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TIME TRENDS IN PREEMPTIVE KIDNEY TRANSPLANTATION IN EUROPE: AN ERA REGISTRY STUDY

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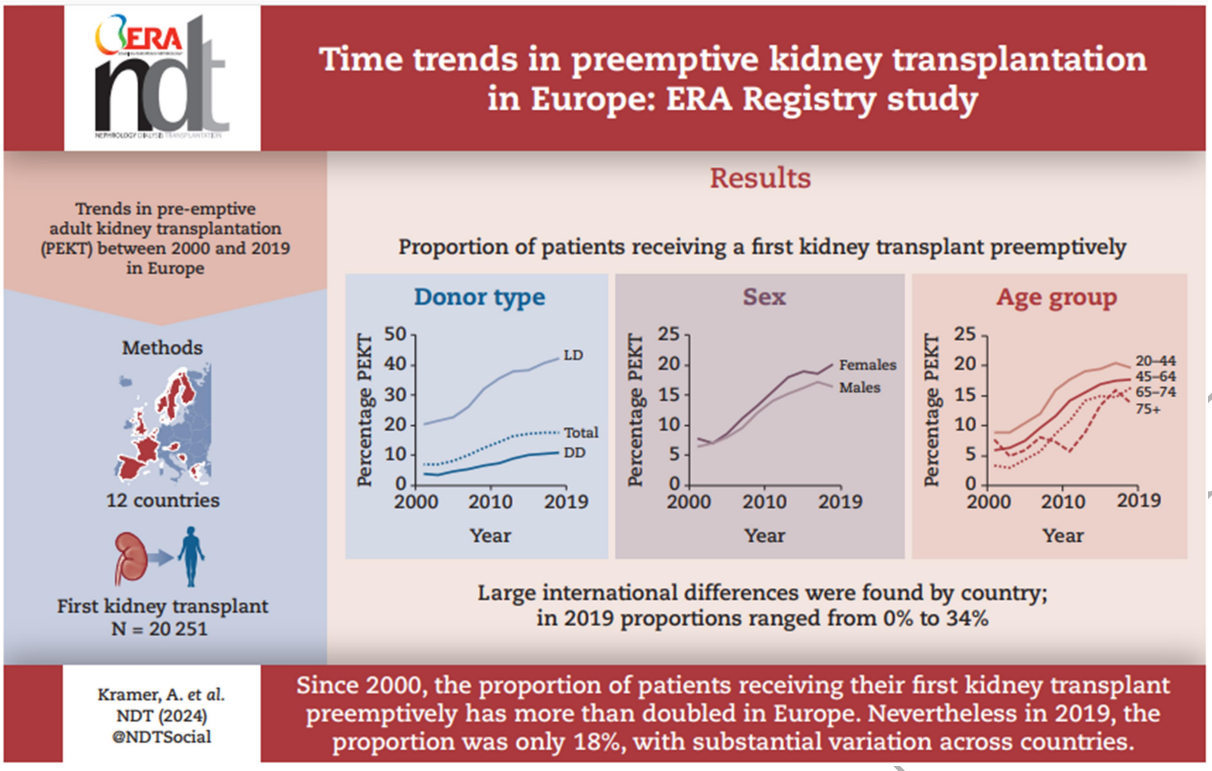
GRAPHICAL ABSTRACT



ABSTRACT

Background. Preemptive kidney transplantation has better outcomes when compared to transplantation after dialysis. We aimed to examine trends in preemptive kidney transplantation between 2000 and 2019 in Europe and to provide an overview of associated policies, barriers and initiatives.

Methods. Adult patients from 12 European countries who received a preemptive kidney transplant were included. The representatives of the registries providing these data were questioned on the policies, barriers and initiatives around preemptive kidney transplantation.

Results. Between 2000 and 2019, 20251 adults underwent preemptive kidney transplantation (11169 from living donors, 8937 from deceased donors). The proportion of first kidney transplantations that were preemptive more than doubled from 7% in 2000 to 18% in 2019, reflecting a similar relative increase for living donor kidney recipients (from 21% to 43%) and deceased donor kidney recipients (from 4% to 11%). Large international differences were found. The increase in preemptive kidney transplantation was observed across all age, sex and primary renal disease groups. Countries had similar criteria for preemptive

waitlisting. Barriers mentioned included donor shortage, late referral to the transplant center and long donor or recipient work-up. Suggested initiatives included raising awareness on the possibility of preemptive kidney transplantation, earlier start and shorter work-up time for recipient and living donor.

Conclusions. Over the last two decades the proportion of patients receiving a first kidney transplant preemptively has more than doubled, reflecting a similar relative increase for living and deceased donor kidney recipients.

KEY LEARNING POINTS

What was known:

- In patients with end-stage kidney disease, both living donor and deceased donor preemptive kidney transplantation are associated with better patient and graft survival compared with post dialysis kidney transplantation.
- Over the years, initiatives and guidelines have been published promoting preemptive kidney transplantation. Nevertheless, countries have also faced barriers in increasing the number of preemptive kidney transplantations.
- There is currently no overview of time trends in PEKT rates for European countries over the past decade. This, combined with knowledge on current initiatives, barriers and policies to performing PEKT, could identify areas for improvement in order to increase the rates of PEKT

This study adds:

- We showed that the proportion of patients receiving a first kidney transplant while not yet receiving dialysis has more than doubled from 7% in 2000 to 18% in 2019.
- However, in 2019 there still were striking differences between countries. Some of the main reasons included: shortage of kidney donors, late referral to the transplant center and long recipient or donor work-up.

Potential impact:

- This study suggests that more can be done to increase the number of transplants before dialysis, such as making the process of getting a transplant referral easier, educating patients and doctors better, and making the donor evaluation and transplant candidates work-up processes more efficient.

Keywords: barriers, Europe, preemptive kidney transplantation, trends

INTRODUCTION

Due to the advantages associated with avoiding dialysis [1-3] in patients with end-stage kidney disease (ESKD), kidney transplantation should ideally occur just before dialysis would become necessary, which is known as preemptive kidney transplantation (PEKT). Despite this, in 2019 in Europe only 19% of all kidney transplantations performed were without a preceding period of dialysis, with substantial differences between [4]. About half of these PEKTs were performed with a kidney from a deceased donor (DD) and the other half with a kidney from a living donor (LD) [4].

Due to the superior outcomes following PEKT, the transplant community has been continuously looking for initiatives to increase PEKT rates, such as early referral of chronic kidney disease (CKD) patients to the transplant center, and timely education of CKD patients and family members about living donation [5, 6]. At the same time, some countries might face barriers to perform PEKT such as legislative, financial and logistical issues [7]. These initiatives, barriers and policies to performing PEKT may differ between European countries. To date, there is no overview of time trends in PEKT rates for European countries. An overview on trends in PEKT, combined with knowledge on current initiatives, barriers and policies to performing PEKT, could identify areas for improvement in order to increase the rates of PEKT.

The aims of this study are to examine the trends in PEKT in adults between 2000 and 2019 in Europe, and to provide overview of current policies, perceived barriers and potential initiatives with regard to PEKT in the participating countries.

MATERIALS AND METHODS

Patient population

The European Renal Association (ERA) Registry collects data on patients with ESKD receiving kidney replacement therapy (KRT) through national and regional renal registries in Europe [4]. In this study, we included data on patients aged 20 years and older from 9 national registries (Austria, Bosnia and Herzegovina, Denmark, Finland, France, Greece, The Netherlands, Norway, Sweden) and from 16 regional registries (Belgium: Dutch-and French speaking part; Spain: Andalusia, Aragon, Asturias, Basque country, Cantabria, Castile and Léon, Castile-La Mancha, Catalonia, Community of Madrid, Extremadura, Galicia, and Valencia; United Kingdom: England, Northern Ireland, Wales and Scotland). For France, patients from 13 (of the 27) regions could be included: Auvergne, Bourgogne, Basse-Normandie, Bretagne, Centre, Champagne-Ardenne, Languedoc-Roussillon, Limousin, Lorraine, Midi-Pyrénées, Nord-Pas-de-Calais, Provence-Alpes-Côte-d'Azur, and Rhône-Alpes.

For most countries, data were included for the period 2000-2019 except for France (from 2005) and Bosnia and Herzegovina (from 2011). For each country, the data represented the complete KRT population, except for France (55.2%), Spain (increasing coverage from 52.9% in 2000 to 87.7% in 2008) and UK (increasing coverage from 52.3% in 2000 to 100% in 2007).

Informed consent was obtained in accordance with national and/or regional regulations for each individual registry. Compliance with ethical standards was confirmed by the medical ethical committee of the Amsterdam Medical Centre (W21_123 No. 21.136).

Definitions

PEKT was defined as a kidney transplantation performed as the first KRT, including first kidney transplantations combined with other organs. This paper focusses on PEKT as percentage of the total number of first kidney transplantations performed. Additionally, PEKT was expressed per million population, by dividing the PEKT count by the general population, multiplied by one million.

The PRD groups consisted of autosomal dominant polycystic kidney disease (ADPKD), congenital anomalies of kidney and urinary tract (CAKUT), diabetes mellitus, hypertension / renal vascular disease (RVD), glomerulonephritis, and 'other PRD' for the rest of the groups and unknown or missing data [4].

Time trend analyses

In this study Joinpoint regression analysis [8] was used to determine annual percentage changes (APC) with 95% confidence intervals (95% CI) for time trends. Joinpoint Regression is designed to test whether a multi-segmented line is a statistically significantly better fit then a straight or less-segmented line [9]. With this approach, points in time are identified where there was a change in the trend of PEKT, and therefore these points could differ across subgroups. Corresponding to the availability of 20 years in our study period a maximum of two joinpoints (three trend periods) were allowed [9].

Analyses were performed for all PEKT (total PEKT) and separately for DD PEKT and LD PEKT. Recipients from an unknown donor (N=145, 0.7%), representing less than 1% of all patients, were included in the total PEKT group. Data were analysed for all countries together, by country, and in subgroups of age, sex and PRD. A sensitivity analysis was performed excluding countries that did not have data available for the entire study period (UK (England / Wales / Northern Ireland), France, Spain and Bosnia and Herzegovina).

The analyses were performed using SAS 9.4 [10] or Joinpoint 4.2.0.4 [8]. P-values below 0.05 were considered statistically significant.

Survey of PEKT policies, barriers and initiatives

To better understand the policies, barriers and potential initiatives concerning PEKT, a short survey was sent to the representatives of the renal registries that provided data for this study. They were asked about 1) whether DD PEKT was permitted in their country during the study period 2) whether patients on the waiting list received waiting time points when not yet on dialysis, 3) what the criteria were to place patients preemptively on the waiting list, 4) which barriers currently had a negative effect on the rate of DD PEKT and LD PEKT, and 5) which initiatives could contribute to overcome these barriers.

RESULTS

Between 2000 and 2019, 148,108 adult patients received a first kidney transplant in the participating countries, of which 32,404 were from living donors, and 114,572 from deceased donors. Out of these, 20251 patients (13.7%) received a PEKT (**Table S1**). With 34.5% the proportion of PEKT was higher for living donor recipients (N=11,169) than for deceased donor recipients (7.8%, N=8937). Over time the proportion of kidney transplantations that was preemptive increased from 6.8% in 2000 to 18.1% in 2019 (**Table S2**), which was largely due to an increase between 2003 and 2010 (APC: 11.5, 95%CI: 9.7; 13.2; **Figure 1**, **Table S2**). Sensitivity analyses including only patients from countries with full coverage for the entire study period revealed similar results (**Figure S1**).

Time trends in PEKT were also examined as rate per million population (**Figure 1**). These results are shown in the Supplement (**Figures S2-S5**, **Table S3**), but will not further be discussed.

Trends in living donor preemptive kidney transplantation

Overall, the proportion of LD recipients who underwent PEKT increased from 20.8% in 2000 to 43.4% in 2019, with the most prominent increase between 2005 and 2010 (APC: 9.2, 95%CI: 5.8; 12.8; **Figure 1**, **Table S2**). In 2019, the proportion of LD PEKT was highest in Spain (55.3%) and the Netherlands (53.2%) and lowest in Bosnia and Herzegovina (0.0%) and Greece (16.1%; **Table S2**). In most countries, an upward trend was seen, with the exception of Austria and Bosnia and Herzegovina (**Figure 2**). The biggest increase between 2000 and 2019 was found in Finland (from 0% to 47.1%) and in Spain (from 11.1% to 55.3%; **Table S2**).

The median age of patients receiving a LD PEKT increased from 41.5 years in 2000 to 52.8 years in 2019, which was a more substantial increase than for all patients receiving a first kidney transplantation (from 48.5 to 55.4; **Figure S6**). While in 2000, the proportion of LD recipients who underwent PEKT was around 20% for each of the age groups 20-44, 45-64 and 65-74 (**Figure 3**), in 2019 36.5% of 20-44 year old, 44.2% of 45-64 year old and 50.2% of 65-74 year old LD recipients received their transplant preemptively. In 2000, no LD PEKT were performed in patients aged 75+ (**Table S1**), however, in 2019, 19 out of 38 (50%)

LD recipients aged 75+ received a PEKT (**Table S1**, **Figure 3**). Analyses by sex showed similar proportions of LD male and female recipients who received a PEKT, and these proportions continued to increase during the study period for both sexes (**Figure 4**). The proportion of LD recipients who underwent PEKT was highest among recipients with ADPKD and CAKUT, and lowest among recipients with hypertension/RVD and diabetes. For all PRDs, proportions continued to increase during the study period (**Figure 5**).

Trends in deceased donor preemptive kidney transplantation

The proportion of DD recipients receiving a PEKT increased from 4.0% in 2000 to 11.0% in 2019, mostly due to a steep increase between 2003 and 2008 (APC: 13.6, 95%CI: 6.8; 20.8) (**Figure 1**, **Table S2**). In 2019, the proportion of DD PEKT was highest in Norway (20.0%) and Denmark (18.3%) and lowest in Bosnia and Herzegovina and Greece (both 0.0%; **Table S2**). The largest increase over time was found in Sweden (from 4.1% in 2000 to 16.5% in 2019) and the United Kingdom (from 4.7% to 15.3%). In all countries, except for Austria, Bosnia and Herzegovina and Greece, the proportion of PEKT out of all DD kidney transplantations performed increased during (a part of) the study period (**Figure 2**).

The median age of patients receiving a DD PEKT increased from 46.0 years in 2000 to 56.7 years in 2019, and was on average 4 years higher than for patients receiving a LD PEKT (**Figure S6**). In 2019 the proportion of DD recipients receiving a PEKT was similar across the age groups 20-44, 45-64 and 65-74 (around 11%), and somewhat lower for patients aged 75 years and over (8.6%). In all age groups an increase over time was found, however, in patients aged 20-44 the proportion DD recipients who underwent PEKT became stable from 2017, while in patients aged 75 years and over the proportion only started to increase after 2005 (**Figure 3**). For males and females DD recipients the proportion PEKT was similar, and increased in both groups (**Figure 4**). For all PRDs the proportion of DD PEKT increased during the study period (**Figure 5**). In 2019, the highest proportions were found for patients with ADPKD and for patients with unknown or missing PRD, and the lowest proportions for patients with hypertension/RVD and glomerulonephritis as PRD.

Policies, barriers and initiatives for preemptive kidney transplantation

Representatives from the 12 participating renal registries in this study were approached to provide information on the policies, barriers and initiatives regarding LD PEKT and DD PEKT in their country. Eleven (92%) registry representatives replied (**Tables 1, 2** and **3**).

The most frequently mentioned barriers for LD PEKT were late referral to the transplant center (N=7), long donor work-up (N=6), patient's hesitation, or preference to postpone the work-up (N=5), and fear that living kidney donation is damaging the donor's health (N=4; **Table 2**). Initiatives mentioned to overcome these barriers aimed at increasing the knowledge/awareness among nephrologists and patients of the possibility of PEKT (N=6, **Table 3**).

In all countries from which a response was received, DD PEKT was permitted during the entire study period, or during a part of the study period (Finland from 2018; **Table 1**). Only in France, Norway, Sweden and the United Kingdom patients received waiting time points when not yet on dialysis, while in Spain there was no nation-wide policy. In 6 countries patients may be placed on the waiting list preemptively with an eGFR <15 ml/min, and/or the expectation to require dialysis within 6 or 12 months. In the other four countries placement on the waiting list was based on clinical judgement (**Table 1**), or there was no nation-wide policy. For DD PEKT the following barriers were most frequently mentioned: shortage of kidney donors (N=9), late referral to the transplant center (N=7), long recipient work-up (N=5), and lack of knowledge of the physician on the possibility of PEKT (N=4; **Table 2**). Initiatives mentioned that may help to overcome the barriers for DD PEKT were mostly aimed at increasing the knowledge/awareness among nephrologists and patients (N=6) and increasing the potential donor pool (N=5; **Table 3**).

DISCUSSION

This study is the first to detail the trends in PEKT in Europe over the past two decades. Overall, the proportion of patients receiving a first kidney transplant while not yet receiving dialysis has more than doubled from 7% in 2000 to 18% in 2019, reflecting a similar relative increase from 21% to 43% for living donor kidney recipients and from 4% to 11% for deceased donor kidney recipients.

Historically, kidney transplantation was generally reserved for kidney failure patients who were already treated with maintenance dialysis. Between 1985 and 1992 in Europe only 7% of the transplantations performed were preemptive [11]. In 2002 Kasiske et al. [12] and Meier-Kriesche et al. [13] were among the first to demonstrate that both LD and DD PEKT were associated with better patient and graft survival compared with post dialysis kidney transplantation. This prompted initiatives [5, 14] and guidelines promoting PEKT [15-17]. Besides, in Europe the overall kidney transplantation rate increased, amongst others due to initiatives aimed at enlarging the donor pool, increasing the availability of donor grafts for PEKT [18]. The increase in the proportion of kidney transplant recipients receiving a PEKT in Europe was also found in other parts of the world. In the US, Australia and New Zealand the proportion PEKT was higher in 2000, but showed a less substantial increase thereafter (in the US from 15% in 2000 to 18% in 2019 [19], in Australia from 9% to 12% and in New Zealand from 16% to 18% [20, 21]) compared to Europe.

However, even after doubling, in Europe PEKT rates remain low with 43% of the first LD recipients and 11% of the first DD recipients in 2019. Moreover, in 2019 in some countries PEKT was still rarely or never performed, while in others DD PEKT proportions up to 20% (Denmark, Norway) and LD PEKT up to 55% (Spain, the Netherlands) were achieved.

Living donation is the ideal way to enable PEKT. With the exception of patients who present acutely or late with kidney failure, or have additional medical problems that make transplantation temporarily impossible, there are few reasons that justify delaying LD transplantation until after the start of dialysis. Nevertheless,

our study shows that in most European countries, less than half of LD kidney transplantations occur preemptively. One of the main hurdles, as brought up by registry representatives questioned within our study and confirmed in several studies, is the late referral of candidates to the transplant center and the long recipient work-up time [22-25]. Practical barriers have been suggested for this delay, such as the high workload of the medical staff along with other logistical challenges. In addition, patient-specific factors can play a role, such as co-morbidities, language barriers and socio-economic status [26]. Potential solutions could be earlier patient education regarding the benefits of PEKT [6, 27], to make the evaluation process shorter for low-risk transplant candidates [28], and to restrict to the necessary tests needed to fulfil minimal listing criteria [29]. In addition, an overly long living donor evaluation time presents a barrier for PEKT. A report on LD recipients in Canada showed that between 2004 and 2014 35% of patients had to initiate dialysis after their donor candidate began their evaluation [30], and that the median donor evaluation time was 10.6 months for PEKT and 22.4 months for recipients already established on dialysis. The 2017 Kidney Disease: Improving Global Outcomes (KDIGO) "Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors" [31] recommends keeping the donor evaluation as efficient as possible, and completing the medical and laboratory aspects of the donor evaluation in a short period. Indeed, the implementation of a 1-day donor assessment in 2010 in Northern Ireland [32] resulted in one of the highest LD transplant rates in Europe [4]. Another barrier for LD PEKT as reported by the surveyed registry representatives was the patient's hesitation and fear that kidney donation could be damaging the donor's health. Patients feel reluctant to ask relatives for a kidney and often have concerns about the long-term consequences of kidney donation. Also cultural barriers may play a role [33]. Culturally sensitive education programs that facilitate discussions about LD transplantation with patients and members of their social network during home-based educational meetings have proved to be effective in overcoming these issues [33-35]. Also the use of a friend, relative or volunteer who is trained to speak to friends and family about donation on the patient's behalf has shown encouraging results [36].

Somewhat counterintuitively, our study shows that the proportion of LD PEKT increased with recipient age. A similar finding was reported for the US, where it was postulated that this may reflect the transplant clinicians' awareness of the risks of waiting for a kidney and prolonged dialysis in older

candidates[37]. In addition, the increased acceptance of older living kidney donors [38] may have contributed to the higher proportion LD PEKT found for the older recipients. Moreover, despite sex-based disparities generally reported for all phases of kidney transplantation [39], we found comparable proportions of LD PEKT and DD PEKT for male and female recipients.

In the absence of a living donor, a PEKT from a deceased donor is recommended [16]. However, we showed that in 2019 still the vast majority of the patients underwent a period of dialysis prior to DD kidney transplantation. Here again, DD PEKT requires a timely initiation and smooth progression of the transplant work-up, aiming to have the work-up finalized before dialysis need, or to minimize time on dialysis on the waiting list [13]. However, in candidates for a DD transplant, an early work-up may only seem worthwhile if the patient actually has a chance of receiving a kidney offer preemptively. In all countries represented in the study, patients are allowed to be preemptively transplanted with a DD kidney. Nevertheless, in most countries the allocation program does not assign points for waiting time to those who are not yet on dialysis, which means that these patients have a lower chance of receiving a kidney preemptively compared to patients already receiving dialysis. Possibly the assumption that patients are hardly likely to receive an offer contributes to inertia. However, DD PEKT proportions up to 20% in Norway, a country where waiting time points are assigned to patients not yet receiving dialysis, show that DD PEKT is achievable, and a revision of the current criteria to place patients preemptively on the waiting list may be a possibility for countries aiming at achieving higher rates of DD PEKT. Also the shortage of deceased donors does reduce the chance of receiving a kidney preemptively, and this was considered the main barrier for DD PEKT by the questioned registry representatives. It is therefore essential to consider policy and clinical measures to increase access to kidney transplantation. The European Commission Joint Statement has identified measures that have been most successful in increasing donation rates, such as maximizing the role of donor coordinators, optimizing the role of intensive care professionals, minimizing the duration of the donation process, and the use of expanded criteria donors [40]. Also ethical concerns could play a role, as some physicians may feel that the scarce DD kidneys available should be offered to patients receiving dialysis first. A simulation study performed by Kiberd et al. [41], comparing the allocation of a DD kidney to a

preemptively waitlisted patient or to a patient receiving dialysis, suggested that preemptive waitlisting for patients with a low likelihood of needing dialysis may result in more people being waitlisted. Also a study by Charpentier et al. [42] on timing of PEKT concluded that transplant programs should avoid performing PEKT too early in the course of CKD. Nevertheless, recent guidelines [43, 44] recommend referral of potential kidney transplant candidates for evaluation at least 6 to 12 months before anticipated dialysis initiation. Although it remains very difficult to accurately predict the progression of kidney failure, it seems reasonable to try to avoid an overly early PEKT, but rather to aim for transplantation (or at least waitlisting, in the absence of a living donor) shortly or a few months before the expected start of dialysis.

Differences in the extent to which the abovementioned barriers hold for the countries participating in this study, as well as in the measures taken to overcome these issues, may partly explain the variability in PEKT rates across countries. Nevertheless, the exact reasons for this variation remain speculative, as literature on country-specific initiatives and barriers and the effects of these on the PEKT rates was not found.

The main strength of this study is that for the first time we were able to analyze the trends in total, LD and DD PEKT in 12 European countries over a considerable period of two decades, using data from more than 20.000 patients. A limitation of our study is that we included predominantly data from Western European countries, as those from Central and Eastern European countries were unavailable. Therefore, the results may not be generalizable to the whole of Europe. Secondly, the data are presented on the national level but differences might occur between regions or even between centers, due to differences in patient population, environment and clinical practice. In addition, countries might have changed their criteria to determine the PRD of potential kidney transplant recipients over the last two decades. This could have contributed to a change in the percentage or rate of PEKT for a certain PRD. Furthermore, our survey was not validated. Lastly, more detailed information on recipients and the transplantation procedures (e.g. blood type, comorbidities, education level, sensitization and HLA mismatching) could have contributed to a better understanding of the differences in PEKT rates between countries, but were unfortunately not available for this study cohort.

Data from the ERA Registry show that the proportion of first kidney transplant recipients receiving a preemptive kidney transplant has increased from 7% in 2000 to 18% in 2019. PEKT is still performed much more frequently in the setting of living than deceased kidney donation, yet we found a similar relative increase for both donor types. Rates varied widely across Europe, suggesting great variability in clinical practice. Initiatives aimed at streamlining the transplant referral process, improving the education of patients and referring nephrologists, and increasing the efficiency of the donor evaluation and transplant candidate work-up processes may contribute to increasing preemptive kidney transplantation rates.

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CONFLICT OF INTEREST STATEMENT

The authors declare the following financial interests/personal relationships:
MOV received travel grants from Baxter and Vifor. PF received grants or contracts from Finska läkaresällskapet and Liv och Hälsa; and consulting fees from Baxter, GSK, Astellas, and AstraZeneca. MMS received grants or contracts from Swedish Kidney Foundation, Skane University Hospital Foundations, IngaBritt and Arne Lundbergs Foundation; and consulting fees from Hansa Biopharma, Astra Zeneca, Vifor, and Otsuka. PMF received royalties or licenses from UpToDate; consulting fees from Allena Pharmaceuticals, Alnylam, AstraZeneca, Bayer, NovoNordisk, and Otsuka Pharmaceuticals; speaker fees from AstraZeneca, Gilead, and Alnylam; travel fees from Alnylam and Amgen; and participated in data safety monitoring or advisory boards from Allena Pharmaceuticals, Alnylam, AstraZeneca, and NovoNordisk; and participated in other boards, society, committees or advocacy groups from ERKNet, EULIS, and ERA Registry. MA received consulting fees from Fresenius Medical Care Slovenia; speaker fees from Astellas, Novartis, Chiesi, AstraZeneca, Bayer, Amgen, Medison Pharma, Takeda, and Boehringer; travel fees from Chiesi and Bayer Pharma; and participated in advisory boards from Bayer Pharma, AstraZeneca, Medison Pharma, and Takeda. MA received speaker fees from Amgen, Astellas, Astra Zeneca, Bayer, Boehringer Ingelheim, Menarini, Novo Nordisk, and Sanofi; travel fees from Astra Zeneca, Menarini, and Sanofi; and participated in data safety monitoring or advisory boards from Astellas, Astra Zeneca, Bayer, Boehringer Ingelheim, and Novo Nordisk. AO received support for medical writing from Astellas and Open health Group; grants from Sanofi; consultancy or speaker fees or travel support from Advicciene, Astellas, Astrazeneca, Amicus, Amgen, Fresenius Medical Care, GSK, Bayer, Sanofi-Genzyme, Menarini, Kyowa Kirin, Alexion, Idorsia, Chiesi, Otsuka, Novo-Nordisk, and Vifor Fresenius Medical Care Renal Pharma; and is Director of the Catedra Mundipharma-UAM of diabetic kidney disease and the Catedra Astrazeneca-

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AUTHORS' CONTRIBUTIONS

Conceptualization: AK, CGMV, KJJ, DA, VSS and RH; Methodology: AK, CGMV, DA, VSS and RH; Formal analysis: AK and CGMV; Writing–original draft: AK, RB, CGMV, KJJ, DA, VSS and RH; Writing–review & editing: SM, JK, OLRA, AM, APJV, AVR, EHSW, TL, MOV, FAOA, EM, PF, MS, CC, SSS, PMF, MA, MA, AO; All authors read and approved the final manuscript.

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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 ERA Registry remain the owners of the data.

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Table 1. Waitlist policies for patients not yet on dialysis

Country	Deceased donor PEKT permitted between 2000-2019	Waiting time points on the waiting list when not yet on dialysis	Current criteria to place patients preemptively on the waiting list
Austria	Yes	No	Clinical judgment
Belgium	Yes	No	Clinical judgment
Bosnia and Herzegovina	Yes	No	Within 6 months of requiring dialysis
Denmark	Yes	NA	eGFR <15ml/min
Finland	Yes, from 9/2018	No	eGFR <15ml/min and decreasing eGFR
France	Yes	Yes, but for a maximum of 1 year	CKD stage 4 and within 12 months of requiring dialysis
Greece	-	-	-
Netherlands	Yes	No	Clinical judgment
Norway	Yes	Yes	eGFR <15ml/min
Spain	Yes	No nation-wide policy	No nation-wide policy
Sweden	Yes	Yes	Clinical judgment
United Kingdom	Yes	Yes, from 2019	eGFR <15ml/min and within 6 months of requiring dialysis

Table 2. Potential barriers for living and deceased donor preemptive kidney transplantation

Potential barriers that may have a negative effect on the rate of PEKT	**for LD PEKT**	**for DD PEKT**
	N respondents	**N respondents**
Shortage of kidney donors	NA	9
Lack of knowledge of the physician on the possibility of PEKT	NA	4
Lack of knowledge of the survival benefit with PEKT	3	2
Physicians believe that time on dialysis will improve compliance after transplantation	2	2
Patient's hesitation, or preference to postpone the work-up	5	2
Hospitals or dialysis centers lose a source of financial revenue after referring for PEKT	0	1
Nephrologists lose a source of financial revenue after referring for PEKT	0	1
Workload too high for physicians and transplant coordinators	NA	3
Workload too high for physicians	3	NA
Long recipient work-up	3	5
Long donor work-up	6	NA
Late referral to the nephrologist	3	3
Late referral to the transplant center	7	7
Language barriers	3	2
Logistical barriers	1	1
Fear that kidney donation is damaging the donor's health	4	NA
Legal barriers	NA	1
Ethical concerns	1	0
Other barriers mentioned that may have a negative effect on the rate of PEKT (free text)		
- Too few donors / no suitable candidates	2	
- Economic and social precariousness for older recipients	1	
- Lack of psychological support / coaching / education & awareness	1	

Table 3. Initiatives that may help to overcome the barriers affecting the rate of living and deceased donor preemptive kidney transplantation

Theme	Quotes
Initiatives that may help to overcome the barriers affecting the rate of PEKT from living donor	
To increase the knowledge / awareness among nephrologists and patients (N=6)	"Information for physicians and doctors" "Comprehensive education of doctors participating in the transplant program, hospital coordinators in particular, and transparency in all aspects of transplantation at the national level of the country" "We have to work with attitudes to living donor KE, informing patients and educating nephrologists" "Information regarding advantages and opportunities…" "Better educational resources" "Training of young physicians"
To increase the potential donor pool (N=5)	"Raising the awareness of the entire population about organ donation, raising national awareness about the number of dialysis patients, and raising quality of life after transplantation" "Informing social environment to lead to more living transplantations" "Better community based local initiatives and awareness campaigns" "More human resources to organize assessments and follow-up of donors and future recipients" "A general investigation into the reasons for the decline in LD transplantation might give us a road map for increasing LD (preemptive and not)"
To reduce the chance of having to start dialysis first (N=3)	"Earlier start of the transplant work-up and shorter work-up time leading for both the recipient and potential donor (better organization of the 'kidney failure clinic' for example with dedicated nurse who coordinates the work-up)" "Resources to the nephrology departments doing the work up" "Resources to improve logistics at transplant center"
Initiatives that may help to overcome the barriers affecting the rate of PEKT from deceased donor	
To increase the knowledge / awareness among nephrologists and patients (N=6)	"Information for physicians and doctors" "Reporting and comparing the rates of PEKT in the various healthcare districts" "Keep the issue of PEKT on the agenda of national nephrology meetings" "National guidelines for early registration on the waiting list" "Information regarding advantages and opportunities" "Better educational resources"
To increase the potential donor pool (N=5)	"Professionalize the work of hospital coordinators who find possible cadaveric donors" "Knowledge of possibility" "More human resources to identify potential donors and organize organ harvesting, and public information on organ transplantation to decrease opposition to organ harvesting." "Better community based local initiatives and awareness campaigns" "A mass campaign to raise awareness and decrease opposition of organ donation"
To reduce the chance of having to start dialysis first (N=2)	"Early referral" "Earlier start of the transplant work-up and shorter work-up time leading to faster referral to the transplant center (better organization of the 'kidney failure clinic' for example with dedicated nurse who coordinates the work-up)"

Figure 1) PEKT between 2000 and 2019, total and by donor type. Data is presented as percentage of all first kidney transplantations performed (upper panel) and per million population (lower panel). The annual percent change (APC) reflects the trend over time. An asterisk (*) indicates whether the APC was statistically significant (p<0.05).

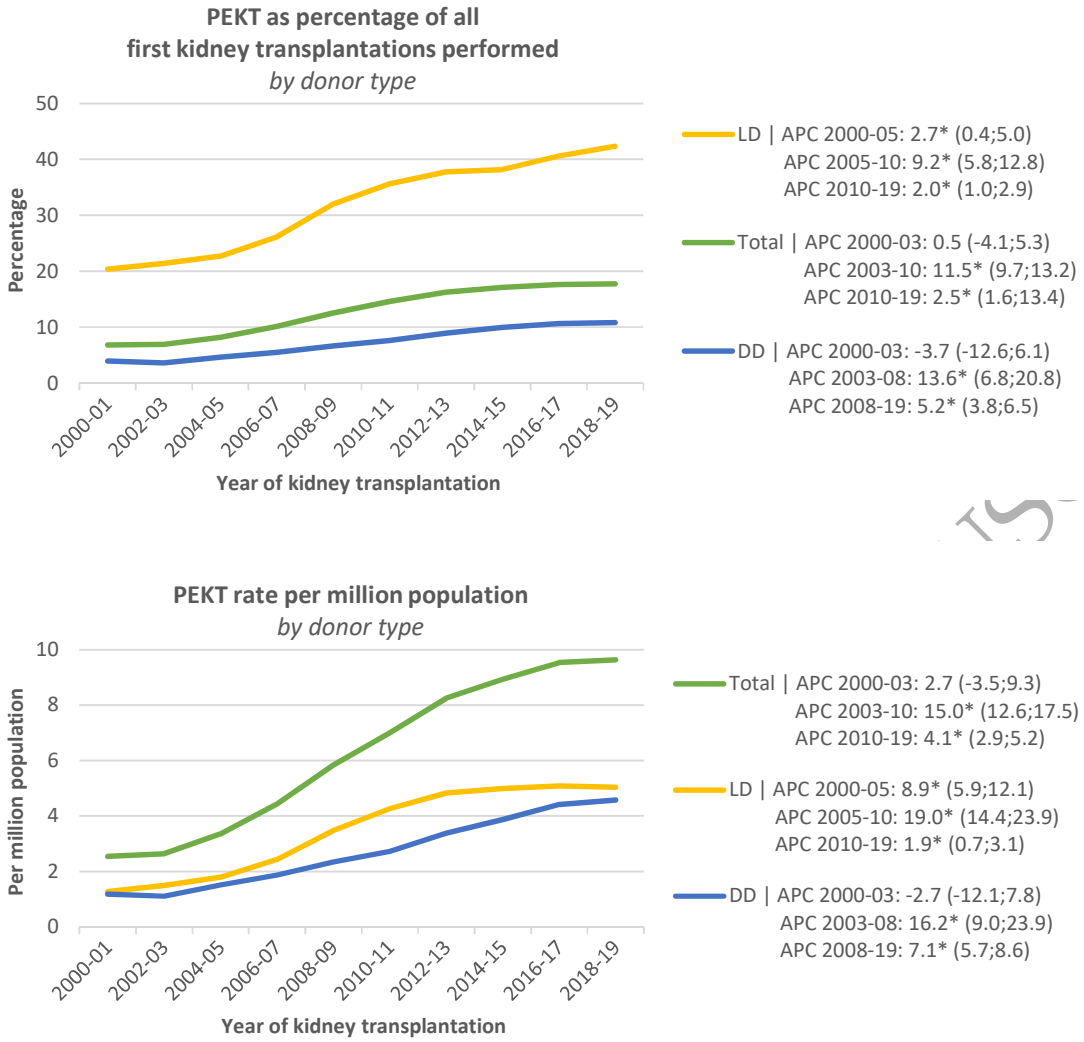
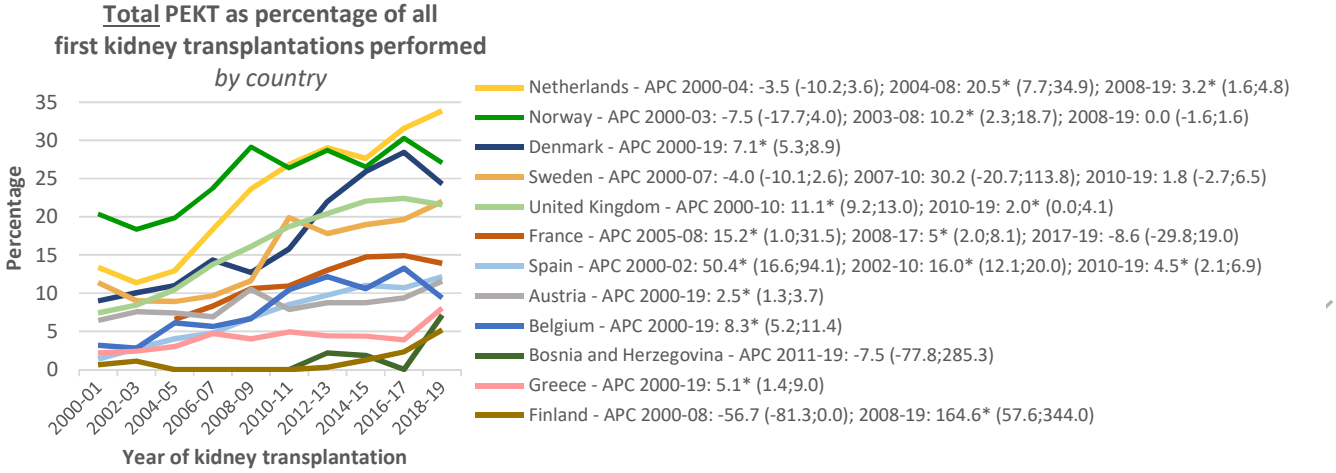
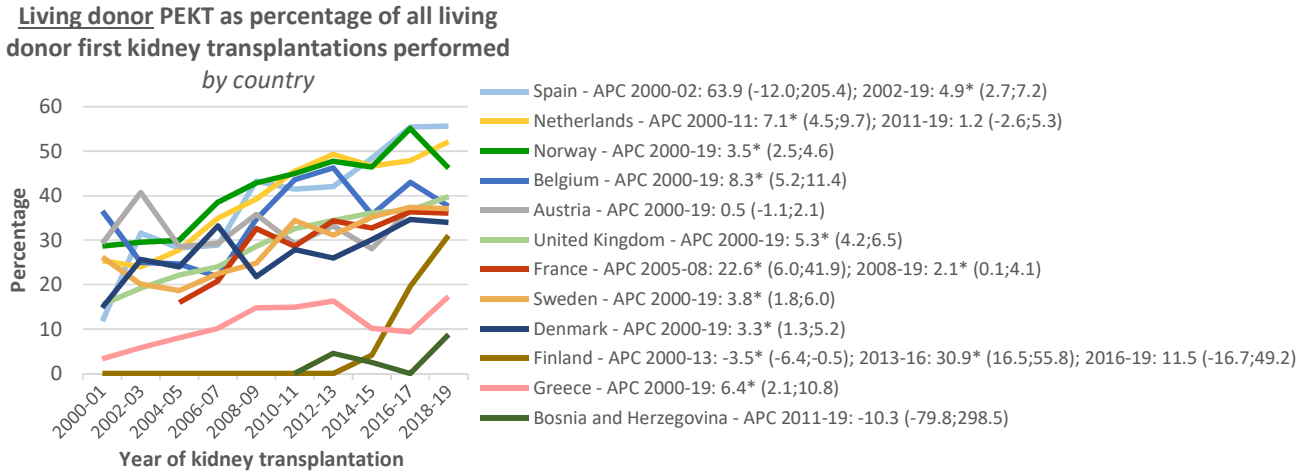


Figure 2) PEKT as percentage of all first kidney transplantations performed, by country. Data is presented separately for all PEKT (upper panel), living donor PEKT (middle panel) and deceased donor PEKT (lower panel). The scale of the vertical axis differs by panel. The annual percent change (APC) reflects the trend over time. An asterisk (*) indicates whether the APC was statistically significant (p<0.05).





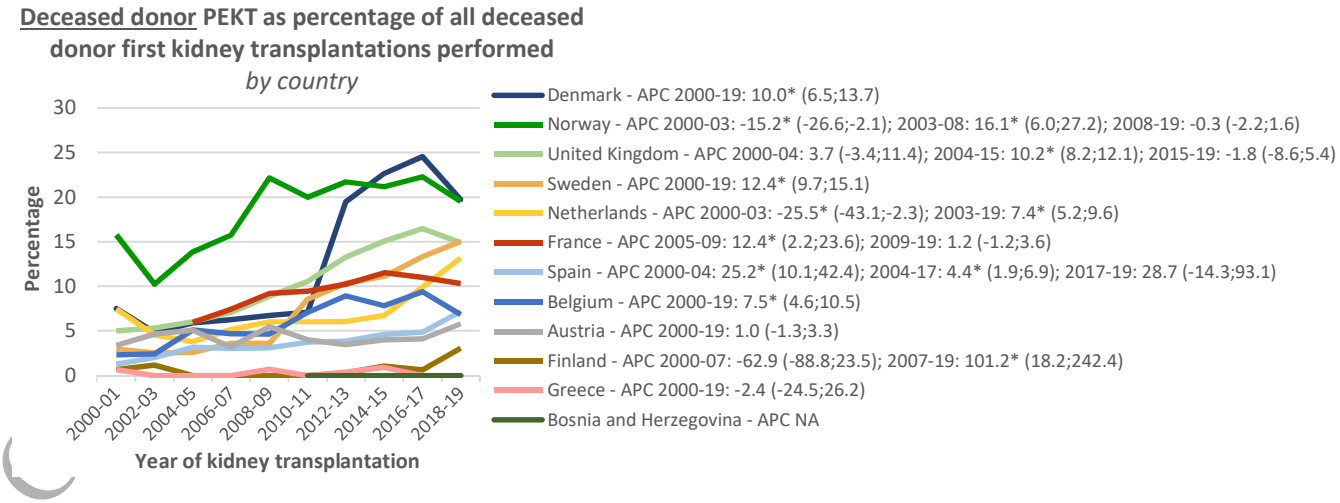
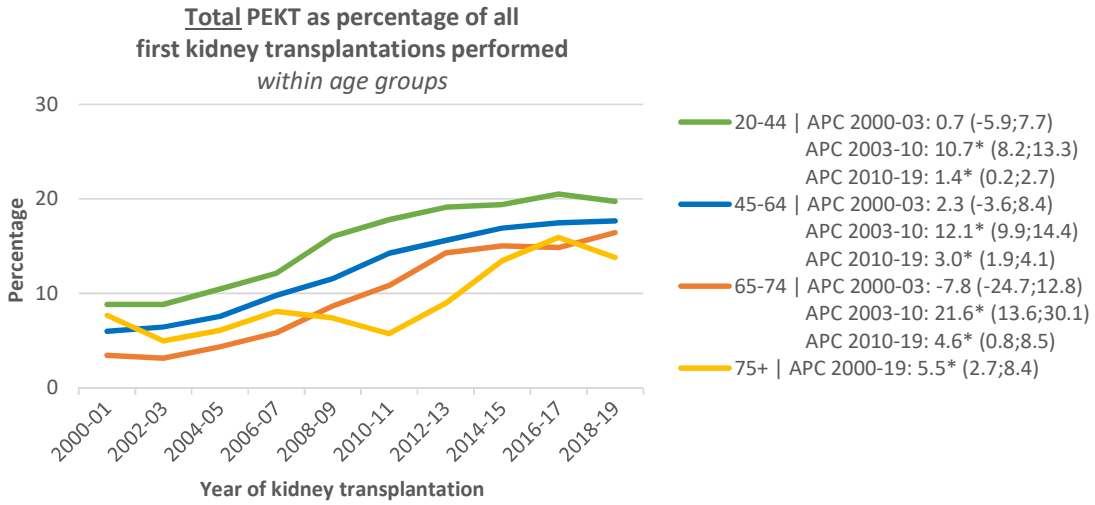


Figure 3) PEKT as percentage of all first kidney transplantations performed, by age group. Data is presented separately for all PEKT (upper panel), living donor PEKT (middle panel) and deceased donor PEKT (lower panel). For the age group 75+ the percentage fluctuates as the number of transplantations performed in this age group is very low. The scale of the vertical axis differs by panel. The annual percent change (APC) reflects the trend over time. An asterisk (*) indicates whether the APC was statistically significant (p<0.05).



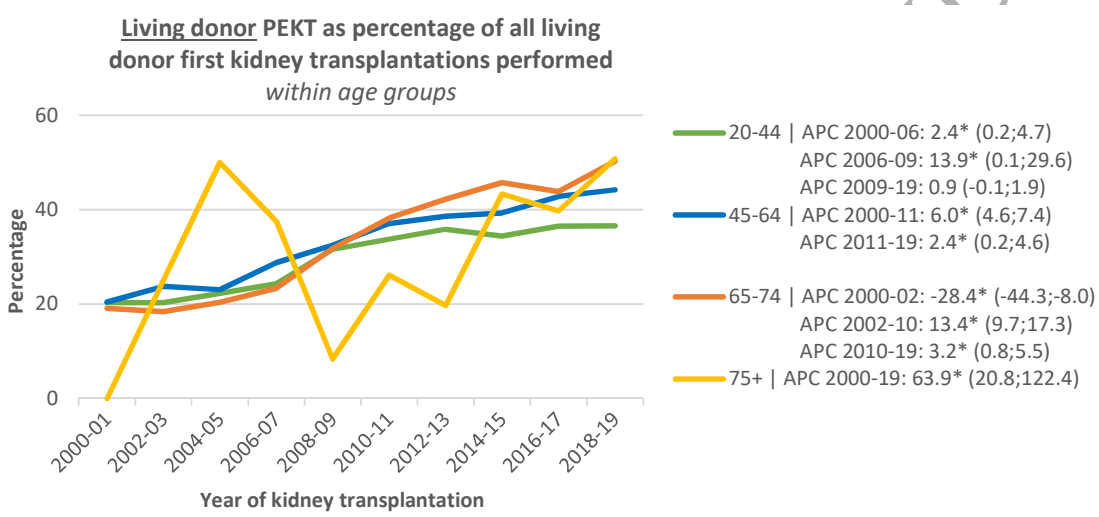


Figure 4) PEKT as percentage of all first kidney transplantations performed, by sex. Data is presented separately for all PEKT (upper panel), living donor PEKT (middle panel) and deceased donor PEKT (lower panel). The scale of the vertical axis differs by panel. The annual percent change (APC) reflects the trend over time. An asterisk (*) indicates whether the APC was statistically significant (p<0.05).

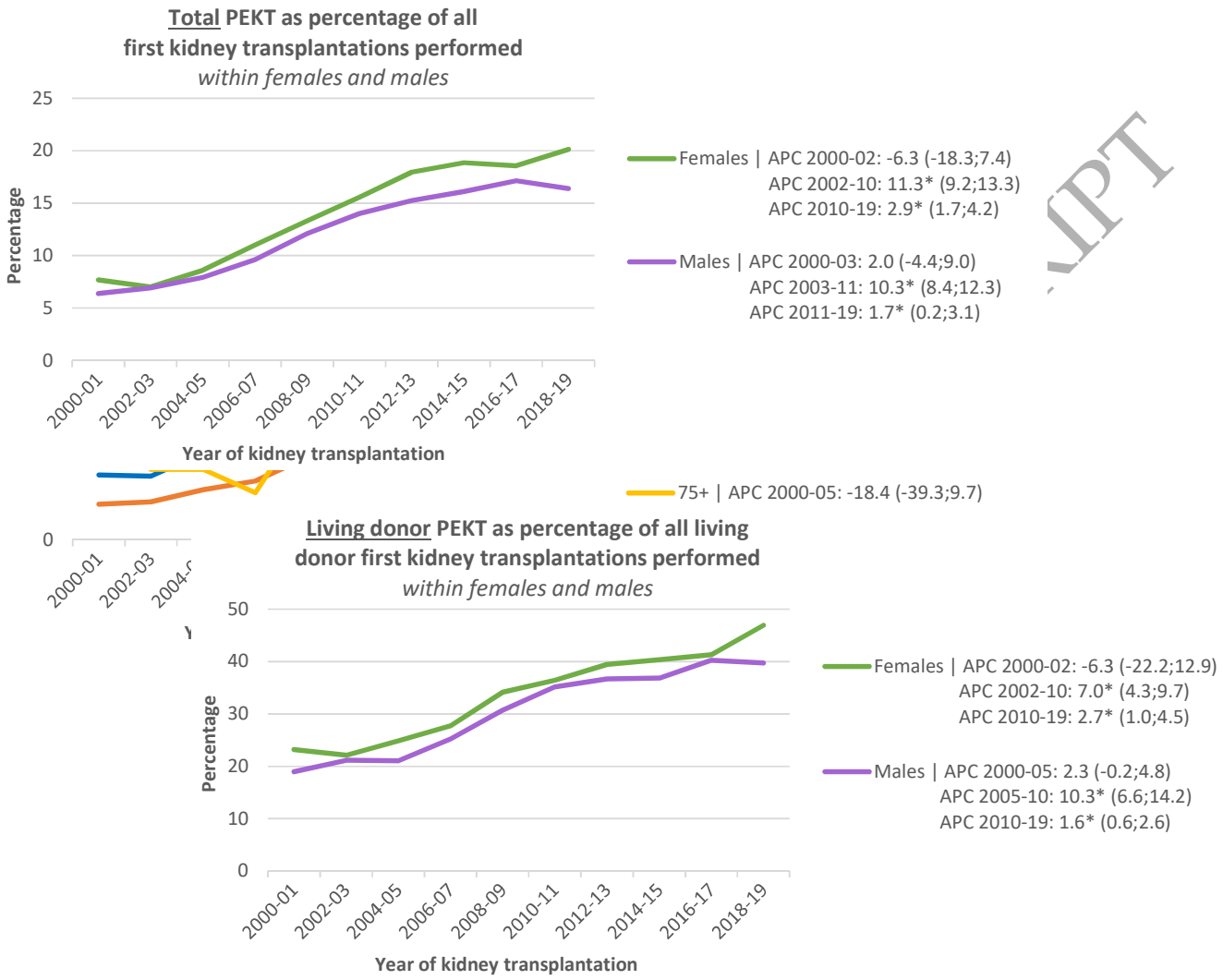


Figure 5) PEKT as percentage of all first kidney transplantations performed, by primary renal disease group. Data is presented separately for all PEKT (upper panel), living donor PEKT (middle panel) and deceased donor PEKT (lower panel). The scale of the vertical axis differs by panel. The annual percent change (APC) reflects the trend over time. An asterisk (*) indicates whether the APC was statistically significant (p<0.05).