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Access to kidney transplantation and re-transplantation from childhood to adulthood: long-term data from the ERA Registry

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ABSTRACT

Background and hypothesis. Knowledge regarding access to first kidney transplantation (KT) and subsequent KT in patients commencing kidney replacement therapy (KRT) in childhood is limited.

Methods. Using European Renal Association (ERA) Registry data, we investigated European patients who started KRT below 20 years of age between 1978 and 2019. Access and determinants to first, second, and third KT were assessed using multivariable Cox regression.

Results. Totals of 12 623, 4077, and 1186 patients were included while awaiting first, second, and third KT, at median ages of 13.8 (IQR: 7.5–17.4), 20.9 (IQR: 16.5–26.1), and 26.6 (IQR: 20.3–32.8) years, respectively. During the study period, overall access was 87.8%, 72.7%, and 60.5% for first, second, and third KT, respectively, and median time to each KT was 0.9 (IQR: 0.2–2.1), 1.9 (0.6–4.5), and 2.6 (IQR: 1.0–5.3) years. Younger age at KRT initiation (aHR 0-4 vs. 10–14 years: 0.54; 95%CI: 0.51–0.57) and female sex (HR: 0.94; 95%CI: 0.90–0.98) were

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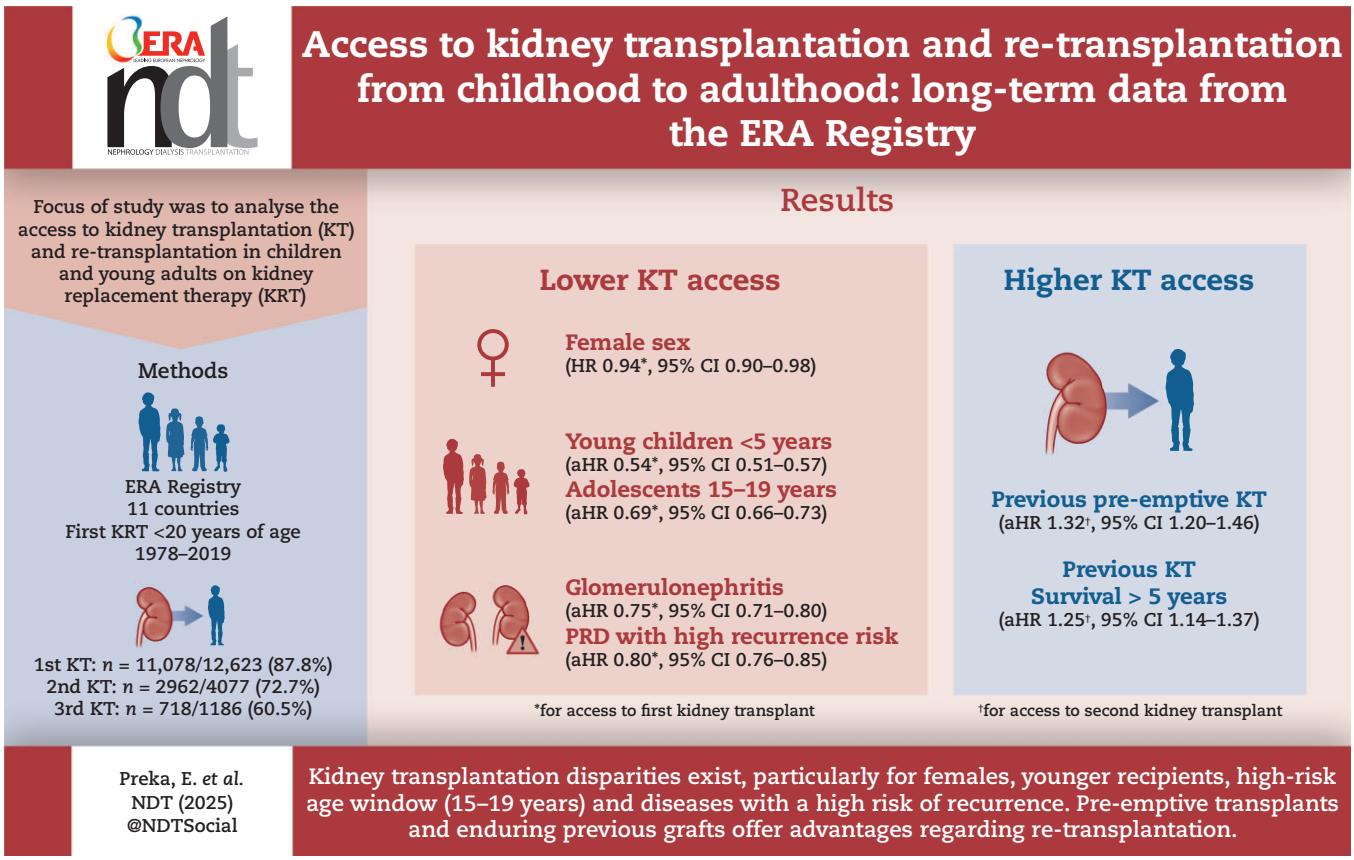
associated with lower access to first KT. KT candidates between 15 and 19 years had lower access to first and second KT (aHR: 0.69; 95%CI: 0.66–0.73, and aHR: 0.70; 95%CI: 0.61–0.81) compared to 10–14 year-olds. Compared to CAKUT, glomerulonephritis patients had lower access to KT (aHR: 0.75; 95%CI: 0.71–0.80 for first, aHR: 0.89; 95%CI: 0.81–0.98 for second, and aHR: 0.80; 95%CI: 0.66–0.97 for third KT). Similarly, patients with primary renal diseases with high risk of recurrence, had lower chances of receiving a first and second KT (aHR: 0.80; 95%CI: 0.76–0.85 for first, aHR: 0.86; 95%CI: 0.78–0.95 for second KT). Access to re-transplantation was also higher with previous pre-emptive KT and previous graft survival exceeding 5 years.

Conclusion. Our study highlights KT access disparities particularly for females, the youngest recipients, high-risk age (15–19 years), and diseases with recurrence risk. Notably, pre-emptive transplants and enduring previous grafts offer advantages regarding re-transplantation.

Keywords: epidemiology, high-risk age window, kidney transplantation, paediatric, re-transplantation

GRAPHICAL ABSTRACT



KEY LEARNING POINTS

What was known:

- A recent increase in paediatric patients awaiting kidney transplants, along with extended waiting periods, has been observed.
- Access to first kidney transplantation (KT) varies by age and sex, with longer waiting times for adolescents and women.
- There is limited European data on re-transplantation in children.

This study adds:

- Adolescents (15–19 years) have lower access to first and second KT compared to younger children, whereas access to first KT was lower for the youngest patients (0–4 years).
- Females have lower access to first KT, mainly due to fewer pre-emptive transplants.
- Glomerulonephritis and diseases with high recurrence risk decrease transplantation and re-transplantation likelihood.
- Prior pre-emptive transplants and longer-lasting grafts increase re-transplantation likelihood.

Potential impact:

- This study highlights the need for research on improving KT access for specific groups (adolescents, young children, females, and specific diseases).
- The findings emphasize the importance of promoting pre-emptive KT.
- Understanding sex disparities in KT access is crucial for improving equity in paediatric kidney transplantation.

INTRODUCTION

Kidney transplantation (KT) and re-transplantation significantly enhance survival and quality of life for paediatric patients with kidney failure, as opposed to remaining on dialysis [1–3]. Nevertheless, a recent rise in paediatric patients awaiting transplantation and prolonged waiting times have been observed [3–5].

With more children on kidney replacement therapy (KRT) reaching adulthood [6], repeat KT becomes common. US Scientific Registry of Transplant Recipients data revealed that 20%–25% of the paediatric waitlists comprise children with previous kidney transplants, and over half undergo re-transplantation [7]. Optimizing access, longevity, and outcomes in children requiring KRT is imperative.

European and US data showed that access to first KT for children and adolescents varies by age [8] with kidney graft loss being significantly greater during late adolescence and early adulthood (17–24 years) due to socio-behavioural and biological mechanisms, termed the 'high-risk age window' [7]. Females present a 23% lower likelihood of receiving a pre-emptive first KT than males [9]. Disparities also exist among ethnic minorities [5, 10] and countries with different income levels [11].

While USA data offer insights into re-transplantation post-initial KT [12–15], European data remain sparse. To address this gap, we examined European paediatric KT candidates' profiles, their access to and factors associated with first, second, and third KTs, with follow-up from childhood into adulthood, using data from the European Renal Association (ERA) Registry.

MATERIALS AND METHODS

Data source and study population

Patient data were derived from the ERA Registry, a population-based registry collecting data on KRT patients in Europe [3]. The current study included data from countries that contributed with individual patient data: Austria, Denmark, Finland, France, Greece, Iceland, the Netherlands, Norway, Spain (Andalusia, Aragon, Asturias, Basque Country, Catalonia, Extremadura, Galicia, Community of Madrid, and Valencia region), Sweden, and UK (Supplementary Table 1).

Data were collected from these 11 countries for all patients with kidney failure initiating KRT before the age of 20 years between 1978 and 2019. Patients were followed from KRT initiation until receiving their first KT, from first KT failure until receiving their second KT and from second KT failure until receiving their third KT, or until death, loss to follow-up (LFU) or end of study (31 December 2019) (Fig. 1). All patients were included, regardless of the allocation system in place (Supplementary Table 2), whether they were on the paediatric priority waiting list or not. Inclusion was completed before the onset of the COVID-19 era to mitigate potential bias in the results due to the pandemic.

Country, age, sex, primary renal disease (PRD), donor type, cause of death and events, including changes in KRT modalities, death, and LFU were reported to the Registry. PRDs were categorized following the ERA coding system adapted for children [3]. Based on literature [16], patients with high risk of disease recurrence and subsequent risk for graft loss were identified based on their PRD, including idiopathic focal and segmental glomerulosclerosis (FSGS), haemolytic uremic syndrome (HUS), and membranoproliferative glomerulonephritis (MPGN) Type I and II (dense deposit disease), labelled as C3 glomerulopathy with changing terminology over time, together with kidney diseases with a high risk of disease recurrence but lower risk of graft loss, namely IgA nephropathy, Henoch–Schönlein Purpura (HSP/IgA vasculitis), and systemic lupus erythematosus (SLE). All other PRDs were grouped as non-recurrent.

The study focused on analysing characteristics of candidates for first, second, and third KT, emphasizing factors affecting access to KT and re-transplantation. Access to KT is defined as receiving a KT either pre-emptively or following dialysis. A patient who presented native or allograft kidney failure was automatically considered a KT candidate, recognizing that waiting list data are unavailable in the ERA Registry. For all analyses, the waiting time was defined as the period from kidney failure (native or allograft) until the patient received the transplant. Pre-emptive kidney transplants, including cases without dialysis time between graft failures, were considered to have no waiting time. The waiting time was censored if the patient died, was lost to follow-up, or reached the end of the study period.

Following previous Registry studies [8] and recognizing a non-linear relationship between patient age and outcomes, patients were divided into clinically relevant age groups: 0–4, 5–9, 10–14, 15–19, 20–24, and >25 years. Additionally, acknowledging differ-

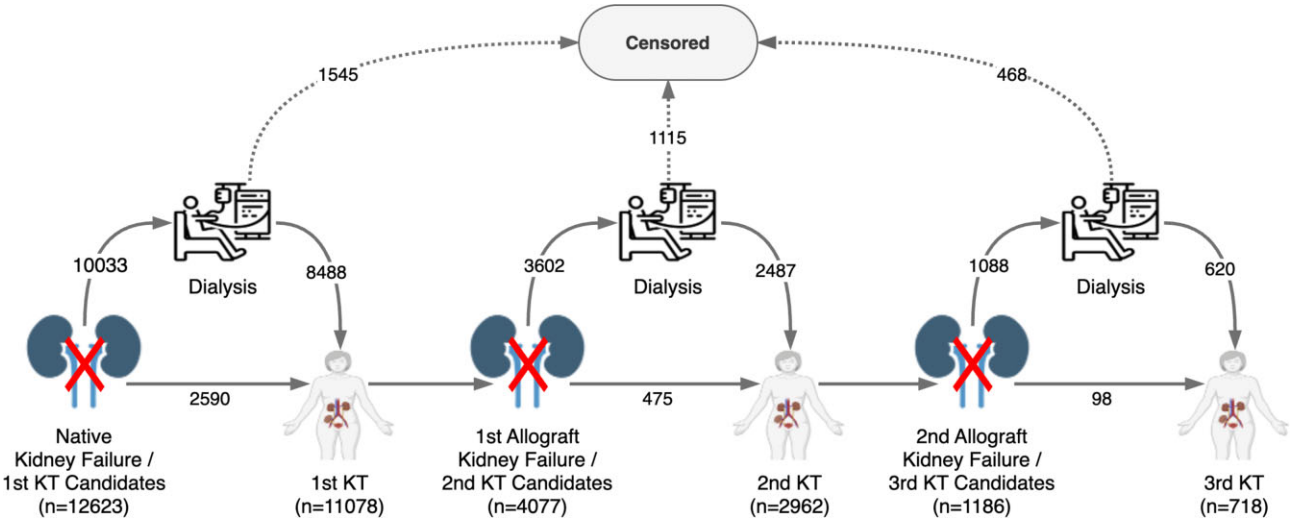


Figure 1: A patient's journey from initial KT candidacy until last follow-up. Note that the censoring criteria were death, loss to follow-up, and end of study.

ent immunosuppressive regimens (no tacrolimus use before 2000) and aiming for similar sample sizes, we divided the era of kidney failure/transplantation into the following categories: 1978–1999, 2000–2009, and 2010–2019.

Statistical analyses

Cox regression models assessed (un)adjusted hazard ratios for factors associated with accessing first, second, and third KT. We hypothesized causal pathways based on existing literature and expert opinion [17]. Models were adjusted for country, sex, PRD, era and patient age at kidney failure or at respective KT, and type of previous KT donor, as appropriate following criteria for confounding [17].

We performed an interaction analysis to assess the direct effect of sex on access to KT after accounting for the mediator (PRD), as PRD lies within the causal pathway and is not a confounder.

We primarily analysed initial dialysis modality (intention-to-treat) at the time of native or allograft kidney failure, although some patients used multiple modalities between KTs. To address the effect of modality changes, we conducted a sensitivity analysis involving patients predominantly using a single dialysis modality (>80% of their waiting time) between transplants.

The proportional hazards assumption was tested for any exposure variable using a proportional hazards test [18]. Wherever assumptions were violated (mainly for access to first KT), we applied robust standard errors. All analyses were conducted using lifelines [19] version 0.27.4 in Python 3.9 and SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Characteristics of KT candidates

During the study period, 12 623 patients initiated KRT before 20 years of age. Among them, 1545 (12%) did not receive a KT during the study period (until LFU, end of study or death). Median ages at the beginning of first, second, and third KT candidacy were 13.8 (IQR: 7.5–17.4), 20.9 (IQR: 16.5–26.1), and 26.6 (IQR: 20.3–32.8) years, respectively. After median waiting times of 0.9 (IQR: 0.2–2.1), 1.9 (0.6–4.5), and 2.6 (1.0–5.3) years, 11 078 (87.8%) received a first KT, 2962 (72.7%) received a second KT, and 718 (60.5%) received a third KT [Table 1].

The most frequent diagnosis was CAKUT (34%), followed by glomerulonephritis (GN; 19%). PRDs with recurrence risk were present in 14%, with higher numbers among those waiting for second and third KT (16% and 18%, respectively).

Most KT candidates received mainly HD (48%, 69%, and 79% for first, second, and third KT candidates, respectively), and their median time on dialysis [HD or peritoneal dialysis (PD)] awaiting KT was 1.3 (0.6–2.5), 2.4 (1.0–5.1), and 2.9 (1.4–5.7) years for first, second, and third KT candidates, respectively.

Pre-emptive KT was performed in 20.5% of first, 11.7% of second, and 8.3% of third KT recipients. Most first and second KT grafts were still functioning beyond 5 years (Table 1).

Access to kidney (re)transplantation in patient subgroups

Age at kidney failure

Early childhood (0–4 years) KT candidates were less likely to receive their first KT than those at 10–14 years (aHR 0.54; 95%CI 0.51–0.57) but had similar chances of second and third KT after graft failure. Candidates with kidney failure between 15 and 19 years had lower likelihoods of receiving their first (aHR 0.69; 95%CI 0.66–0.73) and second KT (aHR 0.70; 95%CI 0.61–0.81). Patients with first graft failure in early adulthood (>20 years old) also had less chance of receiving their second KT compared to 10–14-year-olds [Fig. 2a]. However, when analysing the effect of age at native or allograft kidney failure on KT access by donor type, we only observed a reduced access to deceased donor (DD) KT for patients aged 15 years or older, ultimately leading to lower access (data not shown).

A sensitivity analysis within the 0–4-year-old group revealed reduced likelihoods of first KT access for both 0–2 year-olds and 3–4 year-olds compared to the reference group of 10–14 year-olds (Supplementary Table 3).

Sex

Females had a slightly lower likelihood of first KT than males (HR 0.94; 95%CI 0.90–0.98) but not for their second and third KT [Fig. 2b]. Even if the magnitude of this finding was modest with dialysis vintage being alike between the two sexes, the pre-emptive KT rates differed. Notably, median dialysis times were similar [1.25 (0.60–2.52) for females and 1.26 (0.60–2.50) for males], however, among those receiving a first KT, pre-emptive transplantation was performed in 22.9% of male versus 17.2% of female candidates.

Interaction analysis of sex with CAKUT (vs. non-CAKUT) PRD, revealed that patients with CAKUT (irrespective of their sex) had higher changes of getting a KT compared to patients with no CAKUT. Males with CAKUT showed the highest rates of pre-emptive first KT (Supplementary Table 4).

Primary renal disease

Compared to those with CAKUT, patients with GN (aHR 0.75; 95%CI 0.71–0.80), HUS (aHR 0.65; 95%CI 0.57–0.73), ischaemic renal disease (aHR 0.78; 95%CI 0.67–0.92), vasculitis (aHR 0.55; 95%CI 0.50–0.61), and miscellaneous (aHR 0.76; 95%CI 0.70–0.82) or missing diagnosis (aHR 0.75; 95%CI 0.70–0.81) were less likely to receive a first KT. This lower likelihood was also found in GN patients waiting for their second and third KT (aHR 0.89; 95%CI 0.81–0.98 and aHR 0.80; 95%CI 0.66–0.97, respectively), but not for any other PRD group (Fig. 2c).

Patients with PRDs at risk of disease recurrence were less likely to receive a first (aHR 0.80; 95%CI 0.76–0.85) and second KT (aHR 0.86; 95%CI 0.78–0.95). A similar trend was observed for patients awaiting their third KT (aHR 0.85; 95%CI 0.70–1.04) (Fig. 2c).

Kidney replacement therapy characteristics

Pre-emptive previous KT was associated with an increased likelihood of receiving a second (aHR 1.23; 95%CI 1.20–1.46) and third (aHR 1.31; 95%CI 1.05–1.65) KT (Table 2). Candidates of whom the previous graft failed after >5 years had higher access to a second and third KT (aHR 1.25; 95%CI 1.14–1.37 and aHR 1.22; 95%CI 1.02–1.47, respectively) compared to those for which the graft failed between 1 and 5 years after KT.

Candidates receiving PD as their first modality had higher access to the first and second KT than patients starting on HD. Among candidates who received only one dialysis modality before KT (72.7%, 82.3%, and 84.6% for the first, second, and third KT, respectively), PD patients were more likely to receive a first and second KT (aHR 1.19; 95%CI 1.13–1.26, aHR 1.66; 95%CI 1.50–1.85, respectively) (Table 2).

There was no difference in access to subsequent KT according to previous donation type (living vs. deceased) (Table 2). However, when analysing LD and DD cohorts separately, access to second

Table 1: KT candidates' baseline characteristics.

	Candidates for a first KT (*n* = 12 623) N (%)	Candidates for a second KT (*n* = 4077) N (%)	Candidates for a third KT (*n* = 1186) N (%)
Age at kidney failure [(median (IQR), (years)][a]	13.8 (7.5–17.4)	20.9 (16.5–26.1)	26.6 (20.3–32.8)
0–4 years	2378 (18.8)	155 (3.8)	7 (0.6)
5–9 years	1809 (14.3)	223 (5.5)	39 (3.3)
10–14 years	3091 (24.5)	426 (10.4)	70 (5.9)
15–19 years	5345 (42.3)	1022 (25.1)	164 (3.8)
20–24 years	N/A	1056 (25.9)	242 (0.4)
≥25 years	N/A	1195 (29.3)	664 (56.0)
Males, *n* (%)	7392 (58.6)	2311 (56.7)	665 (56.1)
PRD, *n* (%)			
CAKUT	4290 (34.0)	1488 (36.5)	432 (6.4)
Cystic kidney disease	1053 (8.3)	341 (8.4)	107 (9.0)
GN	2419 (19.2)	992 (24.3)	324 (27.3)
HUS	375 (3.0)	112 (2.7)	36 (3.0)
Hereditary	972 (7.7)	267 (6.5)	63 (5.3)
Ischaemic renal disease (IRD)	196 (1.6)	40 (1.0)	11 (0.9)
Metabolic	319 (2.5)	111 (2.7)	27 (2.3)
Miscellaneous	983 (7.8)	248 (6.1)	63 (5.3)
Vasculitis	405 (3.2)	141 (3.5)	40 (3.4)
Unknown/missing	1611 (12.8)	337 (8.3)	83 (7.0)
PRD with risk of recurrence[b]	1739 (13.8)	662 (16.2)	216 (18.2)
KRT modality at start of native kidney failure (for 1st KT)/kidney graft failure (for 2nd, 3rd KT), *n* (%)[c]			
HD	6093 (48.3)	2812 (69.0)	941 (79.3)
PD	3940 (31.2)	790 (19.4)	147 (12.4)
Pre-emptive KT	2590 (20.5)	475 (11.7)	98 (8.3)
Dialysis time [(median (IQR), (years)]	1.3 (0.6–2.5)	2.4 (1.0–5.1)	2.9 (1.4–5.7)
Previous pre-emptive KT, *n* (%)	N/A	792 (19.4)	150 (12.6)
Lifespan of previous KT, (%)			
0 up to 3 months	N/A	617 (15.1)	192 (16.2)
≥3 months up to 1 year	N/A	238 (5.8)	85 (7.0)
≥1 up to 5 years	N/A	1074 (26.3)	381 (32.1)
>5 years	N/A	2148 (52.7)	530 (44.7)
Previous LD graft, *n* (%)	N/A	1198 (29.4)	221 (18.6)
Follow-up duration since KRT onset [median (IQR), (years)]	10.9 (4.6–19.1)	19.3 (12.8–26.8)	24.3 (17.7–30.7)
Waiting time with kidney failure before receiving a KT or being censored [median (IQR), years]	0.9 (0.2–2.1)	1.9 (0.6–4.5)	2.6 (1.0–5.3)
Candidates awaiting KT by era of kidney failure, *n* (%)			
1978–1999	3950 (31.3)	1112 (27.3)	284 (23.9)
2000–2009	4032 (31.9)	1194 (29.3)	348 (29.3)
2010–2019	4641 (36.8)	1771 (43.4)	554 (46.7)
Access to KT, *n* (%)	11 078 (87.8)	2962 (72.7)	718 (60.5)

CAKUT; congenital anomalies of the kidneys and the urinary tract, GN; glomerulonephritis.
Results are presented in numbers and percentages for categorical variables and median [IQR] for continuous variables
[a]Kidney failure regarding their native kidneys for candidates of 1st KT and kidney transplant failure for candidates of 2nd and 3rd KT;
[b]PRD with risk of recurrence includes: idiopathic focal and segmental glomerulosclerosis (FSGS), HUS, membranoproliferative glomerulonephritis (MPGN) and mesangiocapillary glomerulonephritis Type I and II (dense deposit disease), together with those kidney diseases with a high risk of disease recurrence but in which the risk of graft loss is expected to be low(er), namely IgA nephropathy, Henoch–Schönlein Purpura (HSP/IgA) and SLE;
[c]Starting dialysis modality includes patients who might have changed dialysis modalities during the same pre-KT period. The patients for whom dialysis modality was documented as unknown in the Registry are not presented here.

and third LD transplants was higher, particularly if their previous graft was from an LD or had lasted >5 years (data not presented).

Last, before 2010 the likelihood of receiving a first KT was significantly lower compared to the more recent era (Supplementary Table 5).

DISCUSSION

Our study provides a 40-year overview of KT patterns in the European paediatric KRT population, investigating the characteristics and access to first KT and re-transplantation.

Our study revealed that patients experiencing kidney failure between 15 and 20 years had lower chances of receiving first and second KT compared to those aged 10–14, consistent with US and European studies, which emphasize the negative impact of the 'high-risk' age window (particularly 17–24 years) on graft failure rates [7, 20–23]. Socio-behavioural traits and biological mechanisms, such as adherence challenges and hyperfiltration injury, may contribute to these disparities [7, 21 24–27]. Moreover, transitioning to adult services not only increases graft failure risk during adaptation [25] but patients also face longer waiting times, given paediatric prioritization (<16 or <18 years) by key European organ-sharing organizations such as Eurotransplant, Scandiatransplant, Agence de Biomédecine, and NHSBT [28, 29]. Conversely, children under five had lower first KT access but improved access to second

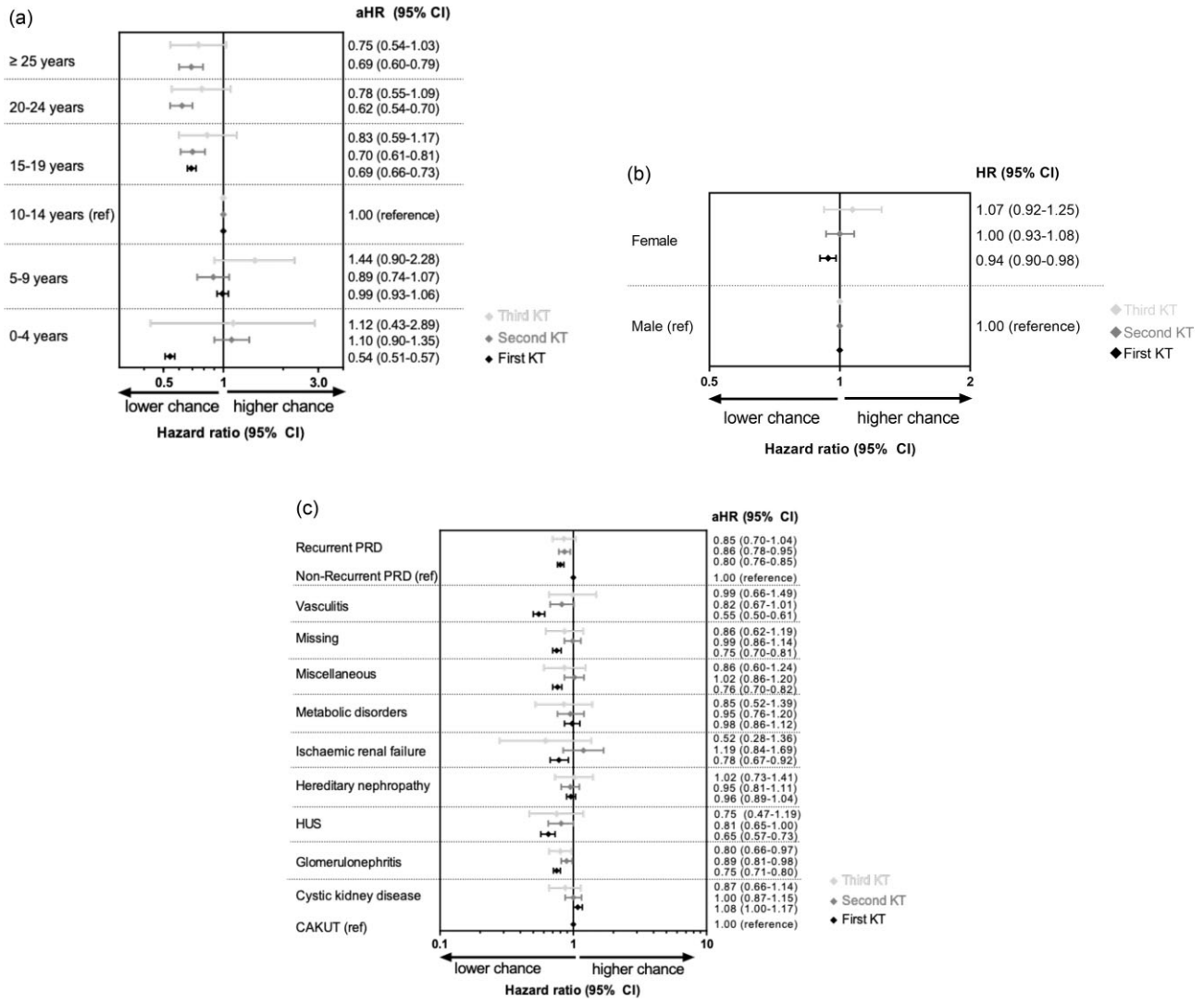


Figure 2: (a) Access to first, second, and third KTs, by age at native kidney failure (for first KT) and kidney graft failure (for second and third KT). *For all KT in our main analysis, 20 years old is considered as the time of transfer to adult services (adjusted for country, sex, PRD, and era of failure). (b) Access to first, second, and third KTs by sex (no adjustments). (c) Access to first, second, and third KTs by PRD (adjusted for: country, sex, age at failure, and era of failure).

transplants, probably as they met size and weight criteria over time.

Consistent with previous European [9] and US [27] findings, our study also showed lower access to first KT for females than for males. Female sex has been associated with lower registration on the transplant waiting list and longer time to be listed [30–33]. Furthermore, previous research has shown a 23% lower rate of pre-emptive KT in females across 35 European countries [9]. However, our data lacked information on the waiting list to explain this disparity fully. Faster eGFR decline in females with glomerular disease may partly contribute [34, 35], but in our study, the main difference was seen in the CAKUT group, suggesting potential non-medical barriers. While previous adult studies showed that women are 10% less likely to receive LD transplants [36], no such difference was observed in our dataset. Non-medical factors, influencing sex disparities in KT access potentially include female perceptions of surgery and immunosuppressive risks, which may lead to non-adherence [7, 30, 37]. Adult findings suggest that physicians recommend transplantation less frequently to females [37, 38], although its relevance to younger patients is unclear. Analysing non-medical and social determinants of KT access is essential to addressing these inequities and improving patients' outcomes.

GN patients had significantly lower access to first, second, and third KTs compared to CAKUT patients. KT access was particularly reduced in those with diseases prone to recurrence, such as FSGS, HUS, vasculitides, and C3 glomerulopathy, which are associated with high graft loss rates [39–41] resulting in a preference for deceased donation [42]. In an ESPN/ERA Registry study [16] among 1955 paediatric patients with PRDs at high risk of recurrence, pre-emptive transplantation was less frequent (52%–80%) than in CAKUT patients. Furthermore, patients with FSGS and SLE were more likely to receive a DD graft compared to CAKUT patients. Identifying genetic causes of recurrence [43–45] may enable more pre-emptive and LD transplants.

We observed a higher likelihood of accessing a first and second KT in patients receiving PD (versus HD) before KT, likely reflecting selection bias towards 'healthier' patients starting PD. Notably, our PD population included more CAKUT (33.1%) and younger patients (53.1% between 0 and 4 and 11% between

Table 2: Hazard ratios for access to KT.

	First transplant candidates		Second transplant candidates		Third transplant candidates	
	Unadjusted HR	**Adjusted HR**	**Unadjusted HR**	**Adjusted HR**	**Unadjusted HR**	**Adjusted HR**
Starting dialysis modality (or first dialysis modality while waiting for the KT)						
HD (ref)	1.00	1.00	1.00	1.00	1.00	1.00
PD	**1.06 (1.01–1.10)**	**1.05 (1.00–1.10)**	**1.31 (1.19–1.43)**	**1.14 (1.03–1.26)**	1.18 (0.94–1.47)	1.04 (0.82–1.32)
Main dialysis modality[a]						
HD (ref)	1.00	1.00	1.00	1.00	1.00	1.00
PD	**1.19 (1.14–1.24)**	**1.19 (1.13–1.26)**	**1.90 (1.72–2.10)**	**1.66 (1.50–1.85)**	**1.55 (1.21–1.99)**	1.29 (0.99–1.68)
Pre-emptive previous KT[b]	N/A	N/A	**1.54 (1.41–1.68)**	**1.32 (1.20–1.46)**	**1.48 (1.20–1.82)**	**1.31 (1.05–1.65)**
Not pre-emptive previous KT (ref.)	N/A	N/A	1.00	1.00	1.00	1.00
Lifespan of previous KT[b]						
0–3 months	N/A	N/A	**1.42 (1.27–1.59)**	**1.30 (1.16–1.46)**	0.96 (0.77–1.20)	0.93 (0.74–1.17)
≥3 months–1 year	N/A	N/A	1.11 (0.95–1.31)	1.05 (0.89–1.24)	0.84 (0.60–1.17)	0.79 (0.56–1.11)
≥1–5 years (ref)	N/A	N/A	1.00	1.00	1.00	1.00
>5 years	N/A	N/A	**1.38 (1.27–1.51)**	**1.25 (1.14–1.37)**	**1.34 (1.13–1.59)**	**1.22 (1.02–1.47)**
Type of previous KT[c]						
LD	N/A	N/A	1.03 (0.95–1.12)	1.06 (0.96–1.16)	1.03 (0.85–1.26)	0.93 (0.75–1.15)
DD (ref.)			1.00	1.00	1.00	1.00

LD; live donor
[a]Adjusted for country, sex, PRD, age at failure, and era at failure. The main dialysis modality group excludes patients with modality changes.
[b]Adjusted for country, sex, PRD, age at previous KT, era of previous KT, and donor type of previous KT
[c]Adjusted for country, sex, PRD, age at previous KT, era of previous KT, and previous pre-emptive KT; only data with known previous donor type (LD or DD) were included in the analysis. In total, 413 (10.1%) of the second and 62 (5.2%) third KT candidates had unknown previous KT type, so these data have been excluded from the analysis.
Values in bold represent statistical significant differences ($P < 0.05$)

5 and 9 years). While our analysis adjusted for PRD and age PD is typically offered to patients with fewer comorbidities and less intensive management needs. Generalizability of our results to lower-income countries may be limited, as 10 out of the 11 participating countries have high macroeconomic levels. Furthermore, young children, who naturally tend to undergo PD more frequently, showed lower KT access rates than children >5 years.

Pre-emptive previous KT was associated with a higher likelihood of receiving second and third KT irrespective of donor type, similar to US findings [13]. As most pre-emptive KTs involve living donors, improved human leucocyte antigen (HLA) matching may play a significant role. Foster *et al.* studied 8433 paediatric patients who received a first DD KT and found that poorer HLA matching in first DD KTs was associated with increased waiting time for the second transplant [46]. In contrast to van Arendonk *et al.*, who reported longer times to second KT in US paediatric recipients after first DD vs. LD graft failure [12], in our study, previous KT donor type did not influence subsequent KT likelihood. However, a recent analysis of US patients found no difference in re-transplant probability based on donor type, despite longer waiting and dialysis times for prior DD recipients [15]. Discrepancies between studies may be attributed to differences in HLA matching policies or sensitization. While advances in desensitization protocols have improved transplantation prospects, carefully considering HLA compatibility remains crucial for optimizing access to subsequent KT [46, 47].

According to a study of organ procurement and transplant network (OPTN) from 1987 to 2009 [14], patients whose first kidney grafts survived over 5 years had significantly better second graft survival compared to those with graft survival between 30 days and 5 years (median second kidney allograft survival 9.4 vs. 5.8 years). We also observed that patients with first and second KTs lasting >5 years were more likely to undergo subsequent transplants, potentially due to hesitancy for retransplanting patients with shorter-lived previous grafts.

Our findings may have significant implications for European healthcare policy. Addressing age-related disparities requires tailored transitional care programmes to support adolescents during their shift to adult services. Promoting pre-emptive KT, particularly for females and high-risk groups, through standardized evaluation processes and targeted education could enhance equity. Additionally, prioritizing research into recurrent conditions and integrating precision medicine approaches could optimize transplant strategies for high-risk patients. Harmonizing allocation policies across European countries could further enhance equitable access and outcomes.

Our study comprises a large European cohort investigating long-term data on KT and re-transplantation in patients starting KRT in childhood. Limitations include missing data on waiting list registration (criteria, timing), and on clinical and non-clinical characteristics, including weight, BMI, race/ethnicity, socioeconomic data, and sensitization. However, a US study using OPTN data between 1996 and 2004 found no association between HLA mismatching of a first DD graft and further sensitization [48]. Moreover, recent advances in desensitization and kidney-paired donation schemes challenge concerns on re-transplantation barriers [49–51]. Given our study's observational nature, causation cannot be proved and residual confounding may exist. Moreover, some factors influencing KT access may be unaccounted for. While adjustments were made for the era of KT, changes in access over time and differences in allocation programmes between countries cannot be excluded [29, 52]. However, similarities are expected due to the inclusion of mainly high-income countries, and macroeconomic factors are main drivers for access to KT [8]. Future research should explore specific factors affecting KT access to better address paediatric KT challenges and opportunities.

CONCLUSION

Our study highlights age-related disparities in (repeat) KT access, with those aged 15–19 facing lower chances compared to those aged 10–14 years old. Patients aged 0–4 years experienced reduced first transplant likelihood, but similar access for subsequent KTs. Females presented lower first KT access, primarily due to fewer pre-emptive transplants. Patients having GN or diseases with risk of recurrence have reduced access to both first and second transplants. Previous pre-emptive transplants and grafts lasting over 5 years increased the likelihood of re-transplantation, while previous donation type had no impact.

Our findings emphasize the importance of prioritizing research on high-risk recurrent conditions and young recipients and further promoting pre-emptive KT for repeat transplant recipients. Finally, our study underscores sex disparities in KT, highlighting the urgency for expedited pre-transplant evaluations for females and promoting sex-focused and equity-oriented research.

SUPPLEMENTARY DATA

Supplementary data are available at *Nephrology Dialysis Transplantation* online.

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AUTHORS' CONTRIBUTIONS

E.P., and M.B., designed the study, revised and analysed data and wrote the manuscript. S.D.M., A.K., V.S.S., J.H., and K.J.J. designed the study, reviewed, and edited the manuscript. A.P.J.V., S.S.S., S.A.B., C.B., T.J., O.R.A., L.B., M.S., J.E.S., M.A., F.A.O-A., F.C-O., L.A.P.,

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DATA AVAILABILITY STATEMENT

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

CONFLICT OF INTEREST STATEMENT

None declared.

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