Sociodemographic Drivers of Donor and Recipient Gender Disparities in Living Kidney Donation in Australia

Siah Kim[1,2], Anita van Zwieten[1,2], Melanie Wyld[1,2,3], Maleeka Ladhani[4,5], Chandana Guha[1,2], Amanda Dominello[1,2], Kylie-Ann Mallitt[1,2], Anna Francis[6,7], Roslyn B. Mannon[8] and Germaine Wong[1,2,3]

[1]Centre for Kidney Research, The Children's Hospital at Westmead, Westmead, New South Wales, Australia; [2]Sydney School of Public Health, University of Sydney, Camperdown, New South Wales, Australia; [3]Department of Renal and Transplantation Medicine, Westmead Hospital, Sydney, New South Wales, Australia; [4]Department of Renal Medicine, Lyell McEwin Hospital, Adelaide, South Australia, Australia; [5]Faculty of Health and Medical Science, Adelaide University Medical School, Adelaide, South Australia, Australia; [6]School of Medicine, The University of Queensland, Brisbane, Queensland, Australia; [7]Child and Adolescent Renal Service, Queensland Children's Hospital, South Brisbane, Queensland, Australia; and [8]Division of Nephrology, University of Nebraska Medical Centre, Omaha Nebraska, USA

Background: Females account for 60% of all living kidney donors worldwide. We defined the proportion of female to male donors for living donor kidney transplantation stratified by recipient gender, and explored the factors associated with female kidney donation.

Methods: Data from the ANZDATA (Australian and New Zealand Dialysis and Transplantation) and ANZOD (Australian and New Zealand Organ Donor) registries (2002–2019) were used to identify the sociodemographic characteristics and their interactions associated with living donation from female donors. We derived the predicted probabilities from adjusted logistic models using marginal means.

Results: Of 3523 living donor pairs, 2203 (63%) recipients were male, and 2012 (57%) donors were female. Male recipients were more likely to receive kidneys from female donors than male donors. Donor and recipient sex association was modified by donor-recipient relationship ($P < 0.01$), with sensitivity analysis suggesting that spousal donor-recipient pairs drive this interaction. Older recipients residing in regional or remote areas were more likely to receive kidneys from female donors compared with those from major cities (aged ≥60 years: 0.67 [0.63–0.71] vs. aged <60 years: 0.57 [0.53–0.60]).

Conclusions: Factors associated with female donation include recipient sex, with spousal donors contributing to the interaction between recipient gender and donor-recipient relationship. Recipient age and location of residence have interactive effects on the likelihood of living donor transplantation from female donors.

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Disparity in access to kidney transplantation is a key public health issue. In North America, women are less likely to be waitlisted for a deceased donor kidney transplant compared with men. Girls with kidney failure are also 14% less likely to be listed on the deceased donor waiting list compared with boys, and women are 18% less likely to be listed compared with men.[1] Compared with their male counterparts, access to transplantation has been found to be worse particularly for older women, and women with comorbidities.[2] Women who are obese are 34% less likely to be waitlisted for deceased donor kidney transplantation, compared with 14% less likely for obese men.[3] Women are also less likely to receive a deceased donor kidney transplant once waitlisted. This may be attributed partly to their greater levels of sensitization because of pregnancy.[4] Similarly, women are less likely to be the recipient of a living donor kidney when compared with men, and sensitization of women through pregnancy appears to be a key contributor to this disparity through

Correspondence: Siah Kim, Centre for Kidney Research, The Children's Hospital at Westmead Locked Bag 4001 Westmead, New South Wales 2145 Australia. E-mail: siah.kim@health.nsw.gov.au

SK and AVZ contributed equally to this work as joint first authors.

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impacts on donor histocompatibility, which is particularly apparent for spouses.[5]

Conversely, women are more likely to be living donors than men, with female donors accounting for 60% of living donor kidney transplants globally.[6] Across the Asia-Pacific region, women account for approximately 60% of living donors, in both low-income and middle-income countries such as Malaysia and Indonesia and high-income countries such as Japan, Korea, and Australia.[7] Reasons for this are thought to be multifactorial, including medical and sensitization-related, social, and economic factors.[8] Medical reasons may relate to higher rates of exclusion of male donors because of comorbidities, along with lower rates of male spousal donation because of sensitization during pregnancy for women.[5] There are multilevel influences which may contribute to barriers to living donation from men. Families may be burdened by the indirect and direct costs of living organ donation and may be reluctant for men to donate if they are the primary income earner.[5,9] This is also reflected at a population level in the United States with a greater decline in male donation rates among lower income families since 2005 to 2015.[10] Social factors include the expectations on women to fill a carer role, with a qualitative study identifying wives may be motivated to be donors for their husbands to avoid carer's burden and to protect their children from becoming donors.[11]

Knowledge of the reasons that drive the preponderance of female donation is crucial because this will enable policymakers, health professionals, and researchers to target potential factors and barriers for change and mitigate the gender disparities in living kidney donation. This study aimed to define the proportion of female to male donors for living donor kidney transplantation stratified by recipient gender and explore factors that are associated with female kidney donation.

METHODS

This was a cross-sectional study, using data on kidney transplant recipient and donor pairs from the ANZDATA and the ANZOD. Ethics approval was obtained from Western Sydney Local Health District Human Research Ethics Committee (2020/PID03115). The study included all people who had received their first kidney transplant in Australia from a living donor from January 2003 to December 2019. We excluded patients who had multiorgan transplants and subsequent living donor transplants.

Outcome and Covariates of Interest

The outcome of interest was the probability of receiving a kidney from a female (as opposed to a male) donor. Explanatory variables included donor and recipient age (in years), ethnicity (European Australian vs. other), state of residence, remoteness (major city vs. regional or remote), area-level socioeconomic status (decile as determined by socioeconomic indexes for areas),[12] transplant era, donor-recipient relationship, recipient gender, and donor-recipient human leukocyte antigen A, B, and DR mismatches. Donor-recipient relationship was classified to reflect the social relationship between donor and recipient, rather than the biological or genetic relationship. Ethnicity was collapsed into European Australian and others, given the small number of participants within individual ethnic groups. Recipient weight at transplant, primary kidney disease, smoking status, maximum panel reactive antibody (PRA) and time on dialysis, as well as recipient comorbidities of cardiovascular disease, coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic lung disease, and diabetes mellitus were considered as explanatory variables.

The terms "gender" and "sex" were used interchangeably within the registry. Before May 2016, "sex" was used to identify sex (with 3 categories: male or female and intersex) but since May 2016, "sex" was renamed to 'gender' as an identifier within the data collection form (with 2 categories: male and female). Because the data item was collected by clinicians, it is unclear if it was biological sex as determined by karyotype, or gender, which refers to the socially constructed characteristics of men and women, and/or self-identification as male or female. For this reason, the term 'gender' was used, and defined it as a binary term of female (woman) or male (man) because we feel that this terminology most likely reflects the societal construct rather than genetic karyotype.

Statistical Analysis

Baseline characteristics of the study cohort were expressed as the number and proportion of patients or median (interquartile range) for continuous variables, stratified by donor gender. Recipient and donor age, maximum PRA, time on dialysis, and weight at transplant were modeled as continuous variables, whereas the others were modeled categorically. *t*-Tests were used to compare differences between means, nonparametric K-sample test on the equality of medians, and χ^2 test was used to compare differences in categorical variables. Multiple imputation using chained equations was used to create 10 imputed datasets for variables with less and equal to 10% missingness. This procedure was repeated in all 10 datasets. All variables were included in the imputation model, with continuous variables imputed using linear regression and categorical variables using logistic regression. We used group

Least Absolute Shrinkage Selector Operator to identify variables to be included in the multivariable logistic model. Group Least Absolute Shrinkage Selector Operator selects variables for model inclusion by introducing a penalty term into the regression equation, which forces the model to reduce the impact of less important variables by shrinkage of their coefficients toward zero. As a result, models are influenced by important variables, and we then identified the optimal model using lowest Akaike Information Criterion. Variables were selected for subsequent multivariable analyses if they were included across >80% of the imputed datasets. Analyses were conducted using multivariable logistic regression with the 10 imputed datasets. We tested for interactions between the variables selected and included interactions with a $P < 0.01$. We used penalized splines through the application of a generalized additive model to assess for linearity of the continuous covariates and maximum PRA was then transformed with square and cubic terms. The predicted probabilities were extracted using marginal means, with individual margins estimates for each imputed data set, combined with Rubins's rules using the STATA mimrgns command. By definition, marginal effects are averaged over other variables in the model and therefore differences cannot be tested for significance. Analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina) and STATA 16.0 (StataCorp, College Station, Texas).

RESULTS

Participant Characteristics

There were 3591 living donor kidney transplants included in our study (Figure 1). Of these, 68 donors were of unknown gender and were excluded from the analysis, leaving 3523 donor-recipient pairs in the final study sample. Of these, 2203 (63%) recipients were male, whereas 2012 (57%) donors were female.

Donor and recipient characteristics are presented in Tables 1 and 2, respectively, stratified by donor gender. A greater proportion of female donors donated to recipients living in remote and regional Australia compared with male donors (31% vs. 27%, $P < 0.02$). A higher proportion of female donors donated to European Australian recipients (84% vs. 81%, $P = 0.05$), to recipients with coronary artery disease (10% vs. 7%, $P < 0.01$), and former or active smokers (35% vs. 29%, $P < 0.01$) compared with male donors (Table 1). Female donors were more likely to donate to male (70%) compared with female (30%) recipients. For male donors, donation across male (53%) and female recipients (47%) was more equally distributed (Table 1). Distribution of the relationship between donor and recipient was different for female and male donors, with a greater proportion of female donors donating to their spouse compared with male donors (30% vs. 19%) (Table 2).

The proportion of female donors across donor relationship groups varied by recipient gender (Table 3).

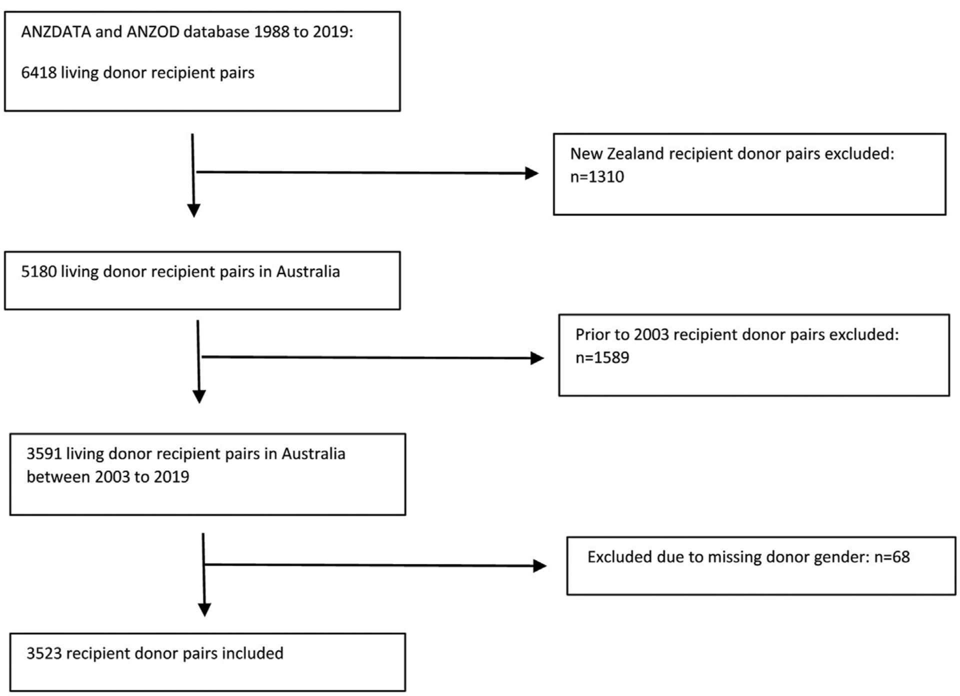

Figure 1. Study flow diagram. ANZDATA, Australian and New Zealand Dialysis, and Transplantation; ANZOD, Australian, and New Zealand Organ Donor.

Table 1. Recipient characteristics stratified by donor gender ($N = 3523$)

Recipient Characteristics (*n* with complete data)	Male Donor *n* (%)[a] Total 1511	Female Donor *n* (%)[b] Total 2012	*P*-value
Recipient gender ($n = 3523$)			< 0.01
Male	800 (53)	1403 (70)	
Female	711 (47)	609 (30)	
Recipient age ($n = 3523$)			< 0.01
Median years (IQR)	43 (28–56)	45 (32–57)	
Transplant era			0.77
2003–2007	449 (30)	572 (28)	
2008–2012	489 (32)	679 (34)	
2013–2017	410 (27)	551 (27)	
2018–2019	163 (11)	210 (10)	
PRA ($n = 3515$)			<0.01
Median % (IQR)	0 (0 – 0)	0 (0 – 0)	
Recipient ethnicity ($n = 3225$)			0.05
European Australian	1125 (81)	1539 (84)	
Other	262 (19)	299 (16)	
Recipient SEIFA - area-level SES ($n = 3455$)			0.19
Median (IQR)	1006 (958 – 1065)	1001 (955 – 1061)	
Recipient remoteness ($n = 3460$)			0.02
Major city	1084 (73)	1375 (69)	
Regional/remote	397 (27)	604 (31)	
Primary renal disease ($n = 3477$)			0.02
Glomerular disease	619 (42)	851 (43)	
Diabetic nephropathy	118 (8)	183 (9)	
Cystic kidney disease	248 (17)	337 (17)	
CAKUT	165 (11)	221 (11)	
Hypertension	52 (4)	86 (4)	
Other	279 (19)	288 (15)	
Recipient weight ($n = 3428$)			<0.01
Median kg (IQR)	71 (57 – 84)	76 (62 – 88)	
Time on dialysis ($n = 3523$)			0.39
Median days (IQR)	180 (0 – 571)	167 (0 – 551)	
Recipient coronary artery disease ($n = 3505$)			<0.01
No	1401 (93)	1810 (90)	
Yes	103 (7)	191 (10)	
Recipient diabetes ($n = 3501$)			0.11
No	1343 (89)	1748 (88)	
Yes	161 (11)	249 (12)	
Recipient smoking status ($n = 3426$)			<0.01
Never	1038 (71)	1264 (65)	
Active/former	434 (29)	690(35)	

CAKUT, Congenital anomalies of the kidney and urinary tract; IQR, interquartile range; PRA, panel reactive antibody; SEIFA, Socioeconomic Indexes for Areas; SES, socioeconomic status.
[a]Column % exclude missing data.

Twenty-two percent of female recipients received a donor kidney from their spouses, compared with 27% of male recipients. If the donor was a parent or sibling, female recipients were more likely to receive it from their mothers (61%) or sisters (61%) compared with their fathers or brothers. If a male recipient was to receive a kidney from a parent, they were more likely to receive a kidney from their mother (56%). However across most other donor groups aside from spouse, male recipients were more likely to receive a kidney from a male donor.

Table 2. Donor characteristics stratified by donor gender

Donor Characteristics	Male Donor *n* (%)[a] Total 1511	Female Donor *n* (%)[a] Total 2012	*P*-value
Relationship to recipient ($n = 3523$)			< 0.01
Spouse	281 (19)	597 (30)	
Parent	420 (28)	578 (29)	
Sibling	331 (22)	393 (20)	
Child	63 (4)	59 (3)	
Friend	108 (7)	102 (5)	
Other related	115 (8)	129 (6)	
Other nonrelated	47 (3)	52 (3)	
Paired exchange	123 (8)	81 (4)	
Altruistic	23 (2)	21 (1)	
Donor SEIFA - area-level SES ($n = 3258$)			0.06
Median (IQR)	1004 (957–1058)	997 (953–1052)	
Donor remoteness ($n = 3262$)			0.31
Major city	980 (70)	1284 (69)	
Regional/Remote	413 (30)	585 (31)	
Donor ethnicity ($n = 3322$)			0.08
European Australian	1211 (85)	1663 (87)	
Other	208 (15)	240 (13)	
Donor age ($n = 3523$)			0.04
Median (IQR)	50 (42–59)	51 (44–58)	
Donor smoking status ($n = 3335$)			< 0.01
Never	759 (53)	1258 (66)	
Former/Active	671 (47)	647 (34)	
Donor hypertension status ($n = 3685$)			< 0.01
No	1242 (86)	1729 (89)	
Yes	197 (14)	202 (11)	
Donor weight kg ($n = 3329$)	84 (13)	69 (12)	<0.01
HLA mismatches A ($n = 3417$)			0.85
0	342 (23)	438 (23)	
1	820 (56)	1102 (57)	
2	308 (21)	407 (21)	
HLA mismatches B ($n = 3417$)			0.52
0	227 (15)	290 (15)	
1	783 (53)	1012 (51)	
2	460 (31)	645 (33)	
HLA mismatches DR ($n = 3414$)			0.38
0	329 (22)	415 (21)	
1	806 (55)	1053 (54)	
2	332 (23)	479 (25)	

HLA, human leukocyte antigen; IQR, interquartile range; SEIFA, Socioeconomic Indexes for Areas; SES, socioeconomic status.
[a]Column % exclude missing data.

Predictors of Receiving a Kidney From a Female Donor

Findings of the predicted probabilities of receiving a kidney from a female donor are shown in Table 4 and further details of the full model are shown in Supplementary Table S1 of the Supplementary Appendix. The key predictors for female living donations were male recipient gender, recipient spousal relationship with donor, recipient residing in regional or remote area, recipients being of European Australian

Table 3. Proportion of female and male donors stratified by recipient gender and recipient and donor relationship

Relationships	Spouse, *n* (%)[a]	Parent, *n* (%)	Sibling, *n* (%)	Child, *n* (%)	Friend, *n* (%)	Other Related, *n* (%)	Other Nonrelated, *n* (%)	Paired Exchange, *n* (%)	Altruistic, *n* (%)
Male recipient *n* (%)[b]	*n* = 591 (27)	*n* = 635 (29)	*n* = 447(20)	*n* = 70 (3)	*n* = 133 (6)	*n* = 150 (7)	*n* = 65 (3)	*n* = 94 (4)	*n* = 18 (1)
Male donor	5 (1)	279 (44)	223 (50)	40 (57)	80 (60)	78 (52)	29 (45)	58 (62)	8 (44)
Female donor	586 (99)	356 (56)	224 (50)	30 (43)	53 (40)	72 (48)	36 (55)	36 (38)	10 (56)
Female recipient	*n* = 287 (22)	*n* = 363 (28)	*n* = 277 (21)	*n* = 52 (4)	*n* = 77 (6)	*n* = 94 (7)	*n* = 34 (3)	*n* = 110 (8)	*n* = 26 (2)
Male donor	276 (96)	141 (39)	108 (39)	23 (44)	28 (36)	37 (39)	18 (53)	65 (59)	15 (58)
Female donor	11 (4)	222 (61)	169 (61)	29 (56)	49 (64)	57 (61)	16 (47)	45 (41)	11 (42)

[a]Denominator for column percentages is number of female or male recipients receiving kidney from different donor relationship groups, denoted in bold with (%) representing total number of donors from each donor relationship group.
[b]Denominator for row percentages is the number of male or female recipients who received a kidney from each donor relationship group.

ethnicity, increasing recipient age, increasing recipient weight, history of cardiovascular disease, and history of smoking. We tested for interactions between these predictors. There was effect modification between recipient gender and donor relationship (P-value for interaction < 0.01) as well as recipient remoteness and age (P-value for interaction < 0.01). The interpretability of the odds ratio of the final model was difficult in the presence of 2 different interactions within the same model. For this reason, we have presented the predicted probabilities instead.

After adjusting for other factors, recipients of other ethnicities were less likely to receive a kidney from a female donor (predicted probability, 95% confidence interval) (0.53, 0.50–0.57) than recipients of European Australian ethnicity (0.58, 0.56–0.59). Recipients with a history of coronary artery disease were also more likely to receive a kidney from a female donor (0.65, 0.61–0.69) compared with recipients without a history of coronary artery disease (0.56, 0.55–0.58). Recipients who were active or former smokers had a higher probability of receiving a kidney from a female donor (0.61, 0.59–0.64) compared with recipients who were nonsmokers (0.55, 0.53–0.57). There was an increase in the chance of receiving a kidney from a female donor with increasing weight of the recipient (Table 4); however overall, the effect was small. The proportion of sensitized participants in our study was small with the 90th centile for maximum PRA for men and women with 7% and 12%, respectively. Sensitization as measured by PRA had a nonlinear effect on the probability of receiving a kidney from a female donor (Table 4); however, this did not differ by recipient gender.

There was an interaction between donor relationship and recipient gender in determining the probability of receiving a kidney from a female donor (P-value for interaction < 0.01). Compared with men, women were more likely to receive a kidney from a female donor if their donor was a sibling (0.61, 0.55–0.67 compared with 0.50, 0.45–0.55), friend (0.64, 0.53–0.74 compared with 0.40, 0.32–0.48) or child (0.56, 0.42–0.69 compared with 0.43, 0.31–0.54).

For younger recipients, the probability of receiving a kidney from a female donor was comparable between recipients residing in major cities (age 20: 0.55, 0.52–0.58) and regional or remote areas (age 20: 0.53, 0.49–0.58). However, the probability of receiving a kidney from female donors increased linearly with advancing recipient age for those residing in regional or remote areas compared with recipients living in major cities (age 60: 0.67, 0.63–0.71 compared with 0.57, 0.53–0.60).

A sensitivity analysis was performed excluding spousal donor-recipient pairs in the analyses. (Supplementary Table S2). We found that the probability of a female recipient receiving a kidney from a female donor was similar to male recipients receiving a kidney from female donor irrespective of their relationships (0.58, 0.55–0.61 compared with 0.51, 0.48–0.53). The interaction between recipient age and remoteness remained statistically significant (P for interaction < 0.01) however the interaction between recipient gender and donor relationship was no longer statistically significant (P for interaction $= 0.08$).

DISCUSSION

In this national registry analysis, we found a predominance of female over male living kidney donors with women accounting for 67% of the living donors. The key predictors for female living donations were male recipient gender, recipient spousal relationship with donor, recipient residing in a regional or remote area, recipient being of European Australian ethnicity, increasing recipient age, increasing recipient weight, history of cardiovascular disease, and history of smoking. The relationship between these factors and female donation was not modified by recipient comorbidities and smoking status. The probability of receiving a kidney from a female donor if the recipient is female is approximately 50%, compared with 64% if the recipient is male. We identified 2 key sociodemographic interactions, including recipient gender and donor relationship, as well as recipient age and the

Table 4. Predicted probabilities of receiving a kidney from a female living donor

Covariate		Predicted probabilities of receiving a kidney from a female living donor (95% CI)	Subgroup	Predicted probabilities of receiving a kidney from a female living donor (95% CI)
Recipient gender	Female recipient	0.46 (0.44–0.49)	Female recipient –husband	0.03 (0.02–0.06)
			Female recipient – parent	0.61 (0.56–0.66)
			Female recipient - sibling	0.61 (0.55–0.67)
			Female recipient - child	0.56 (0.42–0.69)
			Female recipient - friend	0.64 (0.53–0.74)
			Female recipient - other related	0.61 (0.51–0.70)
			Female recipient - other nonrelated	0.47 (0.30–0.64)
			Female recipient - paired exchange	0.41 (0.32–0.50)
			Female recipient - altruistic	0.42 (0.23–0.61)
	Male recipient	0.64 (0.62–0.65)	Male recipient – wife	0.99 (0.98–1.00)
			Male recipient - parent	0.56 (0.52–0.60)
			Male recipient - sibling	0.50 (0.46–0.55)
			Male recipient - child	0.43 (0.31–0.54)
			Male recipient - friend	0.40 (0.32–0.48)
			Male recipient - other related	0.48 (0.40–0.56)
			Male recipient - other nonrelated	0.55 (0.43–0.67)
			Male recipient - paired exchange	0.38 (0.29–0.48)
			Male recipient - altruistic	0.56 (0.33–0.78)
Area of residence	Major city	0.56 (0.54–0.58)	Age 20	0.55 (0.52–0.58)
			Age 40	0.56 (0.54–0.58)
			Age 60	0.57 (0.53–0.60)
	Regional/remote	0.60 (0.58–0.63)	Age 20	0.53 (0.49–0.58)
			Age 40	0.60 (0.58–0.63)
			Age 60	0.67 (0.63–0.71)
Ethnicity	European Australian	0.58 (0.56–0.59)		
	Other	0.53 (0.50–0.57)		
Coronary artery disease	None	0.56 (0.55–0.58)		
	Coronary artery disease	0.65 (0.61–0.69)		
Smoking	Never	0.55 (0.53–0.57)		
	Active/former smoker	0.61 (0.59–0.64)		
Weight at transplant	20 kg	0.56 (0.51–0.60)		
	40 kg	0.56 (0.53–0.59)		
	60 kg	0.57 (0.55–0.58)		
	80 kg	0.57 (0.56–0.59)		
	100 kg	0.58 (0.55–0.61)		
Sensitization	cPRA 0%	0.58 (0.56–0.60)		
	cPRA 20%	0.51 (0.47–0.56)		
	cPRA 40%	0.50 (0.43–0.56)		
	cPRA 60%	0.62 (0.23–1.00)		
	cPRA 80%	0.54 (0.44–0.66)		
	cPRA 100%	0.56 (0.31–0.82)		

CI, confidence interval; cPRA, maximum panel reactive antibody; PRA, panel reactive antibody.

location in which the recipients reside. Whereas female recipients were less likely to receive kidneys from female donors when compared with men (46% vs. 64%), there was variability in the probability of receiving a kidney from a female donor based on the recipient's relationship with the donor. This is reflected in the interactive effects between recipient gender and donor relationship, with female recipients more likely to receive a kidney from a female donor if the donor was a sibling, friend, or child. On the contrary, male recipients were less likely to receive a kidney from a female donor if the donor was a child or sibling. With increasing age, recipients residing in regional and remote Australia were more likely to receive a kidney from a female living donor than those in urban Australia, but this was not observed in younger recipients. Among younger recipients, the probability of receiving a kidney from female donor was similar among recipients residing in urban and regional or remote Australia. On the contrary, the probability of receiving a kidney from a female living donor among older recipients living in regional and remote Australia was 10% higher than that of recipients living in urban settings.

The influence of the donor-recipient relationship on the gender of the living donor has been identified previously across several countries. Across Canada, the United States, and Norway, the proportion of female living donors who were siblings, parents and other related donors was significantly higher than male living donors, and among spousal donation wife to husband donation was disproportionally represented.[9,13,14] In this study, we have only included the donor-recipient pairs that had progressed to transplantation as recorded by the ANZDATA registry. We did not have information and details of the donor-recipient pairs that were assessed but deemed unsuitable for donation. Therefore, we were unable to conclude if the observed sex/gender disparity was the consequences of selection biases or whether it was a true reflection of the gender differences of potential donors who underwent assessment. The higher rates of kidney failure in men may have contributed to donor-recipient gender disparity. Between 2003 and 2019, a greater proportion of men (approximately 60% prevalent patients) received kidney replacement therapies than women (Supplementary Table S3). The interaction between donor-recipient relationship and recipient gender was no longer statistically significant when the spousal relationship was excluded in the sensitivity analyses, suggesting that these pairs may have contributed to the observed differential effects between spousal relationships and the donor-recipient gender disparity in living kidney donation.

Previous studies have investigated the reasons for the lower spousal donation rates to female recipients. A large prospective single center study identified sensitization because of pregnancy as the major contributor to reduced rates of spousal and child donation to female recipients, with the rates of attrition of potential male and female living donors for medical or social reasons being otherwise similar.[5] The authors of this study also noted that women who were sensitized during pregnancy were able to find suitable living donors through the paired kidney exchange at a rate similar to that of men who were sensitized. Therefore, the paired exchange program may be an important strategy to resolve the gender disparity issues in living kidney donation. This current data set was limited to recipient donor pairs who underwent kidney transplantation (excluding those who did not proceed), and therefore we are unable to dissect the granular details and reasons for the gender differences in spousal donation. Sensitization resulting from pregnancy alone may not necessarily explain the disparity. Other factors such as higher rates of medical contraindications among potential male donors as well as social and financial factors may contribute to the underrepresentation of spousal donations from male donors. A previous study from Canada identified a greater number of medical exclusions among male spousal donors than female donors, with 11% of male spousal donors excluded for medical comorbidities compared with 5% of female spousal donors.[9] Within our cohort, male donors were more likely to be hypertensive (13% vs. 10%) and have a history of smoking (39% vs. 29%) compared with female donors. A prior study has suggested that Australia has a greater tolerance of relative contraindications for living donors than other countries,[15] with higher rates of hypertension, history of smoking, and the number of relative and absolute contraindications increasing with age.[15] Data from United States suggest that there is a greater tolerance of obesity among female donors, with female living donors being more likely to be obese than male living donors.[16]

We hypothesize that the increased rates of female donors to older recipients in regional or remote Australia were driven by the higher risk of comorbidities such as diabetes, hypertension, and obesity in men. Despite a greater proportion of men residing in rural Australia (than women), a greater proportion of women donated to men. For recipients residing in regional and remote Australia, the probability of receiving a kidney from a female donor increased with age at a higher rate than for recipients who resided in major cities. In Australia, living in remote areas is associated with increased risks of poor health with higher rates of cardiovascular disease, diabetes, and other chronic medical conditions reported in patients living in areas of increasing remoteness,[17] and the greatest impacts being among men living in regional and remote Australia.[18] Therefore, the observed higher rates of female donation with increasing recipient age in regional and remote Australia may reflect this disparity in general health between sexes. Furthermore, financial considerations may contribute to this disparity, with people in regional and remote Australia having an 18% lower average weekly household income than that of people living in major cities,[19] and in the context of financial strain, women may be more likely to donate to minimize impact on the household income. A prior study in the United States identified that donor gender modified the relationship between income status and rates of living kidney donation over time. Men were less likely to donate if the average income was below the top quartile of income ($>$ $61,902) compared with men whose average income was in the lower quartiles ($<$ $61,902) with such a marked effect of income not observed in women.[10] The Supporting Living Donor Program, introduced in 2017 and funded by the Commonwealth, is a program that provides financial reimbursement of both out of pocket expenses associated with donation and reimbursement of up to 342 hours of paid leave at the national minimum wage to minimize the financial penalty to living donors. In addition, this program also funds out of pocket expenses such as accommodation, airfares, petrol, and public transport up to $1000. Our analysis was restricted to the past 20 years (2003–2019) during which the rates of female donors remained constant (see Supplementary Figure S1) and future analyses should assess if the observed disparity persists after the program was introduced in 2017.

Our analysis has several strengths. Utilizing a national data set with 3523 donor and recipient pairs, we were able to investigate the contribution of a wide range of donor and recipient characteristics to receiving a living kidney donation from a female donor in Australia. We used a machine learning approach for variable selection for the predictive model, and multiple imputation to account for missingness. However, given the complex interactions we identified within the data, we opted to present our results as predicted probabilities using marginal means, which suggests extrapolation to other populations may not be possible. Historically within ANZDATA, sex and gender were collected by clinicians and consequently may not correctly identify gender by self-report. Given the inclusion of only donor-recipient pairs who proceeded to transplantation, we are unable to assess whether this disparity is the result of donor selection or in differences in the gender of potential donors who undergo assessment. It also remains unclear if the differences in donor gender are solely driven by the higher proportion of men who have kidney failure, because female spousal donors are the largest donor group. Our study was also restricted to the most recent era because there was limited information available about donor characteristics before 2003, and we have limited ability to assess if there has been temporal changes in female living donation. Our analysis provides limited insight into the reasons for gender disparities in living kidney donation, with further qualitative work likely to be key to understanding the economic, cultural, and social factors which contribute in Australia, as well as a prospective studies to understand what medical factors during the assessment of living donors contribute to the higher number of female donors. Exploration of the differences in the prevalence of relative and absolute contraindications between female and male donors would also be useful to identify if there is greater tolerance of comorbidities among female donors.

In conclusion, our findings suggest that the observed differences in living kidney donation by gender are influenced by both recipient and donor characteristics, with the intersection of donor-recipient relationship and recipient gender, age, and location of the recipients' residence being the key factors for living kidney donation from female donors. Further work is needed to determine the relative contribution of economic, medical, and sociocultural barriers to living kidney donation by men and to evaluate if such obstacles differ with remoteness. If economic barriers are found to be a major contributor, the government should consider additional financial support for living donors in regional and rural Australia above what is currently provided. Focusing on improving the health and access to health care in regional and remote Australia will also minimize medical contraindications to living kidney donation among men.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the ANZDATA (Australian and New Zealand Dialysis and Transplantation) and ANZOD (Australian and New Zealand Organ Donor) registries. Restrictions apply to the availability of these data, which were provided by ANZDATA and ANZOD following ethics approval for this study.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Table S1. Factors associated with the odds of receiving a kidney from a female living donor.

Supplementary Table S2. Predicted probabilities of receiving kidney from female living donor – sensitivity analysis excluding spousal relationship.

Supplementary Table S3. Incident and prevalent patients receiving renal replacement therapy.

Supplementary Figure S1. Proportion of female donors over time.

STROBE Checklist.

Supplementary Reference.

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