Bailey, P., Tomson, C., MacNeill, S., Marsden, A., Cooke, R., Cook, D., ... Ben-Shlomo, Y. (2017). A multicenter cohort study of potential living kidney donors provides predictors of living kidney donation and non-donation. *Kidney International*, *92*(5), 1249-1260. https://doi.org/10.1016/j.kint.2017.04.020

Predictors of living kidney donation and non-donation: a UK multicentre cohort study of potential living kidney donors

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Running headline

Predictors of living kidney donation and withdrawal

Abstract

This multicentre prospective potential living kidney donor cohort study investigated which sociodemographic and other factors predict progression to living kidney donation or donor withdrawal, as little is known on this topic.

Data were collected on individuals undergoing living donor assessment at 7 UK hospitals from 01/08/14 to 31/1/16. Multivariable logistic regression was used to explore the relationships between donor and recipient characteristics and likelihood of kidney donation.

805 individuals presented for directed donation to 498 intended recipients. 112 intended recipients received a transplant from a living-donor. Potential donors were less likely to donate if their intended recipient was female rather than male (Odds Ratio (OR) 0.60 (0.38-0.94) p=0.03), a friend rather than relative (OR 0.18 (0.05-0.60) p=0.01), or had renal failure due to a systemic disease rather than another cause (OR 0.41 (0.21-0.80) p=0.01). The most socioeconomically deprived quintile were less likely to donate than the least (OR 0.49 (0.24-1.00) p=0.05), but the trend with deprivation was consistent with chance (p=0.12). Higher BMI was associated with a lower odds of donation (OR per +1kg/m^2 0.92 (95% Confidence Interval 0.88-0.96) p<0.001)). Younger potential donors (OR per +1 year 0.97 (0.95-0.98) p<0.001), those of non-white ethnicity (OR 2.98 (1.05-8.44) p=0.04) and friend donors (OR 2.43 (1.31-4.51) p=0.01) were more likely to withdraw from work-up.

This is the first UK study of potential living kidney donors to describe predictors of non-donation. Qualitative work with individuals who withdraw might identify possible ways of supporting those who wish to donate but experience difficulties doing so.

Keywords

Living donors; Kidney donation; Transplantation; Sociodemographic predictors.

Introduction

In the UK, national data are collected on potential and actual deceased organ donors by NHS Blood and Transplant.[1] Whilst data are collected on actual living kidney donors (LKDs),[2] no national data are collected on people who undergo assessment for living donation, that is, potential living donors. Therefore little is known about what factors influence progression to donation or withdrawal.

Two UK single-centre cohort studies have reported the proportion of potential donors that actually go on to donate as 13%[3] and 18%.[4] Studies from the Republic of Ireland,[5] the Netherlands,[6] Poland,[7] South Africa,[8] and the USA,[9-11] have reported varied estimates of between 8-49% of potential donors becoming actual donors. Almost all of these studies were single-centre and the predictors of donation and of non-donation have not been well described. Identifying predictors of non-donation, and potential donor withdrawal in particular, may identify groups of potential donors who would benefit from further support, and may identify ways of making this process more efficient. There has been a recent call from the renal transplant community to address this gap in knowledge.[12]

This is the first UK multicentre prospective cohort study of potential LKDs to investigate the sociodemographic predictors of living kidney donation, and the main reasons for non-donation: i) donor withdrawal, and ii) donors being clinically unfit for donation. In the UK,[13] the Netherlands,[14] the USA[15-17] and Australia,[18] socioeconomically deprived patients with renal failure are less likely to receive a living-donor kidney transplant (LDKT) than less deprived patients. Therefore, we were particularly interested in investigating whether this observed socioeconomic inequity is in part explained by socioeconomic inequity in potential donor progression and retention.

Results

A total of 856 potential donors were recruited (Figure 1 – Flow chart of study participants). After the exclusion of non-directed 'altruistic' donors on whom no recipient information was available (n=51), 805 potential donors linked to 498 intended recipients remained. 74.3% (n=598) of donors had their first assessment for donation in a face-to-face meeting with a living donor coordinator. The remainder (25.6% (n=206)) were initially assessed over the telephone or via a posted and returned questionnaire. For one individual information on the mode of first assessment was missing.

Potential donor characteristics

Characteristics for all potential donors and by level of socioeconomic deprivation (SED) are provided in Table 1. More deprived potential donors were younger than the less deprived ($p<0.001$): the median age of potential donors in Index of Multiple Deprivation (IMD) quintile 5 was more than 10 years less than that of those in IMD quintile 1. A greater proportion of deprived than less deprived donors were ethnicities other than white ($p=0.02$). The median body mass index (BMI) of donors was high ('overweight') across all levels of SED. 26.9% of potential donors had a BMI ≥30kg/m^2. Donor marital status differed with SED ($p<0.001$): more deprived donors were less likely to be married, and more likely to be in a long-term relationship without being married. Less deprived donors were more likely to be retired than more deprived donors ($p=0.02$). There was no evidence that more deprived individuals who had presented for donation had more comorbidities than the less deprived ($p=0.41$).

The different renal units evaluated potential donors with different levels of SED (Supplementary Table 1) reflecting differences in the populations they serve.[19] In Cambridge and Bristol, <6% of

the potential donors evaluated were from IMD quintile 5, whereas >25% of the potential donors evaluated in Cardiff, Newcastle and Preston were from this quintile.

Intended recipient characteristics

Intended recipient characteristics by level of SED are presented in Table 2. As with potential donors, more deprived intended recipients were younger than less deprived recipients (p=0.01). . More deprived intended recipients were at a more advanced stage of renal disease than less deprived recipients: intended recipients in IMD quintiles 4 and 5 were less likely to be at Chronic Kidney Disease (CKD) stages G4 or G4T, and were more likely to be at CKD stage 5 or on dialysis (p<0.001).

Donors and recipients came from the same IMD quintile in 58.8% of donor-recipients pairs for which no IMD data was missing (n=682, agreement 81.8%, expected agreement 59.8%, weighted-kappa 0.55, p<0.001).

Potential donor outcomes

Of the 805 potential donors, 735 had outcomes at the close of the study, and 70 were censored as they were still undergoing assessment. The characteristics of censored individuals were compared to those of potential donors included in the analysis; no evidence was found for any differences between the two groups. 112 (15.2%) individuals had donated by the close of the study. 110 (15.0%) individuals had withdrawn. Outcomes for potential donors by level of SED are available as Supplementary Table 2.

Median duration of donor assessment for those who donated was 308 days (Inter-quartile range (IQR) 176 days). Donors who withdrew were in work-up for a median of 61 days (IQR 157 days).

One donor withdrew from evaluation after 754 days. Median duration of donor evaluation for potential donors who were deemed medically unsuitable was 76 days (IQR 162 days), surgically unsuitable 152 days (IQR 438 days), and psychologically unsuitable 183 days (IQR 153 days), reflecting the order in which these evaluations are typically undertaken in work-up.

Predictors of living kidney donation

182 potential donors were excluded from this analysis as their progress was dependent on the progress of other potential donors (see 'Methods'). The characteristics of these donors were compared to those who progressed (Supplementary Table 3). Of multiple potential donors for the same recipient, those who were not selected to proceed with donor assessment were younger (p=0.001), more likely to be single (p=0.02), more likely to be a friend (p=0.005), and more likely to be HLA/ABO incompatible (p=0.006). This suggests that at this early stage, discussions between potential donors, recipients and donor coordinators result in older donors, closer relatives and better immunological matches being selected over younger potential donors and friends.

Univariable analyses (Table 3) found that if the potential donor was the parent of the intended recipient they were more likely to donate (Odds Ratio 1.95 (95% Confidence Interval (CI) 1.16-3.26) p=0.01). This association was not altered after adjustment for donor age (OR 1.97 (95%CI 1.14-3.42) p=0.02) but it was weakened after adjustment for recipient age (OR 1.75 (95%CI 0.98-3.13) p=0.06), suggesting that the parents of young children are more likely to progress through to donation. Potential donors who were friends rather than relatives were less likely to donate (OR 0.18 (95%CI 0.05-0.60) p=0.01). This strong association remained even after adjustment for donor and recipient age, sex, donor BMI, donor SED, comorbidity and recipient primary renal disease (PRD) (OR 0.18 (95%CI 0.05-0.60) p=0.005). Higher BMI was associated with a lower likelihood of

donation (OR per 1kg/m^2 increase 0.92 (95%CI 0.88-0.96) p<0.001). This did not change after adjustment for donor age and sex (OR 0.92 (95%CI 0.88-0.96) p<0.001).

If the potential donor's intended recipient had a glomerular PRD the potential donor was more likely to donate (OR 1.74 (95%CI 1.10-2.77) p=0.02). This remained after adjustment for donor and intended recipient age, sex, SED level, and donor comorbidity (OR 1.78 (95%CI 1.09-2.90) p=0.02). Potential donors were less likely to donate if their intended recipient had a systemic PRD (OR 0.41 (95%CI 0.21-0.80) p=0.01). 61.3% of those with systemic PRDs had diabetes mellitus as the cause of their renal failure. Further exploration revealed that those donating to an individual with a systemic PRD were more likely to not donate due to their intended recipient being unfit (OR of non-donation as recipient unfit 2.65 (95%CI 1.07-6.59) p=0.04).

Socioeconomic deprivation, potential donors and likelihood of living kidney donation

Although the greatest level of SED appeared to be associated with a halving of the likelihood of donation (IMD quintile 5 versus 1, OR 0.49 (95%CI 0.24-1.00) p=0.05), the trend with deprivation was non-linear and consistent with chance (OR per IMD quintile increase 0.88 (95%CI 0.75-1.03) p=0.12). In the donor and recipient sex-adjusted analysis (Supplementary Table 4), the most deprived potential donors remained the least likely to donate, but as expected this didn't persist after adjustment for possible mediators of SED on living donation with most IMD quintiles showing attenuation of the effect estimates. No evidence was found of interaction between SED and age, sex or transplant centre.

Predictors of potential donor withdrawal

Younger donors were more likely to withdraw from donor work-up (Table 4). This association remained after adjustment for donor and recipient sex, and recipient age. Non-white potential donors were almost three times as likely to withdraw than whites (OR 2.98 (95%CI 1.05-8.44) p=0.04) but this finding must be treated with caution as the number of non-white individuals was very small. Those without comorbidities were more likely to withdraw from donor assessment. This association was diminished after adjustment for donor age (adjusted OR 0.66 (95%CI 0.39-1.11) p=0.11) as those with comorbidities are more likely to be older individuals who were much less likely to withdraw from donor work-up. Parental donors were much less likely to withdraw from work-up, but this association was weakened after adjustment for donor age (OR 0.47 (95%CI 0.20-1.08) p=0.08). Friends rather than relatives were more likely to withdraw. This association remained after adjustment for donor and recipient age, sex and level of SED (OR 2.32 (95%CI 1.13-4.78) p=0.02). People donating to more deprived recipients were more likely to withdraw, but this association was not statistically significant at the 5% level after adjustment for donor age (OR of withdrawal per unit increase in IMD quintile 1.13 (95%CI 0.95-1.34) p=0.17).

Predictors of potential donor clinical unsuitability

Older donor age (OR per +1 year 1.02 (95%CI 1.01-1.04) p=0.01), and active comorbidities (OR ≥1 comorbidities vs none 3.30 (95%CI 2.22-4.90) p<0.001) were associated with an increased likelihood of a donor being assessed as unsuitable. No association between donor clinical unsuitability and SED or recipient PRD was found.

Predictors of renal transplantation for a recipient

Findings of unadjusted analyses examining intended recipient likelihood of receiving a LDKT are presented in Supplementary Table 5. Transplant candidates who had three potential donors under

review were twice as likely to receive a LDKT than those with one under evaluation (OR 2.21 (95%CI 1.00-4.88) p=0.05): having >3 potential donors did not confer any added benefit ('threshold effect'). There was no evidence that more deprived transplant candidates were less likely to receive a LDKT once they had a potential donor under review (p value for trend of increasing IMD quintile=0.46).

Missing data

7.1% (n=57) of the 805 potential donors and 12.1% (n=60) of the 498 intended recipients were missing an IMD score. No pattern of missingness was identified. Missing scores resulted from postcodes not being recorded in the medical notes, new postcodes not yet having a corresponding IMD score, or the participant not being from England/Wales. Missing covariate information was <5% for all donor and recipient covariates, and no patterns of missingness were identified. Due to the small amount of missing data, the associations did not significantly differ between the complete cases analysis and the analyses with missing variables imputed (Supplementary Table 6).

The analyses performed separately for Wales and England, and then pooled, were comparable to those generated in the combined analyses (Supplementary Figures).

Discussion

15.2% of potential donors with end-points at the close of the study had donated. Our findings suggest that of those individuals who begin LKD assessment, potential donors who i) are friends of their intended recipient, ii) have a higher BMI, iii) are donating to female recipients, and iv) donating to an individual with a systemic PRD are less likely to progress to donating a kidney.

Donors living in the most socioeconomically deprived 20% of areas were less likely to donate when compared to the least deprived but there was no strong evidence of a linear trend.

The majority of individuals who volunteer for possible living kidney donation do not go on to donate. This study has identified which potential donors are the least likely to donate and has identified predictors of withdrawal. Identifying those potential donors who are least likely to progress helps to identify barriers to living kidney donation, and identify opportunities to support potential donors and improve living donor retention. This is of particular importance in countries, including the UK and USA, in which rates of living-donor kidney transplantation have recently plateaued or even declined.[20, 21]

With respect to understanding the socioeconomic inequity in living-donor kidney transplantation, our study suggests that while the most deprived potential donors were the least likely to donate a kidney, there was no trend with SED, and therefore deprivation may affect donor recruitment rather than progress once recruited.

Predictors of living kidney donation and non-donation

Women were less likely to receive a LDKT; this has been described previously,[22, 23] and is thought to be due at least in part to the greater level of lymphocytotoxic antibodies from sensitizing events including pregnancy, which provide a barrier to transplantation.[24] Transplant candidates with a systemic PRD were less likely to receive a LDKT, whilst those with a glomerular PRD were more likely, something that has also been suggested previously in the UK.[25] Individuals with glomerular diseases may be less likely to have multiple comorbidities (as compared to individuals with systemic diseases) which may impact on maintained intended recipient fitness for transplantation while a potential donor is being evaluated.[25] In keeping with this, those donating to an individual

with a systemic PRD were more likely to not donate because their recipient was unfit. This was due to individuals listed as suitable for transplantation becoming unsuitable, and donor evaluation starting prior to the recipient's transplant fitness being ascertained. Ensuring intended recipients are fit before a potential living donor begins assessment may prevent disappointment on the donor's part, and prevent money being spent on unnecessary investigations.

High BMI in the potential donor population is a problem; the median BMI of donors across all socioeconomic levels was classed as 'overweight', and potential donors with higher BMIs were less likely to donate. Our findings suggest that national and international guidelines for living kidney donation are being followed: UK guidelines[26] recommend that moderately obese individuals are counselled about increased peri-operative and longer-term risks following donation, and those with BMIs >35kg/m^2 are discouraged from donating. In our study higher BMI was not a predictor of being deemed clinically unsuitable, suggesting that those with high BMIs are suspended from work-up in order to lose weight, rather than classified as completely unsuitable.

The UK guidelines are slightly more conservative than international guidelines. Draft 'Kidney Disease: Improving Global Outcomes' (KDIGO) guidelines[27] recommend that up to BMIs of 40 kg/m^2 can be considered for donation, but obese individuals should still be counselled regarding high risks. It would be interesting to see if BMI is such a strong predictor of non-donation in countries in which those with higher BMIs are allowed to donate.

Predictors of potential donor withdrawal

19.9% (n=110) of independent donors withdrew from work-up. This is comparable to the 17.5% figure reported in another UK donor attrition study.[3] Friends were more likely to withdraw from donor assessment than relatives. This might reflect weaker emotional relationships, but a lack of

family support for the donor may be of importance, as has been suggested in the progress of non-directed kidney donors.[28]

Both UK and KDIGO guidelines[26, 27, 29] reference recent studies which reported that certain individuals, including younger and black individuals, have a greater lifetime risk of developing renal failure following donation.[30-32] Communication of these increased risks may explain the increased likelihood of withdrawal in younger and non-white potential donors in our study. In addition, for younger people, the impact of donor evaluation on the lifestyle, including caring responsibilities, may be too great. Detailed qualitative work is urgently required[12] to understand the reasons for withdrawal.

Socioeconomic deprivation and living kidney donation

In the UK, as in the Netherlands,[14] the USA[15-17] and Australia,[18] renal patients from socioeconomically deprived populations are less likely to receive a LDKT[13] than less deprived individuals, despite being more likely to have renal failure.[33-36] Thus far, it has not been clear whether socioeconomic barriers to living-donor kidney transplantation exist once a transplant candidate has one or more potential donors under evaluation. This study hasn't provided strong evidence that, once under review, more deprived donors are less likely to progress through to donation though the study may have been underpowered to demonstrate a weaker effect. Whilst one might have expected that donors from areas of greater deprivation would have poorer health[37-41] and hence may not progress, our failure to observe this may be explained by pre-hospital screening or self-selection (those with health problems don't present), and/or because donors from more deprived areas were more likely to be younger.

If failure to progress once being assessed is not the reason, then other explanations need to be considered such as delays in both transplant referral[42] and in renal patient listing for

transplantation,[43, 44] and possible barriers to the pursuit of a LDKT and recruitment of a potential donor.[45, 46]

Socioeconomic deprivation, potential donors and transplant candidates

Potential donors for more deprived transplant candidates start donor assessment when the transplant candidates are at more advanced stages of renal disease (CKD 5 and dialysis) when compared to less deprived transplant candidates. This is in keeping with previous research that suggests that socioeconomically deprived individuals are less likely to receive a pre-emptive kidney transplant.[17, 18, 47-49] This may reflect the association of SED with more rapid progression of renal disease towards renal failure,[50] later presentation to secondary care[51, 52] and later listing for transplantation.[43, 44, 53, 54] Qualitative work also suggests that a lack of a long-term health perspective might mean that LDKTs aren't considered until a situation makes it of importance in the short-term.[45] Starting discussions about living-donor kidney transplantation early, and trying to encourage a longer-term perspective may help to encourage a more timely pursuit of live-donor kidney transplantation.

Strengths and limitations

This prospective cohort study is the first UK study to collect multicentre data on potential LKDs. To our knowledge, it is also the first to explore the relationship between SED and potential LKD conversion to actual donor. Only seven individuals (0.8%) declined to participate. The amount of missing data was <10% for donor exposure variable and covariates. However, there are some important limitations: i) This study does not capture possible variation in the informal 'screening' of potential donors by healthcare workers when they accompany candidates to clinic, by intended recipients or potential donors themselves, that occurs prior to the potential donor being assessed at the renal unit. ii) Practice at all the participating centres was similar so study findings may not

be generalizable to renal centres with differences in donor evaluation (for example, one day assessment)[55] or in healthcare systems with different models of funding; iii) The cohort study population was predominantly (92.8%) white so our findings might not be generalizable to populations in other ethnic groups; iv) Whilst this study is reasonably large, we may have been underpowered to detect modest effects; v) The study was based at seven renal units, and therefore we could not test for variation between centres.

Future work

This study has identified groups worthy of further study. Longitudinal qualitative research with those donors this study has identified are most likely to withdraw may provide greater understanding of the reasons for withdrawal, and of ways in which individuals could be supported through the process if their desire to donate remains. Ethnographic work in renal units, and consultation analysis could be used to investigate the influence of physicians on potential donor decision-making. This study also emphasises the need to address obesity in the potential donor population.[56] Ensuring potential donors know at the time a relative or friend is diagnosed with renal disease that a high BMI will prevent donation and offering weightloss support at this stage will not only improve the health of potential donors, but also increase the likelihood of them being suitable for donation if this is something they wish to pursue in the future. Engaging with weightloss in advance of a possible kidney donation will help clinicians assess if the weightloss is sustainable, and likely to be maintained after donation.[57]

We believe the establishment of a national reporting system of potential living-donor evaluations from all UK renal units (as with deceased donors[1]), would enable centre variation and practice patterns to be investigated, as well as provide far greater power to examine the relationships

between ethnicity, SED and donor progression in greater detail. National reporting of unit donor progression might also highlight best practice and may help with the initiation and monitoring of multi-arm trials of interventions aimed at supporting and facilitating living kidney donation.

Conclusions

This study has described several predictors of living kidney donation and potential donor withdrawal. It has suggested that barriers to socioeconomically deprived renal patients prior to the recruitment of potential donors may be important as a strong association between SED and progress or retention of potential donors once under review was not demonstrated.

Methods

Detailed methods are provided as a supplementary file.

The study was based at seven renal units in England and Wales: Southmead Hospital, Bristol; Addenbrooke's Hospital, Cambridge; The Freeman Hospital, Newcastle-upon-Tyne; Royal Stoke University Hospital, Stoke-on-Trent; Royal Preston Hospital, Preston; University Hospital of Wales, Cardiff; and Morriston Hospital, Swansea. Four units are transplant centres, perform donor nephrectomy and transplantation operations. Three units refer candidates to another centre for final approval/surgery. During the study period, the annual proportion of those active on the transplant waiting list who received a LDKT at each participating centre (or the transplant unit to which they refer) ranged between 13.1% and 32.8%.[21] All centres participate in the UK paired exchange program. Data was collected on all individuals who presented for LKD assessment between 1/8/14 and 31/1/16.

The cohort population consisted of potential LKDs and their intended recipients. 'Potential donors' comprised all individuals who underwent a formal documented initial assessment for living kidney donation during the study period. Initial assessments could be conducted over the telephone, in person, or via written communication (e.g. questionnaire, email). All potential donors were eligible. Information regarding the study was provided in a detailed patient information leaflet. An opt-out consent procedure was approved for use as no data were collected other than that routinely collected in donor assessment. Participants were identified by the LKD co-ordinators at each centre, and a list maintained at each site. Individuals were followed until reaching the primary outcome (of donation or confirmed non-donation), or until 31/7/16, whichever occurred first, allowing for a minimum of 6 months follow-up. Donor assessment at the study sites is undertaken in stages (see Supplementary Methods) so individuals could leave the process after different degrees of investigation and assessment. For example, an individual could withdraw from the process after an initial meeting, before any investigations, whilst another might progress to final surgical review and only be deemed unsuitable at this stage. Individuals who remained in donor work-up at study closure were censored for analysis. Multiple potential donors could undergo donor evaluation for the same intended recipient. When multiple donors presented, a decision was typically made early in the process regarding which individual would progress through to further investigations and clinical review.

Data collection

The study was approved by NHS Research Ethics Committee South East Coast (Ref.13/LO/1820). Anonymised data were extracted from the study sites every 4-6 months using REDCap.[58]

The primary outcome for potential donors was whether they did or did not donate a kidney. The primary outcome for recipients was whether or not they received a LDKT. Reasons for non-donation or non-transplantation were recorded (Box 1).

Box 1 Outcomes

Potential donor outcomes

- Living kidney donation/Donor nephrectomy
- Donor did not donate
    - Donor withdrew from work-up
    - Donor medically/surgically/psychologically unfit
    - Donor work-up suspended e.g. to lose weight, to gain BP control
    - Donor unable to proceed – recipient unfit/died
    - Donor did not proceed – alternative donor selected to proceed
    - HLAi/ABOi – Options or options unsuccessful
    - Donor suitable – in pool, awaiting match for exchange

Intended recipient outcomes

- Recipient received LDKT/date planned for transplantation
- Recipient did not receive LDKT
    - Recipient decided against LDKT
    - Recipient unfit/died
    - Recipient received a DDKT
    - Donor withdrew from work-up
    - Donor medically/surgically/psychologically unfit to proceed
    - Donor work-up suspended e.g. to lose weight, to gain BP control
    - HLAi/ABOi – Options or options unsuccessful
    - Donor suitable – in pool, awaiting match for exchange

The exposure variables under investigation were donor and recipient sex, age, level of SED, and donor comorbidity. The IMD was used as an ecological measure of SED at the small area level. At each study site participant postcodes were converted into the English IMD 2010 and Welsh IMD 2011[59, 60] scores using the UK Data Service Census Support's GeoConvert tool.[61] Each participant's country specific IMD quintile was calculated according to their individual IMD score using English and Welsh government data reports.[59, 60] Higher scores represent greater levels of deprivation.

Living donor evaluation is carried out with reference to the UK Guidelines for Living Donor Kidney Transplantation.[26] Information collected routinely during LKD evaluation was recorded, including medical history, clinical examinations, and investigations. The intended recipient's PRD was coded according to the European Renal Association-European Dialysis and Transplantation Association (ERA-EDTA) PRD registry codes,[62] and grouped into the ERA-EDTA disease groups ('major headings').

Statistical analysis

Potential donor and intended recipient characteristics were compared across different levels of SED by simple cross-tabulations. Means and standard deviations were calculated for normally distributed continuous variables. Medians and IQRs are presented for continuous variables whose distribution was not normal. One-way analysis of variance (ANOVA), Chi-squared test, Fisher's exact test, and Cuzick's test for trend were used to compare baseline characteristics between IMD quintile subgroups of patients. The concordance of IMD quintiles of potential donors and their intended recipients were compared using the weighted kappa-statistic.

Multivariable logistic regression models (ORs, 95% CIs, p-values) were used to explore the relationship between potential donor sociodemographic exposure variables (sex, age, BMI, SED, donor-recipient relationship, PRD) and the likelihood of living kidney donation. Potential donors for the same recipient are likely to be more similar than potential donors for different recipients, so we derived robust standard errors, to account for clustering by intended recipient. When multiple potential donors present to donate to the same intended recipient then the progression of each donor may not be independent of the other(s). In Figure 2 (Figure 2 - Illustration of potential non-independence of potential donor progression through donor evaluation), the

intended recipient has three potential donors. Potential donor 3 is found to be medically unsuitable for donation, whilst both 1 and 2 are suitable at the first assessment. Potential donor 2 however is a better match, and therefore the assessment of potential donor 1 is halted, whilst potential donor 2 proceeds. Therefore, the progression of potential donor 2 and the progression of potential donor 3 are independent, whereas the progression of potential donor 1 and that of potential donor 2 are not independent. Individuals whose work-up was discontinued because an alternative donor progressed were excluded from the logistic regression analysis; only independently progressing potential donors were included.

For the analysis with SED we undertook three models: i) unadjusted, ii) adjusted for potential confounders, and iii) adjusted for potential mediators. We specified, *a priori*, potential confounders such as donor and recipient sex, and potential mediators of the effect of SED on likelihood of living kidney donation including donor and recipient age at work-up, donor comorbidity and recipient PRD. As there were very few non-white participants donor and recipient ethnicity were omitted from the models. We tested for *a priori* interactions between SED and the following covariates: age, sex, and renal centre, for both potential donors and intended recipients.

To explore possible sociodemographic variation in the reasons for non-donation, we created binary outcome variables for reasons for non-donation e.g. 'Potential donor withdrew from work-up (Yes/No)'.

We repeated our multivariable logistic regression models to look at recipient outcomes, and to explore the relationship between sociodemographic variables and their prediction of receiving a LDKT, using robust standard errors to account for clustering within renal centres. The analysis was performed both unadjusted and adjusted for the following recipient variables: age-group

(quartiles), sex, number of potential donors the intended recipient had under review, and whether the recipient was based at a transplanting or non-transplanting centre.

Analyses were performed using the combined Welsh and English IMD quintiles as measures of SED. However, as Welsh and English IMD scores are not directly comparable, sensitivity analyses were also performed separately for Wales and England, and the results pooled.

We performed a complete case analysis but also undertook a sensitivity analysis using multiple imputation using chained equations to derive 20 imputed datasets per group, for the exposure variable and potential confounders and then combined using Rubin's rules using the multiple imputation procedure in Stata 14.[63]

The report was prepared with adherence to the 'STrengthening the Reporting of OBservational studies in Epidemiology' (STROBE) statement.[64]

Supplementary information is available at Kidney International's website.

Figure legends

Figure 1 - Flow chart of study participants

Figure 2 - Illustration of potential non-independence of potential donor progression through donor evaluation

Disclosure

All the authors declare no competing interests.

Acknowledgements

This report is independent research arising from a Doctoral Research Fellowship (PKB) supported by the National Institute for Health Research (NIHR). YB-S is the equity theme lead for the NIHR Collaboration for Leadership in Applied Health Research and Care West (CLAHRC West) at University Hospitals Bristol NHS Foundation Trust. CLAHRC West is part of the NIHR, and is a partnership between University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health.

The authors would like to thank all the study participants, and the living donor coordinators at each site who facilitated the study. They would also like to thank the anonymous reviewers who reviewed an earlier version of this work and whose comments helped the authors to make improvements to the paper.

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