ORIGINAL ARTICLE

Access to kidney transplantation in European adults aged 75–84 years and related outcomes: an analysis of the European Renal Association–European Dialysis and Transplant Association Registry

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SUMMARY

To what extent access to, and allocation of kidney transplants and survival outcomes in patients aged ≥75 years have changed over time in Europe is unclear. We included patients aged ≥75–84 years (termed older adults) receiving renal replacement therapy in thirteen European countries between 2005 and 2014. Country differences and time trends in access to, and allocation of kidney transplants were examined. Survival outcomes were determined by Cox regression analyses. Between 2005 and 2014, 1392 older adult patients received 1406 transplants. Access to kidney transplantation varied from ~0% (Slovenia, Greece and Denmark) to ~4% (Norway and various Spanish regions) of all older adult dialysis patients, and overall increased from 0.3% (2005) to 0.9% (2014). Allocation of kidney transplants to older adults overall increased from 0.8% (2005) to 3.2% (2014). Seven-year unadjusted patient and graft survival probabilities were 49.1% (95% confidence interval, 95% CI: 43.6; 54.4) and 41.7% (95% CI: 36.5; 46.8), respectively, with a temporal trend towards improved survival outcomes. In conclusion, in the European dialysis population aged ≥75–84 years access to kidney transplantation is low, and allocation of kidney transplants remains a rare event. Though both are increasing with time and vary considerably between countries. The trend towards improved survival outcomes is encouraging. This information can aid informed decision-making regarding treatment options.

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Introduction

The overall number of patients aged ≥75 years commencing renal replacement therapy (RRT) for end-stage renal disease (ESRD) in most European countries continues to grow [1]. In 2014, patients aged ≥75 years made up 29% of Europe's incident RRT patients and 21% of the prevalent RRT population [2]. The European Renal Association–European Dialysis and Transplantation Association (ERA-EDTA) and the European Union Geriatric Medicine Society recently included kidney transplantation among their topics of interest for inclusion in the new European guidelines on managing chronic kidney disease in older patients [3].

Most transplant guidelines do not consider older age *per se* as a contraindication to kidney transplantation [4–6]. Nevertheless within Europe, only 2.1% of kidney transplants performed in 2012 were allocated to patients aged ≥75 years [7]. Within the United States of America (USA) in 2014, the same percentage (2.1%) of kidney transplants performed in adults were allocated to those aged ≥75–84 years, having increased 10-fold from 0.18% in 1996 [8]. To what extent kidney transplant allocation in patients aged ≥75 years has changed over time in Europe is unclear.

Reports from the USA have shown an improved survival of kidney transplant recipients aged ≥75 years between the 1990s and 2000s [8,9]. Whilst a few European studies with small sample sizes have examined survival of older kidney transplant recipients [10–13], the prognosis of recipients aged ≥75 years in a large European cohort is lacking. Given the reported differences in patient characteristics and treatment outcomes between the USA and European kidney transplant recipients [14], one cannot predict patient outcomes in the European setting based on USA data. Knowledge of transplant outcomes in this age group is necessary for both healthcare professionals and potential recipients to make informed decisions regarding treatment options.

Using data from 13 European countries for patients aged ≥75–84 years receiving RRT over the past decade, we investigated trends in (i) access to kidney transplantation, (ii) kidney transplant allocation rates, (iii) the type of donor utilized for this age group and (iv) the prognosis of these recipients and their grafts.

Methods

The study population comprised prevalent patients aged ≥75–84 years (henceforth termed 'older adults') receiving RRT for ESRD between 2005 and 2014, from 25 national/regional renal registries supplying individual patient data to the ERA-EDTA Registry. These countries/regions were Austria, Dutch- and French-speaking Belgium, Denmark, Finland, France, Greece, Iceland, the Netherlands, Norway, Slovenia (2008–2013), the Spanish regions of Andalusia, Aragon, Asturias, Basque country, Catalonia, Cantabria, Castile-La Mancha, Castile and Leon, Extremadura, Galicia (from 2007), Madrid (from 2008), and Valencia, Sweden and Scotland. In 2014, all registries had 100% coverage of the general population in their region, accounting for 235 million Europeans (30% of the European population). Details of the methods used for data collection can be found in the ERA-EDTA Registry Annual Report [15]. In addition, 20 of the 25 registries with the available data provided details on donor age and deceased donor type (heart beating and nonheart beating donor).

We calculated the following trends:

1. Access to kidney transplantation among older adult patients receiving RRT

We defined access to kidney transplantation as the number of transplants performed in older adult patients per calendar year, divided by the number of prevalent older adult dialysis patients on the 31st December of that year.

2. Allocation of kidney transplants to older adult patients

This was defined as the number of kidney transplants performed in older adult patients per calendar year divided by the total number of transplants performed in adults (≥20 years) in the year in question.

3. Age and type of donor utilized in transplanting older adult patients

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For the above three analyses, we included first and subsequent kidney transplants from a living or deceased donor. Analyses were performed separately by country/region, and for all countries/regions combined. For all countries/regions combined, we examined time trends in kidney transplantation using Joinpoint regression [16]. The year was taken as the explanatory variable and the observed rate as the outcome. The annual percentage change (APC) was computed using Poisson's regression as provided by the Joinpoint regression program [17].

4. Patient and graft survival

Survival analyses were restricted to kidney transplant recipients who received their first transplant when aged ≥75–84 years, between 2005 and 2013. The survival time started with the date of transplantation and ended with the event of interest, a censored observation which included loss to follow-up, or with the end of the follow-up period (31 December 2014). For patient survival, the event of interest was patient death. For graft survival, there were two types of analyses; for death-censored graft survival, the event of interest was graft failure and the censored event was patient death with a functioning graft. For graft survival, both death with a functioning graft and graft failure were considered events of interest. The kidney transplant recipients were divided into three cohorts, based on the year of transplantation; cohort 1: 2005–2007, cohort 2: 2008–2010, and cohort 3: 2011–2013.

Death and graft failure rates per 1000-patient years were calculated by dividing the total number of events (deaths or graft failure, respectively) by the total person-time at risk. Total person time at risk was calculated by summation of the individual survival times. The Kaplan-Meier method was used to calculate unadjusted survival probabilities and Cox regression analysis to compare adjusted survival probabilities. For the Cox regression analysis, we investigated the effect of the year of transplantation on the hazard of patient death, graft failure and graft failure censored for death. The transplant year 2009 was considered the reference year. Adjustments were made for country of transplantation, age at transplantation, primary renal disease, sex, dialysis vintage, donor age and donor type (living versus deceased donor). In addition, a competing risk analysis was performed whereby patient death was considered the event of interest and graft failure resulting in a return to dialysis or re-transplantation and loss to follow-up were considered competing events.

All analyses were performed using SAS software 9.4, R version 3.3.1 and Joinpoint 4.0.4 [17]. A *P*-value of less than 0.05 was considered statistically significant.

Results

Between 2005 and 2014, 1392 older adult patients received 1406 kidney transplants (Table S1). Ninety-six per cent ($N = 1331$) received a first kidney transplant, 4.1% ($N = 58$) a second and 0.2% ($N = 3$) a third. Fourteen patients received two transplants during the 10-year timeframe whilst aged ≥75–84 years. In 2014, the median age at transplantation was 77.0 years [interquartile range (IQR): 75.9–78.1]. Only 8.9% ($N = 125$) of the older adults were aged ≥80–84 years at the time of transplantation. In 2014, 71% of all transplant recipients were male, whereas 60% of the prevalent older adult dialysis population were male. There was no statistically significant change in the sex distribution of either group over time.

Of the 1331 first kidney transplant recipients, 8.3% ($N = 111$) received a pre-emptive transplant, with the majority (77.5%, $N = 86$) occurring during the years 2011–2014. Only 15% ($N = 17$) of pre-emptive transplants were from living donors. For the non-pre-emptive transplant recipients, the median dialysis time prior to the first transplant was 2.0 years (IQR: 1.20–3.40).

Access to kidney transplantation among older adult patients receiving RRT

The percentage of older adult patients on RRT for ESRD who received a kidney transplant, by country/region and overall, and by year 2005–2014, is shown in Table 1. Access to kidney transplantation was consistently highest in Norway (approximately 4% per year), and the Spanish regions of Aragon, Asturias, Castile-La Mancha and Madrid, whilst in Slovenia, Greece and Denmark, this was 0% or nearly 0%. For all countries/regions combined, access to kidney transplantation in older adult patients rose from 0.30% to 0.90% between 2005 and 2014 [APC: 13.9%, 95% confidence interval (95% CI): 11.5; 16.3].

Allocation of kidney transplants to older adult patients

Between 2005 and 2014, 1.8% of the 76 202 transplants performed in patients aged ≥20–84 years in these combined countries/regions were allocated to patients aged ≥75–84 years. Over the 10-year period, the proportion of kidneys allocated to older patients quadrupled from 0.8% in 2005 to 3.2% in 2014 (APC

Table 1. Percentage of prevalent dialysis patients aged ≥75–84 years on renal replacement therapy for end-stage renal disease who received a kidney transplant, by country/region and overall, and by year during 2005–2014. Where cells are empty data are unavailable.

	Year									
Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Austria	0.48	0.59	0.47	0.46	0.32	0.83	0.50	0.90	0.30	0.59
Belgium: Dutch-speaking	0.08	0.15	0.22	0.07	0.13	0.13	0.24	0.18	0.12	0.12
Belgium: French-speaking	0.00	0.00	0.00	0.11	0.22	0.32	0.21	0.31	0.39	0.29
Denmark	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.00
Finland	0.00	0.56	0.00	0.28	0.85	0.27	0.81	0.26	0.78	1.02
France	0.23	0.27	0.26	0.26	0.41	0.42	0.40	0.61	0.71	0.92
Greece	0.00	0.00	0.04	0.00	0.04	0.00	0.04	0.00	0.03	0.00
Iceland	0.00	0.00	0.00	0.00	0.00	5.00	0.00	0.00	0.00	0.00
Netherlands	0.75	0.15	0.50	0.26	0.75	0.72	0.75	1.12	1.10	1.02
Norway	2.70	3.34	1.89	2.77	2.88	2.07	4.99	4.06	2.97	3.76
Slovenia			0.00	0.00	0.00	0.00	0.00	0.00	0.00	
Spain: Andalusia	0.73	0.32	0.10	0.09	0.17	0.17	0.41	0.48	0.40	0.48
Spain: Aragon	0.56	1.14	1.60	0.50	2.05	1.86	2.46	2.35	2.67	2.73
Spain: Asturias	0.74	3.97	1.29	0.64	3.36	0.65	0.00	0.56	0.55	2.42
Spain: Basque	0.00	0.00	0.41	0.41	1.85	0.76	1.05	1.37	0.96	0.98
Spain: Catalonia	0.52	0.51	0.34	0.65	0.85	0.89	1.52	1.51	1.72	2.66
Spain: Cantabria	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Spain: Castile-La Mancha	0.76	2.12	2.11	1.31	0.65	0.97	2.63	1.66	2.19	0.72
Spain: Castile and Leon	0.54	0.26	0.46	0.00	0.44	0.88	1.27	1.07	2.56	2.55
Spain: Extremadura	0.00	0.00	0.00	1.43	0.63	0.59	0.00	0.00	0.00	0.52
Spain: Galicia			0.24	0.22	0.00	0.00	0.56	0.19	0.00	0.00
Spain: Madrid				3.07	2.79	2.96	1.92	2.10	2.59	3.70
Spain: Valencia	0.00	0.00	0.11	0.11	0.20	0.10	0.00	0.37	0.09	0.09
Sweden	0.00	0.00	0.21	0.31	0.00	0.31	0.00	0.92	0.20	0.80
UK: Scotland	0.26	0.00	0.26	0.48	0.24	0.44	0.90	0.23	0.45	0.69
All	0.30	0.31	0.29	0.36	0.49	0.49	0.56	0.67	0.70	0.90

16.3%, 95% CI: 13.4; 19.2; Table 2 and Tables S1 and S2), with a substantial variation seen across Europe. In the later years, 2–5% of all adult kidney transplantations in France, Norway, the Netherlands and Spain (when analysing all regions together and covering 87.5% of the Spanish population) were allocated to older adult RRT patients. Conversely, in Denmark, Greece and Slovenia, this was 0% or nearly 0% (Table 2). Overall the percentage of prevalent older adults (aged ≥75–84 years) receiving dialysis as a proportion of all adult dialysis patients (aged ≥20–84 years) increased from 26.3% in 2005 to 31.1% in 2014 (APC 1.8%, 95% CI: 1.4; 2.2; Table S3). Again this varied across the countries/regions, from 21.8% in Scotland (2014) to 41.8% in Dutch-speaking Belgium (2014). Norway was the only country where the percentage of prevalent older adults receiving dialysis as a proportion of all adult dialysis patients significantly declined over the 10-year time period.

Age and type of kidney donor utilized in transplanting older adult patients

Ninety-one per cent ($N = 1286$) of kidney transplants performed in older adult patients originated from deceased donors, 5.1% ($N = 71$) from living donors and 3.5% ($N = 49$) from unknown donor sources. For the majority of countries, all kidney allografts in this age group came from deceased donors (Fig. 1, left panel). Some countries transplanted kidneys from living donors; however, compared with the percentage of living donor kidney transplants performed in recipients aged ≥20–74 years in the same time period, even these countries had a comparatively low number of living donor transplants in older adult patients (Fig. 1, right panel). Over the 10-year period, the proportion of deceased donor transplants increased (APC 2.8%, 95% CI: 0.7; 5.0), whilst the percentage of living donor transplants appeared to decline (APC

Table 2. Percentage of transplants carried out in adults (≥20 years) which were performed in recipients aged ≥75–84 years, by country/region and overall and by year during 2005–2014. Where cells are empty, data are unavailable.

	Year									
Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Austria	1.1	1.3	0.9	1.3	0.8	2.2	1.1	2.1	0.8	1.6
Belgium: Dutch-speaking	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Belgium: French-speaking	0.0	0.0	0.0	0.6	1.1	1.7	1.0	1.6	2.2	1.8
Denmark	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0
Finland	0.0	1.0	0.0	0.7	1.8	0.6	1.8	0.5	1.7	1.8
France	0.6	0.8	0.8	0.9	1.6	1.8	1.7	2.6	3.1	3.9
Greece	0.0	0.0	0.4	0.0	0.6	0.0	0.5	0.0	0.6	0.0
Iceland	0.0	0.0	0.0	0.0	0.0	9.1	0.0	0.0	0.0	0.0
Netherlands	1.3	0.3	0.9	0.6	1.6	1.5	1.7	2.3	2.3	2.1
Norway	3.7	4.8	2.3	3.3	3.5	2.8	5.7	4.8	3.8	4.9
Slovenia				0.0	0.0	0.0	0.0	0.0	0.0	
Spain: Andalusia	1.9	0.8	0.3	0.3	0.5	0.6	1.2	1.3	1.2	1.3
Spain: Aragon	1.4	3.1	3.8	1.7	5.6	5.9	6.3	7.0	6.7	7.2
Spain: Asturias	2.1	9.2	3.6	2.5	10.9	2.3	0.0	2.0	1.9	7.8
Spain: Basque	0.0	0.0	0.9	0.9	4.8	1.7	2.7	3.4	1.9	2.4
Spain: Catalonia	1.3	1.5	0.9	1.7	2.2	2.7	3.7	3.8	4.9	6.5
Spain: Cantabria	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Spain: Castile-La Mancha	2.4	7.0	6.9	4.0	2.4	3.7	9.8	5.2	5.6	2.1
Spain: Castile and Leon	1.7	0.9	2.0	0.0	2.2	3.8	5.9	3.9	9.0	8.7
Spain: Extremadura	0.0	0.0	0.0	5.0	2.2	2.4	0.0	0.0	0.0	1.8
Spain: Galicia			1.0	0.8	0.0	0.0	2.1	0.7	0.0	0.0
Spain: Madrid				6.9	6.3	6.6	4.6	4.6	5.9	8.1
Spain: Valencia	0.0	0.0	0.5	0.5	1.0	0.5	0.0	1.8	0.4	0.5
Sweden	0.0	0.0	0.5	0.8	0.0	0.9	0.0	2.4	0.5	1.9
UK: Scotland	0.7	0.0	0.5	1.0	0.5	1.1	2.0	0.4	0.8	1.2
All	0.8	1.0	0.9	1.2	1.7	1.9	2.0	2.5	2.5	3.2

−5.8%, 95% CI: −14.7; 4.1). The median age of deceased donors rose by 10 years, from 67 years (IQR: 57; 73) in 2005 to 77 years (IQR: 70; 80) in 2014 (Fig. 2). There were too few living donors to examine annual trends. However, overall the median age of the living donors was lower than that of the deceased donors (60 years, IQR: 52; 71). The median age of deceased donors appeared to be higher in countries/regions with higher transplantation rates in the older adult age group (Table S4).

Patient and graft survival

Between 2005 and 2013, 1080 older adult patients received their first kidney transplant (Table 3). There were no significant differences in the characteristics of the three transplant cohorts. With each passing transplant cohort, the mortality rate per 1000-patient years declined, whereas the number of graft-failure events per 1000-patient years varied from 140.2 (95% CI: 115.1; 165.3) to 115.2 (95% CI: 96.5; 134.0), to 135.5 (95% CI: 113.6; 157.5) over the three time cohorts (Table 4). Seven-year patient survival probability was 48.0% (95% CI: 42.7; 53.0), graft survival probability was 41.3% (95% CI: 36.4; 46.2) and death-censored graft survival probability was 79.2% (95% CI: 75.0; 82.7; Fig. 3a–c, respectively). There was a trend towards improved adjusted patient and graft survival with each passing year (Fig. 4). The competing risk analysis for the outcome death-censored graft failure is presented in Fig. S1. The most common cause of death was infection (31.7%), followed by a cardiac cause (ischaemic heart disease, heart failure or cardiac arrest) or a cerebrovascular event (21.7%) and death from malignancy (11.3%). The cause of death was unknown for 15.8% of the kidney transplant recipients.

Discussion

Using data from 13 European countries, we found a limited access to and allocation of kidney

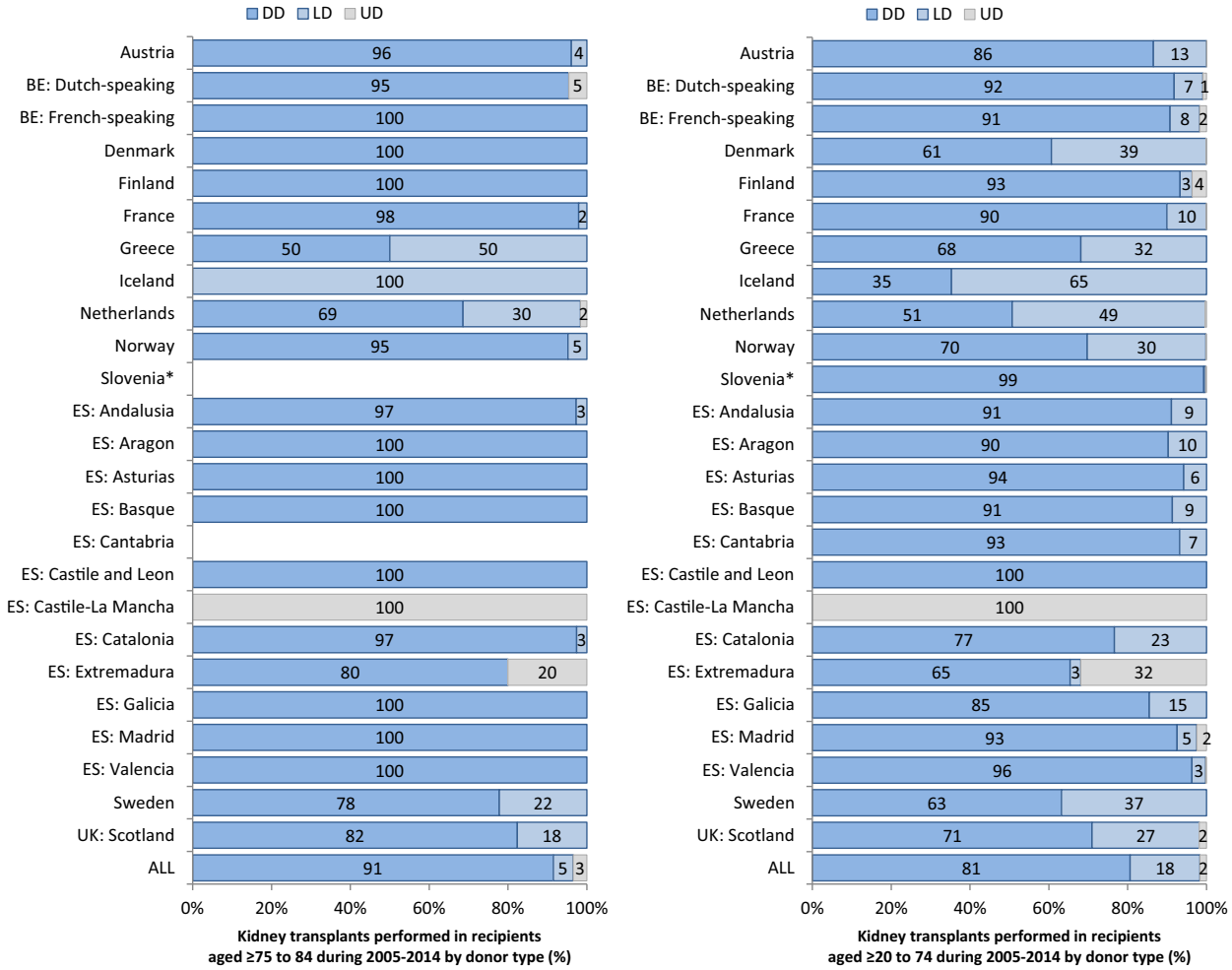


Figure 1 Percentage of kidney transplants performed in patients aged ≥75–84 (left panel) and ≥20–74 years (right panel) in 2005–2014, by donor type; deceased donor, living donor and unknown donor type. The absence of a bar indicates that no transplants were performed in this age group. *Data from Slovenia are for 2005–2013; data for Galicia are for 2007–2014; and data for Madrid are for 2008–2014. BE, Belgium; ES, Spain.

transplantation among older adult patients. Although the access to kidney transplantation and allocation of kidneys to older adult patients increased over time, both varied considerably between European countries. As the RRT population continues to age, the number of potential older adults eligible for kidney transplantation is likely to increase. Hence, the identification of time trends and international variation in access to kidney transplantation is an essential first step in finding explanations for the differences between countries. This is the largest European study on the prognosis of patients receiving a kidney transplant whilst aged ≥75–84 years. We found a trend towards improved patient and graft survival after the first year of transplantation. This information is important for both healthcare professionals and older adult patients with ESRD when considering kidney transplantation as a treatment modality.

Access to and allocation of kidney transplants to older adult patients is increasing but varies across countries

Within the European countries combined, access to kidney transplantation increased somewhat, from 0.3% of all prevalent older adults receiving RRT in 2005 to 0.9% in 2014. In comparison, this figure was 0.3% in 2005 and only 0.4% in 2014 in the USA [8]. Allocation of kidney transplants to this age group, although relatively rare, has increased over time, from 0.8% of all kidney transplants performed in adults (≥20 years) in 2005 to 3.2% in 2014. In the USA, the increase in the allocation of all kidney transplants performed in adults (≥18 years) increased modestly from 1.4% to 2.0% over the 10-year period [8].

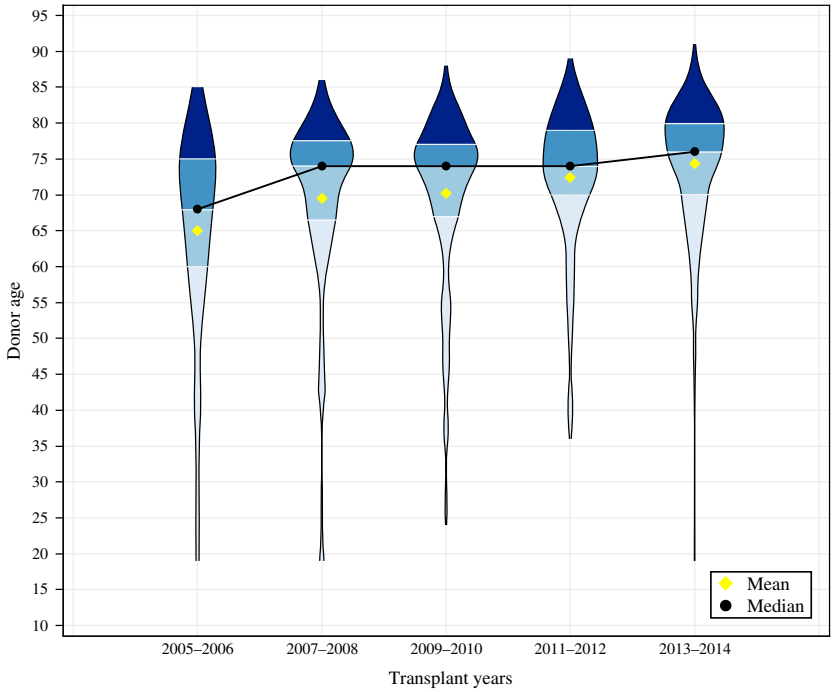


Figure 2 The age of deceased donors who donated a kidney, during 2005–2014 to prevalent patients on renal replacement therapy for end-stage renal disease, aged ≥75–84 years, presented by year of transplant. Donor age presented by median (black circle), mean (yellow diamond) and quartiles. Based on data from Austria, Denmark, Finland, France, Greece, Iceland, the Netherlands, Norway, the Spanish regions of Andalusia, Aragon, Asturias, Basque, Catalonia, Cantabria, Castile-La Mancha, Castile and Leon, Extremadura, Galicia (from 2007), Madrid (from 2008) and Scotland.

Table 3. Baseline characteristics of patients aged ≥75–84 years who received their first kidney transplant during 2005–2013, and the donor features, by transplant cohort.

	Cohort			
Characteristic	2005–2007	2008–2010	2011–2013	*P*-value
Number of recipients	205	333	542	
Male, %/*N*	68.8/141	66.1/219	68.3/368	0.74
Age at RRT onset, median (IQR)	74.7 (73.4, 76.2)	74.7 (73.1, 76.4)	75.0 (73.4, 76.6)	0.29
Age at transplantation, median (IQR)	76.3 (75.6, 78.0)	76.8 (75.8, 78.0)	76.9 (75.8, 78.3)	0.70
Dialysis time, median (IQR)	1.8 (0.97, 3.0)	2.0 (1.1, 3.3)	1.8 (0.9, 3.2)	0.23
Primary renal disease, %/*N*				
Diabetes mellitus type I & II	15.6/32	13.2/44	12.0/65	0.30
Hypertension/renovascular disease	26.3/54	26.7/89	28.2/153	
Glomerulonephritis/sclerosis	19.0/39	17.1/57	12.9/70	
Other	36.6/75	41.4/138	45.0/244	
Missing	2.4/5	1.5/5	1.9/10	
Initial RRT modality, %/*N*				
Haemodialysis	71.2/146	76.6/255	71.4/387	<0.001
Peritoneal dialysis	15.6/32	10.8/36	15.7/85	
Kidney transplant	4.9/10	5.1/17	9.6/52	
Missing	8.3/17	7.5/25	3.3/18	
Donor type, %/*N*				
Living donor	5.4/11	5.1/17	4.8/26	0.03
Deceased donor	86.8/178	92.5/308	91.5/496	
Unknown donor	7.8/16	2.4/8	3.7/20	
Donor age, median (IQR)				
Living donor	67.5 (55.0, 74.0)	59.0 (25.0, 66.0)	60.0 (47.0, 71.0)	0.24
Deceased donor	71.0 (61.0, 76.0)	74.0 (68.0, 78.0)	75.0 (70.0, 79.0)	<0.001
% Missing (*N*)	19.7 (34)	10.5 (35)	7.9 (43)	

RRT, renal replacement therapy.

Table 4. Death and graft failure rates per 1000-patient years with the 95% confidence interval (95% CI) for patients aged ≥75–84 years who received their first kidney transplant during 2005–2013, by transplant cohort.

	2005–2007	2008–2010	2011–2013
Number of recipients	205	333	542
Patient death			
Number of death events	111	118	94
Total person-time at risk (years)	939.9	1400.9	1182.7
Death rate per 1000-patient years (95% CI)	118.1 (96.1; 140.1)	84.2 (69.0; 99.4)	79.5 (63.4; 95.5)
Graft failure			
Number of graft failure events	120	145	146
Total person-time at risk (years)	856.0	1258.2	1077.2
Graft failure rate per 1000-patient years (95% CI)	140.2 (115.1; 165.3)	115.2 (96.5; 134.0)	135.5 (113.6; 157.5)

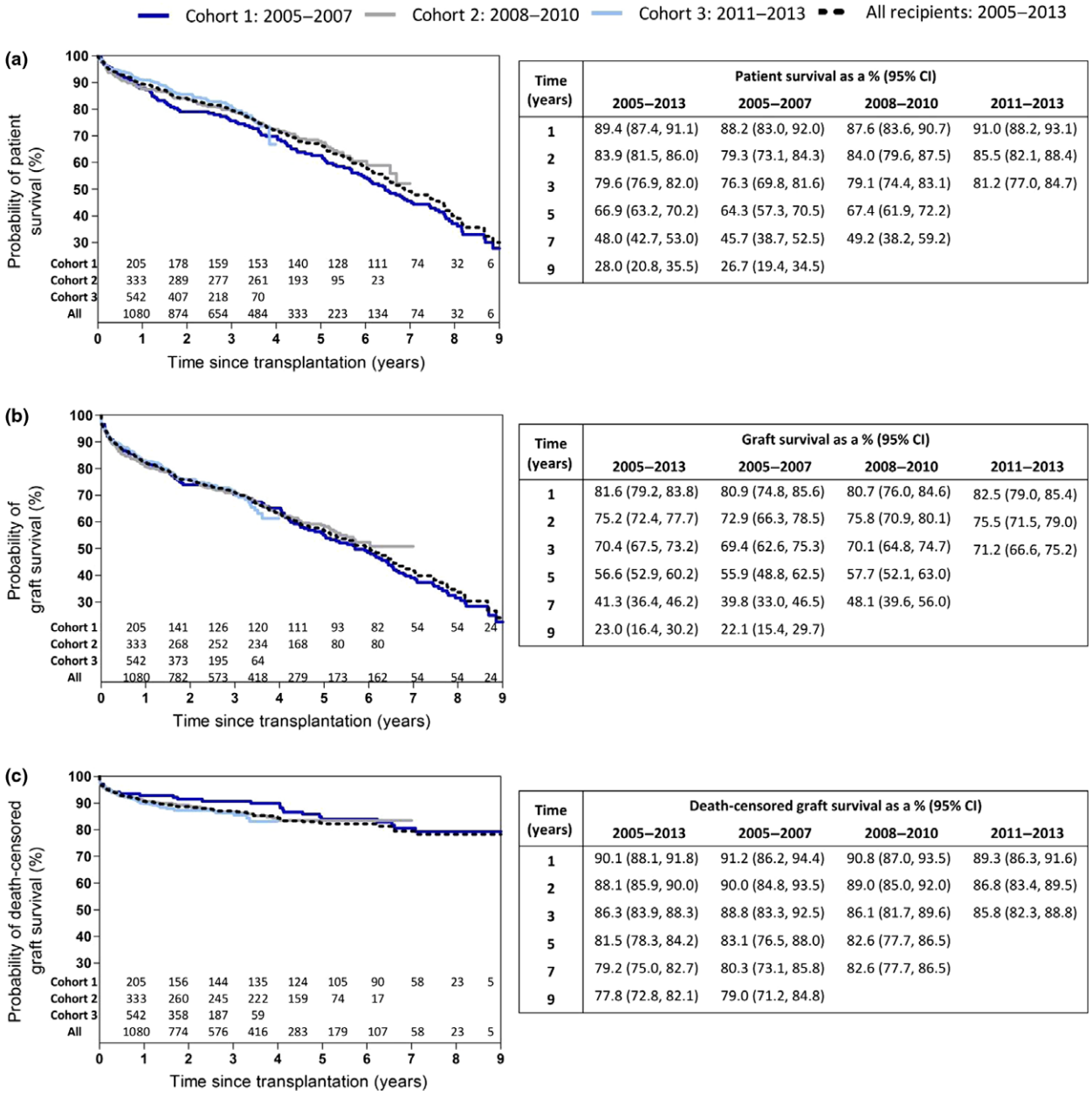
A striking finding of this study is the substantial variation in the access to and allocation of kidneys to older adult patients across Europe. For example, in Norway, where the access to transplantation was highest, 3–4% of prevalent older adult dialysis patients received a kidney transplant each year, whereas in the neighbouring Scandinavian countries, this was only 0–1% per year. Possible explanations for this variation include differences between countries in attitudes towards dialysis and kidney transplantation in the older adult, both among healthcare professionals and patients, country-specific healthcare expenditures, organ allocation policies and the number of available kidneys from older donors. The Eurotransplant Senior Program is a strategy aimed at increasing kidney transplantation rates in older adults [18]. Organs from deceased donors aged >65 years are allocated without human leukocyte antigen (HLA) matching to potential recipients aged >65 years, thereby simultaneously increasing the donor pool for older and younger patients. Although active since 1999 in four countries included in this study [Austria, Dutch- and French-speaking Belgium, Slovenia (since 2000) and the Netherlands], the percentage of older adults receiving a deceased donor kidney transplant varied between these countries. Therefore, the difference cannot, in this case, be explained exclusively by a relative shortage of kidneys from older deceased donors or differences in national allocation policies. It is well-known that even within countries such as Spain, which has one of the highest organ transplantation rates overall, regional differences do exist [19]. In this study, we noted a substantial difference in access to and the allocation of kidney transplants in older adults among the regions of Spain, suggesting that access to transplantation in older adult patients may also vary within a country despite having the same allocation policy.

The differences may also lie with the attitudes towards transplantation in general, and transplanting older adults in particular. For example, whilst Greece has one of the highest incidences of RRT in Europe for both young and older patients, the deceased donor kidney transplantation rates are among the lowest in Europe for both young and old individuals [7]. Limited education among healthcare professionals about organ donation and poor media interest have been suggested as possible causes for the low uptake of organ donation [20,21]. In the United Kingdom, the Netherlands and the USA, a systematic review reported that nephrologists recommending transplantation to patients aged >60 years varied from 10% to 59% [22].

It should be noted that access to kidney transplantation in this study reflects the proportion of older adults from the older adult dialysis population receiving a transplant. However, the incidence and the prevalence of older adults receiving dialysis vary between countries [7]. The greater the percentage of patients receiving a kidney transplant may therefore reflect a lower incidence of RRT within a country or a lower percentage of prevalent older adults as a proportion of the adult dialysis population. Furthermore, given our definition of access to kidney transplantation, we do not account for the proportion of older adult patients listed on the kidney transplant waiting list (as these data were unavailable to us). It is likely that this also varies substantially between countries and will play a role in the subsequent allocation of kidney transplants to this age group.

The majority of allografts utilized in this age group are from old deceased donors

The vast majority of kidney allografts were from deceased donors, even in countries with traditionally



Time (years)	Patient survival as a % (95% CI)			
	2005–2013	2005–2007	2008–2010	2011–2013
1	89.4 (87.4, 91.1)	88.2 (83.0, 92.0)	87.6 (83.6, 90.7)	91.0 (88.2, 93.1)
2	83.9 (81.5, 86.0)	79.3 (73.1, 84.3)	84.0 (79.6, 87.5)	85.5 (82.1, 88.4)
3	79.6 (76.9, 82.0)	76.3 (69.8, 81.6)	79.1 (74.4, 83.1)	81.2 (77.0, 84.7)
5	66.9 (63.2, 70.2)	64.3 (57.3, 70.5)	67.4 (61.9, 72.2)	
7	48.0 (42.7, 53.0)	45.7 (38.7, 52.5)	49.2 (38.2, 59.2)	
9	28.0 (20.8, 35.5)	26.7 (19.4, 34.5)		

Time (years)	Graft survival as a % (95% CI)			
	2005–2013	2005–2007	2008–2010	2011–2013
1	81.6 (79.2, 83.8)	80.9 (74.8, 85.6)	80.7 (76.0, 84.6)	82.5 (79.0, 85.4)
2	75.2 (72.4, 77.7)	72.9 (66.3, 78.5)	75.8 (70.9, 80.1)	75.5 (71.5, 79.0)
3	70.4 (67.5, 73.2)	69.4 (62.6, 75.3)	70.1 (64.8, 74.7)	71.2 (66.6, 75.2)
5	56.6 (52.9, 60.2)	55.9 (48.8, 62.5)	57.7 (52.1, 63.0)	
7	41.3 (36.4, 46.2)	39.8 (33.0, 46.5)	48.1 (39.6, 56.0)	
9	23.0 (16.4, 30.2)	22.1 (15.4, 29.7)		

Time (years)	Death-censored graft survival as a % (95% CI)			
	2005–2013	2005–2007	2008–2010	2011–2013
1	90.1 (88.1, 91.8)	91.2 (86.2, 94.4)	90.8 (87.0, 93.5)	89.3 (86.3, 91.6)
2	88.1 (85.9, 90.0)	90.0 (84.8, 93.5)	89.0 (85.0, 92.0)	86.8 (83.4, 89.5)
3	86.3 (83.9, 88.3)	88.8 (83.3, 92.5)	86.1 (81.7, 89.6)	85.8 (82.3, 88.8)
5	81.5 (78.3, 84.2)	83.1 (76.5, 88.0)	82.6 (77.7, 86.5)	
7	79.2 (75.0, 82.7)	80.3 (73.1, 85.8)	82.6 (77.7, 86.5)	
9	77.8 (72.8, 82.1)	79.0 (71.2, 84.8)		

Figure 3 Probability of patient survival (a), graft survival (b), and death-censored graft survival (c) in patients aged ≥75–84 years who received their first kidney transplant in 2005–2013 and by transplant cohort.

high living donor rates such as the Netherlands and Norway. This could reflect a patient's and/or clinician's apprehension of placing undue risk on either a younger (i.e. offspring) or older (i.e. spouse/partner) donor to surgery for the benefit of an older adult patient. Only 5% of all renal allografts transplanted in this age group were from living donors (8.5% at best, assuming all unknown donor types were living donors). This is in stark contrast to the USA where 20% of renal allografts transplanted in this age group were from living donors [8]. The difference in the practice of utilizing living kidney donors between Europe and the USA is well-known [23]. Although still relatively small, the number of living donor kidney transplants in patients >65 years in the USA has been slowly increasing [24]. In our study, the number of kidney grafts from living donors transplanted into older adult patients appeared to decrease. The outcomes of older, that is ≥70 years, living donor renal allografts in older recipients have been shown to be equivalent to those from standard criteria donors (SCD) aged 50–59 years [25]. Therefore, clinically, the greater utilization of older living donors may

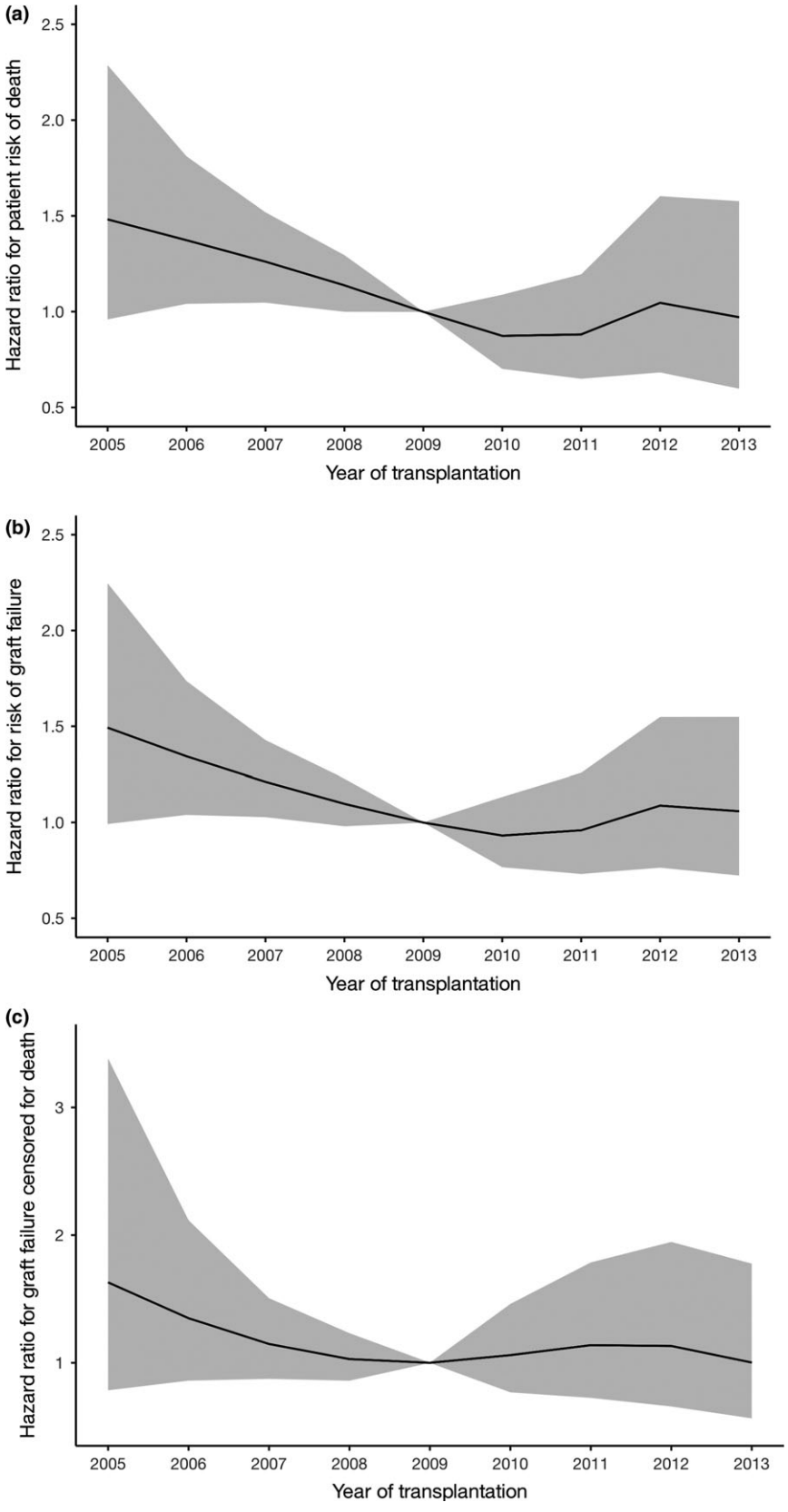


Figure 4 Effect of transplant year on the hazard of patient death (a), graft failure (b) and death-censored graft failure (c), with 95% confidence bands for patients aged ≥75–84 years receiving their first kidney transplant between 2005 and 2013, and adjusted for country of transplantation, age at transplantation, sex, primary renal disease, dialysis vintage, and donor age and type (living versus deceased donor). The year 2009 was taken as the reference year.

prove a useful for increasing the access to transplantation in this age group.

Deceased kidney donors utilized in this age group are getting older

During the study period, the median age of the deceased kidney donors rose from 67 to 77 years. This may well reflect the increased acceptance of utilizing extended criteria donor (ECD) kidneys, which by definition includes all donors aged >60 years. Patients aged ≥65 years who accept an ECD kidney within 2 years of commencing dialysis have a slightly longer life expectancy compared with their counterparts waiting for a SCD or a living donor kidney [26]. For patients aged >70 years, there is no relative survival benefit from medium compared with low-quality kidneys [27]. Furthermore, in recipients >70 years, ECD kidneys are not significant predictor of death or graft loss [28]. In clinical practice, reducing the time spent on dialysis with a kidney transplant from either an older living donor or an ECD may reduce mortality in this age group. Although the median time on dialysis prior to the first kidney transplantation in this study did not change, 77% of the pre-emptive transplants occurred in the last 4 years, which in future may translate to improved survival.

Survival of older kidney transplant recipients may well be improving, although death-censored graft survival remains unchanged

The trend towards improved post-transplant patient and graft survival over the past decade observed in this study is consistent with outcomes seen in older transplant recipients in the USA [9] and in younger recipients in Europe [1]. Although this remains, to our knowledge, the largest analysis of transplant outcomes in older adult European recipients, the relatively small sample size may explain the statistically nonsignificant trends. Of the older patients who received a kidney transplant during 2005–2013, the 2-year patient survival was 84%. This finding is in line with studies from the USA where the reported 2-year probability of patient survival in recipients aged ≥70–79 years and transplanted in 2000–2008 was 85%, whereas the 2-year patient survival in those ≥80 years was lower at 74% [29]. In comparison with graft failure rates, death-censored graft survival rates were very high, indicating that these patients are dying with a functioning graft as a result of their age and/or comorbidities or transplant-related complications.

The main strength of this study is the inclusion of 13 European countries, with coverage of 235 million individuals, over a 10-year time period in the analysis of kidney transplantation rates, donor sources and survival outcomes of kidney transplantation, which is a rare event in the older RRT population. By contrast, the study is limited by the lack of information regarding comorbidities and, most importantly, transplant waiting list status, donor-related factors, such as cause of death, and transplant-related factors, including HLA-match, immunosuppression regimes and acute rejection episodes which have been shown to influence survival outcomes [30]. As patient selection patterns and immunosuppression regimes are likely to vary between transplant centres, the survival outcomes will vary at the transplant centre level; therefore, these results cannot be considered generalizable to all older adult patients. In this study, we defined access to kidney transplantation as the number of patients receiving a transplant as opposed to the number of wait-listed patients, with the former dependent on the number of available donors. As the number of available donors in countries will vary, our definition is not the ideal approach for country comparisons. However, without access to kidney transplant waiting list data, we can only provide this type of comparison. It should be noted, however, that being defined as having access to the waiting list is not what patients would consider most important; it is actually receiving a kidney transplant. Furthermore, without access to waiting list data, we were unable to compare survival outcomes between older adult transplant recipients and those receiving dialysis whilst listed on the kidney transplant waiting list. Knowledge of survival outcomes of patients receiving these different RRT modalities aid informed decision-making regarding treatment options.

Conclusion

Over the past 10 years, the frequency with which the European RRT population aged ≥75–84 years had access to and were allocated allografts increased. Despite this, kidney transplantation in this older adult age group remains a rare event whose occurrence varies considerably across Europe because of known and unknown reasons. The trend towards improved patient and graft survival is encouraging. Changes in clinical practice policies, such as reducing pretransplant dialysis time by performing an early transplantation using an older living donor kidney or eliminating pretransplant dialysis

altogether by carrying out a pre-emptive transplant, may over time further improve patient survival. However, it should be kept in mind that the older adult RRT population in this study are a very select group of individuals. It is vital that older patients are only transplanted when they are likely to benefit from the procedure, and therefore, prediction models identifying which older RRT patients will benefit from kidney transplantation are warranted.

Authorship

MP: participated in research design, data analysis and in the writing of the manuscript, she is the guarantor. VSS and KJJ: participated in research design and in the writing of the manuscript. AK: participated in data analysis and in the writing of the manuscript. JMAD, NA-F, CA, JB, FC, CC, JDM, JGH, IH, MHH, MK, JP, RP, AVR and JPT: supplied data for the study and participated in the writing of the manuscript. FJC, MN and ZM: participated in the writing of the manuscript.

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Conflicts of interest

The authors have declared no conflicts of interest.

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Affiliated registries

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Transparency declarations

All authors declare not receiving support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

The results presented in this manuscript have not been published previously in whole or part, except in abstract format.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article:

Figure S1 Cumulative risk of graft failure from all causes (i.e. graft failure and death) for patients aged

≥75–84 years who received their first kidney transplant between either 2005–2007 (cohort 1, 10-year follow-up), 2008–2010 (cohort 2, 7-year follow-up) and 2011–2013 (cohort 3, 4-year follow-up).

Table S1. Number of prevalent patients aged ≥75–84 years on dialysis for end-stage renal disease, who received a kidney transplant, by country/region and overall, and by year during 2005–2014.

Table S2. Number of prevalent patients aged ≥75–84 years on dialysis for end-stage renal disease, by country/region and overall, and by year during 2005–2014.

Table S3. Percentage of prevalent patients aged ≥75–84 years on dialysis for end-stage renal disease expressed as a percentage of all adult dialysis patients aged ≥20–84 years, and the annual percentage change (APC) with 95% confidence interval (95% CI) by country/region and overall, and by year between 2005 and 2014.

Table S4. The median age and interquartile range (IQR) of deceased donors for recipients of kidney transplants aged ≥75–84 years performed between 2005 and 2014, by country/region.

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