is possible that KT needs were already met in middle- and high-GDP countries while low-GDP countries were catching up. Additionally, possibilities to increase pre-emptive KT should be investigated. Most of the dialysis patients included in the ESPN/ERA Registry who did not receive a kidney transplant during the study period were on KRT for <1 year. Thus it is likely that at least part of these patients are on the waiting list for KT; unfortunately these data are not fully reported to the ESPN/ERA Registry. Additionally, most children receiving long-term dialysis appear to be more complex cases with severe comorbidities, or small children, making KT difficult. Some children may also be highly sensitised due to previous transplantations or blood transfusions [9, 22–25].

In addition, stable paediatric KT rates may be partly explained by the absence of major changes in paediatric waitlist priority during our study period. Although it is difficult to be certain because of the wide variation in transplantation policies between countries, most well-resourced countries seem to have established policies prioritizing paediatric KT candidates <18 years of age, whereas information on these policies in low-GDP countries is scarce [1, 26]. In fact, despite the overall stable




Abbreviations: APC, annual percentage change; CI, confidence interval; GDP, gross domestic product; AL, Albania; AT, Austria; BG, Bulgaria; BY, Belarus; CZ, Czech Republic; DE, Germany; DK, Denmark; EE, Estonia; ES, Spain; FI, Finland; FR, France; GR, Greece; HR, Croatia; HU, Hungary; IS, Iceland; LT, Lithuania; MK, North Macedonia; MT, Malta; NL, Netherlands; NO, Norway; PL, Poland; PT, Portugal; RO, Romania; RS, Serbia; RU, Russia; SE, Sweden; SI, Slovenia; SK, Slovakia; TR, Turkey; UA, Ukraine; UK, United Kingdom.
The total number of kidney transplants performed between 2010 and 2021 were very low (<10) for EE, MT, and IS, this may lead to very steep differences per period.
Data from the German transplantation registry are not based on all the transplantation centers in the country. The incidence in Turkey is an underestimation of the true incidence. Therefore, Germany and Turkey were excluded from the incidence calculations overall and per GDP group.

**Figure 1:** Average kidney transplantation rate (pmarp) in 0-17 year-olds overall, by GDP, and by country, in the periods of 2010-2014, 2015-2019 and 2020-2021. Annual trends were calculated by the APC (95% CI).

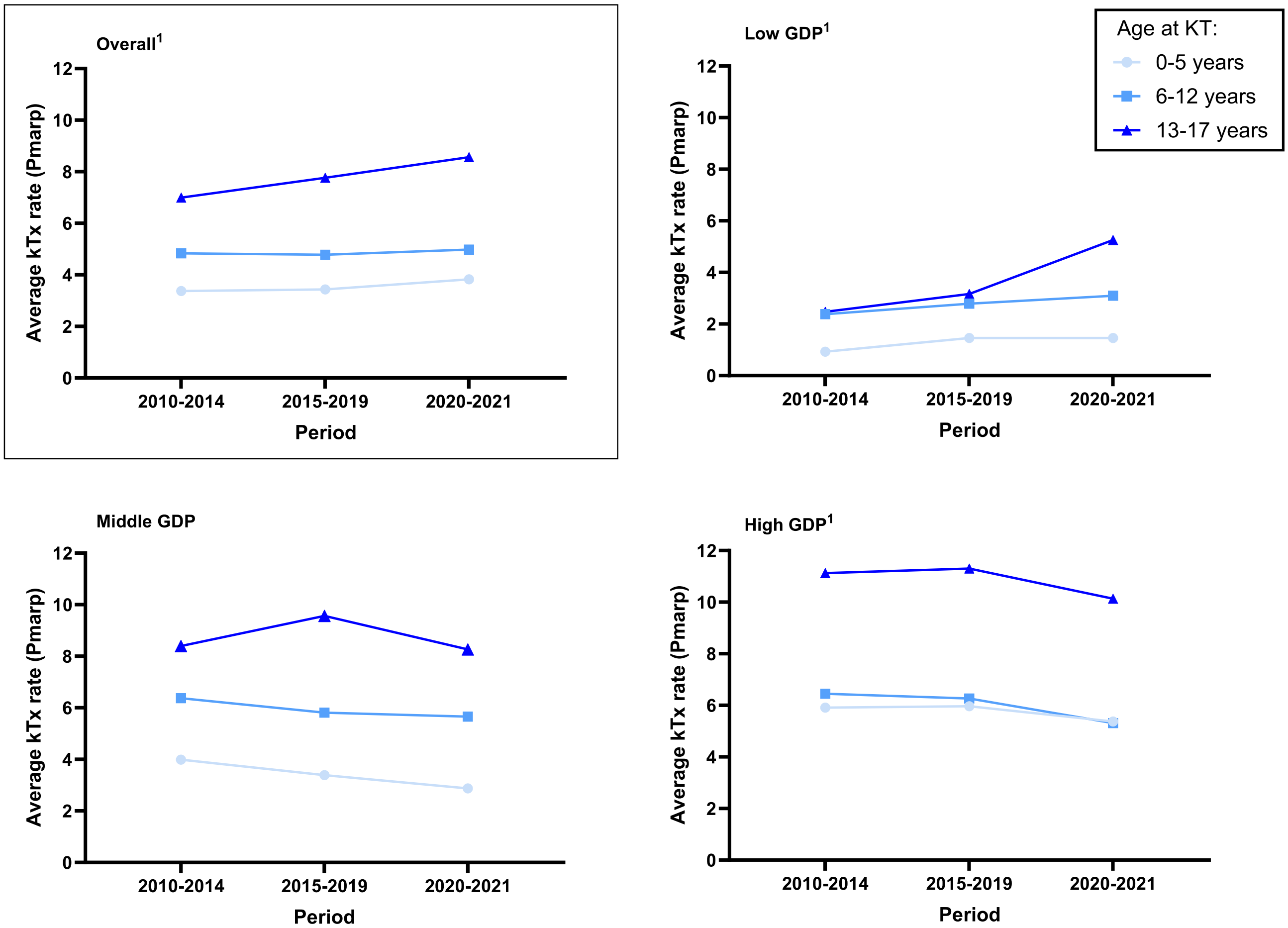
KT rates, there were significant differences between GDP levels. These disparities may be due to economic and sociocultural aspects, differences in evaluation processes for KT and differences in organ availability in each country [1, 27]. Also, organ donation rates might have impacted trends in paediatric KT rates in each GDP group. Additionally, religious and cultural beliefs, more prominent in some regions, may also represent a barrier for paediatric KT [28]. Despite the lowest paediatric KT rates, only in low-GDP countries was there an increase over time. Still, between 2010 and 2019, on average less than half of the prevalent paediatric KRT patients in low-GDP countries had a functioning kidney transplant by the end of the year, whereas in the middle-/high-GDP groups this proportion was >70%. These results are consistent with previous findings describing disparities in KRT provision, particularly in the likelihood of receiving a kidney transplant according to country income [5, 29]. We believe that countries, particularly the ones with lower KT rates, would benefit from informed discussions on successful models to further prioritize paediatric candidates on organ donation waitlists, to continue promoting living donation and further increase deceased donor organ availability and consequently improve (pre-emptive) KT rates.

## Trends in KT by patient subgroup

### Age at KT, sex, PRD and donor type

The overall trends in KT rates by age at KT, sex and PRD were stable. Yet in the low-GDP group, KT rates increased significantly in males (with a similar non-significant trend in females) and in very young children. Younger patients potentially benefit most from timely KT, with better growth potential and the greatest gain in years of life [26, 30]. Young children have a narrow window of opportunity for KT before suffering lifelong consequences, yet they may remain on dialysis due to allocation (organ size limitations) and medical challenges (high level of medical expertise required) [23, 26]. The KRT incidence in 0- to 5-year-olds in Europe has remained stable over the last decade [8], so the increase in KT rates in very young children in low-GDP countries suggests a catch-up in KT access and care in this group.

In the high-GDP group, there was an increase in the number of KTRs diagnosed with cystic kidney disease and a decrease in patients with PRDs classified as 'other'. These changes may have various causes, such as improvements in diagnostic capacity (i.e. genetic testing) and in the availability of advanced care [31, 32]. Moreover, the rate of living donor KT increased, especially in low-GDP countries, and the rate of deceased donor KT remained stable. It appears that country efforts were successful in increasing living donor paediatric KT rates, particularly in low-GDP countries. Whereas in adults the increase in KT rates between 2010 and 2018 was mostly attributed to deceased donor kidney transplants, it is likely that this increase was mostly due to older donors and recipients [33, 34]. Policies that allowed for the increase in deceased donor KT rates in adults may not have impacted KT rates in children due to lower-quality kidneys, which are considered unsuitable for children [35]. Still, compared with adults, a larger




Abbreviations: KT, kidney transplantation.
Data from Russia are not included in the period of 2020-21.
[1]Data from the German transplantation registry are not based on all the transplantation centers in the country. The incidence in Turkey is an underestimation of the true incidence. Therefore, Germany and Turkey were excluded from the overall incidence. UK data does not include Scottish patients.

**Figure 2:** Kidney transplantation rate (pmarp) in 0-17 year-olds overall and per GDP, stratified by age at kidney transplantation in 2010-2014, 2015-2019 and 2020-2021.

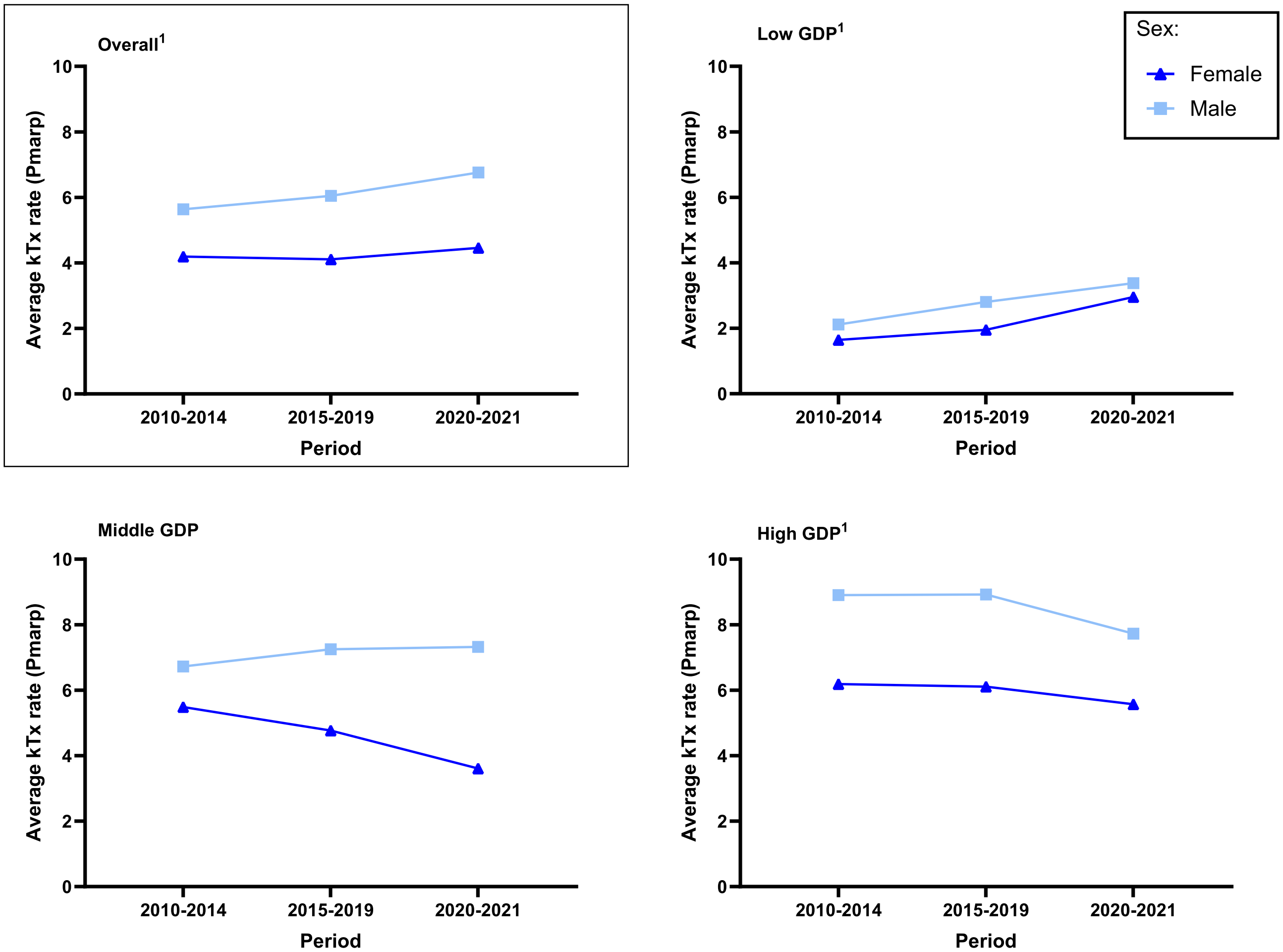
proportion of paediatric KRT patients have received a kidney transplant [8, 34].

## Growth, BMI, anaemia and hyperparathyroidism

The proportion of patients with short stature in the first year post-transplant decreased slightly over time, which is a positive result, as short stature is generally associated with worse prognosis and quality of care [10, 36]. A higher proportion of short stature was observed in the low-GDP group. A previous ESPN/ERA Registry study suggested limited reimbursement for recombinant human growth hormone in some low-income countries that may have contributed to this result [37]. Steroid use may also have impacted growth and body composition of paediatric KRT patients; unfortunately, limited data on these treatments are reported to the ESPN/ERA Registry, hence we were unable to study this in detail [37]. The proportion of anaemia, which has been associated with poorer graft and patient outcomes [11], seemed to increase, possibly due to a decrease in the use of erythropoietin-stimulating agents (ESAs) [38]. Previous studies have also shown that more challenging patients, including those with comorbidities, have recently been accepted for KT, particularly in high-GDP countries, which may account for the higher rates of anaemia, hypertension and overweight in the high-GDP group [9].

## COVID-19 period (2020–21)

The COVID-19 pandemic did not have a significant impact on paediatric KT rates in our study population, whereas in adults there was a decrease of ≈20% in 2020 compared with 2017–19 [39]. This discrepancy may be due to the suspension of adult KT in many European countries, from which paediatric patients were generally excluded [39]. Nevertheless, there were slight (yet non-significant) decreases in KT rates in middle- and high-GDP countries, particularly in adolescents (ages 13–17 years) and in KTs from deceased donors. Yet low-GDP countries seemed less affected. Although exact reasons for this remain unclear, the larger proportion of living donor KTs in low-GDP countries could have contributed to this result. Similar to adults, the decrease in deceased donor organs may be a consequence of limited access to intensive care units for organ preservation, lower donor availability due to fewer road traffic accidents and rejection of COVID-19-positive donors [39]. The larger proportion of living donors




Data from Russia are not included in the period of 2020-21.
[1]Data from the German transplantation registry are not based on all the transplantation centers in the country. The incidence in Turkey is an underestimation of the true incidence. Therefore, Germany and Turkey were excluded from the overall incidence. UK data does not include Scottish patients.

**Figure 3:** Kidney transplantation rate (pmarp) in 0-17 year-olds overall and per GDP, stratified by sex in 2010-2014, 2015-2019 and 2020-2021.

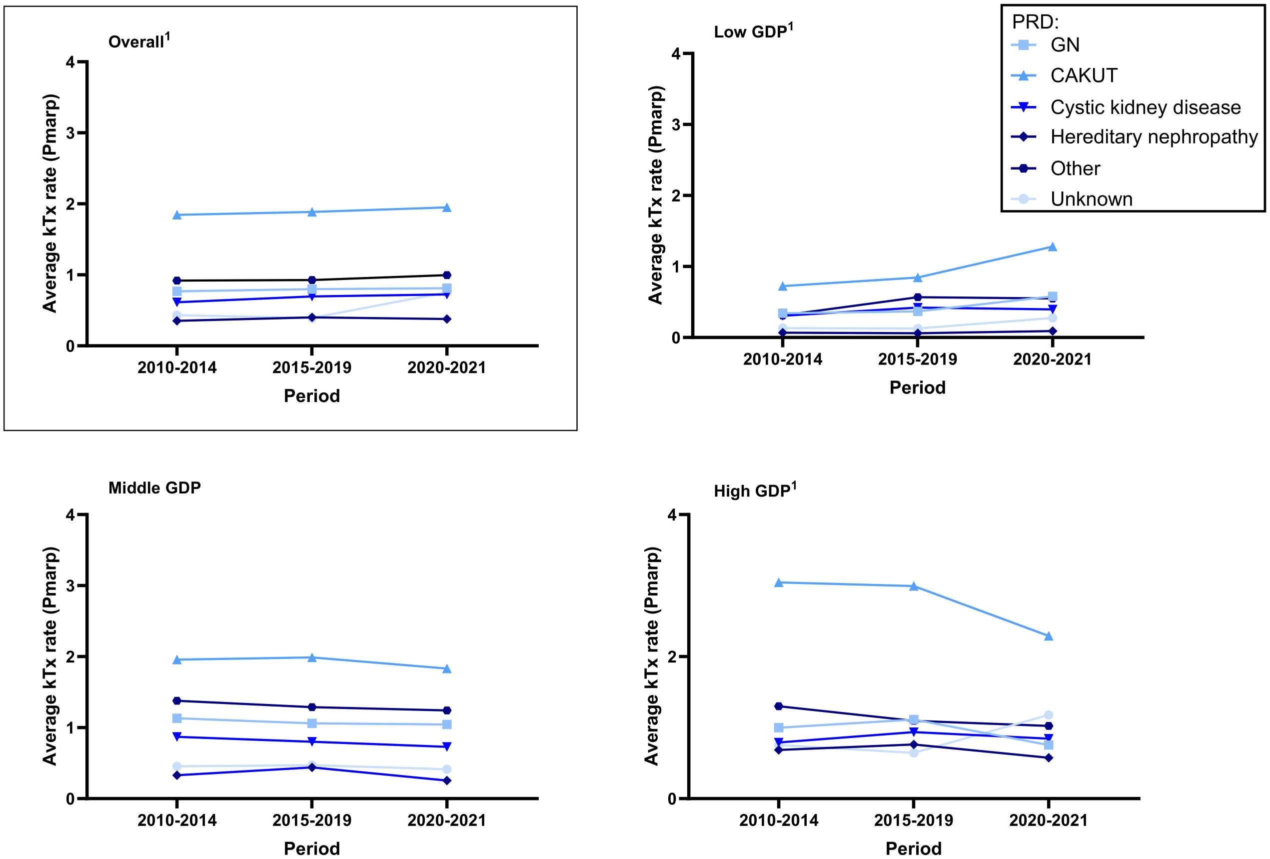
among children may explain the limited impact of the COVID-19 pandemic in paediatric KT rates. There were also fewer pre-emptive KTs, particularly in high-GDP countries. Although waiting times for KT were longer, this did not affect the overall number of paediatric KTs.

### Strengths and limitations

This study provides an overview of trends in paediatric KT over the last decade covering most European countries and including the COVID-19 period. However, some limitations should be considered when interpreting our findings. The ESPN/ERA Registry typically has 100% coverage of the general population in the participating countries, however (pre-emptive) KT numbers are somewhat underestimated in The Netherlands, particularly since 2017. It was difficult to report trends at the country level due to the small number of patients, so we grouped countries according to GDP level, but there may be differences between countries within GDP groups. Additionally, we do not have full knowledge of all KT policies in every country, so we can only hypothesise about reasons for our findings. Furthermore, the ESPN/ERA Registry collects limited data on waitlist registration, use of growth hormone, immunosuppressive drugs and ESAs. Lastly, data on comorbidities and clinical variables were only available for a subset of patients, yet the characteristics of patients for whom data were available did not differ from all patients included in the study.

## CONCLUSION

In Europe, overall paediatric KT rates and pre-emptive KT rates have remained stable over the last decade. There were significant differences between GDP groups. Although KT rates were lowest in low-GDP countries, an increase over time was observed, particularly in very young children and kidneys from living donors, suggesting improvements in KT care. Only the middle-GDP group showed an increase in pre-emptive KT rates. Additionally, the COVID-19 pandemic did not seem to impact paediatric KT rates. Given the benefits of KT in paediatric patients, particularly of pre-emptive KT, it is important to identify the reasons for the stable rates, with the aim of promoting equitable access and optimizing long-term outcomes for children in need of KRT. Our findings may help identify areas for improvement or successful




Abbreviations: PRD, primary renal diagnosis; GN, glomerulonephritis; CAKUT, congenital anomalies of the kidney and urinary tract.
The PRD category "other" includes ischaemic kidney failure, haemolytic uremic syndrome, metabolic diseases, vasculitis, miscellaneous and others.
Data from Russia are not included in the period of 2020-21.
[1]Data from the German transplantation registry are not based on all the transplantation centers in the country. The incidence in Turkey is an underestimation of the true incidence. Therefore, Germany and Turkey were excluded from the overall incidence. UK data does not include Scotish patients.

**Figure 4:** Kidney transplantation rate (pmarp) in 0-17 year-olds overall and per GDP, stratified by PRD in 2010-2014, 2015-2019 and 2020-2021.

**Table 4: Clinical variables of paediatric KTRs overall and stratified by period of KT.**

| | Period of kidney transplantation | | | |
|---|---|---|---|---|
| Clinical variables[a] | 2010–19 | 2010–14 | 2015–19 | 2020–21[b] |
| Hypertension, % (95% CI) | $n = 2553$<br>33.1 (31.6–34.7) | $n = 1254$<br>34.3 (32.1–36.6) | $n = 1300$<br>32.1 (30.0–34.3) | $n = 406$<br>31.5 (27.7–35.6) |
| Short stature, % (95% CI) | $n = 3496$<br>43.1 (41.6–44.7) | $n = 1706$<br>45.1 (42.8–47.4) | $n = 1795$<br>41.2 (39.1–43.4) | $n = 454$<br>35.4 (31.2–39.7) |
| Overweight, % (95% CI) | $n = 3490$<br>32.8 (31.2–34.5) | $n = 1704$<br>33.9 (31.5–36.3) | $n = 1791$<br>32.0 (29.7–34.3) | $n = 454$<br>31.8 (27.7–36.3) |
| Anaemia, % (95% CI) | $n = 2807$<br>16.7 (15.6–17.9) | $n = 1400$<br>14.5 (13.1–16.0) | $n = 1407$<br>18.5 (17.0–20.3) | $n = 457$<br>16.9 (14.2–20.0) |
| Hyperparathyroidism, % (95% CI) | $n = 1267$<br>53.1 (50.5–55.6) | $n = 615$<br>50.3 (46.6–54.0) | $n = 652$<br>55.8 (52.3–59.3) | $n = 228$<br>55.4 (48.7–61.8) |

[a]Generalized estimating equation models were used to correct for correlations of multiple measurements within the same patient.
[b]Data from Russia are not included in the period of 2020–21.
Definitions of each clinical variable are provided in Supplementary Table S2.

**Table 5: Clinical variables of paediatric KTRs stratified by GDP group between 2010 and 2019.**

| | GDP group | | |
|---|---|---|---|
| Clinical variables[a] | Low | Middle | High |
| Hypertension, % (95% CI) | $n = 246$<br>28.9 (24.6–33.7) | $n = 1032$<br>29.4 (26.8–32.2) | $n = 1275$<br>35.5 (33.5–37.6) |
| Short stature, % (95% CI) | $n = 817$<br>54.3 (51.0–57.7) | $n = 1116$<br>37.8 (35.1–40.7) | $n = 1563$<br>41.3 (39.0–43.6) |
| Overweight, % (95% CI) | $n = 816$<br>29.3 (25.9–32.9) | $n = 1116$<br>29.8 (27.1–32.6) | $n = 1558$<br>35.2 (32.8–37.7) |
| Anaemia, % (95% CI) | $n = 313$<br>10.2 (7.9–13.0) | $n = 823$<br>11.9 (10.0–14.1) | $n = 1671$<br>18.4 (17.0–19.8) |
| Hyperparathyroidism, % (95% CI) | $n = 153$<br>52.6 (45.8–59.3) | $n = 648$<br>53.8 (50.2–57.3) | $n = 466$<br>52.7 (48.7–56.6) |

[a]Generalized estimating equation models were used to correct for correlations of multiple measurements within the same patient.
Definitions of each clinical variable are provided in Supplementary Table S2.

strategies to further optimize access to paediatric KT across regions. Countries may obtain insights from one another on successful measures for increasing transplantation rates.

## SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.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## AUTHORS' CONTRIBUTIONS

I.R.M.d.S., M.B., V.S.S. and K.J.J. were responsible for the conceptualization, methodology and writing the original draft. I.R.M.d.S. performed the formal analysis. I.R.M.d.S., M.B., V.S.S., K.J.J., A.C.G., A.J., B.S., B.T., C.P., D.S., V.A., G.R., G.N., G.M.-K., I.Z., J.S., J.H., K.V., L.R., L.P, M.S.M., M.A.G.J.t.D., N.A.-E., O.D., S.B., S.A.B., S.S.S., S.P.F., T.J., T.L., V.E. and W.M. contributed to the review and editing. All authors read and approved the final manuscript.

## DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared with any third party because the national and regional registries that provided data to the ESPN/ERA Registry remain the owners of the data.

## CONFLICT OF INTEREST STATEMENT

G.N. reports speaker fees from Baxter. J.H. reports consulting fees from Alnylam and Rhythm Parmaceuticals; speaker fees from Recordati rare disease; and travel support from Hansa Pharma. N.A.-E. reports speaker fees/travel support from Genesis Pharma and Swixx BioPharma. S.S.S. reports consulting fees from Novo Nordisk; Travel support from and board membership of Amicus. S.P.F. reports board membership of the Ukrainian Association of Nephrologists and Kidney Transplant Specialists. T.L. reports board membership of Scandiatransplant. V.E. reports board membership of the Swedish Orphan Biovitrum. K.J.J. reports research funding to the Institution from ESPN and ERA. V.S.S. reports research funding to the Institution from ERA. The remaining authors declare that they have no conflicts of interest.

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