CJASN Clinical Journal of the American Society of Nephrology

Inequity in Access to Transplantation in the UK

Journal:	*Clinical Journal of the American Society of Nephrology*
Manuscript ID	CJASN-1146-09-19.R3
Manuscript Type:	Original Articles
Date Submitted by the Author:	22-Apr-2020
Complete List of Authors:	Pruthi, Rishi; Guy's and Saint Thomas' NHS Foundation Trust, Transplant, Renal and Urology Directorate Robb, Matthew; NHS Blood and Transplant Organ Donation and Transplantation Directorate Oniscu, Gabriel; Edinburgh Transplant Centre, Royal Infirmary of Edinburgh, Edinburgh, EH16 4SA, UK Tomson, Charles; Freeman Hospital, Department of Renal Medicine Bradley, John; Transplant Unit, Cambridge University Hospitals NHS Foundation Trust, Hills Road Forsythe, John; NHS Blood and Transplant Organ Donation and Transplantation Directorate Metcalfe, Wendy; Edinburgh Transplant Centre, Royal Infirmary of Edinburgh, Edinburgh, EH16 4SA, UK Bradley, Clare; Royal Holloway, University of London, Health Psychology Research Unit Dudley, Christopher; Southmead Hospital, Richard Bright Renal Unit Johnson, Rachel; NHS Blood and Transplant Organ Donation and Transplantation Directorate Watson, Christopher; Transplant Unit, Cambridge University Hospitals NHS Foundation Trust, Hills Road Draper, Heather; University of Birmingham, Institute of Applied Health Research Fogarty, Damian; Belfast Health and Social Care Trust, Department of Renal Medicine Ravanan, Rommel; Southmead Hospital, Richard Bright Renal Unit Roderick, Paul
Keywords:	clinical epidemiology, Epidemiology and outcomes, ethnicity, kidney transplantation, inequity, socio-economic deprivation, transplant waiting list, renal dialysis, Ethnic Groups, Minority Groups, Universal Health Care, Cohort Studies, Body Mass Index, Prospective Studies, Social Class, Renal Replacement Therapy, African Americans, Diagnosis-Related Groups, Outcome Assessment, Health Care

Inequity in Access to Transplantation in the United Kingdom

Running Title: Inequity in Access to Transplantation

Rishi Pruthi PhD[1,2], Matthew L Robb PhD[3], Gabriel C. Oniscu MD[4], Charles Tomson DM[5], Andrew Bradley PhD[6], John L. Forsythe MD[4], Wendy Metcalfe MD[4], Clare Bradley PhD[7], Christopher Dudley MD[8], Rachel J Johnson MSc[3], Christopher Watson MD[6], Heather Draper PhD[9], Damian Fogarty MD[10], *Rommel Ravanan MD[8], *Paul J. Roderick MD[2]. On Behalf of the ATTOM Investigators

1. Guy's and St Thomas' NHS Foundation Trust, London, SE1 9RT, UK
2. Primary Care and Population Sciences, Faculty of Medicine, University of Southampton, SO17 1BJ, UK
3. NHS Blood and Transplant, Bristol, BS34 7QH, UK
4. Edinburgh Transplant Centre, Royal Infirmary of Edinburgh, Edinburgh, EH16 4SA, UK
5. Renal Unit, Freeman Hospital, Newcastle, NE7 7DN, UK
6. Department of Surgery, University of Cambridge and the NIHR Cambridge Biomedical Research Centre, Cambridge, CB2 0QQ, UK
7. Health Psychology Research Unit, Royal Holloway, University of London, Egham, TW20 0EX, UK
8. Richard Bright Renal Unit, Southmead Hospital, Bristol, BS10 5NB, UK
9. Institute for Applied Health Research, University of Birmingham, Birmingham, B15 2TT, UK
10. Belfast Health and Social Care Trust, Belfast, Northern Ireland, BT9 7ABUK

*denotes joint final author

Corresponding author:

Rishi Pruthi,

Consultant Nephrologist,

Guy's Hospital, London SE1 9RT

Tel: 020 7188 7188

Email: rishi.pruthi@nhs.net

Word Count: 3454

Abstract

Background and objectives: Despite the presence of a universal healthcare system it is unclear if there is inter-centre variation in access to kidney transplantation in the UK. This study aims to assess whether equity exists in access to kidney transplantation in the UK after adjustment for patient specific factors and centre practice patterns.

Design, setting, participants, and measurements: Prospective observational cohort study including all 71 UK kidney Centers. Incident kidney replacement therapy (KRT) patients recruited between November 2011-March 2013 as part of the Access to Transplantation and Transplant Outcome Measures study (ATTOM) were analysed to assess pre-emptive listing (n=2676) and listing within 2 years of starting dialysis (n=1970) by centre.

Results: 706 participants (26%) were listed pre-emptively whilst 585 (30%) were listed within 2 years of commencing dialysis. The IQR across Centers was 6-33% for pre-emptive listing and 25-40% for listing after starting dialysis. Patient-factors including increasing age, most co-morbidities, BMI >35kg/m^2 and lower socioeconomic status were associated with a lower likelihood of being listed and accounted for 89% and 97% of measured inter-centre variation, for pre-emptive listing and listing within 2 years of starting dialysis respectively. Ethnic minority associations were inconsistent and reduced access was only seen for pre-emptive listing with Asian (OR 1.42; CI:1.12-1.79) and Black (OR 1.04; CI:0.76-1.43) participants associated with reduced access. As for centre factors, being registered at a transplanting-centre (OR 3.1; CI: 2.36-4.07) and a universal approach to discussing transplantation (OR 1.4; CI: 1.08-1.78) were associated with higher pre-emptive listing, whilst utilising a written protocol was associated negatively with listing within 2 years of starting dialysis (OR 0.7; CI: 0.58-0.9).

Conclusions: Patient case-mix accounts for most of the inter-centre variation seen in access to transplantation in the UK with practice patterns also contributing some variation. Socioeconomic inequity exists despite having a universal healthcare system.

Introduction

In the UK, it is expected that 2.6 million adults are living with CKD stage 3-5[1], with over sixty-three thousand patients receiving renal replacement therapy (RRT) for end-stage kidney disease (ESKD)[2]. Rates of RRT have risen in most high income countries in the last few decades (including the UK)[3,4] and are greater in lower socioeconomic groups[5,6] and in ethnic minorities[5,7]. Though many undergo dialysis, it is recognized that for 'suitable patients' with ESKD, kidney transplantation confers both better clinical outcomes compared to dialysis[8,9], and leads to improvements in self-reported health[10], and is therefore the preferred RRT modality.

The UK National Health Service was founded on the principle of delivering equitable healthcare based on need and not the ability to pay and was ranked first on equity in a recent international healthcare comparison[11]. Equity is a key consideration for assessing the pathway to kidney transplantation for patients with ESKD. Achieving prompt assessment and timely activation on the transplant waiting list is crucial to accessing transplantation. Increasing length of time on dialysis adversely affects graft and patient survival[12], and

deceased donor organ allocation algorithms in many countries (including the UK) give priority to those who have spent greater time on the waiting list.

Despite national clinical practice guidelines for transplant assessment, retrospective analyses of UK Renal and Transplant Registries data suggest there is variation in access to listing for transplantation between kidney Centers[13-15]; and that although ethnic minorities and individuals from lower socioeconomic groups have a higher incidence of ESKD[5-7], they have reduced access to transplantation[14-17]. It is not known whether this difference is due to a higher burden of co-morbidity associated with ethnic minority status or lower socioeconomic status, or due to differences in centre practices that might disadvantage these groups[14]. Studies to date have been limited in their ability to examine these factors due to their retrospective design and use of routine and limited registry data.

This study uses a prospective cohort of patients starting RRT recruited to the Access to Transplantation and Transplant Outcome Measures (ATTOM) study[18] to determine (i) if access to pre-emptive listing (being listed before starting dialysis) and to listing within 2 years of starting dialysis, is equitable for socially deprived and ethnic minority populations in the UK after morbidity adjustment; and ii) whether centre-specific factors are associated with access to transplant listing.

Methods

Study Population

In the UK there are 71 kidney Centers (23 transplanting and 48 non-transplanting Centers) which collectively provide RRT for all patients in the UK as well as managing all patients approaching ESKD. In each centre, over a 12-month period, between 1 November 2011 and 31 March 2013 all incident dialysis patients and incident kidney transplant recipients aged 18-75 years of age were recruited at the time of starting dialysis or transplantation as part of the ATTOM Study. ATTOM is a national prospective cohort study investigating the factors

that influence access, clinical and patient-reported outcomes and cost-effectiveness of kidney transplantation in the UK. Dedicated research nurses collected clinical and demographic information from the case notes and local electronic databases, and collected health status and well-being data from participants. The data were uploaded onto a secure website designed, developed and maintained by the UK Renal Registry (UKRR). A full description of the ATTOM study methods and protocol has been reported previously[18].

For the analysis of access to pre-emptive listing all incident dialysis participants (n=2623) and all incident transplant participants with a pre-emptive transplant (n=431) recruited to ATTOM were considered for inclusion (Figure 1). Participants excluded were those with a previous transplant (n=251), those listed for multi-organ transplantation (n=4), those who recovered kidney function (n=25) and those that could not be linked to the UKRR/NHS Blood and Transplant (NHSBT) database (n=6). Lastly, participants who were suspended from the waiting list for > 30 days within 90 days of first activation (n=92) were also excluded to avoid any potential bias from Centers that may activate patients on the transplant list and then immediately suspend them before more permanent activation at a later date after more formal medical assessment of the patient's suitability.

For analysis of access to the transplant waiting list within 2 years of starting dialysis, all incident dialysis participants that were not pre-emptively listed i.e. who were not listed before starting dialysis were considered (n=2348) using the same exclusion criteria (Figure 1).

Data collection

Patient variables

Demographic, socioeconomic, clinical and comorbidity data were collected for each patient at the time of recruitment. Trained research nurses collected uniformly defined data items from patient interviews, case notes and local electronic patient information systems across the UK. Patient variables collected and analysed included, age, gender, ethnicity, BMI, co-

morbidities and primary renal diagnosis. Several measures of socioeconomic status were also explored including: education status, employment status, accommodation and car ownership. Civil status, number of children in household, number of adults in household and total numbers in household were other measures. Other demographic data collected and explored included place of birth, whether English was their first language, whether any assistance was needed with reading, the length of time a patient was known to kidney services pre RRT and in the case of listing after starting dialysis, their dialysis modality. Full details of how these variables were categorized can be found in Appendix S1.

Centre Variables

Thematic analysis of 45 semi-structured qualitative interviews with key stakeholders and 53 patients conducted across 9 kidney Centers in the UK informed the development of an online survey, which was distributed to the Clinical Directors of all 71 UK kidney Centers[19]. This survey achieved a 100% response rate and was utilized to derive and quantify centre variables for analysis in this study. Centre variables examined were chosen by study investigators who examined the level of variance across centre responses for each potential variable and took into account the ability to readily categorize them. A full list of centre variables chosen for analysis can be found in Appendix S1.

Outcomes

Date of activation on the waiting list and, where applicable, the date of transplantation, were extracted from the UK Transplant Registry held by the Organ Donation and Transplantation Directorate of NHS Blood and Transplant. Date of death was retrieved from the UKRR database and the Scottish Renal Registry (SRR).

Statistical methods

For access to pre-emptive listing a multi-level logistic regression model was constructed to analyse the association of patient variables (level 1) and centre factors (level 2). Individual

participants (Level 1) were nested within kidney Centers (Level 2) to allow for clustering of participants within Centers. Analysis of each patient-level factor was adjusted for all other patient-level factors and analysis of each centre factor was adjusted for those patient-level factors found to be associated with pre-emptive listing. The difference in -2*log-likelihood was used to compare model fit between nested models. The overall effect of centre in the analysis was considered by including kidney centre as a random effect. A significance level of <0.05 was taken as evidence of a significant association.

For access to the transplant waiting list within 2 years of starting dialysis, time to listing was analysed using a multi-level Cox proportional hazards regression model. The time to listing was taken to be the time from start of dialysis to activation on the kidney transplant list. Participants were censored at 2 years or at patient death. Statistical significance was defined a priori as p<0.05. Proportional hazards assumptions were tested using Schoenfeld residuals. The presence of an overall kidney centre effect was considered using a frailty term whilst death was also considered as a competing risk using a Fine and Gray model in a separate competing risk analysis.

Multiple imputation was used to account for missing data in each analysis. For access to preemptive listing, data were missing for BMI (n=243), comorbidity (n= 30), time since first seen by a nephrologist (n=24) and socioeconomic variables (n=146). For access to listing after starting dialysis, data were missing for BMI (n=220), comorbidity (n=22) and socioeconomic variables (n=104). No participants were lost to follow up. Sensitivity analysis using complete case analysis did not change conclusions.

All data were analysed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

The baseline characteristics of participants analysed for pre-emptive listing and listing within 2 years of starting dialysis are shown in Table 1. For pre-emptive listing, 2676 participants were analysed following exclusion of 378 participants (12%), see methods. This study cohort had a median age of 57 years (interquartile range 45-66), of which 64% were male, 81% reported their ethnicity as White and diabetes was the most prevalent comorbidity (39%). Amongst socio-demographic factors, 54% of participants reported owning their own home with 69% owning their own car.

As for listing within 2 years of starting dialysis, of 2348 eligible participants, 1970 participants were analysed following exclusion of 378 patients (16%), see methods. The median age of this cohort was 58 years (interquartile range 47-67 years), of which 65% were male, 80% reported their ethnicity as White and 45% had diabetes listed as a co-morbidity. Amongst socio-demographic factors, 49% of participants reported owning their own home whilst 16% of participants reported being in employment. Full details of these baseline characteristics are shown in Table 1.

Access to Pre-emptive Listing

Of 2676 participants, 706 participants (26%) were pre-emptively listed with a mean age of 49 years. The IQR across Centers was 6%-33%. An unadjusted funnel plot showing centre variation in the percentage of participants pre-emptively listed is shown in Figure 2a. Associations between patient and centre variables and the likelihood of being pre-emptively listed were characterized using univariable (Appendix S2 & S3) and multivariable (Appendix S4) logistic regression; before proceeding to analyse them in a final multivariable logistic regression including imputed missing data (table 2).

Several patient factors were independently associated with reduced access to pre-emptive listing. These included: increasing age, ethnicity (both Asian and Black participants), most co-morbidities, having a BMI of >35, and not being seen by a nephrologist for at least 12

months before starting RRT. Lower socioeconomic status as indicated by housing tenure and car ownership status was also associated with reduced access.

Three centre level factors were negatively associated with pre-emptive listing: being cared for primarily in a non-transplanting centre, having <6 Whole Time Equivalent (WTE) consultant nephrologists in the centre, and not adopting an approach where transplantation is discussed with all patients. The impact on centre variation of adjusting for these centre factors, along with patient factors, is shown in figure 2(b). Whilst inter-centre variation in pre-emptive listing significantly reduced following the addition of centre as a random effect to the model there was still evidence of variation/unaccounted confounding (p=0.0007 1 df). Of the 1020.9 (2679.2-1658.3) difference in -2logL between the null model and model with patient and centre variables, 89% (907) of the difference was observed when including the patient factors only (Appendix S5).

Access to the Transplant Waiting List After Starting Dialysis

Of 1970 participants included in this analysis, 585 (30%) were listed within 2 years of starting dialysis with a mean age of 49 years. The IQR across Centers was 25%-40%. Associations between patient and centre variables and the likelihood of being listed after starting dialysis were characterized using univariable (Appendix S6 & S7) and multivariable (Appendix S8) Cox regression; before proceeding to analyse them in a final multivariable Cox proportional hazards regression model including imputed missing data (table 3).

Several patient factors were independently associated with reduced access to listing after starting dialysis. These included: increasing age, female gender, having vascular disease, heart failure, type II diabetes, the presence of blood borne viruses, a previous history of malignancy, being a current smoker, and having a BMI >35.

As with pre-emptive listing, lower socioeconomic status was associated with reduced access to listing after starting dialysis. Living in rented/housing association accommodation, lack of

car ownership, and being long term sick/disabled or being retired from paid work, as compared to being in full time/part time employment, were all negatively associated with being listed within 2 years of starting dialysis. In contrast, having a university degree, being on Peritoneal Dialysis as opposed to Haemodialysis, and Asian ethnicity were all associated with an higher likelihood of being listed.

Amongst centre practice patterns, having >6 consultant nephrologists in the centre (OR 1.3 CI: 1.00-1.59) was associated positively with being listed within 2 years of starting dialysis as was having a multidisciplinary team (MDT) approach to listing all patients for transplantation (OR 1.2 CI: 0.99-1.52). An MDT approach was defined as having a multi-disciplinary team of physicians, surgeons and other allied health care professionals who regularly convened to discuss patients under consideration for transplant listing before activation.

Utilisation of a written protocol for listing patients for transplantation (OR 0.7 CI: 0.58-0.90) was negatively associated with being listed within 2 years of starting dialysis. Of the (7166.2-6566.8) 599.4 difference in -2logL between the null model and model with patient and centre variables, 97% (583.8) of the difference was observed when including the patient factors only (Appendix S9). After adjusting centre factors along with patient factors though much of the observed inter-centre variation from unadjusted analyses was again reduced there was still evidence of a difference between the Centers (p=0.041, 1df).

Interactions and Competing Risk Analysis

When considering age as a linear factor, an interaction with type 2 diabetes was found to be important in the model (p=0.002, 1df). The association between increasing age and time to listing was stronger in participants with type 2 diabetes (data not shown). As for the competing risk analysis, sub-hazard ratios derived did not highlight any significant differences.

Discussion

This national prospective cohort study of patients aged <75 years starting RRT in the UK found significant variation between kidney Centers in access to pre-emptive listing for kidney transplantation and listing after starting dialysis. This was largely explained by patient case-mix factors though some centre level effects were also found to be important. There was evidence of socioeconomic inequity in both measures of listing, despite extensive comorbidity adjustment; ethnic minority associations were inconsistent and inequity was only seen for pre-emptive listing.

Strengths and Limitations

The main strengths of this study are its prospective cohort design, national representativeness and high levels of data completeness (especially for socioeconomic status and co-morbidity) which meant that it was not subject to the inherent weaknesses of retrospective studies that have affected studies exploring access to transplantation to date. As for limitations, this study was observational so causal relationships cannot be determined. There was also no adjustment for comorbidity severity, or for pre transplant work-up. In the case of access to pre-emptive listing, analyses could not take into account all those patients who had CKD 5 or who were approaching the need for dialysis and were being worked up for listing, as these patients were not recruited as part of ATTOM. There may also be residual confounding factors not accounted for, as suggested by the persistence of a centre effect in the final models.

Comparison with Other Studies and Implications on Health Policy

Lower socioeconomic status was independently associated with both lower pre-emptive transplant listing and a lower likelihood of being listed after starting dialysis, even after extensive adjustment for demographic factors and comorbidity. Though this observation could arise in part from residual confounding by comorbidity due to lack of data on disease severity, this inequity is consistent with multiple studies in the US and the UK which have

highlighted reduced access to the transplant waiting list in socially deprived patients[14,20]. Similarly, several studies around the world have also shown that socioeconomically deprived individuals are less likely to undergo pre-emptive transplantation[21,22], though this has never been reported in the UK to date. As for potential explanations, studies, primarily in the US, have suggested that socially deprived patients may not appreciate the advantages of kidney transplantation and may be less likely to complete the pre-transplant work up[20]. Additionally, clinicians may consciously or subconsciously manage patients in ways that make it less likely for socially deprived patients to be listed for transplantation[23]. Another possible reason may be lower levels of health literacy amongst patients of lower socioeconomic status. This hypothesis is supported by studies from the US and UK[24,25] and may represent an area for targeted interventions to reduce inequity caused by social deprivation.

As for the association of ethnicity and the transplant pathway, this was seen to vary by measure; both Asian and Black participants being less likely to be pre-emptively listed as compared to white participants; but Asian ethnicity was associated with an higher likelihood of being listed after starting dialysis. Other studies have also found conflicting associations in terms of ethnicity. Many studies in the US[16,17,20,23] and UK[14,15] have reported that ethnic minorities have decreased access to the transplant waiting list, whilst other studies have reported equal access[26]. One explanation for differing historical outcomes may be that previous studies reporting that ethnic minorities having reduced access to listing may have been confounded, by combining and analysing pre-emptive listing and listing after starting dialysis together; whilst in the present study they were treated independently. It is also possible that the lower likelihood of pre-emptive listing in ethnic minorities is partly a reflection of their lower rates of live donor transplantation, found in both the US and in the UK[27]. Institutional prejudice, distrust and reluctance to engage with the medical system, cultural and religious beliefs, and lack of suitable donors or concern over a higher risk for living donors from minority ethnic backgrounds have all been cited as possible reasons for these disparities[28-31]. Further research is clearly needed to understand potential reasons.

In contrast the reasons for the observation that Asian participants had an higher likelihood of being listed once starting dialysis are unclear. Likewise, the reasons for the observation that female gender was negatively associated with listing after starting dialysis but not pre-emptive listing is uncertain; it is revealed by analyzing these cohorts separately rather than combining them as in studies to date, and may be due to chance.

Whilst patient case-mix was seen to account for the majority of inter-centre variation, some centre practice patterns were also seen to be associated with being listed. Being registered at a transplanting centre was associated with an increase in pre-emptive listing but not post-dialysis listing. This has been described in previous retrospective studies[24-25], and may reflect more efficient listing processes in transplanting Centers as a consequence of having access to on-site specialist clinicians to assist in assessing suitability; and to on-site live donor co-ordinators to aid earlier identification of potential living donors.

The observation that a critical mass of consultant nephrologist availability (> 6 consultant nephrologists) was independently associated with a higher likelihood of listing also suggests a direct link between improved quality of patient care (i.e. early wait-listing) and senior workforce capacity. Whilst we are not able to clarify why this may be the case, a possible explanation is the ability to embed sub-specialist interest in transplantation and/or CKD pathway progress which may be more likely in larger units.

The finding that discussing transplantation with all patients and not utilising a written protocol both improve listing is intriguing and has not been reported before. An inclusive approach to discussion about transplantation is likely to help eliminate personal bias and assist in a more patient-centred approach that may result in more open conversation, as well as aid in the early identification of potential live donors. Likewise, clinicians at Centers not using a written protocol (i.e. Centers which do not list patients using defined criteria as part of a in house

centre protocol), might benefit from listing more patients due to the ability to exercise more flexibility and their own personal clinical judgment which would otherwise be hampered by restrictions imposed by local guidelines.

Conclusions

This study has shown that patient case-mix and, to a lesser extent, centre practice patterns account for the majority of observed inter-centre variation in access to pre-emptive listing and listing after starting dialysis in the UK. However, socioeconomic inequity exists in access to kidney transplantation in the UK despite the existence of a universal healthcare system. Further research is needed to understand the causal pathways between socioeconomic status and listing for transplantation including the role of health literacy in influencing access to transplantation to reduce inequity.

Disclosures: Dr. Draper was a member of UK DEC 2010-2016. Dr. Fogarty reports “other” from Vifor Pharmaceuticals (anemia products), personal fees from ACI clinical, “other” from Amicus Pharmaceuticals (Treatment for Fabry Disease), and personal fees from Pharmacosmos Pharmaceuticals anemia products), outside the submitted work. Dr. Bradley, Dr. Dudley, Dr. Forsythe, Dr. Johnson, Dr. Metcalfe Dr. Oniscu, Dr. Pruthi, Dr. Ravanan, Dr. Robb, Dr. Roderick, Dr. Tomson, and Dr. Watson have nothing to disclose.

Funding: This article presents independent research funded by the National Institute for Health Research (NIHR) under the Programme Grants for Applied Research scheme (RP-PG-0109-10116).

Acknowledgments: The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. Ethical approval for this study was obtained from the NHS/HSC Research Ethics Committee via Cambridgeshire Central REC (Ref:11/EE/0120), and all data were collected and stored in keeping with the requirements of the UK Data Protection Act 1998.

Supplemental Material Table of Contents

References

1. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/612303/ChronickidneydiseaseCKDprevalencemodelbriefing.pdf
2. MacNeill SJ, Ford D, Evans K, Medcalf JF. Chapter 2 UK Renal Replacement Therapy Adult Prevalence in 2016: National and Centre-specific Analyses. Nephron. 2018;139 Suppl 1:47-74. doi: 10.1159/000490960
3. Gilg J, Methven S, Casula A, Castledine C. UK Renal Registry 19th Annual Report: Chapter 1 UK RRT Adult Incidence in 2015: National and Centre-specific Analyses. Nephron. 2017;137 Suppl 1:11-44. doi: 10.1159/000481363.
4. United States Renal Data System. 2017 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2017.
5. Volkova N, McClellan W, Klein M, et al. Neighbourhood poverty and racial differences in ESRD incidence. J Am Soc Nephol 2008;19(2):356-64
6. Ward MM. Socioeconmic status and the incidence of ESRD. Am J Kidney Dis 2008;51(4):563-72.
7. Roderick PJ, Raleigh VS, Hallam L, Mallick NP. The need and demand for renal replacement therapy in ethnic minorities in England. Journal of Epidemiology and Community Health. 1996;50(3):334-339.
8. Wolfe RA, Ashby VB, Milford EL*, et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999; 341: 1725-1730.
9. Oniscu GC, Brown H, Forsythe JL. Impact of cadaveric renal transplantation on survival in patients listed for transplantation. *J Am Soc Nephrol* 2005; 16: 1859-1865.
10. Neipp M, Karavul B, Jackobs S*, et al.* Quality of life in adult transplant recipients more than 15 years after kidney transplantation. *Transplantation* 2006; 81: 1640-1644.

11. https://www.commonwealthfund.org/publications/fund-reports/2017/jul/mirror-mirror-2017-international-comparison-reflects-flaws-and
12. Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis. Transplantation.2002;74:1377-1381.
13. Taylor D, Robb M, Casula A, Caskey F. UK Renal Registry 19th Annual Report: Chapter 11 Centre Variation in Access to Kidney Transplantation (2010-2015). Nephron 2017;137(suppl 1):259-268. doi: 10.1159/000481373
14. Oniscu GC, Schalkwijk AA, Johnson RJ, Brown H, Forsythe JL. Equity of access to renal transplant waiting list and renal transplantation in Scotland: cohort study. BMJ2003;327:1261.
15. Ravanan R, Udayaraj U, Ansell D, et al. Variation between Centers in access to renal transplantation in UK: longitudinal cohort study. BMJ. 2010 Jul 20;341:c3451. doi: 10.1136/bmj.c3451.
16. Kasiske BL, London W, Ellison MD. Race and socioeconomic factors influencing early placement on the kidney transplant waiting list. J Am soc Nephrol 1998;9(11):2142-7.
17. Yeates KE, Schaubel DE, Cass A, Sequist TD, Ayanian JZ. Access to renal transplantation for minority patients with ESRD in Canada. Am J Kidney Dis 2004;44(6):1083-9.
18. Oniscu GC, Ravanan R, Wu D, et al. Access to Transplantation and Transplant Outcome Measures (ATTOM): study protocol of a UK wide, in-depth, prospective cohort analysis. BMJ Open. 2016;6(2):e010377. doi:10.1136/bmjopen-2015-010377.
19. Pruthi R, Tonkin-Crine S, Calestani M, et al. Variation in Practice Patterns for Listing Patients for Renal Transplantation in the United Kingdom: A National Survey. Transplantation. 2018 Jun;102(6):961-968. doi: 10.1097/TP.0000000000002046.
20. Alexander GC, Sehgal AR. Barriers to cadaveric transplantation among blacks, women and the poor. JAMA 1998;280(13):1148-52.

21. Grams ME, Chen BP, Coresh J, Segev DL. Preemptive deceased donor kidney transplantation: considerations of equity and utility. Clin J Am Soc Nephrol. 2013 Apr;8(4):575-82.

22. Riffaut N, Lobbedez T, Hazzan M, et al. Access to preemptive registration on the waiting list for renal transplantation: a hierarchical modeling approach. Transpl Int. 2015 Sep;28(9):1066-73.

23. Navaneethan SD, Singh S. A systematic review of barriers in access to renal transplantation among African Americans in the United States. Clin Transplant 2006;20(6):769-75.

24. Taylor DM, Bradley JA, Bradley C, et al. Limited health literacy in advanced kidney disease. Kidney Int. 2016 Sep;90(3):685-95. doi: 10.1016/j.kint.2016.05.033.

25. V. Grubbs, S.E. Gregorich, E.J. Perez-Stable, C.Y. Hsu. Health literacy and access to kidney transplantation. Clin J Am Soc Nephrol, 4 (2009), pp. 195-200.

26. Jeffrey RF, Woodrow G, Mahler J, Johnson R, Newstead CG. Indo-asian experience of renal transplantation in Yorkshire: results of a 10 year survey. Transplantation 2002;73(10):1652-7.

27. Udayaraj U, Ben-Shlomo Y, Roderick P, et al. Social deprivation, ethnicity, and uptake of living kidney donor transplantation in the United Kingdom. Transplantation. 2012 Mar 27;93(6):610-6.

28. Norris KC, Agodoa LY. Unraveling the racial disparities associated with kidney disease. Kidney Int. 2005 Sep;68(3):914-24.

29. Boulware LE, Cooper LA, Ratner LE, LaVeist TA, Powe NR. Race and trust in the health care system. Public Health Rep 2003;118(4):358-65.

30. Bratton C, Chavin K, Baliga P. Racial disparities in organ donation and why. Current opinion in organ transplantation 2011;16(2):243-9.

31. Doshi M, Garg AX, Gibney E, Parikh C. Race and renal function early after live kidney donation: an analysis of the United States Organ Procurement and Transplantation Network Database. Clin Transplant 2010;24(5):E153-7.

Table 1: Baseline characteristics of participants in the Access to Transplantation and Transplant Outcome Measures study, United Kingdom, analysed for access to pre-emptive kidney transplant listing and kidney transplant listing within two years of starting dialysis

Variable	Access to Pre-emptive Listing		Access to Listing within 2 years of Starting Dialysis	
	Total N (%)	Number Pre-emptively listed N (%)	Total N (%)	Number Listed within 2 years of starting Dialysis N, (%)
Age (Mean, (SD))	55 (13.6)	49 (12.9)	57 (13)	49 (14)
Gender				
Male	1706 (64)	421 (60)	1285 (65)	406 (69)
Female	970 (36)	285 (40)	685 (35)	179 (31)
Ethnic Group				
White	2177 (81)	611 (87)	1566 (80)	416 (71)
Asian	293 (11)	60 (8)	233 (12)	103 (18)
Black	177 (7)	31 (4)	146 (7)	54 (9)
Other	29 (1)	4 (1)	25 (1)	12 (2)
Primary Renal Disease				
Diabetes	711 (28)	112 (16)	599 (30)	119 (20)
Glomerulonephritis	428 (16)	148 (21)	280 (14)	142 (24)
Hypertension	171 (6)	40 (6)	131 (7)	50 (9)
Missing	30 (1)	10 (1)	20 (1)	14 (2)
Other	388 (15)	88 (13)	300 (15)	75 (13)
Polycystic	249 (9)	135 (19)	114 (6)	56 (10)
Pyelonephritis	221 (8)	91 (13)	130 (7)	31 (5)
Renal vascular disease	95 (4)	12 (2)	83 (4)	9 (2)
Uncertain	383 (14)	70 (10)	313 (16)	89 (15)
BMI				
Less than 20	165 (6)	40 (6)	125 (6)	41 (7)
20 - <25	729 (27)	232 (33)	497 (25)	195 (33)
25 - <30	771 (29)	274 (39)	497 (25)	186 (32)
30 - <35	435 (16)	107 (15)	328 (17)	91 (16)
35 - <40	202 (8)	24 (3)	178 (9)	34 (6)
≥ 40	131 (5)	6 (1)	125 (6)	8 (1)
Missing	243 (9)	23 (3)	220 (11)	30 (5)
Diabetes				

No	1614 (60)	552 (78)	1065 (54)	398 (68)
Type 1	256 (10)	80 (11)	176 (9)	60 (10)
Type 2	776 (29)	67 (10)	709 (36)	115 (20)
Missing	27 (1.0)	7 (1)	20 (1)	12 (2)
Heart Disease				
No	2159 (81)	650 (92)	1509 (77)	508 (87)
Yes	488 (18)	48 (7)	440 (22)	63 (11)
Missing	29 (1)	8 (1)	21 (1)	14 (2)
Heart Failure				
No	2467 (92)	691 (98)	1776 (90)	551 (94)
Yes	178 (7)	7 (1)	171 (9)	18 (3)
Missing	31 (1)	8 (1)	23 (1)	16 (3)
Atrial Fibrillation				
No	2547 (95)	687 (97)	1860 (94)	559 (96)
Yes	97 (4)	11 (2)	86 (4)	10 (2)
Missing	32 (1)	8 (1)	24 (1)	16 (3)
Cardiac Valve Replacement				
No	2612 (98)	689 (98)	1923 (98)	568 (97)
Yes	31 (1)	7 (1)	24 (1)	1 (0.2)
Missing	33 (1)	10 (1)	23 (1)	17 (3)
Pacemaker				
No	2604 (97)	694 (98)	1910 (97)	567 (97)
Yes	41 (2)	4 (0.6)	37 (2)	2 (0.3)
Missing	31 (1)	8 (1)	23 (1)	16 (3)
Cerebrovascular Disease				
No	2422 (91)	674 (96)	1748 (89)	541 (93)
Yes	222 (8)	23 (3)	199 (10)	28 (5)
Missing	32 (1)	9 (1)	23 (1)	16 (3)
Vascular Disease				
No	2432 (91)	686 (97)	1746 (89)	545 (93)
Yes	212 (8)	12 (2)	200 (10)	24 (4)
Missing	32 (1)	8 (1)	24 (1)	16 (4)
Abdominal Aortic Aneurysm				
No	2597 (97)	693 (98)	1904 (97)	569 (97)
Yes	46 (2)	4 (0.6)	42 (2)	1 (0.2)
Missing	33 (1)	9 (1)	24 (1)	15 (3)
Respiratory Disease				
No	2335 (87)	643 (91)	1692 (86)	523 (89)
Yes	310 (12)	55 (8)	255 (13)	47 (8)
Missing	31 (1)	8 (1)	23 (1)	15 (3)
Liver Disease				

No	2582 (97)	691 (98)	1891 (96)	563 (96)
Yes	64 (2)	7 (1)	57 (3)	7 (1)
Missing	30 (1)	8 (1)	22 (1)	15 (3)
Blood Borne Viruses				
No	2576 (96)	688 (98)	1888 (96)	562 (96)
Yes	70 (3)	10 (1)	60 (3)	9 (2)
Missing	30 (1)	8 (1)	22 (1)	14 (2)
Malignancy				
No	2328 (87)	659 93)	1669 (85)	545 (93)
Yes	321 (12)	39 (6)	282 (14)	25 (4)
Missing	27 (1)	8 (1)	19 (1)	14 (2)
Mental Illness				
No	2422 (91)	657 (93)	1765 (90)	532 (91)
Yes	225 (8)	41 (6)	184 (9)	39 (7)
Missing	29 (1)	8 (1)	21 (1)	14 (2)
Dementia				
No	2637 (99)	697 (99)	1940 (99)	568 (97)
Yes	8 (0.3)	1 (0.1)	7 (0.4)	1 (0.2)
Missing	31 (1)	8 (1)	23 (1)	16 (3)
Smoking				
No	1145 (43)	364 (52)	781 (40)	253 (43)
Current	381 (14)	66 (9)	315 (16)	73 (13)
Ex-smoker	763 (29)	185 (26)	578 (29)	158 (27)
Don't Know	370 (14)	85 (12)	285 (15)	93 (16)
Missing	17 (0.6)	6 (1)	11 (0.6)	8 (1)
Born in UK				
No	485 (18)	86 (12)	399 (20)	149 (26)
Yes	2032 (76)	578 (82)	1454 (74)	404 (69)
Missing	159 (6)	42 (6)	117 (6)	32 (6)
English First Language				
No	325 (12)	58 (8)	267 (14)	110 (19)
Yes	2192 (82)	606 (86)	1586 (81)	443 (76)
Missing	159 (6)	42 (6)	117 (6)	32 (6)
Read Help				
No	2058 (77)	597 (85)	1461 (74)	459 (78)
Yes	457 (17)	66 (9)	391 (20)	94 (16)
Missing	161 (6)	43 (6)	118 (6)	32 (6)
Accommodation				
Owned by you (outright or with a mortgage)	1436 (54)	468 (66)	968 (49)	281 (48)
Part rent, part owned (shared ownership)	55 (2)	11 (2)	44 (2)	17 (3)

Rented privately from Council/ Housing Association	861 (32)	145 (21)	716 (36)	203 (35)
Other	154 (6)	37 (5)	117 (6)	49 (8)
Missing	170 (6)	45 (6)	125 (6)	35 (6)
Employment				
Working PT/FT	627 (23)	316 (45)	311 (16)	185 (32)
Long term sick/disabled	700 (26)	132 (19)	568 (29)	156 (27)
Retired from paid work	889 (33)	124 (18)	765 (39)	114 (20)
Unemployed	173 (7)	37 (5)	136 (7)	65 (11)
Other	122 (5)	52 (7)	70 (4)	33 (6)
Missing	165 (6)	45 (6)	120 (6)	32 (6)
Education				
Degree, Higher or NVQ 4-5	446 (17)	160 (23)	286 (15)	137 (23)
GCSE, A-level or NVQ 1-3	1051 (39)	346 (49)	705 (36)	241 (41)
No Qualifications	1023 (38)	160 (23)	863 (44)	175 (30)
Missing	156 (6)	40 (6)	116 (6)	32 (6)
Car Ownership				
No	658 (25)	76 (11)	582 (30)	153 (26)
Yes	1852 (69)	586 (83)	1266 (64)	399 (68)
Missing	166 (6)	44 (6)	122 (6)	33 (6)
Civil Status				
Single (never married)	480 (18)	136 (19)	344 (17)	136 (23)
Married	1386 (52)	388 (55)	998 (50)	286 (49)
Living with partner	173 (7)	64 (9)	109 (6)	43 (8)
Divorced	238 (9)	49 (7)	189 (10)	49 (8)
Separated (but still legally married)	81 (3)	12 (2)	69 (4)	19 (3)
Widowed	148 (6)	14 (2)	134 (7)	17 (3)
Missing	170 (6)	43 (6)	127 (6)	35 (6)
Children in Household				
None	1978 (74)	472 (67)	1506 (76)	387 (66)
1	264 (10)	97 (14)	167 (9)	76 (13)
2 or more	265 (10)	92 (13)	173 (9)	88 (15)
Missing	169 (6)	45 (6)	124 (6)	34 (6)
Adults in Household				
0-1	699 (26)	127 (18)	572 (29)	154 (26)
2	1261 (47)	378 (54)	883 (45)	263 (45)
3 or more	545 (20)	156 (22)	389 (20)	134 (23)
Missing	171 (6)	45 (6)	126 (6)	34 (6)

Table 2 – Associations of patient-level and centre-level characteristics with listing for pre-emptive kidney transplantation*.

Variable	N	Adjusted Odds Ratio (95% Confidence Interval)	p-value
Patient Variables±			
Age			<0.0001
18-29	149	1	
30-39	235	0.9 (0.51-1.57)	
40-49	455	0.79 (0.47-1.32)	
50-59	657	0.57 (0.34-0.97)	
60-64	372	0.47 (0.26-0.87)	
65-75	808	0.19 (0.1-0.37)	
Ethnic Group			<0.0001
White	2177	1	
Asian	293	0.49 (0.33-0.72)	
Black	177	0.43 (0.26-0.71)	
Other	29	0.23 (0.07-0.8)	
BMI			<0.0001
Less than 20	184	0.66 (0.4-1.09)	
20 - <25	798	1	
25 - <30	845	1.31 (0.99-1.73)	
30 - <35	482	0.97 (0.69-1.38)	
35 - <40	223	0.31 (0.18-0.54)	
≥ 40	144	0.12 (0.05-0.28)	
Time Since First Seen by Nephrologist			<0.0001
<1 Year	701	1	
1-3 Years	619	8.12 (5.44-12.1)	
>3 Years	1355	11.55 (8.05-16.55)	
Diabetes			<0.0001
No	1626	1	
Type 1	266	1.12 (0.76-1.64)	

Type 2	784	0.37 (0.26-0.52)	
Peripheral Vascular Disease			
No	2456	1	
Yes	220	0.29 (0.13-0.61)	0.0013
Heart Disease			
No	2170	1	
Yes	506	0.55 (0.36-0.82)	0.004
Heart Failure			
No	2490	1	
Yes	186	0.25 (0.08-0.77)	0.016
Cerebrovascular Disease			
No	2448	1	
Yes	228	0.53 (0.3-0.92)	0.025
Malignancy			
No	2340	1	
Yes	336	0.33 (0.2-0.53)	<0.0001
Smoking			0.0005
No	1148	1	
Current	383	0.53 (0.36-0.78)	
Ex-smoker	769	0.95 (0.72-1.25)	
Don't know	377	0.75 (0.52-1.07)	
Socioeconomic Variables			
Employment			<0.0001
Working full time/ part time	667	1	
Long term sick/disabled	746	0.42 (0.3-0.58)	
Retired from paid work	948	0.55 (0.37-0.82)	
Unemployed	185	0.51 (0.31-0.85)	
Other	130	0.93 (0.54-1.6)	
Accommodation			<0.0001
Owned by you (Outright or with a Mortgage)	1533	1	
Other	166	0.58 (0.34-1.0)	
Part rent, Part owned (shared ownership)	59	0.32 (0.13-0.74)	
Rented Privately from Council / Housing Association	918	0.55 (0.41-0.75)	
Car ownership			
No	701	1	
Yes	1975	1.98 (1.41-2.76)	<0.0001
Education			0.08

GCSE, A-level or NVQ 1-3	1115	1.26 (0.96-1.67)	
Degree, Higher or NVQ 4-5	477	1.06 (0.74-1.51)	
No Qualifications	1084	1	
Centre Level Variables			
Transplanting Centre			
No	48	1	
Yes	23	3.1 (2.36-4.07)	<0.0001
No. of Consultant Nephrologists			
≤6	30	1	
>6	41	2.16 (1.5-3.1)	<0.0001
Transplantation Discussed with All Patients			
No	20	1	
Yes	51	1.39 (1.08-1.78)	0.0094

***** Derived using multivariable logistic regression and multiple imputation. 20 imputed data sets were modelled separately then combined to produce final parameter estimates.
± Missing data was imputed for BMI (n=243), comorbidity (n= 30), time since first seen by a nephrologist (n=24) and socioeconomic variables (n=146).

Table 3 – Associations of patient-level and centre-level characteristics with listing for kidney transplantation within 2 years of starting dialysis*

Variable	N	Adjusted Hazard Ratio (95% Confidence Interval)	p-value
Patient Variables			
Age			<0.0001
18-29	86	1	
30-39	137	0.8 (0.56-1.12)	
40-49	280	0.64 (0.46-0.89)	
50-59	462	0.35 (0.25-0.49)	
60-64	290	0.27 (0.18-0.41)	
65-75	715	0.15 (0.1-0.23)	
Gender			
Male	1285	1	
Female	685	0.82 (0.68-0.99)	0.035
Ethnic Group			0.002
White	1566	1	
Asian	233	1.42 (1.12-1.79)	
Black	146	1.04 (0.76-1.43)	
Other	25	1.56 (0.85-2.87)	
BMI			<0.0001
Less than 20	143	0.85 (0.6-1.21)	
20 - <25	561	1	
25 - <30	558	1.15 (0.93-1.42)	
30 - <35	369	0.88 (0.67-1.14)	
35 - <40	200	0.48 (0.33-0.7)	
≥ 40	141	0.15 (0.08-0.3)	
Dialysis Modality			
Haemodialysis	1603	1	
Peritoneal dialysis	367	1.34 (1.1-1.64)	0.004
Diabetes			<0.0001

No	1085	1	
Type 1	176	0.76 (0.57-1.02)	
Type 2	709	0.62 (0.49-0.79)	
Peripheral Vascular Disease			
No	1764	1	
Yes	206	0.6 (0.37-0.96)	0.035
Heart Disease			
No	1520	1	
Yes	451	0.8 (0.59-1.09)	0.16
Heart Failure			
No	1797	1	
Yes	173	0.58 (0.36-0.93)	0.025
Blood Borne Viruses			
No	1906	1	
Yes	64	0.36 (0.18-0.71)	0.0035
Malignancy			
No	1677	1	
Yes	293	0.33 (0.2-0.53)	<0.0001
Smoking			0.05
No	784	1	
Current	316	0.76 (0.58-1.0)	
Ex-smoker	582	1.17 (0.95-1.45)	
Don't know	289	1.06 (0.82-1.36)	
Socioeconomic Variables			
Employment			<0.0001
Working full time/ part time	331	1	
Long term sick/disabled	606	0.54 (0.43-0.68)	
Retired from paid work	814	0.58 (0.42-0.8)	
Unemployed	144	0.77 (0.56-1.06)	
Other	75	0.74 (0.5-1.1)	
Accommodation			0.009
Owned by you (Outright or with a Mortgage)	1035	1	
Other	126	0.81 (0.58-1.13)	
Part rent, Part owned (shared ownership)	47	1.07 (0.64-1.8)	
Rented Privately from Council / Housing Association	762	0.76 (0.61-0.94)	
Car ownership			
No	619	0.73 (0.6-0.9)	0.0026
Yes	1351	1	
Education			0.01

GCSE, A-level or NVQ 1-3	749	1.05 (0.85-1.3)	
Degree, Higher or NVQ 4-5	305	1.38 (1.07-1.79)	
No Qualifications	916	1	
Centre Level Variables			
Consultant Nephrologists			
≤6	30	1	
>6	41	1.26 (1.0-1.59)	0.054
MDT			
No	17	1	
Yes	54	1.23 (0.99-1.52)	0.057
Written Protocol for listing			
No	21	1	
Yes	50	0.72 (0.58-0.9)	0.0033

***** Derived using multivariable Cox regression and multiple imputation. 20 imputed data sets were modelled separately then combined to produce final parameter estimates.
± Missing data was imputed for BMI (n=220), comorbidity (n=22) and socioeconomic variables (n=104).

Figure Legend

Figure 1(a). Flow diagram showing the study recruitment of participants (with inclusion and exclusion criteria) for (1) access to pre-emptive listing and (2) listing after starting dialysis
Figure 1 (b). Flow diagram showing the study recruitment of participants (with inclusion and exclusion criteria) for (1) access to pre-emptive listing and (2) listing after starting dialysis

Figure 2 (a). Unadjusted funnel plot showing variation in proportion listed for pre-emptive kidney transplant by centre according to number of participants evaluated.
*Centers with less than 10 observations are not shown
** Number of Patients, denotes the number of participants from a given centre that were analysed (from cohort of patients recruited at each centre for the ATTOM study)
Figure 2(b). Risk adjusted funnel plot showing variation in proportion listed for pre-emptive kidney transplant by centre according to number of participants evaluated
*Risk adjusted for all patient and centre factors, using the mean of each adjustment variable across the cohort, associated with pre-emptive listing as highlighted in table 2. Centers with less than 10 observations are not shown.
** Number of Patients, denotes the number of participants from a given centre that were analysed (from cohort of patients recruited at each centre for the ATTOM study)

Figure 1(a)

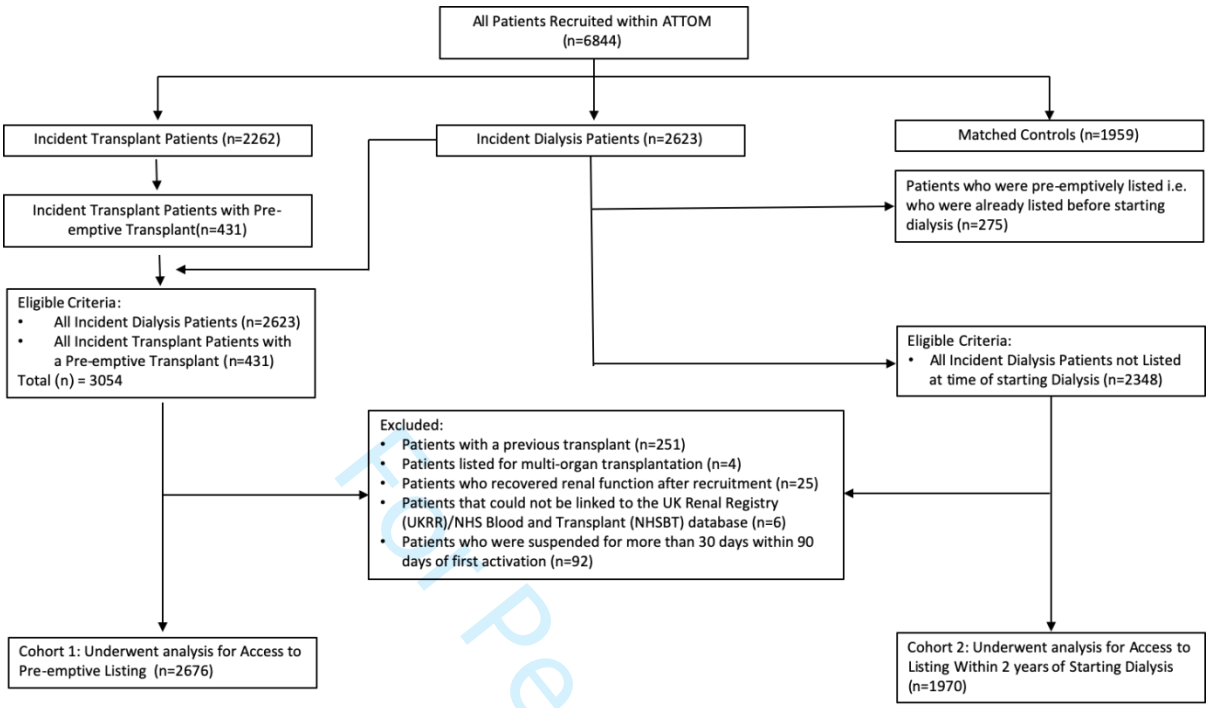
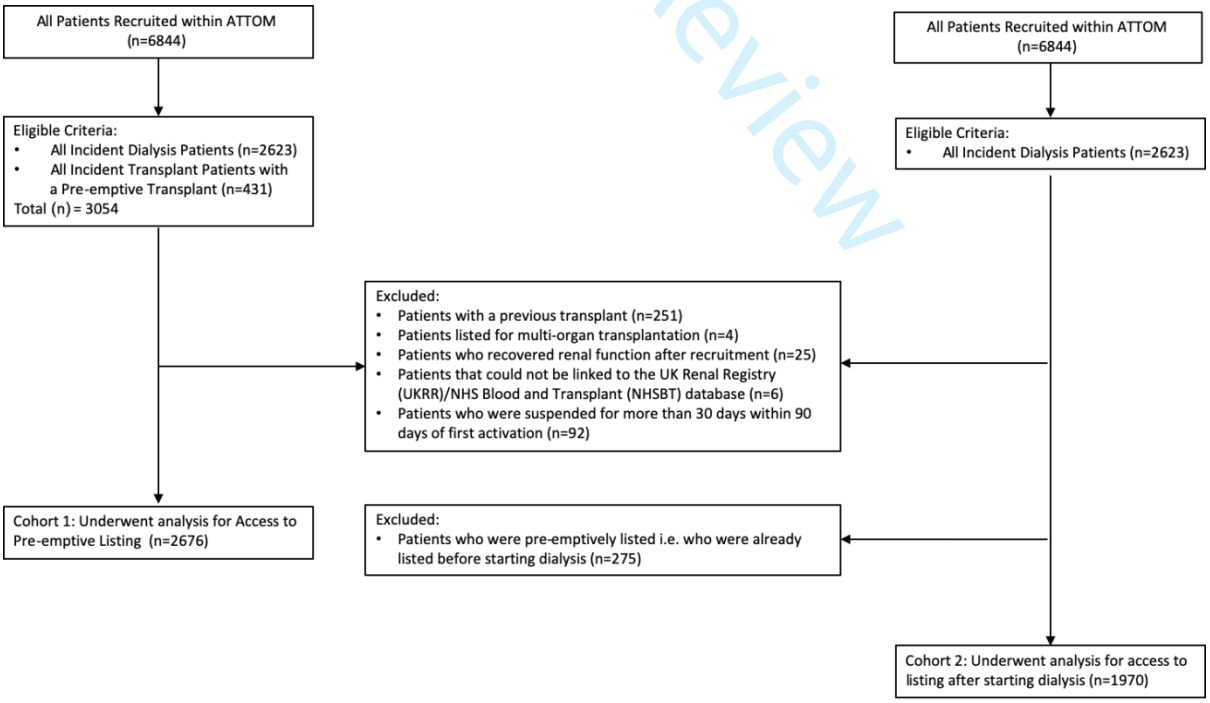


Figure 2(b)



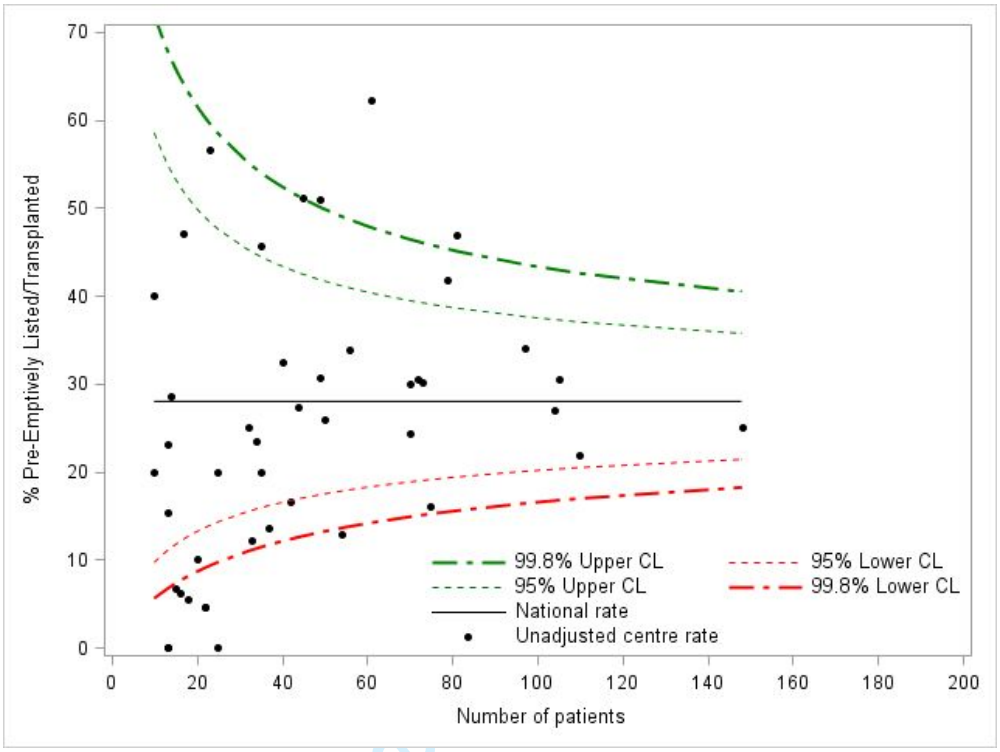


Figure 2 (a)

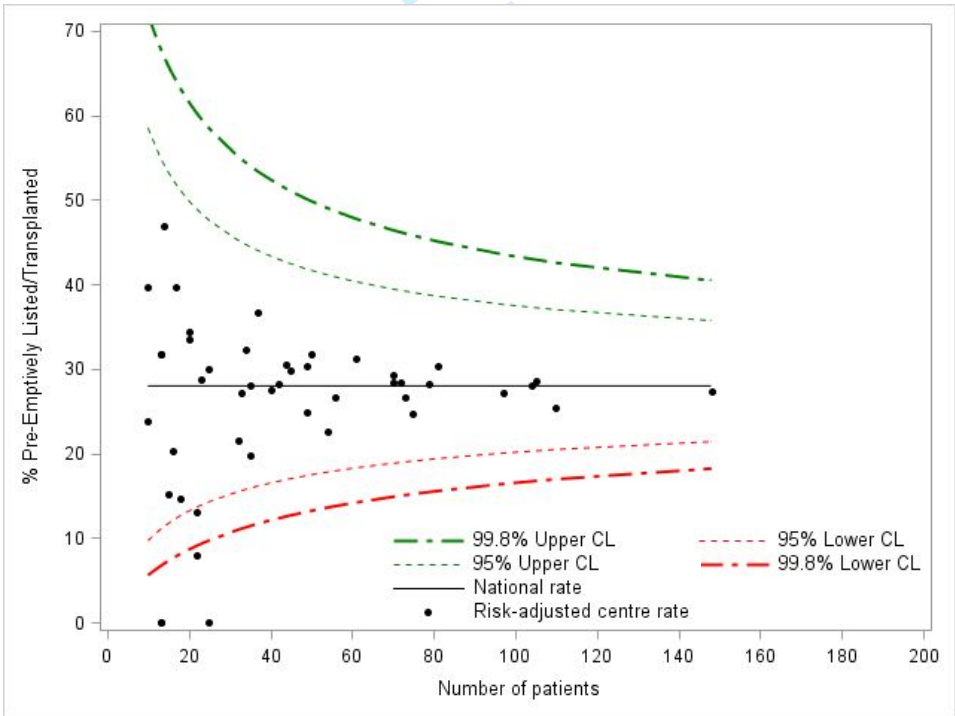


Figure 2(b)

Is there inequity in access to kidney transplantation in the United Kingdom?

CJASN
Clinical Journal of American Society of Nephrology

Methods and Cohort

Prospective observational cohort study

72 UK kidney centers

Incident KRT patients in ATTOM study

Nov 2011-March 2013

Results

Preemptive listing

26%

of 2676 incident KRT patients

	Lower likelihood	Higher likelihood
Patient factors	• Older age • Non-white • Most co-morbidities • BMI >35	• Working full time • Car ownership
Center factors		• Transplanting center • Transplantation discussed with all patients

Listing within 2 years of initiating dialysis

30%

of 1970 patients starting dialysis

	Lower likelihood	Higher likelihood
Patient factors	• Older age • Most co-morbidities • BMI >35	• Peritoneal dialysis • Working full time • Car ownership
Center factors	• Written protocol for listing	

Conclusion Patient case-mix accounts for most of the inter-center variation seen in access to transplantation in the UK. Socioeconomic inequity exists despite having a universal healthcare system.

Rishi Pruthi, Matthew Robb, Gabriel Oniscu, Charles Tomson, et al. ***Inequity in Access to Transplantation in the UK: A Prospective Observational Cohort Study.*** CJASN doi: 10.2215/CJN.11460919. **Visual Abstract by Beatrice Concepcion, MD.**

Inequity in Access to Transplantation in the United Kingdom

Running Title: Inequity in Access to Transplantation

Rishi Pruthi PhD[1,2], Matthew L Robb PhD[3], Gabriel C. Oniscu MD[4], Charles Tomson DM[5], Andrew Bradley PhD[6], John L. Forsythe MD[4], Wendy Metcalfe MD[4], Clare Bradley PhD[7], Christopher Dudley MD[8], Rachel J Johnson MSc[3], Christopher Watson MD[6], Heather Draper PhD[9], Damian Fogarty MD[10], *Rommel Ravanan MD[8], *Paul J. Roderick MD[2]. On Behalf of the ATTOM Investigators

1. Guy's and St Thomas' NHS Foundation Trust, London, SE1 9RT, UK
2. Primary Care and Population Sciences, Faculty of Medicine, University of Southampton, SO17 1BJ, UK
3. NHS Blood and Transplant, Bristol, BS34 7QH, UK
4. Edinburgh Transplant Centre, Royal Infirmary of Edinburgh, Edinburgh, EH16 4SA, UK
5. Renal Unit, Freeman Hospital, Newcastle, NE7 7DN, UK
6. Department of Surgery, University of Cambridge and the NIHR Cambridge Biomedical Research Centre, Cambridge, CB2 0QQ, UK
7. Health Psychology Research Unit, Royal Holloway, University of London, Egham, TW20 0EX, UK
8. Richard Bright Renal Unit, Southmead Hospital, Bristol, BS10 5NB, UK
9. Institute for Applied Health Research, University of Birmingham, Birmingham, B15 2TT, UK
10. Belfast Health and Social Care Trust, Belfast, Northern Ireland, BT9 7ABUK

*denotes joint final author

Corresponding author:

Rishi Pruthi,

Consultant Nephrologist,

Guy's Hospital, London SE1 9RT

Tel: 020 7188 7188

Email: rishi.pruthi@nhs.net

Word Count: 3454

Abstract

Background and objectives: Despite the presence of a universal healthcare system it is unclear if there is inter-centre variation in access to kidney transplantation in the UK. This study aims to assess whether equity exists in access to kidney transplantation in the UK after adjustment for patient specific factors and centre practice patterns.

Design, setting, participants, and measurements: Prospective observational cohort study including all 71 UK kidney centres. Incident kidney replacement therapy (KRT) patients recruited between November 2011-March 2013 as part of the Access to Transplantation and Transplant Outcome Measures study (ATTOM) were analysed to assess pre-emptive listing (n=2676) and listing within 2 years of starting dialysis (n=1970) by centre.

Results: 706 participants (26%) were listed pre-emptively whilst 585 (30%) were listed within 2 years of commencing dialysis. The IQR across centres was 6-33% for pre-emptive listing and 25-40% for listing after starting dialysis. Patient-factors including increasing age, most co-morbidities, BMI >35kg/m^2 and lower socioeconomic status were associated with a lower likelihood of being listed and accounted for 89% and 97% of measured inter-centre variation, for pre-emptive listing and listing within 2 years of starting dialysis respectively. Ethnic minority associations were inconsistent and reduced access was only seen for pre-emptive listing with Asian (OR 1.42; CI:1.12-1.79) and Black (OR 1.04; CI:0.76-1.43) participants associated with reduced access. As for centre factors, being registered at a transplanting-centre (OR 3.1; CI: 2.36-4.07) and a universal approach to discussing transplantation (OR 1.4; CI: 1.08-1.78) were associated with higher pre-emptive listing, whilst utilising a written protocol was associated negatively with listing within 2 years of starting dialysis (OR 0.7; CI: 0.58-0.9).

Conclusions: Patient case-mix accounts for most of the inter-centre variation seen in access to transplantation in the UK with practice patterns also contributing some variation. Socioeconomic inequity exists despite having a universal healthcare system.

Introduction

In the UK, it is expected that 2.6 million adults are living with CKD stage 3-5[1], with over sixty-three thousand patients receiving renal replacement therapy (RRT) for end-stage kidney disease (ESKD)[2]. Rates of RRT have risen in most high income countries in the last few decades (including the UK)[3,4] and are greater in lower socioeconomic groups[5,6] and in ethnic minorities[5,7]. Though many undergo dialysis, it is recognized that for 'suitable patients' with ESKD, kidney transplantation confers both better clinical outcomes compared to dialysis[8,9], and leads to improvements in self-reported health[10], and is therefore the preferred RRT modality.

The UK National Health Service was founded on the principle of delivering equitable healthcare based on need and not the ability to pay and was ranked first on equity in a recent international healthcare comparison[11]. Equity is a key consideration for assessing the pathway to kidney transplantation for patients with ESKD. Achieving prompt assessment and timely activation on the transplant waiting list is crucial to accessing transplantation. Increasing length of time on dialysis adversely affects graft and patient survival[12], and

deceased donor organ allocation algorithms in many countries (including the UK) give priority to those who have spent greater time on the waiting list.

Despite national clinical practice guidelines for transplant assessment, retrospective analyses of UK Renal and Transplant Registries data suggest there is variation in access to listing for transplantation between kidney centres[13-15]; and that although ethnic minorities and individuals from lower socioeconomic groups have a higher incidence of ESKD[5-7], they have reduced access to transplantation[14-17]. It is not known whether this difference is due to a higher burden of co-morbidity associated with ethnic minority status or lower socioeconomic status, or due to differences in centre practices that might disadvantage these groups[14]. Studies to date have been limited in their ability to examine these factors due to their retrospective design and use of routine and limited registry data.

This study uses a prospective cohort of patients starting RRT recruited to the Access to Transplantation and Transplant Outcome Measures (ATTOM) study[18] to determine (i) if access to pre-emptive listing (being listed before starting dialysis) and to listing within 2 years of starting dialysis, is equitable for socially deprived and ethnic minority populations in the UK after morbidity adjustment; and ii) whether centre-specific factors are associated with access to transplant listing.

Methods

Study Population

In the UK there are 71 kidney centres (23 transplanting and 48 non-transplanting centres) which collectively provide RRT for all patients in the UK as well as managing all patients approaching ESKD. In each centre, over a 12-month period, between 1 November 2011 and 31 March 2013 all incident dialysis patients and incident kidney transplant recipients aged 18-75 years of age were recruited at the time of starting dialysis or transplantation as part of the ATTOM Study. ATTOM is a national prospective cohort study investigating the factors

that influence access, clinical and patient-reported outcomes and cost-effectiveness of kidney transplantation in the UK. Dedicated research nurses collected clinical and demographic information from the case notes and local electronic databases, and collected health status and well-being data from participants. The data were uploaded onto a secure website designed, developed and maintained by the UK Renal Registry (UKRR). A full description of the ATTOM study methods and protocol has been reported previously[18].

For the analysis of access to pre-emptive listing all incident dialysis participants (n=2623) and all incident transplant participants with a pre-emptive transplant (n=431) recruited to ATTOM were considered for inclusion (Figure 1). Participants excluded were those with a previous transplant (n=251), those listed for multi-organ transplantation (n=4), those who recovered kidney function (n=25) and those that could not be linked to the UKRR/NHS Blood and Transplant (NHSBT) database (n=6). Lastly, participants who were suspended from the waiting list for > 30 days within 90 days of first activation (n=92) were also excluded to avoid any potential bias from centres that may activate patients on the transplant list and then immediately suspend them before more permanent activation at a later date after more formal medical assessment of the patient's suitability.

For analysis of access to the transplant waiting list within 2 years of starting dialysis, all incident dialysis participants that were not pre-emptively listed i.e. who were not listed before starting dialysis were considered (n=2348) using the same exclusion criteria (Figure 1).

Data collection

Patient variables

Demographic, socioeconomic, clinical and comorbidity data were collected for each patient at the time of recruitment. Trained research nurses collected uniformly defined data items from patient interviews, case notes and local electronic patient information systems across the UK. Patient variables collected and analysed included, age, gender, ethnicity, BMI, co-

morbidities and primary renal diagnosis. Several measures of socioeconomic status were also explored including: education status, employment status, accommodation and car ownership. Civil status, number of children in household, number of adults in household and total numbers in household were other measures. Other demographic data collected and explored included place of birth, whether English was their first language, whether any assistance was needed with reading, the length of time a patient was known to kidney services pre RRT and in the case of listing after starting dialysis, their dialysis modality. Full details of how these variables were categorized can be found in Appendix S1.

Centre Variables

Thematic analysis of 45 semi-structured qualitative interviews with key stakeholders and 53 patients conducted across 9 kidney centres in the UK informed the development of an online survey, which was distributed to the Clinical Directors of all 71 UK kidney centres[19]. This survey achieved a 100% response rate and was utilized to derive and quantify centre variables for analysis in this study. Centre variables examined were chosen by study investigators who examined the level of variance across centre responses for each potential variable and took into account the ability to readily categorize them. A full list of centre variables chosen for analysis can be found in Appendix S1.

Outcomes

Date of activation on the waiting list and, where applicable, the date of transplantation, were extracted from the UK Transplant Registry held by the Organ Donation and Transplantation Directorate of NHS Blood and Transplant. Date of death was retrieved from the UKRR database and the Scottish Renal Registry (SRR).

Statistical methods

For access to pre-emptive listing a multi-level logistic regression model was constructed to analyse the association of patient variables (level 1) and centre factors (level 2). Individual

participants (Level 1) were nested within kidney centres (Level 2) to allow for clustering of participants within centres. Analysis of each patient-level factor was adjusted for all other patient-level factors and analysis of each centre factor was adjusted for those patient-level factors found to be associated with pre-emptive listing. The difference in -2*log-likelihood was used to compare model fit between nested models. The overall effect of centre in the analysis was considered by including kidney centre as a random effect. A significance level of <0.05 was taken as evidence of a significant association.

For access to the transplant waiting list within 2 years of starting dialysis, time to listing was analysed using a multi-level Cox proportional hazards regression model. The time to listing was taken to be the time from start of dialysis to activation on the kidney transplant list. Participants were censored at 2 years or at patient death. Statistical significance was defined a priori as p<0.05. Proportional hazards assumptions were tested using Schoenfeld residuals. The presence of an overall kidney centre effect was considered using a frailty term whilst death was also considered as a competing risk using a Fine and Gray model in a separate competing risk analysis.

Multiple imputation was used to account for missing data in each analysis. For access to preemptive listing, data were missing for BMI (n=243), comorbidity (n= 30), time since first seen by a nephrologist (n=24) and socioeconomic variables (n=146). For access to listing after starting dialysis, data were missing for BMI (n=220), comorbidity (n=22) and socioeconomic variables (n=104). No participants were lost to follow up. Sensitivity analysis using complete case analysis did not change conclusions.

All data were analysed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

The baseline characteristics of participants analysed for pre-emptive listing and listing within 2 years of starting dialysis are shown in Table 1. For pre-emptive listing, 2676 participants were analysed following exclusion of 378 participants (12%), see methods. This study cohort had a median age of 57 years (interquartile range 45-66), of which 64% were male, 81% reported their ethnicity as White and diabetes was the most prevalent comorbidity (39%). Amongst socio-demographic factors, 54% of participants reported owning their own home with 69% owning their own car.

As for listing within 2 years of starting dialysis, of 2348 eligible participants, 1970 participants were analysed following exclusion of 378 patients (16%), see methods. The median age of this cohort was 58 years (interquartile range 47-67 years), of which 65% were male, 80% reported their ethnicity as White and 45% had diabetes listed as a co-morbidity. Amongst socio-demographic factors, 49% of participants reported owning their own home whilst 16% of participants reported being in employment. Full details of these baseline characteristics are shown in Table 1.

Access to Pre-emptive Listing

Of 2676 participants, 706 participants (26%) were pre-emptively listed with a mean age of 49 years. The IQR across centres was 6%-33%. An unadjusted funnel plot showing centre variation in the percentage of participants pre-emptively listed is shown in Figure 2a. Associations between patient and centre variables and the likelihood of being pre-emptively listed were characterized using univariable (Appendix S2 & S3) and multivariable (Appendix S4) logistic regression; before proceeding to analyse them in a final multivariable logistic regression including imputed missing data (table 2).

Several patient factors were independently associated with reduced access to pre-emptive listing. These included: increasing age, ethnicity (both Asian and Black participants), most co-morbidities, having a BMI of >35, and not being seen by a nephrologist for at least 12

months before starting RRT. Lower socioeconomic status as indicated by housing tenure and car ownership status was also associated with reduced access.

Three centre level factors were negatively associated with pre-emptive listing: being cared for primarily in a non-transplanting centre, having <6 Whole Time Equivalent (WTE) consultant nephrologists in the centre, and not adopting an approach where transplantation is discussed with all patients. The impact on centre variation of adjusting for these centre factors, along with patient factors, is shown in figure 2(b). Whilst inter-centre variation in pre-emptive listing significantly reduced following the addition of centre as a random effect to the model there was still evidence of variation/unaccounted confounding (p=0.0007 1 df). Of the 1020.9 (2679.2-1658.3) difference in -2logL between the null model and model with patient and centre variables, 89% (907) of the difference was observed when including the patient factors only (Appendix S5).

Access to the Transplant Waiting List After Starting Dialysis

Of 1970 participants included in this analysis, 585 (30%) were listed within 2 years of starting dialysis with a mean age of 49 years. The IQR across centres was 25%-40%. Associations between patient and centre variables and the likelihood of being listed after starting dialysis were characterized using univariable (Appendix S6 & S7) and multivariable (Appendix S8) Cox regression; before proceeding to analyse them in a final multivariable Cox proportional hazards regression model including imputed missing data (table 3).

Several patient factors were independently associated with reduced access to listing after starting dialysis. These included: increasing age, female gender, having vascular disease, heart failure, type II diabetes, the presence of blood borne viruses, a previous history of malignancy, being a current smoker, and having a BMI >35.

As with pre-emptive listing, lower socioeconomic status was associated with reduced access to listing after starting dialysis. Living in rented/housing association accommodation, lack of

car ownership, and being long term sick/disabled or being retired from paid work, as compared to being in full time/part time employment, were all negatively associated with being listed within 2 years of starting dialysis. In contrast, having a university degree, being on Peritoneal Dialysis as opposed to Haemodialysis, and Asian ethnicity were all associated with an higher likelihood of being listed.

Amongst centre practice patterns, having >6 consultant nephrologists in the centre (OR 1.3 CI: 1.00-1.59) was associated positively with being listed within 2 years of starting dialysis as was having a multidisciplinary team (MDT) approach to listing all patients for transplantation (OR 1.2 CI: 0.99-1.52). An MDT approach was defined as having a multi-disciplinary team of physicians, surgeons and other allied health care professionals who regularly convened to discuss patients under consideration for transplant listing before activation.

Utilisation of a written protocol for listing patients for transplantation (OR 0.7 CI: 0.58-0.90) was negatively associated with being listed within 2 years of starting dialysis. Of the (7166.2-6566.8) 599.4 difference in -2logL between the null model and model with patient and centre variables, 97% (583.8) of the difference was observed when including the patient factors only (Appendix S9). After adjusting centre factors along with patient factors though much of the observed inter-centre variation from unadjusted analyses was again reduced there was still evidence of a difference between the centres (p=0.041, 1df).

Interactions and Competing Risk Analysis

When considering age as a linear factor, an interaction with type 2 diabetes was found to be important in the model (p=0.002, 1df). The association between increasing age and time to listing was stronger in participants with type 2 diabetes (data not shown). As for the competing risk analysis, sub-hazard ratios derived did not highlight any significant differences.

Discussion

This national prospective cohort study of patients aged <75 years starting RRT in the UK found significant variation between kidney centres in access to pre-emptive listing for kidney transplantation and listing after starting dialysis. This was largely explained by patient case-mix factors though some centre level effects were also found to be important. There was evidence of socioeconomic inequity in both measures of listing, despite extensive comorbidity adjustment; ethnic minority associations were inconsistent and inequity was only seen for pre-emptive listing.

Strengths and Limitations

The main strengths of this study are its prospective cohort design, national representativeness and high levels of data completeness (especially for socioeconomic status and co-morbidity) which meant that it was not subject to the inherent weaknesses of retrospective studies that have affected studies exploring access to transplantation to date. As for limitations, this study was observational so causal relationships cannot be determined. There was also no adjustment for comorbidity severity, or for pre transplant work-up. In the case of access to pre-emptive listing, analyses could not take into account all those patients who had CKD 5 or who were approaching the need for dialysis and were being worked up for listing, as these patients were not recruited as part of ATTOM. There may also be residual confounding factors not accounted for, as suggested by the persistence of a centre effect in the final models.

Comparison with Other Studies and Implications on Health Policy

Lower socioeconomic status was independently associated with both lower pre-emptive transplant listing and a lower likelihood of being listed after starting dialysis, even after extensive adjustment for demographic factors and comorbidity. Though this observation could arise in part from residual confounding by comorbidity due to lack of data on disease severity, this inequity is consistent with multiple studies in the US and the UK which have

highlighted reduced access to the transplant waiting list in socially deprived patients[14,20]. Similarly, several studies around the world have also shown that socioeconomically deprived individuals are less likely to undergo pre-emptive transplantation[21,22], though this has never been reported in the UK to date. As for potential explanations, studies, primarily in the US, have suggested that socially deprived patients may not appreciate the advantages of kidney transplantation and may be less likely to complete the pre-transplant work up[20]. Additionally, clinicians may consciously or subconsciously manage patients in ways that make it less likely for socially deprived patients to be listed for transplantation[23]. Another possible reason may be lower levels of health literacy amongst patients of lower socioeconomic status. This hypothesis is supported by studies from the US and UK[24,25] and may represent an area for targeted interventions to reduce inequity caused by social deprivation.

As for the association of ethnicity and the transplant pathway, this was seen to vary by measure; both Asian and Black participants being less likely to be pre-emptively listed as compared to white participants; but Asian ethnicity was associated with an higher likelihood of being listed after starting dialysis. Other studies have also found conflicting associations in terms of ethnicity. Many studies in the US[16,17,20,23] and UK[14,15] have reported that ethnic minorities have decreased access to the transplant waiting list, whilst other studies have reported equal access[26]. One explanation for differing historical outcomes may be that previous studies reporting that ethnic minorities having reduced access to listing may have been confounded, by combining and analysing pre-emptive listing and listing after starting dialysis together; whilst in the present study they were treated independently. It is also possible that the lower likelihood of pre-emptive listing in ethnic minorities is partly a reflection of their lower rates of live donor transplantation, found in both the US and in the UK[27]. Institutional prejudice, distrust and reluctance to engage with the medical system, cultural and religious beliefs, and lack of suitable donors or concern over a higher risk for living donors from minority ethnic backgrounds have all been cited as possible reasons for these disparities[28-31]. Further research is clearly needed to understand potential reasons.

In contrast the reasons for the observation that Asian participants had an higher likelihood of being listed once starting dialysis are unclear. Likewise, the reasons for the observation that female gender was negatively associated with listing after starting dialysis but not pre-emptive listing is uncertain; it is revealed by analyzing these cohorts separately rather than combining them as in studies to date, and may be due to chance.

Whilst patient case-mix was seen to account for the majority of inter-centre variation, some centre practice patterns were also seen to be associated with being listed. Being registered at a transplanting centre was associated with an increase in pre-emptive listing but not post-dialysis listing. This has been described in previous retrospective studies[24-25], and may reflect more efficient listing processes in transplanting centres as a consequence of having access to on-site specialist clinicians to assist in assessing suitability; and to on-site live donor co-ordinators to aid earlier identification of potential living donors.

The observation that a critical mass of consultant nephrologist availability (> 6 consultant nephrologists) was independently associated with a higher likelihood of listing also suggests a direct link between improved quality of patient care (i.e. early wait-listing) and senior workforce capacity. Whilst we are not able to clarify why this may be the case, a possible explanation is the ability to embed sub-specialist interest in transplantation and/or CKD pathway progress which may be more likely in larger units.

The finding that discussing transplantation with all patients and not utilising a written protocol both improve listing is intriguing and has not been reported before. An inclusive approach to discussion about transplantation is likely to help eliminate personal bias and assist in a more patient-centred approach that may result in more open conversation, as well as aid in the early identification of potential live donors. Likewise, clinicians at centres not using a written protocol (i.e. centres which do not list patients using defined criteria as part of a in house

centre protocol), might benefit from listing more patients due to the ability to exercise more flexibility and their own personal clinical judgment which would otherwise be hampered by restrictions imposed by local guidelines.

Conclusions

This study has shown that patient case-mix and, to a lesser extent, centre practice patterns account for the majority of observed inter-centre variation in access to pre-emptive listing and listing after starting dialysis in the UK. However, socioeconomic inequity exists in access to kidney transplantation in the UK despite the existence of a universal healthcare system. Further research is needed to understand the causal pathways between socioeconomic status and listing for transplantation including the role of health literacy in influencing access to transplantation to reduce inequity.

Disclosures: None

Acknowledgments: This article presents independent research funded by the National Institute for Health Research (NIHR) under the Programme Grants for Applied Research scheme (RP-PG-0109-10116). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. Ethical approval for this study was obtained from the NHS/HSC Research Ethics Committee via Cambridgeshire Central REC (Ref:11/EE/0120), and all data were collected and stored in keeping with the requirements of the UK Data Protection Act 1998.

Supplemental Material Table of Contents

References

1. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/612303/ChronickidneydiseaseCKDprevalencemodelbriefing.pdf
2. MacNeill SJ, Ford D, Evans K, Medcalf JF. Chapter 2 UK Renal Replacement Therapy Adult Prevalence in 2016: National and Centre-specific Analyses. Nephron. 2018;139 Suppl 1:47-74. doi: 10.1159/000490960
3. Gilg J, Methven S, Casula A, Castledine C. UK Renal Registry 19th Annual Report: Chapter 1 UK RRT Adult Incidence in 2015: National and Centre-specific Analyses. Nephron. 2017;137 Suppl 1:11-44. doi: 10.1159/000481363.
4. United States Renal Data System. 2017 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2017.
5. Volkova N, McClellan W, Klein M, et al. Neighbourhood poverty and racial differences in ESRD incidence. J Am Soc Nephol 2008;19(2):356-64
6. Ward MM. Socioeconmic status and the incidence of ESRD. Am J Kidney Dis 2008;51(4):563-72.
7. Roderick PJ, Raleigh VS, Hallam L, Mallick NP. The need and demand for renal replacement therapy in ethnic minorities in England. Journal of Epidemiology and Community Health. 1996;50(3):334-339.
8. Wolfe RA, Ashby VB, Milford EL*, et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999; 341: 1725-1730.
9. Oniscu GC, Brown H, Forsythe JL. Impact of cadaveric renal transplantation on survival in patients listed for transplantation. *J Am Soc Nephrol* 2005; 16: 1859-1865.
10. Neipp M, Karavul B, Jackobs S*, et al.* Quality of life in adult transplant recipients more than 15 years after kidney transplantation. *Transplantation* 2006; 81: 1640-1644.

11. https://www.commonwealthfund.org/publications/fund-reports/2017/jul/mirror-mirror-2017-international-comparison-reflects-flaws-and
12. Meier-Kriesche HU, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis. Transplantation.2002;74:1377-1381.
13. Taylor D, Robb M, Casula A, Caskey F. UK Renal Registry 19th Annual Report: Chapter 11 Centre Variation in Access to Kidney Transplantation (2010-2015). Nephron 2017;137(suppl 1):259-268. doi: 10.1159/000481373
14. Oniscu GC, Schalkwijk AA, Johnson RJ, Brown H, Forsythe JL. Equity of access to renal transplant waiting list and renal transplantation in Scotland: cohort study. BMJ2003;327:1261.
15. Ravanan R, Udayaraj U, Ansell D, et al. Variation between centres in access to renal transplantation in UK: longitudinal cohort study. BMJ. 2010 Jul 20;341:c3451. doi: 10.1136/bmj.c3451.
16. Kasiske BL, London W, Ellison MD. Race and socioeconomic factors influencing early placement on the kidney transplant waiting list. J Am soc Nephrol 1998;9(11):2142-7.
17. Yeates KE, Schaubel DE, Cass A, Sequist TD, Ayanian JZ. Access to renal transplantation for minority patients with ESRD in Canada. Am J Kidney Dis 2004;44(6):1083-9.
18. Oniscu GC, Ravanan R, Wu D, et al. Access to Transplantation and Transplant Outcome Measures (ATTOM): study protocol of a UK wide, in-depth, prospective cohort analysis. BMJ Open. 2016;6(2):e010377. doi:10.1136/bmjopen-2015-010377.
19. Pruthi R, Tonkin-Crine S, Calestani M, et al. Variation in Practice Patterns for Listing Patients for Renal Transplantation in the United Kingdom: A National Survey. Transplantation. 2018 Jun;102(6):961-968. doi: 10.1097/TP.0000000000002046.
20. Alexander GC, Sehgal AR. Barriers to cadaveric transplantation among blacks, women and the poor. JAMA 1998;280(13):1148-52.

21. Grams ME, Chen BP, Coresh J, Segev DL. Preemptive deceased donor kidney transplantation: considerations of equity and utility. Clin J Am Soc Nephrol. 2013 Apr;8(4):575-82.

22. Riffaut N, Lobbedez T, Hazzan M, et al. Access to preemptive registration on the waiting list for renal transplantation: a hierarchical modeling approach. Transpl Int. 2015 Sep;28(9):1066-73.

23. Navaneethan SD, Singh S. A systematic review of barriers in access to renal transplantation among African Americans in the United States. Clin Transplant 2006;20(6):769-75.

24. Taylor DM, Bradley JA, Bradley C, et al. Limited health literacy in advanced kidney disease. Kidney Int. 2016 Sep;90(3):685-95. doi: 10.1016/j.kint.2016.05.033.

25. V. Grubbs, S.E. Gregorich, E.J. Perez-Stable, C.Y. Hsu. Health literacy and access to kidney transplantation. Clin J Am Soc Nephrol, 4 (2009), pp. 195-200.

26. Jeffrey RF, Woodrow G, Mahler J, Johnson R, Newstead CG. Indo-asian experience of renal transplantation in Yorkshire: results of a 10 year survey. Transplantation 2002;73(10):1652-7.

27. Udayaraj U, Ben-Shlomo Y, Roderick P, et al. Social deprivation, ethnicity, and uptake of living kidney donor transplantation in the United Kingdom. Transplantation. 2012 Mar 27;93(6):610-6.

28. Norris KC, Agodoa LY. Unraveling the racial disparities associated with kidney disease. Kidney Int. 2005 Sep;68(3):914-24.

29. Boulware LE, Cooper LA, Ratner LE, LaVeist TA, Powe NR. Race and trust in the health care system. Public Health Rep 2003;118(4):358-65.

30. Bratton C, Chavin K, Baliga P. Racial disparities in organ donation and why. Current opinion in organ transplantation 2011;16(2):243-9.

31. Doshi M, Garg AX, Gibney E, Parikh C. Race and renal function early after live kidney donation: an analysis of the United States Organ Procurement and Transplantation Network Database. Clin Transplant 2010;24(5):E153-7.

Table 1: Baseline characteristics of participants in the Access to Transplantation and Transplant Outcome Measures study, United Kingdom, analysed for access to pre-emptive kidney transplant listing and kidney transplant listing within two years of starting dialysis

Variable	Access to Pre-emptive Listing		Access to Listing within 2 years of Starting Dialysis	
	Total N (%)	Number Pre-emptively listed N (%)	Total N (%)	Number Listed within 2 years of starting Dialysis N, (%)
Age (Mean, (SD))	55 (13.6)	49 (12.9)	57 (13)	49 (14)
Gender				
Male	1706 (64)	421 (60)	1285 (65)	406 (69)
Female	970 (36)	285 (40)	685 (35)	179 (31)
Ethnic Group				
White	2177 (81)	611 (87)	1566 (80)	416 (71)
Asian	293 (11)	60 (8)	233 (12)	103 (18)
Black	177 (7)	31 (4)	146 (7)	54 (9)
Other	29 (1)	4 (1)	25 (1)	12 (2)
Primary Renal Disease				
Diabetes	711 (28)	112 (16)	599 (30)	119 (20)
Glomerulonephritis	428 (16)	148 (21)	280 (14)	142 (24)
Hypertension	171 (6)	40 (6)	131 (7)	50 (9)
Missing	30 (1)	10 (1)	20 (1)	14 (2)
Other	388 (15)	88 (13)	300 (15)	75 (13)
Polycystic	249 (9)	135 (19)	114 (6)	56 (10)
Pyelonephritis	221 (8)	91 (13)	130 (7)	31 (5)
Renal vascular disease	95 (4)	12 (2)	83 (4)	9 (2)
Uncertain	383 (14)	70 (10)	313 (16)	89 (15)
BMI				
Less than 20	165 (6)	40 (6)	125 (6)	41 (7)
20 - <25	729 (27)	232 (33)	497 (25)	195 (33)
25 - <30	771 (29)	274 (39)	497 (25)	186 (32)
30 - <35	435 (16)	107 (15)	328 (17)	91 (16)
35 - <40	202 (8)	24 (3)	178 (9)	34 (6)
≥ 40	131 (5)	6 (1)	125 (6)	8 (1)
Missing	243 (9)	23 (3)	220 (11)	30 (5)
Diabetes				

No	1614 (60)	552 (78)	1065 (54)	398 (68)
Type 1	256 (10)	80 (11)	176 (9)	60 (10)
Type 2	776 (29)	67 (10)	709 (36)	115 (20)
Missing	27 (1.0)	7 (1)	20 (1)	12 (2)
Heart Disease				
No	2159 (81)	650 (92)	1509 (77)	508 (87)
Yes	488 (18)	48 (7)	440 (22)	63 (11)
Missing	29 (1)	8 (1)	21 (1)	14 (2)
Heart Failure				
No	2467 (92)	691 (98)	1776 (90)	551 (94)
Yes	178 (7)	7 (1)	171 (9)	18 (3)
Missing	31 (1)	8 (1)	23 (1)	16 (3)
Atrial Fibrillation				
No	2547 (95)	687 (97)	1860 (94)	559 (96)
Yes	97 (4)	11 (2)	86 (4)	10 (2)
Missing	32 (1)	8 (1)	24 (1)	16 (3)
Cardiac Valve Replacement				
No	2612 (98)	689 (98)	1923 (98)	568 (97)
Yes	31 (1)	7 (1)	24 (1)	1 (0.2)
Missing	33 (1)	10 (1)	23 (1)	17 (3)
Pacemaker				
No	2604 (97)	694 (98)	1910 (97)	567 (97)
Yes	41 (2)	4 (0.6)	37 (2)	2 (0.3)
Missing	31 (1)	8 (1)	23 (1)	16 (3)
Cerebrovascular Disease				
No	2422 (91)	674 (96)	1748 (89)	541 (93)
Yes	222 (8)	23 (3)	199 (10)	28 (5)
Missing	32 (1)	9 (1)	23 (1)	16 (3)
Vascular Disease				
No	2432 (91)	686 (97)	1746 (89)	545 (93)
Yes	212 (8)	12 (2)	200 (10)	24 (4)
Missing	32 (1)	8 (1)	24 (1)	16 (4)
Abdominal Aortic Aneurysm				
No	2597 (97)	693 (98)	1904 (97)	569 (97)
Yes	46 (2)	4 (0.6)	42 (2)	1 (0.2)
Missing	33 (1)	9 (1)	24 (1)	15 (3)
Respiratory Disease				
No	2335 (87)	643 (91)	1692 (86)	523 (89)
Yes	310 (12)	55 (8)	255 (13)	47 (8)
Missing	31 (1)	8 (1)	23 (1)	15 (3)
Liver Disease				

No	2582 (97)	691 (98)	1891 (96)	563 (96)
Yes	64 (2)	7 (1)	57 (3)	7 (1)
Missing	30 (1)	8 (1)	22 (1)	15 (3)
Blood Borne Viruses				
No	2576 (96)	688 (98)	1888 (96)	562 (96)
Yes	70 (3)	10 (1)	60 (3)	9 (2)
Missing	30 (1)	8 (1)	22 (1)	14 (2)
Malignancy				
No	2328 (87)	659 93)	1669 (85)	545 (93)
Yes	321 (12)	39 (6)	282 (14)	25 (4)
Missing	27 (1)	8 (1)	19 (1)	14 (2)
Mental Illness				
No	2422 (91)	657 (93)	1765 (90)	532 (91)
Yes	225 (8)	41 (6)	184 (9)	39 (7)
Missing	29 (1)	8 (1)	21 (1)	14 (2)
Dementia				
No	2637 (99)	697 (99)	1940 (99)	568 (97)
Yes	8 (0.3)	1 (0.1)	7 (0.4)	1 (0.2)
Missing	31 (1)	8 (1)	23 (1)	16 (3)
Smoking				
No	1145 (43)	364 (52)	781 (40)	253 (43)
Current	381 (14)	66 (9)	315 (16)	73 (13)
Ex-smoker	763 (29)	185 (26)	578 (29)	158 (27)
Don't Know	370 (14)	85 (12)	285 (15)	93 (16)
Missing	17 (0.6)	6 (1)	11 (0.6)	8 (1)
Born in UK				
No	485 (18)	86 (12)	399 (20)	149 (26)
Yes	2032 (76)	578 (82)	1454 (74)	404 (69)
Missing	159 (6)	42 (6)	117 (6)	32 (6)
English First Language				
No	325 (12)	58 (8)	267 (14)	110 (19)
Yes	2192 (82)	606 (86)	1586 (81)	443 (76)
Missing	159 (6)	42 (6)	117 (6)	32 (6)
Read Help				
No	2058 (77)	597 (85)	1461 (74)	459 (78)
Yes	457 (17)	66 (9)	391 (20)	94 (16)
Missing	161 (6)	43 (6)	118 (6)	32 (6)
Accommodation				
Owned by you (outright or with a mortgage)	1436 (54)	468 (66)	968 (49)	281 (48)
Part rent, part owned (shared ownership)	55 (2)	11 (2)	44 (2)	17 (3)

Rented privately from Council/ Housing Association	861 (32)	145 (21)	716 (36)	203 (35)
Other	154 (6)	37 (5)	117 (6)	49 (8)
Missing	170 (6)	45 (6)	125 (6)	35 (6)
Employment				
Working PT/FT	627 (23)	316 (45)	311 (16)	185 (32)
Long term sick/disabled	700 (26)	132 (19)	568 (29)	156 (27)
Retired from paid work	889 (33)	124 (18)	765 (39)	114 (20)
Unemployed	173 (7)	37 (5)	136 (7)	65 (11)
Other	122 (5)	52 (7)	70 (4)	33 (6)
Missing	165 (6)	45 (6)	120 (6)	32 (6)
Education				
Degree, Higher or NVQ 4-5	446 (17)	160 (23)	286 (15)	137 (23)
GCSE, A-level or NVQ 1-3	1051 (39)	346 (49)	705 (36)	241 (41)
No Qualifications	1023 (38)	160 (23)	863 (44)	175 (30)
Missing	156 (6)	40 (6)	116 (6)	32 (6)
Car Ownership				
No	658 (25)	76 (11)	582 (30)	153 (26)
Yes	1852 (69)	586 (83)	1266 (64)	399 (68)
Missing	166 (6)	44 (6)	122 (6)	33 (6)
Civil Status				
Single (never married)	480 (18)	136 (19)	344 (17)	136 (23)
Married	1386 (52)	388 (55)	998 (50)	286 (49)
Living with partner	173 (7)	64 (9)	109 (6)	43 (8)
Divorced	238 (9)	49 (7)	189 (10)	49 (8)
Separated (but still legally married)	81 (3)	12 (2)	69 (4)	19 (3)
Widowed	148 (6)	14 (2)	134 (7)	17 (3)
Missing	170 (6)	43 (6)	127 (6)	35 (6)
Children in Household				
None	1978 (74)	472 (67)	1506 (76)	387 (66)
1	264 (10)	97 (14)	167 (9)	76 (13)
2 or more	265 (10)	92 (13)	173 (9)	88 (15)
Missing	169 (6)	45 (6)	124 (6)	34 (6)
Adults in Household				
0-1	699 (26)	127 (18)	572 (29)	154 (26)
2	1261 (47)	378 (54)	883 (45)	263 (45)
3 or more	545 (20)	156 (22)	389 (20)	134 (23)
Missing	171 (6)	45 (6)	126 (6)	34 (6)

Table 2 – Associations of patient-level and centre-level characteristics with listing for pre-emptive kidney transplantation*.

Variable	N	Adjusted Odds Ratio (95% Confidence Interval)	p-value
Patient Variables[±]			
Age			<0.0001
18-29	149	1	
30-39	235	0.9 (0.51-1.57)	
40-49	455	0.79 (0.47-1.32)	
50-59	657	0.57 (0.34-0.97)	
60-64	372	0.47 (0.26-0.87)	
65-75	808	0.19 (0.1-0.37)	
Ethnic Group			<0.0001
White	2177	1	
Asian	293	0.49 (0.33-0.72)	
Black	177	0.43 (0.26-0.71)	
Other	29	0.23 (0.07-0.8)	
BMI			<0.0001
Less than 20	184	0.66 (0.4-1.09)	
20 - <25	798	1	
25 - <30	845	1.31 (0.99-1.73)	
30 - <35	482	0.97 (0.69-1.38)	
35 - <40	223	0.31 (0.18-0.54)	
≥ 40	144	0.12 (0.05-0.28)	
Time Since First Seen by Nephrologist			<0.0001
<1 Year	701	1	
1-3 Years	619	8.12 (5.44-12.1)	
>3 Years	1355	11.55 (8.05-16.55)	
Diabetes			<0.0001
No	1626	1	
Type 1	266	1.12 (0.76-1.64)	

Type 2	784	0.37 (0.26-0.52)	
Peripheral Vascular Disease			
No	2456	1	
Yes	220	0.29 (0.13-0.61)	0.0013
Heart Disease			
No	2170	1	
Yes	506	0.55 (0.36-0.82)	0.004
Heart Failure			
No	2490	1	
Yes	186	0.25 (0.08-0.77)	0.016
Cerebrovascular Disease			
No	2448	1	
Yes	228	0.53 (0.3-0.92)	0.025
Malignancy			
No	2340	1	
Yes	336	0.33 (0.2-0.53)	<0.0001
Smoking			0.0005
No	1148	1	
Current	383	0.53 (0.36-0.78)	
Ex-smoker	769	0.95 (0.72-1.25)	
Don't know	377	0.75 (0.52-1.07)	
Socioeconomic Variables			
Employment			<0.0001
Working full time/ part time	667	1	
Long term sick/disabled	746	0.42 (0.3-0.58)	
Retired from paid work	948	0.55 (0.37-0.82)	
Unemployed	185	0.51 (0.31-0.85)	
Other	130	0.93 (0.54-1.6)	
Accommodation			<0.0001
Owned by you (Outright or with a Mortgage)	1533	1	
Other	166	0.58 (0.34-1.0)	
Part rent, Part owned (shared ownership)	59	0.32 (0.13-0.74)	
Rented Privately from Council / Housing Association	918	0.55 (0.41-0.75)	
Car ownership			
No	701	1	
Yes	1975	1.98 (1.41-2.76)	<0.0001
Education			0.08

GCSE, A-level or NVQ 1-3	1115	1.26 (0.96-1.67)	
Degree, Higher or NVQ 4-5	477	1.06 (0.74-1.51)	
No Qualifications	1084	1	
Centre Level Variables			
Transplanting Centre			
No	48	1	
Yes	23	3.1 (2.36-4.07)	<0.0001
No. of Consultant Nephrologists			
≤6	30	1	
>6	41	2.16 (1.5-3.1)	<0.0001
Transplantation Discussed with All Patients			
No	20	1	
Yes	51	1.39 (1.08-1.78)	0.0094

***** Derived using multivariable logistic regression and multiple imputation. 20 imputed data sets were modelled separately then combined to produce final parameter estimates.
± Missing data was imputed for BMI (n=243), comorbidity (n= 30), time since first seen by a nephrologist (n=24) and socioeconomic variables (n=146).

Table 3 – Associations of patient-level and centre-level characteristics with listing for kidney transplantation within 2 years of starting dialysis*

Variable	N	Adjusted Hazard Ratio (95% Confidence Interval)	p-value
Patient Variables			
Age			<0.0001
18-29	86	1	
30-39	137	0.8 (0.56-1.12)	
40-49	280	0.64 (0.46-0.89)	
50-59	462	0.35 (0.25-0.49)	
60-64	290	0.27 (0.18-0.41)	
65-75	715	0.15 (0.1-0.23)	
Gender			
Male	1285	1	
Female	685	0.82 (0.68-0.99)	0.035
Ethnic Group			0.002
White	1566	1	
Asian	233	1.42 (1.12-1.79)	
Black	146	1.04 (0.76-1.43)	
Other	25	1.56 (0.85-2.87)	
BMI			<0.0001
Less than 20	143	0.85 (0.6-1.21)	
20 - <25	561	1	
25 - <30	558	1.15 (0.93-1.42)	
30 - <35	369	0.88 (0.67-1.14)	
35 - <40	200	0.48 (0.33-0.7)	
≥ 40	141	0.15 (0.08-0.3)	
Dialysis Modality			
Haemodialysis	1603	1	
Peritoneal dialysis	367	1.34 (1.1-1.64)	0.004
Diabetes			<0.0001

No	1085	1	
Type 1	176	0.76 (0.57-1.02)	
Type 2	709	0.62 (0.49-0.79)	
Peripheral Vascular Disease			
No	1764	1	
Yes	206	0.6 (0.37-0.96)	0.035
Heart Disease			
No	1520	1	
Yes	451	0.8 (0.59-1.09)	0.16
Heart Failure			
No	1797	1	
Yes	173	0.58 (0.36-0.93)	0.025
Blood Borne Viruses			
No	1906	1	
Yes	64	0.36 (0.18-0.71)	0.0035
Malignancy			
No	1677	1	
Yes	293	0.33 (0.2-0.53)	<0.0001
Smoking			0.05
No	784	1	
Current	316	0.76 (0.58-1.0)	
Ex-smoker	582	1.17 (0.95-1.45)	
Don't know	289	1.06 (0.82-1.36)	
Socioeconomic Variables			
Employment			<0.0001
Working full time/ part time	331	1	
Long term sick/disabled	606	0.54 (0.43-0.68)	
Retired from paid work	814	0.58 (0.42-0.8)	
Unemployed	144	0.77 (0.56-1.06)	
Other	75	0.74 (0.5-1.1)	
Accommodation			0.009
Owned by you (Outright or with a Mortgage)	1035	1	
Other	126	0.81 (0.58-1.13)	
Part rent, Part owned (shared ownership)	47	1.07 (0.64-1.8)	
Rented Privately from Council / Housing Association	762	0.76 (0.61-0.94)	
Car ownership			
No	619	0.73 (0.6-0.9)	0.0026
Yes	1351	1	
Education			0.01

GCSE, A-level or NVQ 1-3	749	1.05 (0.85-1.3)	
Degree, Higher or NVQ 4-5	305	1.38 (1.07-1.79)	
No Qualifications	916	1	
Centre Level Variables			
Consultant Nephrologists			
≤6	30	1	
>6	41	1.26 (1.0-1.59)	0.054
MDT			
No	17	1	
Yes	54	1.23 (0.99-1.52)	0.057
Written Protocol for listing			
No	21	1	
Yes	50	0.72 (0.58-0.9)	0.0033

***** Derived using multivariable Cox regression and multiple imputation. 20 imputed data sets were modelled separately then combined to produce final parameter estimates.
± Missing data was imputed for BMI (n=220), comorbidity (n=22) and socioeconomic variables (n=104).

Figure 1: Flow diagram showing the study recruitment of participants (with inclusion and exclusion criteria) for (1) access to pre-emptive listing and (2) listing after starting dialysis

(Option A)

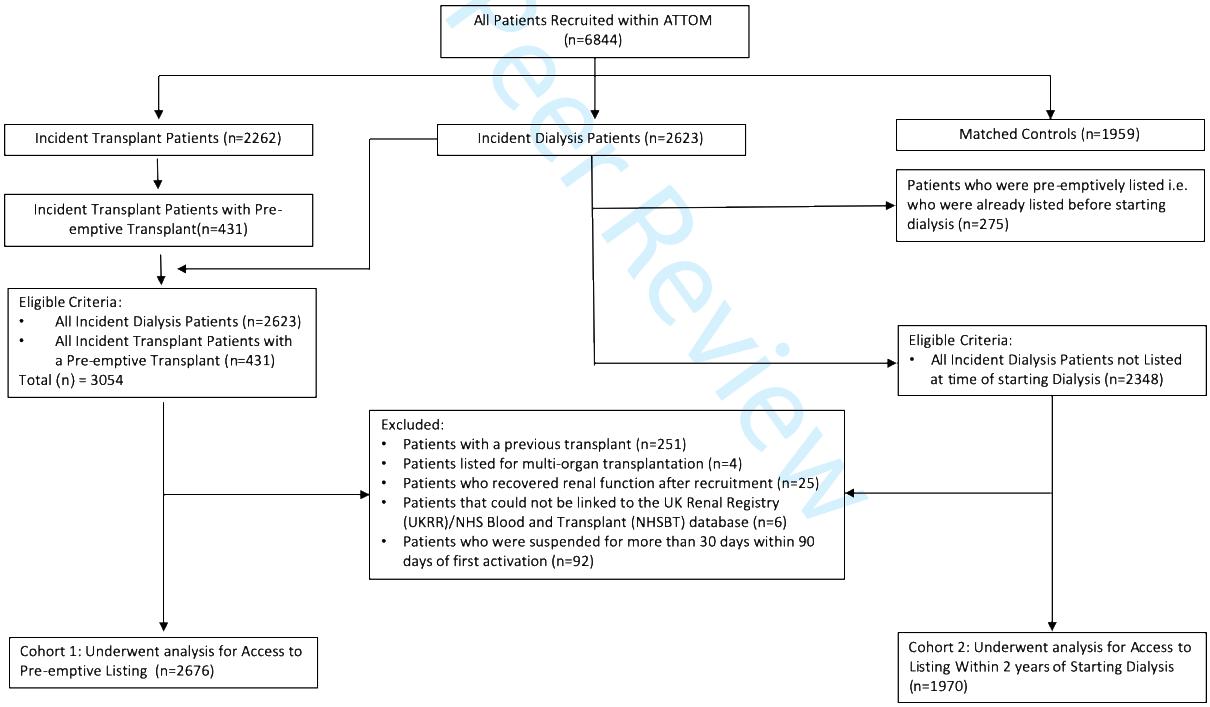
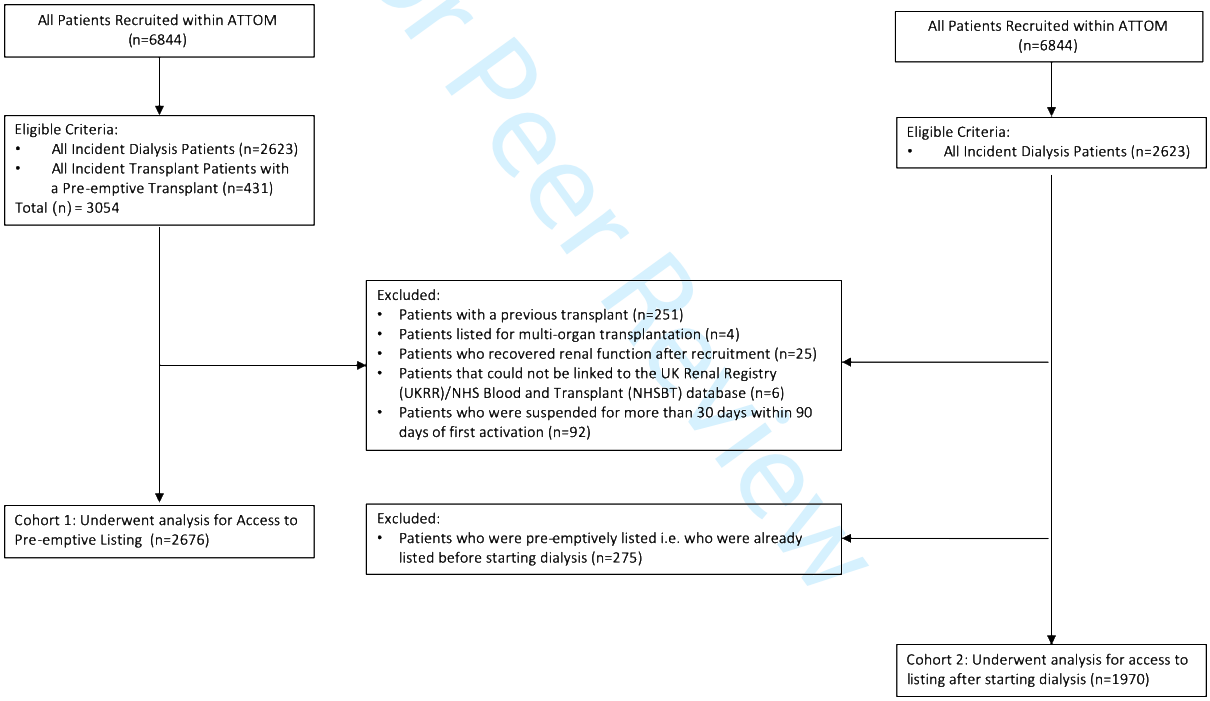


Figure 1: Flow diagram showing the study recruitment of participants (with inclusion and exclusion criteria) for (1) access to pre-emptive listing and (2) listing after starting dialysis (Option B)



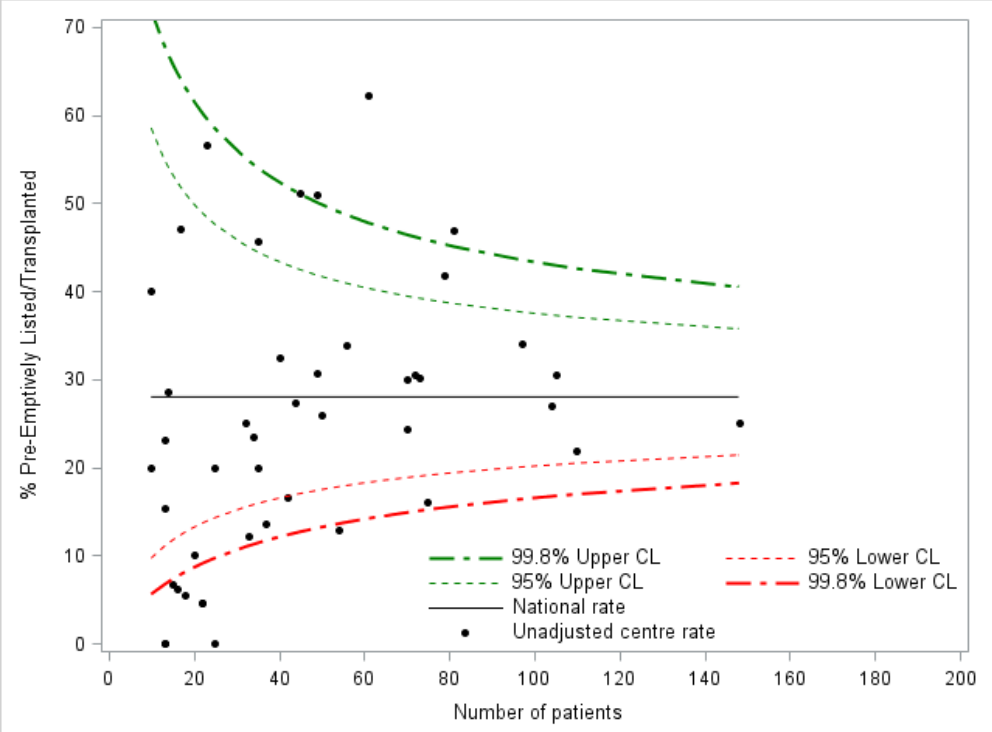


Figure 2 (a) – Unadjusted funnel plot showing variation in proportion listed for pre-emptive kidney transplant by centre according to number of participants evaluated.

*Centres with less than 10 observations are not shown

** Number of Patients, denotes the number of participants from a given centre that were analysed (from cohort of patients recruited at each centre for the ATTOM study)

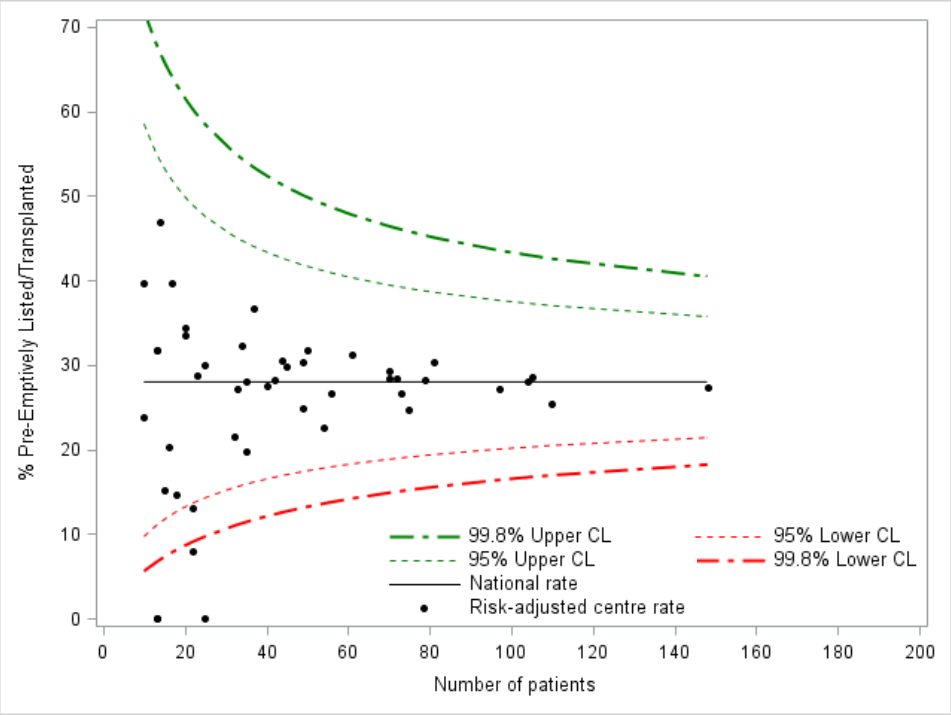


Figure 2(b)* – emptive kidney transplant by centre according to number of participants evaluated

*Risk adjusted for all patient and centre factors, using the mean of each adjustment variable across the cohort, associated with pre-emptive listing as highlighted in table 2. Centres with less than 10 observations are not shown.

** Number of Patients, denotes the number of participants from a given centre that were analysed (from cohort of patients recruited at each centre for the ATTOM study)