

A Kidney Graft Survival Calculator that Accounts for Mismatches in Age, Sex, HLA, and Body Size

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Abstract

Background and objectives Outcomes for transplants from living unrelated donors are of particular interest in kidney paired donation (KPD) programs where exchanges can be arranged between incompatible donor-recipient pairs or chains created from nondirected/altruistic donors.

Design, setting, participants, & measurements Using Scientific Registry of Transplant Recipients data, we analyzed 232,705 recipients of kidney-alone transplants from 1998 to 2012. Graft failure rates were estimated using Cox models for recipients of kidney transplants from living unrelated, living related, and deceased donors. Models were adjusted for year of transplant and donor and recipient characteristics, with particular attention to mismatches in age, sex, human leukocyte antigens (HLA), body size, and weight.

Results The dependence of graft failure on increasing donor age was less pronounced for living-donor than for deceased-donor transplants. Male donor-to-male recipient transplants had lower graft failure, particularly better than female to male (5%–13% lower risk). HLA mismatch was important in all donor types. Obesity of both the recipient (8%–18% higher risk) and donor (5%–11% higher risk) was associated with higher graft loss, as were donor-recipient weight ratios of <75%, compared with transplants where both parties were of similar weight (9%–12% higher risk). These models are used to create a calculator of estimated graft survival for living donors.

Conclusions This calculator provides useful information to donors, candidates, and physicians of estimated outcomes and potentially in allowing candidates to choose among several living donors. It may also help inform candidates with compatible donors on the advisability of joining a KPD program.

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Introduction

Graft survival after kidney transplantation is of considerable interest to donors, candidates, health professionals, and payers. We examine the donor and recipient characteristics that are associated with graft survival for transplants from living related (LR), living unrelated (LUR), and deceased donors (DD), and develop models that are useful in estimating outcomes on the basis of these characteristics.

It is well known that characteristics of both donors and recipients are related to outcomes and there have been numerous studies that examine these relationships, especially with regard to donor and recipient age and human leukocyte antigen (HLA) mismatch (MM). Except for HLA MM, previous studies have generally considered donor and candidate characteristics separately, and most studies have been confined to either DDs or living donors (LDs) (1–21). A pediatric study reported on differences in graft survival for all three types of donors, but did not examine other factors (22). On the basis of a 15-year time period, we examine graft survival as a function of donor and recipient age, sex, HLA MM, and body size with an emphasis on the outcome's possible dependence

on MMs between donors and recipients. These results are used to develop a calculator that estimates the probabilities of graft survival at 5 and 10 years on the basis of recipient and donor characteristics. This study was partially motivated by consideration of kidney paired donation (KPD) programs, where all transplants are from LUR donors (23–26). This provides useful information to candidates, donors, and physicians, but has particular possible benefit in helping to guide decisions, where, for example, a candidate might have the opportunity to choose between several LDs, or a candidate with a compatible LD might join a KPD program to find another donor predicted to yield better post-transplant outcomes. The incorporation of compatible pairs in a KPD program can also be beneficial to other candidates in the program (25,26).

Materials and Methods

This study used data on a 15-year cohort of 232,705 kidney-alone transplant recipients from 1998 to 2012 from the Scientific Registry of Transplant Recipients (SRTR). The SRTR system includes data on all donors, wait-listed candidates, and transplant recipients in the

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United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight to the activities of its OPTN and SRTR contractors.

Analyses were performed separately for three donor types: LR, LUR, and DD. Transplants were considered to be LR if there was a biologic relationship between the donor and recipient. LD transplants with a pediatric donor or an unknown relationship between donor and recipient were excluded ($n=97$). Five- and 10-year rates of graft failure were estimated for transplants from 32,349 LUR donors, 56,660 LR donors, and 143,696 DD. The origin for analysis was the time of transplant and the event of interest was the first of graft failure or death. Patients were censored at December 31, 2013 or at loss to follow-up. All models were adjusted for transplant year, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, insurance, recipient and donor race and ethnicity, donor history of cigarette use, and the following donor-recipient combinations: age, sex, obesity status (body mass index ≥ 30), weight ratio, height ratio, HLA MM, and ABO compatibility. These models concentrate attention on the potential association with MM between donor and recipient and, in so doing, account for interactions between donor and recipient characteristics. Results are presented in terms of hazard ratios (HR) and 5- or 10-year graft survival rates and are on the basis of the Cox model (27). For a given donor and recipient, these models inform a calculator that estimates the probability of surviving with a functioning graft 5 and 10 years post-transplant. For 10-year outcomes in the calculator, the Cox model was stratified into two time segments from 0 to 5 years and 5 to 10 years with separate

relative risk parameters for each segment. The 10-year graft survival probability given by the calculator is the product of the probability of graft survival for the first 5 years with the probability of survival for the second 5 years given the first.

Results

Figure 1 shows the probability of graft failure at 5 years for each donor type and transplant year from 1998 to 2008. Among transplants performed from 1998 to 2000, the average 5-year graft failure was 33%, 21%, and 20% for DD, LUR, and LR transplant recipients, respectively. For transplant recipients from 2006 to 2008, these average failure probabilities were substantially reduced to 28%, 16%, and 15%, respectively. It is important to account for this trend in the models and in the calculator developed in this paper.

Table 1 presents the counts, distribution, and comparative risks of graft failure for the first 5 post-transplant years on the basis of separate models for three donor groups, LUR, LR, and DD. Results concentrate on five characteristics of particular interest that relate to donor/recipient MM: age, sex, HLA differences, body mass index, and weight.

Age

Table 1 shows that the distributions of both recipient and donor age differ across the three donor types, although the recipient age distributions for LUR donors and DDs are similar. For all three classes of donors, the risk of graft failure is higher within the 13–17, 18–29, and 60+ years recipient age categories. Tables 2–5 show the estimated probability of graft failure at 5 and 10 years by donor-recipient age groups for LD and DD transplant recipients.

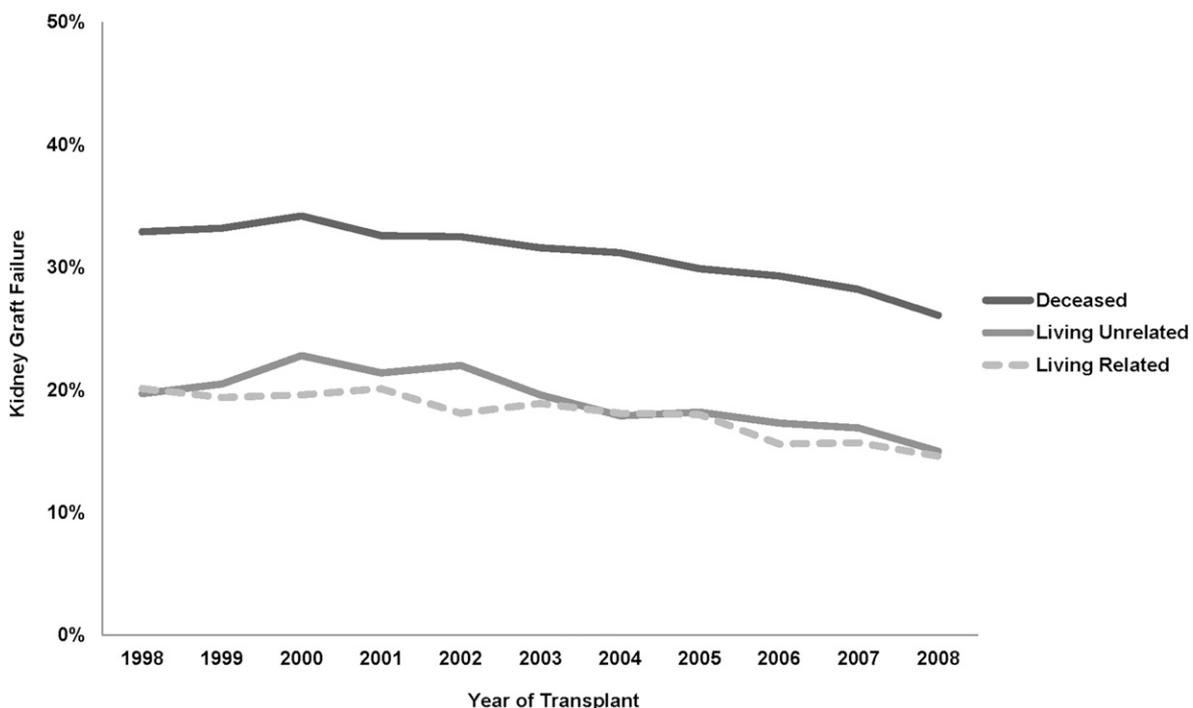


Figure 1. | Trends in the unadjusted probability of graft failure at 5 years for deceased donor, living unrelated donor, and living related transplant recipients, 1998–2008. Graft failure probabilities shown for years in which five years of followup is available.

Table 1. Adjusted risk of graft failure at 5 years by characteristic for each transplant donor type for transplants from 1998 to 2012

Characteristic ^a	LUR Donor (n=32,349)		LR Donor (n=56,660)		Deceased Donor (n=143,696)	
	N (%)	HR (95% CI)	N (%)	HR (95% CI)	N	HR (95% CI)
Recipient age, yr						
<13	316 (1)	1.12 (0.77 to 1.63)	2594 (5)	1.01 (0.88 to 1.16)	2791 (2)	1.40 (1.28 to 1.54)
13-17	304 (1)	2.49 (1.93 to 3.21)	2123 (4)	2.02 (1.80 to 2.26)	3454 (2)	2.05 (1.90 to 2.20)
18-29	2577 (8)	1.72 (1.53 to 1.94)	9104 (16)	1.59 (1.48 to 1.72)	9461 (7)	1.48 (1.41 to 1.55)
30-39	5384 (17)	1.11 (1.00 to 1.23)	9818 (17)	1.10 (1.02 to 1.19)	18,601 (13)	1.10 (1.06 to 1.14)
40-49	8709 (27)	1.00 (Ref)	11,019 (19)	1.00 (Ref)	29,918 (21)	1.00 (Ref)
50-59	9031 (28)	1.08 (0.99 to 1.18)	11,853 (21)	1.10 (1.02 to 1.18)	39,454 (28)	1.12 (1.09 to 1.16)
60+	6028 (19)	1.57 (1.43 to 1.73)	10,149 (18)	1.39 (1.29 to 1.50)	40,017 (28)	1.46 (1.41 to 1.51)
Donor age, yr						
<18	—	—	—	—	18,812 (13)	0.78 (0.75 to 0.81)
18-29	4141 (13)	0.88 (0.80 to 0.98)	12,609 (22)	0.89 (0.84 to 0.95)	33,500 (23)	0.76 (0.73 to 0.79)
30-39	7845 (24)	0.93 (0.85 to 1.01)	17,090 (30)	0.92 (0.87 to 0.98)	20,835 (15)	0.84 (0.81 to 0.87)
40-49	10,448 (32)	1.00 (Ref)	16,472 (29)	1.00 (Ref)	30,744 (21)	1.00 (Ref)
50-59	7698 (24)	1.14 (1.05 to 1.24)	8691 (15)	1.07 (1.00 to 1.14)	27,289 (19)	1.20 (1.17 to 1.24)
60+	2217 (7)	1.38 (1.23 to 1.56)	1798 (3)	1.42 (1.26 to 1.59)	12,516 (9)	1.52 (1.46 to 1.58)
Donor-recipient sex						
Female-female	5828 (18)	1.01 (0.92 to 1.11)	14,549 (26)	1.07 (1.00 to 1.14)	23,567 (16)	0.93 (0.89 to 0.96)
Male-female	5922 (18)	1.07 (0.96 to 1.19)	9371 (17)	1.03 (0.95 to 1.12)	33,227 (23)	0.94 (0.91 to 0.98)
Female-male	14,765 (46)	1.00 (Ref)	17,773 (31)	1.00 (Ref)	34,420 (24)	1.00 (Ref)
Male-male	5834 (18)	0.87 (0.79 to 0.95)	14,967 (26)	0.89 (0.83 to 0.95)	52,482 (37)	0.95 (0.92 to 0.98)
HLA ABDR mismatch						
0 MM	162 (1)	0.69 (0.42 to 1.12)	7869 (14)	0.62 (0.57 to 0.67)	15,171 (11)	0.83 (0.80 to 0.86)
1-2 MM, 0 DR MM	847 (3)	0.73 (0.59 to 0.91)	8512 (15)	0.93 (0.88 to 1.00)	5796 (4)	0.87 (0.82 to 0.92)
1-2 MM, 1-2 DR MM	993 (3)	0.85 (0.70 to 1.02)	10,308 (18)	0.95 (0.89 to 1.01)	6103 (4)	0.95 (0.90 to 1.00)
3-4 MM, 0 DR MM	1350 (4)	0.91 (0.77 to 1.06)	532 (1)	0.99 (0.79 to 1.24)	10,557 (7)	0.91 (0.87 to 0.95)
3-4 MM, 1-2 DR MM	12,149 (38)	1.00 (Ref)	23,413 (41)	1.00 (Ref)	44,692 (31)	1.00 (Ref)
5,6, missing MM	16,848 (52)	1.06 (1.00 to 1.13)	6026 (11)	1.06 (0.99 to 1.14)	61,377 (43)	1.08 (1.06 to 1.11)
Recipient BMI (kg/m²)						
Not obese (<30)	20,508 (63)	1.00 (Ref)	36,876 (65)	1.00 (Ref)	88,565 (62)	1.00 (Ref)
Obese (>30)	8637 (27)	1.18 (1.09 to 1.28)	12,112 (21)	1.15 (1.08 to 1.22)	37,269 (26)	1.08 (1.05 to 1.11)
Missing	3204 (10)	1.03 (0.89 to 1.19)	7672 (14)	1.17 (1.07 to 1.28)	17,862 (12)	0.93 (0.86 to 1.01)
Donor BMI						
Not obese (<30)	22,355 (69)	1.00 (Ref)	35,679 (63)	1.00 (Ref)	109,771 (76)	1.00 (Ref)
Obese (>30)	6307 (20)	1.11 (1.02 to 1.20)	10,948 (19)	1.05 (0.98 to 1.11)	33,268 (23)	1.07 (1.04 to 1.10)
Missing	3687 (11)	0.94 (0.78 to 1.13)	10,033 (18)	1.08 (0.95 to 1.22)	657 (1)	1.05 (0.90 to 1.22)
Donor-recipient weight ratio						
<0.75	6388 (20)	1.12 (1.01 to 1.25)	6526 (12)	1.09 (1.00 to 1.19)	30,333 (21)	1.12 (1.08 to 1.16)
0.75-0.90	6239 (19)	1.06 (0.96 to 1.16)	8568 (15)	0.98 (0.91 to 1.06)	23,538 (16)	1.04 (1.00 to 1.08)

Table 1. (Continued)

Characteristic ^a	LUR Donor (n=32,349)		LR Donor (n=56,660)		Deceased Donor (n=143,696)	
	N (%)	HR (95% CI)	N (%)	HR (95% CI)	N	HR (95% CI)
0.90–1.15	8113 (25)	1.00 (Ref)	14,951 (26)	1.00 (Ref)	35,606 (25)	1.00 (Ref)
>1.15	7606 (24)	1.09 (0.99 to 1.21)	16,193 (29)	0.97 (0.90 to 1.03)	43,162 (30)	1.00 (0.96 to 1.03)
Missing	4003 (12)	1.16 (0.99 to 1.36)	10,422 (18)	1.06 (0.95 to 1.18)	11,057 (8)	1.26 (1.18 to 1.35)
Donor-recipient height ratio						
<0.94	8480 (26)	1.13 (1.01 to 1.27)	8978 (16)	1.08 (0.99 to 1.18)	30,240 (21)	1.05 (1.02 to 1.09)
0.94–1.00	6851 (21)	1.02 (0.92 to 1.13)	11,053 (20)	1.00 (0.93 to 1.08)	29,183 (20)	1.00 (0.97 to 1.03)
1.00–1.06	6180 (19)	1.00 (Ref)	13,042 (23)	1.00 (Ref)	34,057 (24)	1.00 (Ref)
>1.06	5757 (18)	0.96 (0.86 to 1.07)	10,748 (19)	0.98 (0.91 to 1.07)	38,460 (27)	0.94 (0.91 to 0.98)
Missing	5081 (16)	1.04 (0.87 to 1.25)	12,839 (23)	0.91 (0.81 to 1.02)	11,756 (8)	1.11 (1.04 to 1.19)
Recipient race/ethnicity						
White	23,515 (73)	1.00 (Ref)	36,590 (65)	1.00 (Ref)	69,709 (49)	1.00 (Ref)
Black	3930 (12)	1.22 (1.09 to 1.38)	8863 (16)	1.28 (1.06 to 1.53)	43,656 (30)	1.15 (1.12 to 1.18)
Hispanic	3166 (10)	0.96 (0.83 to 1.10)	8391 (15)	0.85 (0.73 to 0.98)	20,065 (14)	0.79 (0.76 to 0.82)
Other	1738 (5)	0.82 (0.71 to 0.96)	2816 (5)	0.67 (0.59 to 0.76)	10,266 (7)	0.75 (0.71 to 0.78)
Donor race/ethnicity						
Not black or Hispanic	26,676 (83)	1.00 (Ref)	39,484 (70)	1.00 (Ref)	105,874 (74)	1.00 (Ref)
Black	2703 (8)	1.12 (0.97 to 1.28)	8708 (15)	1.10 (0.91 to 1.32)	18,700 (13)	1.24 (1.20 to 1.27)
Hispanic	2970 (9)	0.84 (0.73 to 0.97)	8468 (15)	0.91 (0.79 to 1.05)	19,122 (13)	1.02 (0.98 to 1.05)
Donor history of cigarette use						
No	15,537 (48)	1.00 (Ref)	20,611 (36)	1.00 (Ref)	6108 (4)	1.00 (Ref)
Yes	4917 (15)	1.09 (0.99 to 1.20)	6744 (12)	1.08 (0.99 to 1.17)	43,128 (30)	1.09 (1.04 to 1.15)
Missing	11,895 (37)	1.15 (1.05 to 1.26)	29,305 (52)	1.18 (1.10 to 1.27)	94,460 (66)	1.04 (0.99 to 1.10)
ABO compatibility						
Not incompatible	31,895 (99)	1.00 (Ref)	56,086 (99)	1.00 (Ref)	143,374 (100)	1.00 (Ref)
Incompatible	454 (1)	1.51 (1.22 to 1.87)	574 (1)	1.36 (1.11 to 1.66)	322 (0)	1.16 (0.94 to 1.43)
PRA						
0–9	26,473 (82)	1.00 (Ref)	47,022 (83)	1.00 (Ref)	111,404 (78)	1.00 (Ref)
10–79	4079 (13)	1.09 (0.99 to 1.20)	6408 (11)	1.11 (1.03 to 1.19)	21,784 (15)	1.11 (1.07 to 1.14)
80+	730 (2)	1.35 (1.12 to 1.63)	1321 (2)	1.45 (1.27 to 1.65)	8278 (6)	1.27 (1.21 to 1.34)
Missing	1067 (3)	0.87 (0.71 to 1.06)	1909 (3)	0.93 (0.81 to 1.07)	2230 (2)	1.22 (1.10 to 1.34)
Recipient diagnosis						
Not diabetes	25,264 (78)	1.00 (Ref)	45,337 (80)	1.00 (Ref)	110,370 (77)	1.00 (Ref)
Diabetes	7085 (22)	1.32 (1.23 to 1.41)	11,323 (20)	1.30 (1.23 to 1.37)	33,326 (23)	1.27 (1.24 to 1.30)
Previous transplant						
No	28,584 (88)	1.00 (Ref)	51,219 (90)	1.00 (Ref)	125,104 (87)	1.00 (Ref)
Yes	3765 (12)	1.41 (1.29 to 1.55)	5441 (10)	1.16 (1.08 to 1.25)	18,592 (13)	1.19 (1.15 to 1.23)

Table 1. (Continued)

Characteristic ^a	LUR Donor (n=32,349)		LR Donor (n=56,660)		Deceased Donor (n=143,696)	
	N (%)	HR (95% CI)	N (%)	HR (95% CI)	N	HR (95% CI)
Time on dialysis						
Preemptive transplant	10,712 (33)	0.71 (0.65 to 0.77)	18,103 (32)	0.64 (0.60 to 0.68)	16,749 (12)	0.86 (0.82 to 0.90)
0–1 yr	8948 (28)	0.82 (0.75 to 0.89)	17,441 (31)	0.85 (0.80 to 0.91)	15,984 (11)	0.98 (0.94 to 1.02)
1–2 yr	5864 (18)	1.00 (Ref)	10,684 (19)	1.00 (Ref)	21,618 (15)	1.00 (Ref)
2–3 yr	2905 (9)	0.97 (0.86 to 1.08)	4681 (8)	0.99 (0.91 to 1.08)	22,147 (15)	1.03 (0.99 to 1.07)
3+ yr	3920 (12)	1.07 (0.96 to 1.18)	5751 (10)	1.05 (0.97 to 1.13)	67,198 (47)	1.12 (1.08 to 1.15)
Recipient hepatitis C serology						
Negative or missing	31,419 (97)	1.00 (Ref)	55,147 (97)	1.00 (Ref)	134,430 (94)	1.00 (Ref)
Positive	930 (3)	1.51 (1.31 to 1.74)	1513 (3)	1.46 (1.31 to 1.63)	9266 (6)	1.45 (1.40 to 1.51)
Recipient insurance						
Public primary payer	11,346 (35)	1.00 (Ref)	22,824 (40)	1.00 (Ref)	96,508 (67)	1.00 (Ref)
Private primary payer	20,184 (62)	0.77 (0.72 to 0.82)	31,892 (56)	0.80 (0.77 to 0.84)	42,478 (30)	0.82 (0.80 to 0.84)
Other/missing	819 (3)	0.83 (0.69 to 1.01)	1944 (3)	0.92 (0.81 to 1.03)	4710 (3)	0.94 (0.89 to 1.00)
Transplant year						
1998–2002	7013 (22)	1.00 (Ref)	19,810 (35)	1.00 (Ref)	40,977 (29)	1.00 (Ref)
2003–2007	11,609 (36)	0.83 (0.76 to 0.90)	20,553 (36)	0.93 (0.87 to 0.99)	49,191 (34)	0.82 (0.80 to 0.84)
2008–2012	13,727 (42)	0.63 (0.55 to 0.71)	16,297 (29)	0.78 (0.71 to 0.85)	53,528 (37)	0.62 (0.60 to 0.64)

LUR, living unrelated; LR, living related; HR, hazard ratio; 95% CI, 95% confidence interval; Ref, reference group; —, not included in study; MM, mismatch; BMI, body mass index; PRA, panel reactive antibody;

^aAdjusted for transplant year, ESRD cause, PRA at transplant, previous transplant, years of ESRD, hepatitis C serology, insurance, and recipient and donor race and ethnicity, donor history of cigarette use, and the following donor-recipient combinations: age, sex, obesity status, weight ratio, height ratio, HLA mismatch, and ABO compatibility.

Table 2. Adjusted probability (and 95% confidence interval) of graft failure at 5 years by donor-recipient age group for living-donor transplant recipients, 1998–2012

Donor Age ^a (yr)	Recipient Age (yr)					
	<18	18–29	30–39	40–49	50–59	60+
18–29	19.4 (16.5 to 22.1)	18.1 (16.8 to 19.5)	13.8 (12.4 to 15.1)	12.7 (11.5 to 13.9)	12.7 (11.6 to 13.7)	16.0 (14.0 to 17.9)
30–39	17.3 (15.4 to 19.2)	20.3 (18.3 to 22.2)	13.2 (12.3 to 14.1)	13.1 (12.0 to 14.1)	13.5 (12.5 to 14.5)	17.0 (15.8 to 18.1)
40–49	20.5 (18.2 to 22.8)	23.8 (22.1 to 25.5)	14.7 (13.3 to 16.0)	12.3 (11.6 to 13.0)	13.7 (12.7 to 14.7)	19.3 (18.1 to 20.4)
50–59	21.5 (16.1 to 26.5)	22.0 (20.0 to 24.0)	16.3 (14.5 to 18.0)	13.8 (12.3 to 15.2)	15.6 (14.6 to 16.6)	20.2 (18.5 to 21.9)
60+	Not shown ^b	26.2 (17.5 to 34.1)	20.5 (16.9 to 23.9)	18.5 (14.6 to 22.3)	18.9 (15.7 to 22.0)	25.6 (23.3 to 27.8)

^aAdjusted for transplant year, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, insurance, and recipient and donor race and ethnicity, donor history of cigarette use, and the following donor-recipient combinations: sex, obesity status, weight ratio, height ratio, HLA mismatch, and ABO compatibility. Each probability pertains to the average donor and recipient characteristic for each model.

^bBecause of small cell size, graft failure results are not shown for the pediatric age group (<18) with donors of age 60 years or older.

The LR and LUR groups were merged into one group because they have similar graft failure rates.

For DD transplant recipients of all age groups, receipt of a kidney from a donor 60 years or older was associated with the greatest probability of graft loss. For recipients of LD transplants, graft failure with increasing donor age was not as pronounced as it was with recipients of DD transplants. The youngest and oldest recipient groups showed the highest 5-year graft failure. Similarly, for recipients of LDs, Figure 2 gives a graph of estimated HRs of graft failure by donor and recipient age group relative to the reference group. In the model for the calculator, the log HR of age of donor is modeled, conditional on the age of recipient, as a series of connected straight lines as illustrated in Figure 2. This has the effect of smoothing the dependence on donor age in the calculator, so that donors who are close in age have similar estimates of graft survival, a desirable feature in comparing potential donors for a given candidate.

Sex

Among LDs, the combination of a male donor and male recipient had better graft survival than all other donor-recipient combinations (Table 1). Male recipients with a male LUR donor had a 13% lower overall risk of graft failure (HR, 0.87; 95% confidence interval [95% CI], 0.79 to 0.95) compared with male recipients who received a kidney from a female LUR donor. These differences exist despite adjustment for donor and recipient body size and the other listed recipient and donor characteristics.

This dependence is also reflected in the probability of graft failure at 5 and 10 years by donor-recipient sex as shown in Figure 3. At 5 years for the LUR and LR donor types, male donor-to-male recipient transplants had lower graft failure (13.6% and 14.0%) compared with all other donor-recipient combinations and, in particular, lower graft failure than female donor-to-male recipient transplants (15.8% both LD categories). Among recipients of DDs, female donors to male recipients have the highest graft failure (29.0%) compared with all other donor-recipient combinations (26.6%–27.5%). Similar trends are also shown for graft failure at 10 years.

HLA MM

For all donor types, recipients of a zero MM kidney had the lowest risk of graft failure (Table 1). Recipients with 0 MM make up about 14% and 11% of the LR donor and the DD groups, respectively, but <1% of the LUR donor group. The high frequency in the DD group is due to the preference given to such transplants for candidates on the DD wait list. Those recipients with a 1–2 HLA MM and a 0 DR MM have a 7%–27% lower risk of graft failure when compared with the reference group (3–4 HLA MM with a 1–2 DR MM) across all donor types. However, most LUR transplant recipients (93%) have a 3–6 or unknown HLA MM. Recipients with 5–6 or unknown HLA MM have the highest risk of graft failure in all donor groups.

Body Size

For all donor groups, Table 1 shows that obesity of either the recipient or donor was associated with a higher probability of graft loss. Obese LUR, LR, and DD recipients had

Table 3. Adjusted probability (and 95% confidence interval) of graft failure at 10 years by donor-recipient age group for living-donor transplant recipients, 1998–2012

Donor Age ^a (yr)	Recipient Age (yr)					
	<18	18–29	30–39	40–49	50–59	60+
18–29	35.3 (31.0 to 39.3)	33.8 (31.7 to 35.9)	27.4 (25.2 to 29.6)	27.4 (25.3 to 29.4)	31.5 (29.4 to 33.6)	40.1 (36.2 to 43.8)
30–39	35.1 (32.1 to 38.0)	38.1 (35.2 to 41.0)	26.4 (24.9 to 27.8)	26.9 (25.2 to 28.7)	30.5 (28.8 to 32.3)	40.2 (38.1 to 42.2)
40–49	40.9 (37.3 to 44.3)	44.5 (42.0 to 46.9)	28.8 (26.6 to 30.9)	27.1 (25.7 to 28.3)	30.6 (28.8 to 32.4)	46.0 (43.8 to 48.2)
50–59	45.9 (37.1 to 53.5)	41.1 (38.0 to 44.1)	34.6 (31.6 to 37.5)	31.2 (28.6 to 33.7)	34.8 (33.0 to 36.6)	48.0 (44.7 to 51.2)
60+	Not shown ^b	44.0 (29.4 to 55.6)	38.1 (32.6 to 43.2)	40.5 (33.8 to 46.6)	41.0 (35.1 to 46.3)	52.3 (48.1 to 56.1)

^aAdjusted for transplant year, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, insurance, and recipient and donor race and ethnicity, donor history of cigarette use, and the following donor-recipient combinations: sex, obesity status, weight ratio, height ratio, HLA mismatch, and ABO compatibility. Each probability pertains to the average donor and recipient characteristic for each model.

^bBecause of small cell size, graft failure results are not shown for the pediatric age group (<18) with donors of age 60 years or older.

an 18%, 15%, and 8% higher risk of graft failure, respectively, than those LUR, LR, and DD recipients who were not obese. Similarly, recipients with obese donors had a 5%–11% higher risk of failure than those recipients who did not have an obese donor. Table 6 shows the majority of kidney transplant recipients are not obese and do not have an obese donor. Recipients who are both obese and have an obese donor have the highest probability of graft failure. If a donor weighed <75% of the recipient's weight, the recipient had a 9%–12% higher overall risk of graft failure than if the donor and recipient were of similar weight (Table 1). These differences are seen while accounting for the effects of sex and obesity on graft failure as well as recipient and donor height and age.

Using Estimates to Assess and Compare Donor-Recipient Outcomes

On the basis of the model described above, we developed a calculator that estimates the probability of graft survival given the characteristics of the candidate and potential donor. The parameter estimates for graft failure derived from the LD model are shown in Supplemental Table 1. LR and LUR models were combined and a covariate for LD type (unrelated, related first-degree, related second-degree) was added to the model. The recipient and donor age were fitted using splines as described above. The C-statistic for the 5-year model is 0.64, which compares favorably with other models for graft survival (2,28,29). It should be noted that the C-statistic estimates the probability that the model would allow us to correctly predict which of two randomly chosen individuals would fail first. It does not, however, reflect the ability of the model to discriminate between particular individuals in the population (28,30).

The following example in Table 7 illustrates the use of this calculator in a hypothetical situation of a 50-year-old male candidate with three potential donors. Donor 1 is a 55-year-old sister who is not obese and the donor-recipient weight ratio is 0.70. They have a 3 HLA ABDR MM and 1 DR MM. Donor 2 is not related and is a 25-year-old man. He is not obese, but the donor weight ratio is 1.20. They have a 2 HLA ABDR MM and 2 DR MM. Donor 3 is also not related and is a 35-year-old woman. She is obese and the donor weight ratio is 0.95. They have a 5 ABDR MM with a 2 DR MM. In this example, the graft failure at 5 years is estimated to be 16.0% (95% CI, 14.2% to 17.8%) for donor 1, his sister; 9.8% (95% CI, 8.6% to 11.0%) for donor 2, a much younger man who is less well matched; and 13.6% (95% CI, 12.1% to 15.1%) for donor 3, a much younger woman, also less well matched and obese. At 5 years, there is a clear preference for the candidate to select donor 2 and take advantage of the lower risk of graft failure. At 10 years, although the estimated graft failure probability is much lower for donor 2 than donor 1, the difference is not statistically significant. The computation of the graft survival estimates is shown in the footnote of Table 7.

Discussion

This calculator has particular potential as a guide to candidates with a compatible LD who may be able to improve their predicted graft or patient survival through participation in a KPD program. Candidates with a compatible donor could

Table 4. Adjusted probability (and 95% confidence interval) of graft failure at 5 years by donor-recipient age group for deceased-donor transplant recipients, 1998–2012

Donor age ^a (yr)	Recipient Age (yr)					
	<18	18–29	30–39	40–49	50–59	60+
<18	32.7 (30.1 to 35.2)	27.5 (25.3 to 29.6)	21.5 (19.9 to 23.1)	18.2 (17.0 to 19.5)	20.7 (19.4 to 22.0)	29.1 (27.3 to 30.7)
18–29	33.2 (30.8 to 35.5)	29.7 (27.7 to 31.6)	21.0 (19.8 to 22.3)	19.0 (18.0 to 20.0)	20.6 (19.7 to 21.6)	26.4 (25.1 to 27.5)
30–39	34.9 (30.9 to 38.7)	32.4 (29.8 to 35.0)	23.2 (21.6 to 24.8)	21.0 (19.8 to 22.3)	22.1 (21.0 to 23.3)	28.5 (27.0 to 30.0)
40–49	37.8 (32.4 to 42.8)	32.2 (29.8 to 34.5)	26.9 (25.5 to 28.4)	23.8 (22.7 to 24.9)	26.7 (25.7 to 27.7)	34.4 (33.2 to 35.6)
50–59	40.4 (30.9 to 48.6)	39.9 (36.4 to 43.2)	29.5 (27.7 to 31.3)	29.2 (27.8 to 30.5)	31.0 (29.9 to 32.1)	37.5 (36.3 to 38.6)
60+	Not shown ^b	48.1 (39.5 to 55.4)	39.9 (35.2 to 44.3)	36.5 (33.7 to 39.2)	36.7 (35.0 to 38.4)	44.0 (42.6 to 45.3)

^aAdjusted for transplant year, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, insurance, and recipient and donor race and ethnicity, donor history of cigarette use, and the following donor-recipient combinations: sex, obesity status, weight ratio, HLA mismatch, and ABO compatibility. Each probability pertains to the average donor and recipient characteristic for each model.

^bBecause of small cell size, graft failure results are not shown for the pediatric age group (<18) with donors of age 60 years or older.

Table 5. Adjusted probability (and 95% confidence interval) of graft failure at 10 years by donor-recipient age group for deceased-donor transplant recipients, 1998–2012

Donor Age ^a (yr)	Recipient Age (yr)					
	<18	18–29	30–39	40–49	50–59	60+
<18	49.4 (45.9 to 52.7)	44.3 (41.3 to 47.2)	37.4 (35.0 to 39.6)	35.0 (33.0 to 36.9)	41.3 (39.2 to 43.3)	54.8 (52.3 to 57.2)
18–29	55.5 (51.9 to 58.9)	47.8 (45.1 to 50.4)	37.8 (35.9 to 39.7)	36.7 (35.1 to 38.2)	40.6 (39.0 to 42.1)	52.4 (50.4 to 54.3)
30–39	61.6 (55.9 to 66.6)	51.3 (47.7 to 54.7)	42.4 (39.9 to 44.8)	40.0 (38.0 to 42.0)	43.6 (41.6 to 45.5)	55.3 (52.9 to 57.6)
40–49	61.0 (54.7 to 66.4)	52.9 (49.6 to 55.9)	46.9 (44.7 to 48.9)	45.0 (43.2 to 46.6)	49.6 (48.0 to 51.2)	62.5 (60.6 to 64.3)
50–59	60.9 (50.3 to 69.3)	58.3 (53.9 to 62.2)	50.5 (47.9 to 52.9)	50.5 (48.6 to 52.4)	56.3 (54.6 to 57.9)	66.7 (64.8 to 68.4)
60+	Not shown ^b	71.4 (61.6 to 78.7)	60.9 (55.1 to 65.9)	61.8 (58.0 to 65.3)	61.3 (58.8 to 63.6)	73.0 (71.0 to 74.8)

^aAdjusted for transplant year, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, insurance, and recipient and donor race and ethnicity, donor history of cigarette use, and the following donor-recipient combinations: sex, obesity status, weight ratio, HLA mismatch, and ABO compatibility. Each probability pertains to the average donor and recipient characteristic for each model.

^bBecause of small cell size, graft failure results are not shown for the pediatric age group (<18) with donors of age 60 years or older.

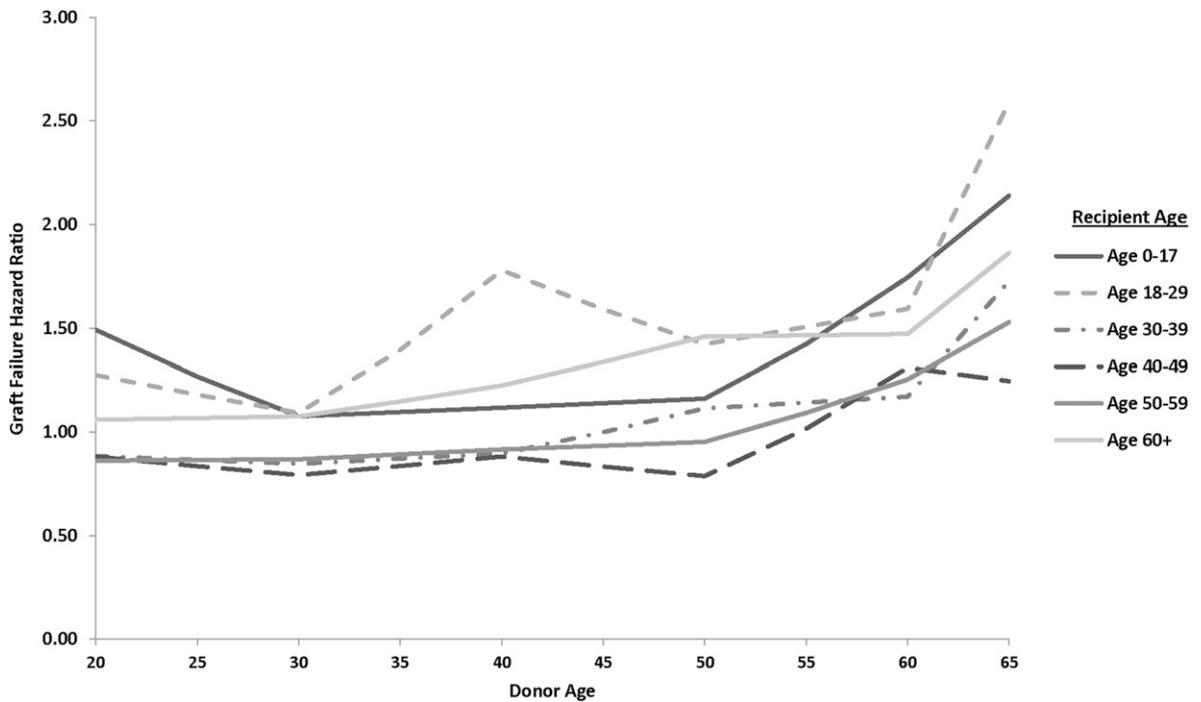


Figure 2. | Adjusted risk of graft failure hazard ratio comparisons for donor and recipient age group among living donor kidney transplant recipients, 1998–2012. Adjusted for calendar year as well as recipient race and ethnicity, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, and insurance. In addition, all models were adjusted for the following donor-recipient combinations: sex, obesity status (obese if body mass index ≥ 30), weight ratio, height ratio, and HLA mismatch.

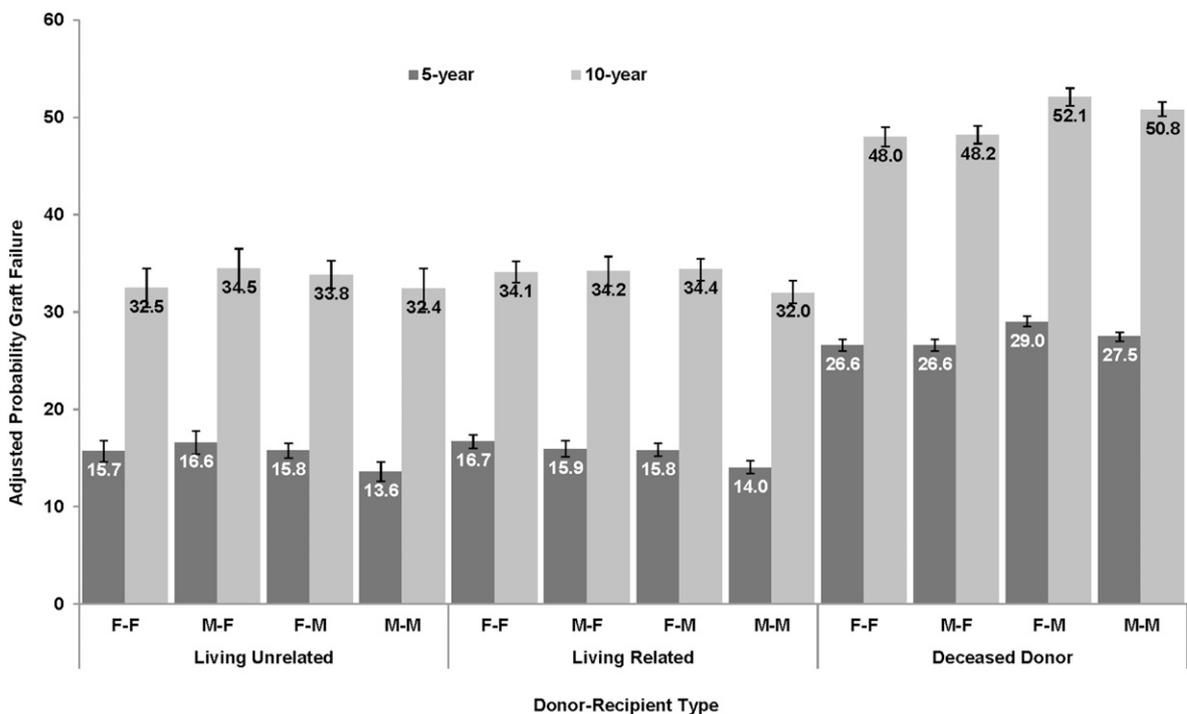


Figure 3. | Adjusted probability (and 95% confidence interval) of graft failure at 5 and 10 years by donor-recipient sex for recipients of living unrelated, living related, and deceased donor transplants, 1998–2012. Adjusted for calendar year as well as recipient race and ethnicity, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, and insurance. In addition, all models were adjusted for the following donor-recipient combinations: age, obesity status (obese if body mass index ≥ 30), weight ratio, height ratio, and HLA mismatch. Each probability pertains to the average donor and recipient characteristic for each model. F, female; M, male.

Table 6. Adjusted probability (and 95% confidence interval) of graft failure at 5 and 10 years by obesity of recipient and donor and donor type, 1998–2012^a

Donor Type ^a	Donor Obese? ^b	Recipient Obese? ^b	N	%	5 yr	10 yr
Living unrelated	No	No	15,043	46.5	14.6 (13.8 to 15.4)	31.5 (29.9 to 33.1)
	Yes	No	3687	11.4	16.0 (14.4 to 17.5)	31.4 (28.6 to 34.1)
	No	Yes	5817	18.0	15.9 (14.6 to 17.3)	35.1 (32.4 to 37.8)
	Yes	Yes	2205	6.8	18.1 (16.1 to 20.0)	40.7 (36.7 to 44.4)
Living related	No	No	25,463	44.9	15.4 (14.6 to 16.1)	33.5 (32.1 to 34.8)
	Yes	No	6516	11.5	15.9 (14.7 to 17.0)	35.6 (33.4 to 37.7)
	No	Yes	7277	12.8	16.3 (15.1 to 17.4)	35.0 (32.8 to 37.1)
	Yes	Yes	3555	6.3	17.9 (16.4 to 19.4)	40.6 (37.8 to 43.4)
Deceased donor	No	No	68,229	47.5	26.8 (26.4 to 27.3)	48.7 (48.1 to 49.4)
	Yes	No	19,948	13.9	28.0 (27.2 to 28.8)	50.5 (49.2 to 51.8)
	No	Yes	27,293	19.0	28.4 (27.7 to 29.1)	53.6 (52.4 to 54.7)
	Yes	Yes	9811	6.8	31.5 (30.4 to 32.7)	56.8 (54.9 to 58.7)

^aAdjusted for transplant year, ESRD cause, panel reactive antibody at transplant, previous transplant, years of ESRD, hepatitis C serology, insurance, and recipient and donor race and ethnicity, donor history of cigarette use, and the following donor-recipient combinations: age, sex, weight ratio, height ratio, HLA mismatch, and ABO compatibility. Each probability pertains to the average donor and recipient characteristic for each model.

^bRecipients with missing body mass index (BMI) and/or missing donor BMI are not shown (living unrelated LUR: *n*=5597, 17%; living related LR: *n*=13,848, 24%; deceased donor DD *n*=18,415, 13%)

be provided with information on the possibility of improving their expected outcomes through entering and obtaining a match with a donor in a KPD pool. Involvement of compatible pairs in this way would also enrich the KPD program by increasing the number of possible matches perhaps by potentially offsetting the deficiency of O donors commonly observed in KPD programs. Generally, we suggest that a candidate with a compatible donor consider the possibility of risk reduction through joining a KPD system. However, one

concern is that exchanges may be suggested to compatible pairs on the basis of compatibility with other pairs within the KPD pool, but the compatible pair would be unable to assess whether the recipient would improve his or her potential outcomes. In such cases, there might be some pressure, whether overt or implicit, to participate in an exchange for altruistic reasons. The calculator developed in this paper would offer valuable information for such compatible pairs to evaluate their options and to participate when it is to their

Table 7. Kidney graft failure estimates for a 50-year-old man with three potential donors

Characteristic ^a	Donor 1 (Sister)	Donor 2 (Unrelated)	Donor 3 (Unrelated)
Donor age, yr	55	25	35
Donor sex	Female	Male	Female
Donor BMI	Not obese	Not obese	Obese
Donor-recipient weight ratio	0.70	1.20	0.95
HLA	3 HLA MM 1 DR	2 HLA MM 2 DR	5 HLA MM 2 DR
Estimated graft failure at 5 yr ^b (95% confidence interval), %	16.0 (14.2 to 17.8)	9.8 (8.6 to 11.0)	13.6 (12.1 to 15.1)
Estimated graft failure at 10 yr ^c (95% confidence interval), %	39.6 (31.4 to 47.8)	30.2 (22.9 to 37.6)	36.2 (28.3 to 44.0)

BMI, body mass index; MM, mismatch.

^aIn these examples, all recipient and donor characteristics with the exception of transplant year not described are the reference characteristic found in Supplemental Table 1. The transplant year is 2008–2012, the most recent cohort, in these examples.

^bTo compute the probability of graft failure at 5 yr, use the parameter estimates and baseline survival curve found in Supplemental Table 1: Probability (graft failure at 5 yr)= $1-0.7995^A$ where $A=\exp(0.0112 \times I[\text{related first-degree}]+0.0434 \times I[\text{related second-degree}]+0.0263 \times I[\text{recipient age } <13]+0.5365 \times I[\text{recipient age } 13-17]+0.4375 \times I[\text{recipient age } 18-29]-0.1087 \times I[\text{recipient age } 30-39]-0.2557 \times I[\text{recipient age } 50-59]-0.050 I[\text{recipient age } \geq 60]+ \dots + 0.396 \times I[\text{recipient hepatitis C serology positive}]-0.227 \times I[\text{insurance private primary payer}]-0.0748 \times I[\text{insurance other/missing}]-0.1098 \times I[\text{transplant year } 2003-2007]-0.3330 \times I[\text{transplant year } 2008-2012])$, where $I(A)$ is set to 1 if condition A applies (*i.e.*, if the recipient/donor possesses condition A), and otherwise it is set to 0. Our calculator does the computation at <https://kecc.shinyapps.io/SurvivalCalculator/>.

^cThe probability of graft failure at 10 yr is computed as follows. The probability of graft failure= $1 - \text{probability of graft survival}$. Compute the probability of graft survival for the first 5 years (=F) and then compute the probability of graft failure for the second 5 years (=T). The probability of graft failure at 10 years= $1 - (F \times T)$. Our calculator does the computation at <https://kecc.shinyapps.io/SurvivalCalculator/>.

advantage and to the advantage of one or more other candidates in the KPD pool. Provision of suitable decision support tools would be helpful; summarizing the potential for risk reduction in an existing pool or simulating risk reductions on the basis of characteristics of previous donors are possibilities. The presence of such compatible donors in the KPD pool could be accommodated through the use of existing algorithms fine-tuned to prioritize them with an advantage in selection.

Of particular interest is the advantage to male candidates who receive kidney transplants from male donors. This suggests that the rather common situation of a wife donating to her husband may be one where consideration should be given to entering a KPD program, where a male donor, perhaps with better matches in HLA and body size, might be found. Figure 4 shows the donor-recipient sex distribution by kidney transplant type for each donor and recipient combination. For LD transplants, female donor-to-male recipient is the largest group among all sex combinations. Among LUR, LR, and KPD groups, 46%, 31%, and 34% of transplants were female to male recipient; this can be compared with the DD group where only 24% of transplants were female to male. Note also that for all donor groups, there is no evidence of any advantage to a female candidate of a male donor. All else being equal, this suggests that there may be benefit for KPD programs to reserve male donors for male candidates whenever possible.

Compatible pairs with 5 or more HLA MMs might also consider joining a KPD pool. If, despite the MM with her or his donor, the candidate has a genotype that is relatively common in the population, there may be a preferable match with, say, only 1 or 2 HLA MMs in the KPD. This could result in a decrease in risk of from 20% to 31% (Table 1). The comparisons in Table 7 are on the basis of a model with “all else equal” and so need to be carefully interpreted when the factors investigated are typically associated with important

differences. For example, the apparent advantage in survival of LUR transplants may be mitigated to some degree by the fact that LR transplants typically have fewer HLA MMs than LUR transplants.

A use of the calculator that first motivated our investigations arises in the context of allocations in a KPD program where algorithms are developed to optimize the number of transplants or some other measure of utility (31–34). An alternative approach defines the value of a potential transplant from a given donor to a given recipient as the estimated probability that the graft would survive for 5 (or 10) years.

Recently, Massie *et al.* (2) considered a joint model with the aim of extending the kidney donor profile index for DDs to include LDs. Methodologic differences in their work include use of 10 versus 15 years of data, considering only adults with no previous transplants, and specifying models in which the effects of candidate characteristics are assumed to be the same for all donor types, a restriction that is not supported by the data (see differences in Table 1). They also do not include a time trend in their analyses, which could have major implications on estimating the association with graft survival of any donor or recipient characteristic whose distribution is changing over time. Because the kidney donor profile index only gives the percentile ranking among all donors and, as used with DD, does not reflect donor/recipient MMs or other interactions, we believe that our calculator (located at <https://kecc.shinyapps.io/SurvivalCalculator/>) gives metrics that are more relevant to the kidney transplant candidate.

We plan to develop further a DD calculator that can be used with the living donor calculator; this could aid in understanding the consequences of utilizing DDs as non-directed donors in instituting chains within a KPD program (19). This could be done without disadvantaging those on

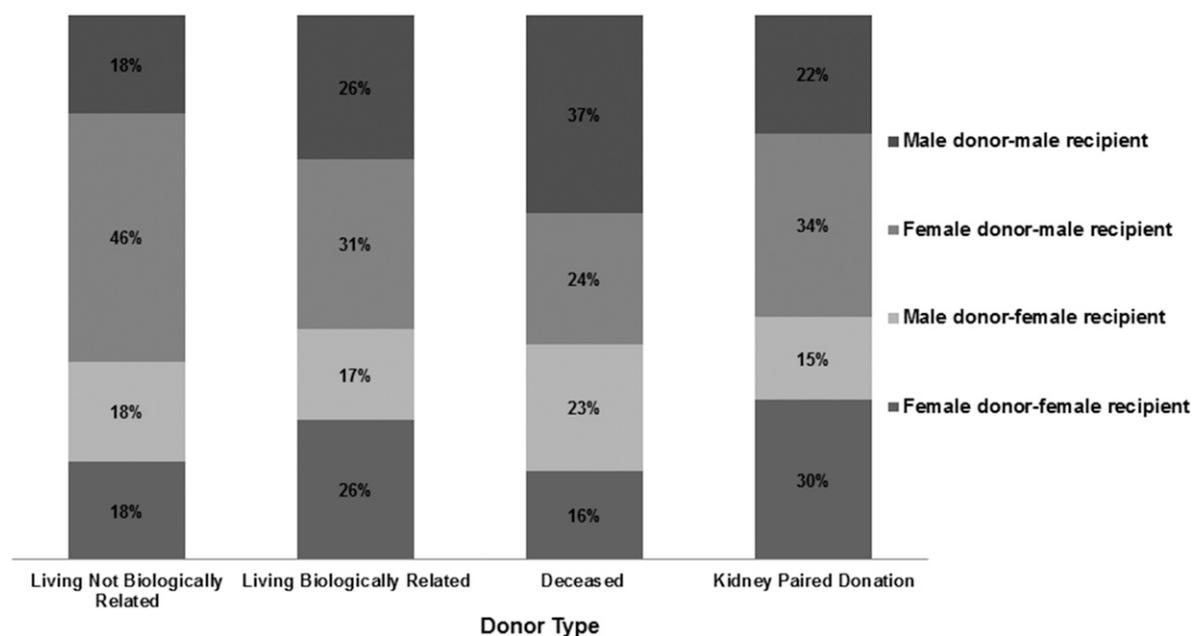


Figure 4. | Donor-recipient sex distribution for living not biologically related, living biologically related, deceased, and kidney paired donation groups, 1998–2012.

the waiting list by having the chains end with a transplant to the DD waiting list. Such use of DDs has the potential to increase substantially the number of transplants.

This calculator is on the basis of 15 years of United States data during which transplant technology has changed, resulting in substantially better outcomes. We have predicted the outcomes as they would apply in the most recent 5-year period, but this may underestimate survival rates given this continuous improvement of outcomes. It should be noted, however, that relative differences due to most risk factors have not changed appreciably, so comparative statements are less affected by these secular trends.

As in many such studies (1,5,15–18), we have confined attention to graft survival so that the outcome corresponds to graft failure as indicated by return to dialysis or death without graft failure. We cannot determine the length of time the graft would have functioned had the patient lived when a patient dies or if graft failure was a cause of death. Thus, this endpoint has the advantage of being relatively unambiguous and seems an important one from a clinical perspective. However, it is comprised of two competing risks and these can be examined separately (1) to see to what extent the risk factors affect differently the rates of graft failure and death without graft failure. As has been noted elsewhere (1), transplantation of adolescent and young adult recipients is associated with a substantially higher rate of graft failure and a somewhat lower death rate. Similarly, the higher risk for black recipients is primarily due to graft failure. Females have a lower risk of graft failure than males, but a higher risk of death. In Supplemental Table 2, we have provided parameter estimates for a 5-year Cox model for death-censored graft failure and for death. The estimated probabilities of these events up to 5 years for donors 1–3 are given in Supplemental Table 3.

In conclusion, we believe that the calculator for the combined event of graft survival is of potential interest to kidney transplant candidates and clinicians, and could help guide decisions to choose among multiple compatible donors, or decisions of compatible pairs with respect to joining a KPD program.

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Disclosures

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