

## **Title**

Utilisation and clinical outcomes of kidney transplants from deceased donors with albuminuria in the UK: a national cohort study

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## **Abbreviations**

AKI, acute kidney injury

BMI, body mass index

CI, confidence interval

CIT, cold ischaemia time

CVA, cerebrovascular accident

cRF, calculated reaction frequency

DBD, donation after brain death

DCD, donation after circulatory death

DGF, delayed graft function

eGFR, estimated glomerular filtration rate

HLA, human leucocyte antigen

HR, hazard ratio

IQR, interquartile range

NHSBT, National Health Service Blood and Transplant

OR, odds ratio

uPCR, urine protein : creatinine ratio

PNF, primary non-function

SD, standard deviation

KDRI, kidney donor risk index

UKTR, United Kingdom transplant registry

## **Abstract**

### **Background**

Urinalysis is a standard component of potential deceased kidney donor assessment in the UK. The value of albuminuria as a biomarker for organ quality is uncertain. We examined the relationship between deceased donor albuminuria and kidney utilisation, survival, and function.

### **Methods**

We performed a national cohort study on adult deceased donors and kidney transplant recipients between 2016 and 2020, using data from the UK Transplant Registry. We examined the influence of donor albuminuria, defined as  $\geq 2+$  on dipstick testing, on kidney utilisation, early graft function, graft failure, and estimated glomerular filtration rate (eGFR).

### **Results**

Eighteen percent (1,681/9,309) of consented donors had albuminuria. After adjustment for confounders, kidneys from donors with albuminuria were less likely to be accepted for transplantation (74% vs 82%; OR 0.70, 95% CI 0.61 to 0.81). Of 9,834 kidney transplants included in our study, 1,550 (16%) came from donors with albuminuria. After a median follow-up of 2 years, 8% (118/1,550) and 9% (706/8,284) of transplants from donors with and without albuminuria failed, respectively. There was no association between donor albuminuria and graft failure (HR 0.91, 95% CI 0.74 to 1.11). There was also no association with delayed graft function, patient survival, or eGFR at 1 or 3 years.

### **Conclusions**

Our study suggests reluctance in the UK to utilise kidneys from deceased donors with dipstick albuminuria but no evidence of an association with graft survival or function. This

may represent a potential to expand organ utilisation without negatively impacting transplant outcomes.

## **Key learning points**

### **What is already known about this subject**

- While there is good evidence linking albuminuria to adverse outcomes in patients with chronic kidney disease, the significance of deceased donor albuminuria in relation to kidney transplantation is uncertain.
- Small studies have shown more chronic damage in biopsies at the time of organ retrieval in donors with proteinuria, but there is no evidence that urinary abnormalities predict clinical outcomes following transplantation.
- Some clinicians are wary of accepting a kidney transplant offer from a donor with albuminuria, but it is not known whether this is justified.

### **What this study adds**

- We found strong evidence that kidneys from UK deceased donors with albuminuria detected on dipstick are less likely to be accepted for transplantation.
- At the same time, in the kidneys that were utilised, there was no association between donor albuminuria and graft survival or function following transplantation.

### **What impact this may have on practice or policy**

- Although we cannot prove a causal link, our findings challenge existing beliefs about the significance of dipstick albuminuria in deceased donor assessment.
- Dipstick albuminuria does not appear to be a reliable marker of organ quality in this context.
- It may be possible to expand organ utilisation without negatively impacting outcomes.

## **Keywords**

Kidney transplantation; albuminuria; deceased organ donation; proteinuria; biomarkers

# 1 Introduction

Kidney transplantation offers the best survival benefit for suitable patients with end-stage renal failure.<sup>1,2</sup> While deceased donation rates in the UK have increased, demand for organs still exceeds supply, such that each year hundreds of patients waiting for a transplant die or become too unwell to undergo the operation.<sup>3,4</sup> Reliable donor risk assessment underpins appropriate organ allocation and clinical decision-making. Although there is good evidence that certain donor attributes influence graft survival and function,<sup>5,6</sup> it is important to critically assess all potential markers of organ quality in order to widen access to transplantation.<sup>7</sup>

Albuminuria is a commonly used biomarker of glomerular dysfunction. There is a consistent association between albuminuria and renal function decline in the general population.<sup>8-11</sup> Dipstick urinalysis is a readily available, low-cost means of detecting albuminuria with reasonable performance as a screening tool.<sup>12-14</sup> Albuminuria is common in critical care patients, and is associated with a greater risk of, and lower recovery from, acute kidney injury (AKI) in this population.<sup>15-18</sup> It might therefore be useful as a marker of organ quality in the context of kidney donation. As such, urine dipstick testing is now a standard component of deceased donor assessment in the UK.

Although albuminuria may indicate established kidney disease, it can occur in the absence of renal pathology, as a result of factors that are often seen in deceased donors.<sup>19</sup> Systemic inflammation and cytokine release, as seen in sepsis, trauma or brain death, can increase glomerular permeability, while obesity or severe hypertension may cause glomerular hyperfiltration.<sup>20-23</sup> Furthermore, polyuria or oliguria, which may result from diabetes insipidus or AKI, can influence the reliability of dipstick urinalysis. Therefore, it may not be appropriate to extrapolate evidence from the general or critical care population to deceased donors.

There is little evidence to guide clinical practice in this area. Although grafts from donors with proteinuria may have more acute and chronic injury at the time of implantation, a relationship with clinical outcomes is unproven.<sup>24-28</sup> Evidence on deceased donors mainly comes from

studies in which donors with brain death (DBD) predominate; this may not be generalisable to transplant programs with more donation after cardiac death (DCD), such as in the UK. Furthermore, urine protein : creatinine ratio (uPCR) is often unavailable at the time of donor assessment; consequently, substantial missing data reduces the power of previous studies and may introduce selection bias. The clinical utility of dipstick albuminuria, a readily available test in widespread use by organ donation specialists, is unclear. Formal examination of organ utilisation in this context is also lacking.

We studied the UK experience of kidney transplantation from deceased donors with albuminuria detected by dipstick measurement. We first assessed whether donor albuminuria influences the likelihood of a kidney being accepted for transplantation. We then examined the association between donor albuminuria and subsequent graft survival and function.

## **2 Materials and Methods**

### **2.1 Study design, population and exposure**

This was a national cohort study of deceased donors and kidney transplant recipients. All data came from the UK Transplant Registry (UKTR), which is maintained by National Health Service Blood and Transplant (NHSBT). The UKTR has recorded donor urinalysis results in standardised format since 2016. This was a service evaluation project using anonymised data, carried out within NHSBT as part of its duty to monitor the national transplant program. Additional ethical approval was not required.

The main exposure in this study was donor albuminuria, defined as 2+ or higher on dipstick testing (equating to an albuminuria concentration of approximately 100 mg/dL) recorded at the time of donor assessment. Hereafter, donors with  $\geq 2+$  and  $< 2+$  albuminuria are termed “donors with/without albuminuria”, respectively.



This study comprised two linked cohorts. The donor cohort consisted of all adult (age  $\geq 18$  years) consented donors (defined as individuals with no absolute contraindications to becoming an organ donor,<sup>29</sup> where consent/authorisation for donation had been granted) with an albuminuria record available, between 1 January 2016 and 31 December 2020. The recipient cohort was all adult recipients of single kidney transplants from the donor cohort. To maintain the assumption of independent observations in our survival analyses, we included only the first transplant for each recipient during the study period. We excluded multi-organ transplants (e.g. simultaneous kidney-pancreas transplants), and recipients with no follow-up data.

## **2.2 Outcomes**

Outcomes of interest in the donor cohort were kidney offer acceptance, kidney transplantation (acceptance and transplantation of at least one kidney, respectively), and the number of kidneys transplanted per donor. It is standard practice in the UK to only retrieve an organ for the purposes of transplantation if it has been accepted by a transplanting centre.<sup>30</sup>

The primary outcome in the recipient cohort was graft failure, defined as the earliest of graft nephrectomy, re-transplantation or resumption of long-term dialysis, censored at death.

Secondary outcomes were delayed graft function (DGF, defined as at least one session of dialysis in the first 7 post-operative days), primary non-function (PNF, failure ever to achieve independence from dialysis following transplantation),<sup>31</sup> 1 and 3 year estimated glomerular filtration rate (eGFR, calculated using the Modification of Diet in Renal Disease equation to calculate eGFR from serum creatinine results reported to NHSBT, without adjustment for ethnicity),<sup>32,33</sup> and death. Follow-up ended on 18<sup>th</sup> October 2021.

## **2.3 Covariates**

Donor covariates were age, sex, donor type (donation after brain death [DBD], donation after circulatory death [DCD]), cause of death, body mass index (BMI), smoking status, diabetes,

hypertension, terminal creatinine (defined as the last recorded donor serum creatinine result prior to organ retrieval) and, where available, creatinine prior to and at the time of hospital admission, 24-hour urine volume at the time of donor assessment, and urine protein : creatinine ratio (uPCR). We also calculated the UK Kidney Donor Risk Index (KDRI), a validated prognostic score for predicting graft failure in deceased donor transplants.<sup>6</sup> In addition, we identified donors with AKI stage 2 or 3, defined using the admission and terminal creatinine results according to AKI Network criteria ( $\geq 2$ -fold rise, increase of  $\geq 44$   $\mu\text{mol/L}$  to  $\geq 354$   $\mu\text{mol/L}$ , or initiation or renal replacement therapy).

Recipient factors were age, sex, graft number, diabetes, dialysis status at the time of transplant, sensitisation (defined as a calculated reaction frequency [cRF] of  $<10\%$  [unsensitised], 10 to  $<85\%$  [sensitised], and  $\geq 85\%$  [highly sensitised]),<sup>34</sup> human leucocyte antigen (HLA) mismatch level (grouped according to the 2006 UK National Kidney Allocation Scheme as level 1 [0 mismatches]; level 2 [0 HLA-DR mismatches and 0/1 HLA-B mismatch]; level 3 [0 HLA-DR mismatches and 2 HLA-B mismatches or 1 HLA-DR mismatch and 0/1 HLA-B mismatch]; and level 4 [2 HLA-DR mismatches or 1 HLA-DR and 2 HLA-B mismatches]),<sup>35</sup> and cold ischaemia time (CIT, the time from *in situ* cold preservation fluid flushing to reperfusion with recipient blood).

## 2.4 Statistical analysis

We used Cox proportional hazards modelling, logistic regression or linear regression, as appropriate, to compare outcomes of interest in our donor and recipient cohorts, with adjustment for potential confounders. All utilisation analyses (offer acceptance, transplantation, number of transplants) were restricted to donors whose kidneys were offered for transplantation, and adjusted for the following donor factors: age (18 to  $<40$ , 40 to  $<50$ , 50 to  $<60$ , and  $\geq 60$  years), sex, type, cause of death (cerebrovascular accident [CVA] vs other), BMI ( $<20$ , 20 to  $<25$ , 25 to  $<30$ , and  $\geq 30$   $\text{kg/m}^2$ ), smoking status (ever vs never), diabetes, hypertension and terminal creatinine ( $<100$ , 100 to 150, and  $>150$   $\mu\text{mol/L}$ ). To investigate the possibility of unmeasured donor factors confounding our results, we

conducted a negative control analysis by looking for an association between donor albuminuria and liver, heart or lung offer acceptance, using the same multivariable approach in our donor cohort (with restriction to donors where the organ in question was offered for transplantation). Because we had no *a priori* reason to expect that donor albuminuria should influence acceptance of other organs, any association here would suggest that other (unmeasured) factors led clinicians to decline organs from these donors, reducing the likelihood of a causal relationship between albuminuria and kidney offer acceptance.

Transplant outcome analyses (graft/patient survival, DGF, PNF, eGFR) were adjusted for the donor factors above, as well as the following recipient factors: age (grouped as for donors), sex, graft number (first vs other), diabetes, dialysis status, sensitisation, HLA mismatch grade and CIT (<12, 12 to <18, ≥18 hours), with random effects to account for clustering by transplant unit. To check the proportional hazards assumption, we fitted a time-varying interaction term in an unadjusted Cox regression model of graft survival.

#### **2.4.1 Additional analyses**

Using likelihood ratio tests, we looked for an interaction between donor albuminuria and (1) donor diabetes (because this may affect the clinical significance of albuminuria), and (2) donor type (since DBD donors are more likely to develop diabetes insipidus, which could influence the reliability of albuminuria measurement), in our main graft survival model.

In a subgroup with data available, we repeated our utilisation and survival analyses using donor uPCR as the exposure, with a cut-off of ≥100 mg/mmol. Due to data sparsity, these models were adjusted for donor age and type, terminal creatinine and (in the survival model) recipient age.

#### **2.4.2 Sensitivity analyses**

To assess the robustness of our findings, we modified our survival analysis as follows: (1) using all-cause graft failure as the outcome; (2) restricting to primary (i.e. first ever) kidney transplants; (3) varying the threshold for donor albuminuria (≥1+ [≥30 mg/dL] or ≥3+

[ $\geq 300$  mg/dL] on dipstick); (4) using three levels of albuminuria (“negative / trace”, 1+ to 2+, 3+ to 4+) to look for a “dose-response” effect; (5) additionally adjusting for donor pre-admission creatinine (grouped as for terminal creatinine); and (6) additionally adjusting for donor AKI (stage 2 or 3).

We also repeated our utilisation analysis with additional adjustment for (1) pre-admission donor creatinine; (2) AKI; and (3) 24-hour urine volume (<1.5L, 1.5 to 3L,  $\geq 3$ L); on the grounds that both of these factors could confound the relationship between donor albuminuria and kidney utilisation.

After examining the distribution of missing information on each covariate, all models used a complete case analysis. All statistical tests were two-sided with a 5% significance level. All analyses used SAS Enterprise Guide v7.13 (SAS Institute Inc, Cary, NC, USA).

## **3 Results**

### **3.1 Study population**

Figure 1 summarises the development of our study cohorts. There were 10,315 consented donors during our study period, of which 9,309 (90%) had a dipstick albuminuria result recorded. The recipient cohort comprised 9,834 individuals.

### **3.2 Donors**

Mean (standard deviation, SD) donor age was 55 (15) years; 57% were male, and 18% (1,681/9,309) had  $\geq 2+$  albuminuria. Dipstick urinalysis was performed within 1 day of referral for donor assessment in 96% (8,947/9,309) of donors. More detailed categorisation of dipstick results showed that 52% (4,864) had negative/trace, 30% (2,764) had 1+ (30 mg/dL), 13% (1,225) had 2+ (100 mg/dL), 4% (402) had 3+ (300 mg/dL), and 1% (54) had 4+ (2000 mg/dL) albuminuria. Consented donors with albuminuria had more co-

morbidities, worse renal function, and were more likely to be donating after circulatory death. UK KDRI was similar in the two donor groups (Table 1).

Kidneys were offered for transplantation in 97% (9,063/9,309) of consented donors. Among these, the rate of offer acceptance was 74% (1,180/1,597) vs 82% (6,098/7,466) in donors with vs without albuminuria (OR 0.63, 95% confidence interval [CI] 0.56 to 0.72; nine donors had missing offer acceptance data). All covariates in our utilisation models had <4% missing data. After adjustment for donor confounders, there was strong evidence of lower kidney acceptance in donors with albuminuria (OR 0.70, 0.61 to 0.81; Appendix Table S1). Kidney utilisation was similarly lower (60% vs 69%; adjusted OR 0.78, 0.68 to 0.88. Appendix Table S2), and fewer kidneys were transplanted (1.1 vs 1.3 per donor, difference 0.1, 0.05 to 0.14). The negative control analysis showed no association between donor albuminuria and liver (OR 0.95, 0.83 to 1.10), heart (OR 0.96, 0.77 to 1.19) or lung (OR 0.96, 0.81 to 1.14) offer acceptance.

### **3.3 Recipients**

Mean (SD) recipient age was 53 (13) years; 63% were male. Sixteen percent (1,550/9,834) of transplants were from donors with albuminuria. Recipient characteristics were similar between the two groups (Table 2).

Over a median (interquartile range, IQR) of 2 (1 to 3) years, 8% (118/1,550) of grafts from donors with albuminuria and 9% (706/8,284) of grafts from donors without albuminuria failed (hazard ratio [HR] 0.87, 95% CI 0.72 to 1.06; Figure 2). All covariates in our transplant outcome models had <4% missing data. After adjustment for donor and recipient confounders, there was no association between donor albuminuria and graft failure (HR 0.91, 0.74 to 1.11; Appendix Table S3).

Patient death occurred in 6% of both transplants from donors with (92/1,550) and without (537/8,284) albuminuria (adjusted HR 0.80, 0.63 to 1.01). Early graft outcomes (DGF and PNF) were available for 90% (8,836/9,834) of recipients. Twenty-four percent (344/1,410) of

grafts from donors with albuminuria and 22% (1,667/7,426) of grafts from donors without albuminuria had DGF (adjusted OR 1.05, 0.91 to 1.22). The rate of PNF was 2% (28/1,410) vs 3% (218/7,426; adjusted OR 0.74, 0.50 to 1.12).

Among 7,288 (64%) recipients with data available, mean (SD) 1 year eGFR was 51 (21) vs 50 (20) mL/min/1.73m<sup>2</sup> in transplants from donors with vs without albuminuria (adjusted difference 0.1, -1.3 to 1.1). At 3 years, the corresponding values were 51 (22) vs 50 (21) mL/min/1.73m<sup>2</sup> (n=3,265; adjusted difference 0.3, -1.5 to 2.1).

### **3.4 Additional analyses**

Although transplants from donors with albuminuria had a lower rate of failure in the context of donor diabetes and DCD donation, there was no evidence of an interaction between donor albuminuria and either diabetes ( $p=0.23$ ) or donor type ( $p=0.56$ ; Figure 3).

uPCR results were available for 777 (8%) of the consented donors in our cohort, of which 134 (17%) had a result  $\geq 100$  mg/mmol. Although the rates were lower, there was no evidence of an association between donor uPCR and kidney offer acceptance (72% vs 79%; adjusted OR 0.75, 0.47 to 1.19) or kidney transplantation (56% vs 67%; adjusted OR 0.68, 0.45 to 1.04). Among 815 kidney transplants with donor uPCR results recorded, there was no association between donor uPCR and graft failure (5% [6/120] vs 7% [46/695]; adjusted HR 0.71, 0.30 to 1.68).

### **3.5 Sensitivity analyses**

The results of our sensitivity analyses were consistent with our main graft survival analysis (Figure 3). All models showed a lower rate of failure in grafts from donors with albuminuria, but the confidence intervals of all adjusted HRs included the null value. All-cause graft failure showed the strongest association with albuminuria. There was no evidence of a dose-response effect when using three levels of albuminuria.

The relationship between donor albuminuria and kidney utilisation did not alter meaningfully with adjustment for pre-admission creatinine (n=3,988; OR 0.74, 0.61 to 0.89), AKI (n=7,054; OR 0.76, 0.66 to 0.88) or 24-hour urine volume (n=5,932; OR 0.83, 0.71 to 0.96), or after exclusion of DCD donors (n=4,108; OR 0.76, 0.61 to 0.95).

## **4 Discussion**

In this national cohort study of deceased donor kidney transplantation, we found no evidence of a relationship between donor albuminuria, detected by dipstick analysis, and both early and long-term clinical outcomes. The rate of DGF, PNF and graft failure, and eGFR at 1 and 3 years, were comparable in transplants from donors with and without albuminuria. At the same time, there was strong evidence that kidneys from donors with albuminuria were less likely to be accepted for transplantation; this association was independent of other markers of donor quality and only apparent in relation to kidney transplant offers.

Most evidence in this area comes from secondary analyses in small studies with short follow-up. A single centre study in Austria found that while donor uPCR, but not dipstick albuminuria, was associated with chronic damage on pre-implantation biopsies, there was no relationship with 1-year graft survival or function.<sup>24</sup> The outcomes here are consistent with our results, although we are unable to judge the relationship between dipstick albuminuria and histological findings. A multi-centre study in the USA showed no association between donor albuminuria and DGF or 6-month eGFR, although the degree of albuminuria was somewhat lower than in our cohort.<sup>28</sup> Recently, a national cohort study in Switzerland, which had a smaller sample size but longer follow-up than ours, found no association between deceased donor proteinuria, defined as uPCR >30mg/mmol, and graft survival or function.<sup>26</sup> Our findings add to the literature by showing consistent results in an adequately powered study that includes more DCD transplants, using a biomarker that is more widely reported at the time of donor assessment. In the subgroup of donors with uPCR recorded, we found

consistent results despite applying a higher threshold ( $\geq 100$  mg/mmol), although low numbers and potential selection bias limit interpretation of this result. Studies in living donor transplants have suggested greater histological damage at implantation and inferior long-term function in association with donor albuminuria; inevitably, stricter exclusion criteria limit comparison with our study.<sup>25,27</sup> Our utilisation analysis supports recent work, suggesting that urinary findings are taken into account when considering kidney offers.<sup>26</sup>

The strengths of this study are its size, national coverage, data completeness and minimal loss to follow-up. We were able to account for several potential confounders of the relationships in question, and our results were consistent across several outcomes and when using other categorisations of albuminuria. The negative control analysis, which showed no relationship between donor albuminuria and acceptance of other organs, supports a true relationship between albuminuria and kidney offer acceptance, which has not been shown previously.

This study also has some limitations. We defined our exposure as dipstick albuminuria, a result that is usually available at the time of organ offering, using a threshold that is generally considered to be clinically significant.<sup>36</sup> While this improves the generalisability of our results, some measurement error is inevitable.<sup>37-39</sup> Urinalysis is most accurate in “steady state” conditions; unstable physiology is likely to have reduced the reliability of dipstick testing in some donors.<sup>13,14</sup> Iodinated contrast, raised specific gravity or gross haematuria can result in false positive albuminuria on dipstick urinalysis;<sup>40</sup> we were unable to account for these factors. Alterations in urine concentration, blood pressure or renal function may also influence the detection of albuminuria; although our sensitivity analyses accounted for some of these factors, missing data limits these results. There was also only one dipstick result recorded for each donor. All of these sources of measurement bias could explain the lack of association with transplant outcomes. Because donor urine dipstick results have been a standard data item in the UKTR since 2016, 3-year eGFR was only available for a relatively



small subset of our cohort; although this reduced the power of this analysis, it is unlikely to have biased the results.

Selection bias may also have influenced our results. Although the KDRI did not meaningfully differ between the two groups, donors that were utilised despite having albuminuria may have had a more favourable profile which our covariates did not capture, so some residual confounding is possible. Indeed, our findings are consistent with slightly better outcomes in transplants from donors with albuminuria. Ultimately, we cannot know what the outcomes would have been in kidneys that were not utilised. There are many potential reasons for declining an organ for transplantation; our analysis cannot capture all of these. Factors such as inflammation or sepsis can cause albuminuria and could therefore have confounded our organ acceptance analysis.<sup>21,22</sup> Without standardised information on chronic kidney disease or pre-implantation biopsies, we cannot determine the role of dipstick albuminuria in detecting established donor renal pathology. Lastly, low power limits our secondary analyses. While we found no evidence of effect modification, the relationship between donor albuminuria and graft survival may be different in the context of DCD donation or donor diabetes.

Our findings clearly show lower offer acceptance and utilisation of kidneys from donors with albuminuria, which are independent of other measures of donor risk. This is consistent with a reluctance among UK transplant clinicians to accept kidneys from these donors. At the same time, in the organs that were transplanted, donor albuminuria does not appear to predict transplant survival or function. Optimal organ utilisation aims to maximise the benefits of any national transplant program, so it is important to evaluate markers of organ quality.<sup>7</sup> We have not found evidence supporting the value of dipstick albuminuria in this context, although the role of donor uPCR remains to be determined. This study examined the clinical utility of a bedside test in the real-world setting, so the results are likely to be generalisable to deceased donor transplant programs with a similar case mix to the UK. Our findings challenge the view that dipstick albuminuria *per se* should preclude kidney donation, going

against extrapolation of evidence from the general population to deceased donors (and, by extension, recipients of their organs). While we cannot exclude a modest, longer-term influence of donor albuminuria on graft survival, any potential effect should be considered in light of the substantially higher mortality among patients waiting for a transplant.<sup>41</sup>

The decision to accept any kidney depends on an individualised risk assessment. Though widely used in donor assessment, we have found no evidence that dipstick albuminuria predicts the survival of deceased donor kidney transplants. Therefore, our results do not support reliance on dipstick albuminuria *per se* in organ acceptance decision making.

Clinicians should interpret urinalysis results within the context of a donor's overall risk profile, and the potential benefits to a recipient, when considering organ offers. Expanded use of kidneys from donors with dipstick albuminuria could benefit more patients on the transplant waiting list.

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## **Conflict of interest statement**

R Hilton has received speaker honorarium from Chiesi Ltd. C Watson has received speaker fees from OrganOx and consultancy fees from Nefro health and Jazz Pharmaceuticals. All other authors declare no conflicts of interest in relation to this work.

## **Authors' contributions**

GG: Conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing – original draft, writing – review & editing

MR: Methodology, writing – review & editing

RJ: Conceptualization, supervision, methodology, writing – review & editing

MI: Methodology, writing – review & editing

RH: Conceptualization, writing – review & editing

LT: Conceptualization, supervision, writing – review & editing

CC: Conceptualization, supervision, writing – review & editing

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## **Data availability statement**

The data underlying this article will be shared on reasonable request to the data controller (NHSBT), after appropriate information governance clearances.

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## Tables

**Table 1. Characteristics of donor cohort**

	<b>Consented donors <sup>a</sup> with &lt;2+ albuminuria (n=7,628)</b>	<b>Consented donors <sup>a</sup> with ≥2+ albuminuria (n=1,681)</b>
<b>Female sex</b>	3,295 (43%)	690 (41%)
<b>Age (years)</b>	56 (46 to 66)	56 (44 to 66)
<b>DCD</b>	3,890 (51%)	912 (54%)
<b>Cause of death</b>		
<b>CVA</b>	4,125 (54%)	782 (47%)
<b>Other</b>	3,205 (42%)	838 (50%)
<b>Diabetes</b>	723 (9%)	223 (13%)
<b>Hypertension</b>	2,536 (33%)	628 (37%)
<b>BMI (kg/m<sup>2</sup>)</b>	27 (23 to 30)	27 (24 to 31)
<b>Smoking history</b>	4,986 (65%)	1,110 (66%)
<b>UK KDRI</b>	1.33 (1.00 to 1.58)	1.35 (1.01 to 1.60)
<b>Creatinine (µmol/L)</b>		
<b>Pre-admission</b>	72 (61 to 84)	75 (63 to 86)
<b>Admission</b>	77 (61 to 99)	87 (67 to 110)
<b>Terminal</b>	65 (52 to 86)	75 (57 to 114)
<b>AKI (stage 2 or 3)</b>	258 (3%)	152 (9%)
<b>24-hour urine volume (L)</b>	2.3 (1.5 to 3.3)	1.9 (1.2 to 2.8)

Values are n (%) or median (interquartile range)

AKI, acute kidney injury; CVA, cerebrovascular accident; DBD, donation after brain death; DCD, donation after circulatory death; BMI, body mass index; UK KDRI, United Kingdom Kidney Donor Risk Index.<sup>6</sup>

Missing data (n): cause of death (359), diabetes (87), hypertension (168), BMI (52), smoking (60), UK KDRI (1,737), pre-admission creatinine (4,887), admission creatinine (1,552), terminal creatinine (7), AKI (1,552), 24-hr urine volume (2,732)

<sup>a</sup> Individuals with no absolute contraindications, where consent/authorisation for donation had been granted.

Table 2. Characteristics of recipient cohort

	Transplants from donors with <2+ albuminuria (n=8,284)	Transplants from donors with ≥2+ albuminuria (n=1,550)
<b>Donor age (years)</b>		
18 to <40	1,509 (18%)	344 (22%)
40 to <50	1,479 (18%)	296 (19%)
50 to <60	2,473 (30%)	421 (27%)
≥60	2,823 (34%)	489 (32%)
<b>DCD</b>	3,306 (40%)	682 (44%)
<b>Donor cause of death</b>		
CVA	4,744 (57%)	742 (48%)
Other	3,250 (39%)	762 (49%)
<b>Donor diabetes</b>	625 (8%)	128 (8%)
<b>Donor hypertension</b>	2,466 (30%)	451 (29%)
<b>Donor smoking</b>	5,372 (65%)	1,038 (67%)
<b>Donor BMI (kg/m<sup>2</sup>)</b>		
<20	387 (5%)	71 (5%)
20 to <25	2,599 (31%)	486 (31%)
25 to <30	3,075 (37%)	618 (40%)
≥30	2,180 (26%)	367 (24%)
<b>Donor terminal creatinine (µmol/L)</b>		
<100	7,060 (85%)	1,151 (74%)
100 to <150	852 (10%)	253 (16%)
≥150	368 (4%)	144 (9%)
<b>Donor UK KDRI</b>	1.12 (0.99 to 1.51)	1.09 (0.98 to 1.51)
<b>Recipient female</b>	3,106 (37%)	568 (37%)
<b>Recipient age (years)</b>		
18 to <40	1,527 (18%)	299 (19%)
40 to <50	1,552 (19%)	283 (18%)
50 to <60	2,380 (29%)	398 (26%)
≥60	2,825 (34%)	570 (37%)
<b>Recipient diabetes</b>	1,009 (12%)	188 (12%)
<b>On dialysis at transplant</b>	7,048 (85%)	1,283 (83%)
<b>Graft number</b>		
First	6,966 (84%)	1,343 (86%)
Second or more	1,318 (16%)	207 (13%)
<b>Sensitisation (cRF)</b>		
Non-sensitised (<10%)	5,192 (63%)	1,023 (66%)
Sensitised (10 to <85%)	1,999 (24%)	360 (23%)
Highly sensitised (≥85%)	1,093 (13%)	167 (11%)
<b>HLA mismatch grade <sup>35</sup></b>		
1	664 (8%)	105 (7%)
2	2,524 (30%)	462 (30%)
3	4,179 (50%)	795 (51%)
4	917 (11%)	188 (12%)
<b>Cold ischaemia time (hours)</b>		
<12	3,553 (43%)	644 (42%)
12 to <18	3,214 (39%)	624 (40%)
≥18	1,512 (18%)	281 (18%)

Values are n (%) or median (interquartile range). CVA, cerebrovascular accident; DBD, donation after brain death; DCD, donation after circulatory death; BMI, body mass index; cRF, calculated reaction frequency; HLA, human leucocyte antigen; UK KDRI, United Kingdom Kidney Donor Risk Index.<sup>6</sup> Values are n (%). Missing data (n): donor cause of death (344), donor diabetes (78), donor hypertension (146), donor smoking (57), donor BMI (51), donor terminal creatinine (6), recipient sex (3), dialysis status (1), CIT (6). recipient dialysis status (5), CIT (10). UK KDRI (1,834).

## **Figure legends**

### **Figure 1**

Title:

Donor and recipient cohort creation

Footnote:

Numbers on arrows represent missing data

### **Figure 2**

Title:

Kaplan-Meier plot of death-censored graft survival in kidney transplants from deceased donors with vs without albuminuria

### **Figure 3**

Title:

Forest plot of main, subgroup and sensitivity analyses: adjusted hazard ratio of death-censored graft failure in kidney transplants from deceased donors with vs without albuminuria

Footnote:

AKI, acute kidney injury; DBD, donation after brain death; DCD, donation after circulatory death; HR, hazard ratio; CI, confidence interval. <sup>a</sup> Adjusted using Cox regression for donor age, sex, type, cause of death, diabetes, hypertension, smoking, BMI and terminal creatinine; recipient age, sex, graft number, diabetes, dialysis status, sensitisation, HLA mismatch and cold ischaemia time; grouped by transplant unit (n=23) using random effects.

<sup>b</sup> AKIN stage 2 or 3.