UNIVERSITY OF SOUTHAMPTON

FACULTY OF MEDICINE

Primary Care and Population Sciences

Exploring Inequity in Access to Renal Transplantation

by

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Thesis for the degree of Doctor of Philosophy

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ABSTRACT

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EXPLORING INEQUITY IN ACCESS TO RENAL TRANSPLANTATION

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Transplantation is the most cost effective treatment for end stage renal disease (ESRD), but demand outstrips supply. In the UK, retrospective analyses of Registry data show there is variation in access to transplantation between renal centres, and that despite ethnic minority populations and those from lower socioeconomic groups having a higher incidence of ESRD, they have reduced access to transplantation. As part of the NIHR funded ATTOM (Access to Transplantation and Transplant Outcome Measures) study, a mixed methods approach explored the impact of both the compositional properties of a centre and modifiable centre factors relating to organisation and processes of care, on access to transplant listing. The inter-personal relationships between living kidney donors and their recipients were also examined.

Thematic analysis of 45 semi-structured qualitative interviews with key stakeholders conducted across 9 renal centres in the UK informed the development of an online survey, which was, distributed to the Clinical Directors of all 71 UK renal centres. Major themes identified were pathways of care relating to transplant recipient assessment and chronic kidney disease management as well as cardiac assessment and decision-making. The subsequent national survey achieved a 100% response rate and demonstrated significant variation in the assessment criteria of patients, delivery of care, role of multi-disciplinary teams and level of transplant surgical involvement prior to listing. A prospective cohort of incident renal replacement therapy (RRT) patients in ATTOM with 18 month follow up were subsequently analysed to assess listing for transplantation. A multi-level hierarchical logistic regression model was used to assess factors associated with listing. The majority of observed inter-centre variation was accounted for by patient factors including independently age, ethnicity, socioeconomic status and several co-morbidities. Centre factors included the use of a written protocol to wait-list, whether the centre was a transplanting centre, and the universal discussion of transplantation with all patients. The study on living donor-recipient relationships demonstrated that living-kidney donation is subject to significant unexplained relationship differences amongst ethnic-minorities. Spousal donation is significantly lower in the Black population and gender disparity greatest in the Asian spousal population.

Further research is need to understand these observed differences to tackle inequity in access to transplantation for socially deprived patients and ethnic minorities as well as to to increase donation rates in ethnic minorities. There is also need for consensus on recipient work up and between centre harmonisation, as well as research to examine cardiovascular screening utility in potential transplant recipients.

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Declaration of Authorship

I, Rishi Pruthi, declare that the thesis entitled "Exploring inequity in access to renal transplantation" and the work presented in the thesis are both my own, and have been generated by me as the result of my own original research. I confirm that:

- this work was done wholly or mainly while in candidature for a research degree at this University;
- where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;
- where I have consulted the published work of others, this is always clearly attributed;
- where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
- I have acknowledged all main sources of help;
- where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;

Parts of this work have been published as:

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Detailed Account of Contribution to Presented work

This thesis was part of a larger study exploring Access to Transplant and Transplant Outcome Measures (ATTOM), which was funded by the NIHR. For the purpose of clarity, a detailed account of my contribution to the presented work is given below:

- The detailed review of existing literature presented in Chapter 1 was all my own work
- The original study design of ATTOM and its recruitment (described in Chapter 2) was developed by the ATTOM group of investigators. I took the lead role in examining work-stream 1 of the ATTOM study, looking at access to transplantation for which I planned the detailed analyses which have been reported in this thesis.
- The idea of exploring living-donor relationships, described in chapter 3 was my own. The study design described and statistical analyses were all planned and conducted by myself.
- The early methodology for the qualitative study exploring healthcare professionals' perspectives on listing patients for transplantation (described in chapter 4) was originally described in the ATTOM Study proposal by the ATTOM investigators. This methodology was developed further by myself for this thesis. The subsequent data collection/qualitative interviews were all conducted by myself, as was the subsequent coding and analysis.
- The national survey (reported in chapter 5) was designed, administered and analysed by myself. All statistical analyses were also conducted by myself.
- The final analysis of access to transplantation using data from patients recruited in the ATTOM study was my own work. The study design, inclusion and exclusion criteria, and the statistical analyses conducted were all my own work. Assistance with conducting the multi-level modeling using SAS version 9.3. was provided by Dr. Matthew Robb, Statistician at NHSBT.

Dedication

To my wife Vinit, my son Puneet, my brothers Ashutosh, Naveen and Neeraj and my parents for all their love, support and encouragement.

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Lastly, I would like to thank my fellow research registrars at the UKRR, Anirudh Rao, Catriona Shaw, Lynsey Webb and Clare Castledine who made the whole journey a lot more enjoyable.

Abbreviations

APD	Automated peritoneal dialysis
APOL1	Apolipoprotein L1
ATTOM	Access to Transplantation and Transplant Outcome Measures
BME	Black and Minority Ethnic
BMI	Body Mass Index
BTS	British Transplant Society
CAD	Coronary artery disease
CAPD	Continuous ambulatory peritoneal dialysis
CARI	Caring for Australians with Renal Impairment
CKD	Chronic kidney disease
CTS	Collaborative Transplant Study
CVD	Cardiovascular disease
DBD	Donation after brainstem death
DCD	Donation after circulatory death
ECG	Electrocardiogram
EPR	Electronic patient record
ESRD	End stage renal disease
GFR	Glomerular filtration rate
GN	Glomerulonephritis
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HD	Haemodialysis
HDF	Hemodiafiltration
HES	Hospital Episode Statistics
HIV	Human immunodeficiency virus
HLA	Human Leucocyte Antigen
IMD	Index of Multiple Deprivation
IT	Information technology
LCC	Low clearance clinic
Mbp	Mega base pair
MCM	Maximum conservative management

MDT	Multidisciplinary team
NHS	National Health Service
NHSBT	NHS Blood and Transplant
NICE	National Institute of Health and Clinical Excellence
NIHR	National Institute for Health Research
ODT	Organ Donation and Transplantation
ONS	Office for National Statistics
OPTN	Organ Procurement and Transplantation Network
OR	Odds Ratio
PD	Peritoneal dialysis
PKD	Polycystic kidney disease
PMP	Per million population
PRD	Primary renal diagnosis
QoL	Quality of life
RRDSS	Renal Registry Data Set Specification
RRT	Renal replacement therapy
SES	Socioeconomic status
SD	Standard deviation
UKRR	United Kingdom Renal Registry
USRDS	United States Renal Data System
WTE	Whole-time equivalent

Chapter 1: Background

1.1 Introduction

Since its inception in 1948, the aim of the National Health Service has been "to provide care that is universal, comprehensive and based on need and not ability to pay". These principles have guided the development of the NHS for over 60 years and are also enshrined in the NHS constitution. The NHS also has a wider social duty to promote equality through the services it provides and to pay particular attention to groups or sections of society where improvements in health and life expectancy are not keeping pace with the rest of the population[1].

Health inequalities can be defined as differences in the health status or distribution of health determinants between population groups[2-3]. Health inequity refers to those inequalities that are avoidable, unnecessary and deemed to be unfair or stemming from some form of injustice [2-3]. Commissioners of health care are responsible for assessing health needs, commissioning services to meet those needs, evaluating services and ensuring that there is equity.

For suitable patients with end stage renal disease (ESRD), renal transplantation is widely accepted as conferring both better quality of life and life expectancy than dialysis[4-7]; with live kidney transplantation offering the best clinical outcomes[8-10]. In the UK, retrospective analyses of registry data suggest there is variation in access to transplantation between renal centres[11-12], and that despite ethnic minorities and individuals from lower socioeconomic groups having a higher incidence of ESRD[13-23], they are associated with reduced access to transplantation[11-12, 24-36]. It is unclear which patient-specific or centre-specific factors are responsible for such variations.

In this study, a mixed-methods approach is adopted to explore if access to kidney transplantation is equitable for socially deprived and ethnic minority populations in the UK and explores the impact of patient variables and centre-specific factors on access to transplantation.

This introductory Chapter describes the functions of the human kidney, chronic kidney disease and the available treatment options for ESRD, assesses suitability criteria for kidney transplantation, reviews the organ allocation scheme and reviews the existing literature on the impact of ethnicity, socioeconomic status and practice patterns on access to transplantation.

1.2 Functions of the Kidney

The kidneys play an integral role in maintaining human existence by virtue of performing a range of important excretory and metabolic functions. The primary excretory function involves the selective elimination of the waste products of cellular metabolism and the maintenance of fluid homeostasis. The metabolic functions of the kidney include the regulation of concentrations of electrolytes such as sodium, potassium, chloride, calcium and phosphate and the maintenance of acid base homeostasis. The kidneys also help convert inactive vitamin D3 to an activated form (1-25 hydroxy vitamin D3 which is essential for maintaining calcium-phosphate homeostasis in the body and are also involved in the synthesis of a hormone called erythropoietin which stimulates the bone marrow to produce red blood cells.

Failure of these processes can be caused by a wide range of conditions affecting the kidney. These can occur acutely with dramatic onset leading to acute kidney injury, but more commonly follow a slower more insidious course leading to chronic kidney disease.

1.3 Chronic Kidney Disease

Chronic kidney Disease (CKD) refers to a state of irreversible kidney damage and/or reduction of kidney function. The National Institute of Health and Clinical Excellence (NICE) has classified CKD into 5 stages (Figure 1.1) based on the level of kidney function and degree of proteinuria[37]. The level of kidney function is reported as glomerular filtration rate (GFR) which can be either directly measured by injecting radio isotope drugs into the body or more commonly estimated from a variety of mathematical equations. NICE recommends using use the Chronic Kidney Disease Epidemiology Collaboration (CKD‑EPI) creatinine equation to estimate GFR, using creatinine assays with calibration traceable to standardised reference material. An

eGFR of less than 15 ml/min/1.73 m2 (GFR category G5) is referred to as kidney failure (or commonly described as end stage renal disease, ESRD), the point at which renal replacement therapy (RRT) is necessary to prolong life.

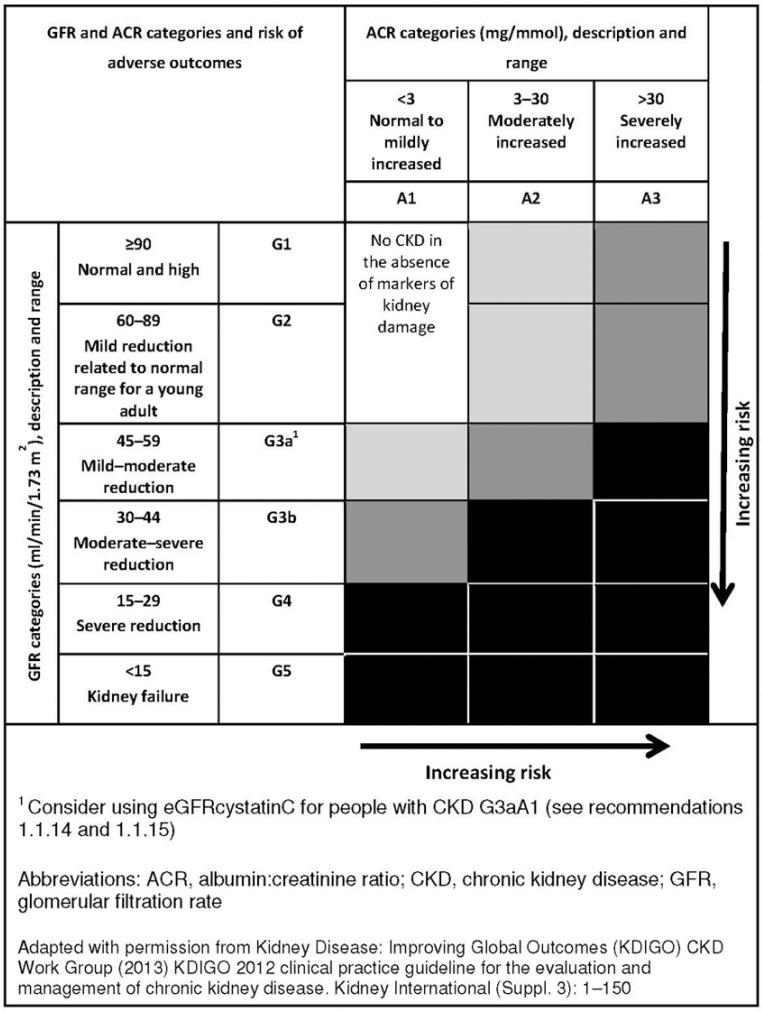

Figure 1.1: NICE classification of chronic kidney disease

CKD is increasingly recognised as being a major public health problem[38-39] imposing a substantial burden on the patients affected and on the health-care systems caring for them. Studies from around the world have reported varying prevalence rates of CKD stages 3-5 (eGFR<60) , from 4.7% to 11.2%[40-43], with both socioeconomic deprivation [14, 43-45] and non-white ethnicity[20, 44, 46-49] being associated with higher prevalence rates of CKD. In the UK, a large population based study, which also included institutionalised people, reported an age-standardised adult prevalence of stage 3–5 CKD of 8.5% (10.6% for females and 5.8% for males)[50]. A number of risk factors have been associated with CKD including increasing age, ethnicity

socioeconomic deprivation, structural abnormalities of the urinary tract and several comorbidities including diabetes, hypertension, heart failure and atherosclerotic vascular disease.

Amongst patients with CKD, cohort studies indicate that the risk of mortality in CKD far outweighs the risk of progression to end-stage renal disease[15, 51-54]. Cardiovascular causes account for nearly 50% of the mortality and CKD is an independent predictor of cardiovascular comorbidity [40-41, 51, 55-57]. Indeed, only a small proportion of patients with early stages of CKD progress to reach ESRD[51] necessitating the need to consider either conservative care or renal replacement therapy (RRT).

1.4 Conservative Care

There is increasing evidence that for some elderly patients with other chronic illnesses initiating RRT may offer only minimal survival advantage and come at a cost in terms of reducing their quality of life[58]. As a consequence, patients with ESRD may make an informed decision not to have RRT and instead opt for conservative care management focusing primarily on symptom control. Assigning patients to this care pathway is gaining in recognition, with the U.S. Renal Physicians Association current guidelines also now suggesting that MCM (maximum conservative management) should be considered for individuals aged 75 and older with a Charlson Comorbidity Index of 8 or greater, because these individuals are predicted to have poor outcomes and are unlikely to have their lives extended by initiation of dialysis[59].

The Charlson comorbidity index[60], is a method of predicting mortality by classifying or weighting comorbid conditions (comorbidities) and has been widely utilized by health researchers to measure burden of disease and case mix[61]. Each comorbidity category has an associated weight (from 1 to 6), based on the adjusted risk of mortality or resource use, and the sum of all the weights results in a single comorbidity score for a patient. A score of zero indicates that no comorbidities were found. The higher the score, the more likely the predicted outcome will result in mortality or higher resource use[60].

1.4 Renal Replacement Therapy

Renal replacement therapy can take the form of one of three modalities: haemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation. In the UK at the end of 2014, 0.09% (n-58,968) of the population were reported as undergoing RRT[62] accounting for an estimated 1-2% of the total healthcare spending budget[63]. Of these, 24,166 patients were receiving haemodialysis, 3,638 patients were receiving peritoneal dialysis and 27,804 patients had a functioning transplant. The incident number of dialysis patients for 2014 was 6796, of which 5319 patients started on haemodialysis. As for transplantation, 3,200 kidney or kidney plus other organ transplants were performed in 2014[62].

1.4.1 Haemodialysis

HD is the commonest mode of RRT worldwide[64] and involves pumping a patient's blood through an extracorporeal artificial kidney, consisting of a semi-permeable membrane, through which waste products and excess fluid are removed. To undertake haemodialysis, it is necessary to have safe and reliable access to a patients' circulating blood volume which can be achieved via creating an arteriovenous fistula, arteriovenous graft or by inserting a dialysis catheter into a central vein. Traditionally HD occurs three times a week with each session lasting 4 hours (though variations exist as per different patients' circumstances). The setting for HD can also vary with the majority of patients (95.1%) receiving HD in a unit within the confines of a hospital or within a satellite unit located offsite, while a small proportion opt to have HD at home (4.9% of prevalent RRT patients in 2014)[62].

1.4.2 Peritoneal Dialysis

In PD, the patient's peritoneal membrane which has a rich supply of tiny blood vessels (capillaries) serves as the filter across which waste products and excess fluid are removed. Dialysate fluid (consisting of glucose or other osmotically active solutes) is instilled into the patient's peritoneal cavity through a semi-permanent soft silastic tube in the abdominal wall. The fluid is allowed to equilibrate for a variable length of time, and then removed and replaced (or 'exchanged' for) fresh fluid. This process is repeated manually by the patient up to five times a day in continuous ambulatory

peritoneal dialysis (CAPD) during the daytime or automatically up to 10 times overnight via a machine in automated peritoneal dialysis (APD). In contrast to HD, PD is usually performed at home

1.4.3 Kidney Transplantation

Kidney transplantation involves surgically placing a functioning donated kidney, into the abdomen of a patient with ESRD and connecting it to the patient's arterial and venous systems, as well as to their bladder. Thereafter, long term immunosuppressant medications need to be taken by the patient for the life of the transplanted kidney to prevent the body's immune system from rejecting the foreign tissue. Kidney donations may come from either deceased donors or living donors.

In 2014 living donor kidney transplants represented 34% of the total kidney transplant programme in the UK[65], with most living donor transplants being 'directed'. This means that a kidney is donated to a specific recipient known to the donor - a close family member or friend. In addition, there are now a number of 'non-directed' living donor transplants (also known as altruistic donor transplants) which represent less than 10% of all live kidney donations[66].

As for deceased donors, these can be either from donation after brainstem death (DBD) or donation after circulatory death (DCD). In the case of DBD, kidneys are retrieved from patients who have suffered permanent and irreversible brain injury though whose circulation is intact, whilst in DCD, kidneys are retrieved after the heart has stopped beating. Due to the DCD kidneys being retrieved after cessation of blood flow in the donor, these organs are more susceptible to ischaemic injury and are associated with poor early graft function, although long term graft survival has been reported to be compatible to that of DBD transplants[67-69].

Amongst the three RRT options available to patients with ESRD, kidney transplantation is widely regarded as the optimal modality of RRT, conferring better survival[4-5] and quality of life[6, 70-73], than dialysis. This, coupled with progressively improving transplant (kidney) survival rates which are now are now >90%, >70% and >60%, at 1-year, 5-year and 10-year respectively, has driven demand for renal

transplantation in the UK and across the world over the last decade. Whilst the number of deceased organ donors available has also risen during this time in the UK, the rise has been relatively modest in comparison to the number of patients wait-listed, resulting in an increasing gap between supply and demand (see Figure 1.2)[74].

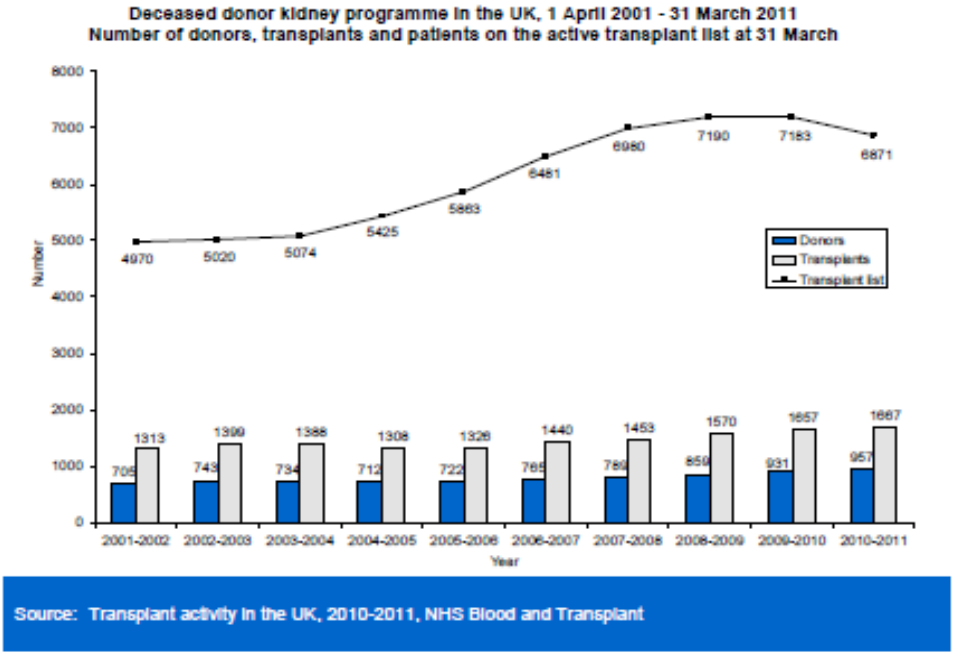

Figure 1.2: Showing the Number of patients listed for deceased donor kidney transplantation, the number transplants performed and the number of contributing donors between 1st April 2001-31st March 2011.

To address this shortfall, more emphasis has been placed on improving living donor kidney transplantation rates in the UK. Indeed, living kidney donor transplantation rates have increased progressively over recent years and (as mentioned earlier) now account for 34% of all kidney transplants performed in the UK[65]. Living donor kidney transplantation has significant benefits over deceased donor kidney transplantation, including offering better patient and graft outcomes compared to deceased donor transplantation[8-10, 75-76]. It also allows the procedure to be scheduled at a time convenient to both the donor and the recipient and can help facilitate pre-emptive transplantation (that is performing the transplant prior to the patient starting dialysis).

Pre-emptive transplantation is recommended as the gold standard by the UK Renal Association in suitable patients and has been reported to be associated with better survival compared to transplantation after a period of dialysis[77-78]. Although it should

be acknowledged that these analyses are also fraught with confounding and bias with no data from randomised controlled trials available.

1.5 UK Kidney Transplant Allocation Scheme

As the number of patients needing a kidney transplant in the United Kingdom is greater than the number of deceased donors available, to ensure equitable distribution of donated organs, all kidneys from deceased donors whose death has been defined by brain-stem death (DBD) criteria are allocated through the National Allocation Scheme managed by NHSBT. The current scheme was implemented in 2006 to meet agreed objectives and address issues of inequity of access to transplantation and utilises an evidence-based computer algorithm[79]. The decision to allocate a kidney to a particular patient depends on several factors including Human Leucocyte Antigen (HLA) type.

HLA proteins are coded by the major histocompatibility complex genes on a 3 Mbp (mega base pair) stretch within chromosome 6p21. These cell-surface proteins are responsible for the regulation of the immune system in humans and assisting in the identification of 'foreign' cells. When two people share the same Human Leukocyte Antigens, they are said to be a "match", that is, their tissues are immunologically compatible with each other. The closer the match between the recipient and donor HLA, the lower risk of rejection of the donor organ by the recipient.

There are 2 classes of HLA: Class 1 antigens (A, B and C) and Class 2 antigens (DP, DQ and DR). Amongst these antigens HLA-DR, HLA-B and HLA-A are the most important for the purposes of transplantation, and are used to match donor and recipients. The impact of mismatches for any of these HLA antigens varies and is recognised in the organ allocation algorithm. The Collaborative Transplant Study (CTS) analysis showed that the major impact comes from the DR and B antigens, with little additional effect from the A antigens[80-81]. The UK Transplant and Eurotransplant data are similar, with DR matching having a much greater effect than that of B or A[82-83]. Another study found that HLA-DR mismatches correlated with poorer long-term survival[84].

The Renal Organ Allocation scheme has been revised on several occasions since its introduction in the 1970s. The current scheme was implemented in 2006 and is based on a tier system, with all patients listed for kidney transplantation being allocated into one of five tiers (see Fig 1.3).

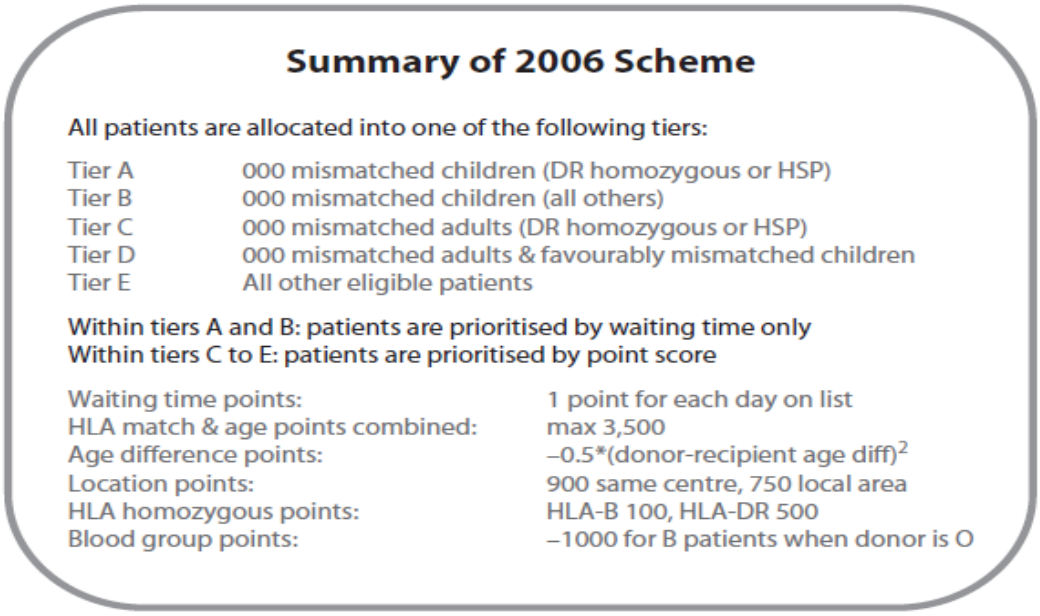

Figure 1.3. Summary of 2006 National Allocation Scheme for DBD Kidneys

Paediatric patients are prioritised within Tiers A and B according to waiting time, whilst within tiers C, D and E patients are prioritised according to a points based system (highest score first), based on seven elements. These are: waiting time, human leucocyte antigen (HLA) match and age combined, donor-recipient age difference, geographical location of patient relative to donor, HLA-DR homozygosity, HLA-B homozygosity and blood group match (figure 1.3).

Whilst these rules apply in the allocation of DBD Kidneys, they do not apply in totality when allocating DCD kidneys. The reason for this is that as mentioned earlier DCD kidneys are more likely to have sustained ischaemic injury before their retrieval due to loss of circulatory support. In light of this DCD kidneys are allocated regionally according to the 2006 allocation scheme principles, although one kidney is always offered preferentially to the local transplant centre.

If the donor HLA-type is known at the time of offering, one of the kidneys from DCD donors is retained locally and if available, the second ‘paired’ kidney is shared

regionally within four defined regions (see table 1.1). Alternatively, if the donor HLA-type is not known at the time of offering one of the kidneys from DCD donors is retained locally and if available, the second 'paired' kidney will be offered for simultaneous kidney and pancreas transplantation via the Pancreas Fast Track Scheme. If the retained kidney is declined locally then it is shared regionally[79]. Full details of the allocation policy can be accessed at: http://www.odt.nhs.uk/pdf/kidney_allocation_policy.pd

Table 1.1: Showing the four DCD kidney sharing regions, and their corresponding transplant centres

North	Midlands	South West	London
Belfast	Birmingham	Bristol	Great Ormond Street Hospital
Edinburgh	Cambridge	Cardiff	Guy's
Glasgow	Coventry	Oxford	The Royal Free
Leeds	Leicester	Plymouth	The Royal London
Liverpool	Nottingham	Portsmouth	St George's
Manchester	Sheffield		West London Renal Transplant Centre
Newcastle			

1.6 Demography of Patients Listed for Transplantation in the UK

In the UK, patients have to be registered on the National Kidney Transplant Waiting List in order to receive a deceased donor kidney transplant. This list is maintained by the UK Transplant Registry held by the Organ Donation and Transplantation Directorate of NHS Blood and Transplant (NHSBT). NHSBT is a special health authority which not only maintains the national transplant waiting list and national donor register but also regulates the allocation of organs nationally[85].

In the absence of any published data, the demography of those waitlisted for kidney transplantation in the UK was recently described as part of preliminary work for this thesis. It was anticipated that by gaining an understanding of the demography of those listed, it could provide useful insights into centre practices in listing patients for transplantation as well as help to inform the objectives and study design of this thesis. Full details of this analysis have been published in Nephron Clinical Practice and can be found in Appendix A. Before proceeding it is worth highlighting some important findings from this study relevant to this thesis.

1.6.1 Prevalent Patient Numbers Listed for Transplantation

At the beginning of 2011, 6699 patients were recorded as being active on the 'kidney only' transplant list, giving a UK population prevalence rate for listing for kidney transplantation of 107 pmp compared with a dialysis prevalence rate of 424 pmp. There were no significant differences in prevalence rates for dialysis in all four of the UK countries; however, prevalence rates for listing were significantly lower in Wales at 79 pmp. This may be explained by the higher prevalence rate of dialysis for patients aged >80 seen in Wales[86] who are less likely to be listed. Figure 1.4 shows that Northern Ireland had a higher prevalence rate for listing patients aged 65+ compared with the other UK countries, mirroring the trend seen in prevalence of dialysis patients in UK countries[86]. The number of prevalent patients listed for transplantation in each renal centre and the distribution of their treatment modalities varied widely with wide inter-centre variation also seen in listing patients pre-emptively between transplant centres with 11 to 125 patients (median 32; IQR: 23-59) listed across 24 transplanting centres.

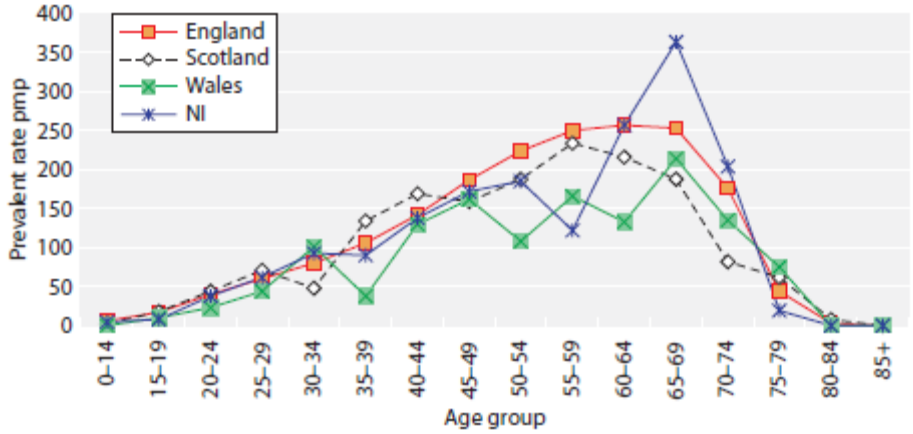

Fig. 1.4. Prevalence rates of registration for kidney transplantation in the UK per million population (pmp) by age group and UK country on 01/01/2011

1.6.2 Age

The median age of prevalent listed patients on dialysis and those pre-emptively listed in the UK at 1st January 2011 was 53 years and 52 years respectively, which was significantly lower than the median age of the prevalent HD patients (66.3 years) and those on PD (61.7 years), $p<0.0001$. Eighty percent of the UK prevalent listed population was aged between 35-69 years, with only 8% of patients aged 70 or above. The proportion of patients listed aged 70 or more was 8% in England, 11% in Wales, 7% in Northern Ireland and 6% in Scotland. Analysis by centre showed wide variation in the proportion of patients listed aged 70 or above by centre with 4 centres (Basildon, Colchester, Ipswich and London Barts) listing no patients, compared to Dorset, Portsmouth, Truro and Bangor, where more than a sixth of their listed patients were aged 70 or more. These differences may be due to variation in local listing practices, though could also reflect variation in the age distribution of the population as a whole, ethnic make-up of the catchment population and the social deprivation index of the local population.

1.6.3 Gender

The gender distribution of patients listed for transplantation in the UK is similar to that seen in the prevalent dialysis population with 59% of patients listed being male. There is wide inter-centre variation however with a range of 37-91%, and only 11 centres (15.5%) having a preponderance of women listed. Sub-analysis by modality has not shown any significant gender differences.

1.6.4 Ethnicity

A quarter of the patients listed for kidney only transplantation in the UK (25%) were from ethnic minority groups (Black or Asian) which compared to 12% of the UK general population who were designated as belonging to an ethnic minority[87] at the time of the analysis. Whilst there was little difference across modalities, Black patients were seen to have the lowest proportion of pre-emptively listed patients, with only 10% (61/593) of listed black patients being pre-emptively listed compared to 17% (817/4835) and 16% (175/1089) of White and Asian listed patients respectively. Amongst renal centres there was wide variation between centres with respect to the proportion of patients listed from ethnic minorities, ranging from zero percent (0%) in 12 centres to over 50% in London Barts (72%), London West (70%), London St Georges (69%), London Kings (69%), London Royal Free (65%), Birmingham Heartlands (61%) and London Guys (53%). These differences are likely to reflect variation in the ethnic make-up of the catchment population served but could also be due to to higher prevalence of CKD causing co-morbidity e.g. diabetes associated with higher levels of socioeconomic deprivation.

1.6.5 Primary Renal Diagnosis

Glomerulonephritis (GN) was the most common primary renal diagnosis amongst patients listed for transplantation on 1st January 2011 at 22%, whilst hypertension only accounted for 7% and renovascular disease only 2%. This may be explained by the fact that younger patients (age <65 years) who are more likely to be listed are more likely to have GN or pyelonephritis and less likely to have renal vascular disease or hypertension as the cause of their renal failure which are more prominent in older age. Diabetes accounted for just 10% of listed patients which contrasts with the pattern seen in incident patients where diabetes is the predominant specific diagnostic code at 24% of new RRT patients. Amongst patients pre-emptively listed the most common diagnosis was polycystic kidney disease (PKD), which is probably a reflection of the fact that these patients are often known to renal services for many years prior to starting dialysis allowing their timely work up to be pre-emptively listed.

Though these analyses describe variation in the demographics of those listed, it is important to note that they were unadjusted for diabetes and other socio-demographic

characteristics. They also did not account for differing local policies in listing patients for transplantation which may have had an impact on the types of patients that were successfully listed. Indeed, listing policies play an integral role in getting patients onto the transplant waiting and will be explored next in this chapter.

1.7 Suitability for kidney transplantation

Achieving prompt and timely activation on the waiting list is important not least because increasing length of time on dialysis adversely affects graft and patient survival, but also because the current organ allocation algorithm introduced in April 2006 takes time spent on the waiting list into account when allocating deceased donor kidneys in the UK[79]. Thus, centres that achieve earlier listing for transplantation provide an advantage for their patients compared with centres that take longer.

Guidelines from the UK Renal Association recommend that patients with progressive deterioration in renal function 'suitable' for transplantation should be placed on the national transplant list within six months of their anticipated dialysis start date and that pre-emptive transplantation should be the treatment of choice for all suitable patients whenever a living donor is available[88].

The term 'suitable' used in these guidelines and other international guidelines often poses clinicians with a conundrum. As defining suitability in an ever increasing co-morbid population of pre-dialysis and dialysis patients can be extremely challenging and requires navigation through a plethora of issues including evaluating the benefit of transplantation against potential risks and understanding the ethical issues associated with allocating a scare resource.

To aid decision-making prior to being listed for transplantation, potential kidney transplant recipients are carefully evaluated in order to detect and treat coexisting illnesses, which may affect perioperative risk and survival after transplantation, as well as transplant candidacy. This process should be as efficient and cost effective as possible and is guided by local physician and surgical experience, local protocols, or availability of investigations. To assist this process, guidelines for the evaluation of candidates for renal transplantation have been published by many organisations.

These guidelines, provide assistance in decision making aiming to balance utility for the community as a whole and equity for each individual and to minimise potential harms for kidney transplant recipients[89]. Examples of organisations that have published guidelines include the American Society of Transplantation[90], Caring for Australians with Renal Impairment (CARI)[91] group and the European Renal Association and European Society for Organ Transplantation[92]. In the United Kingdom, the Renal Association have published guidelines on the assessment of potential renal transplant recipients which are also endorsed by the British Transplantation Society[88].

1.7.1 Variability in Eligibility Criteria

Having described the existence of numerous guidelines it is worth exploring their similarities and any differences that exist which might be affecting listing practices.

1.7.1.1 Absolute Contraindications

Overall there are few absolute contraindications to renal transplantation. These include: active systemic infections, uncontrolled malignancy, active substance abuse, reversible renal failure and ongoing treatment non-adherence. Significantly reduced life expectancy is also cited as a contra-indication though guidelines differ in the life expectancy below which an individual should be deemed ineligible from less than 2 years[93] to less than 5 years[94-96].

Whilst most national and international clinical practice guidelines on wait-listing of patients for kidney transplantation agree in terms of the absolute contraindications, consensus regarding other patient variables is lacking with significant variation noted amongst several variables. Table 1.2 summarises the major differences between guidelines published in the UK, EU and US for assessing suitability for transplantation.

Table 1.2. A summary of the major differences between guidelines published in the UK, EU and US for assessing suitability for transplantation.

Clinical Variable	Summary of advice given by UK, EU and US guidelines published on assessing suitability for transplantation
Age	No upper limit/Age restriction (UK, EU and US)
CVD	Serious or untreatable cardiovascular diseases (cardiac dysfunction not amenable to surgical reconstruction) absolute contraindication in UK, EU and US. Screening tests may be best used to identify high-risk patients for exclusion from the transplant waiting list though there is no compelling evidence that in ESRD patients pre-transplantation screening tests for coronary artery disease in asymptomatic patients is effective in preventing future cardiac events or reducing mortality after transplantation (UK and endorsed by EU) Correction of coronary artery disease before wait-listing because of its impact on postoperative mortality (US)
Diabetes	Not seen as a contraindication (UK, EU and US) Recommend patients with Type 1 DM should be considered for Simultaneous Pancreas-kidney transplantation (UK, EU, US)
HIV	HIV is seen as a relative contraindication (UK, EU and US)
Hepatitis B	Relative contraindication though prior to listing recommended that infection be individually assessed and wait-listing deferred until treatment completion.
Hepatitis C	Relative contraindication though prior to listing recommended that infection be individually assessed and wait-listing deferred until treatment completion.
Obesity	Not seen as a absolute contraindication in US, though patients encouraged to diet, exercise, and adopt behavioral modifications to achieve a target body mass index(BMI) of 30 kg/m2 before transplantation. Relative contraindication in UK and EU, Obese patients (BMI >30 kg/m2) present technical difficulties and are at increased risk of peri-operative complications. They should be screened rigorously for cardiovascular disease and each case considered individually. Although obesity is not an absolute contra-indication to transplantation, individuals with a BMI >40 kg/m2 are less likely to benefit.
Malignancy	Current or active malignancy an absolute contraindication (UK, EU, US)
Smoking	Smoking not seen as a absolute contraindications though smoking cessation should be strongly encouraged before and after transplantation (UK, EU and US)

Each of the variables described in the table, will now be discussed in greater detail with the addition of reviewing other international guidelines.

1.7.1.2 Age

The majority of published guidelines (including guidance from the UK Renal Association) do not define an age limit for wait-listing, recommending instead that recipient age alone is not a contraindication to transplantation but that age-related comorbidities could be considered a relative contraindication to transplantation. Whilst there is evidence that older patients are more susceptible to surgical complications including mortality from infection or acute cardiovascular episodes[97-99], many patients aged >70 years have been transplanted safely and achieved good long-term graft function[100].

In contrast to this guidance, two guidelines have been identified as imposing an age limit for listing patients for transplantation. One from Malaysia, recommending exclusion of patients older than 60 years and suggesting that patients aged 55 to 65 years be evaluated individually[95]. Whilst another guideline (from an American Transplanting Centre) stated that candidates older than 70 years may be wait-listed though stated that no clear evidence was available to support improved outcomes[101].

1.7.1.3 Cardiovascular Disease

Cardiovascular disease (CVD) is a significant cause of morbidity and mortality for wait-listed kidney transplant candidates[102-103], and is the leading cause of death in transplant recipients[65, 104]. In recognition of this, several clinical guidelines recommend screening for cardiovascular disease prior to listing and cite that untreatable cardiovascular diseases (including severe coronary artery disease not amenable to intervention), severe ischemic cardiomyopathy (ejection fraction <30 percent or a recent myocardial infarction within the past three to six months as a relative contraindication to transplantation[95,98].

Further support for screening for CVD is provided by studies which have shown that asymptomatic chronic kidney disease (CKD) patients often have significant coronary artery disease (CAD), with prevalence estimates of 37–53% for at least one coronary artery with 50% or greater stenosis[105-109]. Additionally, the risk of having a major cardiac event has been shown to be greatest in the immediate post-operative period[110-

[114], suggesting screening for CVD could help reduce these early events and improve both early and long-term outcomes.

Whilst there are strong arguments in favour of screening for CVD and a large number of guidelines which support some form of risk stratified cardiac screening, it is not clear whether screening asymptomatic patients prior to transplantation provides any benefit[115]. Indeed, large randomised controlled trials in non-transplant (but high-risk) populations have not shown benefit to screening or revascularisation for asymptomatic CAD[116] (although these trials may not be applicable to a population with advanced CKD and a high prevalence of asymptomatic CAD). This uncertainty in the clinical utility of screening for CVD in asymptomatic patients is reflected in guidance from the UK Renal Association who suggest

> "that there is no compelling evidence that in ESRD patients pre-transplantation screening tests for coronary artery disease in asymptomatic patients is effective in preventing future cardiac events or reducing mortality after transplantation. Until better evidence emerges, screening tests may be best used to identify high-risk patients for exclusion from the transplant waiting list.[88]"

As for the optimal screening method, whilst non-invasive tests are often preferred the optimal non-invasive test is unclear[117.] A Cochrane review of the accuracy of non-invasive cardiac screening tests compared with coronary angiography to detect CAD in patients who are potential kidney transplant recipients found that dobutamine stress echocardiography and thallium myocardial perfusion scan both have relatively low sensitivity and specificity among high risk kidney transplant candidates[118]. Thus, suggesting that a significant number of patients will either have their significant CAD missed (false negatives) or be referred unnecessarily for coronary angiography (false positive). It is perhaps unsurprising therefore that several studies have reported variation in transplant centre practice patterns in screening asymptomatic kidney transplant candidates for coronary artery disease[119-120].

1.7.1.4 Diabetes

Diabetes is not seen as a contraindication to transplantation with evidence from numerous retrospective cohort studies[4, 121-123] as well as a systematic review[124] reporting superior survival rates in diabetic patients who are transplanted, as compared to diabetic patients who remain on dialysis. Indeed, all guidelines recommend that diabetics should be considered for transplantation with those with type 1 diabetes being considered for simultaneous pancreas-kidney transplantation. Many guidelines also recommend that diabetics should undergo screening for cardiovascular disease to be considered for transplantation. Screening methods for cardiovascular disease in diabetics are seen to vary with no clear consensus. This may be partially explained by several studies reporting that non-invasive tests have limitations in their ability to detect CAD in patients with CKD, particularly those with diabetes[117-125].

1.7.1.5 HIV and Hepatitis Viruses

Whilst there is consensus that transplant recipients should be free from active infections prior to transplantation. Eligibility of patients with HIV and hepatitis is more ambiguous and an evolving area in view of newer treatments for hepatitis and the advent of highly active antiviral therapy which has revolutionised the prognosis of HIV patients. Many guidelines still cite HIV as a relative contraindication [88, 90-91, 94,96, 99] having previously been cited as an absolute contraindication in the old European Best Practice Guidelines. However, early experience suggests similar early graft and patient survival rates between HIV positive and negative renal transplant recipients[126]. Another recent study reporting on the UK experience of transplantation in HIV positive patients also reports similar findings with patient survival at 1 and 3 years reported as 91.3%, and graft survival 91.3% and 84.7%, respectively[127]. This study did identify a higher cumulative incidence of acute rejection (48%) suggesting that the optimal immune suppression strategy in this population remains to be refined.

As for potential recipients with active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, transplantation has been shown to improve their survival as compared with remaining on dialysis[128-129]. Prior to listing however, the majority of

guidelines recommend that infection be individually assessed and wait-listing deferred until treatment completion. Several also suggest that chronic active hepatitis and patients with hepatitis unresponsive to treatment may still be considered for transplantation[91, 98].

1.7.1.6 Obesity

Obesity is not seen as a contraindication to transplantation with 58.8% of patients transplanted in the US alone being categorised as either overweight or obese[130]. However, several studies report an increased risk of technical difficulties and perioperative complications amongst obese patients[131-132]. Evidence in favour of imposing a BMI limit on the basis of more hard end-points (patient and graft survival) is however conflicting[133-138]. A number of reports from nationwide databases, including the USA, Australia and the Netherlands[133, 136, 138], have shown decreased patient and graft survival in obese recipients, whilst others showed no differences in survival between obese and non-obese transplant recipients[137].

It is unclear in studies where an increase in risk was noted, how much would be mitigated once co-existing cardiovascular disease was accounted for. This raises the notion that if technically feasible, and cardiovascular disease has been ruled out, most patients should be considered for transplantation irrespective of their BMI.

In the UK the Renal Association recommends that

> "Obese patients (BMI >30 kg/m2) present technical difficulties and are at increased risk of peri-operative complications. They should be screened rigorously for cardiovascular disease and each case considered individually. Although obesity is not an absolute contra-indication to transplantation, individuals with a BMI >40 kg/m2 are less likely to benefit.[88]"

Whilst this advice is consistent with many other international guidelines, others (from Malaysia and Canada) suggest aiming for a much lower BMI of 30 kg/m2 before transplantation[95,97].

1.7.1.7 Malignancy

Whilst active malignancy is considered an absolute contraindication to transplantation many guidelines recommend that patients with previous malignancy should be considered, although recommend varying cancer-free periods of 2-5years depending on the type of malignancy[97-98, 139]. This is to minimise the risk of recurrence due to the enhanced development of micrometastasis by immunosuppressive medications[140]. The Israel Penn International Transplant Tumor Registry is a US-based database which is often recommended for consultation for tumour specific advice[141]. As for cancer surveillance post transplantation although there is evidence that dialysis patients have an increased incidence of cancer compared with the general population[142], currently there is no evidence that dialysis patients on the transplant waiting list should have increased cancer surveillance strategies over that recommended for the general population[143].

1.7.1.8 Smoking

Only a few studies have examined the effect of cigarette smoking on renal transplantation but all show an association with reduced patient and graft survival[88]. Smoking cessation prior to transplantation has also been shown to reduce the relative risk of graft failure and improve death-censored graft survival[144-145]. In light of this the UK Renal Association recommends that

> "patients should be strongly encouraged to stop smoking before and after transplantation. Formal smoking cessation programmes should be offered and accessed in primary care.[88]"

This advice is similar to the majority of published guidelines where smoking is mentioned[90, 101].

To conclude, significant variation in assessing transplant suitability and differing eligibility criteria, exists between national and international guidelines. Whilst the impact of this on listing patients for transplantation is not known, it raises the possibility of physicians differing in their decisions-making to list patients for

transplantation based on their co-morbidities thereby becoming a source of inequity in terms of accessing the transplant list.

1.8 Access to Healthcare

Despite the National Health Service aiming to provide access to healthcare that is universal and equitable for all, there are many examples where this does not take place. Examples of areas of healthcare where inequity has been demonstrated include: referral for coronary angiography from a rapid chest pain clinic[146], access to hospice beds for palliative care patients[147], access to general practitioner services[144], access to breast screening[149-150], access to total knee replacements[151-152] as well as access to transplantation[11-12] which this thesis will focus on.

1.9 Variation in Access to Transplantation

In recognition of the benefits of transplantation and in keeping with the NHS constitution the UK Renal Association recommend that

> "There must be demonstrable equity of access to donor organs irrespective of gender, race or district of residence. All patients on dialysis should be considered formally by physicians and surgeons for transplantation or for exclusion from the transplant waiting list.[88]"

However, despite this recommendation and providing guidelines to assist in assessing patient suitability for transplantation numerous studies having shown that access to transplantation varies in the UK[11-12, 153]. Currently, fewer than 40% of all patients with ESRD in the UK are listed as suitable candidates for transplantation, with significant centre variation noted in the proportion of prevalent patients on RRT listed for transplantation[154].

Ravanan et al in a large registry based, longitudinal cohort study highlighted, significant inter-centre variability existed in the UK in access to the transplant list as well as in the time taken to register patients on the waiting list, and in receipt of a renal transplant from a donor after brain stem death[12]. Similarly, Oniscu et al in

another registry based study also showed significant centre variation in Scotland, with patients having a 28% better chance of listing when they started dialysis in a renal centre in a hospital with a transplant unit[11]. It is likely that some of this variation may be due to differences in centres' approach to assessing recipient suitability, driven partly by guidelines for assessing suitability for transplantation lacking consensus (previously described). This is supported by evidence that despite published guidelines the fitness for transplantation criteria employed in renal centres varies widely throughout the UK[155]. Patient specific factors and other centre practices may also be responsible for this variation.

1.10 Patient Specific Factors and Access to Transplantation

1.10.1 Age, Sex and Comorbidities

Amongst patient specific factors numerous studies have shown that both increasing age[11-12, 156-160] and female gender[11-12, 26, 156-157, 161] are associated with reduced access to the transplant waiting list in the UK and in other countries. Several co-morbidities have also been highlighted to reduce access to the transplant waiting list. These include cardiovascular disease (including congestive heart failure, coronary artery disease and left ventricular hypertrophy), past history of malignancy, peripheral vascular disease, diabetes, obesity, primary renal disease, low BMI and having a psychiatric disorder[11-12, 153, 157, 160, 162].

The majority of studies relating to the impact of co-morbidities on access to transplantation have been conducted in the US with several reliant on using retrospective registry data with significant missing data leading to potential bias. One study reports that 88% of patients analysed had missing data for at least one of the co-morbidity variables[157].

In the UK, studies looking at access to transplantation have tried to adjust for co-morbidities however again due to reliance on registry data they too have been limited by missing data and have only been able to adjust for diabetes which was shown to reduce access to transplantation[11-12]. This has been recognised as a limitation with the

authors recommending the need for a prospective study which includes collecting and analysing co-morbidity data.

1.11 Ethnicity

According to the 2011 UK National Census, 86% of the population classified themselves as White, 7.5% Asian, 3.3% Black and 3.2% Other[163]. Although the ethnic make-up of the UK is increasingly diverse, this thesis will concentrate on outcomes from the three main ethnic groups: White, South Asian (Indian, Pakistani, Bangladeshi, Sri Lankan) and Black (Caribbean and African origin). This is in keeping with standard national and international registry practice to report using this classification system. Additionally, patients from other ethnic groups are a heterogeneous population which account for only a small proportion of all patients on RRT and are therefore not discussed in detail in this thesis.

1.11.1 Ethnicity and RRT

The incidence of ESRD and acceptance onto RRT has been reported as being higher amongst ethnic minorities[13, 15-20] as compared to the white population by numerous studies. Ethnic differences in ESRD have been attributed to the larger burden of the primary causes of ESRD, including diabetes, hypertension, and glomerulonephritis, in ethnic minorities[15-20]. However, research on these differences has revealed that those primary causes do not explain most of the differences seen[164-165]. Another possible determinant of ethnic differences in ESRD is the *APOL1* gene, which is now recognised as a risk factor for ESRD in non-diabetic black patients[166]. Other studies have described faster progression of chronic kidney disease to ESRD[167-168], a lack of access to appropriate medical care and psychosocial factors[19, 169-172], and social deprivation[2, 22-25 33] as potential reasons for the higher rate of ESRD seen in ethnic minorities. However, even after adjusting for these factors residual association has persisted and highlights the need for further research to understand this association.

In the UK, the UK Renal Registry report that the age–gender standardised incidence ratio of RRT is higher (2–3 times) in regions with a high ethnic minority population compared to those with a low ethnic minority population[169]. As a large proportion of ethnic minorities live in areas of high deprivation it is unclear how much of the

regional variation reported in these analyses is due to their ethnic composition and/or the socioeconomic characteristics of the area.

The higher incidence of RRT amongst ethnic minorities is particularly pronounced in older people, with Black and South Asian patients over the age of 65 having an incidence rate of 1,191 and 1,133 per million population (pmp) as compared to 283 (pmp) in the white populations (see figure 1.5)[169]. As life expectancy estimates for ethnic minorities in the general population are lower than for the White population[173] the higher incidence amongst the elderly ethnic minority patients cannot be attributed to the possibility of them living longer to reach ESRD.

Whilst the incidence of RRT is higher in ethnic minorities, several studies, both in the UK and US have reported better adjusted survival on dialysis in ethnic minorities compared to the white population[169, 174-175]. The reasons for this are unclear with lower co-morbidity at the start of RRT, better adaptation to dialysis as well as the possibility of a 'healthy survivor bias' (ethnic minorities with significant co-morbidities dying prematurely before reaching ESRD) being cited as possible reasons.

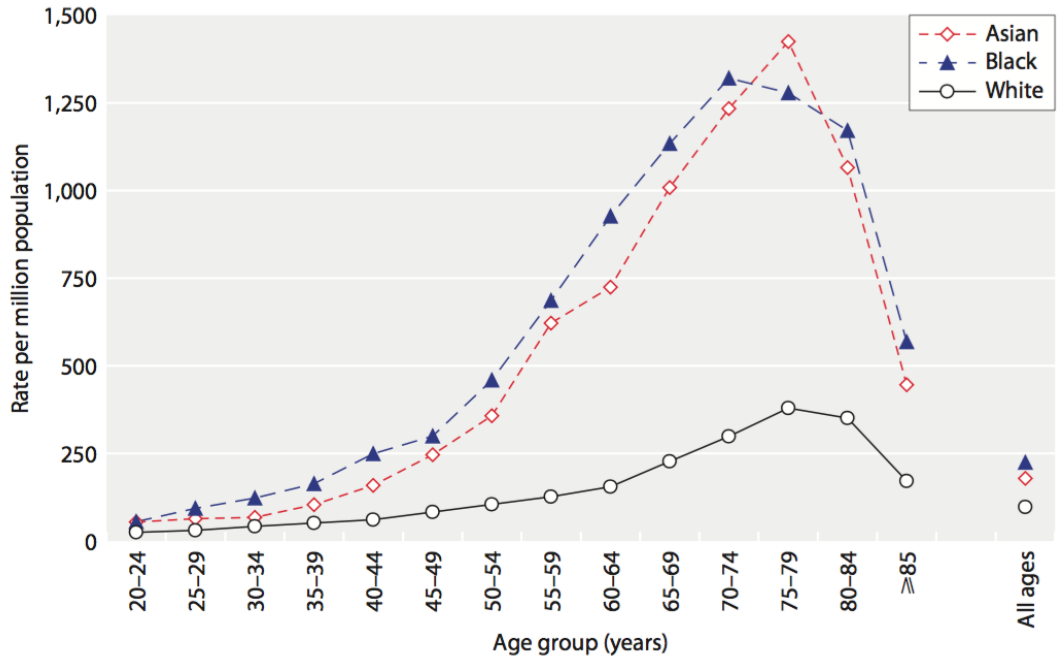

Fig. 1.5. Age profile of incident RRT patients (2010–2012), by ethnicity, in England and Wales[169]

1.11.2 Ethnicity and Access to Transplantation

Despite having an increased incidence of ESRD and better survival on dialysis, several studies in the US have reported that ethnic minorities have decreased access to both the transplant waiting list and access to transplantation once listed[25-36]. In the UK, NHSBT also reports lower rates of transplantation amongst ethnic minorities active on the transplant waiting list. Their report in 2007 cited that despite representing a fifth of the prevalent patients on the transplant waiting list (in 2005) they only represented 13% of the proportion of patients who received a transplant in 2003-2004. Furthermore, the median time to transplant once wait-listed was significantly higher for Asian (1368 days) and Black patients (1419 days) compared to White patients (719 days)[176].

The lower rates of transplantation reported amongst ethnic minorities may be due to the higher prevalence of diabetes and related co-morbidities in ethnic minorities. Furthermore, ethnic minority individuals are at a significant disadvantage due to blood group and HLA disparity compared to the predominantly White donor pool in the UK. Ethnic minority populations contribute only 6% of the kidneys that enter the UK donor pool yet comprise 14% of the general population and 29.5% of the patients on the cadaveric waiting list[85]. This is again highlighted in another study commissioned by NHSBT which showed that only 10% of Asian and 5% of Black patients on the waiting list had HLA antigens which were easy to match compared to 24% of White patients; and that 38% of Asians and 24% of Black patients awaiting a kidney transplant in the UK were blood group B compared to 10% of White patients[176].

In attempt to address some of these disparities several changes have been made to the allocation scheme over the years. In 2002 kidneys from blood group O donors were allowed to be allocated to blood group B recipients in certain circumstances with the aim of producing greater equality between group O and B recipients. Whilst in 2006, changes were introduced to reduce inequity arising from biological differences: rare HLA antigens would be defaulted to a more common equivalent (on the basis of serology and sequence data) thus improving the likelihood of receiving a matched kidney; HLA matching would be ignored for older patients likely to receive only one

transplant, for whom sensitisation and re-transplantation are of less relevance and a greater emphasis would be given in the point scoring system to patients waiting longer for a transplant.

As for access to the transplant waiting list in the UK, some studies have described that ethnic minorities have decreased access to the transplant waiting list in the UK[11-12, 149], whereas others have reported equal access[177-178]. A reason for this discrepancy may be that studies reporting reduced access did not adjust for socioeconomic status which may have led to confounding. Indeed, in Udayaraj et al study looking at access to transplantation in England and Wales, whilst non-white patients had a lower chance of being waitlisted than white patients, these differences were attenuated after adjusting for socioeconomic status[178].

Ethnic differences in living donor[34-35] and pre-emptive transplantation[24, 33] have also been described with lower rates of transplantation amongst both Black and Asian patients compared to White patients in the US. Similarly, ethnic minorities have also been found to have reduced access to living donor transplantation in the UK with Udayaraj et al reporting that both South Asians (OR: 0.55, CI: 0.34-0.90) and Black (OR: 0.31, CI: 0.18-0.54) patients had lower odds of living donor transplantation compared with white patients, though there was an interaction with age so that this disparity was observed only in those younger than 50 years[179]. It is not known if ethnic differences in pre-emptive transplantation in the UK exist as there are no published data examining this available. Possible reasons cited for lower levels of living donor transplantation amongst ethnic minorities include institutional prejudice[171], distrust and reluctance to engage with the medical system[180-181], cultural and religious beliefs[27, 182], and lack of suitable donors or concern over a higher risk for living donors from minority ethnic backgrounds[183-186].

1.12 Socioeconomic Status

Socioeconomic deprivation is often described as being multidimensional, including both material and social elements, and is relative to societal norms affecting people in all societies[187]. Amongst many definitions perhaps one of the most famous and most quoted is that of Peter Townsend who describes it as

> "People can be said to be deprived if they lack the types of diet, clothing, housing, household facilities and fuel and environmental, educational, working and social conditions, activities and facilities which are customary, or at least widely encouraged and approved, in the societies to which they belong" (Townsend, P)[187]

1.12.1 Measuring Socioeconomic Deprivation

Socioeconomic deprivation can be measured at either an area level or individual level. Individual level socioeconomic deprivation data variables include: income, education, housing tenure, and car ownership.

As for measuring area level socioeconomic deprivation, several instruments exist including, the Townsend Index[188], the Carstairs Deprivation Index[189], the Jarman Index[190] and the Index of Multiple Deprivation (IMD)[191].

The Townsend Index focuses primarily on material differences using 4 variables derived from the 2011 national census. These include:

1. Percentage of private households that had no car ownership
2. Percentage of economically active residents who are unemployed
3. Percentage of households with more than one person per room (overcrowding)
4. Percentage of households not owner-occupied

Z scores are calculated for each of these percentages which are then combined to create the overall Townsend Score.

The Cairstairs Deprivation Index like the Townsend Index also utilises national census data relating to 4 areas: male unemployment, overcrowding, car ownership and social class.

The Jarman Index give an indication of social deprivation, based on the weight of eight variables:-

1. Unemployment - unemployed residents aged 16+ as a proportion of all economically active residents aged 16+.

2. Overcrowding - persons in households with 1 and more persons per room as a proportion of all residents in households.
3. Lone pensioners - lone pensioner households as a proportion of all residents in households.
4. Single parents - lone 'parents' as a proportion of all residents in households.
5. Born in New Commonwealth - residents born in the New Commonwealth as a proportion of all residents.
6. Children aged under 5 - children aged 0-4 years of age as a proportion of all residents.
7. Low social class - persons in households with economically active head of household in socio-economic group 11 (unskilled manual workers) as a proportion of all persons in households.
8. One year migrants - residents with a different address one year before the Census as a proportion of all residents.

The Index of Multiple Deprivation (IMD) combines information from seven domains to produce an overall relative measure of deprivation. The domains are:

1. Income Deprivation
2. Employment Deprivation
3. Crime
4. Health Deprivation and Disability
5. Barriers to Housing and Services
6. Living Environment Deprivation
7. Education, Skills and Training Deprivation

Area based measures of socioeconomic deprivation have often been utilised in studies exploring equity in access to healthcare services to act as a proxy for data on personal/household income or wealth which have not routinely been collected. However, people of high socioeconomic position live in deprived areas, and vice versa[192-193]. Thus adjusting for area deprivation leads to non-differential misclassification and tends to the null for socioeconomic associations and alternatively may leave residual confounding for any exposure-outcome association in which socioeconomic position is strongly implicated leading to underestimation or overestimation of a socioeconomic effect[194].

1.12.2 Socioeconomic Deprivation and RRT

The incidence of ESRD has been reported as higher amongst socially deprived patients by several studies[16, 21-23, 44]. This could be due to the higher prevalence of CKD in socially deprived populations[14, 43, 45-46, 195], faster progression of CKD to ESRD[196-197] or higher late referral rates seen amongst socially deprived patients[198-200]. Several studies have also shown that mortality on dialysis is higher amongst socially deprived patients in the UK and US[198, 201], however after adjusting for co-morbidity this association is attenuated[198].

1.12.3 Socioeconomic Deprivation and Access to Transplantation

Several studies in the US and UK have reported that socially deprived patients have reduced access to deceased donor kidney transplantation, both in terms of access to the transplant waiting list and access to transplantation once listed[11, 24, 26-27]. Greater comorbidities[202], lower rates of adherence to medical treatment[203], lack of medical insurance (in the US) and reduced awareness of the benefits of transplantation[26] have all been identified as possible causes behind these differences. Additionally, clinicians may consciously or subconsciously manage patients in ways that make it less likely for socially deprived patients to be listed for transplantation[27].

It should be noted that the majority of studies exploring the impact of socioeconomic deprivation on access to transplantation have been performed in the US where access to healthcare could be influenced by availability of private health insurance[204].

In the UK, Oniscu et al have shown that patients from socially deprived areas in Scotland were less likely to be on the transplant waiting list, but once on the waiting list patients had an equal chance of attaining a transplant irrespective of their socioeconomic status[11]. This study however did not adjust for differences between deprivation groups in ethnic composition or co-morbidity, both of which have been independently associated with a low probability of listing for transplantation[25-26, 28-31]. In a more recent study performed by Udayaraj et al looking at the impact of social deprivation on access to transplantation in the England and Wales (using UK Renal

Registry data), individuals living in socially deprived areas were also seen to have reduced access to transplantation with the effect of deprivation more pronounced amongst those aged over 50 years[178]. Whilst this study adjusted for ethnicity it could again not adjust for co-morbidity due to incomplete registry data returns.

As for access to live donor transplantation several studies have also demonstrated that socially deprived patients are less likely to receive a live donor transplant[205-209]. In the UK, a study involving only white patients found that lower socioeconomic status was associated with lower odds of living donor transplantation at within 3 years of starting RRT, with the effect being greater in male patients[179]. Similarly, several studies around the world have also shown that socioeconomically deprived individuals are also less likely to undergo pre-emptive transplantation[210-211], though there have been no studies exploring this in the UK to date.

A summary of the patient factors described above and their influence on being wait-listed for renal transplantation is shown in Figure 1.6.

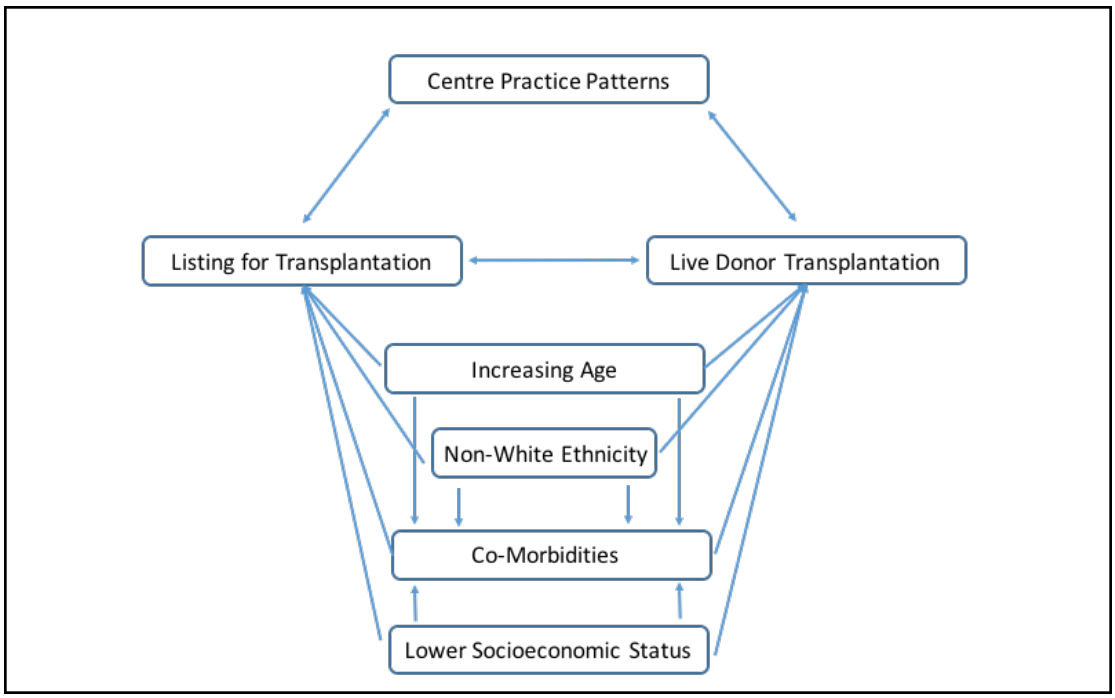

Figure 1.6. A summary of the impact of patient factors on listing for transplantation. (direction of arrow denotes which factor is being influenced, whilst bi-directional arrows denote potential impact of factors in both directions)

1.13 Practice Patterns and Variation in Healthcare

Understanding the impact of practice patterns and service organisation on variation in healthcare is increasingly recognised as important in improving quality in healthcare. This has been driven by variation in clinical outcomes being reported in-between different organisations/centres providing care, despite adjustment for case-mix, suggesting that there is variation in quality between organisations/centres. Understanding these centre effects is key to understanding how to deliver high quality care equitably to populations served by different organisations.

In healthcare the impact of practice patterns has been explored in several areas including: exploring variation in knee/hip replacement rates[152], hysterectomy rates[212] and in examining door to balloon times in cardiac catheterisation for acute myocardial infarction[213-214]. All these studies found that variation in rates/times were in part as a consequence of clinician practice patterns.

In the case of exploring variation in hip replacement rates, the knowledge and willingness of GPs to attempt non-surgical interventions in the first instance was seen as important[152] whilst another study found that the presence of a GP trainer within the practice reduced referral rates[215]. Having a hysterectomy was described as more likely if the clinician making the decision was middle aged, female, had more than 15 years of experience and when more hospital beds, surgeons and anaesthetists were available to perform the procedure[216].

As for practice patterns in cardiac revascularisation for acute myocardial infarction, six strategies were identified as significantly reducing door to balloon time. These included: having emergency medicine physicians activate the catheterisation laboratory, having a single call to a central page operator activate the laboratory, having the emergency department activate the catheterization laboratory while the patient was en route to the hospital, expecting staff to arrive in the catheterization laboratory within 20 minutes after being paged, having an attending cardiologist always on site, and having staff in the emergency department and the catheterization laboratory use real-time data feedback[213].

1.13.1 Practice patterns and RRT

Several studies have also tried examining practice patterns in patients receiving RRT. Plantinga et al described that more frequent sit-down rounds in hemodialysis units was associated with better patient outcomes, including an increased chance of meeting the albumin clinical performance target, decreased hospitalization, and decreased risk of mortality[217-218]. The Identifying Best Practices in Dialysis Care Study which also looked at dialysis unit practice patterns in relation to mortality found that units where patients were more engaged in their care, physician communication was stronger and dieticians were empowered were associated with lower mortality rates[219]. In another study, Castledine et al described several centre factors which were associated with a higher probability of home dialysis including: physicians aspiring to a higher 'ideal' peritoneal dialysis rate, early use of peritoneal dialysis and the use of home visits to educate patients pre-dialysis[220].

1.13.2 Practice patterns and Access to Transplantation

The observations of centre variation in time to listing for a kidney transplant[11], variation in fitness for transplantation criteria employed in UK renal centres[155] and that centre variation in access to transplantation persists despite 'limited' case-mix adjustment[12] all suggest that centre factors/practice patterns may be playing a role. However, despite this awareness there are little published data on the impact of practice patterns on access to transplantation. In the UK, Dudley et al. found in a cross-sectional study of prevalent adult dialysis patients from 41 renal centres across England and Wales that larger renal centres with smaller living donor programs and centres with different listing practices for living donor recipients (listing <60% of live transplant recipients on the deceased donor waiting list before transplant as compared to >60%) were significant centre-level factors associated with reduced probability of listing[153]. In this study having pre-transplant care at a transplanting centre did not improve access to listing, in contrary to studies from France and Scotland who found a positive association towards improving access to listing[11, 160,].

Whilst the French study used an incident cohort, the major limitation of the Scottish study was that it was a cross-sectional analysis of prevalent data rather than an

incident cohort and the rate of transplantation within a centre may have influenced the size of its waiting list. Additionally, by using prevalent data there could have been enrichment of the prevalent dialysis population with patients who are unsuitable for transplantation resulting in the centre differences observed. More recently, another study conducted in France showed that being registered at a transplanting centre improved the likelihood of being pre-emptively listed[211].

1.14 Persistence in Variation in Access to Renal Transplantation

Following the reporting of inter-centre variation in access to transplantation in the UK[11-12], a range of initiatives have been undertaken to improve listing rates and access to transplantation in the UK, including the 'Transplant First' initiative led by NHSBT and NHS kidney care[221]. Whilst the impact of some of these may take some time to make a measurable impact, before finalising the aims of this thesis a decision was made to re-evaluate whether variation was still present and the degree of variation using more up-to-date UK Renal Registry data.

Analysing a cohort of incident RRT patients (between 1st January 2006 and 31st December 2008) across all UK renal centres this analysis found that after adjusting for patient specific variables that were shown to influence outcome (age, ethnicity, gender, PRD), significant centre effects were identified for the probability of being activated on the waiting list prior to or within two years of starting dialysis. This is depicted in the funnel plot below (Figure 1.7) which shows several centres lying outside the 99.8% confidence interval.

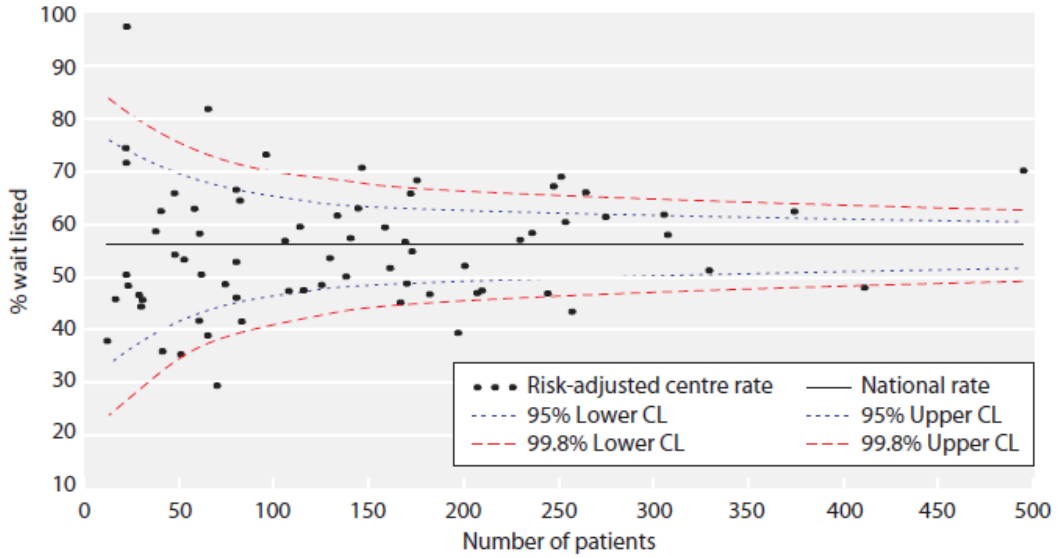

Fig. 1.7. The percentage of patients wait listed for a kidney transplant by renal centre, prior to or within two years of starting dialysis (centres with <10 patients excluded)[222]

After adjustment for patient variables, significant centre differences were also seen in the probability of receiving a renal transplant from a donor after brainstem death or a donor after cardiac death/living kidney donor. Increasing age, non-white ethnicity and diabetes (as the primary renal diagnosis) were all associated with a reduced likelihood of accessing the kidney transplant waiting list and receiving a kidney transplant (although it should be noted that these analyses did not adjust for social deprivation – a known confounder). A patient starting dialysis in a non-transplanting renal centre was also less likely to be registered for transplantation (OR 0.80, 95% CI 0.74–0.87) or receive a transplant from a donor after cardiac death or a living kidney donor (OR 0.69, 95% CI 0.61–0.77) compared with patients cared for in transplanting renal centres. Once registered for kidney transplantation, patients in both transplanting and non-transplanting renal centres had an equal chance of receiving a transplant from a donor after brainstem death (OR 0.92, 95% CI 0.79–1.08)[222]. Full details of this analysis have been published in Nephron Clinical Practice[222]

1.15 Summary

This review has demonstrated that for suitable patients with ESRD, renal transplantation confers both better quality of life and life expectancy than dialysis; with live kidney transplantation offering the best clinical outcomes. Whilst the UK Kidney Transplant Allocation Scheme facilitates equitable access to renal transplantation once listed, retrospective analyses of registry data suggest there is inter-centre variation in access to both live and deceased donor transplantation.

Furthermore, despite the National Health Service being funded via public taxation and being free at the point of use, retrospective studies also report inequity in access amongst ethnic minorities and individuals from lower socioeconomic status, both of which are seen to have reduced access to both live and deceased donor transplantation despite having a higher incidence of ESRD.

Increased comorbidity burden amongst these populations and or differing centre processes in assessing patient suitability for transplantation (driven by significant variation in published national and international guidelines) may be amongst contributory factors however studies to date have been limited in their ability to adjust for these factors. It thus remains unclear which patient-specific and centre-specific factors are responsible for such variations, or indeed which centre practices represent the optimal approach for listing patients.

Additionally, in reference to live donor transplantation, cultural/religious beliefs alongside lack of suitable donors may also be contributing to lower rates of live transplantation (especially amongst ethnic minorities) as may the relationships between donors and their respective recipients though there are no published UK data on the latter.

1.16 Aims and Objectives

The primary aims of this thesis is to explore inequity in access to renal transplantation in the UK focusing on two areas:

1. To identify patient-specific and centre-specific factors that influence access to the transplant waiting-list
2. To understand if inter-personal relationships between living kidney donors and their recipients differ by ethnicity

The Specific Objectives to achieve these aims are:

1. To investigate the relationships that exist between living kidney donors and their recipients (Chapter 3).
2. To identify centre specific factors that might influence access to the national transplant waiting list (Chapters 4 & 5).
3. To investigate the independent effects of patient factors including ethnicity, social economic status and co-morbidity as well as centre effects on (i) access to pre-emptive transplantation/listing and (ii) access to transplantation/listing after starting dialysis, in conjunction with the Access to Transplantation and Transplant Outcome Measures (ATTOM) study (Chapter 6).

Chapter 2 describes general methods of data collection and data extraction used by the national registries providing data for this thesis (UKRR and NHSBT) and also details the recruitment and data collection processes involved in the ATTOM study which provided the prospective data utilised in achieving objective 3. The individual methods and results for each of the objectives are described separately in Chapters 3-6. Each set of results is also followed by a detailed discussion, whilst Chapter 7 seeks to provide a few concluding remarks and discusses the implications of this study for clinical practice and ideas for future research.

Chapter 2: General Methods

2.1 Introduction

This chapter describes the study design, recruitment, validation processes, data completeness and demographic details of patients recruited in the ATTOM study, which provided the prospective data utilised in achieving objective 3. It also outlines the general methods of data collection and data extraction used by the UKRR and the UK Transplant Registry which provided additional data items needed for the analyses in this thesis.

2.2 Access to Transplantation and Transplant Outcome Measures (ATTOM)

The UK National Institute for Health Research (NIHR) funded Access to Transplantation and Transplant Outcome Measures (ATTOM) research programme was developed by a consortium involving all renal and transplant units in the UK following the identification of inter-centre variability in access to transplantation in the UK[11-12]. The overarching aims of this study were to improve equity of access to kidney and kidney–pancreas transplantation across the UK and to optimise organ allocation to maximise the benefit and cost-effectiveness of transplantation. This study involved five key work streams:

1. To identify patient-specific and centre-specific factors that influence (a) access to the transplant waiting-list (which is also one of the key objectives of this thesis) and to develop a survival probability model as a basis for standardising access to the transplant waiting-list and (b) access to transplantation (deceased donor kidney and pancreas and living donor kidney) for wait-listed patients.
2. To identify patient-specific and centre-specific factors that influence patient survival for transplant wait-listed dialysis patients, after deceased donor kidney transplantation, after simultaneous pancreas and kidney (SPK) transplantation, after living donor kidney transplantation and after pre-emptive transplantation (transplantation as a first mode of RRT prior to the initiation of dialysis treatment).

3. To evaluate quality of life (QoL) and other patient-reported outcome measures (PROMs) for patients on dialysis, after deceased donor kidney transplantation, after SPK transplantation, after living donor kidney transplantation, after pre-emptive transplantation, in waiting-list controls for kidney and SPK transplantation and in those whose transplants have failed following recruitment to ATTOM.
4. To perform a health economic analysis to explore costs and outcomes associated with alternative approaches to organ allocation.
5. To utilise survival, health status, QoL, treatment satisfaction and costs to determine an optimal organ allocation policy as defined by the maximisation of clinical and cost–benefits derived from transplantation.

2.2.1 Study population

All 71 renal units (of which 23 are renal transplant units) in the UK contributed to the ATTOM programme. Between 1 November 2011 and 31 March 2013, 6360 patients aged 18–75 years were recruited in three cohorts: incident dialysis patients, incident kidney and SPK transplant patients and prevalent listed patients selected as controls for transplanted patients (figure 2.1).

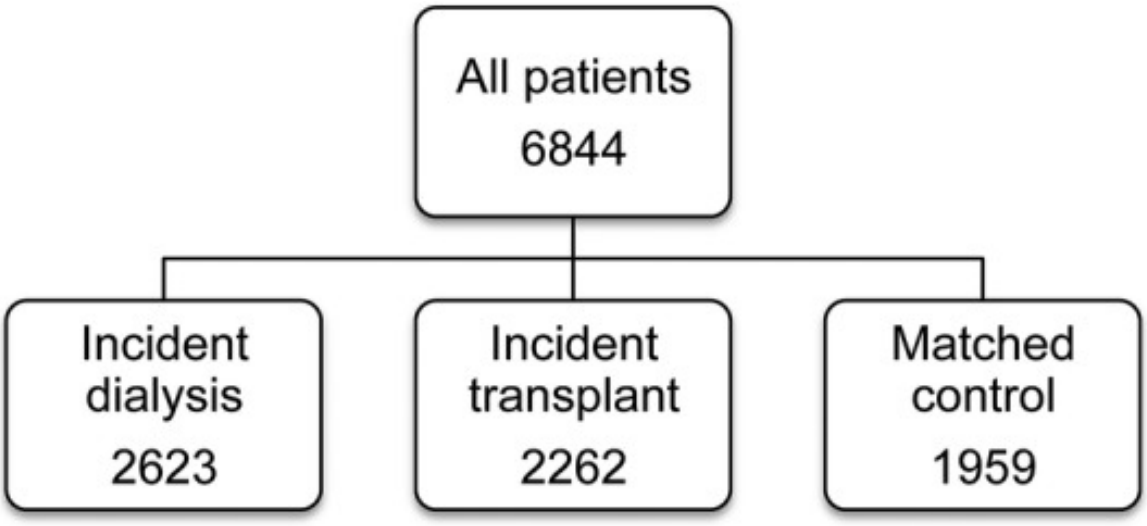

Figure 2.1: Access to Transplantation and Transplant Outcome Measures (ATTOM) study patient recruitment and cohort distribution

A total of 484 patients moved cohorts (13 patients moved twice) resulting in 6844 registrations within ATTOM (figure 2.2). This cohort represented 72% of all incident

renal transplants performed in the UK during the study period and and 52% of all incident dialysis patients starting dialysis in the UK during the study period.

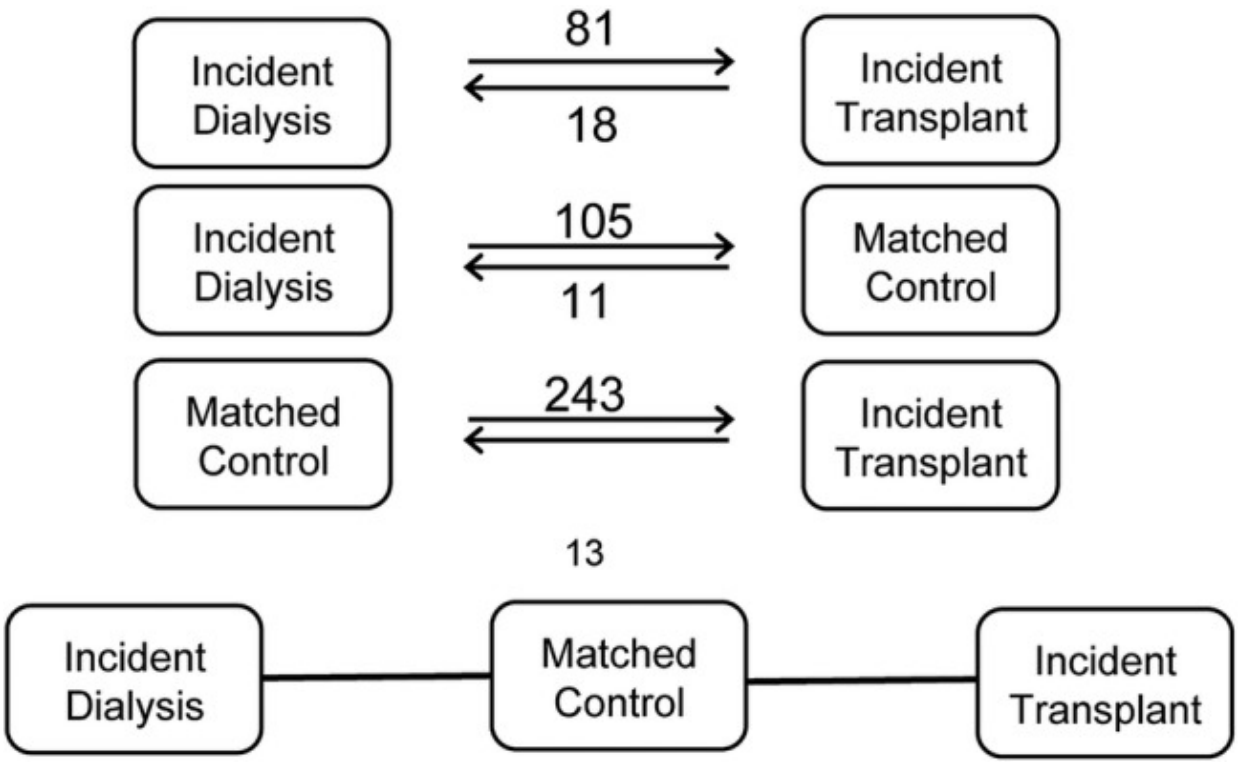

Figure 2.2: Number of patients changing between the ATTOM study cohorts and the direction of change.

In each centre, recruitment took place over a 1-year period aiming to include every patient <75 years of age starting RRT. Controls were selected automatically from the UK Transplant Registry database on a fortnightly basis and were matched for: age (within 5 years), time on the list, pre-emptive/on dialysis and the type of transplant (deceased donor or living donor). Only patients aged <75 were recruited due to funding limitations which did not allow for patients aged > 75 to be recruited.

Patient-level data (see Appendix B) were collected prospectively at the time of starting dialysis, at the time of transplantation or when identified as a control from the transplant list. 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 patients via completion of the EuroQoL five dimensions (EQ-5D)[223] and 12-item Well-being Questionnaire (W-BQ12)[224-227]. The

data were uploaded onto a secure website designed, developed and maintained by the UK Renal Registry (UKRR). Data completeness for the items recorded is illustrated in figure 2.3a and b.

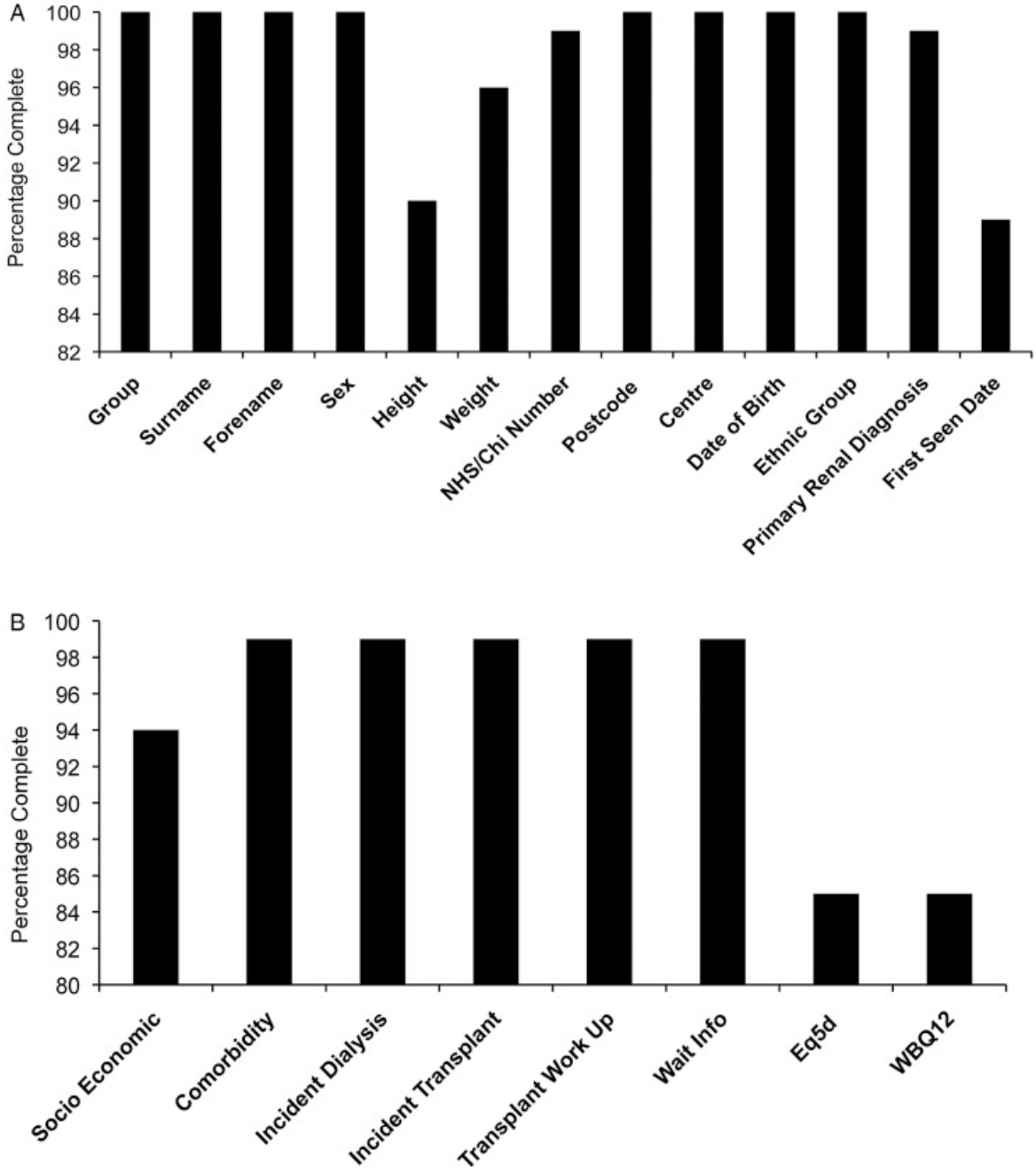

Figure 2.3 A and B: Data completeness for each study item collected in the ATTOM study.

Data collection accuracy was ensured using uniform definitions and a training process for the research nurses. An independent data validation of coding of 5% of case notes in all research sites confirmed >98% concordance for all coded fields.

The demographic characteristics of the three study cohorts are illustrated in table 2.1. Detailed comparisons of the demographics of those recruited within ATTOM and those registered as starting dialysis or having a transplant during the study period at the UKRR are discussed in Chapter 6.

Table 2.1: Demographic characteristics of the ATTOM study cohorts

	Incident dialysis	**Incident Transplant**	**Matched controls**
N	**2623**	**2262**	**1959**
Age at Registration to ATTOM			
Mean ±SD	56.18±13.55	49.34±13.44	50.38±12.83
Median (IQR)	58.39 (47.48–67.14)	50.28 (40.07–59.89)	51.14 (41.67–60.34)
Gender (%)			
Male	64.93	62.81	57.91
Female	35.07	37.19	42.09
Ethnicity (%)			
White	79.95	82.45	74.54
Asian	11.23	9.4	12.42
Black	7.09	6.21	10.93
Chinese	0.69	0.75	0.92
Mixed	0.65	0.8	0.87
Not specified	0.38	0.4	0.31
Age First Seen by Nephrologist			
Mean ±SD	50.14±15.66	39.85±15.36	39.38±15.41
Median (IQR)	52.76 (39.85–62.68)	40.59 (28.65–51.61)	39.91 (28.24–51.48)

2.3 UK Renal Registry

The UK Renal Registry (UKRR) is part of the Renal Association, a not for profit organisation registered with the Charity Commission (Registered in England No. 2229663). It was established in 1997 by the Renal Association with support from the

Department of Health, the British Association of Paediatric Nephrologists and the British Transplantation Society, to act as a source of comparative data for audit of compliance with national clinical practice standards and to assist in the development of patient care in renal disease. The UKRR collects, analyses and reports on data from all 71 adult and all 13 paediatric renal centres in the UK. Though data collection began in 1997, complete coverage was only achieved in 2008. Participation is mandated in England through the NHS National Service Specification and the Chief Executive of each Trust is responsible for adherence to this contract.

The collection and analysis of sequential biochemical and haematological data is a unique feature of the UKRR. The Renal Registry Data Set Specification (RRDSS) defines the data items that are required to be sent from participating renal centres for analysis by the UKRR. Data are downloaded quarterly from the renal information technology (IT) systems of each renal centre and as a condensed dataset from the Scottish Renal Registry in the case of patients attending a Scottish renal centre. This is facilitated by extraction routines written by the suppliers of the IT software and based on original routines written by the UKRR for the Proton IT system. Following extraction, data is transferred to the UKRR via encryption systems, where it is subject to automated validation routines and manual checks by the data management team to identify inconsistencies, missing data and out of range results. Once validated data is uploaded on to the UKRR database where it undergoes further statistical checks to ensure there are no inconsistencies prior to it being available for release. Full details of the data validation process are described in the eleventh annual report[228].

The collection of patient identifiable data is regulated by the National Health Service Act 2006 with the UKRR being granted temporary approval to hold data without patient consent by the Secretary of State under section 251 of this Act.[229] Funding for the UKRR comes from an annual capitation fee levied on RRT patients (per patient from each renal centre). Further information relating to the function and operation of the UKRR can be found in 'Appendix A: The Registry Rationale' of the 2015 Annual Report[229]

2.3.1 Data Items Used from UKRR

In examining the impact of patient and centre variables on access to transplant listing Chapter 6) survival data for the ATTOM cohort being analysed (in the form of date of death), was extracted from the UKRR database using patient identifiers. ATTOM cohort patients were matched to their data held in the UKRR using their NHS number and details of their survival were extracted from their registry timelines.

2.4 NHS Blood and Transplant

NHS Blood and Transplant (NHSBT) was formed in October 2005 as a result of the merger of the National Blood Service and Bio Products Laboratory with UK Transplant. This was given the status of a Special Health Authority within the NHS responsible for encouraging donation, optimising the supply of organs, blood, stem cells and tissues; as well as improving the quality, effectiveness and clinical outcomes of blood and transplant services. The Organ Donation and Transplantation (ODT) Directorate of NHS Blood and Transplant maintains the national transplant waiting list, national donor register, and stores details of all patients transplanted in the UK as well as regulating the allocation of organs nationally[85]. All UK renal centres send paper based clinical outcome data returns to ODT annually for all individuals who have undergone transplantation. These data are analysed and published annually in their annual report.

2.4.1 Data Items Used from NHSBT

In examining the impact of patient and centre variables on access to transplantation (Chapter 6) data on whether patients were wait-listed or not were retrieved from NHSBT. This was undertaken by matching ATTOM recruited patients to those listed for transplantation using their NHS number. Data on the relationship between live donors and their recipients were also retrieved from the NHSBT database for the analyses in Chapter 3.

2.5 Ethics and governance

All research undertaken in this thesis was in line with the Research Governance Framework for Health and Social Care (DH, 2005) and in line with other appropriate professional guidance/regulations. 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.

The UKRR and NHSBT already hold permission to collect and report on anonymised data. Patient identifiable information was directly electronically uploaded onto the secure UKRR server in real time by the research nurses. After authentication of data accuracy, outputs from the UKRR server were anonymised for use in subsequent analyses to ensure there was no danger of compromising patient confidentiality.

Chapter 3: Living Kidney Donor-Recipient Relationships: Gender and Ethnic Variations in the UK

3.1 Introduction

Whilst the number of deceased organ donors available has risen in the UK, the rise has been relatively modest in comparison to the number of patients wait-listed, resulting in an increasing gap between supply and demand. Ethnic minorities face a dual problem of having a higher incidence of ESRD[13, 15-20] and reduced access to cadaveric donors due to HLA matching requirements[230]. As a result, they constitute a disproportionate number on the waiting list in the UK and are subject to longer waiting times in the UK[164, 230] and in other high-income countries[28, 231].

The shortage of deceased donor organs has also placed more emphasis on improving living donor kidney transplantation which itself is often referred to as the 'gold-standard' in terms of transplantation due to conferring better patient and graft outcomes compared to deceased donor transplantation[8-10, 75-76]. Despite this awareness (and national drives to improve living donation) there remains variation amongst ethnic groups with regards to volunteering for living donation. Indeed, significant ethnic differences have been described in both living donor[34-35, 179] and pre-emptive transplantation[24, 33] in the UK and North America, with lower rates of transplantation amongst Black and South Asian patients compared to White patients.

Living donation is made possible only by healthy and willing adults who meet eligibility criteria agreeing to serve as living donors. Motivations behind donation can be complex and have been described in published literature to include compelled altruism, sense of duty/responsibility towards recipient, meeting expectations, perception of personal gain and spiritual[232-234]. These motivational factors are a consequence of the personal relationships that exists between donors and their potential recipients. Despite the fundamental role these relationships play in decision making very little is known about them and whether they differ across ethnic groups.

To improve living donation rates and understand the inequity that exists in live donor transplantation in ethnic minorities, a better understanding of the relationships that

exist between a recipient and their successful donor within different ethnic groups is needed. Studies to date have been restricted to single centre experiences[235-236] with results confounded by local population demography thereby limiting generalizability. Given the absence of robust multi-centre or national data, this study aimed to investigate the personal relationships between those individuals who successfully donate a kidney in the UK and their respective recipients; and to examine any ethnic and gender differences as well as any changes over time, thereby gaining a better understanding of the donor population for different ethnic groups. Analysing observed differences might also lead to a better understanding of the disparity seen in living kidney transplantation across ethnic groups, and highlight areas of further research in improving living donation in ethnic minorities

3.2 Methods

Data for this retrospective observational cohort study were obtained from the UK Transplant Registry held by the Organ Donation and Transplantation Directorate of NHS Blood and Transplant (NHSBT). The Registry was used to identify all living donor renal transplant recipients and their respective donors between 1st January 2001 and 31st December 2010 in the UK (n= 6596).

Using anonymised patient data, we reviewed the demographic characteristics of all living donor renal transplant recipients and their respective donors. The relationship between recipients and their donors was also analysed together with their ethnicity and gender. Relationships were defined as describing 'the relationship of the donor to the recipient', and were categorised into five groups: 'Parent', 'Partner', 'Sibling', 'Offspring' and 'Other'; with each group being further divided by gender. Ethnicity analysis involved categorising all donors and recipients into one of 4 groups: 'White', 'South Asian/Asian' (Indian, Pakistani, Bangladeshi, Sri Lankan), 'Black' (Caribbean and African origin), and 'Other' which included all other reported ethnic groups.

Group/categorical comparisons were performed using a Fisher's exact test, paired non-parametric t test or a Kruskal Wallis test as appropriate. All statistical analyses were performed using SAS version 9.3.

3.3 Results

3.3.1 Gender & Ethnicity

Of the 6596 patients identified as having undergone living kidney transplantation, 16 patients (0.24%) were excluded as the relationship between the donor and recipient could not be deduced due to missing data. Table 3.1 shows the ethnicity and gender distribution of the remaining 6580 patients who received a kidney transplant. For comparison the gender and ethnicity distribution of those listed for transplantation at the beginning of 2012, and those who donated a kidney are shown in tables 3.2 and 3.3 respectively.

Table 3.1. Showing the distribution of patients who received a kidney transplant from a living donor, by gender and ethnicity.

	Male		Female		
Ethnicity	***number***	***%***	***number***	***%***	**Total**
White	3374	*59.1%*	2334	*40.9%*	5708
Asian	326	*69.2%*	145	*30.8%*	471
Black	144	*59.0%*	100	*41.0%*	244
Other	96	*61.1%*	61	*38.9%*	157
Total	***3940***	***59.9%***	***2640***	***40.1%***	***6580***

Table 3.2. Showing the distribution of patients active on the transplant waiting list in the UK on 04/01/12, by gender and ethnicity.

	Male		Female		
Ethnicity	***number***	***%***	***Number***	***%***	***Total***
White	2801	*59.2%*	1934	*40.8%*	4735
Asian	638	*56.3%*	496	*43.7%*	1134
Black	365	*58.4%*	260	*41.6%*	626*
Other	119	*53.6%*	103	*46.4%*	222
Total	***3923***	***58.4%***	***2793***	***41.6%***	***6717****

* includes 1 case where gender not specified

Table 3.3. Showing the distribution of patients who donated a kidney, by gender and ethnicity

	Male		Female		
Ethnicity	***Number***	***%***	***number***	***%***	**Total**
White	2586	*45.5%*	3009	*54.5%*	5687
Asian	197	*45.4%*	237	*54.6%*	434
Black	126	*54.1%*	107	*45.9%*	233
Other	69	*44.5%*	86	*55.5%*	155
Total	***2978***	***45.8%***	***3529***	***54.2%***	***6507****

* 73 patients excluded due to missing ethnicity data

Ethnic minorities were the beneficiaries in only 13.3% (n=872) of all living donor transplantations despite representing 29.5% (n= 1982) of all patients listed for transplantation in the UK. The number of Asian (n=471, 7.2%) and Black (n=244, 3.7%) recipients were both significantly lower than their proportional representation on the waiting list; Asian 16.9% (n=1134) and Black 9.3% (n=626), $p<0.0001$. Amongst recipients, men were the beneficiaries' in nearly 60% of cases (in keeping with their representation on the waiting list). This gender disparity was similar across all ethnic groups though significantly greater in the Asian population where women benefited in only 30.8% of cases, $p<0.0001$ (see table 3.1). In contrast there were no significant differences within ethnic groups amongst those active on the transplant list, with 58.4% of patients listed being male (see table 3.2).

Whilst women received fewer live kidney transplants, amongst those donating a kidney there was a preponderance of women, with 54.2% of all donors being women, which was similar across all ethnic groups except in the Black population, where this observation was reversed and men donated more often (54.1%), $p<0.0001$ (table 3.3).

3.3.2 Donor-recipient Age and Ethnicity

The mean age of donors was 46.2 years (SD=11.6, CI: 45.9-46.5yrs), which was significantly higher (p value <0.0001) than the mean recipient age of 40.2 years (SD =15.5, CI: 39.8-40.5yrs). This age difference was most pronounced in the White population (see table 3.4).

Table 3.4. Showing the age distribution of patients who received a live donor kidney transplant between 2001-2010 in the UK and their respective donors, across different ethnic groups.

	Overall	White	Asian	Black	Other
Recipient					
Mean Recipient Age (years)	40.16	40.19	40.44	41.81	35.09
95% Confidence Interval	(39.78-40.53)	(39.79-40.59)	(39.02-41.87)	(40.15-43.46)	(32.54-37.64)
Median	41	41	41	42	35
IQR	29-52	29-52	30-53	34-51	23-48
Donor					
Mean Donor Age (years)	46.2	46.99	42.46	39.41	39.46
95% Confidence Interval	(45.94-46.5)	(46.69-47.29)	(41.37-43.55)	(38.06-40.76)	(37.63-41.30)
Median	46	47	42	39	39
IQR	38-55	39-55	34-51	31-46	29-48

3.3.3 Living Kidney Donor-Recipient Relationships

Parental, spousal and sibling donation accounted for more than 80% of all living kidney donations in the UK between 2001-2010, with significant female preponderance seen within both spousal and parental donation. However, the pattern of donor-recipient relationships varied by ethnicity ($p < 0.001$), see table 3.5.

Table 3.5: Showing the gender distribution and relationship between live kidney donors and their respective recipients by ethnic group, for all live kidney transplants performed in the UK between 2001-2010.

Donor Ethnicity*		Relationship of Donor to Recipient				
		Parent	**Partner**	**Sibling**	**Offspring**	**Other**
White	N-total (%)	1774 (31.2)	1367 (24.1)	1571 (27.6)	357 (6.3)	616 (10.8)
	% Female	55.7%	61.5%	50.4%	47.1%	50.7%
Asian	N-total (%)	108 (24.9)	88 (20.3)	132 (30.4)	46 (10.6)	60 (13.8)
	% Female	57.4%	78.4%	45.5%	52.2%	36.7%
Black	N-total (%)	39 (16.7)	24 (10.3)	110 (47.2)	32 (13.7)	28 (12.0)
	% Female	61.5%	70.8%	40.0%	46.9%	25.0%
Other	N-total (%)	44 (28.4)	18 (11.6)	54 (34.8)	22 (14.2)	17 (11.0)
	% Female	61.4%	83.3%	53.7%	31.8%	47.1%

* 73 patients were excluded due to missing donor ethnicity data

Spousal donation was similar in both White 24% (n=1367) and Asian 20.3% (n=88) populations, but significantly reduced in the Black population 10.3% (n=24) p=0.0001 (fig. 3.1), which had significantly higher sibling donation (47.2%) p<0.0001. Though spousal gender disparity (female preponderance) was universal in all groups this was significantly greater in the Asian population where women donated 78.4% compared to Black 70.8% and White 61.5% donors, p<0.0001 (fig. 3.1). Gender disparity was not seen amongst offspring donating to parents.

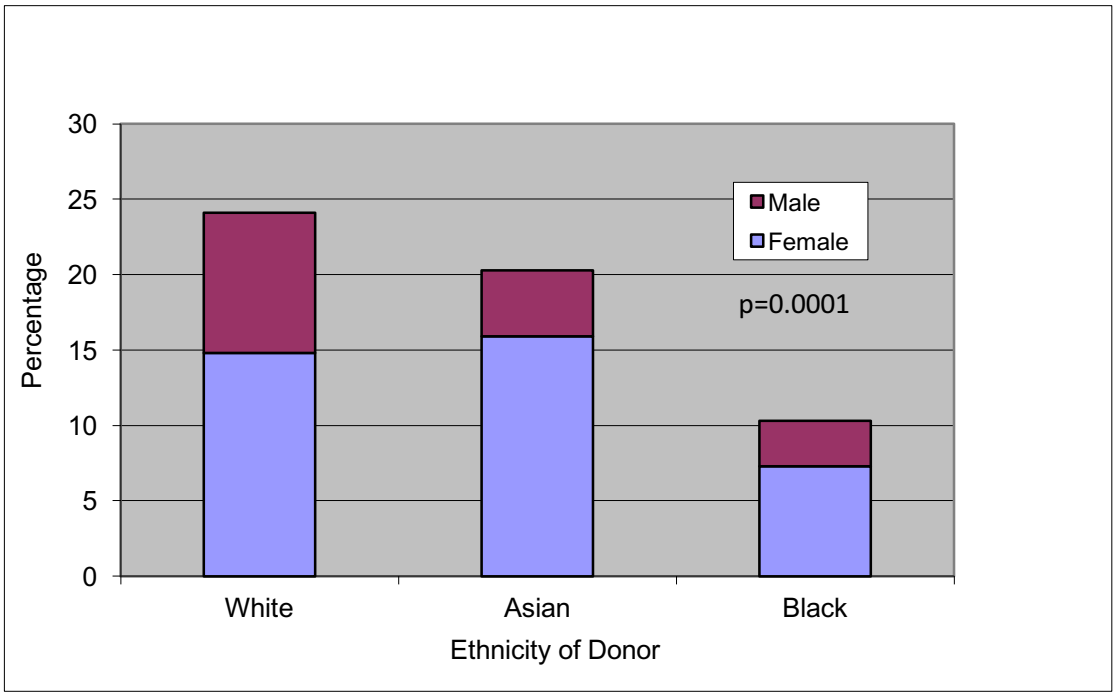

Figure 3.1. The proportion of all live kidney transplants between 2001-2010 in the UK from a spouse/partner, by ethnic group, and the gender distribution within each ethnic group.

Analysis of living kidney donor relationships over time shows that the proportion of parental donations has reduced, with a rise in kidney donation from 'offspring' and from 'other' relationships $p<0.001$(fig 3.2). This trend was also significant in the Asian sub-group analysis $p<0.01$.

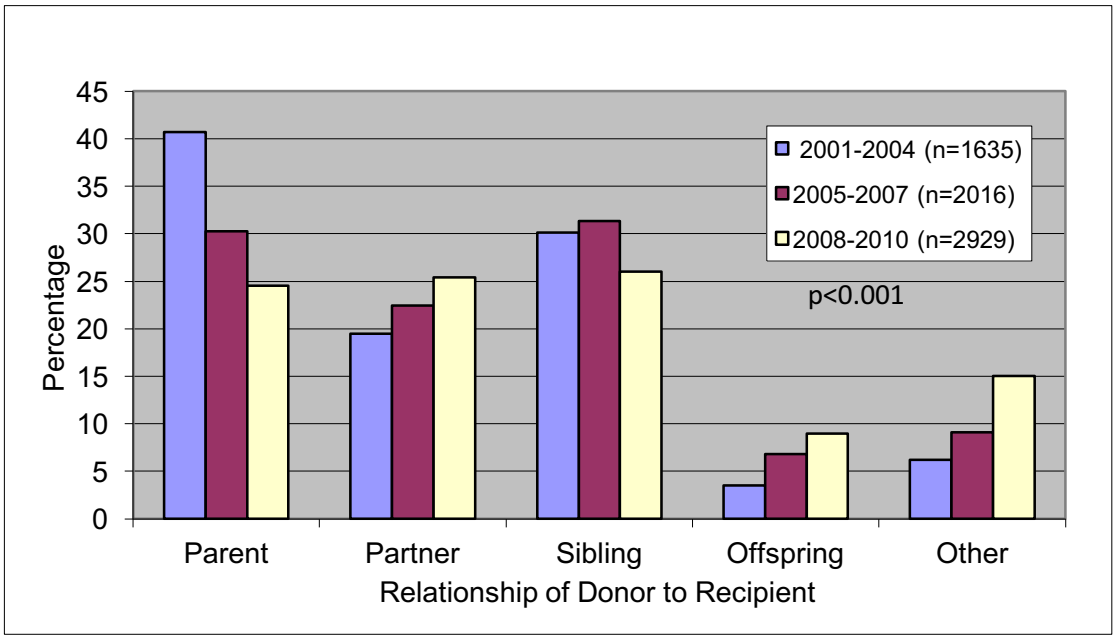

Figure 3.2: Changes in the percentage distribution of the relationships between live kidney donors and their respective recipients between 2001-2010.

3.4 Discussion

This study represents the largest analyses to date of the relationships between recipients and their respective live kidney donors and highlights several important ethnic and gender differences. Despite representing more than a quarter of all patients listed for transplantation in the UK, living kidney donation occurs less frequently than expected in ethnic minorities (as compared to their proportional representation on the waiting list), and is subject to several significant unexplained relationship differences.

The observation that men are the beneficiaries in the majority of live donations (in keeping with their representation on the waiting list) is not surprising and similar to other international reports[237]. However, our study highlights that this gender imbalance is significantly greater in women of Asian ethnicity who not only benefit least from live donation (31% versus 40.1% for overall group) but are also the recipient of a 'spousal kidney' in just 21.6% of Asian spousal donations – much lower than all other ethnic groups. Thus raising the notion that Asian women are subject to a 'double inequity' with reduced likelihood of receiving not only a deceased donor kidney (as a consequence of their ethnic minority status)[176, 178] but are also least likely to receive a live donor kidney, especially not from their male spouse.

One of the reasons behind this gender imbalance might be the increased prevalence of co-morbidities, in particular diabetes in the Asian population[169], which might have rendered many potential Asian male donors unsuitable for donation. Indeed, as this analysis only examines successful donors we are unable to comment on those that 'intended to donate' though were deemed medically unsuitable. Other potential reasons for Asian women not benefitting from living donation may include language and cultural barriers, greater difficulties negotiating healthcare systems as well as poorer health literacy[235-236].

As for female preponderance amongst live kidney donors, this is well known and has been reported in several studies[238-239], with a higher incidence of kidney disease in men, fear of losing the earning male member, and perception of renal donation as an extension of responsibility toward family in females all being cited as reasons[236]. In

contrast, the observation in this study that amongst black ethnic groups men actually donate more than women has not been reported before.

The reason for why this trend would be reversed in the black community in the UK is unclear with cultural and socioeconomic factors likely to be playing a role. This observation should also be interpreted with caution as it may be a consequence of having small numbers in the analysis though certainly warrants further investigation. In contrast, the lower spousal donation rates seen in the black ethnic group has previously been noted in a single centre study in the United States where it was thought to have arisen as a result of centre efforts to find a healthy younger cohort of donors in African American populations with less extensive donor testing[235]. Similar bias may well be affecting choice of live donors amongst black ethnic groups in the UK driving more donation from offspring and siblings.

Such practices (where donation occurs from someone with a shared genotype) may need to be reviewed especially in light of mounting evidence regarding mutations in the APOL1 gene, which has been shown to be highly associated with ESRD and is more common in those of African ancestry[166]. As our understanding of these mutations improves and more long-term outcome data becomes available on black ethnic group donors it is seems likely that donation patterns may change and will need to be factored in when interpreting donor-recipient relationships in black ethnic groups[239].

As for the relationships between living donors and their recipients changing over time (fall in parental donation with a rise in kidney donation from 'offspring' and from 'other' relationships), these observations are similar to trends observed in the United States[237]. This may reflect improved awareness of the benefits of transplantation amongst recipients' relatives, improved living donor focus in centres and better education as well as changing public attitudes. These changes are also in keeping with the rise in emotionally uninvolved donors (altruistic or non-directed donors) seen both in the UK and USA[237, 240-241].

Though this study utilised a large national dataset with accurate characterisation of donor-recipient relationships, some limitations of this registry-based analysis require consideration. The lack of data on who was approached for living donation and

refused as well as who intended to donate or underwent assessment for possible live kidney donation but were deemed medically unsuitable must be acknowledged when interpreting the results of this study. Also, despite collating the entire UK transplant experience over a decade, some sub-groups still have small numbers introducing statistical uncertainty. Finally, this study does not adjust for socioeconomic status, which has been shown to influence sources of living kidney transplants in the white population, with recipients from lower socioeconomic status being less likely to receive a spousal kidney and more likely to receive a kidney from a sibling or their child[241].

To conclude despite representing more than a quarter of all patients listed for transplantation in the UK, living kidney donation occurs less frequently than expected, and is subject to significant unexplained relationship differences amongst ethnic minorities with changes noted over time. It is anticipated that these insights into living donor-recipient relationships in the UK will assist clinicians in better tailoring their approach to exploring potential kidney donors with patients as well as facilitating more targeted educational programs for ethnic minorities thereby improving live kidney transplantation especially in ethnic minorities. Further research is warranted to understand these relationship differences, so as to help develop strategies to increase donation rates in ethnic minorities especially from male spouses.

Having described the relationships that exist between living kidney donors and their recipients in this chapter, the rest of this thesis focuses on the second aim; to explore which patient-specific and centre-specific factors influence access to the transplant waiting-list. For this purpose, a mixed methods approach has been adopted, which includes a qualitative study (chapter 4), national survey (chapter 5) and quantitative analysis using prospectively collected data from the ATTOM study (chapter 6).

Chapter 4: Qualitative Study Exploring Centre Practice Patterns in Listing Patients for Transplantation

4.1 Introduction

4.1.1 Epistemology approaches

Historically, research in nephrology has primarily been experimental and quantitative in nature in order to try and eliminate bias from research and to obtain objective results, following a 'realist' approach. A realist approach aims to maintain the perspective that there is one true reality, independent of human thought and experience, and that by undertaking rigorous research studies, scientists can uncover that true reality[242]. Researchers supporting this view believe that research studies should try to minimise bias as much as possible in order to make objective observations about the physical world (Yardley and Marks, 2004)[242].

Whilst this approach has many benefits (especially in basic science studies/ experiments) critics of this perspective have argued that humans are unable to view the world objectively and that our interpretation of the physical world will always be influenced by our understandings and interpretations[242]. Those who support this idea believe more in (i) constructivism which represents the idea that humans "construct" the world around them and interpret their interactions with their physical environment in a way which fits in with their existing knowledge (Yardley and Marks, 2004), or (ii) relativism which is the concept that points of view have no absolute truth or validity, having only relative, subjective value according to differences in perception and consideration[242].

Appreciation of these different epistemological approaches has greatly increased amongst researchers over recent years not least amongst those involved in clinical medicine (including nephrology) which in turn has seen a shift from performing only 'quantitative' research to also adopting the use of qualitative methodology which lends itself more towards constructivism and relativism. This shift may have come about through a realisation that "real life" cannot be replicated in a laboratory experiment (Eisner, 2003)[243], with researchers noting significant advantage in being

able to understand peoples' experiences and behaviour by exploring their perceptions, ideas and judgements about different topics[243].

4.1.2 Rationale behind adopting qualitative methodology

In exploring individuals' understandings of the world, for example, their understanding of a particular procedure or process, qualitative research can appear to be naturally more driven by a relativist perspective. For example, in asking about healthcare professionals' understanding of the processes involved in listing patients for transplantation, and accepting that individuals may have different perspectives on this, gives rise to the idea that there can be multiple realities about going through a particular process.

Indeed, Eisner (2003) states "that in one sense all research is qualitative because all experience is in some way qualitative; qualities are the sources our senses pick up as we have intercourse with the environment" (pp. 20)[243]. Eisner (2003) suggests that both qualitative and quantitative research report on qualities which are experienced by humans but that these approaches differ in how they report these qualities. He states that quantitative research uses quantification which "describes with respect of magnitude" and qualitative research uses qualification which "describes through the use of descriptive language and the meanings associated with such language" (pp. 20)[243].

Qualitative research is aimed at gaining a deep understanding of how individuals derive meaning from their surroundings or experiences. Rather than generating numbers as in quantitative research, qualitative methodologies use participants' language in order to provide a detailed, descriptive account of a situation[244]. This is beneficial in studies where a new area is being explored and/or where little is previously known about individuals' behaviours, thoughts or experiences.
This is also beneficial in studies seeking to provide insight into how complex organisations work (including renal centres) where a quantitative approach might be too restrictive whilst a qualitative approach would help gather multiple perspectives and as a consequence a more detailed understanding of the overarching process within an organisation.

As there has been very little exploration of health professionals' views and experiences of practice patterns for listing patients for transplantation, a qualitative approach was considered appropriate for exploring this process and experience. As well as capturing any variations across renal centres across the UK, qualitative research methodology would also provide an opportunity to search for more in-depth understanding about perceived barriers and facilitators for listing and seek explanations as to why that may be the case. The results from this study could then be utilised to design a survey tool, facilitating a mixed methods approach, which would allow one to capture the reality of how centres are organized and the practices that operate to list patients for transplantation.

Using qualitative methods would also allow one to retain the context in which results were obtained in order to help explain data. This can be beneficial when exploring a process such as access to transplantation which may differ in factors which can influence results. For example, in renal centres which have a large population of patients from different cultural and ethnic backgrounds the presence of a 'multi-linguistic education team' may be viewed very differently but this may not be apparent if using a purely quantitative measure of education provision which did not consider culture and ethnicity.

4.1.3 Rationale for qualitative semi-structured interviews

In this study qualitative semi-structured interviews were considered the appropriate form of data collection rather than focus groups. Qualitative semi structured interviews and focus groups both allow for exploration of set topics from a guide and allow for exploration of emergent views. However, adopting a focus group approach may have hindered the ability of all participants to discuss their feelings and opinions openly due to feeling inhibited by the presence of their seniors and different professional groups[245-246]. Semi-structured interviews are also more practical for doing research in the field, especially when researching sensitive topics or when there is little prior knowledge about a unit's listing process before the interview commences. Qualitative semi-structured interviews allow the generation of in-depth data as it

allows the perspectives and priorities of individuals to be revealed without imposing the preconceptions of the researcher (Seale, 2004)[247].

Qualitative semi structured interviews also give an opportunity to encourage and probe the respondent for more information and clarify meaning as well as observe non-verbal behaviour to assess the validity of the respondent's answer[247-248]. One could also ask questions to confirm that their understanding of a particular question is correct, and observe the respondents' non-verbal behaviour. For example, if the respondent does not want to talk, does not make eye contact while answering a question, laughs or looks angry while talking about something. Finally, using qualitative methods would also allow one to identify factors which may influence the behaviour of interest and explore these in relation to the contexts in which they appear. This then allows for the possibilities of finding "multiple truths" which may represent multiple realities or offer perspectives on a true reality depending on one's epistemological perspectives.

4.1.4 Types of Qualitative Analysis Methods

Several methods exist to analyse qualitative data each with their own merits and limitations. For the purpose of this study two main methods were considered for use: Framework Analysis and Thematic analysis.

4.1.4.1 Framework analysis

Framework analysis was developed by Jane Ritchie and Liz Spencer, from the Qualitative Research Unit at the National Centre for Social Research in the United Kingdom in the late 1980s as a qualitative analysis approach which provided a systematic way of handling a large data set for use in large-scale policy research[248]. Framework analysis is now used widely in other areas, including health research[249-252] where research studies are carried out to answer specific questions to inform policy and/or practice. The analysis involves several stages: familiarisation, identifying a thematic framework, indexing, charting, and mapping and identification[248].

- Familiarisation: involves re-listening to the audio recording and or re-reading transcripts with any contextual or reflective notes that were recorded by the interviewer several times so as to develop an understanding of the data as a whole begin the process of identifying important topics within the data.

- Identifying a thematic framework: After familiarisation, transcripts are coded line by line adopting either inductive or deductive approaches depending on the research question. In more inductive studies, 'open coding' takes place, i.e. coding anything that might be relevant from as many different perspectives as possible. In contrast, in deductive studies the codes may have been pre-defined (e.g. by an existing theory, or specific areas of interest to the project). Coding aims to classify all of the data so that it can be compared systematically with other parts of the data set. After coding a sample of transcripts, codes undergo categorisation and an analytical framework is constructed which often requires several iterations to ensure no further codes emerge.

- Indexing: After constructing an analytical framework, it is then applied by indexing subsequent transcripts using the existing categories and codes. Indexing ensures that each data source, is analysed and indexed according to the thematic framework to ensure that data analysis is comprehensive and covers all the relevant data available.

- Charting: This involves summarising the data by category from each transcript. Care must be taken to strike a balance between reducing the data on the one hand and retaining the original meanings and 'feel' of the interviewees' words on the other. A spreadsheet is often used to generate a matrix and the data are 'charted' into the matrix.

- Interpretation: This final stage involves looking at the patterns and relationships emerging between categories and data sources. The matrix structure is helpful in facilitating recognition of patterns in the data including through drawing attention to contradictory data, deviant cases or empty cells.

Whilst the structured approach recommended in analysing data using Framework analysis aids both data analysis and transparency in data analysis, the main disadvantage of adopting this approach is that Framework analysis is not suitable for accommodating highly heterogeneous data; as data must cover similar topics to facilitate categorisation[253]. Additionally, alongside being time consuming and resource intensive (similar to other qualitative analysis methods) there is a high training component to successfully utilising the method[253].

4.1.4.2 Thematic analysis

Thematic analysis is the most common form of analysis in qualitative research providing a systematic way of handling large sets of raw data[254]. It also offers an inductive approach and can provide a description of the phenomena as well develop meaningful themes without generating theory, and is theoretically flexible for the purpose of a mixed methods or pragmatic study. Braun & Clarke (2006)[255] outline six steps in conducting thematic analysis these include: familiarisation with data, generating initial codes, searching for themes among codes, reviewing themes, defining and naming themes, and producing the final report[255].

- Familiarisation with data: This step involves the researcher immersing themselves in the data becoming familiar with the content, breadth and depth. This often involves re-listening to the audio recording and or re-reading transcripts with any contextual or reflective notes that were recorded by the interviewer several times whilst searching for patterns.

- Generating initial codes: This involves systematically working through the entire dataset, and identifying important issues which are being discussed and then coding on a line by line basis, assigning labels to identify common sections of text. This process can be carried out inductively, with code labels staying closely linked to the raw data, or deductively where an existing framework or theory is applied to the data

- Searching for themes among codes: This step involves analysing the low level codes and combining them to form overarching themes emerging from the data.

- Reviewing Themes: This step involves reviewing each of the themes and associated data to see if they formulate a coherent pattern or if they require refining.

- Naming Themes: This step involves defining what each theme is about and determining what aspect of the data each theme captures.

- Producing final report: The final step after finalising a set of fully worked-out themes is to write up the analysis providing sufficient evidence of the themes within the data.

As with other qualitative methodologies thematic analysis also has several limitations. These include: the potential to miss nuanced data, organising data as per the researcher's own views instead of representing an individual participant's story and the potential to produce superficial themes, over more conceptual ideas[256].

4.1.5 Rationale for Choosing Thematic Analysis

Despite the above listed limitations thematic analysis was chosen as the preferred analysis method for this study as it had several advantages above the other methods. Firstly, this method did not require a high training component and was less resource-intensive than Framework Analysis[257]. Secondly, thematic analysis lends itself better to understanding and identifying barriers in complex health processes, as in this study, where there is already a body of existing information as compared to adopting a grounded theory approach which is more explorative and theory generating[258]. Another advantage of thematic analysis is that themes often directly relate to practice or policy (as can Framework) and can therefore be used to help address and answer questions in these areas without the need for policy makers to undertake further interpretation[254, 259].

4.2 Participants and Methods

4.2.1 Design and Setting

Having identified the benefit of pursuing qualitative research, in conjunction with the NIHR funded ATTOM project, this qualitative study was designed to explore the practice patterns in listing patients for transplantation across the UK. This was performed with the objective that by understanding the different practice patterns that exist one might be able to explain some of the inter-centre variation that exists between centres, and to use the results to devise, develop and test a credible structured questionnaire for use in a survey of all UK renal centres (transplanting and non-transplanting).

The study design focused on conducting semi-structured interviews with 'key stake holders' involved in listing patients for transplantation within a purposive sample of 9 renal centres across the UK. Semi-structured interviews allowed pre-determined questions to be devised using known published literature so that the aims of the study could be addressed but they also permitted flexibility (as discussed earlier).

Whilst all UK renal centres (n=71) were deemed eligible for this study, nine centres were purposively sampled using maximum variation sampling to include a range of variables including: degree of listing for transplantation (using data available from the UKRR), whether the centre was a transplant or non-transplanting renal unit and geography which included capturing a spread in deprivation and ethnicity of the centres' catchment areas.

4.2.2 Ethics

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.

4.2.3 Participant Recruitment

The clinical director of each chosen renal unit was formally contacted by email and their unit was invited to participate in the study. Following their approval, a letter of access was sought from the local research and development department of each participating renal unit in keeping with the ethics and clinical governance approvals within the ATTOM grant application. Key stakeholders were then recruited from the four transplanting and five non-transplanting renal centres that had been identified by our sampling. These individuals were identified directly by contacting the clinical director at each respective unit by email and asking them to identify which individuals they believed played an important role in the provision of renal services locally, in particular listing patients for transplantation. These individuals were then contacted and invited to participate. By allowing any healthcare professional involved in listing patients for transplantation to be included, this enabled the views of a diverse range of individuals recruited to be analysed including: clinical directors, consultant nephrologists, consultant transplant surgeons, staff grades, low clearance clinic nurses, nurse educators, ethnic liaison officers, transplant co-ordinators and living donor nurse co-ordinators.

4.2.4 Data Collection

To guide the semi-structured interviews an interview guide was designed, which was informed by a literature review of existing qualitative and quantitative research, and input from several experts (Consultant Nephrologists, Transplant Surgeons, Transplant Co-ordinators and Low Clearance Nurses). The interview guide was piloted in 4 pilot interviews conducted in a local renal centre to enable its' further development in terms of its flow, question design and acceptability as well as to identify additional questions. Interviewees included a consultant nephrologist, a consultant transplant surgeon, a dialysis nurse and a transplant co-ordinator. The topic guide was then continually refined in an iterative manner throughout subsequent interviews as new topics were introduced by participants. The following topics were explored within each interview: the local chronic kidney disease service, information provision on transplantation and the transplant recipient assessment process (including perceived barriers and enablers). Please refer to Appendix: C: Staff Interview Guide.

Face-to-face semi-structured interviews with key stakeholders were conducted between February and September 2012. Interviews took place in a private office chosen by the participant at their place of work, and consent was obtained prior to commencing the interview. Interviews were conducted until theoretical saturation[252] was reached with no new information or themes being identified. All interviews were audio-recorded and transcribed verbatim in preparation for analysis. Transcripts were transcribed by a professional transcriber familiar with handling qualitative data, and were then proof checked by RP for errors by listening to the audio against the transcript. Participants were assured that all information would be kept confidential and that transcripts of interviews would be anonymised. This included anonymising all participant and centre names.

4.2.5 Analysis

A thematic analysis based on the data-driven inductive approach of Braun & Clarke (2006)[255] was conducted (as described earlier). Analysis of transcripts was facilitated by NVivo 10 software.

The analysis involved an iterative and reflective process and began as soon as data collection commenced. RP initially became familiar with the data which involved reading through the transcripts repeatedly, and reviewing the original audio recordings to ensure that there were no transcription errors. Once familiar with the data, interviews were coded on a line by line basis independently by RP, assigning labels to identify common sections of text. This produced a number of low level codes which were reviewed and combined to produce themes emerging from the data with regular discussion with the research team. Initial transcripts were reviewed in an iterative fashion as themes developed and themes elicited during initial interviews were confirmed in the latter ones.

Themes were continuously revised and refined moving back and forth between transcripts as analysis progressed over the remaining interviews. Agreement on themes and sub themes was sought by members of the research team and inconsistencies were discussed and resolved. Ten transcripts were coded

independently by MC in order to provide a check for the consistency of coding and meaning of themes. Further analysis was conducted to produce a final summary of the themes by RP which were discussed within the wider research team.

Using this grounded, line by line approach to initial coding, to develop a thematic framework for the data, facilitated an inductive approach to data analysis and avoided fitting the data into a pre-existing framework based either on previous research or the researcher's own preconceptions.

4.3 Results

4.3.1 Centre Characteristics and Participant Demographics

In total, forty-five key stakeholders participated in this study from nine centres across the UK (7 from England, and 1 each from Scotland and Wales). Interviews lasted between 35 to 98 minutes, with a median of 57 minutes and were conducted in a hospital office or meeting room. Participants included the clinical director of each of the nine units, alongside a range of individuals with varying roles though each with extensive experience in listing patients for transplantation. Further details on participant characteristics are shown in table 4.1.

As a consequence of purposive sampling, the nine participating centres were a diverse cohort as shown in tables 4.2 and 4.3. The catchment areas served by each centre varied from 0.62 to 2.02 million people, and four of the centres (44%) had an active transplant programme. Incidence and prevalence rates for RRT across these nine centres varied widely as did the proportion of patients belonging to ethnic minorities. Amongst incident patients the proportion of non-white patients ranged between 0 and 63.6%, whilst amongst the prevalent population it ranged between 1.1 and 61.6%. As for access to transplantation, the proportion of patients listed within two years from starting dialysis and the median time to listing also varied between centres from 34.7% to 65.1% (risk adjusted) and 91-1225 days respectively. This was also reflected in outcomes, with nearly a quarter of patients transplanted at 90 days post start of RRT at one centre whilst this was as low as 3.1% at another centre.

Table 4.1: Showing participant characteristics of stakeholders interviewed for qualitative study

Participant Characteristics	N (%)
Total Number of Participants	45
% Female, N (%)	22 (48.9)
Distribution of Participants across UK	
England	35(77.8)
Wales	5(11.1)
Scotland	5(11.1)
Overall	45(100)
Number of Clinical Directors	9 (20)
Role within Renal Centre, N (%)	
Consultant Nephrologist	18(40)
Consultant Surgeon	5(11.1)
Transplant Co-ordinator	6(13.3)
Living Donor Nurse	6(13.3)
Nurse Other (e.g. Low Clearance/Pre-dialysis Nurse)	9(20)
Allied Healthcare Worker	1(2.2)

Centre	Catchment Population (millions)	Incidence Rate of RRT (pmp)	% Incidence Non White	% Transplanted at Day 90	Transplant Centre (Y/N)	Number of Prevalent RRT Patients	Number of Prevalent Dialysis Patients	Prevalence Rate of RRT (pmp)	Median Age of Prevalent RRT Patients	% Prevalence Non white
1	1.83	169	63.6	6.4	Y	2236	1195	1222	55.7	61.6
2	0.62	102	3.2	4.5	N	452	229	731	58.2	3.3
3	0.65	127	40.2	13.3	N	549	244	842	54.7	43.8
4	0.67	118	30.4	3.9	N	575	393	860	60.4	29.8
5	1.16	110	5.5	24.4	Y	1243	398	1073	58.6	8.1
6	2.02	111	6.3	14.6	Y	1595	696	788	58.7	5.9
7	1.09	128	1.5	3.1	N	950	510	872	63.2	1.1
8	0.89	120	0	4.5	N	704	387	795	64	2.3
9	1.62	112	-	16.3	Y	1641	635	1011	56.9	-

Table 4.2: Showing centre characteristics of the incident and prevalent patients having renal replacement therapy at the nine chosen centres in 2012 as reported to the UK Renal Registry.

Centre	RRT* N	Registrations N	% wait listed		Median Time to Listing (Days)
			Unadjusted	Risk-adjusted	
1	441	206	46.7	46.4	816
2	101	50	49.5	47.8	413
3	111	51	45.9	44.7	773
4	131	47	35.9	34.7	765
5	153	91	59.5	56.8	128
6	231	154	66.7	65.1	91
7	149	62	41.6	42.9	1225
8	150	56	37.3	37.1	870
9	257	127	49.4	64.3	548

Table 4.3: Showing the percentage of patients wait-listed for a kidney transplant for each of the nine centres, prior to or within two years of starting dialysis (between 1st January 2008 and 31st December 2010) and the median time to wait listing for a kidney transplant (censoring at the earliest of death or 31st December 2012). *RRT denotes the number of patients starting renal replacement therapy at each centre between 1st January 2006 and 31st December 2008

4.3.2 Qualitative Findings

Eight themes were identified from the interview data, each with subthemes. These are listed in Figure 4.1. A schematic drawing showing the interaction between themes was also constructed and is shown in Figure 4.2.

Figure 4.1. Showing the eight themes identified from the analysis of 'Key Stakeholders' views on listing patients for transplantation

1 - Chronic Kidney Disease Pathway of Care:
- Variation in clinic models for CKD care
- Logistics of delivering outpatient clinical care
- Impact of population demography and geographical spread
- Presence of multi-skilled workforce
- Effective approachable leadership of service

2 - Transplantation Assessment Pathway of care:
- Heterogeneity in assessment protocols
- Variation in timing and logistics of assessment
- Level of surgical involvement
- Implementation of Information Technology systems

3 - Cardiac assessment:
- Cardiac assessment ambiguity
- Clinical utility of screening asymptomatic patients
- Quality of cardiac department service provision
- Importance of designated cardiologist

4 - Education and Information:
- Granularity in delivery processes
- Facilitate engagement and shared decision making
- Tailoring language to patient
- Overcome language barriers in BME groups

5 - Decision making:
- Consultant led approach
- Multi-disciplinary team meeting approach
- Level of transparency in communicating decision
- Role of audit mechanisms

6 - Human drivers:
- Physician Enthusiasm
- Performance Recognition
- Patients activation
- Accessible support

Figure 4.1: Continued. Showing the eighth themes identified from the analysis of 'Key Stakeholders' views on listing patients for transplantation

7 - Efficiency reducing human factors:

- Ineffective teamwork
- Patient passivity and disengagement
- Staff shortages
- Employee disenchantment
- Physician belief driven delay

8 – Strategies for improvement:

- Derive national consensus on recipient assessment
- Research cardiac outcomes
- Provision of resources to improve staff shortages
- Interlinking IT Systems
- Improve education for BME groups

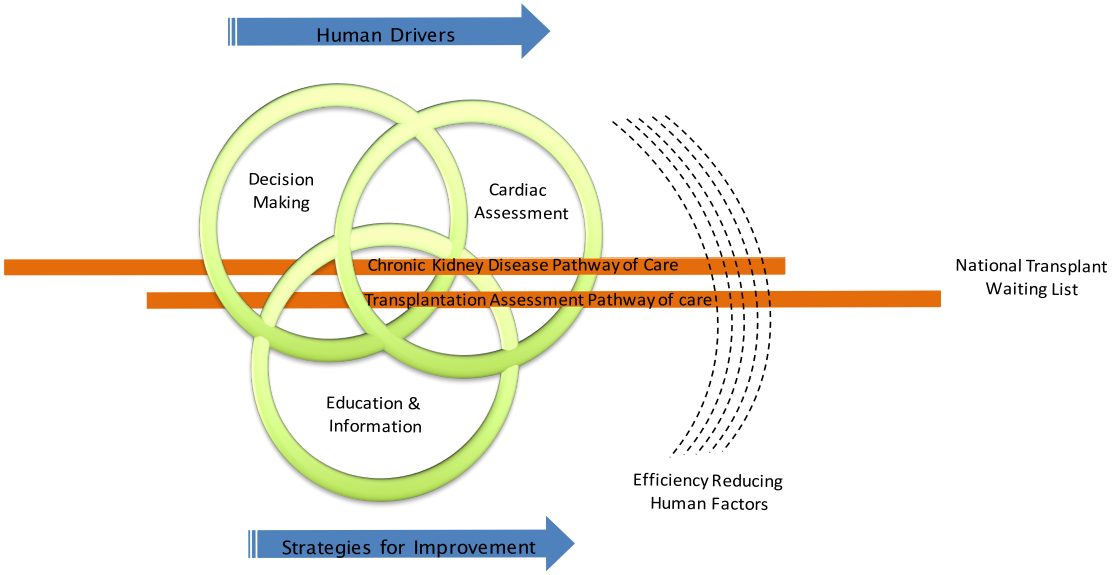

Figure 4.2. A schematic drawing representing the eight themes identified from the analysis of 'Key Stakeholders' views on listing patients for transplantation

Chronic Kidney Disease Pathway of Care:

Participants reported utilising different clinic models for managing chronic kidney disease (CKD) patients, with the majority of participants reporting using a low clearance service – where all pre renal replacement therapy (RRT) patients were seen in a dedicated clinic by a multidisciplinary team.

> "Despite having to cover a wide catchment area, which I'm sure you know. We make sure that all of our low clearance patients are seen in a low clearance clinic. All the consultants here believe it offers the best model of care….We have an excellent multi-disciplinary team present so patients can see a dietician, [name of nurse] our education nurse or whoever on the same day too…I think it works really well" (Consultant, 1)

> "As soon as their eGFR hits 20, they get moved into a low clearance clinic where they get seen by [name of consultant lead for low clearance], the anaemia nurses, transplant co-ordinator, dietician etc..etc…" (Consultant, 6)

Other participants reported seeing patients in isolated 'mixed nephrology' clinics as they did not believe that the low clearance clinic model offered any additional benefit suggesting it could adversely affect patient-physician continuity of care and lead to longer commuting times for patients.

> "Look, I know they use low clearance clinics in London but we don't. Because frankly speaking I don't think they add anything….I mean, I don't think if I sent a patient of mine to one that they would gain anything…..I manage their whole care from diagnosis to starting dialysis or whatever in my nephrology clinic locally……It's better for the patient as they always see me and don't waste time travelling long distances." (Consultant, 3)

> " No, we don't use low clearance clinics. We have mixed clinics where we see all patients pre dialysis and dialysis patients together" (Nurse, 2)

Clinic models also differed in their logistics in terms of where they were delivered with some opting for a 'hub and spoke' model and others travelling to clinics set up at local hospitals away from the main central renal unit.

> " We have low clearance clinics in [area 1], [area 2], [area 3] and [area 4] so patients don't have to come here [main hospital] and we can generally see them locally" (Consultant, 4)

> "We run a hub and spoke system…..all patients are seen here [main hospital] in our low clearance service irrespective from where they live or are referred from [area 1], [area 2] or [area 3]. " Consultant, 1)

Participants reported that services differed from other centres as a consequence of meeting unique centre specific needs driven by the geographical spread and population demographics of their centre's catchment area.

> "Our service has evolved like I suppose many others have, driven by our local population…I think one should be careful before saying that we should all do something one way as we all have different needs…..We for example have a very elderly population and cover a wide catchment area so have set up our service to avoid making our elderly patients travel long distances….one hat does not fit all in medicine" (Consultant 2)

To meet these needs many participants also stated the importance of having a multi-skilled workforce to help facilitate the delivery of an effective service, with many saying that staff shortages often led to inefficiency and reduced quality.

> "I think the reason why we do so well is because we have an excellent team of physicians, surgeons, and nurses who all make things happen quickly". (Consultant, 7)

> "The hospital I cover in [area], has the best rate in terms of listing patients… the department works well because we have everyone present there so no one needs to go anywhere else. We have access to surgeons, dieticians, an education nurse and even a psychologist" (Consultant, 5)

> "Our listing rates have gone down since our transplant co-ordinator left….we know this as we have audited our data. Unfortunately we have not been able to recruit anyone into the role….I gather there is no money. It's a shame as it's the patients that suffer" (Nurse, 1)

The presence of effective approachable leadership was also seen to be important in delivering a successful CKD service and to champion transplant listing. In most units this leadership was provided by a consultant nephrologist whilst other units opted for a nurse led service.

> "Our low clearance service is very much consultant led. Patients may see a nurse or junior doctor but I oversee everyone's management and review everyone's blood tests results…..Prior to clinic I also remind people to review the transplant status of people that they see in clinic and call me if they are uncertain" (Consultant 8)

> "Dr [name of consultant] is excellent. Ever since she came she has really taken hold of the low clearance clinic service. She is really pro transplantation and tries her best to get most people listed. She makes sure tests get done and if we have any problems we can always go to her. She is lovely." (Nurse 4)

Transplantation Assessment Pathway of care:

The majority of participants reported having written assessment protocols for listing patients for transplantation which included defining essential clinical parameters as well as listing which investigations were necessary prior to a patient being listed. Protocols were seen to vary widely between centres both in design, content and the use of risk stratification on the basis of a range of different risk factors.

> "…in our hospital, patients are worked up for transplantation using this

> [interviewee shows piece of paper] protocol. It lists which tests need to be done and takes into account what your risk factors are; and depending on the results what you need to do afterwards. It's fairly self-explanatory and easy to follow, you can have it for your records if you like…" (Live Donor Nurse, 1)

> " we follow the same protocol as the one in [name of local transplanting centre]. As all our patients get seen there afterwards if makes sense. It stratifies people into different risk groups. It tells you who needs an echo and who doesn't, and takes into account if they are a smoker, are diabetic or overweight…" (Consultant, 20)

Variation was also seen as to the logistics of where investigations were performed with patients having all tests performed on site in some centres, and others needing to refer patients to alternate hospitals to have their investigations performed.

> "all tests in relation to a patients' transplant assessment are conducted here. That includes all their tissue typing and all their cardiac work up" (Transplant Co-ordinator, 3)

> "…we do some of the basic tests, such as ECG, chest x-ray and bloods, but everything else including their tissue typing bloods only get done at [name of transplanting centre] after they are referred there by [name of consultant nephrologist]" (Transplant Co-ordinator, 1)

> "if [name of consultant] thinks that they are suitable, he refers them to [name of transplanting centre] where they get all their tests done. We don't do any tests here" (Nurse, 7)

Alongside heterogeneity amongst the investigations needed to assess a patient's suitability, views on the need for formal surgical review varied. Though the majority of interviewees reported that from a centre perspective surgical review was absolutely necessary, particularly to obtain informed consent and allow accurate surgical assessment, some participants stated that they listed patients without any surgical

review or discussion. On these occasions participants described how they felt self-sufficient to obtain informed consent. Moreover, these participants described how insisting that all potential recipients undergo formal surgical evaluation prior to listing served to delay the assessment process.

> "All patients must be seen by our one of transplant surgeons who will go through the risks of the procedure and get them to fill out the appropriate consent forms if they feel that they are suitable to have the procedure…." (Consultant, 16)

> "Our patients do not need to see a surgeon. If we feel that they are suitable then we can activate them directly…..In this unit, we as a consultant body do not believe that it is a necessity to see a surgeon as we feel perfectly capable of assessing a patient's suitability as well as discussing transplantation and its risks…We are not alone. I know of other units that do the same. If they, and ourselves had to refer all patients to our surgical colleagues at [name of local transplanting centre] then patients would have to wait longer to get listed, and to be honest I do not think that [name of local transplanting centre] could cope with all the extra work" (Consultant, 22)

To ensure the process of assessment was performed efficiently the majority of participants reported utilising a variety of information technology systems and databases to help co-ordinate and facilitate the process as well as enabling accurate audit of their processes.

> "we use this [consultant pointing to software on computer screen] bespoke software package to oversee the entire process.….it allows you to see where every single person is in terms of their work up and see every decision that has been made. It is excellent as it allows me to audit what I'm doing and keep on top of things right here in my office…..it is so much more efficient that paper notes" (Consultant, 9)

Cardiac assessment:

Participants reported much confusion surrounding which cardiac investigations were needed to list patients for transplantation, often citing inter-clinician and inter-centre variation in opinion. This ambiguity was noted even when departments had risk stratifying protocols/guidelines with participants reporting lack of consensus between members of the multi-disciplinary team involved in transplantation.

> "as you will know there is a lot of uncertainty about assessing a patient's cardiac status pre-transplantation. I don't think anyone really knows who to test or which test to use. I know that at [name of a different renal unit] they make everyone have a coronary angio. But where is the evidence for that?....we could never do that here" (Consultant, 6)

> "assessing their cardiac status is the biggest problem to getting a patient listed. There are always arguments no matter what we do. [name of transplanting centre] often tell us that we need to do a different test to the one we have already done. Even though we have followed the protocol….it's very frustrating" (Consultant, 13)

The main reason cited for this conflict was the uncertainty of the clinical utility of screening asymptomatic transplant candidates as well as lack of evidence on managing asymptomatic coronary artery disease once identified through screening.

> "the biggest headache is what do you do with someone who is asymptomatic but has coronary disease. The cardiologists say no need to do anything, whilst the transplant surgeons refuse to list the patient unless they have some intervention done…..we really need hard data on this as the evidence just isn't there…..in the end it causes a lot of delays and it's the patient that suffers most" (Consultant, 11)

> "it's often difficult to get the cardiologists to screen young adults because they often say that they are asymptomatic and low risk.....when we identify coronary artery disease we then get stuck as to what to do….We insist that

> they should be actively treated, but the cardiologists argue that they don't need treatment" (Consultant, 4)

Participants reported that the efficiency of the entire process was also dependent on having access to a sympathetic cardiac department which recognised not only the complexities of cardiac screening in renal transplant recipients but also had the resources to provide timely provision of investigations.

> "we are really lucky here, as we have a fantastic cardiology department. They understand that our patients are complex and are really accommodating at getting our scans done quickly and making sure appointments don't clash with dialysis slots….in other hospitals I've worked at you had to wait ages for an ECHO, but here they are really helpful and get it done on the same day if we explain the situation to them" (Consultant, 8)

Several participants reported that having access to a named cardiologist who regularly deals with listing patients for transplantation was also important as this facilitated decision-making when there was uncertainty and also was seen to provide accountability for the cardiac assessment process as well as make it more efficient.

> "As part of their work up, all patients need to see Dr [name of cardiologist] who has to clear them from a cardiac point of view. He decides which test is needed, reviews the result and then lets us know if they are safe to list….it's really good to have someone who is genuinely interested in our patients working with us to help us make the right decision." (Consultant, 10)

> "Dr [name of cardiology consultant] is our named cardiologist and go to man. If we have any complex patients we tend to run them by him…. He's great, and usually gets back to you quickly with a clear plan, making the whole process smoother" (Consultant, 3)

Education and Information:

Participants reported utilising a range of different educational material in educating patients about transplantation alongside adopting many different delivery methods. One to one education sessions with patients, coupled with take home literature was seen to be the main approach, though group patient sessions, providing DVDs and utilising information technology (webinars, national patient support group website help tools) alongside home visits were also reported by participants.

> "all patients attend a one to one session with me……When they come I tend to go through everything about transplantation with them in detail and avoid using complicated words which I think the doctors don't always do. I also give them these leaflets to take home along with a DVD which they can watch at home with their family" (Nurse, 2)

> "Though we hold group education sessions, I always try to visit people in their own home where they feel more comfortable.…….People often tell me that it is a lot to take in which is why I always leave my contact details so that they can call me if they want to get more info. And I always give them a DVD which has all the information in it too…" (Nurse 7)

The provision of information and informing patients was seen as being important to help patients become more involved in thinking about their own care, and to enable patients to make decisions about their own management thereby facilitating a more patient centred approach.

> "I think we spend a lot of time on education here and rightly so… I personally find that patients who know more about their condition are more likely to get involved in making decisions rather than accepting what we say" (Nurse, 1)

> "I always encourage patients to get involved in making decisions by spending a lot of time giving them the facts" (Consultant, 4)

> "Education is extremely important, as patients who know more about their condition are more likely to express an opinion and be less afraid of pushing us to get them the treatment they want as quickly as possible" (Consultant, 12)

To facilitate education, participants reported that it was crucial that the language used was understandable for the patient and did not include complex terminology or any unexplained abbreviations which patients' were unfamiliar with.

> "Patients often tell me that when they saw the doctors they were so scared and didn't understand what was going on, but after coming to the education day they don't feel as scared and understand more…..I think the difference is that we take our time and try to talk like normal and don't use complicated words so they understand more." (Nurse, 2)

> "Everyone is different. Some want more detail and others less. I think the most important thing is that you speak at their level" (Nurse, 8)

Alongside this, participants also reported the importance of being able to provide education in different languages especially in areas with a high ethnic minority population so that BME groups were not disadvantaged and so that the overall process was not delayed

> "As we serve a large Asian population we always make sure we have information leaflets written in Hindi, Urdu and Punjabi…..several of the staff here also speak Urdu and Punjabi and we sometimes call them to help do the education sessions which patients appreciate" (Transplant Co-ordinator, 3)

Decision making:

Most participants reported that the decision to list a patient for transplantation irrespective of their complexity was made solely by a consultant. In some centres this was the patient's regular CKD consultant, whilst in other centres the decision was made by a consultant nephrologist or consultant surgeon at the transplanting centre to where the patient had been referred.

> "The final decision to list a patient or not is made by the consultant surgeon at the transplanting centre after assessing the patient in clinic" (Transplant Co-ordinator, 6)

> "..ultimately it is the responsibility of the consultant in charge of a patient's dialysis care to decide if a patient should be listed or not" (Consultant, 5)

In contrast, some participants reported that all decisions about whether to list a patient or not were made following discussion at a MDT meeting, as it was felt that this reduced conflict and improved validity of decision making especially when deciding on whether to list a complex patient with multiple co-morbidities.

> " all patients are seen in our joint clinic where they are seen by a nephrologist and one of the transplant surgeons….they are then discussed at our weekly MDT where the final decision to list or not is made. … the meeting is attended by all the surgeons and nephrologists here, it adds weight to the decision so that there are no arguments later…..this is particularly useful if the patient is borderline and has lots of co-morbidities" (Consultant, 18)

After deciding to list a patient for transplantation participants reported that it was important to inform patients of the outcome as the decision involved them and to ensure that they were ready to be called up for a transplant (which was now a possibility as they were now active on the list). Though there was agreement on ensuring 'positive outcomes' were communicated to patients, some participants did

not actively inform patients if it had been decided not to list them, instead opting to answer that question when or if they were asked by the patient. One participant felt it was unfair to 'actively deliver bad news'.

> " once a decision has been made to list a patient for transplantation, our transplant co-ordinator writes to NHSBT to get them activated and also writes to the patient to let them know and to make sure that they are aware that they could be called at any time in the future for a transplant…….if a decision has been made not to list a patient then I always inform the patient formally too as I believe it is good clinical practice that patients' are aware of decisions that we have made about them" (Consultant, 7)

> "if a person is not suitable for transplantation to be honest I don't routinely write to them to tell them that. But of course if they ask me in clinic I will let them know" (Consultant, 13)

Irrespective of the outcome, participants described the importance of auditing decisions and reviewing them over time to see if they were still correct and also to see if further investigations were warranted. Procedures for doing so however differed with some participants describing well defined protocols for this purpose and others reporting no set protocol; instead reviewing patients on a clinic to clinic basis.

> "once a patient is listed, our policy is to reassess their suitability in our transplant assessment clinic every two years to see if the decision is still correct and if they need any further tests" (Consultant, 5)

> " We don't have any agreed review date for patients, but that is because we see them every three months in clinic and we are constantly reassessing if they are still suitable each time we see them." (Consultant, 13)

Human drivers:

Many participants reported that to achieve a successful listing programme it was important that healthcare staff involved in the process were passionate about transplantation and believed in its benefits. Several participants reported that the success of their own programme was largely as a consequence of this prevailing ethos.

> "As you may have heard I am extremely passionate about transplantation….some might say a bit too much [laughs], but you see I truly believe that it is the best treatment. I treat everyone as if they were my own family. If anyone in my family had kidney failure I would want them to have a transplant so why should not all of my patients?...You know I think it is because I am so passionate about transplantation that we have the best figures for listing patients in the department" (Consultant, 14)

Participants also reported that alongside committed staff, it was important to recognise the effort and hard work of those involved and to ensure that they felt appreciated, not just within the department but externally within the trust and by the transplanting centre (where applicable). Participants reported feelings of pride and being recharged when recognised and said it made them want work harder.

> "Some people think my job is crazy as I cover dialysis, transplantation and do all the education days. But to be honest I really don't mind as we all work together here and I know that the consultants appreciate what we do. It really makes a difference when someone tells you you are doing a good job….Last week Dr [name of consultant nephrologist from local transplanting centre] called me to say thanks for sending some documents across so quickly. He didn't have to call me but he did…it's the small things." (Nurse, 9)

> "The consultants recognise that our job is not easy and how hard we work…..we even got a mention in the trust newsletter [laughter]. I was actually quite proud to be honest. It's things like that that keep you motivated to work harder" (Living Donor Nurse, 2)

Achieving high levels of patient activation was also seen to be important in driving the process as participants felt that it led to patients being more pro-active in managing their health and gave them the skills and confidence to do so. Highly activated patients were seen as being more likely to chase outstanding investigations themselves and question healthcare professionals and less likely to passively accept delays and inefficiencies.

> " I think having a person who is clued up about his illness and is proactive makes a huge difference. They are more likely to attend their appointments, chase tests that are pending and less likely to just accept things dragging on." (Consultant, 2)

> "I've definitely found that people who ask lots of questions, read up on the internet and question what you are doing tend to hurry things along as they know what they want" (Consultant, 20)

Ensuring staff felt supported and were able to ask for assistance and or advice easily, was also seen to be important in terms of improving the efficiency of the process and reducing anxieties. This was particularly important for non-consultant grade participants but also for consultants.

> "Our consultants are lovely here. You can ask them anything. If ever I am worried about something or don't know what to do with someone's ECHO result or something, rather than delay things I just knock on Dr [name of consultant nephrologist]'s door and if he's there he will always help. He is lovely" (Transplant Co-ordinator, 1)

Efficiency reducing human factors:

Conversely, participants reported that poor teamwork was a significant cause of inefficiency and delays in listing patients for transplantation. Uncertainty amongst team members of each other's responsibilities, lack of trust, absence of clear objectives and poor cohesion amongst team members were all cited as reasons driving this.

> "I order the tests, I chase the results and then I again refer the patient to the surgeons….we do have a transplant co-ordinator who should be doing a lot of this, but to be honest if I left it up to them it would take a lot longer to get people listed so I tend to do it myself as at least that way I know it is done….this is why I don't think we need any more co-ordinators as I don't really know what they do, or will add. My colleagues may be doing things differently…I'm sure they will tell you when you speak to them." (Consultant, 23)

> "People sometimes tell me they never knew we existed. We are meant to be a team but we really don't feel like it here….it's a shame because it slows things down. If we were near each other we could get things done much more quickly" (Nurse, 8)

> "some of our colleagues [pause] how can I put this…the older ones….do things their own way. We have unit protocols but they refuse to follow them. We have had departmental meetings to get everyone on board but it hasn't worked. Thankfully they will retire soon so hopefully it won't be a problem for much longer [chuckles]" (Consultant, 14)

Participants also reported that having patients who did not take an active role in their management or actively engage/interact with healthcare professionals had often led to delays in listing and in discovering suitable live donors. One participant described that these types of patients were more likely to miss appointments and also less likely to discuss living donation with their family and friends.

> "it's really frustrating when you see patients who are happy to just sit back and

> who don't seem to engage in discussions about transplantation or take on board the importance of getting on with things…..they are the ones that often miss their cardiac tests and delay the whole process" (Consultant, 11)

> "I saw a patient in clinic the other day who had been on dialysis for three years, and only now had he decided to discuss transplantation with his family….it turns out he has three possible donors. If only he had been more proactive earlier on…" (Consultant, 7)

Alongside ineffective teamwork problems stemming from individuals having different approaches and the practical challenges of location; staff shortages were also seen as delaying listing patients. This included shortage of staff within the renal department and externally in other departments (e.g. cardiac department - which played an important role in listing). Participants reported that as a consequence of this, patients were subjected to longer waiting times for investigations and follow-up. This was seen as being a major cause of frustration for participants who also felt that this put additional strain on their own work load and was a source of increasing stress.

> "the reason it takes so long to get people listed is that it takes months to get their cardiac tests done….This is because they are really short down there and so it takes ages….." (Consultant, 10)

> "I think if there were more transplant co-ordinators it would definitely speed things up. I'm the only one here and when I go on leave things generally stop. The CD knows that we need more staff but there is no money at the moment…." (Transplant Co-ordinator, 6)

> "Our transplant co-ordinator left 5 months ago and since then things have slowed down…..they haven't got a replacement so we have all had to take on more work…it's annoying as I was already doing more than I'm paid to do." (Living Donor Nurse, 3)

Participants felt that these feelings played a major role in lowering the morale of staff which was seen to negatively impact their subsequent performance in listing patients

efficiently. Low morale was also seen to be driven by feeling disconnected from the rest of department as well as unappreciated and under-valued. The level of low morale varied, one participant became tearful during the interview when talking about how tough things were on the 'shop floor'. The interview with this participant was subsequently terminated early, and the participant was provided with support and advised to seek counsel, which they subsequently did.

> "….. there is only one of me. I try as hard as I can but just can't do everything. I feel like I'm letting them [patients] down. But what can I do, they [The Trust] don't care about us." (Nurse, 3)

Though all participants agreed on the benefits of transplantation above dialysis some reported facing a moral dilemma when listing patients pre-emptively as they felt that the evidence to do so was slim and that that in doing so the odds of patients on dialysis getting a transplant are unfairly further reduced. As a result some participants reported being less pro-active to pre-emptively list. One expert also said his colleague believed that the experience of dialysis before getting a transplant was in fact beneficial as it allowed patients to truly value their transplant thereafter having experienced dialysis and its associated problems.

> "There are still people who – feel that you need to earn your transplant, and that a bit of dialysis makes people value their transplant more, but I think that that will change; they are very old-fashioned, very old nephrologists, who have very old-fashioned views to other aspects of renal care also, so transplantation is not the only one." (Consultant, 4)

> "Oh absolutely, there's a constant voice of people out there who say if somebody's not on dialysis then why should they get a transplant before somebody who is on dialysis….that it is not morally right" (Consultant, 18)

Strategies for improvement:

Participant accounts suggested that whilst many guidelines were available to assist in the listing of patients for transplantation, there was a need to reach a national

consensus on how best to evaluate the clinical suitability of potential transplant recipients, so as to help reduce centre variation and improve access to transplantation.

> "I think the most important thing that we as a renal community need to do is collectively agree how exactly we should be working people up for transplantation. That's how you will get rid of variation….we all do the same thing in terms of working up living donors because the guidelines are clear whereas the recipients' one are not" (Consultant, 2)

Further research in understanding the utility of cardiac investigations and how to manage asymptomatic coronary artery disease were described as important in addressing this, as well as improved auditing of clinical outcomes.

> "I don't think we should blame guidelines because the reason they are not clear is because the evidence isn't there. What we need is better outcome data on how patients with asymptomatic cardiac disease who get revascularised do compared to those that don't, and see if there really is of any benefit, and end this argument" (Consultant, 5)

> "I'd like to see some research done in terms of which cardiac test is best in our patients and who really needs testing" (Consultant, 11)

In centres where staff vacancies and poor cardiac service provision were reported, participants also reported the need for more resources to address these shortages, whilst in other centres, participants reported that they would like to use additional resources to employ more transplant co-ordinators.

> "If I had a pot of money I would definitely get a transplant co-ordinator as I think that that would make our process a lot more efficient. At the moment we individually chase our patients results and refer them on for listing which is time consuming for us and we are probably not the most efficient at doing it." (Consultant, 15)

> "I don't think we need more doctors, but what we need is money so that we

> can get more nurses to do the education and cardiac technicians to do our scans instead of waiting ages. I'd also like to get a live donor nurse in post to help improve our live kidney programme and get a psychologist" (Consultant, 2)

Interlinking IT systems between hospitals and trusts was also thought to be important as it was felt that this would enable investigation results and clinic letters to be more freely available improving efficiency and reduce time being wasted chasing them.

> "one of our problems is that when patients come to see us we don't always have access to their scans and test results from their local hospital. We are reliant on the referring consultant sending them through which doesn't always happen and is frustrating for us and patients who get cross with us…..It would be good if our IT systems were linked so that we didn't have to chase them for results." (Consultant, 8)

In addition, participants also felt more needed to be done to improve the education amongst ethnic minorities so as to improve listing amongst BME groups as well as live transplantation. Whilst participants described local initiatives to improve education in these groups, there was a suggested need to improve overall outcomes.

> "we have a very large ethnic minority population here, and have done lots of things to improve awareness of transplantation…we've given talks in the local Gurudwara and spoken to local Imams too. But we need to do more if we are going to improve things…. We need to spend more time educating minority groups about kidney donation and about the benefits of having a kidney transplant" (Consultant, 21)

> "I've lost count of the number of times people have told me that donating is against their religion. We have to keep educating people that this is not the case...I often ask them so it's ok to take a kidney but not donate?.." (Nurse, 7)

4.4 Discussion

This is the first qualitative study to describe in-depth, expert healthcare professionals' views toward listing patients for transplantation and highlights the processes and challenges encountered in the UK. Amongst its main findings, the chronic kidney disease pathway of care and transplantation recipient assessment pathway were both identified as crucial in listing patients for transplantation. With considerable heterogeneity noted amongst participating units. These pathways are influenced by local education policies, decision-making practices, and recipient cardiac assessment; the latter being a source of much uncertainty. Several 'human drivers' in particular physician enthusiasm and high levels of patient activation were seen to enhance process outcomes, whilst patient passivity and a disengaged poorly inter-linked workforce were seen to impede the efficient listing of patients. Finally, this study highlighted several strategies to improve listing which included deriving a national consensus on recipient assessment alongside improving resources to improve service delivery and reduce staff fatigue and improve staff morale. Before discussing the merits and limitations of this study some of these important findings are discussed in more detail and how this fits with existing knowledge and the literature.

The finding that the chronic kidney disease pathway of care was viewed has having an integral role in facilitating the listing of patients for kidney transplantation likely stems from the reality that it is here that patients are often first introduced to the concept of transplantation, undergo referral and often begin their assessment process. It is interesting however to see that the models of care utilised differed and to note heterogeneity in the enthusiasm for / take up of low clearance clinics despite the renal association recommending that patients should be managed in a dedicated clinic by a multidisciplinary team[260]. The extent of variation nationally and the impact this may have on listing is unclear but will be explored in more detail in Chapters 5 and 6 of this thesis.

It is also interesting to note that the assessment of patients' suitability for transplantation was a heterogeneous process with considerable variation in clinical

suitability parameters. This finding is consistent with previously published work (involving only transplanting centres)[261], and raises concerns of a postcode lottery whereby this variation is a source of inequity in access to transplantation. Participants responses from this study would suggest a patient with a BMI of 38 could be declined access to a transplant at one centre (where the limit is 30), but be accepted if they lived near to a different centre where the limit is 40. The extent and impact of such variation is again unclear but will be explored in more detail in Chapters 5 and 6 of this thesis.

Similar inequity could result as a consequence of differences in cardiac performance criteria between centres, with participants varying in their objective, assessment processes and management of any identified pathology following screening. Cardiovascular disease (CVD) is known to be a significant cause of morbidity and mortality for wait-listed kidney transplant candidates[102-103], and it is the most common cause of death in transplant recipients[65, 104]. It is understandable that clinicians would be highly motivated to screen for CVD before transplant, hoping to prevent events early after transplant and to improve long-term outcomes. However, as described earlier the clinical utility of screening asymptomatic transplant candidates remains unclear both in terms of the benefits and whether the benefits outweigh the risks[115]. As well as being a source of frustration amongst clinicians, this uncertainty was one of the major reasons participants talked about the need for a national consensus on recipient assessment.

The importance of providing a comprehensive 'patient specific' education programme both in terms of improving patient activation/engagement and facilitating shared decision making is in keeping with recommendations from published renal specific national guidelines[262]. The clinical practice guidelines issued by the Renal Physicians' Association (Moss, 2010)[263] and the National Kidney Foundation (2002)[264] recommend that physicians engage in practices (including partnering with patients in the decision-making process, assessing patients' desired roles in decision making, and discussion of evidence regarding risks and benefits of treatment options) that will encourage shared and informed decision making prior to RRT initiation.

These themes have also been reported in other qualitative studies exploring healthcare provision as well as in qualitative studies in renal care in other countries[265-266]. Most notably, Hanson's (2016) exploration of nephrologists' perspectives on recipient eligibility and access to living transplantation highlighted similar themes relating to using education to enhance shared decision-making and to help improve patient accountability[266]. Similarly, the themes identified in this study compliment qualitative studies that have explored patient attitudes towards kidney transplant listing. Calestani et al. (2014) described that the timing of information provision and volume of information offered was important, as well as the use of accessible terminology or tailoring language according to the individual patient[267]. Likewise, a recent systematic review of qualitative studies of factors related to patients' and families' decision making regarding RRT identified a number of patients' concerns that were important to decision making[268]. These included concerns about confronting mortality, perceived or actual lack of choice regarding RRTs, having knowledge about treatment, and the degree to which patients weigh the pros and cons of alternative treatment options as important to decision making (Morton et al., 2010)[268].

It is interesting to note that participants in this study differed in their approach to communicating decisions made about whether to list a patient or not, with some opting to inform all patients and others using a more selective approach, whereby 'bad news' deliveries were avoided thereby relying on patients to pro-actively enquire whether they had or had not been listed. Similar findings were reported (though amongst patients) by Calestani et al who found that the majority of patient participants being considered for transplant listing in their interview study described a lack of information or communication with healthcare professionals about the waiting list and whether they were on it; with patients also reporting that the process was an emotional one and a source of anxiety[267]. In keeping with good clinical governance, a 'patient centred approach' would dictate that all options and decisions are communicated with a patient following a 'no decision about me without me' approach as recommended in The White Paper, Equity and Excellence: Liberating the NHS[269]. Whilst this is not always possible (e.g. in the presence of severe cognitive impairment) or appropriate (e.g. in a patient with metastatic cancer, where discussion of a clearly non-viable treatment option might be deemed completely insensitive). By choosing to not communicate a decision however on the basis that it might cause distress signals a

paternalistic approach to patient care, that, whilst on the surface may be well intended, risks being a source of frustration, with patients being in limbo and potentially disempowering for patients.

This study also highlighted several 'human drivers' for listing in particular physician enthusiasm and high levels of patient activation to enhance process outcomes whilst patient disengagement was seen to impede the efficient listing of patients alongside ineffective team work and resource shortages (similar to other qualitative studies)[266, 270]. Low or limited engagement of patients in their own care and decision making could be due to a variety of factors including patients' denial of their need for RRT (Lunsford et al., 2006)[270], and limited engagement in education about the range of available treatments for RRT (Ayanian et al., 1999)[271]. Participants uniformly described how, irrespective of the cause, addressing patient disengagement/passivity as well as providing such patients with extra support as important not just to assist them to get listed but also to improve their overall well-being.

Lastly, strategies to improve listing were identified and these focused on reducing variation and improving equity. Developing a national consensus on recipient work up and promoting research in understanding cardiovascular screening utility in potential transplant recipients was uniformly described as area for development for reasons previously discussed. Additionally, participant accounts also indicated that it was important to have some robust evidence that screening was cost-effective, with the benefits outweighing the harms. Considering the fundamental basis of an effective screening test in general is that it must improve outcomes of importance to patients, not consume resources that would be better spent in other ways, and not produce harms that outweigh the benefits this seems entirely appropriate.

Another area of improvement included tackling inequity in access to transplantation and live donor transplantation in ethnic minorities. Improved education and making healthcare systems more user friendly and easier to navigate for BME patients in particular were strategies described as crucial in reducing variation in access. In the United States several qualitative studies exploring ethnic disparities in accessing renal transplantation have found that ethnic minorities are less likely than white patients to participate in medical decision making, particularly when treated by a white physician,

and have shown large differences in the extent to which black and white patients with ESRD agree with and trust their physicians and understand their illness[270-272]. The results of these studies speak to the need for more intensive and targeted interventions, such as education and outreach, to improve the timely listing of patients form ethnic minorities with ESRD and echo views captured in this study.

Study strengths and limitations

This is the first qualitative study to describe in-depth, expert healthcare professionals' views toward and experiences of listing patients for transplantation, exploring both the processes and challenges encountered in the UK. Purposive maximum variation sampling of nine units across the UK meant that interviews were conducted with a range of participants who varied across a number of variables thought to be important: their centre's degree of listing for transplantation (using data available from the UKRR), whether the centre was a transplanting or non-transplanting renal unit, UK geography, level of social deprivation and ethnicity and role (in terms of seniority and expertise).

Whilst this study managed to successfully interview a large number of participants, from across the UK, it was not the aim to claim representation of the population of all healthcare professionals involved in listing patients for transplantation, to do this would require a larger scale project. Rather, the interview findings help identify important, in-depth views of participants and the way in which some of the findings resonate with the existing literature lends confidence to the sense and relevance of the findings reported. As with all studies, research participants may differ from. decliners/non-participants in important ways. Here, participants may have volunteered to take part in the study because they held particularly strong views on the subject of listing patients for transplantation, whether positive or negative, and therefore may represent a biased sample in this respect. Nevertheless, the risk of bias in this way is present for many studies and it remains the case that interviews were the most appropriate way to gain depth information on participant views and experiences.

In qualitative research, there is always a risk that participants will only express socially desirable views. To avoid this, the interviewer reassured participants that they

were conducting independent research and that individual views would not be shared with renal unit staff and individual responses would be treated in a confidential way, ensuring individual anonymity. With this in mind, it was reassuring to see that participants reported both positive and negative experiences of their centre practices, which suggests that participants were comfortable discussing the issues explored.

Finally, this study highlights only the views of healthcare professionals involved in listing and does not provide insights into how patients perceive the process and how decisions are made. A separate study (in which I was involved) carried out under the ATTOM project explored patients views of transplant listing has now been published and provides complimentary insights[267]. This study highlighted variation in patients' experiences of the decision making process as well as their understanding of the transplant waiting list process and on the provision of information about treatment options and listing. It also highlighted additional themes on patients' attitudes towards live donation, the meanings and feelings attached to transplantation as well as differing perceptions of support available to patients[267].

4.5 Conclusions

This study provided a unique insight into healthcare professionals' perceptions of kidney transplant listing. In summary, the chronic kidney disease pathway of care and transplantation recipient assessment process were both described as crucial in listing patients for transplantation and demonstrated considerable heterogeneity amongst participants. These pathways were influenced by local education policies, decision making practices, and recipient cardiac assessment, the latter of which was a source of much ambiguity. Several 'human drivers' in particular physician enthusiasm and high levels of patient activation were seen to enhance process outcomes whilst patient passivity and a disengaged poorly inter-linked workforce were seen to impede the efficient listing of patients. Lastly, within the data strategies to improve listing were identified and seen to focus on reducing variation and improving equity. These results have important implications with respect to understanding the complex challenges faced by centres and the individuals that make them work, together with a strong sense of a need to have clear strategies to increase equity of access to renal transplantation.

Having explored healthcare professionals' perceptions of kidney transplant listing the next chapter of this thesis attempts to build on the findings of this qualitative study by trying to identify centre specific factors that may influence access to transplantation through a national survey.

Chapter 5: Variation in Practice Patterns for Listing Patients for Renal Transplantation in the United Kingdom: a National Survey

5.1 Introduction

Numerous guidelines on the timing of referral for renal transplantation are available from professional organisations across the world[88, 98, 273]. Guidelines from the United States Organ Procurement and Transplantation Network (OPTN) Minority Affairs Committee state that the goal for referral should be that all potential candidates are referred for transplant at an estimated glomerular filtration rate (eGFR) above 20 ml/min/1.73m^2 to favour early transplantation and avoid the development of comorbidities associated with dialysis as well as allowing patients to accrue waiting time that increases their chance of being allocated a donor organ[273]. In comparison the UK Renal Association guidelines recommend that patients with progressive deterioration in renal function suitable for transplantation should be placed on the national transplant list within six months of their anticipated dialysis start date and that pre-emptive transplantation should be the treatment of choice for all suitable patients whenever a living donor is available[88].

The term 'suitable' used in these guidelines often poses a conundrum for clinicians as objective criteria to confirm suitability for transplantation are not clearly defined and hence are open to interpretation. To assist this process guidelines for the evaluation of candidates for renal transplantation have been published by the American Society of Transplantation[90], the European Renal Association and European Society for Organ Transplantation[274], the UK Renal Association[88], the British Transplantation Society[275] and Caring for Australasians with Renal Impairment[91]. Despite the availability of clinical guidelines, significant variations in the assessment practices among transplant centres have been reported in the United States as well as Europe[119, 261, 276].

Whilst inter-clinician variability in decision-making is recognised, we hypothesised that inter-centre variability in organisation / processes governing the patient pathway may also impact on differences seen in listing practices. To explore this further, we undertook a national survey as part of the NIHR funded Access to Transplantation

and Transplant Outcome Measures (ATTOM) programme to examine whether variation exists in the organisation of renal services in listing patients as well as exploring how decisions are made.

5.2 Materials and Methods

A structured online and paper-based survey consisting of 96 questions was developed using the results of two qualitative studies carried out within the ATTOM programme[267, 277]. Qualitative studies included 53 patients and 45 healthcare professionals (Chapter 4), and explored patients' views and experiences of joining the transplant waiting list and staff members' experiences of listing patients for transplantation. Staff and patients were recruited from a purposive maximum variation sample of nine renal centres in the UK. Existing published literature (including results from Chapter 4) was also reviewed and feedback sought and incorporated from a group of experts on the ATTOM steering group. Pilot face-to face interviews with four clinicians were conducted using the first draft survey to guide revision to improve instrument face and content validity and usability prior to distribution.

The questionnaire was designed to establish the practice patterns of the unit relating to listing patients aged <75 years for transplantation. This included exploring the organisation of the chronic kidney disease service and how transplantation education was administered, identifying how transplant recipient assessment was performed and local decision making processes, understanding the re-evaluation policy of the unit once patients were listed, as well as describing the attitudes and interpersonal relationships between staff and between transplanting and non-transplanting units.

Once finalised, both versions (online and paper-based) of the survey were sent to the lead physicians and surgeons of all 71 adult renal centres in the United Kingdom in January 2014 (Appendix D). Clinicians were invited either to complete the survey personally or to nominate a representative within the unit to respond. It was specified that the respondent's answers should reflect current practice in the unit rather than individual preference. Follow-up contact was made to non–responders after 4 weeks to request completion of questionnaire.

In order to measure how much time renal staff were involved in transplantation listing, Whole-time equivalent (WTE) time was asked. An WTE of 1.0 indicates that a person is equivalent to a Whole-time worker, or 2 persons working half-time.
Statistical analyses were performed using SAS version 9.3. Results for each question were expressed as a percentage of the total number of centres responding to the question. We identified several factors a priori as 'exposure' variables (including transplanting centre status, use of low clearance clinic, BMI, surgical review and use of a MDT or written protocol for suitability assessment) and tested for associations of these categorical variables with care processes using Chi squared test or Mann Whitney test. Given the potential for multiple testing and false positives we only report associations that were significant at $p<0.01$.

5.3 Results

A completed survey was received from all 71 (100%) adult centres in the UK, of which 23 were transplanting and 48 were non-transplanting renal centres. The reported roles of respondents were: Clinical Director (42.3%, n=30), Consultant Nephrologist (49.3%, n=35), Consultant Transplant Surgeon (2.8%, n=2) and 'Other health professional' (5.6%, n=4). Forty centres (56.3%) completed the web-based version and 31 centres (43.7%) the paper version of the survey. The responding centres had a total of 6699 patients active on the UK transplant waiting list at the end of 2012 and reported a national workforce involved in listing patients for transplantation which comprised of 488 WTE Consultant Nephrologists, 113 WTE Transplant Surgeons, 57 WTE Associate Specialists, 73 WTE Transplant Co-ordinators and 75 WTE Live Kidney Donor Nurses. The median number of Consultant Nephrologists was significantly greater at transplanting centres (8.5; IQR 8-11) compared with non-transplanting centres (4.5; IQR 3-6), $p<0.001$).

Chronic Kidney Disease Workforce and Organisation

Almost 48% (47.9%, n=34) of centres reported seeing all pre-dialysis patients in a dedicated low-clearance clinic (LCC), whilst 33.8% (n=24) of centres used a LCC for some (but not all) of their patients. The remaining 18.3% (n=13) of centres did not have a designated LCC service. There was no significant difference between non-

transplanting and transplanting centres in terms of the pattern of LCC utilisation. In centres where only some patients were referred to a low clearance clinic, avoidance of longer commuting times (62.5%, n=15) was cited as the main reason not to refer a patient to the LCC, with 25% (n=6) also believing that a LCC would not add any additional benefit. Similar reasons were cited for not having a LCC, with centres also citing 'consultant wish to maintain continuity' as a major reason. LCCs were mostly joint (consultant with nurse, 48.3%, n=28) or consultant-led (43.1%, n=25), with only 8.6% (n=5) of centres having a nurse-led service. When LCCs were present, 30% of non-transplanting centres did not have a specified protocol for referral for transplantation compared with 11.1% of transplanting centres ($p<0.001$).

Transplantation Education

Transplantation was discussed as a treatment option with all patients under the age of 75 in 51 (71.8%) of centres, with other centres reporting a more selective policy. The decision not to discuss was made mostly by a consultant led multi-disciplinary team (MDT) (55%) or solely by a consultant nephrologist (40%). Discussions regarding transplantation were led most often by a consultant nephrologist (64.8%, n=46), with nurses leading the discussion in 19.7% (n=14), transplant surgeons in 2.8% (n=2) and 'other' healthcare professionals in 12.6% (n=9) of centres. Despite reporting a wide range of educational delivery tools, education almost always took the form of a one-to-one consultation (98.6%) where patients were given literature to take home to read (91.5%). In 37 centres (52.1%) patients considering transplantation were also given the opportunity to talk to other patients who had successfully been transplanted.

Transplant Listing Pathway and Role of Transplant Surgeons

The majority of centres (93%) were able to medically assess patients locally, whilst the remaining 7% (n=5) of centres (all non-transplanting centres) referred patients to be assessed at the transplanting centre after completing some baseline investigations. The clinical setting for transplant assessment varied, with 36.4% of centres utilising a LCC, 21.2% seeing patients in their usual CKD clinic and 19.7% utilising a specific transplant assessment clinic. The remaining 22.7% of centres reported a mix of 'other' clinical settings. The use of specific transplant assessment clinics was similar in non-transplanting centres and transplanting centres, though the frequency varied widely, with clinics occurring monthly or less frequently in 55% of non-transplanting centres,

as compared with 100% of transplanting centres running these clinics fortnightly or more frequently, p<0.001. Overall 88.2% (n=63) of centres required all patients to be seen by a Transplant Surgeon prior to being listed; of the remaining 8 centres that did not require direct surgical review, 4 centres (1 transplanting and 3 non-transplanting) reported that all patients were discussed with a Transplant Surgeon, whilst 4 centres reported no surgical involvement in the decision to list for transplantation.

The Assessment Process

Nationally 30% (n=21) of centres did not have a written transplant work-up protocol for recipient assessment, which included 3 transplant centres. Figure 5.1 shows the frequency with which different investigations were used for the routine assessment of potential renal transplant recipients amongst the 71 centres.

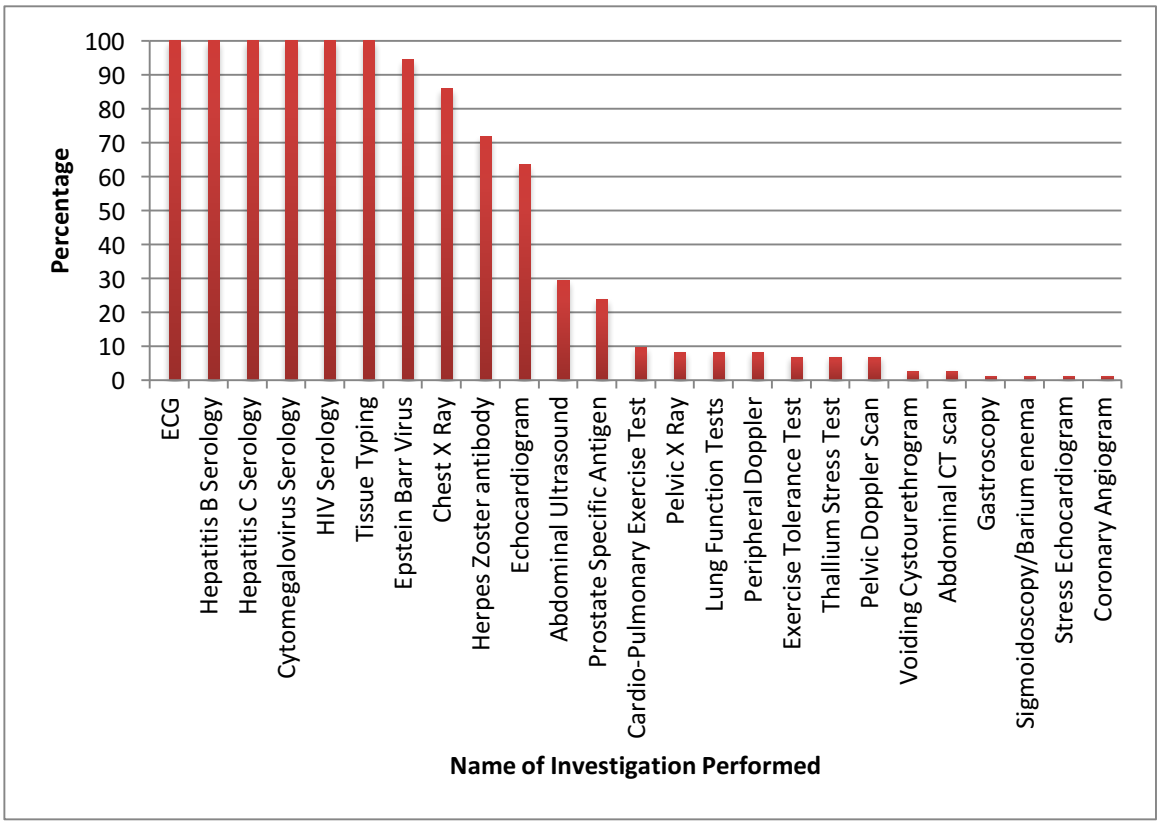

Figure 5.1: Proportion of UK Centres performing each investigation as part of their routine assessment of patients under consideration for renal transplantation wait listing at UK renal centres

Three non-transplanting centres reported having an upper age limit of 75 years (above which patients were only considered in exceptional circumstances for transplantation) whilst all other centres (n=68, 95.6%) did not report any age restrictions. In comparison, Body Mass Index (BMI) was widely used as an exclusion criterion for listing patients, with 81.7% (n=58) of centres excluding patients for transplantation based on BMI. The overall median upper BMI cut off, in these centres was 35 (IQR: 33.25-35), with 36 centres reporting an upper limit of 35, and 5 centres an upper limit of 40. The reasons stated for using BMI as an exclusion criterion are summarised in Table 5.1.

	Transplanting Centre		Non-Transplanting Centre		Overall Nationally	
	N	% (of Centres)	N	% (of Centres)	N	% (of Centres)
Increased post-operative complication risk	16	88.9	34	85	50	86.2
Increased technical difficulty in performing procedure	14	77.8	30	75	44	75.9
Increased cardiovascular risk	6	33.3	21	52.5	27	46.6
Lower Graft survival compared to a normal BMI	6	33.3	9	22.5	15	25.9
Lower patient survival compared to normal BMI	6	33.3	9	22.5	15	25.9
Other (please specify)	2	11.1	10	25	12	20.7

Table 5.1: Reasons for considering raised BMI as a contraindication for transplantation by the 58 centres adopting a maximum exclusion criterion

These did not differ between centres (n=58) other than perceived increased cardiovascular risk, which appeared to be more of an issue for non-transplanting centres (52.5%) than transplanting centres (33.3%), $p<0.01$.

All transplanting centres, and 87.5% (n=65) of non-transplanting centres reported stratifying patients by risk when deciding which cardiac investigations to perform, with age (median 50 years; IQR: 50-55) (88%), diabetes (97%), previous cardiovascular disease (91%), and an abnormal ECG (89%) being the factors used when determining risk. Thirty-one centres (44%) conducted some form of 'cardiac stress testing' even in low risk patients whilst significant variation was seen in the

first-line investigation of choice for the assessment of coronary artery disease in high risk patients (Table 5.2).

	Transplanting Centre		Non-Transplanting Centre		Overall Nationally	
	N	% (of Centres)	N	% (of Centres)	N	% (of Centres)
Exercise Tolerance Test	5	21.7	10	20.8	15	21.1
Thallium Stress Test	7	30.4	17	35.4	24	33.8
Stress Echocardiography	2	8.7	7	14.6	9	12.7
Dobutamine Stress Tc Scan	3	13.0	6	12.5	9	12.7
Coronary Angiography	1	4.3	2	4.2	3	4.2
CPEX Testing*	1	4.3	2	4.2	3	4.2
Other (please specify)	4	17.4	4	8.3	8	11.3

*Cardio-Pulmonary Exercise Test

Table 5.2: First-line investigation of choice for the assessment of coronary artery disease in high-risk patients

To aid the process of cardiac assessment for suitability for transplantation, 35.2% (n=25) of centres reported having a named cardiologist to provide assistance, though this was significantly greater amongst transplanting centres (70%), $p<0.01$. If a coronary angiogram was deemed necessary for listing a low clearance patient, 5.6% (n=4) of centres reported they would refrain from performing the test until patients were on dialysis to avoid precipitating the need for dialysis, with a further 74.6% stating they would 'sometimes' refrain from proceeding. Only 19.7% reported always proceeding.

Variation was also seen in screening for malignancies with 38% of centres reporting that screening for cancer such as breast, prostate, bladder and colorectal was part of the routine work-up of transplant recipients, in addition to national screening programmes In contrast, formal psychological assessment, or cognitive assessment, of all potential recipients was only performed in 7.0% (n=5) and 5.6% (n=4) of centres respectively, with 13.1% of centres reporting no access to psychologist or counsellor services.

Decision Making

Overall 76.1% (n=54) of centres utilised an MDT approach when listing patients for transplantation. This proportion was greater amongst transplanting centres where all

but one centre (95.7%) used an MDT, compared to 66.7% (n=54) in non-transplanting centres. MDTs occurred more frequently in transplanting centres with a median of 4 meetings a month (IQR 1.25-4) as compared to 2 a month (IQR 1-4;p= 0.001) in non-transplanting centres.

If a patient was not deemed suitable for listing for deceased donor transplantation, 76.1% of centres said that they would consider listing them for living donor transplantation if a suitable donor was available. Living donor availability was generally seen as a positive driver for listing, alongside patient enthusiasm, whilst the majority of centres did not perceive socioeconomic factors, including employment status or level of patient education, as important when deciding whether to list patients for transplantation (Figure 5.2).

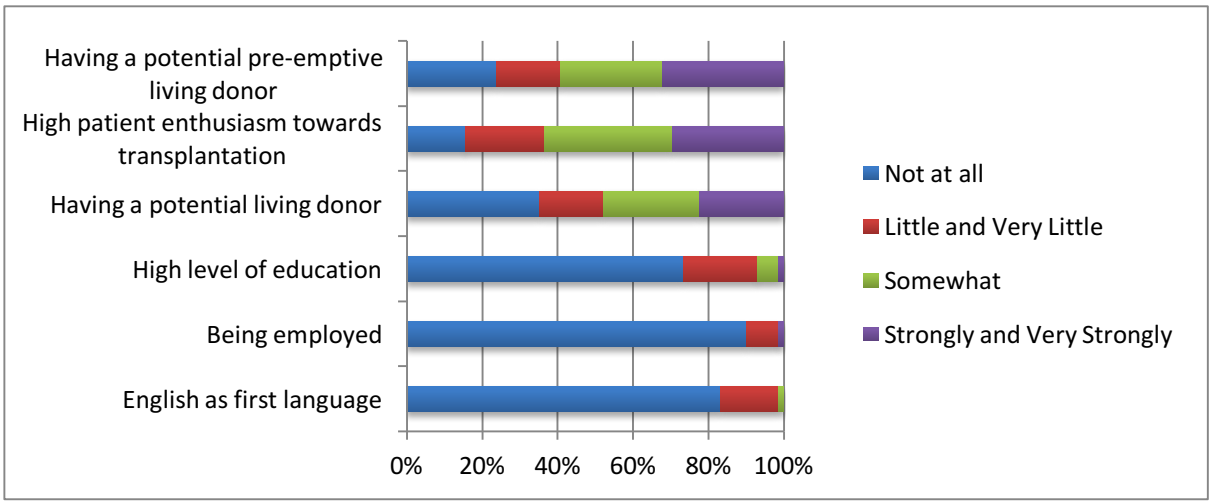

Figure 5.2: Distribution across renal centres of responses to the question: "**Please indicate your views on whether the following factors influence the decision to list a patient"** Please indicate how strongly each would influence a decision. Values are expressed as percentage of units (n=71).

Once a decision regarding listing was made, 50.7% of centres reported informing all patients on dialysis, or with CKD stage 5 under 75 years, of the decision, with 78.6% of centres recording all decisions made on transplant suitability on their electronic patient record (EPR). Once recorded on their EPR, only 61.8% of centres performed regular audit of this information.

After listing, only 38% of centres reported having a protocol in place to monitor patients activated on the transplant list with the majority of centres (53.5%) reviewing

patient suitability annually. Significant variation existed in how centres undertook on-going surveillance for cardiac disease in asymptomatic patients once listed as shown (Table 5.3).

	Transplanting Centre		Non-Transplanting Centre		Overall Nationally	
	N	%	N	%	N	%
No routine surveillance if asymptomatic	6	26.1	13	27.1	19	26.8
All patients screened irrespective of remaining asymptomatic	4	17.4	16	33.3	20	28.2
Surveillance only in high risk groups	12	52.2	11	22.9	23	32.4
Varies, no specific policy	1	4.3	8	16.7	9	12.7
Other (please specify)	0	0.0	0	0.0	0	0.0
Total	**23**	**100.0**	**48**	**100.0**	**71**	**100.0**

Table 5.3: Continued surveillance of cardiac disease in asymptomatic patients on the waiting list reported across UK renal centres

This was also highlighted in centres' responses to questions on improving listing, with 53 centres (74.6%) either agreeing or strongly agreeing with the need for having a national consensus on cardiac work up, and 52 centres (73.2%) also agreeing that there was a need for a consensus on the entire assessment work-up process (Figure 5.3).

Inter-Centre Relationships and Future Development

Although 95% of centres reported having a positive relationship with a 'good', 'very good' or 'excellent' relationship with their associated transplanting/non-transplanting centres, one third (n=16) of non-transplanting centres felt that accessing an appointment at their affiliated transplanting centre was a significant source of delay in listing patients.

Factors reported by centres to be most important in improving listing of patients for transplantation included: providing a better evidence base behind necessary assessment work up; improving the commissioning of transplant work up by funders of the service; and developing a national consensus on the work up of transplant recipients (Figure 5.3).

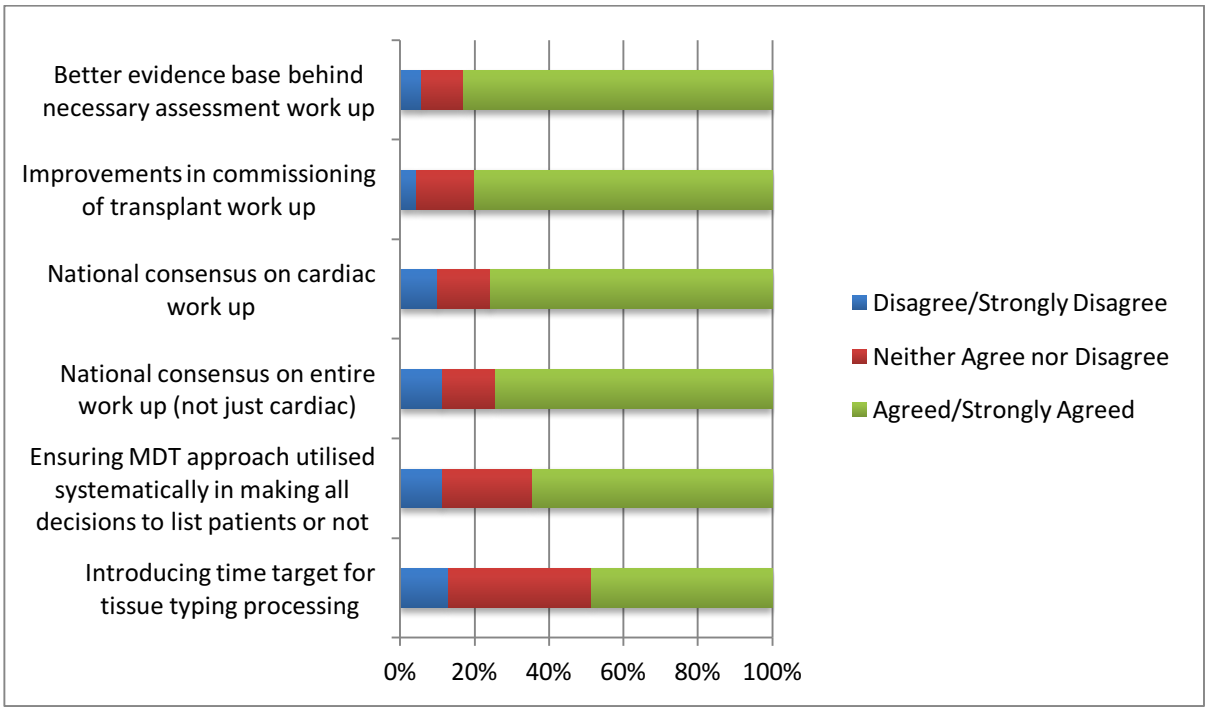

Figure 5.3: Distribution across renal centres of responses to the question: "**What is your opinion on the following statements about whether they would improve listing of patients for transplantation?"** Please indicate how strongly you agree or disagree with each of the following." Values are expressed as percentage of units (n=70).

If extra funding was available, centres stated they would use this to increase the number of transplant co-ordinators and living-donor nurses, increasing the number of operation time slots for transplantation in trusts, and providing administrative support for allied health professionals involved in transplantation would likely improve overall listing and time to listing in their centres (Figure 5.4).

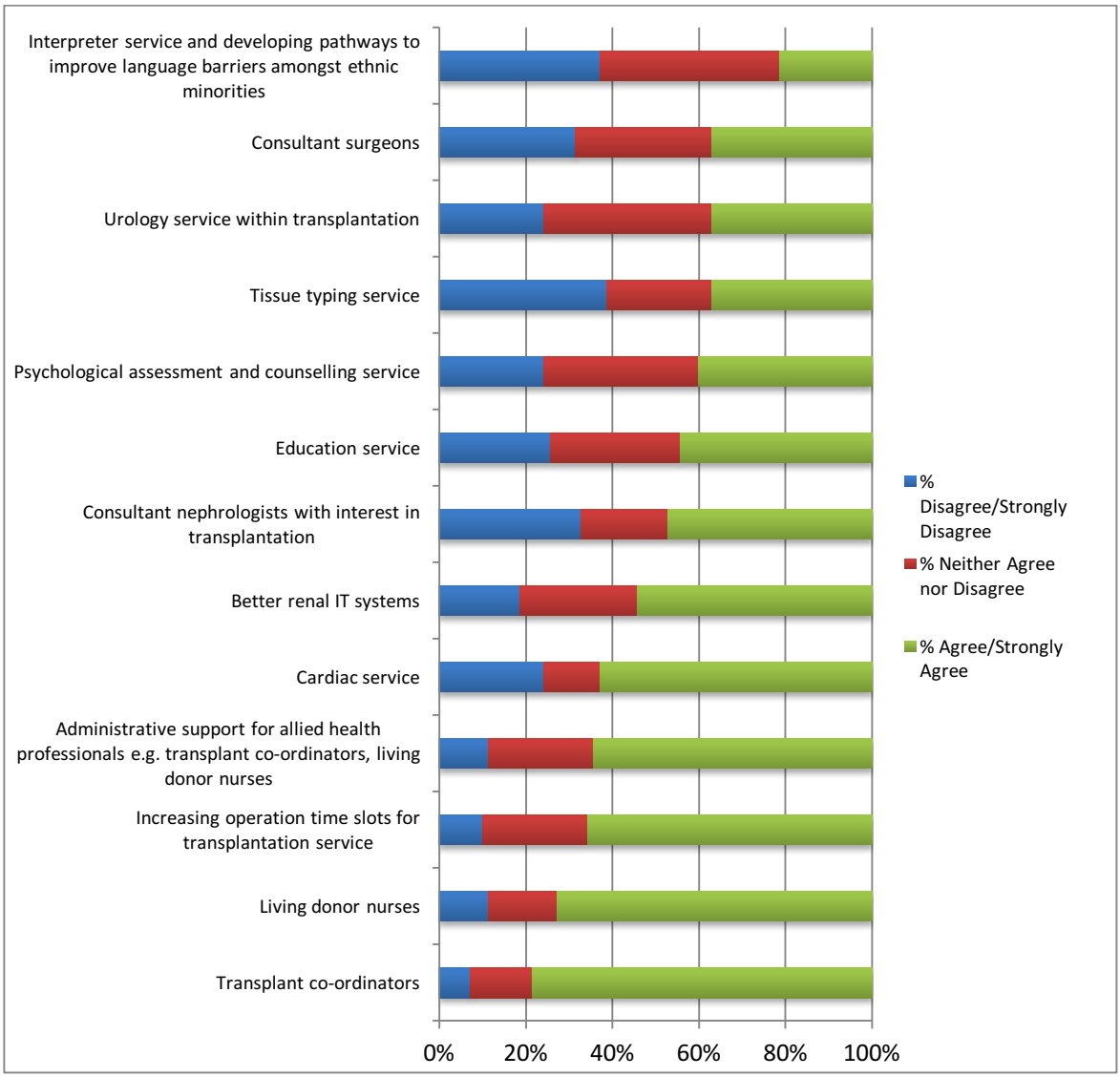

Figure 5.4: Distribution across renal centres of responses to the question: "**What is your opinion on whether more funding for the following resources would improve overall listing and time to listing in your unit?** Please indicate how strongly you agree or disagree with each of the following." Values are expressed as percentage of units (n=70).

5.3 Discussion

This study provides the most extensive exploration to date of clinical practice patterns within renal centres in listing patients for renal transplantation in the UK. It provides a comprehensive overview of the transplant-listing pathway including staffing levels, clinic arrangements, provision of patient education on transplantation, decision-making, recipient assessment, surgical review, criteria for listing, and the role of multidisciplinary teams.

For a national population of 64.1 million[278] the number of consultant transplant surgeons reported (1.76 per million population) (pmp) in this survey remains significantly lower than the 2pmp recommended by the Royal College of Surgeons of England[279]. Indeed, the number of consultant nephrologists (7.61pmp), transplant co-ordinators (1.14pmp) and living-donor nurses (1.17pmp) are all significantly lower than that recommended by the National Renal Workforce Planning Group and point towards an understaffed service[279].

Despite the UK Renal Association recommending that CKD patients pre RRT should be managed in a dedicated clinic by a multidisciplinary team[260], this study also demonstrated wide variation in the utilisation of low-clearance clinics nationally, with variation also seen in their implementation and entry criteria. There are many studies, albeit of small and variable quality, which have shown that a dedicated pre- dialysis clinic is associated with improved outcomes and reduced urgent initiation of dialysis[280-283]. These clinics may provide more focused opportunity to assess transplantation potential and more timely discussion of options including live donation and pre-emptive transplantation. Whilst it may seem intuitive that having a dedicated low clearance service may be advantageous to centres in improving access to transplantation, clear evidence to support such is lacking which may explain its variable implementation. Similarly, specific transplant-assessment clinics (used by a fifth of centres) enable joint assessment by physician and surgeon; whilst the evidence of their effectiveness is lacking they may be more efficient at achieving transplant listing.

Irrespective of the type of CKD service in place, a broad range of educational methods were utilised across the UK, with one-to-one education being the main route. A significant proportion of centres (28%) did not discuss transplantation as a treatment option with all patients under the age of 75 years, and nearly 50% of patients who had had a decision made about them regarding transplantation were not informed of the decision made. This is of concern, as a patient-centred approach would require that all options are communicated to a patient and their family where possible[269]. There may be exceptional circumstances where this may not always be feasible, but such instances would be expected to be less frequent than was reported in the present study.

Another important observation from this study was that some centres did not consider surgical review to be an absolute requirement for listing patients for transplantation. Eight centres listed without formal review, four of which cited no surgical involvement at all. The UK Renal Transplant Service specification stipulates that patients should undergo surgical assessment prior to being placed on the transplant list[284]. It is questionable whether without surgical input, patients can make an adequately informed choice and be involved in shared decision-making about transplantation and associated surgical risks as well as raising validity issues surrounding any pre-listing obtained consent. Chronic understaffing described earlier may partly explain why centres have adopted such practices, though it's impact on outcome is not known.

Several national guidelines recommend that centres should have written criteria for acceptance of patients onto the waiting list[88], yet nearly a third of centres reported not having a protocol, including three transplanting centres. The lack of standardisation in these units could lead to variation in assessment, stereotyping, individual clinician bias and personal idiosyncrasies contributing to inequity. It was reassuring that the majority of centres (95.6%) did not use chronological age per se as an exclusion criterion, acknowledging that age must not be used as a proxy for the proper assessment of individual need and suitability. It also highlights how clinicians are aware that chronological age can be very different to biological age in different individuals, and how assessment needs to be tailored on a case- by- case basis to avoid unwarranted age discrimination.

In contrast to age, the majority of centres used BMI as an exclusion criterion with a wide upper BMI limit of 30-40. In the context of an increasingly obese population, such a broad range has the potential to cause variation in terms of access to transplantation. Obese patients are certainly at an increased risk of technical difficulties and peri-operative complications[131-132] though evidence in favour of imposing a BMI limit on the basis of more hard end-points (patient and graft survival) is conflicting[134-138]. A number of reports from nationwide databases, including the USA, Australia and the Netherlands[133, 136, 138], have shown decreased patient and graft survival in obese recipients, whilst others showed no differences in survival between obese and non-obese transplant recipients[137]. It is unclear in studies where an increase in risk was noted, how much would be mitigated once co-existing cardiovascular disease was accounted for. This raises the notion that if technically feasible, and cardiovascular disease has been ruled out, most patients should be considered for transplantation irrespective of their BMI.

As cardiovascular disease remains the main cause of death in transplant recipients[104], it is unsurprising that most centres invest a great deal of time and resource in its investigation and management. This study showed that most centres stratify patients on their level of risk, though the choice of ensuing investigation varied greatly with no clear consensus, irrespective of risk, from non-invasive functional tests to invasive angiography. This variation is likely due to a combination of factors including lack of evidence on superiority for any one investigation, as well as local cardiac service availability and experience. Centres also differed in their perception of risk associated with angiography in low-clearance patients and access to a dedicated named cardiologist to assist in decision making, both of which may influence their listing practices.

MDTs were seen to be used more often in deciding whether to list patients than to decide whether to discuss transplantation with a patient. Of the 54 centres that reported using an MDT approach in listing patients, only 17 centres (31.5%) used them to discuss all patients prior to them being listed. Further research is required to assess the impact of MDTs on transplant decision-making as views on their effectiveness are mixed[285-286] and the degree to which MDT meetings have been incorporated into other clinical settings varies widely[287]. Once a decision is made,

despite recommendations regarding the re-evaluation of patients on the waiting list being available for sometime[120, 288], only 38% of centres reported having a protocol in place to monitor wait-listed patients. In addition, only two thirds of centres regularly audited transplant status information stored on patients' electronic patient record where present.

Although this study received a 100% response rate across all parts of the UK and though the survey instrument was piloted and refined to enhance relevance, understandability, and usability; some limitations need to be acknowledged. The survey responses were self-reported by self-selecting renal staff e.g. the clinical lead for transplantation, and their responses will not necessarily reflect those of the broader consultant community. Equally, we could not check the validity of responses garnered and some of these data were necessarily estimates and so should be regarded with caution. Furthermore, most questions in the survey were multiple-choice questions that invited respondents to select the best possible answer out of the choices available. This approach necessarily limits their responses, although an option to select "other" was provided and the survey was designed following detailed qualitative interviews with patients and staff to identify core domains.

In conclusion there is wide variation in UK practice patterns for listing patients for renal transplantation, though the impact this has on access to transplantation is unclear. The extent to which of the above described centre-specific factors, as well as patient-specific factors, affects access to transplantation requires further analysis in a prospective cohort of patients which will be investigated next in Chapter 6.

Chapter 6: A Prospective, Observational Study Investigating the Impact of Patient Factors and Centre Practice Patterns, on Access to Transplantation

6.1 Introduction

There is increasing evidence that access to transplantation varies between renal centres both internationally and in the UK[11-12, 153]. Inequity in access has been noted amongst disadvantaged groups including ethnic minorities[11-12, 25-36, 153] and individuals from lower socioeconomic status[11, 24, 26-27], both of which are seen to have reduced access to both live and deceased donor transplantation despite having a higher incidence of ESRD[15-23, 44].

Increased comorbidity burden amongst these populations and or differing centre processes in assessing patient suitability for transplantation may be amongst contributory factors[11], however, studies to date have been limited in their ability to adjust for these factors. It thus remains unclear which patient-specific and centre-specific factors are responsible for such variations, or indeed which centre practices represent the optimal approach for listing patients.

Having identified variation in centre practices in listing patients for transplantation in the UK in chapter 5, this chapter examines which centre practices are positively (or negatively) associated with transplant listing, alongside examining the independent impact of patient variables including comorbidity, ethnicity and socioeconomic status on access to transplantation.

6.2 Methods

When examining listing for transplantation it is important to recognise that there are many time points in a patient's care pathway when they might be listed. As figure 6.1 shows patients may be listed prior to starting dialysis (pre-emptive listing-often referred to as the 'gold standard' by the Renal Association[88]) or indeed after starting dialysis. Additionally, in some centres patients may also undergo live transplantation without even being officially listed for transplantation on the national waiting list.

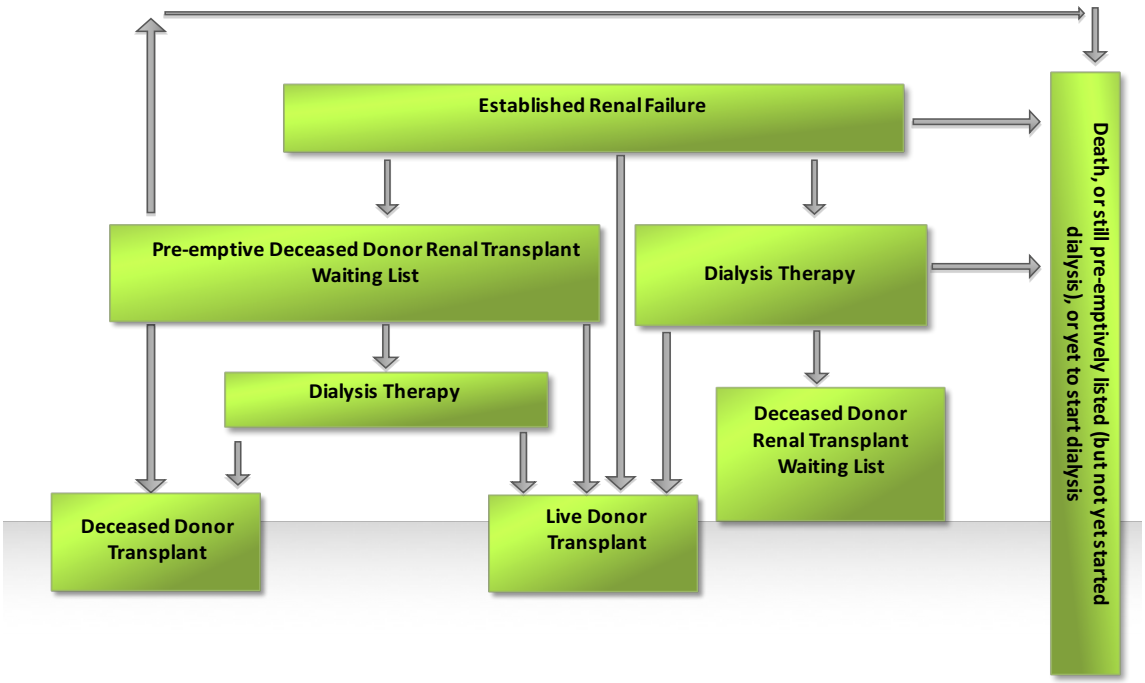

Figure 6.1: Care pathways for patients with Established Renal Failure

Despite this variation in listing practices, analyses to date examining access to transplantation undertaken in the US and UK have often chosen to combine these different groups together and analyse their outcomes collectively. Whilst this is a well utilised approach, a fundamental problem with adopting this approach in examining the impact of practice patterns on listing is that it may bias results. As pre-emptively listed patients and patients listed after dialysis are likely to be fundamentally different both in terms of their co-morbid profile and in terms of their susceptibility to different practice patterns, thus by combining the two, important associations may be missed or their impact altered.

For example, the impact of being registered at a transplanting centre as opposed to a non-transplanting centre may be greater in terms of pre-emptive listing as the presence of on-site transplant surgeons and live donor co-ordinators may make it easier to list patients pre-emptively than at non-transplanting centres. Similarly, the benefit of centres which utilise dedicated low clearance clinics in an attempt at maximising focus on preparing patients for dialysis and enabling more prompt listing

for transplantation might be lost in a combined analysis. Pre-emptively listed patients are also more likely to be less co-morbid, well known to renal services and have more CKD with less acute complications facilitating their earlier listing. Areas with higher levels of deprivation and ethnic minorities with a greater prevalence of co-morbidities may have lower pre-emptive transplant rates though this would be less apparent in a combined analysis. i.e. the impact of ethnicity and deprivation may be attenuated.

Finally, another limitation of combining these groups is that in keeping with the Renal Association's guidance that pre-emptive transplantation should be regarded as the gold standard and recognising that the national algorithm for allocating deceased kidneys takes time accrued on the waiting list into account, one could describe pre-emptive listing as an important measure of quality in terms of patient care and 'best practice' which should be highlighted to improve patient care though would be overlooked in a combined analysis.

Recognising the limitations of analysing all listed patients together, this study was designed to analyse each group separately i.e examining the impact of centre practice patterns, ethnicity and socioeconomic status on

(i) Access to pre-emptive listing and

(ii) Access to listing after starting dialysis.

6.2 Methods: Analysis 1 - Access to Pre-emptive Listing/ Transplantation

6.2.1 Study Population

Of the 6844 patients aged 18–75 years recruited in the ATTOM study, between 1st November 2011 and 31st March 2013, all incident dialysis patients starting RRT as either haemodialysis or peritoneal dialysis (n-2281) and incident transplant patients with a pre-emptive transplant (n-424), from renal centres in England and Wales (n=51) were considered eligible for inclusion (n-2705). Following exclusions (listed below, n=62) a final cohort of 2643 patients were analysed in this study, see Figure 6.2.

6.2.1.1 Exclusion Criteria

Incident dialysis patients and incident pre-emptive transplant patients from Scotland and Northern Ireland were not included in this analysis due to data-linkage problems arising at the UKRR. Other exclusion criteria included:

- Patients listed for multi-organ transplants other than pancreas (n=3)
- Patients who were suspended for more than 30 days within 90 days of first activation (n=59). This was 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 fitness.

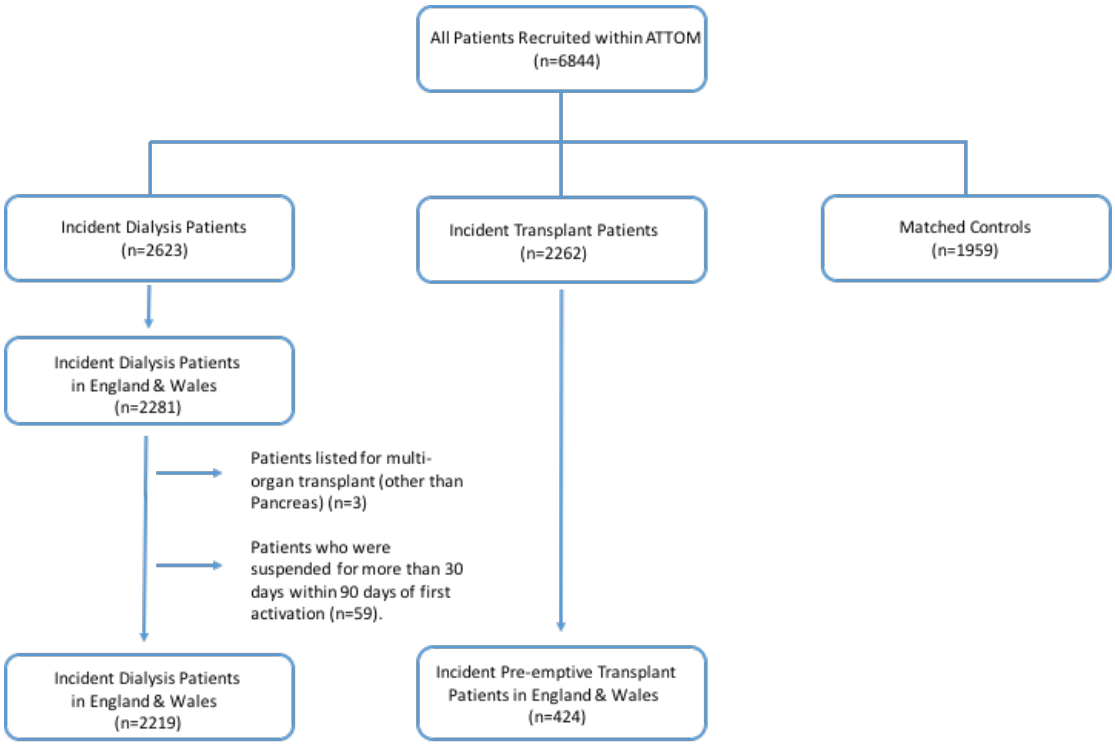

Figure 6.2 Flow diagram showing showing the inclusion and exclusion criteria utilised in the access to pre-emptive listing analysis.

6.2.1.2 Primary Outcome

The Primary Outcome of this analysis was to examine whether patients included in the study cohort were pre-emptively wait-listed for renal transplantation, with data on whether a patient was listed or not at the start of RRT being retrieved from the NHSBT database.

All patients who achieved pre-emptive live donor transplantation without prior activation on the national transplant waiting list were assumed to have been activated for the purposes of this analysis.

6.2.2 Statistical Analyses for Analysis 1: Access to Pre-emptive Listing/Transplantation

As the outcome pursued in this chapter was binary (listed Vs non listed) logistic regression was used to examine the association between the individual patient and renal centre characteristics and the probability of being listed. Mathematically this can be expressed as:

$$\text{Log odds of outcome} = \beta 0 + \beta 1\chi 1 + \beta 2\chi 2 + \ldots..\beta p\chi p$$

Where the log odds of the outcome is the linear predictor of the log odds given the particular values of the predictors. The predictors are labelled 1, 2 to p. The β's are the regression coefficients associated with the predictors and β0 is the log odds of the outcome in the unexposed group. The probability of the outcome is transformed into a log term and is anti-logged to get an exposure odds ratio. The relationship between the predictors moves from additive to multiplicative when anti-logged.

Description of a Multi-level Model

A multi-level model was chosen to analyse the data to account for the hierarchical data structure, patients (level 1) nested within renal centres (level 2) and enable appropriate contextual analysis of the data. It is important to incorporate the hierarchical data structure to ensure that appropriate conclusions are drawn about associations between organisational factors and centre outcomes and to able to adjust for case-mix differences as well as to allow for patient clustering within centres even

when studying the impact of individual factors such as socioeconomic status and ethnicity.

If hierarchical models are not used for this type of analysis the results may be susceptible to fallacy; the ecological fallacy where inferences are drawn about individuals when the data are group level data or the atomistic fallacy where group level inferences are drawn using individual level data. This can result in erroneous associations being drawn between exposure and outcome. Practically, individual level factors i.e case-mix are likely to influence centre level outcomes and so methodology which allows incorporation of these individual level data adds weight to any associations detected if just centre level data (or an ecological study) were performed. However, the statistical model must also account for similarities between individuals within one centre who are all exposed to the same structure and processes. Statistical methods based on individual level only assumes statistical independence between individuals but this is not correct as patients are clustered within centres[289-291].

The multi-level model is a more sophisticated form of regression analysis. The relationship between the predictor variable and the outcome variable are allowed to vary randomly both between individuals and between centres. The model can be specified to include either a variable intercept or slope for each level of the model. Multi-level models can also include random terms such that patients and renal centres are treated as a random sample from a larger population (random rather than fixed effects)[289-291].

Application of multi-level model to describe access to pre-emptive transplant listing

Patient Variables (Level 1)

The process of developing a multi-level logistic regression model to examine access to pre-emptive listing involved several steps/preliminary models. The first model constructed included patient level (level 1) variables only to examine the effect of case mix on centre differences to pre-emptive listing. The level 1 case-mix variables included in the model were:

- Age (categorized as 18-29, 30-39, 40-49, 50-59, 60-64 and 65-75),
- Gender (male/female),
- Ethnicity (White, Asian, Back and Other),
- BMI (categorized as (< 20, 20 - <25, 25 - <30, 30 - <35, 35 - <40 and >40).

Other demographic and socioeconomic variables (categorised as Y/N unless otherwise specified):

- Born in UK,
- English First Language,
- Need Help with Reading (Never, Always, Often, Rarely and Sometimes),
- Accommodation (Owned by you, Other, Part rent, Part owned and Rented Privately from Council / Housing Association),
- Education (GCSE, A-level or NVQ 1-3, Degree, Higher or NVQ 4-5 and No Qualifications),
- Employment (Working full time, Long term sick/disabled, Looking after family home, Not in work for some other reason, Retired from paid work, Student (includes those in training), Unemployed and Working part time),
- Car ownership,
- Civil Status (Single, Divorced, Living with Partner, Married, Separated and Widowed),
- Children in household (None, One or more),
- Adults in household (One, Two or more), Total in household (One, Two or more).

Comorbidities (categorised as Y/N unless otherwise specified)

Diabetes, Heart disease, Heart failure, Atrial fibrillation, Cardiac valve replacement, Pacemaker, Vascular disease, Abdominal aortic aneurysm, Respiratory disease, Liver disease, Blood borne viruses, Previous Malignancy, Smoking (categorised as No, Current, Ex-smoker and Don't know), Mental illness, Dementia.

Other independent patient variables:

- Time Since First Seen by Nephrologist (categorized as (<1 Year, 1-3 Years and >3 Years),

- Previous transplant,
- Primary Renal Disease (Diabetes, Glomerulonephritis, Hypertension, Polycystic, Pyelonephritis, Renal vascular disease, Uncertain and Other).

The effect of these variables on outcome were tested both individually and then in a stepwise process and were kept in the model if they remained significantly predictive after adjustment for all other individual characteristics. The multi-level model calculates a value for -2logL as a test statistic, which can then be used to calculate the difference between two nested models. The difference between the -2logL values for the model including each case mix variable and the unadjusted model were tested using a X^2 distribution with the appropriate number of degrees of freedom depending on the number of variables in the model. Following this, a model which included the significant patient variables and centre as a random effect was analysed prior to examining the impact of centre factors.

Centre Variables (Level 2)

The same analytical approach was used for examining centre variables as was used for patient variables, with centre variables being tested both individually and in a stepwise process. Centre variables analysed in this study were derived from the questionnaire responses (discussed in chapter 5). Centre variables were chosen after a group discussion/review of the questionnaire responses by the investigating team. Variables chosen included those in which there was significant variation between centres alongside those thought to differ greatly from general consensus/advice from guidelines e.g. seeing a surgeon before being listed, having a written protocol...etc. Variables chose for analyses included:

- Number of whole time equivalent Consultant Nephrologists (as continuous),
- Number of whole time equivalent Consultant Nephrologists (categorical),
- Number of Patients Receiving RRT at centre (continuous),
- Number of Patients Receiving RRT (categorical),
- Transplanting Centre (categorical - Y/N),
- Use of Low Clearance Clinic (categorical - Always, Sometimes and Never),
- Transplantation Discussed with All Patients (categorical – Y/N),

- Location of Assessment (categorical-locally or referred to another centre),
- Patients Seen by a Surgeon before wait-listing (Categorical - Y/N),
- Presence of a written protocol to assess suitability (categorical – Y/N),
- Presence of an MDT for listing purposes (categorical Y/N),
- Use of MDT to List All Patients (categorical – Y/N),
- Audit of CKD 5 Patients Listing Status (categorical – Y/N),
- The presence of a named cardiologist to discuss wait-listing (categorical – Y/N).

The unadjusted association of centre variables in a model corrected for patient characteristics were first examined, after which significant centre characteristics were kept to be analysed in a final multi-level multivariable logistic regression model. A significance level of 0.05 was taken as evidence of a significant association.

Sensitivity Analysis

As this analysis included patients who had undergone live pre-emptive transplantation, a separate sensitivity analysis was also conducted in which these patients were excluded. This was to exclude the possibility of the lack of live donors amongst ethnic minorities and socioeconomically deprived patients influencing the results, as the multi-level model may not have been able to fully control for these factors.

Statistical Software

All statistical analyses were performed using SAS software version 9.3 (SAS Institute, Cary, NC).

6.3 Methods: Analysis 2 - Access to Listing after Starting Dialysis

6.3.1 Study Population

Of the 6844 patients aged 18–75 years recruited in the ATTOM study, between 1st November 2011 and 31st March 2013, all incident dialysis patients starting RRT as either haemodialysis or peritoneal dialysis who were not on the transplant waiting list when starting dialysis from renal centres in England and Wales (n=51) were considered eligible for inclusion (n-1776). Following exclusions (listed below, n=62) a final cohort of 1714 patients were analysed in this study, see Figure 6.3.

6.3.1.1 Exclusion Criteria

Incident dialysis patients from Scotland and Northern Ireland were not deemed eligible for this analysis as survival data was not available from the UKRR at the time of analysis to allow their data to be analysed. Other exclusion criteria included:

- Patients listed for multi-organ transplants other than pancreas (n=3)
- Patients who were suspended for more than 30 days within 90 days of first activation (n=59). This was 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 fitness.

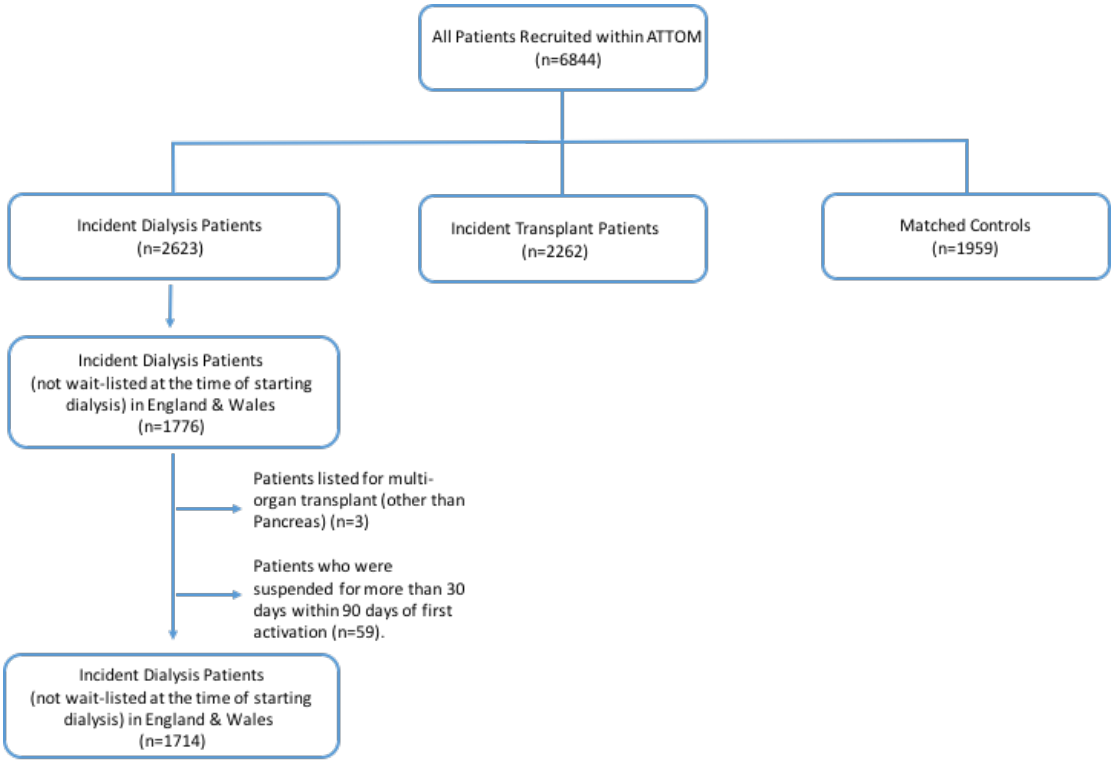

Figure 6.3 Flow diagram showing showing the inclusion and exclusion criteria utilised in the access to listing after starting dialysis analysis.

6.3.1.2 Primary Outcome

The Primary Outcome of this analysis was to whether patients included in the study cohort who started dialysis without being waitlisted were wait-listed for renal

transplantation subsequently, with data on whether a patient was listed or not retrieved from the NHSBT database. To analyse access to the transplant list, the proportion of incident patients with end stage renal disease in each centre who were activated on the waiting list within 18 months of starting dialysis were identified.

All patients who achieved non pre-emptive live donor transplantation without prior activation on the national transplant waiting list were assumed to have been activated for the purposes of this analysis.

6.3.1.3 Follow Up Period

All patients were followed up for 18 months, or until they were put on the waiting list for kidney transplant alone, kidney plus pancreas transplant, or death, whichever was earliest. Patient death whilst on the transplant list was retrieved from NHSBT. Patient death on dialysis (but not on the waiting list) was retrieved from UKRR time-lines using the Health and Social Care Information Service Demographics Batch Service.

6.3.2 Statistical Analyses for Analysis 2: Access to Listing after Starting Dialysis

As the outcome pursued in this analysis was again binary (listed Vs non listed) logistic regression was again used to examine the association between the individual patient and renal centre characteristics and the probability of being listed (as described earlier).

Application of multi-level model to describe access to wait-listing after starting dialysis

A multi-level model was again chosen to analyse the data to account for the hierarchical data structure, patients (level 1) nested within renal centres (level 2) and enable appropriate contextual analysis of the data (as previously discussed). The analytical approach/steps in constructing the model were the same as those used in the pre-emptive listing analysis. Individual patient factors/characteristics (as listed above in pre-emptive listing analysis) were examined first and kept in the model if they remained significantly predictive after adjustment for all other individual characteristics. Dialysis modality was also examined in this model categorized as HD,

HDF, APD and CAPD. This was not examined in pre-emptive listing as patients were not on dialysis.

Following this, centre level characteristics (as described above in pre-emptive listing analysis) were then examined individually, with the addition of one new centre variable (centre pre-emptive listing rate) which was derived from the earlier analysis). Significance testing was performed using a test for heterogeneity for all non-ordered variables and a chi squared test for trend for all ordered categorical variables. A significance level of 0.05 was taken as evidence of a significant association

Statistical Software

All statistical analyses were performed using SAS software version 9.3 (SAS Institute, Cary, NC).

6.4 Results

6.4.1 Comparison of Study Cohort with UKRR Dialysis Population

Prior to undertaking any data analysis to ensure that the cohort of patients analysed in this study were reflective/truly representative of the UK RRT population as a whole, baseline characteristics of those recruited were compared to the baseline characteristics of the entire incident dialysis population starting dialysis during the recruitment time period at all UK renal centres (identified and retrieved from the UKRR database). Baseline characteristics compared included: Gender, Age, Ethnicity, Dialysis modality and Diabetes (as PRD). Results from this comparison did not highlight any significant differences in terms of gender or age, though did show a slightly larger White population in the study population (80.8% vs 68.56% in the UKRR cohort; $p<0.001$) which was likely due to having zero missing data Vs 10.84% missing in the UKRR database. The proportion of patients on PD were also significantly lower than in the UKRR cohort (21.4% Vs 24.9%; $p=0.0005$) though in absolute terms not greatly different and which likely reflected the greater ease for recruiting nurses to seek consent and collect data of patients who attended dialysis on-site three times a week as in the case of haemodialysis versus those patients having peritoneal dialysis at home who would likely be harder to get hold of and consent. As

for the proportion of patients having diabetes as their PRD, this was lower in the ATTOM cohort compared to the UKRR (41% Vs 47%; p<0.001) which is likely to reflect 'real time' better coding of patients' PRD by recruiting nurses as compared to centre data returns the UKRR.

6.4.2 Results Analysis 1: Access to Pre-emptive Listing

6.4.2.1 Overall Baseline Characteristics

Of the 2643 patients eligible for this study, 476 patients were excluded (18%) due to missing data. These included 223 patients with missing BMI data, 27 patients with missing comorbidity data, 45 patients with missing data on time first seen and 181 patients with missing socio-economic data.

The study cohort had a median age of 57 years (interquartile range 45-66), of which 65.4% (n=1418) were male and 80.8% (n=1750) reported their ethnicity as White. Obesity (BMI>25) was present in 1369 patients (63.2%) and more than three quarters (n=1655; 76.4%) had been seen by a nephrologist for >1 year. Amongst examined co-morbidities diabetes was the most prevalent, being present in 35.8% (n= 776) of patients. Diabetes was also the main cause of renal failure (PRD) affecting nearly a quarter (23.8%; n=515) of patients. Amongst socio-demographic factors, 57.8% (n=1252) of patients reported owing their own home with three quarters of patients (75%; n=1624) owing their own car and 17.5% (n=380) of patients reporting being in full-time employment. The baseline characteristics of all patients, stratified by those pre-emptively listed for transplantation and those which were not, are shown in table 6.1.

Study Cohort Group Comparisons

Of the 2167 patients included in this analysis, 600 (27.7%) were pre-emptively listed, with a median of 20% by centre (Range 0-75%, IQR: 5.6% - 33%). In comparison to those that were not listed patients, pre-emptively listed patients were significantly younger (<0.0001), had fewer non-white patients (14.3% Vs 21.1%; p<0.0001), had fewer obese patients (20.3% Vs 35.6; p<0.0001), had fewer diabetic patients (20% Vs 41.9%; p<0.0001), were more likely to be well known to renal services for (known

for >3years 69.7% Vs 48.9%; p<0.0001) and had a lower proportion of patients for each measured comorbidity. Amongst socio-demographic factors, those listed pre-emptively had a significantly higher level of home ownership (71.7 Vs 52.5; p<0.0001), car ownership (88.2% Vs 69.9%; p<0.0001), and a greater proportion in full-time employment 35.3% Vs 10.7%; p<0.0001). Full details of group comparisons are shown in table 6.1

Table 6.1: Showing baseline characteristics of all patients included in analysis for access to pre-emptive listing, stratified by listing status.

Variable	Pre-emptively listed				Total (N)
	No		Yes		
	N	%	N	%	
Age					
18-29	88	5.6	49	8.2	137
30-39	122	7.8	79	13.2	201
40-49	239	15.3	145	24.2	384
50-59	368	23.5	171	28.5	539
60-64	201	12.8	71	11.8	272
65-75	549	35	85	14.2	634
Total	1567	100	600	100	2167
Sex					
Male	1050	67	368	61.3	1418
Female	517	33	232	38.7	749
Total	1567	100	600	100	2167
Ethnic Group					
White	1236	78.9	514	85.7	1750
Asian	177	11.3	55	9.2	232
Back	132	8.4	27	4.5	159
Other	22	1.4	4	0.7	26
Total	1567	100	600	100	2167
BMI					
Less than 20	114	7.3	35	5.8	149
20 - <25	451	28.8	198	33	649
25 - <30	444	28.3	245	40.8	689
30 - <35	294	18.8	98	16.3	392
35 - <40	149	9.5	20	3.3	169
>40	115	7.3	4	0.7	119
Total	1567	100	600	100	2167

Variable	Pre-emptively listed				Total (N)
	No		Yes		
	N	%	N	%	
Time Since First Seen by Nephrologist					
<1 Year	468	29.9	44	7.3	512
1-3 Years	333	21.3	138	23	471
>3 Years	766	48.9	418	69.7	1184
Total	1567	100	600	100	2167
Previous transplant					
No	1395	89	582	97	1977
Yes	172	11	18	3	190
Total	1567	100	600	100	2167
Primary Renal Disease					
Diabetes	423	27	92	15.3	515
Glomerulonephritis	265	16.9	130	21.7	395
Hypertension	115	7.3	37	6.2	152
Other	232	14.8	82	13.7	314
Polycystic	99	6.3	112	18.7	211
Pyelonephritis	114	7.3	75	12.5	189
Renal vascular disease	57	3.6	11	1.8	68
Uncertain	262	16.7	61	10.2	323
Total	1567	100	600	100	2167
Diabetes					
No	911	58.1	480	80	1391
Yes	656	41.9	120	20	776
Total	1567	100	600	100	2167
Heart disease					
No	1232	78.6	560	93.3	1792
Yes	335	21.4	40	6.7	375
Total	1567	100	600	100	2167
Heart failure					
No	1435	91.6	594	99	2029
Yes	132	8.4	6	1	138
Total	1567	100	600	100	2167

Variable	Pre-emptively listed				Total (N)
	No		Yes		
	N	%	N	%	
Atrial fibrillation					
No	1495	95.4	592	98.7	2087
Yes	72	4.6	8	1.3	80
Total	1567	100	600	100	2167
Cardiac valve replacement					
No	1552	99	593	98.8	2145
Yes	15	1	7	1.2	22
Total	1567	100	600	100	2167
Pacemaker					
No	1542	98.4	596	99.3	2138
Yes	25	1.6	4	0.7	29
Total	1567	100	600	100	2167
Vascular disease					
No	1423	90.8	592	98.7	2015
Yes	144	9.2	8	1.3	152
Total	1567	100	600	100	2167
Abdominal aortic aneurysm					
No	1539	98.4	596	99.3	2135
Yes	28	1.6	4	0.7	32
Total	1567	100	600	100	2167
Respiratory disease					
No	1373	87.6	558	93	1931
Yes	194	12.4	42	7	236
Total	1567	100	600	100	2167
Liver disease					
No	1529	97.6	592	98.7	2121
Yes	38	2.4	8	1.3	46
Total	1567	100	600	100	2167
Blood borne viruses					
No	1521	97.1	593	98.8	2114
Yes	46	2.9	7	1.2	53
Total	1567	100	600	100	2167

Variable	Pre-emptively listed				Total (N)
	No		Yes		
	N	%	N	%	
Malignancy					
No	1352	86.3	568	94.7	1920
Yes	215	13.7	32	5.3	247
Total	1567	100	600	100	2167
Smoking					
No	698	44.5	331	55.2	1029
Current	249	15.9	57	9.5	306
Ex-smoker	510	32.5	170	28.3	680
Don’t know	110	7	42	7	152
Total	1567	100	600	100	2167
Mental illness					
No	1431	91.3	572	95.3	2003
Yes	136	8.7	28	4.7	164
Total	1567	100	600	100	2167
Dementia					
No	1560	99.6	600	100	2160
Yes	7	0.4	0	0	7
Total	1567	100	600	100	2167
Born in UK					
No	345	22	82	13.7	427
Yes	1222	78	518	86.3	1740
Total	1567	100	600	100	2167
English First Language					
No	221	14.1	53	8.8	274
Yes	1346	85.9	547	91.2	1893
Total	1567	100	600	100	2167
Need Help Reading					
Never	1144	73	516	86	1660
Always	131	8.4	17	2.8	148
Often	57	3.6	7	1.2	64
Rarely	112	7.1	26	4.3	138
Sometimes	123	7.8	34	5.7	157
Total	1567	100	600	100	2167

Variable	Pre-emptively listed				Total (N)
	No		Yes		
	N	%	N	%	
Accommodation					
Owned by you (Outright or with a Mortgage)	822	52.5	430	71.7	1252
Other	104	6.6	35	5.8	139
Part rent, Part owned (shared ownership)	24	1.5	8	1.3	32
Rented Privately from Council / Housing Association	617	39.4	127	21.2	744
Total	1567	100	600	100	2167
Education					
GCSE, A-level or NVQ 1-3	639	40.8	317	52.8	956
Degree, Higher or NVQ 4-5	245	15.6	151	25.2	396
No Qualifications	683	43.6	132	22	815
Total	1567	100	600	100	2167
Employment					
Working full time	168	10.7	212	35.3	380
Long term sick/disabled	500	31.9	120	20	620
Looking after family home	30	1.9	12	2	42
Not in work for some other reason	17	1.1	19	3.2	36
Retired from paid work	610	38.9	119	19.8	729
Student (includes those in training)	12	0.8	13	2.2	25
Unemployed	125	8	31	5.2	156
Working part time	105	6.7	74	12.3	179
Total	1567	100	600	100	2167
Car ownership					
Yes	1095	69.9	529	88.2	1624
No	472	30.1	71	11.8	543
Total	1567	100	600	100	2167
Civil Status					
Single	304	19.4	130	21.7	434
Divorced	157	10.0	46	7.7	203
Living with Partner	103	6.6	54	9.0	157
Married	845	53.9	344	57.3	1189
Separated (but still legally married)	57	3.6	13	2.2	70
Widowed	101	6.4	13	2.2	114
Total	1567	100	600	100	2167

Variable	Pre-emptively listed				Total (N)
	No		Yes		
	N	%	N	%	
Children in household					
None	1254	80	435	72.5	1689
One or more	313	20	165	27.5	478
Total	1567	100	600	100	2167
Adults in household					
One	462	29.5	116	19.4	578
Two or more	1105	70.5	484	80.6	1589
Total	1567	100	600	100	2167
Total in household					
One	403	25.8	90	15	493
Two or more	1164	74.2	510	85	1674
Total	1567	100	600	100	2167

6.4.2.2 Effect of Case-Mix on Access to pre-emptive Transplantation

Univariate Analysis

The results of the univariate logistic regression model for case mix (patient specific variables) are shown in table 6.2. and the corresponding funnel plot showing each centre's performance compared with its peers in Figure 6.4. Funnel plots are often used by national registries (including the UKRR) to present the results for each outcome of interest, providing a visual comparison of each centre's performance compared with its peers. The solid black straight line in each funnel plot shows the overall average together with the 95% and 99.8% confidence intervals, which correspond to two and three standard deviations. Each point on the plot represents one renal centre. With 57 centres included, for an outcome of interest, two or three centres would be predicted to fall between the 95% and 99.8% confidence intervals (one above and one below) and no centre should fall outside the 99.8% confidence interval.

Excluding the four centres which had no patients pre-emptively listed, in the unadjusted analysis significant centre variation is noted in figure 6.4 with 14 centres lying outside the 95% confidence intervals of which eight are lying outside the 99.8% confidence interval.

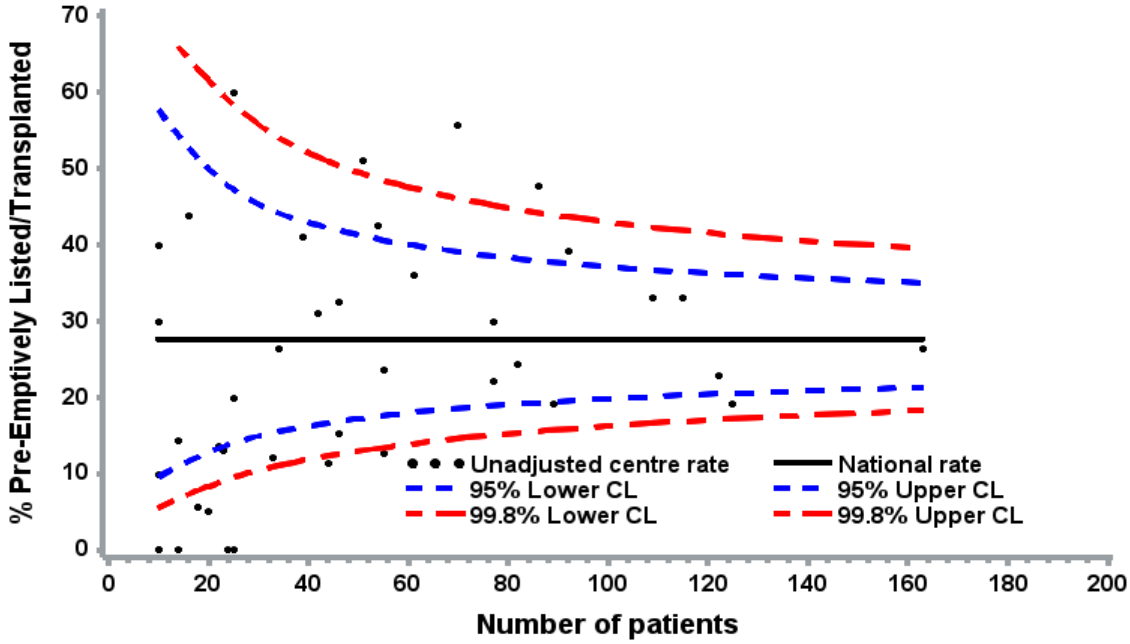

Figure 6.4. – Funnel plot showing the unadjusted percentage of patients pre-emptively listed at each centre in England and Wales.

Table 6.2. Univariate logistic regression for patient level effects on pre-emptive listing in England and Wales.

Variable	Unadjusted Odds Ratio	95% Confidence Limits	Overall p Value
Age Group			
18-29	Ref	-	<0.0001
30-39	1.09	0.73-1.65	
40-49	1.00	0.69-1.44	
50-59	0.73	0.51-1.05	
60-64	0.53	0.36-0.80	
65-75	0.25	0.17-0.36	
Sex			
Male	Ref	-	0.0034
Female	1.31	1.1-1.56	
Ethnic Group			
White	Ref	-	0.0002
Asian	0.67	0.50-0.90	
Black	0.56	0.38-0.82	
Other	0.34	0.12-0.98	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	Overall p Value
BMI (continuous)	0.95	0.94-0.97	<0.0001
BMI			
Less than 20	0.73	0.49-1.1	
20 - <25	Ref	-	<0.0001
25 - <30	1.22	0.98-1.52	
30 - <35	0.75	0.57-0.99	
35 - <40	0.33	0.21-0.52	
>40	0.08	0.03-0.21	
Time Since First Seen by Nephrologist			
<1 Year	Ref	-	<0.0001
1-3 Years	4.72	3.36-6.62	
>3 Years	6.25	4.60-8.49	
Previous transplant			
No	Ref	-	<0.0001
Yes	0.35	0.24-0.52	
Primary Renal Disease			
Diabetes	Ref	-	<0.0001
Glomerulonephritis	2.28	1.72-3.02	
Hypertension	1.57	1.05-2.35	
Other	1.50	1.10-2.05	
Polycystic	5.40	3.90-7.46	
Pyelonephritis	3.03	2.16-4.24	
Renal vascular disease	0.94	0.50-1.77	
Uncertain	1.11	0.80-1.53	
Primary Renal Disease			
Diabetes	Ref	-	<0.0001
Glomerulonephritis	2.51	0.85-1.90	
Glomerulonephritis and Diabetes	0.82	0.43-3.83	
Hypertension	1.72	0.71-2.19	
Hypertension and Diabetes	0.95	0.35-3.77	
Other	1.74	0.85-2.11	
Other and Diabetes	0.46	0.13-1.50	
Polycystic	6.40	1.46-3.71	
Polycystic and Diabetes	0.27	0.01-1.22	
Pyelonephritis	3.67	1.38-3.85	
Pyelonephritis and Diabetes	0.19	0.03-2.03	
Renal vascular disease	0.94	0.50-3.05	
Renal vascular disease and Diabetes	0.94	0.27-4.76	
Uncertain	1.42	0.67-1.72	
Uncertain and Diabetes	0.50	0.31-1.78	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	Overall p Value
Diabetes			
No	Ref	-	<0.0001
Yes	0.35	0.28-0.43	
Heart disease			
No	Ref	-	<0.0001
Yes	0.26	0.19-0.36	
Heart failure			
No	Ref	-	<0.0001
Yes	0.15	0.08-0.29	
Atrial fibrillation			
No	Ref	-	<0.0001
Yes	0.33	0.18-0.62	
Cardiac valve replacement			
No	Ref	-	0.8791
Yes	0.94	0.40-2.21	
Pacemaker			
No	Ref	-	0.0185
Yes	0.34	0.12-0.95	
Vascular disease			
No	Ref	-	<0.0001
Yes	0.15	0.08-0.29	
Abdominal aortic aneurysm			
No	Ref	-	0.0095
Yes	0.31	0.12-0.87	
Respiratory disease			
No	Ref	-	0.0004
Yes	0.58	0.42-0.80	
Liver disease			
No	Ref	-	0.028
Yes	0.48	0.23-0.98	
Blood borne viruses			
No	Ref	-	0.0065
Yes	0.41	0.20-0.84	
Malignancy			
No	Ref	-	<0.0001
Yes	0.35	0.25-0.50	
Smoking			
No	Ref	-	<0.0001
Current	0.51	0.38-0.68	
Ex-smoker	0.72	0.58-0.88	
Don’t know	0.78	0.57-1.07	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	Overall p Value
Mental illness			
No	Ref	-	0.0005
Yes	0.52	0.35-0.77	
Dementia			
No	Ref	-	0.2582
Yes	0.35	0.04-2.80	
Born in UK			
No	Ref	-	<0.0001
Yes	1.79	1.39-2.29	
English First Language			
No	Ref	-	0.0002
Yes	1.74	1.29-2.34	
Need Help Reading			
Never	Ref	-	<0.0001
Always	0.30	0.18-0.49	
Often	0.30	0.140.63	
Rarely	0.58	0.38-0.87	
Sometimes	0.57	0.40-0.83	
Accommodation			
Owned by you (Outright or with a Mortgage)	Ref	-	<0.0001
Other	0.65	0.44-0.95	
Part rent, Part owned (shared ownership)	0.56	0.25-1.23	
Rented Privately from Council / Housing Association	0.41	0.33-0.51	
Education			
GCSE, A-level or NVQ 1-3	Ref	-	<0.0001
Degree, Higher or NVQ 4-5	1.19	0.95-1.50	
No Qualifications	0.38	0.31-0.48	
Employment			
Working full time	Ref	-	<0.0001
Long term sick/disabled	0.20	0.15-0.26	
Looking after family home	0.29	0.15-0.56	
Not in work for some other reason	0.87	0.46-1.63	
Retired from paid work	0.15	0.12-0.20	
Student (includes those in training)	0.75	0.35-1.62	
Unemployed	0.20	0.13-0.31	
Working part time	0.54	0.38-0.76	
Car ownership			
Yes	Ref	-	<0.0001
No	0.31	0.24-0.40	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	Overall p Value
Civil Status			
Single	Ref	-	<0.0001
Divorced	0.69	0.48-0.99	
Living with Partner	1.22	0.84-1.76	
Married	0.95	0.76-1.19	
Separated (but still legally married)	0.54	0.29-0.98	
Widowed	0.30	0.17-0.54	
Children in household			
None	Ref	-	<0.0002
One or more	1.49	1.21-1.84	
Adults in household			
One	Ref	-	<0.0001
Two or more	1.69	1.36-2.10	
Total in household			
One	Ref	-	<0.0001
Two or more	1.90	1.50-2.41	

Multivariate Analysis

Results from the Multivariate logistic regression model for case mix are shown in table 6.3, with several factors seen to have an independent effect on pre-emptive listing. Age 65-75 was seen to be negatively associated with listing with an odds ratio of 0.53 (95% CI: 0.26 to 0.13) compared to those aged 18-29. Other factors negatively associated with pre-emptive listing included: black ethnicity (OR 0.69; CI 0.27-0.79), having had a previous transplant (OR 0.09; CI 0.05-0.16), vascular disease (OR 0.19 CI 0.09-0.43), heart disease (OR 0.51; CI 0.34-0.77), heart failure (OR 0.08-0/51), a previous history of malignancy (OR 0.38; CI: 0.24-0.60), being a current smoker (OR 0.55; CI: 0.37-0.83) and having a BMI of > 35 (with odds ratios of 0.21 (CI: 0.11-0.37) and 0.05 (CI:0.02-0.15) for patients with a BMI of 35-40, and >40 , compared to those with a BMI of 20-25).

Socioeconomic status was also seen to to be associated negatively with listing, with having no educational qualifications (OR 0.63; CI 0.47-0.85), lack of car ownership (OR 0.53; CI 0.37-0.74) and living in rented or housing association accommodation (OR 0.54; CI 0.39-0.74) as opposed to owning your home both reducing the

likelihood of being listed. Employment status too affected the likelihood of being listed, with being long term sick/disabled (OR 0.35; CI 0.24-0.50), looking after the family home (OR 0.25; CI 0.10-0.59), being retired from paid work (OR 0.48; CI 0.30-0.78), being unemployed (OR 0.46; CI 0.26-0.80) or working part time (OR 0.54; CI 0.34-0.84) all being negatively associated with pre-emptive listing when compared to being in full time employment.

In contrast to these negatively associated factors, having a primary renal diagnosis of polycystic kidney disease (OR 2.33; CI 1.46-3.71) or pyelonephritis (OR 2.33; CI 1.38-3.85) compared to diabetes were both seen to increase the likelihood of being listed. Likewise, those seen by a nephrologist 1-3 years before starting RRT (OR 7.93; CI 5.14-12.22) or > 3 years before starting RRT (OR 9.63; CI 6.52-14.22) as compared to < 1 year, were both seen to have a positive impact on pre-emptive listing.

Table 6.3 – Multivariate logistic regression model for the probability of a patient being pre-emptively listed in England and Wales.

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Age				
18-29	137	1	-	-
30-39	201	1.16	0.63-2.13	0.6426
40-49	384	1.05	0.59-1.89	0.8665
50-59	539	0.82	0.46-1.48	0.5093
60-64	272	0.61	0.31-1.19	0.1457
65-75	634	0.26	0.13-0.53	0.0002
Time Since First Seen by Nephrologist				
<1 Year	512	1	-	-
1-3 Years	471	7.93	5.14-12.22	<0.0001
>3 Years	1184	9.63	6.52-14.22	<0.0001
Education				
GCSE, A-level or NVQ 1-3	956	1	-	-
Degree, Higher or NVQ 4-5	396	0.89	0.64-1.23	0.466
No Qualifications	815	0.63	0.47-0.85	0.0027
Car ownership				
Yes	1624	1	-	-
No	543	0.53	0.37-0.74	<0.0001

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Accommodation				
Owned by you (Outright or with a Mortgage)	1252	1	-	-
Other	139	0.60	0.35-1.04	0.0666
Part rent, Part owned (shared ownership)	32	0.48	0.17-1.34	0.1589
Rented Privately from Council / Housing Association	744	0.54	0.39-0.74	0.0001
Employment				
Working full time	380	1	-	-
Long term sick/disabled	620	0.35	0.24-0.50	<0.0001
Looking after family home	42	0.25	0.10-0.59	0.0016
Not in work for some other reason	36	1.45	0.60-3.52	0.4093
Retired from paid work	729	0.48	0.30-0.78	0.0031
Student (includes those in training)	25	1.79	0.60-5.35	0.3
Unemployed	156	0.46	0.26-0.80	0.0062
Working part time	179	0.54	0.34-0.84	0.0064
Malignancy				
No	1920	1	-	-
Yes	247	0.38	0.24-0.60	<0.0001
Smoking				
No	1029	1	-	-
Current	306	0.55	0.37-0.83	0.0042
Ex-smoker	680	0.92	0.69-1.22	0.5541
Don’t know	152	0.81	0.50-1.30	0.379
Vascular Disease				
No	2015	1	-	-
Yes	152	0.19	0.09-0.43	<0.0001
Heart Disease				
No	1792	1	-	-
Yes	375	0.51	0.34-0.77	0.0012
Heart Failure				
No	2029	1	-	-
Yes	138	0.20	0.08-0.51	0.0008
BMI				
Less than 20	149	0.82	0.49-1.38	0.4508
20 - <25	649	1	-	-
25 - <30	689	1.24	0.92-1.67	0.1526
30 - <35	392	0.87	0.60-1.25	0.4441
35 - <40	169	0.21	0.11-0.37	<.0001
>40	119	0.05	0.02-0.15	<.0001

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Ethnic Group				
White	1750	1	-	-
Asian	232	0.69	0.46-1.04	0.073
Black	159	0.46	0.27-0.79	0.0047
Other	26	0.33	0.09-1.24	0.1005
Primary Renal Disease				
Diabetes	515	1	-	-
Glomerulonephritis	359	1.27	0.85-1.90	0.2492
Glomerulonephritis and Diabetes	36	1.29	0.43-3.83	0.6525
Hypertension	123	1.25	0.71-2.19	0.4442
Hypertension and Diabetes	29	1.14	0.35-3.77	0.8264
Other	270	1.34	0.85-2.11	0.2098
Other and Diabetes	44	0.45	0.13-1.50	0.1937
Polycystic	195	2.33	1.46-3.71	0.0004
Polycystic and Diabetes	16	0.13	0.01-1.22	0.0742
Pyelonephritis	166	2.31	1.38-3.85	0.0013
Pyelonephritis and Diabetes	23	0.26	0.03-2.03	0.1979
Renal vascular disease	47	1.23	0.50-3.05	0.6571
Renal vascular disease and Diabetes	21	1.14	0.27-4.76	0.858
Uncertain	231	1.07	0.67-1.72	0.772
Uncertain and Diabetes	92	0.75	0.31-1.78	0.5093
Previous transplant				
None	1977	1	-	-
Yes	190	0.09	0.05-0.16	<.0001

The impact of adjusting for these patient factors on centre variation is shown in shown in the case mix adjusted funnel plot, figure 6.5.

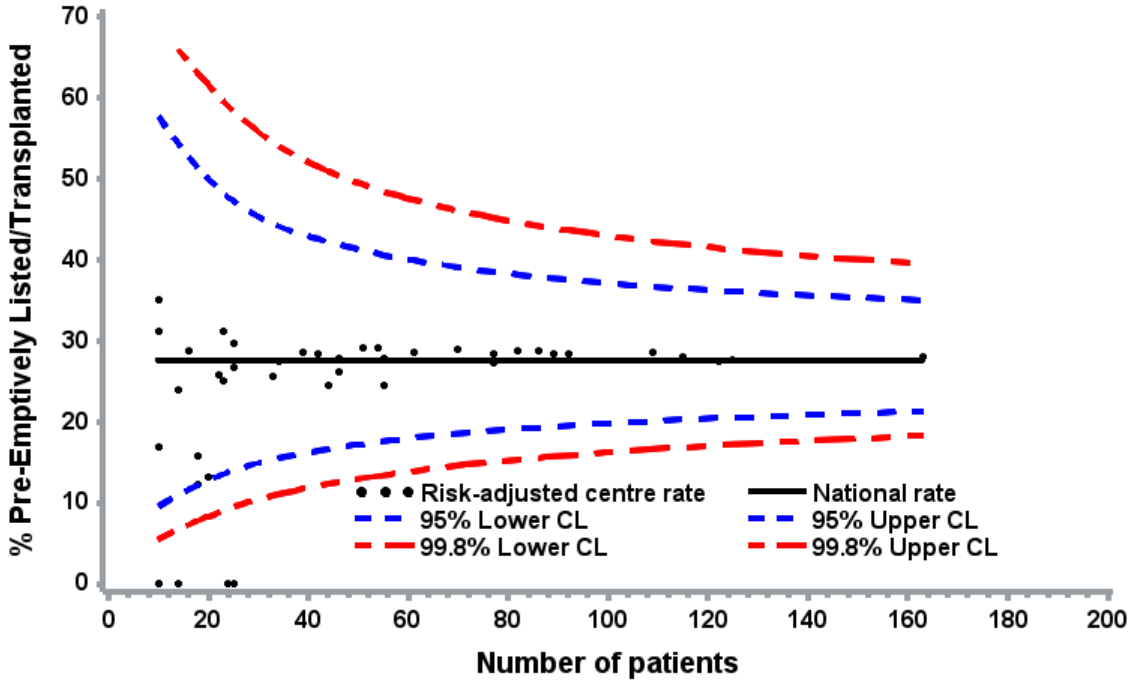

Figure 6.5 – Funnel plot showing the case mix adjusted percentage of patients pre-emptively listed at each centre in England and Wales

As compared to the unadjusted funnel plot (Figure 6.4), this funnel plot shows no centres lying outside either the 95% or 99.8% confidence intervals (other than the 4 centres which had listed no patients) suggesting that much of the variation noted earlier in the unadjusted model had been accounted for in the adjusted model by patent specific factors -which was 'a better fit'. To see if there was still any unaccounted variation, the adjusted model was re-run with the addition of centre as a random effect.

The results of this analysis are shown in table 6.4.; and shows that the model with centre as a random effect was significantly better ($p<0.0001$) suggesting that whilst adjusting for patient variables had accounted for a proportion of centre variation, a degree of variation still persisted which potentially could be accounted for by centre factors.

Table 6.4. – Multivariate patient level model for probability of being pre-emptively listed, including renal unit as a random effect

Model	-2 log L	p-value
Null Model	2557	
Multivariate Patient Level Model	1672.2	
Multivariate Patient Level Model + Random Effect for Renal Unit	1607.8	<0.0001

6.4.2.3 Effect of Centre Practice Patterns on Access to pre-emptive listing

Results from the univariate analysis exploring the impact of centre variables on access to pre-emptive listing (adjusted for case mix) are shown in Table 6.5. After a model building process, several of these factors were highlighted as having an effect on pre-emptive listing in the multivariable analysis (which included both patient and centre factors). These are shown in table 6.6.

Being registered at a transplanting centre (OR 3.89; CI 2.78-5.45), having ≥6 WTE consultant nephrologists (OR 2.06; CI 1.40-3.03), adopting a selective approach in the use of a low clearance clinic (OR 1.73; 1.11-2.73) as compared to never or always using one, and adopting an approach where transplantation is discussed with all patients (OR 1.48; CI 1.09-2.00) were all seen to have a positive impact on pre-emptively listing patients.

Table 6.5. – Univariate logistic regression for centre level effects on pre-emptive listing/transplant, adjusting for patient level factors.

Centre Factor	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Number of Consultant Nephrologists (continuous increase by 1)	1.06	1.04 - 1.09	<0.0001
Number of Consultant Nephrologists (categorical increase by 1)			<0.0001
<6	1	-	-
>=6	2.62	1.88 - 3.65	
Number of Patients Receiving RRT (continuous increase by 1)	1.01	1.07 - 1.09	<0.0001
Number of Patients Receiving RRT (categorical)			<0.0001
1st Quartile	1	-	-
2nd vs 1st Quartile	1.72	1.19 - 2.48	
3rd vs 1st Quartile	2.92	2.04 - 4.17	
4th vs 1st Quartile	3.09	2.13 - 4.47	
Transplanting Centre			<0.0001
Yes	1	-	
No	3.62	2.7 - 4.87	
Use of Low Clearance Clinic			0.817
Never	1	-	
Always	1.13	0.78 - 1.63	
Sometimes	1.21	0.76 - 1.62	
Transplantation Discussed with All Patients			0.1809
Yes	1	-	
No	1.21	0.91 - 1.6	
Location of Assessment			0.0001
Locally	-	-	
Referred to another Centre	0.39	0.24 0.63	
Patients Seen by a Surgeon			0.4756
Yes	1	-	
No	0.85	0.55 - 1.32	
Written Protocol			0.3773
Yes	1	-	
No	1.16	0.83 - 1.63	
Use of MDT			0.0058
Yes	1	-	
No	1.55	1.13 - 2.12	
MDT used to List All Patients			0.0484
Yes	1	-	
No	1.31	1 - 1.71	

Centre Factor	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Audit of CKD 5 Patients Listing Status			0.0014
Never	1	-	
1-2 per year	1.17	0.88 - 1.95	0.82 - 1.67
3-4 per year	1.76	1.11 - 2.86	1.18 - 2.63
5 or more per year	0.54	0.51 5.38	0.13 - 2.21
Other	0.73	0.71 2.09	0.44 - 1.19
Named Cardiologist			<0.0001
Yes	1	-	
No	1.68	1.29 - 2.19	

Table 6.6 – Multivariate logistic regression model for the probability of a patient being pre-emptively listed including centre level factors

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Age				
18-29	137	1	-	-
30-39	201	1.10	0.58-2.08	0.8514
40-49	384	1.01	0.55-1.86	0.9307
50-59	539	0.77	0.42-1.42	0.3575
60-64	272	0.55	0.27-1.11	0.0958
65-75	634	0.24	0.12-0.51	0.0001
Time Since First Seen by Nephrologist				
<1 Year	512	1	-	-
1-3 Years	471	8.70	5.56-13.61	<0.0001
>3 Years	1184	10.33	6.91-15.45	<0.0001
Education				
GCSE, A-level or NVQ 1-3	956	1	-	-
Degree, Higher or NVQ 4-5	396	0.85	0.61-1.20	0.3717
No Qualifications	815	0.74	0.54-1.02	0.0394
Car ownership				
Yes	1624	1	-	-
No	543	0.52	0.37-0.75	0.0002

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Accommodation				
Owned by you (Outright or with a Mortgage)	1252	1	-	-
Other	139	0.59	0.33-1.03	0.0558
Part rent, Part owned (shared ownership)	32	0.34	0.11-1.03	0.076
Rented Privately from Council / Housing Association	744	0.52	0.36-0.72	<0.0001
Employment				
Working full time	380	1	-	-
Long term sick/disabled	620	0.33	0.22-0.48	<0.0001
Looking after family home	42	0.31	0.12-0.78	0.0112
Not in work for some other reason	36	1.26	0.51-3.10	0.6162
Retired from paid work	729	0.47	0.28-0.77	0.0028
Student (includes those in training)	25	2.18	0.68-6.98	0.2573
Unemployed	156	0.37	0.21-0.67	0.0014
Working part time	179	0.57	0.36-0.91	0.0166
Malignancy				
No	1920	1	-	-
Yes	247	0.34	0.21-0.56	<0.0001
Smoking				
No	1029	1	-	-
Current	306	0.56	0.37-0.86	0.0123
Ex-smoker	680	0.93	0.69-1.25	0.6962
Don’t know	152	0.80	0.48-1.33	0.4169
Vascular Disease				
No	2015	1	-	-
Yes	152	0.17	0.07-0.37	<0.0001
Heart Disease				
No	1792	1	-	-
Yes	375	0.45	0.30-0.69	0.0004
Heart Failure				
No	2029	1	-	-
Yes	138	0.20	0.08-0.51	0.0009
BMI				
Less than 20	149	0.83	0.49-1.43	0.5695
20 - <25	649	1	-	-
25 - <30	689	1.31	0.96-1.79	0.0828
30 - <35	392	0.91	0.62-1.33	0.6382
35 - <40	169	0.20	0.11-0.37	<0.0001
>40	119	0.05	0.02-0.14	<0.0001

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Ethnic Group				
White	1750	1	-	-
Asian	232	0.50	0.33-0.77	0.0028
Black	159	0.36	0.21-0.63	0.0002
Other	26	0.23	0.06-0.94	0.0407
Primary Renal Disease				
Diabetes	515	1	-	-
Glomerulonephritis	359	1.19	0.78-1.82	0.3563
Glomerulonephritis and Diabetes	36	1.08	0.35-3.37	0.8903
Hypertension	123	1.46	0.81-2.63	0.1975
Hypertension and Diabetes	29	1.27	0.37-4.32	0.6889
Other	270	1.26	0.78-2.03	0.3249
Other and Diabetes	44	0.42	0.12-1.47	0.1831
Polycystic	195	2.20	1.35-3.59	0.0009
Polycystic and Diabetes	16	0.11	0.01-1.08	0.0522
Pyelonephritis	166	2.04	1.19-3.49	0.0078
Pyelonephritis and Diabetes	23	0.25	0.03-2.03	0.1605
Renal vascular disease	47	1.29	0.48-3.46	0.553
Renal vascular disease and Diabetes	21	0.84	0.18-3.79	0.863
Uncertain	231	0.95	0.57-1.55	0.9021
Uncertain and Diabetes	92	0.61	0.25-1.45	0.2443
Previous transplant				
None	1977	1	-	-
Yes	190	0.09	0.05-0.16	<0.0001
Transplanting Centre				
No	700	1	-	-
Yes	1467	3.89	2.78-5.45	<0.0001
No. of Consultant Nephrologists				
<6	463	1	-	-
>=6	1704	2.06	1.40-3.03	<0.0001
Use of a Low Clearance Clinic				
Never	314	1	-	-
Sometimes	719	1.73	1.11-2.70	<0.0001
Always	1134	1.00	0.66-1.51	
Transplantation Discussed with All Patients				
No	590	1	-	-
Yes	1577	1.48	1.09-2.00	0.041

The impact of adjusting for both patient and centre factors from this analysis on centre variation is shown in the fully adjusted funnel plot, figure 6.6. Again, no centre in this funnel plot is seen to lie outside wither the 95% or 99.8% (other than the 4 centres which had listed no patients). Following this analysis when the model was re-run with the addition of centre as a random effect (see table 6.7), the overall fit of the model did not significantly improve (p=0.222).

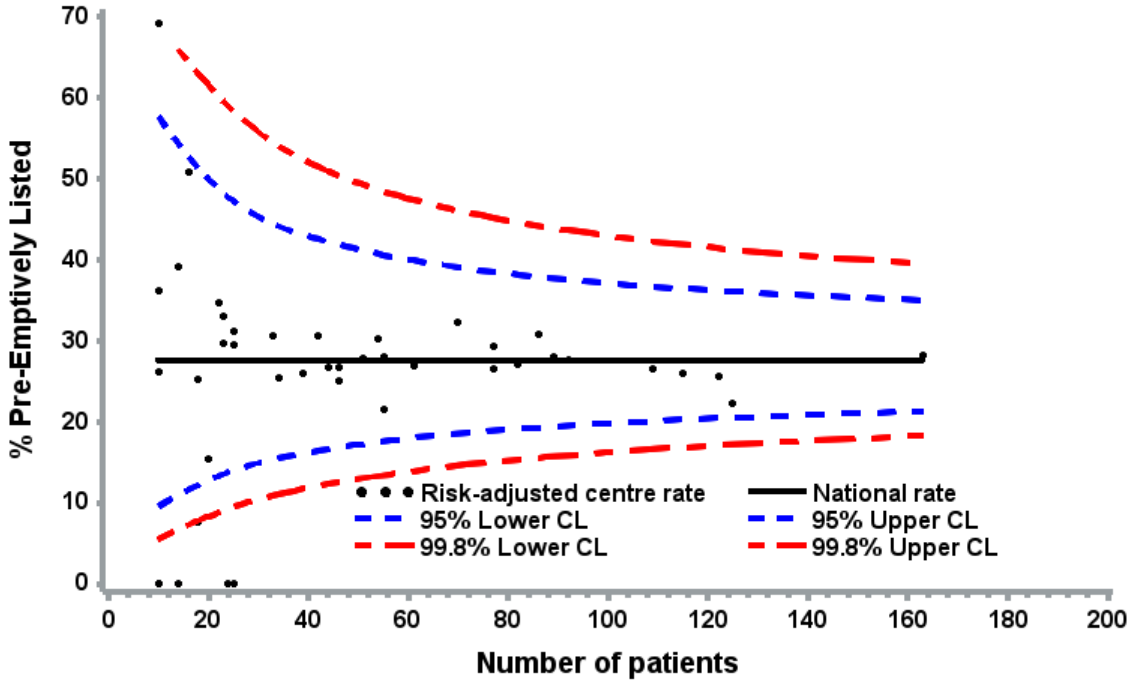

Figure 6.6 – Funnel plot showing the percentage of patients pre-emptively listed at each centre in England and Wales risk-adjusted for patient and centre level factors

Table 6.7. – Multivariate patient and centre level model for probability of being pre-emptively listed/transplanted, including renal centre as a random effect.

Model	-2 log L	p-value
Multivariate Patient and Centre Level Model	1572.3	
Multivariate Patient and Centre Level Model + Random Effect for Renal Unit	1557.5	0.222

Sensitivity Analyses

Of the 2167 patients analysed in this study, 132 patients (n=6.1%) were identified as having had a pre-emptive live transplant. These were excluded in a separate sensitivity analysis which did not show any significant change to the results (data not shown). Another sensitivity analysis was conducted which involved the use of multiple imputation to account for missing data in 476 patients (18%) of the original eligible cohort of 2643 patients. These included 223 patients with missing BMI data, 27 patients with missing comorbidity data, 45 patients with missing data on time first seen and 181 patients with missing socio-economic data. The results from this analysis (which was conducted with the assistance of Dr. Matthew Robb, Statistician at NHSBT) again showed no overall change in the results and can be seen in Appendix E.

6.4.3 Results Analysis 2: Access to Listing after starting dialysis

6.4.3.1 Overall Baseline Characteristics

Of the 1714 patients eligible for this study, 286 patients were excluded (16.7%) due to missing data. These included 163 patients with missing BMI data, 22 patients with missing comorbidity data and 101 patients with missing socio-economic data.

The study cohort had a median age of 58 years (interquartile range 47-67 years), of which 67.9% (n=969) were male and 77.7% (n=1110) reported their ethnicity as White. Obesity was seen in 927 patients (64.9%) and more than two thirds (n=978; 68.5%) had been seen by a nephrologist for >1 year. Amongst examined co-morbidities diabetes was the most prevalent, being present in 40% (n= 571) of patients. Diabetes was also the main cause of renal failure affecting nearly a quarter (25.8%; n=369) of patients. Amongst socio-demographic factors, 51.9% (n=741) of patients reported owing their own home, 70.2% of patients (n=1003) owned their own car; whilst only 11.8% (n=169) of patients reported being in full-time employment. The baseline characteristics of all patients, stratified by those listed for transplantation within 18 months of starting dialysis and those which were not, are shown in table 6.8.

Study Cohort Group Comparisons

Of the 1428 patients included in this analysis, 460 (26.8%) were listed within 18 months of starting dialysis, with a median of 33% by centre (Range 0-100%, IQR: 24.5% - 40%). In comparison to those that were not listed patients, listed patients were significantly younger (<0.0001), had more non-white patients (28.9% Vs 19.4%; p<0.0001) and had fewer diabetic patients (25.7% Vs 46.8%; p<0.0001). Amongst socio-demographic factors, those listed within 18 months of starting dialysis a greater proportion in full-time employment 22.4% Vs 6.8%; p<0.0001). Full details of group comparisons are shown in table 6.8.

Table 6.8: Showing baseline characteristics of all patients included in the analysis for access to listing after starting dialysis, stratified by listing status.

Variable	Listed within 18 months of starting dialysis				Total (N)
	No		Yes		
	N	%	N	%	
Age					
18-29	34	3.5	53	11.5	87
30-39	52	5.4	71	15.4	123
40-49	121	12.5	106	23	227
50-59	234	24.2	110	23.9	344
60-64	138	14.3	43	9.3	181
65-75	389	40.2	77	16.7	466
Total	968	100	460	100	1428
Sex					
Male	660	68.2	309	67.2	969
Female	308	31.8	151	32.8	459
Total	968	100	460	100	1428
Ethnic Group					
White	780	80.6	330	71.7	1110
Asian	95	9.8	72	15.7	167
Back	81	8.4	49	10.7	130
Other	12	1.2	9	2	21
Total	968	100	460	100	1428

Variable	Listed within 18 months of starting dialysis				Total (N)
	No		Yes		
	N	%	N	%	
BMI					
Less than 20	62	6.4	37	8	99
20 - <25	245	25.3	157	34.1	402
25 - <30	267	27.6	162	35.2	429
30 - <35	184	19	75	16.3	259
35 - <40	109	11.3	25	5.4	134
>40	101	10.4	4	0.9	105
Total	968	100	460	100	1428
Time Since First Seen by Nephrologist					
<1 Year	283	29.2	167	36.3	450
1-3 Years	213	22	76	16.5	289
>3 Years	472	48.8	217	47.2	689
Total	968	100	460	100	1428
Previous transplant					
No	867	89.6	382	83	1249
Yes	101	10.4	78	17	179
Total	968	100	460	100	1428
Primary Renal Disease					
Diabetes	293	30.3	76	16.5	369
Glomerulonephritis	125	12.9	130	28.3	255
Hypertension	72	7.4	38	8.3	110
Other	150	15.5	60	13	210
Polycystic	51	5.3	44	9.6	95
Pyelonephritis	75	7.7	30	6.5	105
Renal vascular disease	41	4.2	7	1.5	48
Uncertain	161	16.6	75	16.3	236
Total	968	100	460	100	1428
Diabetes					
No	515	53.2	342	74.3	857
Yes	453	46.8	118	25.7	571
Total	968	100	460	100	1428
Heart disease					
No	729	75.3	410	89.1	1139
Yes	239	24.7	50	10.9	289
Total	968	100	460	100	1428

Variable	Listed within 18 months of starting dialysis				Total (N)
	No		Yes		
	N	%	N	%	
Heart failure					
No	886	91.5	441	95.9	1327
Yes	82	8.5	19	4.1	101
Total	968	100	460	100	1428
Atrial fibrillation					
No	922	95.2	450	97.8	1372
Yes	46	4.8	10	2.2	56
Total	968	100	460	100	1428
Cardiac valve replacement					
No	959	99.1	458	99.6	1417
Yes	9	0.9	2	0.4	11
Total	968	100	460	100	1428
Pacemaker					
No	950	98.1	457	99.3	1407
Yes	18	1.9	3	0.7	21
Total	968	100	460	100	1428
Vascular disease					
No	853	88.1	443	96.3	1296
Yes	115	11.9	17	3.7	132
Total	968	100	460	100	1428
Abdominal aortic aneurysm					
No	944	97.5	459	99.8	1403
Yes	24	2.5	1	0.2	25
Total	968	100	460	100	1428
Respiratory disease					
No	846	87.4	418	90.9	1264
Yes	122	12.6	42	9.1	164
Total	968	100	460	100	1428
Liver disease					
No	950	98.1	454	98.7	1404
Yes	18	1.9	6	1.3	24
Total	968	100	460	100	1428

Variable	Listed within 18 months of starting dialysis				Total (N)
	No		Yes		
	N	%	N	%	
Blood borne viruses					
No	933	96.4	453	98.5	1386
Yes	35	3.6	7	1.5	42
Total	968	100	460	100	1428
Malignancy					
No	810	83.7	438	95.2	1248
Yes	158	16.3	22	4.8	180
Total	968	100	460	100	1428
Smoking					
No	407	42	234	50.9	641
Current	172	17.8	52	11.3	224
Ex-smoker	326	33.7	134	29.1	460
Don’t know	63	6.5	40	8.7	103
Total	968	100	460	100	1428
Mental illness					
No	876	90.5	430	93.5	1306
Yes	92	9.5	30	6.5	122
Total	968	100	460	100	1428
Dementia					
No	963	99.5	459	99.8	1422
Yes	5	0.5	1	0.2	6
Total	968	100	460	100	1428
Born in UK					
No	204	21.1	122	26.5	326
Yes	764	78.9	338	73.5	1102
Total	968	100	460	100	1428
English First Language					
No	130	13.4	78	17	208
Yes	838	86.6	382	83	1220
Total	968	100	460	100	1428

Variable	Listed within 18 months of starting dialysis				Total (N)
	No		Yes		
	N	%	N	%	
Need Help Reading					
Never	685	70.8	364	79.1	1049
Always	95	9.8	20	4.3	115
Often	38	3.9	11	2.4	49
Rarely	68	7	37	8	105
Sometimes	82	8.5	28	6.1	110
Total	968	100	460	100	1428
Accommodation					
Owned by you (Outright or with a Mortgage)	495	51.1	247	53.7	742
Other	57	5.9	43	9.4	100
Part rent, Part owned (shared ownership)	10	1	12	2.6	22
Rented Privately from Council / Housing Association	406	42	158	34.3	564
Total	968	100	460	100	1428
Education					
GCSE, A-level or NVQ 1-3	370	38.2	222	48.3	592
Degree, Higher or NVQ 4-5	127	13.1	114	24.8	241
No Qualifications	471	48.7	124	27	595
Total	968	100	460	100	1428

Variable	Listed within 18 months of starting dialysis				Total (N)
	No		Yes		
	N	%	N	%	
Employment					
Working full time	66	6.8	103	22.4	169
Long term sick/disabled	313	32.3	137	29.8	450
Looking after family home	20	2.1	11	2.4	31
Not in work for some other reason	11	1.1	7	1.5	18
Retired from paid work	434	44.8	89	19.3	523
Student (includes those in training)	5	0.5	8	1.7	13
Unemployed	71	7.3	50	10.9	121
Working part time	48	5	55	12	103
Total	968	100	460	100	1428
Car ownership					
Yes	659	68.1	344	74.8	1003
No	309	31.9	116	25.2	425
Total	968	100	460	100	1428
Type of Dialysis					
HD	701	72.4	301	65.4	1002
HDF	102	10.5	32	7	134
APD	73	7.5	49	10.7	122
CAPD	92	9.5	78	17	170
Total	968	100	460	100	1428
Civil Status					
Single	170	17.6	115	25.0	285
Divorced	101	10.4	38	8.3	139
Living with Partner	56	5.8	38	8.3	94
Married	527	54.4	243	52.8	770
Separated (but still legally married)	39	4.0	14	3.0	53
Widowed	75	7.8	12	2.6	87
Total	968	100	460	100	1428

Variable	Listed within 18 months of starting dialysis				Total (N)
	No		Yes		
	N	%	N	%	
Children in household					
None	810	83.7	314	68.3	1124
One or more	158	16.3	146	31.7	304
Total	968	100	460	100	1428
Adults in household					
One	301	31.1	118	25.7	419
Two or more	667	68.9	342	74.3	1009
Total	968	100	460	100	1428
Total in household					
One	267	27.6	94	20.4	361
Two or more	701	72.4	366	79.6	1067
Total	968	100	460	100	1428

6.4.3.2 Effect of Case-Mix on Access to Listing After Starting Dialysis

Univariate Analysis

The results of the univariate logistic regression model for the impact of case mix (patient specific variables) on listing are shown in table 6.9. and the corresponding unadjusted funnel plot showing centre performance in Figure 6.7. In the unadjusted analysis significant centre variation is noted in figure 6.7 with 5 centres lying outside the 95% confidence interval of which one is seen lying outside the 99.8% confidence interval.

Table 6.9. - Univariate logistic regression for patient level effect of being added to the transplant list within 18 months of starting dialysis

Variable	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Age Group			
18-29	Ref	-	<0.0001
30-39	0.85	0.50-1.43	
40-49	0.50	0.31-0.80	
50-59	0.25	0.16-0.39	
60-64	0.18	0.11-0.30	
65-75	0.10	0.06-0.16	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Sex			
Male	Ref	-	0.7103
Female	0.96	0.77-1.19	
Ethnic Group			
White	Ref	-	0.0008
Asian	1.68	1.25-2.26	
Black	1.46	1.02-2.07	
Other	2.05	0.94-4.47	
BMI (continuous)	0.93	0.92-0.95	<0.0001
BMI			
Less than 20	0.89	0.57-1.39	
20 - <25	Ref	-	<0.0001
25 - <30	0.96	0.74-1.26	
30 - <35	0.66	0.48-0.91	
35 - <40	0.34	0.22-0.55	
>40	0.06	0.02-0.16	
Time Since First Seen by Nephrologist			
<1 Year	Ref	-	0.0462
1-3 Years	0.72	0.54-0.96	
>3 Years	0.80	0.64-1.01	
Previous transplant			
No	Ref	-	0.0001
Yes	1.8	1.33-2.43	
Primary Renal Disease			
Diabetes	Ref	-	<0.0001
Glomerulonephritis	3.48	2.54-4.78	
Hypertension	1.72	1.12-2.66	
Other	1.30	0.91-1.85	
Polycystic	3.10	2.00-4.80	
Pyelonephritis	1.51	0.97-2.37	
Renal vascular disease	0.59	0.27-1.28	
Uncertain	1.61	1.152.25	
Primary Renal Disease			
Diabetes	Ref	-	<0.0001
Glomerulonephritis	3.94	2.83-5.48	
Glomerulonephritis and Diabetes	1.39	0.67-2.88	
Hypertension	1.87	1.18-2.98	
Hypertension and Diabetes	1.18	0.46-3.04	
Other	1.41	0.97-2.04	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Other and Diabetes	0.88	0.41-1.89	
Polycystic	3.30	2.06-5.28	
Polycystic and Diabetes	2.47	0.92-6.65	
Pyelonephritis	1.66	1.03-2.67	
Pyelonephritis and Diabetes	0.88	0.29-2.70	
Renal vascular disease	0.75	0.32-1.74	
Renal vascular disease and Diabetes	0.24	0.03-1.80	
Uncertain	2.17	1.50-3.12	
Uncertain and Diabetes	0.73	0.40-1.32	
Diabetes			
No	Ref	-	<0.0001
Yes	0.45	0.36-0.55	
Heart disease			
No	Ref	-	<0.0001
Yes	0.39	0.29-0.53	
Heart failure			
No	Ref	-	<0.0001
Yes	0.40	0.24-0.66	
Atrial fibrillation			
No	Ref	-	0.0133
Yes	0.49	0.26-0.89	
Cardiac valve replacement			
No	Ref	-	0.0952
Yes	0.33	0.07-1.45	
Pacemaker			
No	Ref	-	0.0145
Yes	0.28	0.08-0.92	
Vascular disease			
No	Ref	-	<0.0001
Yes	0.34	0.21-0.53	
Abdominal aortic aneurysm			
No	Ref	-	<0.0001
Yes	0.07	0.01-0.53	
Respiratory disease			
No	Ref	-	0.0335
Yes	0.69	0.49-0.98	
Liver disease			
No	Ref	-	0.0586
Yes	0.45	0.19-1.10	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Blood borne viruses			
No	Ref	-	0.0032
Yes	0.34	0.15-0.76	
Malignancy			
No	Ref	-	<0.0001
Yes	0.27	0.18-0.40	
Smoking			
No	Ref	-	0.006
Current	0.59	0.43-0.81	
Ex-smoker	0.81	0.64-1.02	
Don't know	1.01	0.70-1.45	
Mental illness			
No	Ref	-	0.0376
Yes	0.66	0.44-0.99	
Dementia			
No	Ref	-	0.2833
Yes	0.36	0.04-2.96	
Born in UK			
No	Ref	-	0.0131
Yes	0.73	0.58-0.94	
English First Language			
No	Ref	-	0.0224
Yes	0.72	0.54-0.95	
Need Help Reading			
Never	Ref	-	0.0031
Always	0.46	0.30-0.73	
Often	0.56	0.29-1.07	
Rarely	1.05	0.70-1.57	
Sometimes	0.84	0.57-1.24	
Accommodation			
Owned by you (Outright or with a Mortgage)	Ref	-	0.0012
Other	1.66	1.12-2.46	
Part rent, Part owned (shared ownership)	2.05	0.94-4.47	
Rented Privately from Council / Housing Association	0.81	0.65-1.01	
Education			
GCSE, A-level or NVQ 1-3	Ref	-	<0.0001
Degree, Higher or NVQ 4-5	0.65	0.49-0.87	
No Qualifications	0.29	0.21-0.39	

Variable	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Employment			
Working full time	Ref	-	<0.0001
Long term sick/disabled	0.28	0.20-0.39	
Looking after family home	0.31	0.15-0.66	
Not in work for some other reason	0.43	0.17-1.10	
Retired from paid work	0.13	0.09-0.19	
Student (includes those in training)	1.29	0.43-3.93	
Unemployed	0.47	0.30-0.73	
Working part time	0.71	0.44-1.12	
Car ownership			
Yes	Ref	-	0.0056
No	0.72	0.57-0.91	
Civil Status			
Single	Ref	-	<0.0001
Divorced	0.56	0.37-0.84	
Living with Partner	1.01	0.65-1.58	
Married	0.67	0.52-0.88	
Separated (but still legally married)	0.54	0.29-0.99	
Widowed	0.24	0.13-0.45	
Children in household			
None	Ref	-	<0.0001
One or more	1.71	1.34-2.17	
Adults in household			
One	Ref	-	0.015
Two or more	1.03	0.80-1.31	
Total in household			
One	Ref	-	<0.0001
Two or more	1.12	0.87-1.46	

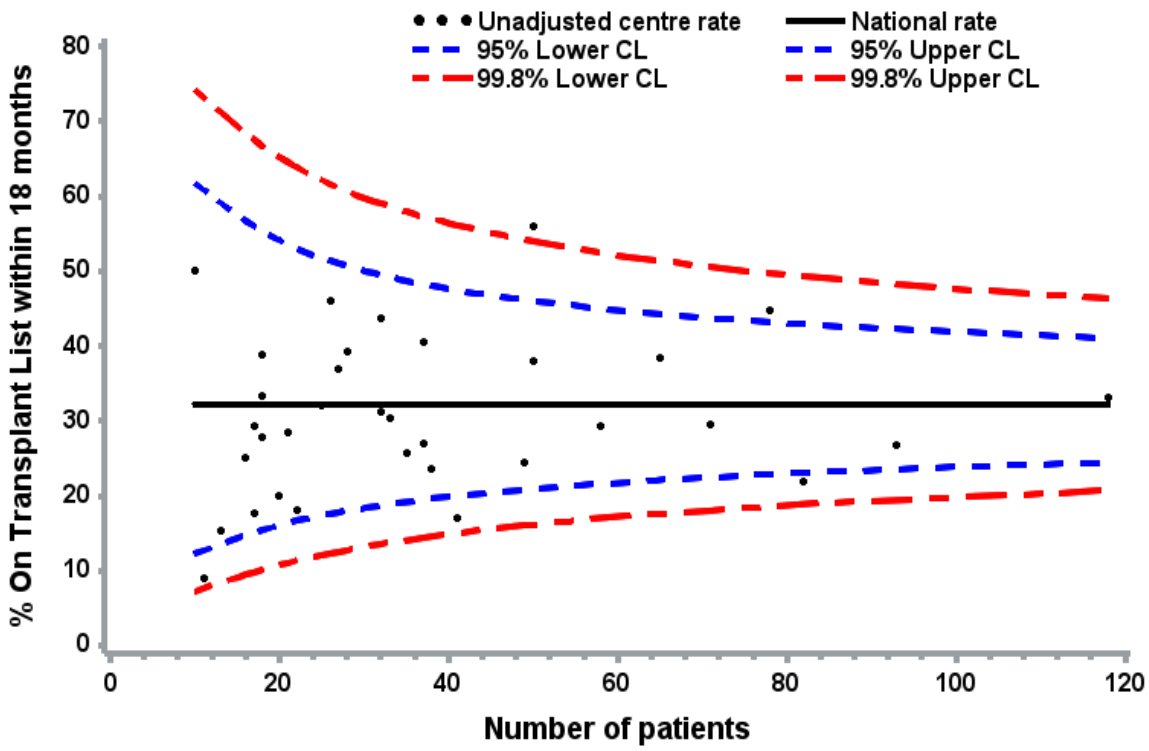

Figure 6.7. – Funnel plot showing the unadjusted percentage of patients listed within 18 months of starting dialysis at each centre in England and Wales.

Multivariate Analysis

After a completing a model building process, the multivariable logistic regression model (table 6.10.) found several factors to have an effect on listing after starting dialysis. This included a negative association with increasing age of recipient with likelihood of being listed being lower if aged 50-59 years (OR 0.40; CI 0.22-0.71), 60-64 years (OR0.32; CI 0.16-0.63) or 65-75 years (OR 0.21; CI 0.10-0.43) as compared to 18-29 years. Other factors negatively associated with listing after starting dialysis included: a previous history of malignancy (OR 0.26; CI: 0.16-0.44), being a current smoker (OR 0.47; CI: 0.31-0.71), presence of blood borne viruses (OR 0.22; CI 0.09-0.54), being on HDF (OR 0.58; CI 0.35-0.96) as opposed to HD, having vascular disease (OR 0.41 CI 0.23-0.73) and having a BMI of > 35 (with odds ratios of 0.31 (CI: 0.18-0.54) and 0.04 (CI:0.02-0.1=3) for patients with a BMI of 35-40, and >40, compared to those with a BMI of 20-25).

Socioeconomic status was also seen to to be associated negatively with listing, with lack of car ownership (OR 0.68; CI 0.50-0.93) reducing the likelihood of being listed.

Employment status too affected the likelihood of being listed, with being long term sick/disabled (OR 0.40; CI 0.26-0.62), looking after the family home (OR 0.37; CI 0.15-0.94), being retired from paid work (OR 0.34; CI 0.19-0.60), being unemployed (OR 0.46; CI 0.26-0.80) or not in work for some other reason (OR 0.27; CI 0.09-0.81) all being negatively associated with listing when compared to being in full time employment.

As opposed to these negatively associated factors, being degree level educated (OR 1.51; 1.04-2.20), being on CAPD (1.54 (1.02-2.30) as opposed to HD, having a primary renal diagnosis of polycystic kidney disease (OR 2.22; CI 1.23-4.00) or glomerulonephritis (OR 2.81; CI 1.81-4.35) compared to diabetes were both seen to increase the likelihood of being listed. In contrast to pre-emptive listing, ethnicity did not appear to have any impact on listing after starting dialysis.

Table 6.10. –Multivariate logistic regression model for the probability of a dialysis patient being added to transplant list within 18 months of starting dialysis

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Age				
18-29	87	1	-	-
30-39	123	0.92	0.48-1.75	0.7898
40-49	227	0.67	0.37-1.22	0.1906
50-59	344	0.40	0.22-0.71	0.002
60-64	181	0.32	0.16-0.63	0.0011
65-75	466	0.21	0.10-0.43	<.0001
Education				
GCSE, A-level or NVQ 1-3	592	1	-	-
Degree, Higher or NVQ 4-5	241	1.51	1.04-2.20	0.0301
No Qualifications	595	0.73	0.53-1.00	0.0518
Employment				
Working full time	169	1	-	-
Long term sick/disabled	450	0.40	0.26-0.62	<.0001
Looking after family home	31	0.37	0.15-0.94	0.0356
Not in work for some other reason	18	0.27	0.09-0.81	0.0198
Retired from paid work	523	0.34	0.19-0.60	0.0002
Student (includes those in training)	13	0.89	0.21-3.74	0.8773
Unemployed	121	0.58	0.32-1.05	0.0699
Working part time	103	0.77	0.43-1.38	0.3822

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Malignancy				
No	1248	1	-	-
Yes	180	0.26	0.16-0.44	<.0001
Smoking				
No	641	1	-	-
Current	224	0.47	0.31-0.71	0.0004
Ex-smoker	460	1.03	0.75-1.42	0.8528
Don’t know	103	1.16	0.70-1.95	0.5654
Vascular Disease				
No	1297	1	-	-
Yes	132	0.41	0.23-0.73	0.0028
BMI				
Less than 20	99	0.93	0.54-1.62	0.8057
20 - <25	402	1	-	-
25 - <30	429	1.37	0.98-1.93	0.0668
30 - <35	259	0.84	0.56-1.26	0.3977
35 - <40	134	0.31	0.18-0.54	<.0001
>40	105	0.04	0.02-0.13	<.0001
Primary Renal Disease				
Diabetes	369	1	-	-
Glomerulonephritis	224	2.81	1.81-4.35	<.0001
Glomerulonephritis and Diabetes	31	1.27	0.45-3.53	0.6508
Hypertension	88	1.56	0.87-2.80	0.1381
Hypertension and Diabetes	22	1.34	0.41-4.40	0.6309
Other	176	0.89	0.54-1.47	0.6524
Other and Diabetes	34	0.69	0.25-1.90	0.4738
Polycystic	81	2.22	1.23-4.00	0.008
Polycystic and Diabetes	14	3.34	0.93-12.01	0.0647
Pyelonephritis	88	1.01	0.54-1.89	0.9853
Pyelonephritis and Diabetes	17	0.65	0.16-2.68	0.5483
Renal vascular disease	34	0.90	0.32-2.53	0.8399
Renal vascular disease and Diabetes	14	0.50	0.06-4.29	0.5284
Uncertain	166	1.56	0.97-2.52	0.0657
Uncertain and Diabetes	70	0.96	0.45-2.07	0.9203
Car Ownership				
Yes	1003	1	-	-
No	425	0.68	0.50-0.93	0.0167

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Blood Borne Viruses				
No	1386	1	-	-
Yes	42	0.22	0.09-0.54	0.0011
Type of Dialysis				
HD	1002	1	-	-
APD	122	1.00	0.63-1.61	0.9898
CAPD	170	1.54	1.02-2.30	0.0378
HDF	134	0.58	0.35-0.96	0.0327

The impact of these patient factors on centre variation is shown in shown in the case mix adjusted funnel plot, figure 6.8. As compared to the unadjusted funnel plot (Figure 6.7), this funnel plot shows no centres lying outside either the 95% or 99.8% confidence intervals with much of the variation noted earlier in the unadjusted model appearing to have diminished. To see if there was still any unaccounted variation, the adjusted model was re-run with the addition of centre as a random effect (table 6.11) which although did not significantly improve the overall fit of the model, was close to significant (p=0.069) warranting further investigation of centre factors.

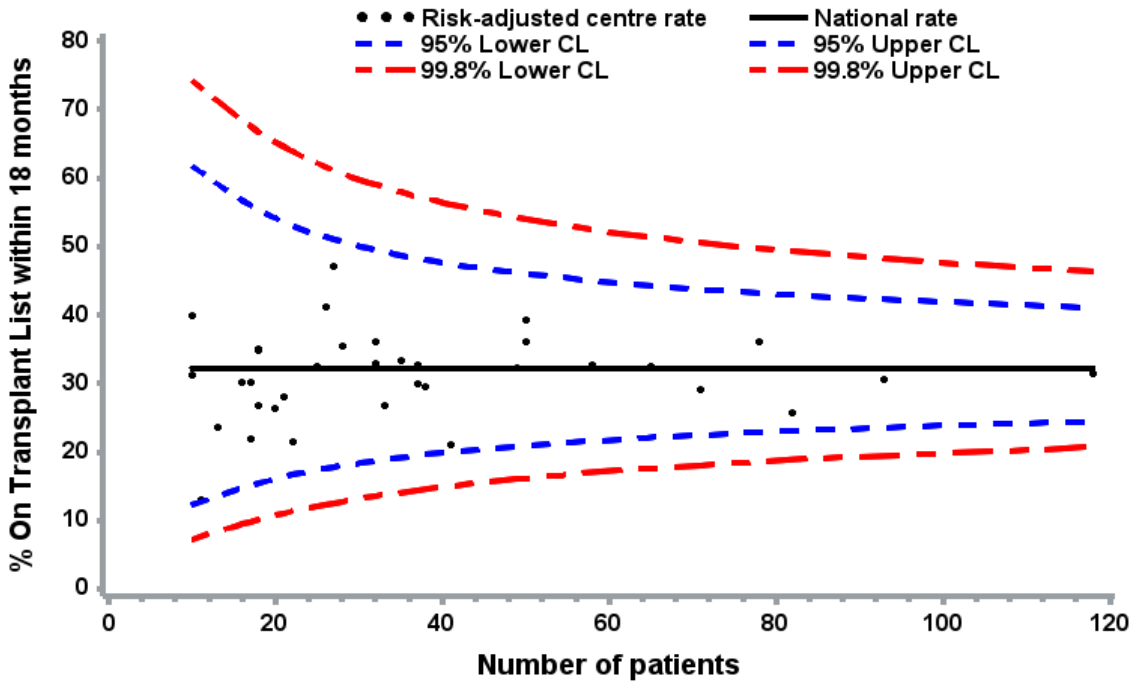

Figure 6.8. – Funnel plot showing the case mix adjusted percentage of patients listed within 18 months of starting dialysis at each centre in England and Wales.

Table 6.11. – Multivariate patient level model for probability of being listed within 18 months of starting dialysis, including renal unit as a random effect

Model	-2 log L	p-value
Null Model	1794.9	
Multivariate Patient Level Model	1338.149	
Multivariate Patient Level Model + Random Effect for Renal Unit	1334.843	0.069

6.4.3.3 Effect of Centre Practice Patterns on Access to Listing after Starting Dialysis

Results from the univariate analysis exploring the impact of centre variables on access to listing after starting dialysis (adjusted for case mix) are shown in Table 6.12. After a Model building process, two of these factors were highlighted as having an effect on pre-emptive listing in the multivariable analysis (which included both patient and centre factors). These are shown in table 6.13.

Having a written protocol for listing patients (OR 1.51; CI 1.03-2.21), and a higher number of consultant nephrologists (OR 1.04; CI 1.02-1.07) were both see to have a positive impact on listing patients (table 6.15).

Table 6.12. – Univariate logistic regression for centre level effects on being added to the transplant list within 18 months of starting dialysis, adjusting for patient level factors

Centre Factor	Unadjusted Odds Ratio	95% Confidence Limits	P Value
Number of Consultant Nephrologists (continuous increase by 1)	1.04	1.01 - 1.06	0.0071
Number of Consultant Nephrologists (categorical increase by 1)			0.243
<6	1	-	-
>=6	1.21	0.88 - 1.68	
Number of Patients Receiving RRT (continuous increase by 1)	1	1.0 - 1.0	0.0235
Number of Patients Receiving RRT (categorical)			0.1
1st Quartile	1	-	-
2nd vs 1st Quartile	1.06	0.73 - 1.54	
3rd vs 1st Quartile	1.26	0.87 - 1.82	
4th vs 1st Quartile	0.97	0.65 - 1.45	
Transplanting Centre			0.1
Yes	1	-	
No	1.28	0.95 - 1.7	
Use of Low Clearance Clinic			0.2532
Never	1	-	
Always	1.33	0.87 - 2.03	
Sometimes	1.45	0.93 - 2.24	
Transplantation Discussed with All Patients			0.3479
Yes	1	-	
No	0.87	0.64-1.17	
Location of Assessment			0.4455
Locally	-	-	
Referred to another Centre	0.81	0.48 - 1.38	
Patients Seen by a Surgeon			0.3911
Yes	1	-	
No	0.8	0.49 - 1.33	
Written Protocol			0.1665
Yes	1	-	
No	0.77	0.54 - 1.11	
Use of MDT			0.1304
Yes	1	-	
No	1.29	0.93 - 1.8	

Centre Factor	Unadjusted Odds Ratio	95% Confidence Limits	P Value
MDT used to List All Patients			0.5926
Yes	1	-	
No	1.09	0.8 - 1.47	
Audit of CKD 5 Patients Listing Status			0.1862
Never	1	-	
1-2 per year	1.31	0.88 - 1.95	
3-4 per year	1.78	1.11 - 2.86	
5 or more per year	1.66	0.51 5.38	
Other	1.22	0.71 2.09	
Named Cardiologist			0.7667
Yes	1	-	
No	1.04	0.78 - 1.39	
Pre-emptive listing rate			0.5828
<=5%	1	-	
5% - <20%	0.93	0.56 - 1.54	
20% - <33%	1.33	0.7 - 1.82	
>=33%	1.26	0.76 - 2.1	

Table 6.13 – Multivariate logistic regression model for the probability of a dialysis patient being added to transplant list within 18 months of starting dialysis adjusted for both patient and centre factors.

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Age				
18-29	87	1	-	-
30-39	123	0.92	0.48-1.75	0.7884
40-49	227	0.63	0.35-1.15	0.1312
50-59	344	0.37	0.21-0.67	0.0009
60-64	181	0.28	0.14-0.57	0.0004
65-75	466	0.20	0.09-0.40	<.0001
Education				
GCSE, A-level or NVQ 1-3	592	1	-	-
Degree, Higher or NVQ 4-5	241	1.48	1.02-2.16	0.0401
No Qualifications	595	0.77	0.56-1.06	0.1052

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Employment				
Working full time	169	1	-	-
Long term sick/disabled	450	0.41	0.26-0.64	<.0001
Looking after family home	31	0.36	0.14-0.90	0.0295
Not in work for some other reason	18	0.27	0.09-0.84	0.023
Retired from paid work	523	0.33	0.18-0.58	0.0001
Student (includes those in training)	13	0.81	0.19-3.46	0.774
Unemployed	121	0.54	0.30-0.98	0.0416
Working part time	103	0.77	0.43-1.38	0.3792
Malignancy				
No	1248	1	-	-
Yes	180	0.27	0.16-0.46	<.0001
Smoking				
No	641	1	-	-
Current	224	0.48	0.32-0.74	0.0008
Ex-smoker	460	1.06	0.77-1.46	0.7186
Don’t know	103	1.21	0.72-2.03	0.4776
Vascular Disease				
No	1297	1	-	-
Yes	132	0.42	0.23-0.75	0.0036
BMI				
Less than 20	99	0.96	0.55-1.67	0.8749
20 - <25	402	1	-	-
25 - <30	429	1.42	1.00-1.99	0.0472
30 - <35	259	0.87	0.58-1.31	0.5042
35 - <40	134	0.33	0.19-0.57	<.0001
>40	105	0.04	0.02-0.13	<.0001
Primary Renal Disease				
Diabetes	369	1	-	-
Glomerulonephritis	224	2.87	1.85-4.46	<.0001
Glomerulonephritis and Diabetes	31	1.26	0.45-3.54	0.6654
Hypertension	88	1.64	0.91-2.97	0.1024
Hypertension and Diabetes	22	1.55	0.47-5.15	0.473
Other	176	0.95	0.57-1.57	0.8261
Other and Diabetes	34	0.70	0.25-1.95	0.4984
Polycystic	81	2.26	1.25-4.10	0.0071
Polycystic and Diabetes	14	3.39	0.95-12.13	0.06
Pyelonephritis	88	1.09	0.58-2.05	0.7881
Pyelonephritis and Diabetes	17	0.70	0.17-2.91	0.6273
Renal vascular disease	34	0.95	0.34-2.67	0.9156

Variable	N	Adjusted Odds Ratio	95% Confidence Limits	P Value
Renal vascular disease and Diabetes	14	0.48	0.06-4.21	0.5074
Uncertain	166	1.56	0.97-2.52	0.0684
Uncertain and Diabetes	70	0.96	0.44-2.08	0.9112
Car Ownership				
Yes	1003	1	-	-
No	425	0.65	0.47-0.89	0.0072
Blood Borne Viruses				
No	1386	1	-	-
Yes	42	0.21	0.08-0.52	0.0008
Type of Dialysis				
HD	1002	1	-	-
APD	122	1.06	0.66-1.70	0.8056
CAPD	170	1.65	1.09-2.48	0.0169
HDF	134	0.58	0.35-0.95	0.0315
Written Protocol				
Yes	40	1	-	-
No	17	1.51	1.03-2.21	0.0337
Consultant Nephrologists (Continuous)	57	1.04	1.02-1.07	0.0018

The impact of adjusting for both patient and centre factors from this analysis on centre variation is shown in the fully adjusted funnel plot, figure 6.9. No centre in this funnel plot is seen to lie outside wither the 99.8% with only two lying outside the 95% confidence interval. When this model was re-run with the addition of centre as a random effect, as shown in table 6.14, the overall fit of the model did not significantly improve (p=0.999).

Figure 6.9 – Funnel plot showing the percentage of patients listed at each centre within 18 months of starting dialysis in England and Wales, risk-adjusted for patient and centre level factors

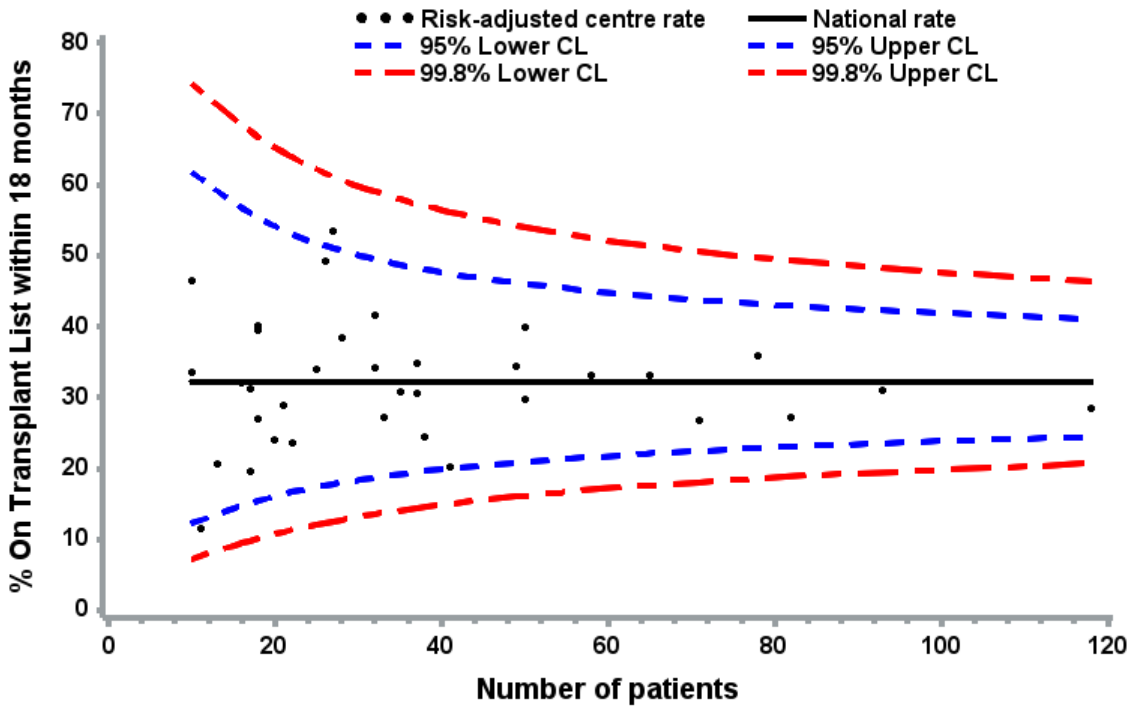

Table 6.14 – Multivariate patient and centre level model for probability of being activated on the transplant list within 18 months of starting dialysis, including renal unit as a random effect

Model	-2 log L	p-value
Multivariate Patient and Centre Level Model	1326.4	
Multivariate Patient and Centre Level Model + Random Effect for Renal Unit	1326.4	0.999

Sensitivity Analyses

A separate sensitivity analysis involving the use of multiple imputation to account for missing data in 286 patients (16.7%) of the original eligible cohort of 1714 patients was also performed. These included 163 patients with missing BMI data, 22 patients with missing comorbidity data and 101 patients with missing socio-economic data.

The results from this analysis (which was conducted with the assistance of Dr. Matthew Robb, Statistician at NHSBT) showed no overall change in the results and can be seen in Appendix E.

6.5 Discussion

6.5.1 Key Findings

This chapter has highlighted that whilst unadjusted analyses show inter-centre variation in access to pre-emptive listing and listing after starting dialysis, the majority of this variation can be accounted for by patient factors/characteristics. In the case of pre-emptive listing these include age, ethnicity, socioeconomic status, previous transplant, cardiovascular disease, smoking status, morbid obesity, previous malignancy, primary renal diagnosis, and length of time known to renal services. As for listing after starting dialysis: age, education, socioeconomic status, vascular disease, smoking status, morbid obesity, presence of blood borne viruses, previous malignancy, primary renal diagnosis, and dialysis modality were all seen to be independently significant.

Though patient variables were seen to account for the majority of variation, centre practice patterns were also seen to be important for pre-emptive listing and to a lesser extent listing after starting dialysis. The number of whole time equivalent consultant nephrologists, being a transplanting centre, the use of a low clearance clinic and whether transplantation is discussed with all patients were all seen to be important for pre-emptive listing, whilst having a written protocol, and the number of WTE consultant nephrologists were seen to be important for listing after starting dialysis.

The rest of this chapter proceeds to discuss these findings and interprets them in the context of knowledge about clinical practice in England and Wales at the time of the study.

6.5.2 Impact of Patient Variables

One of the primary aims of this thesis was to identify patient-specific and centre-specific factors that influence access to the transplant waiting-list and explore if

access to renal transplantation in the UK was truly equitable. In particular, this thesis sought to understand the impact of ethnicity, social deprivation and comorbidity on access to transplantation as well as trying to help identify best practice.

Access to Transplantation and Socioeconomic Status

This thesis has shown that social deprivation is associated with both lower pre-emptive transplant listing and a lower likelihood of being listed after starting dialysis in England and Wales, even after extensive demographic and comorbidity adjustment. These findings are in keeping with results from retrospective studies in the US and the UK which have highlighted reduced access to the transplant waiting list in socially deprived patients[11, 24, 26-27]. Similarly, several studies around the world have also shown that socioeconomically deprived individuals are less likely to undergo pre-emptive transplantation[210-211], though this has never been reported in the UK to date.

A criticism of previously published studies, other than their retrospective design, has been that they have not adjusted for ethnic differences between deprivation groups and co-morbidity, both of which have been independently associated with a lower probability of listing for transplantation. Indeed, the increased co-morbidity burden[154] and increased risk of mortality amongst socially deprived groups[292-294] have often been cited as reasons for lower rates of listing in socially deprived areas. In contrast to these studies, analyses in this thesis did not have these limitations and were able to robustly adjust for co-morbidity despite which social deprivation was still seen to have a negative impact.

As for the reasons for why socially deprived patients appear to have reduced access to listing for transplantation, studies originating 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[26]. Noncompliance with medications post transplantation has also been shown to be more common in socially deprived patients which could also be deterring physicians from listing social deprived patients[295]. Additionally, clinicians may consciously or subconsciously manage patients in ways that make it less likely for socially deprived patients to be listed for transplantation[27]. Whilst most of these studies exploring the reasons behind socioeconomic inequity in access to renal transplantation originate from the US,

where healthcare is not free at the point of use (unlike the NHS) it is possible that similar factors are operational in England and Wales.

Other studies (in the UK and US) have also suggested that higher rates of late referral to renal services in patients of lower SES may lead to a delay in pre-transplant assessment and reduce access to listing in particular pre-emptive listing[178, 296-297]. In this study, whilst there were indeed significantly fewer patients seen for <1 year in the pre-emptively listed group and a positive association observed with being listed and increasing the length of time known to renal services, even after adjusting for this, social deprivation was still seen to have a negative impact.

Lower rates of live donor transplantation in socially deprived patients (noted both in the UK and US)[205-209] may also be a cause of reduced access to transplant listing, in particular pre-emptive listing as having access to a live donor often functions as a driver to assess suitability and get patients transplanted as soon as possible (ideally pre-emptively) so that the maximum benefit can be achieved for the patient. Qualitative work aimed to identify reasons for the observed socioeconomic disparity in live-donor kidney transplantation in the UK has highlighted patient passivity, patient disempowerment, lack of social support and short-term focus in patients of lower SES as important themes for investigation[298]. Also a greater prevalence of 'donor issues' including concerns about returning to normal physical activity[299] and taking unpaid time off work[300] may be more of an issue for deprived patients affecting donation rates and as a consequence listing.

Further research is needed to understand how much of the inequity in access to transplantation described in this study for socially deprived patients can be attributed to these factors and to explore other potential causes driving this disparity.

Education

Having no educational qualifications (another marker of social deprivation) was seen to reduce the likelihood of being pre-emptively listed, whilst being degree educated was seen to increase the likelihood of being listed after starting dialysis as compared to being attaining GCSE, A-level or NVQ 1-3 level education. Though the impact of educational attainment on wait-listing after starting dialysis has not been reported in

the UK to date, studies in the US have reported similar findings with Schaeffner et al reporting that college graduates were three times more likely to be wait-listed compared to those without a high school degree[301]; whilst Goldfarb-Rumyantzev et al reported that racial disparities in access to transplantation were attenuated in African Americans college graduates[302].

As for the impact of education on pre-emptive listing, there is limited published data available. Kasiske et al investigated levels of education among many other factors potentially influencing pre-emptive listing in the United States, and found that higher educational attainment was associated with an increased likelihood of being wait-listed before dialysis[32] and an increased likelihood of undergoing preemptive transplantation[24].

The impact of education on wait-listing may be due to a variety of reasons, including the possibility that those with higher education attainments are more adept at navigating through listing processes and are able to understand the benefits of transplantation and their illness better, as have higher literacy levels[303] and have less difficulty understanding health materials which are often written at above 12th grade reading level[304-305]. This theory is supported by studies from the US which have shown that poorer health literacy is associated with a reduced likelihood of referral for transplantation in US hemodialysis patients[306-307] whilst in the UK, Taylor et al has similarly shown that both transplant wait-listing and preemptive transplantation are associated with increasing health literacy[303].
Further research is needed to understand the mechanisms and processes through which education attainment impacts access to transplantation listing to aid developing education programs which might improve both pre-emptive wait-listing and listing after starting dialysis.

Access to Transplantation and Ethnicity

The impact of ethnicity on access to transplantation was seen to vary significantly in this study. Whilst ethnicity was negatively associated with pre-emptive listing, with both Asian and Black patients being less likely to be pre-emptively listed as compared to white patients; ethnicity was not seen to have any significant effect on being wait-listed after starting dialysis in England and Wales. This variation in effect, whilst

initially surprising, is not unexpected in the context of published literature, with studies showing conflicting views on the impact of ethnicity. Indeed, though many studies in the US[25-36] and UK[11-12, 153] have reported that ethnic minorities have decreased access to both the transplant waiting list and access to transplantation once listed, other studies have reported equal access[177-178].

Udayaraj et al suggested that differing outcomes may be due to studies not adjusting for socioeconomic status, having found that by adjusting for social deprivation in a cohort of patients in England and Wales the initially observed negative impact of ethnicity on wait listing for transplantation was attenuated[178]. Indeed, whilst in this study socioeconomic status was also seen to be important, adjusting for it did not diminish the impact of ethnicity completely in terms of pre-emptive listing. In the absence of any published literature on ethnic differences in pre-emptive listing in the UK, this study poses the idea that non-white ethnicity independently reduces the likelihood of being pre-emptively listed. It also raises the possibility that studies that have reported on ethnic minorities having reduced access to listing to date may have been confounded by grouping and analysing pre-emptive listing and listing after starting dialysis together.

In the US, several health care related and patient related barriers have been proposed for observed ethnic disparities in access to transplantation[27]. Healthcare barriers include physician related barriers, inadequate transplant work-up and referral delays, whilst patient barriers include ethnic minorities reporting better health on dialysis and not believing that transplantation would necessarily improve their quality of life, as well as cultural and religious believes impeding the pursuit of transplantation[27].

In this study, as patients receiving a pre-emptive live transplant without prior listing were considered to have been listed, it is possible that the lower likelihood of pre-emptive listing is a reflection of the lower rates of live donor transplantation seen in ethnic minorities. Ethnic minorities have been shown to undergo lower than expected live donor transplantation as compared to White patients in chapter 3, which has also been reported in several studies both in the US and in the UK[34-35, 179]. Institutional prejudice[171], distrust and reluctance to engage with the medical system[180-181], cultural and religious beliefs[27, 182], and lack of suitable donors or concern over a higher risk for

living donors from minority ethnic backgrounds[183] have all been cited as possible reasons for these disparities.

Lack of donor motivation and failure of donors to complete appropriate investigations have also been reported amongst the Black population, which may in part be due to greater concerns about their future health after donation and the fear of living with one kidney[270-272]. It has also been observed that Black patients on dialysis have more positive coping strategies than White patients which may affect their perception of the need for having a transplant and their persuasiveness in asking for living donations[272]. Additionally, as shown in Chapter 3, live donation in the UK is subject to significant unexplained relationship differences amongst ethnic minorities the reasons for which are unclear as is their impact on pre-emptive listing.

Devising more targeted education of both potential donors and recipients may overcome some of these barriers and improve not only live donor transplantation but also pre-emptive transplantation/listing. This is supported by evidence from a randomised trial conducted in the US, which showed that compared to clinic based education, home-based education combined with clinic based education resulted in more live donor evaluations and transplantation amongst Black patients compared to White patients[308].

Age

This thesis has shown that increasing age is associated with both lower pre-emptive transplant listing and in particular a lower likelihood of being listed after starting dialysis in England and Wales. This is consistent with data from published retrospective studies from around the world[11-12, 152-156], including published UK Renal Registry analyses. As described in Chapter 1, the UK Renal Association does not define an age limit for wait-listing recommending instead that recommends that age-related comorbidities could be considered a relative contraindication to transplantation. The majority of retrospective studies to date have not been able to adjust for comorbidities, though analyses in this thesis have adjusted for many known

age-related comorbidities though despite this age is still seen to have an independent effect.

A reason for this may be, that as shown in the results from the national survey in Chapter 5, contrary to national guidelines several centres (4.4%) reported using chronological age as an exclusion criterion for listing patients. By using age as a proxy for the proper assessment of individual need and suitability some clinicians may fail to appreciate that chronological age can be very different to biological age in different individuals. Indeed, it should also be noted that from 1st October 2012, the Government fully implemented the ban on age discrimination enshrined in the Equality Act 2010, giving protection against age discrimination in services, clubs and associations and in the exercise of public functions making it unlawful for service providers and commissioners to discriminate, victimise, or harass a person because of age. Centres adopting an exclusion criterion on an arbitrary chronological age may now find themselves in breech of this and may be deemed as being unlawful.

Another important reason why increasing age was seen to negatively impact access to transplantation may be individual physician 'beliefs and values' relating to maximizing efficiency/most life-years (or longevity) gained from the kidney in the context of organ scarcity. Tong et al in a recent systematic review reported that this was an important theme amongst nephrologists with many reporting feeling tension in considering the 'individual versus the community' and being worried about "squandering scarce resources"[309]. This was also reflected in nephrologists attitudes to list elderly patients with 10% to 59% of nephrologists recommending transplant for patients aged over 60 years in their study[309]. In another study, Ghahramani et al reported that nephrologists with 10 years or less of practice, or were working in high volume centers, or were transplant nephrologists, were more likely to view transplant as a treatment of choice for older patients[310].

Access to Transplantation and Co-morbidities

Amongst the range of co-morbidities investigated pre-emptive listing appeared more susceptible to their impact with cardiovascular disease, heart failure, vascular disease, a previous history of malignancy and being a current smoker all being negatively associated with pre-emptive listing. A greater impact of co-morbidities on pre-

emptive listing is not surprising as one would expect clinicians to take a longer period of time to investigate the suitability of patients with a larger co-morbidity burden as well as appropriately manage them alongside any associated 'de-listing' complications prior to getting them activated on the waiting list. The greater time needed for this process would likely mean that patients would end up starting dialysis before getting listed.

Another reason for a larger number of comorbidities affecting pre-emptive listing is that some centres may refrain from conducting the necessary investigations to allow a patient to be pre-emptively listed if there was a risk that the investigation itself may potentially render them dialysis dependent. This may particularly be true in the case of investigating coronary artery disease where clinicians may feel the risk of exposing an asymptomatic low clearance patient to nephrotoxic contrast is too great. This theory is supported by evidence from results from the national survey (reported in chapter 5) which highlighted that 4 centres (5.6%) would 'always', and a further 53 centres (74%) would 'sometimes' refrain from performing a coronary angiogram (deemed necessary for listing) until they were on dialysis in a low clearance patient to avoid precipitating the need for dialysis.

Cardiovascular disease) is a significant cause of morbidity and mortality for wait-listed kidney transplant candidates[102-103]. It remains the leading cause of death in transplant recipients[65, 104], with many national and international guidelines recommending screening for cardiovascular disease prior to listing. Whilst there are strong arguments in favour of screening for CVD and a large number of guidelines which support some form of risk stratified cardiac screening. It is not clear whether screening asymptomatic patients prior to transplantation provides any benefit[115]. This uncertainty in the in the clinical utility of screening of cardiac screening for heart disease was reflected in the results of the qualitative study (chapter 4) which highlighted cardiac assessment as an area of ambiguity which needed further research both in terms of which test to use and whom to screen as well as better longitudinal survival data. Indeed, it is highly likely that some part of this ambiguity is a contributory factor in both heart disease and heart failure being negatively associated with access and is an area which needs further research and education to improve outcomes and reduce variation.

The presence of vascular disease as a factor reducing both access to pre-emptive listing and listing after starting dialysis is not surprising as severe vascular disease affecting the iliac vessels and lower limbs can render the operation itself of transplanting a kidney and attaching it to a patient's arterial system as unfeasible. On the contrary, it is interesting to see that being a current smoker is seen to negatively impact both pre-emptive listing and listing after starting dialysis. Only a few studies have examined the effect of cigarette smoking on renal transplantation but all show an association with reduced patient and graft survival[88]. Smoking cessation prior to transplantation has also been shown to reduce the relative risk of graft failure and improve death-censored graft survival[144-145].

In the UK, the Renal Association does not specify stopping smoking prior to being listed as an absolute necessity but rather that patients should be strongly encouraged to stop smoking before and after transplantation. The observation that approximately 15% of all patients analysed in the two analyses were 'current smokers' suggests that that there is room for improvement and that healthcare professionals involved in providing renal care need to do more to try to assist patients in stopping smoking. Additionally, the observation that despite this advice, smoking appears to have a negative impact may be as a consequence of clinicians' personal moral beliefs, with some clinicians believing it better for non-smokers to be listed (as opposed to smokers) to extract the maximum benefit (in terms of graft function and patient survival) from a donated kidney[309]. Indeed, some clinicians may feel that as demand exceeds supply, they have a duty to ensure the best possible outcome for any donated kidney, all be it at the cost of disadvantaging recipients amongst whom donor outcomes may not be as good, such as in the case of smokers. This possible explanation is further supported by the results from the qualitative study (chapter 4) which reported that 'moral dilemmas' often influenced clinician listing practices especially in the case of pre-emptive listing.

Alternatively, another possible reason for the negative impact of smoking may be that some clinicians are simply delaying listing smokers and instead are actively trying to get them to stop before listing. Indeed, some clinicians may feel that the overall health benefits of stopping smoking including reducing cardiovascular events, malignancy

risks..etc, outweigh the disadvantage of being listed late and might use the reward of listing a patient for transplantation as an incentive for getting patients to stop smoking.

Finally, it is unsurprising to see that a previous history of malignancy adversely affects both pre-emptive listing and listing after starting dialysis, as though active malignancy is considered an absolute contraindication to transplantation (as discussed in chapter 1) many guidelines recommend that patients with previous malignancy should be considered, although recommend varying cancer-free periods of 2-5years depending on the type of malignancy[97-98, 139]. This is to minimise the risk of recurrence due to the enhanced development of micrometastases, due in part to alteration of immune surveillance mechanisms with maintenance immunosuppression[140]. As different types of cancer require different disease free intervals before being listed, some patients are likely to have to wait longer before being deemed eligible whereas others may not require any significant delay. For example, patients with non-melanoma skin cancer and in-situ carcinoma of the cervix or bladder would not require any delay as the risk of recurrence is very low, whereas those with colorectal cancer, or breast cancer may need to wait at least 5 years before transplantation depending on circumstances due to higher recurrence risk[88, 311].

Primary Renal Disease

Several primary renal diagnoses were seen as increasing the likelihood of being listed compared to having diabetes. Pyelonephritis and polycystic kidney disease were both seen to increase the likelihood of pre-emptive listing, whilst the later along with glomerulonephritis were seen to increase the likelihood of listing after starting dialysis.

Patients with pyelonephritis and polycystic kidney disease often present early to renal services following recurrent urinary infections (in the case of pyelonephritis) or following familial genetic testing/cyst related complications (in the case of polycystic kidney disease) and is likely one of the major reasons why clinicians manage to list more of these patients pre-emptively. Early presentation, lack of concern regarding post-transplant disease recurrence and a largely insidious complication free disease course post diagnosis makes it easier for patients with these conditions to be prepared for RRT including facilitating pre-emptive listing.

As for patients with glomerulonephritis having a greater likelihood of being listed after starting dialysis than diabetics, this may be due to the fact that patients with glomerulonephritis may have have access to more live donors (as the majority of glomerulonephritides are not hereditary) which may drive listing after starting dialysis. Patients with glomerulonephritis will also not be subject to the same level of microvascular and macrovascular complications, as seen in diabetics, that might need managing before listing i.e. allowing them to get listed more quickly. Indeed, whilst the list of co-morbidities which were adjusted for in the final model were quite extensive, it did not include all potential diabetes associated complications which could delay listing as compared to those patients with glomerulonephritis.

Obesity

This chapter has shown that increasing levels of morbid obesity (BMI>35) are associated with both lower pre-emptive transplant listing and a lower likelihood of being listed after starting dialysis in England and Wales. To my knowledge this is the first study to report on the impact of obesity on pre-emptive listing. As for the impact of obesity on dialysis patients several retrospective studies from the US have reported that obese patients with ESRD have reduced access to the transplantation than do normal-weight patients[312-214].

In contrast to these studies, a recent large retrospective analysis of >700,000 patients with incident ESRD over 12 years using data from the US Renal Data System (USRDS) by Gil et al reported a differential association of BMI with access to kidney transplantation in men and women[315]. In this study they found that a higher BMI was associated with a higher likelihood of activation to the waiting list until the BMI was ≥40.0 kg/m^2 in men and ≥35.0 kg/m^2 in women at which point the likelihood of being listed was lower than normal weight patients. Whilst this study collated 12 years of data, and adjusted for many known confounders its retrospective design and lack of extensive socioeconomic data were highlighted as limitations which may have affected the results. In contrast to this study, results from this chapter were not subject

to these limitations and did not identify any such gender differences (data not shown) whilst identifying the threshold for reducing the likelihood for listing to be >35 kg/m^2 for both genders.

Obesity is not an absolute contraindication to kidney transplantation (as discussed in chapter 1), unlike active infection and malignancy. However, as shown in the results from the national survey of practice patterns in Chapter 6, it is seen as a relative contraindication at many centres, albeit often with subjective and loosely defined BMI cutoffs with clinicians citing an increased risk of technical difficulties and perioperative complications amongst obese patients[131-132] in the survey responses. Other reasons for why a higher BMI may reduce the likelihood of being wait-listed include clinicians' belief that patient and graft survival in obese recipients is reduced, referral bias and increased medical complexity of obese patients as well as some physicians perceiving obese patients as poor surgical candidates or as non-adherent[315].

With 50% of the ESRD population in the US and nearly a third (32.7%) of the study population analysed in this thesis being reported as being obese (BMI >30 kg/m^2) it is important to understand the reasons behind obesity reducing the likelihood of being wait listed. Further research including prospective studies looking at the long term graft outcomes, patient survival and perioperative complications in obese patients are needed to provide necessary insights.

Previous Transplant

Despite recommendations from the BTS that pre-emptive re-transplantation in suitable candidates is the best option for ongoing renal replacement therapy, which should ideally occur when eGFR is 10-15 mL/min. (1D), previous transplantation was seen to be strongly associated with reduced access to pre-emptive transplant listing. Whilst increasing age and greater co-morbidity may be explanations, it is also likely that those with failing grafts have fewer potential live donors having potentially already benefit from live donation when first transplanted. It is estimated that patients with failed transplants currently constitute approximately 4% of the incident dialysis population[316].

As the number of transplants increase it is inevitable that, despite improvements in graft survival, failing grafts will become progressively more common and thus these patients represent an important growing population amongst whom greater research is needed to understand the reasons behind their lower pre-emptive listing rates. This is further supported by the observation that higher mortality rates have been reported amongst patients returning to dialysis after graft failure compared to those with poorly functioning grafts highlighting the need to avoid return to dialysis if possible[317-318].

Dialysis Modality

The observation that haemodiafiltration reduced the likelihood of listing after starting dialysis whilst continuous ambulatory peritoneal dialysis increased the likelihood of listing was unexpected. Potential reasons for this observation may be that patients with CAPD are more likely to be deemed suitable for listing as they are likely to include a greater aggregate of patients who are younger, active and more physically able who have chosen this modality to allow them to pursue a more active life without time constraints brought about by having to attend a dialysis centre several times a week i.e. potential residual confounding of unmeasured factors. Conversely, those with HDF may include a greater aggregate of unsuitable patients with greater morbidity who have been placed on HDF for its better hemodynamic stability[319-320].

Blood Borne Viruses

The presence of HIV/Hep B/Hep C was seen to significantly reduce the likelihood of being listed. Whilst one needs to interpret this result with caution as this was based on a small sample size (42 patients), this reduction is likely to reflect the ambiguity surrounding the eligibility of patients with HIV and/or viral hepatitis. Indeed, newer treatments for hepatitis and the advent of highly active antiviral therapy which have revolutionised the prognosis of HIV patients has changed the outlook for patients with these viruses which are no longer considered an absolute contraindication to kidney transplantation in the UK[88]. Whilst some clinicians may still have a bias against listing patients with blood borne viruses, some may also delay listing whilst patients are treated for their infection/viral load brought under control.

Early experience suggests similar early graft and patient survival rates between HIV positive and negative renal transplant recipients[126]. As for potential recipients with

active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, transplantation has been shown to improve their survival as compared with remaining on dialysis[128-129]. Whilst these early studies are encouraging further long term prospective studies are still needed on patient and graft outcomes if ambiguity surrounding listing of these patients is to be resolved and listing rates improved.

Time Since First Seen by Nephrologist

The observation that being known to renal services for a greater length of time before the need for RRT, is associated with an increased likelihood of being pre-emptively listed has been reported by several studies in the UK and US[321-324]. This is not surprising as it is well known that early referral to renal services with CKD is recommended to facilitate prompt management of the underlying cause of CKD as well as delay progression, manage its associated complications and prepare patients for RRT including transplantation[260]. Conversely, late referral would likely lead to insufficient time to assess transplant suitability to get patients listed before the need for dialysis arises or explore and assess suitability of potential live donors for pre-emptive live donor transplantation.

6.5.3 Impact of Practice Patterns

Results from the multilevel models exploring pre-emptive listing and listing after starting dialysis have both shown that case-mix significantly influences centre performance in terms of listing patients for transplantation and accounts for much of the variation seen in unadjusted analyses. These data suggest that presenting case-mix adjusted as well as unadjusted data is important when presenting performance analyses using UKRR or NHSBT data. The presence of 'residual unaccounted centre variation' despite case-mix adjustment, whilst potentially attributable to unmeasured case-mix variables (residual confounding) suggested structural characteristics and processes within renal centres (practice patterns) could be having an effect which were then investigated (utilising the results of the national survey) in a two level model using patients (level 1) nested within renal centres (level 2).

These analyses highlighted several practice patterns affecting both pre-emptive listing and listing after starting dialysis and are discussed individually below:

Registration at Transplanting Centre

Being registered at a transplanting centre was seen to significantly increase the likelihood of being pre-emptively listed, however, this did not have any impact on listing after starting dialysis. These results were interesting and to some extent helps explain the discrepancies in previous UK registry analyses to date, with Ravanan et al reporting that patients at non-transplanting renal centres were less likely to be registered for transplantation or receive a transplant in their analyses[12] whilst Dudley et al reported that whether the renal unit was also a transplant centre was not significant in terms of listing patients[153].

As previous analyses have not separated pre-emptive listing and listing after starting dialysis, it is likely that the effect of transplanting centre may have been skewed in their analyses. Indeed, as our study shows, transplanting centre status is important however only in terms of pre-emptive listing. One of the reasons for this may be that the presence on-site transplant surgeons (at transplant centres) allows suitable patients to be worked up more efficiently thereby getting them listed before the need for dialysis arises. Alternatively, live donor coordinators which are primarily based at transplanting centres may also be a contributing factor, as they may allow for the earlier identification of potential donors which may prompt clinicians to get patients listed quickly to accommodate pre-emptive transplantation.

Consultant Nephrologists

A greater number of WTE consultant nephrologists were seen to increase the likelihood of being both pre-emptively listed and listed after starting dialysis. This suggests a direct observational link between improved quality in patient care (i.e. getting wait-listed) and senior workforce size. These findings seem logical, as recognizing the integral role consultant nephrologists play in managing CKD and preparing patients for RRT (including assessing transplant suitability), it is unsurprising to see that having more individuals undertaking this role, improves listing outcomes. This finding has potentially greater importance when interpreted in the context of the results of the national survey (chapter 6) which highlighted that the number of consultant nephrologists (7.61pmp) in the UK were significantly lower

than that recommended by the National Renal Workforce Planning Group and pointing towards an understaffed service[279].

Indeed, if improved staffing levels have the potential to improve access to transplantation this represents an area that warrants further investigation alongside research on the impact understaffing might be having on lowering staff morale (as discussed in chapter 4) and its impact on staff performance.

Selective approach to using a Low Clearance Clinic

The observation that using a low clearance clinic for some patients but not all, as opposed to not using a low clearance at all increased your likelihood of being listed was unexpected and initially made one think of the possibility of whether it was a consequence of chance/multiple testing. Indeed, when the analysis was re-run with the use of a low clearance clinic analysed as a binary yes/no outcome, no effect was observed. There are indeed many studies, albeit of small and variable quality, which have shown that a dedicated pre- dialysis clinic is associated with improved outcomes and reduced urgent initiation of dialysis[280-283]. Thus, suggesting that such clinics may provide more focused opportunity to assess transplantation potential and more timely discussion of options including live donation and pre-emptive transplantation. Whilst this may be true, this study does not provide any evidence in support of advocating the use of a low clearance clinic for all patients. As to why selectively using a low clearance set up might be important, it is hard to explain as the reasons for being selective are likely to differ between centre, ranging from financial to heterogeneity in clinician belief within centres, and requires further research.

Discussing Transplantation

The finding that discussing transplantation as an option with all patients increased the likelihood of pre-emptive listing supports what many researchers have cited in the past on the importance of education to improve access to transplantation. Indeed, recently Tamura et al showed that patients who participated in a kidney disease screening and education program (National Kidney Foundation Kidney Early Evaluation Program-KEEP), were associated with significantly higher rates of pre-emptive transplant wait listing (24.2% vs. 17.1%), and transplantation (9.7% vs. 6.4%) than those who did not participate[325]. Likewise, Mehrotra et al, also found that

incomplete presentation of all treatment options to be an important reason for the underutilization of home dialysis modalities and causing a delay in access to transplantation[326].

In addition to these studies, the importance of discussing transplantation with all patient is further supported by qualitative studies exploring patient perspectives on wait-listing with Calestani et al, reporting that many patients were not aware of pre-emptive transplantation and believed they had to be on dialysis before being able to be listed, with incomplete education and poor communication being a source of distress[267]. These findings suggest that there is a need to improve education in particular the discussion of transplantation as a treatment option amongst all patients to improve not only access to pre-emptive transplantation but also patient satisfaction.

Written Protocol to assess suitability

Analyses from this thesis have also shown that the presence of a written protocol is associated with an increased likelihood of being wait-listed for transplantation after starting dialysis. This is an important observation and supports guidance from the UK Renal Association which recommends that all transplant units should have written criteria for acceptance on to the waiting list[88]. It is likely that in the absence of a written protocol, centres are more prone to delays in listing with lack of standardization of assessment leading to greater variation in assessment, with personal bias and individual idiosyncrasies being a potential underlying reason for inequity. The national survey (chapter 6) showed that nearly a third of centres did not have a protocol, including three transplanting centres. It is therefore possible that if these centres were to implement a written protocol then patients registered at those centres may benefit from improved access to transplantation.

6.5.4 Strengths and Limitations of this Study

The main strength of this study was its prospective cohort design which meant that it was not subject to the inherent weaknesses of retrospective studies, which have affected studies exploring access to transplantation to date. Additionally, this study involved analysing a comprehensive dataset including patients from all renal centres in England and Wales, which allowed for the accurate adjustment of ethnicity,

individual level socioeconomic data as well as a comprehensive range of comorbidities, the data for which had been collected by dedicated research nurses. This negated the need for using Registry data which are limited by data completeness, accuracy and validation issues as well as being limited by the dataset collected.

Other strengths of this study included using individual level socioeconomic data and analyzing access to pre-emptive listing and listing after starting dialysis separately as opposed to previous studies, acknowledging that they represent different populations and are the result of different pathways and likewise may be affected by centre practices differently. The mixed method approach in identifying and quantifying centre variables for analysis also provided greater breadth and depth in understanding and highlighting, centre practices for analysis, whilst the 100% response rate to the national survey allowed individual centre level variables to be described and quantified for the purpose of analysis.

As for the main limitations, it is important to first mention that the data analysed are observational and have the difficulties associated with all observational studies that causal relationships cannot be determined. Another limitation is that though centre variables were identified and described on the basis of the survey instrument, which achieved a 100% response rate; the survey responses were self-reported by self-selecting renal staff e.g. the clinical lead for transplantation, and their responses will not necessarily reflect those of the broader consultant community. However, as many of the centre practice data items analysed in this study were highly objective the importance of this is likely to have been minimal. Another limitation is that though this study attempted to account for comorbidity it could not adjust for varying levels of comorbidity severity and also did not adjust for transplant work up investigations (data not available).

Missing data is another limitation to this study, in that though data completeness for all variables was high, as detailed in the methodology, a small proportion of patients were excluded from the analysis due to missing data which may have introduced bias. Whilst it is feasible that excluding these patients may have affected the results, it was reassuring to note that after using multiple imputation to populate missing results, no difference in the outcomes were observed (data not shown).

Another limitation to this study was the follow up time which was restricted to 18 months. Previous analyses have used an arbitrary follow up time of two years on the assumption that in this length of time most patients likely to be listed would have been listed. However, to accommodate university time constraints to complete this thesis, this study followed up patients for a slightly shorter length of time (18months) which may have affect its results. Similarly, the use of a logistic regression model may have diminished the impact of some of the centre variables, which may have had a tendency to improve the efficiency of being listed as opposed to getting listed per se. Indeed, undertaking a cox-regression survival analysis of centre factors and patient factors would be better as it handles time to event, censoring by death if not listed and allows use of all available follow up information. This would have assisted in overcoming this limitation and will be the focus of future work.

The population cohorts analysed for pre-emptive listing and listing after starting dialysis were also subject to limitations. In the case of access to pre-emptive listing, analyses could not take into account all those patients that had CKD 5 or that were approaching the need for dialysis and were being worked up for listing as these patient were not recruited as part of ATTOM neither did either the UKRR or NHSBT have any information on these patients. As for listing after starting dialysis, analyses were restricted to those starting dialysis who were recruited in the ATTOM study and not all patients starting dialysis in England and Wales. Though analyses comparing those recruited in ATTOM with those starting dialysis in the UK to be generally comparable, and the group analysed representative of the dialysis population, it is feasible that using a selective cohort may have influence results.

These data are specific to the RRT population in England and Wales and renal centres in England and Wales and restricted to those aged <75 years (as limited by the recruitment criteria of ATTOM), and it is unknown whether these findings are generalizable to other populations. This would be difficult to test as there are no other prospective studies of this nature comparing performance of renal centres. Finally, though this study has adjusted for many factors known to affect listing there may still be a degree of residual confounding which has not been accounted for.

Chapter 7: Conclusion

This thesis has achieved its aims and described both significant ethnic and gender differences in the relationships between live kidney donors and their recipients; and has identified both case mix variables and organizational factors associated with centre performance in listing patients for transplantation. These findings have a number of potential implications for clinical practice and research.

7.1 Implications for Clinical Practice

Firstly, this thesis shows that living kidney donation is subject to significant unexplained relationship differences amongst ethnic-minorities in the UK. Spousal donation is significantly lower in the Black population and gender disparity greatest in the Asian spousal population. Whilst these observations remain unexplained and represent an area for further research, they suggest that clinicians may need to tailor their approach when exploring live donation with different ethnic groups, as well as develop more targeted educational programs for ethnic minorities to improve live kidney transplantation in ethnic minorities. Indeed, healthcare providers need to ensure that educational programs are flexible and 'patient focused', which along with discussing transplantation, allow for the exploration of patients' beliefs and cultural values to facilitate both better physician-clinician understanding and communication; both of which would assist in tackling inequity in access to transplantation amongst ethnic minorities.

This thesis also shows that case mix differences are associated with transplant listing and accounts for much of the variation seen in unadjusted analyses. This suggests that when interpreting performance both unadjusted and case-mix adjusted data should be presented to renal centres, which would provide a more robust measure of the performance of a given centre. This makes a strong argument for centres to improve data returns to the UK Renal Registry especially relating to comorbidity data to facilitate adjustment. At the time of writing, the UK Renal registry data returns on co-morbidity remain insufficient to provide such adjustment with >90% missing data for some data variables. An alternative way to adjust for comorbidity could be to link

registry data with Hospital Episode Statistics (HES) data which has been shown to reduce missing data and facilitate more robust comparisons between centres. Lack of individual socioeconomic data in these analyses could be overcome by using area level socioeconomic data (IMD) which the registry has used in previous studies.

As for individual patient factors identified in this thesis as influencing access to transplantation though several are non-modifiable (in particular co-morbidities), as discussed earlier, several others could be viewed as potential targets for centres to improve listing. In particular, centres' having an age restriction to listing patients for transplantation need to remove these limitations to ensure that they not only comply with the ban on age discrimination enshrined in the Equality Act 2010 but also to improve listing amongst older patients. Commissioners of healthcare also need to encourage renal centres to take a more proactive approach in addressing obesity and smoking amongst patients with CKD and ESRD. This could include facilitating easier access to weight reduction services including bariatric surgery as well as improving access to smoking cessation services in primary care.

This thesis has also highlighted reduced access to the transplant waiting list (pre-emptive and listing after starting dialysis) for socially deprived patients as well as reduced access to pre-emptive listing for ethnic minorities (despite adjusting for known co-morbidities). To observe this association in a healthcare system which strives for equitable access irrespective of social status and race is disheartening and warrants further investigation into the reasons behind their reduced access (possibly using mixed methods) as well as to guide development of appropriate strategies to overcome them. Limited health literacy has recently been shown to be more prevalent amongst non-waitlisted patients as well as being associated with social deprivation and may represent an area for targeted interventions to reduce inequity caused by social deprivation.

This thesis has also demonstrated the benefit of being referred early to renal services in terms of pre-emptive listing and highlights the need to improve collaboration between primary care physicians and nephrologists so that patients at risk of developing ESRD (in particular socially deprived patients and ethnic minorities) are identified and referred early to improve access to pre-emptive listing. Linking tertiary

centre and GP IT systems to identify 'at risk' patients provides one possible method, though is fraught with technical and logistical difficulties as well as IT governance problems though could be achievable with Clinical Commissioning Group (CCG) support. As part of the North Central London Sustainability and Transformation (STP) CKD group (of which I am a part of) attempts are already underway to co-ordinate this link-up across 5 CCGs in London (Camden, Islington, Barnet, Haringey and Enfield) which if successful in reducing late-referral could be used as a model to be implemented nationally.

As for practice patterns, this thesis has identified a number of centre processes which might be associated with improved transplant listing. This study however is observational and one should not forget that as such the observation might be subject to reverse causality, in that the observational nature of the data makes it difficult to know in which direction the association lies.

In practice, some of the associations seem logical such as have a written protocol, raising the argument that maybe observational data is sufficient for centres to instigate change. Though a counter argument for this might be the cost and resources required to reorganize a care pathway which would support the argument for strengthening evidence via a randomized controlled trial. In the aforementioned example of instigating a written protocol limited resources would be needed and so this study might be considered to provide sufficient evidence for change.

7.2 Ideas for Further Research

There are several areas within this thesis that would be interesting to take further. Firstly, as mentioned in the limitations, the use of a logistic regression model may have diminished the impact of some of the centre variables, which may have had a tendency to improve the efficiency of being listed as opposed to getting listed per se. To improve the analysis undertaking a cox-regression analysis (with an expanded cohort including Northern Ireland and Scotland) of patient and centre factors will be the focus of future work, as will the development of time coefficients for significant centre variables to improve interpretation of their impact.

In addition to this, as highlighted by the literature review, qualitative interviews and results from the national survey, this thesis has shown that uncertainty remains surrounding cardiovascular disease screening pre-transplantation with no clear consensus on which screening tests to undertake or how to manage asymptomatic patients with coronary artery disease. Cardiovascular screening is a key component of being listing for transplantation though the lack of evidence base/clear consensus is concerning and warrants further investigation through a randomized controlled trial (RCT). Indeed, an RCT exploring both the utility of screening and the long and short term benefits of intervening on asymptomatic patients with coronary artery disease in patients with CKD stage 5 would be extremely valuable to patients and clinicians. To facilitate this, I have recently taken up an opportunity to present the findings of my thesis to the the Cardio-Renal Clinical Study Group (a national group dedicated to initiating and supporting clinical research in the cardio-renal field) where I hope to gain support for a research grant application to fund this study.

As for the observation of gender and ethnic differences in the relationships between live kidney donors and their recipients, further qualitative studies are needed to explore these differences as well as further studies investigating the outcome of patients who offered to be donors or were approached but who were deemed unsuitable or decided not to donate. Indeed, a qualitative study would be ideal in trying to understand the beliefs held by different ethnic communities about their own health and healthcare providers, as well as exploring their views on transplantation and live donation. Understanding how these views differ across ethnic groups could facilitate strategies to address differences in living donation practices and improve transplantation especially amongst Asian women who appear most disadvantaged

Another area for future work would be the development of a national consensus on recipient work up and promoting research in understanding cardiovascular screening utility in potential transplant recipients. Results from the qualitative interviews and national survey both highlighted these as important areas for future research and tackling inequity. Following on from this a Delphi consensus meeting involving stakeholders involved in transplantation in the UK has already been conducted exploring contentious areas of recipient work up and is in the process of being published. Additionally, further research is needed on the benefits of transplanting

obese patients and older patients to improve listing amongst these patients. Planned survival and quality of life analyses from the ATTOM study may assist in this and are already in progress.

Finally, it is anticipated that some of the methodological aspects and findings of this thesis may be helpful to researchers in other areas of healthcare who are attempting to improve quality of care for patients through determining the benchmark of quality for a particular healthcare system.

7.3 Personal Reflection

After working as a clinician in the NHS for over a decade it has been a tremendous experience to take time out of clinical practice and work towards attaining a PhD. It has also been an absolute privilege to be able to focus on exploring whether access to transplantation is equitable which is something I feel very passionately about as I strongly believe in the values upon which the NHS was formed and believe it is imperative that health services should be equally accessible irrespective of socioeconomic status or ethnicity.

In the process of completing this thesis there have been so many learning experiences I find it hard to think I could have learnt so much and undergone so much personal development doing anything else during this time. This experience has taught me to think deeply about complex processes and given me a much greater appreciation for conducting research on a national scale. I've learnt to complete research proposals including seek ethics approval and gained experience dealing with multiple Research and Development (R and D) departments across the UK. I have also had the unique privilege to interview senior healthcare professionals about their experiences (as part of Qualitative study) and work alongside leaders in their field of renal transplantation (as part of ATTOM study) both of which have given me greater depth to understanding problems relating to service delivery, as I have been able to learn directly from their experiences.

Alongside this I have had the opportunity to attend a range of courses on research methods, advanced epidemiology, statistics and multi-level modelling and learnt how

to use a range of statistical packages including SPSS, NVivo, STATA, SAS and MLwiN. This process has also given me the opportunity to improve my publishing profile and led to over 20 publications during the study period, several of which were derived directly from this thesis. It has also given me the opportunity to present my work at over 20 national and international conferences both through accepted oral abstracts and as an invited speaker.

Finally, my time studying for this PhD has also coincided with a period of personal growth, as I met my now wife during this process and was also blessed with the birth of my son Puneet, making these last few years even more memorable. I will forever be grateful to my supervisors for agreeing to supervise my PhD and hope to be able to inspire other students to pursue higher degrees in the future, just like my supervisors have inspired me to date.

Appendix A: Demography of Patients Wait- listed for Renal Transplantation in the UK: National and Centre-specific Analyses

UK Renal Registry 16th Annual Report: Chapter 4 Demography of Patients Wait-listed for Renal Transplantation in the UK: National and Centre-specific Analyses

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Key Words
Blood group · Calculated reaction frequency · Demography · End stage renal disease · Established renal failure · Ethnicity · Kidney allocation · Match grade · Prevalence · Renal replacement therapy · Transplantation · Transplant waiting list · Wait listing times

Summary

- There were 6,699 patients registered on the active transplant list for kidney only transplantation at the beginning of 2011.
- The UK population prevalence rate for listing for kidney transplantation was 107 pmp compared with a dialysis prevalence rate of 424 pmp, with wide inter-centre variation.
- A quarter of the patients listed (25%) were from ethnic minority groups (Black or South Asian). Only 10% (61/593) of Black patients were pre-emptively listed compared to 16% of Asian and 17% of White patients.
- The median age of prevalent listed patients on dialysis was 53 years, which was significantly lower than the median age of the prevalent haemodialysis (HD) patients (66.3 years) and those on peritoneal dialysis (PD) (61.7 years), $p < 0.0001$.
- The proportion of patients listed aged 70 or more was 8% in England, 11% in Wales, 7% in Northern Ireland and 6% in Scotland, with wide variation between centres.
- Of patients listed, 50% had blood group type O, whilst blood group AB was the least common accounting for just 3% of listed patients. The percentage of patients listed with blood group B showed inter-centre variation with some centres having more than a quarter of patients listed with blood group B.
- Of all patients listed for kidney transplantation, 43% were sensitised (cRF $\geqslant$10), with nearly a quarter (23%) of all patients listed being highly sensitised (cRF $\geqslant$85). Patients listed on haemodialysis had the largest proportion of highly sensitised patients with 30% having a cRF $\geqslant$85, whilst only 8% of patients listed pre-emptively were highly sensitised.
- Adult White patients had significantly shorter waiting times (1098 days, CI: 1071–1125) as compared to Black patients (1,396 days, CI: 1,301–1,491) or Asian patients (1411 days, CI: 1,334–1,488).
- Median waiting times in highly sensitised patients (2,218 days CI: 1,958–2,478) was more than twice that seen in patients who were not sensitised (1,063 days CI: 1,039–1,087).

Introduction

For suitable patients with established renal failure (ERF), renal transplantation is accepted as the optimal modality of renal replacement therapy, conferring both better quality of life and better life expectancy than dialysis. In the UK, after completing necessary medical and surgical assessment (guided by national guidelines [1]), 'suitable' patients are listed for transplantation on the UK Transplant Registry at NHSBT (National Health Service Blood and Transplant). The number of people registered on this database however are far greater than the number of donor organs available in the UK which has led to the development and implementation of an allocation policy for deceased donor kidneys. This policy aims to ensure equity of allocation whilst taking into account the importance of achieving a good match between donor and recipient.

Allocation policy

All kidneys from deceased donors whose death has been defined by brain-stem death criteria are allocated through the national allocation scheme managed by NHSBT. The current scheme was implemented in 2006 to meet agreed objectives and address issues of inequity of access to transplantation and utilises an evidence-based computer algorithm [2, 3]. This is based on a tier system, with all patients listed for kidney transplantation being allocated into one of five tiers (figure 4.1). Paediatric patients are prioritised within Tiers A and B according to waiting time, whilst within tiers C, D and E patients are prioritised according to a points based system (highest score first), based on seven elements. These are: waiting time, HLA match and age combined, donor-recipient age difference, geographical location of patient relative to donor, HLA-DR homozygosity, HLA-B homozygosity and blood group match (figure 4.1). Full details of the allocation policy can be accessed at: http://www.odt.nhs.uk/pdf/kidney_allocation_policy.pdf.

Whilst the analysis of these variables at a centre level is beyond the scope of a UK Renal Registry (UKRR) report, this report aims to provide clinicians with a better understanding of the 'make-up' of the UK Transplant Registry by:

(i) Defining the prevalence rates of listing, for individual UK countries and by age group
(ii) Providing centre level analysis of listing patterns by age group, ethnicity, gender, calculated HLA antibody reaction frequency (cRF), matchability score, blood group and primary renal disease (PRD)
(iii) Providing median waiting times by ethnicity, blood group and calculated HLA antibody reaction frequency (cRF).

Clinicians may find these analyses provide a better understanding of their practice patterns and service needs.

Methods

These analyses relate to the prevalent patients active on the transplant waiting list in the UK at the beginning of 2011. The cohort was defined as all patients listed for renal transplantation

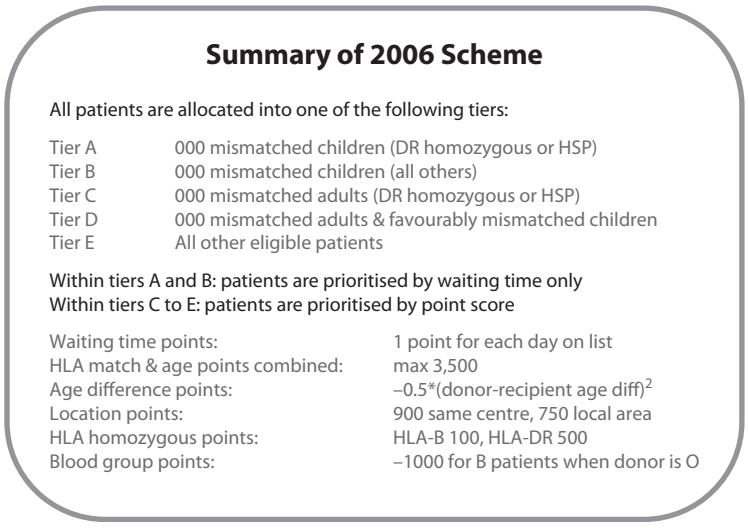

Fig. 4.1. Summary of national allocation scheme

Table 4.1. Prevalence of registration for kidney transplantation and dialysis in the UK on 01/01/2011 (including children <18 years)

	England	N Ireland	Scotland	Wales	**UK**
Total estimated population, mid-2010 (millions)*	52.2	1.8	5.2	3.0	62.3
Total number registered for transplantation	5,748	178	533	240	6,699
Prevalence rate registration for transplantation (pmp)	110	98	102	79	107
Prevalence rate dialysis (pmp)	424	440	415	436	424

*Data from the Office for National Statistics, National Records of Scotland and the Northern Ireland Statistics and Research Agency
pmp = per million population

on the UK Transplant Registry at NHSBT on 1st January 2011. Prevalent listed patients were extracted from the NHSBT database. Patients that had commenced dialysis were matched to the UKRR database. Patients were allocated to renal centres based on the origin of their data returns to the UKRR as opposed to their post-code. Population estimates were obtained from the UK Office of National Statistics (ONS) [4], the National Records of Scotland (NRS) [5] and the Northern Ireland Statistic and Research Agency (NISRA) [6]. Crude prevalence rates were calculated per million population (pmp) and centre level analyses were performed following a merge of data between NHSBT and the UKRR allowing listed patients to be re-allocated to their main renal centre.

The prevalence rate per million population for each centre was calculated using a derived catchment population. For a full description of the methodology used to estimate the catchment populations see appendix E: Methodology for Estimating Catchment Populations (www.renalreg.com). For Scotland, mid-2010 populations of Health Boards (HBs) (from the General Register Office for Scotland) were converted to centre level populations using an approximate mapping of renal centres to HBs supplied by the Scottish Renal Registry. Estimates of the catchment populations in Northern Ireland were supplied by personal communication from Dr D Fogarty.

Throughout this chapter, haemodialysis refers to all modes of HD treatment, including haemodiafiltration (HDF). Several centres reported significant numbers of patients on HDF, but other centres did not differentiate this treatment type in their UKRR returns. Prevalent patients listed for transplantation were examined by gender, ethnicity, age group, primary renal disease, blood group, match grade and calculated HLA antibody reaction frequency (Report appendix H: Coding (www.renalreg.com). Analyses were done for the UK as a whole, by UK country, at centre level and split by treatment modality as appropriate.

Match grade was calculated for each listed patient by NHSBT using a pool of 10,000 donors that were blood group identical, HLA compatible and 000 or favourably (100, 010, 110) HLA mismatched. The match count was then converted into a standardised score, and categorised as: easy to match (1–3), moderate to match (4–7) and difficult to match (8–10). UK and centre analyses were performed using the three generated categories.

Calculated HLA antibody reaction frequency (cRF) for each patient was determined by NHS Blood & Transplant-Organ Donation and Transplantation Directorate (NHSBT–ODT) from the unacceptable HLA specificities reported for each patient. The unacceptable specificities were compared with the HLA types of blood group identical donors from a pool of 10,000 UK donors and the resulting HLA antibody reaction frequency (cRF) was expressed as a percentage of HLA incompatible donors. These were then categorised into five groups: '0–9%', '10–29%', '30–84%', and '⩾85%'; '0–9%' was classed as being un-sensitised, and '⩾85%' was classed as being highly sensitised.

Chi-squared test, Fisher's exact test and Kruskal Wallis tests were used as appropriate to test for significant differences between groups. The data were analysed using SAS 9.3.

Results

Prevalent patient numbers listed for transplantation

There were 6,699 patients registered on the active transplant list for kidney only transplantation at the beginning of 2011, giving a UK population prevalence rate for listing for kidney transplantation of 107 pmp compared with a dialysis prevalence rate of 424 pmp (table 4.1). There were no significant differences in prevalence rates for dialysis in all four of the UK countries; however prevalence rates for listing were significantly lower in Wales at 79 pmp. This may be explained by the higher prevalence rate of dialysis for patients aged >80 seen in Wales who are less likely to be listed. Figure 4.2 shows that Northern Ireland had a higher prevalence rate for listing patients aged 65+ compared with the other UK countries, mirroring the trend seen in prevalence of dialysis patients in UK countries (chapter 2).

Prevalent patients listed for transplantation by RRT modality and centre

The number of prevalent patients listed for transplantation in each renal centre and the distribution of their treatment modalities varied widely (table 4.2). Many factors including geography, local population density, age distribution, ethnic composition, prevalence of diseases predisposing to kidney disease and the social deprivation index of that population may contribute to

Table 4.2. Number of prevalent listed patients by treatment modality and centre on 01/01/2011

Centre	HD	PD	Total number listed on dialysis	Catchment population (millions)	Rate of patients listed on dialysis	
					pmp	95% CI
England						
B Heart	94	13	107	0.74	145	(118–172)
B QEH[a]	208	72	280	1.70	165	(145–184)
Basldn	12	3	15	0.42	36	(18–54)
Bradfd	30	17	47	0.65	72	(51–93)
Brightn	45	21	66	1.30	51	(39–63)
Bristol[a]	83	26	109	1.44	76	(62–90)
Camb[a]	45	6	51	1.16	44	(32–56)
Carlis	13	4	17	0.32	53	(28–78)
Carsh	93	31	124	1.91	65	(53–76)
Chelms	15	13	28	0.51	55	(35–75)
Colchr	14	0	14	0.30	47	(22–71)
Covnt[a]	64	18	82	0.89	92	(72–112)
Derby	36	26	62	0.70	88	(66–110)
Donc	34	9	43	0.41	105	(74–136)
Dorset	59	19	78	0.86	91	(70–111)
Dudley	25	23	48	0.44	109	(78–139)
Exeter	38	22	60	1.09	55	(41–69)
Glouc	23	15	38	0.59	65	(44–85)
Hull	45	17	62	1.02	61	(46–76)
Ipswi	8	10	18	0.40	45	(24–66)
Kent	60	25	85	1.22	69	(55–84)
L Barts[a]	134	61	195	1.83	107	(92–122)
L Guys[a]	100	16	116	1.08	107	(88–127)
L Kings	72	30	102	1.17	87	(70–104)
L Rfree[a]	166	26	192	1.52	126	(109–144)
L St.G[a]	48	13	61	0.80	76	(57–96)
L West[a]	330	14	344	2.40	143	(128–159)
Leeds[a]	111	41	152	1.67	91	(77–105)
Leic[a]	235	71	306	2.44	126	(112–140)
Liv Ain	19	1	20	0.48	41	(23–59)
Liv RI[a]	82	25	107	1.00	107	(87–127)
M RI[a]	115	35	150	1.53	98	(82–114)
Middlbr	58	9	67	1.00	67	(51–83)
Newc[a]	41	25	66	1.12	59	(45–73)
Norwch	40	13	53	0.79	67	(49–86)
Nottm[a]	80	48	128	1.09	118	(97–138)
Oxford[a]	81	43	124	1.69	73	(60–86)
Plymth[ab]	20	13	33	0.47	70	(46–94)
Ports[a]	143	44	187	2.02	92	(79–106)
Prestn	94	30	124	1.49	83	(68–98)
Redng	64	37	101	0.91	111	(89–133)
Salford	99	49	148	1.49	99	(83–115)
Sheff[a]	114	19	133	1.37	97	(80–113)
Shrew	26	8	34	0.50	68	(45–91)
Stevng	83	14	97	1.20	81	(65–97)
Sthend	11	8	19	0.32	60	(33–87)
Stoke	54	20	74	0.89	83	(64–102)
Sund	34	11	45	0.62	73	(52–94)
Truro	28	8	36	0.41	87	(59–116)
Wirral	29	10	39	0.57	68	(47–90)
Wolve	36	19	55	0.67	82	(61–104)
York	28	5	33	0.49	67	(44–90)

Table 4.2. Continued

Centre	HD	PD	Total number listed on dialysis	Catchment population (millions)	Rate of patients listed on dialysis	
					pmp	95% CI
Northern Ireland						
Antrim	11	3	14	0.30	47	(22–71)
Belfast[a]	50	12	62	0.55	113	(85–141)
Newry	20	3	23	0.28	82	(49–116)
Ulster	11	0	11	0.30	37	(15–58)
West NI	36	5	41	0.35	117	(81–153)
Scotland						
Abrdn	37	11	48	0.60	80	(57–103)
Airdrie	27	3	30	0.56	54	(34–73)
D & Gall	10	2	12	0.15	80	(35–125)
Dundee	16	7	23	0.41	56	(33–79)
Dunfn	19	7	26	0.37	70	(43–97)
Edinb[a]	69	22	91	0.96	95	(75–114)
Glasgw[a]	186	24	210	1.51	139	(120–158)
Inverns	14	7	21	0.34	62	(35–88)
Klmarnk	24	11	35	0.37	95	(63–126)
Wales						
Bangor	14	4	18	0.22	83	(44–121)
Cardff[a]	64	29	93	1.42	65	(52–79)
Clwyd	11	2	13	0.19	69	(31–106)
Swanse	45	12	57	0.89	64	(48–81)
Wrexm	8	6	14	0.24	58	(28–89)
England	**3,619**	**1,156**	**4,775**			
N Ireland	**128**	**23**	**151**			
Scotland	**402**	**94**	**496**			
Wales	**142**	**53**	**195**			
UK	**4,291**	**1,326**	**5,617**			

Centres prefixed 'L' are London centres
The numbers of patients calculated for each country quoted above differ marginally from those quoted elsewhere when patients are allocated to areas by their individual postcodes, as some centres treat patients from across national boundaries
[a]Transplant centres
[b]The catchment population for Plymouth may be too low, see appendix E

this. Many of these factors are also likely to be the cause behind the wide inter-centre variation seen in listing patients pre-emptively between transplant centres with a range of 11 to 125 patients listed across 24 transplanting centres (table 4.3).

Case mix in prevalent wait-listed patients

Gender

Table 4.4 shows that the gender distribution of patients listed for transplantation was similar to that seen in the prevalent dialysis population with 59% of patients listed

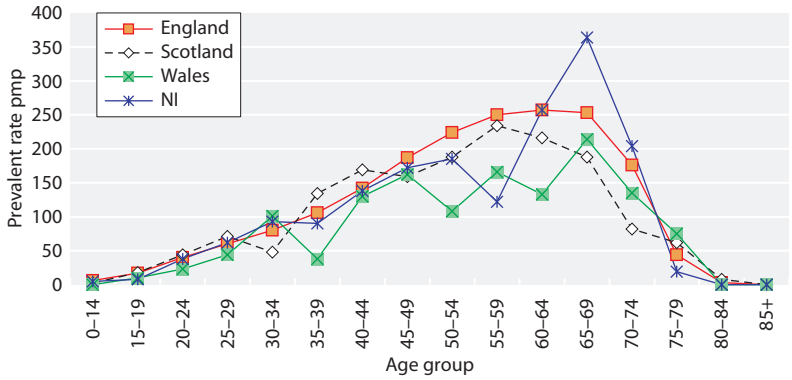

Fig. 4.2. Prevalence rates of registration for kidney transplantation in the UK per million population by age group and UK country on 01/01/2011

Table 4.3. Number of prevalent listed patients pre-emptively listed by transplant centre on 01/01/2011

Transplant centre	Number of pre-emptive listed patients
M RI	125
B QEH	112
Leic	97
L Guys	71
Bristol	67
L Rfree	61
L St.G	56
L West	56
Leeds	50
Oxford	49
Camb	34
Liv RI	33
Nottm	31
Newc	30
Sheff	30
Ports	30
Cardiff	29
Belfast	27
Glasgw	19
L Barts	18
Edin	16
Plymth	15
L GOSH	15
Covnt	11
UK	**1,082**

being male. There was wide inter-centre variation with a range of 37–91%, and only 11 centres had a preponderance of women listed (figure 4.3). Sub-analysis by modality did not show any significant gender differences.

Ethnicity

Ethnicity completeness for prevalent listed patients in the UK was 100% at the beginning of 2011 across all UK countries. Table 4.4 shows that a quarter of the patients listed (25%) were from ethnic minority groups (Black or South Asian) which compared to 12% of the UK general population who were designated as belonging to an ethnic minority. Whilst there was little difference across modalities, Black patients were seen to have the lowest proportion of pre-emptively listed patients, with only 10% (61/593) of listed Black patients being pre-emptively listed compared to 17% (817/4,835) and 16% (175/1,089) of White and South Asian listed patients respectively. Amongst renal centres there was wide variation between centres with respect to the proportion of patients listed from ethnic minorities (table 4.5, figure 4.4), ranging from zero percent (0%) in 12 centres to over 50% in London Barts (72%), London West (70%), London St Georges (69%), London Kings (69%), London Royal Free (65%), Birmingham Heartlands (61%) and London Guys (53%).

Age

The median age of prevalent listed patients on dialysis at 1st January 2011 was 53 years, which was significantly lower than the median age of the prevalent HD patients (66.3 years) and those on PD (61.7 years), $p < 0.0001$. As for those listed pre-emptively the median age was slightly lower than those on dialysis at 52 years. Table 4.4 shows that 79% of the UK prevalent listed

Table 4.4. Number and percentage of prevalent listed patients and their modalities by gender, ethnicity and age group on 01/01/2011

		Modality							
		HD		PD		Pre-emptive		Total	
		N	%	*N*	%	*N*	%	*N*	%
Gender	Male	2,595	60	724	55	614	57	3,933	59
	Female	1,696	40	602	45	468	43	2,766	41
Ethnicity	White	2,968	69	1,050	79	817	76	4,835	72
	Asian	738	17	176	13	175	16	1,089	16
	Black	461	11	71	5	61	6	593	9
	Other	124	3	29	2	29	3	182	3
Age group	0–17	20	0	24	2	52	5	96	1
	18–34	511	12	148	11	111	10	770	11
	35–49	1,265	29	380	29	303	28	1,948	29
	50–59	1,098	26	356	27	261	24	1,715	26
	60–69	1,024	24	334	25	300	28	1,658	25
	70+	373	9	84	6	55	5	512	8

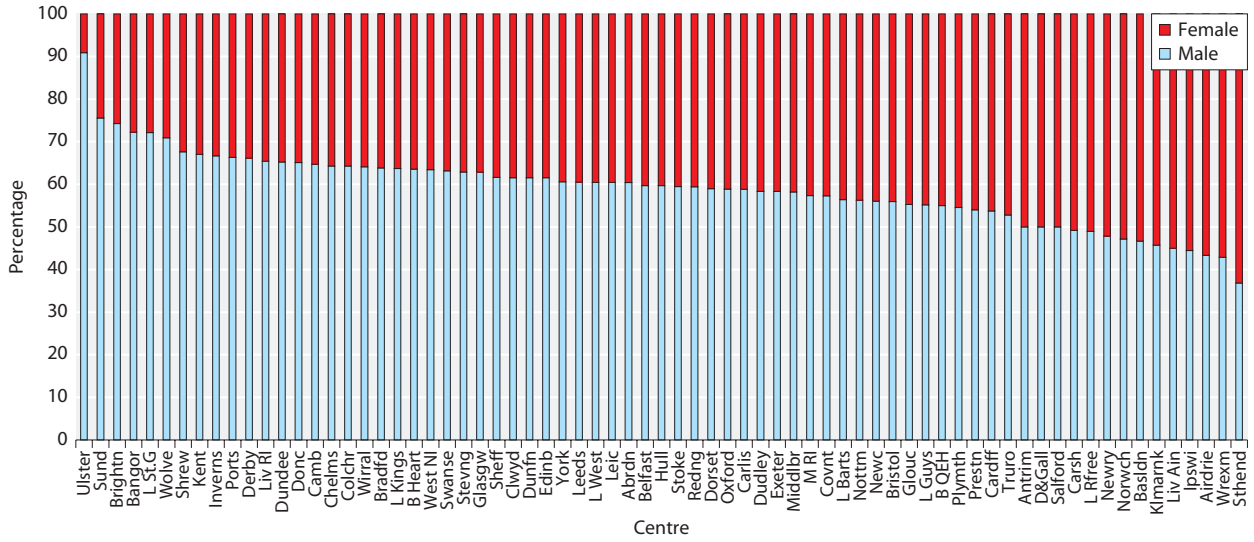

Fig. 4.3. Percentage of prevalent listed patients by gender and centre on 01/01/2011

Table 4.5. Ethnicity of prevalent listed patients by centre on 01/01/2011

		Ethnicity							
		White		Asian		Black		Other	
Centre	*N*	*N*	%	*N*	%	*N*	%	*N*	%
England									
Basldn	15	13	87	1	7	1	7	0	0
B Heart	107	42	39	54	50	10	9	1	1
B QEH	280	151	54	91	33	30	11	8	3
Bradfd	47	25	53	21	45	1	2	0	0
Brightn	66	54	82	4	6	4	6	4	6
Bristol	109	86	79	6	6	8	7	9	8
Camb	51	44	86	4	8	2	4	1	2
Carlis	17	17	100	0	0	0	0	0	0
Carsh	124	74	60	18	15	18	15	14	11
Chelms	28	23	82	1	4	1	4	3	11
Colchr	14	13	93	0	0	0	0	1	7
Covnt	82	52	63	22	27	5	6	3	4
Derby	62	48	77	11	18	3	5	0	0
Donc	43	42	98	1	2	0	0	0	0
Dorset	78	76	97	2	3	0	0	0	0
Dudley	48	38	79	7	15	3	6	0	0
Exeter	60	60	100	0	0	0	0	0	0
Glouc	38	35	92	2	5	1	3	0	0
Hull	62	56	90	2	3	2	3	2	3
Ipswi	18	16	89	0	0	1	6	1	6
Kent	85	84	99	0	0	1	1	0	0
Leeds	152	97	64	38	25	9	6	8	5
Leic	306	209	68	79	26	16	5	2	1
Liv Ain	20	19	95	1	5	0	0	0	0
Liv RI	107	95	89	1	1	5	5	6	6
L Barts	195	55	28	78	40	54	28	8	4
L Guys	116	55	47	4	3	52	45	5	4
L Kings	102	32	31	14	14	51	50	5	5
L Rfree	192	68	35	48	25	70	36	6	3

Table 4.5. Continued

		Ethnicity							
		White		Asian		Black		Other	
Centre	*N*	*N*	%	*N*	%	*N*	%	*N*	%
L St.G	61	19	31	18	30	18	30	6	10
L West	344	104	30	143	42	77	22	20	6
M RI	150	103	69	33	22	11	7	3	2
Middlbr	67	64	96	2	3	1	1	0	0
Newc	66	61	92	4	6	0	0	1	2
Norwch	53	50	94	2	4	0	0	1	2
Nottm	128	106	83	7	5	12	9	3	2
Oxford	124	89	72	21	17	10	8	4	3
Plymth	33	32	97	0	0	0	0	1	3
Ports	187	161	86	10	5	10	5	6	3
Prestn	124	100	81	21	17	2	2	1	1
Redng	101	60	59	32	32	8	8	1	1
Salford	148	111	75	31	21	4	3	2	1
Sheff	133	119	89	8	6	5	4	1	1
Shrew	34	31	91	1	3	2	6	0	0
Sthend	19	15	79	1	5	2	11	1	5
Stevng	97	69	71	16	16	10	10	2	2
Stoke	74	65	88	6	8	2	3	1	1
Sund	45	43	96	1	2	0	0	1	2
Truro	36	35	97	0	0	0	0	1	3
Wirral	39	33	85	3	8	1	3	2	5
Wolve	55	37	67	16	29	2	4	0	0
York	33	32	97	0	0	0	0	1	3
N Ireland									
Antrim	14	14	100	0	0	0	0	0	0
Belfast	62	60	97	1	2	0	0	1	2
Newry	23	22	96	0	0	0	0	1	4
Ulster	11	11	100	0	0	0	0	0	0
West NI	41	41	100	0	0	0	0	0	0
Scotland									
Abrdn	48	45	94	2	4	1	2	0	0
Airdrie	30	30	100	0	0	0	0	0	0
D & Gall	12	12	100	0	0	0	0	0	0
Dundee	23	22	96	1	4	0	0	0	0
Dunfn	26	26	100	0	0	0	0	0	0
Edinb	91	88	97	2	2	0	0	1	1
Glasgw	210	193	92	12	6	4	2	1	0
Inverns	21	21	100	0	0	0	0	0	0
Klmarnk	35	33	94	1	3	0	0	1	3
Wales									
Bangor	18	18	100	0	0	0	0	0	0
Cardff	93	83	89	7	8	1	1	2	2
Clwyd	13	13	100	0	0	0	0	0	0
Swanse	57	54	95	2	4	1	2	0	0
Wrexm	14	14	100	0	0	0	0	0	0
England	**4,775**	**3,218**	**67**	**886**	**19**	**525**	**11**	**146**	**3**
Northern Ireland	**151**	**148**	**98**	**1**	**1**	**0**	**0**	**2**	**1**
Scotland	**496**	**470**	**95**	**18**	**4**	**5**	**1**	**3**	**1**
Wales	**195**	**182**	**93**	**9**	**5**	**2**	**1**	**2**	**1**
UK	**5,617**	**4,018**	**72**	**914**	**16**	**532**	**9**	**153**	**3**

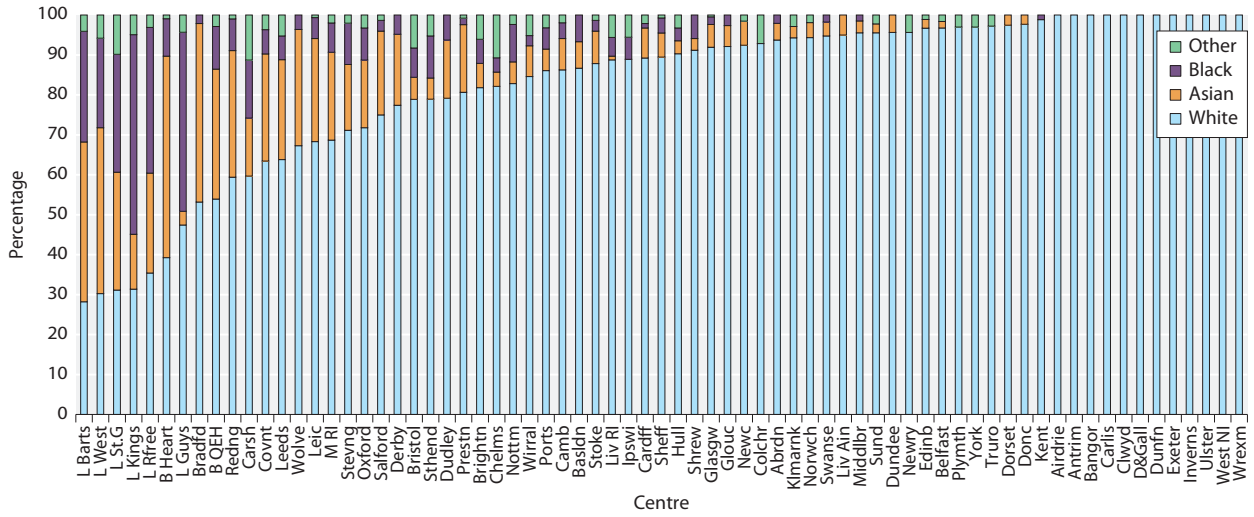

Fig. 4.4. Ethnicity of prevalent listed patients by centre on 01/01/2011

population was aged between 35–69 years, with only 8% of patients aged 70 or above. The proportion of patients listed aged 70 or more was 8% in England, 11% in Wales, 7% in Northern Ireland and 6% in Scotland (table 4.6). Analysis by centre (table 4.6) showed wide variation in the proportion of patients listed aged 70 or above by centre with four centres (Basildon, Colchester, Ipswich and London Barts) listing no patients, compared

Table 4.6. Number and percentage of prevalent listed patients in each age group by centre on 01/01/2011

	Age group (years)											
	0–17		18–34		35–49		50–59		60–69		70+	
Centre	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
England												
Basldn			1	7	5	33	6	40	3	20		
B Heart			17	16	27	25	27	25	24	22	12	11
B QEH	4	1	38	14	73	26	90	32	60	21	15	5
Bradfd			11	23	15	32	10	21	8	17	3	6
Brightn	1	2	7	11	16	24	16	24	17	26	9	14
Bristol	3	3	12	11	35	32	23	21	29	27	7	6
Camb			5	10	17	33	16	31	8	16	5	10
Carlis			2	12	5	29	4	24	5	29	1	6
Carsh			12	10	37	30	28	23	37	30	10	8
Chelms			3	11	8	29	9	32	7	25	1	4
Colchr					3	21	2	14	9	64		
Covnt			6	7	24	29	27	33	19	23	6	7
Derby			8	13	15	24	15	24	20	32	4	6
Donc			6	14	10	23	10	23	13	30	4	9
Dorset			7	9	17	22	12	15	26	33	16	21
Dudley			5	10	15	31	15	31	11	23	2	4
Exeter			4	7	16	27	15	25	22	37	3	5
Glouc			5	13	10	26	9	24	9	24	5	13
Hull			8	13	21	34	16	26	15	24	2	3
Ipswi			4	22	8	44	5	28	1	6		
Kent			8	9	17	20	23	27	31	36	6	7
Leeds	10	7	22	14	47	31	36	24	26	17	11	7
Leic			31	10	71	23	67	22	95	31	42	14
Liv Ain			4	20	5	25	4	20	4	20	3	15
Liv RI			14	13	39	36	30	28	19	18	5	5
L Barts			30	15	63	32	71	36	31	16		

Table 4.6. Continued

	Age group (years)											
	0–17		18–34		35–49		50–59		60–69		70+	
Centre	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
L Guys	1	1	14	12	42	36	32	28	19	16	8	7
L Kings			11	11	37	36	30	29	22	22	2	2
L Rfree			20	10	68	35	44	23	40	21	20	10
L St.G			7	11	19	31	9	15	17	28	9	15
L West	2	1	25	7	86	25	102	30	82	24	47	14
M RI			13	9	57	38	43	29	26	17	11	7
Middlbr			10	15	19	28	18	27	14	21	6	9
Newc	2	3	9	14	8	12	19	29	23	35	5	8
Norwch			7	13	13	25	12	23	18	34	3	6
Nottm	14	11	16	13	38	30	26	20	28	22	6	5
Oxford			12	10	36	29	39	31	30	24	7	6
Plymth			6	18	5	15	9	27	12	36	1	3
Ports			18	10	43	23	38	20	54	29	34	18
Prestn			18	15	34	27	38	31	29	23	5	4
Redng			8	8	35	35	28	28	23	23	7	7
Salford	1	1	19	13	42	28	40	27	38	26	8	5
Sheff			18	14	42	32	39	29	27	20	7	5
Shrew	1	3	7	21	13	38	5	15	7	21	1	3
Sthend			1	5	10	53	3	16	4	21	1	5
Stevng			12	12	35	36	20	21	20	21	10	10
Stoke			10	14	21	28	21	28	16	22	6	8
Sund			7	16	19	42	8	18	6	13	5	11
Truro			2	6	6	17	8	22	14	39	6	17
Wirral			6	15	9	23	14	36	7	18	3	8
Wolve			6	11	16	29	14	25	16	29	3	5
York			2	6	12	36	10	30	5	15	4	12
Northern Ireland												
Antrim					3	21	1	7	8	57	2	14
Belfast			12	19	19	31	12	19	18	29	1	2
Newry			5	22	6	26	2	9	9	39	1	4
Ulster			2	18	3	27	2	18	3	27	1	9
West NI			5	12	10	24	8	20	13	32	5	12
Scotland												
Abrdn			8	17	15	31	14	29	8	17	3	6
Airdrie			4	13	11	37	7	23	6	20	2	7
D & Gall					5	42	3	25	3	25	1	8
Dundee			1	4	9	39	5	22	5	22	3	13
Dunfn			2	8	6	23	10	38	6	23	2	8
Edinb	1	1	9	10	34	37	20	22	21	23	6	7
Glasgw	3	1	26	12	71	34	62	30	38	18	10	5
Inverns			3	14	3	14	6	29	8	38	1	5
Klmarnk			6	17	8	23	6	17	14	40	1	3
Wales												
Bangor			2	11	6	33	1	6	6	33	3	17
Cardff	1	1	12	13	31	33	21	23	20	22	8	9
Clwyd			2	15	5	38	2	15	3	23	1	8
Swanse			5	9	12	21	13	23	19	33	8	14
Wrexm			1	7	4	29	4	29	4	29	1	7
England	**39**	**1**	**554**	**12**	**1,384**	**29**	**1,255**	**26**	**1,146**	**24**	**397**	**8**
N Ireland	**0**	**0**	**24**	**16**	**41**	**27**	**25**	**17**	**51**	**34**	**10**	**7**
Scotland	**4**	**1**	**59**	**12**	**162**	**33**	**133**	**27**	**109**	**22**	**29**	**6**
Wales	**1**	**1**	**22**	**11**	**58**	**30**	**41**	**21**	**52**	**27**	**21**	**11**
UK	**44**	**1**	**659**	**12**	**1,645**	**29**	**1,454**	**26**	**1,358**	**24**	**457**	**8**

The numbers of patients calculated for each country quoted above differ marginally from those quoted elsewhere when patients are allocated to areas by their individual postcodes, as some centres treat patients from across national boundaries
Blank cells denote no patients listed for that age group within corresponding centre

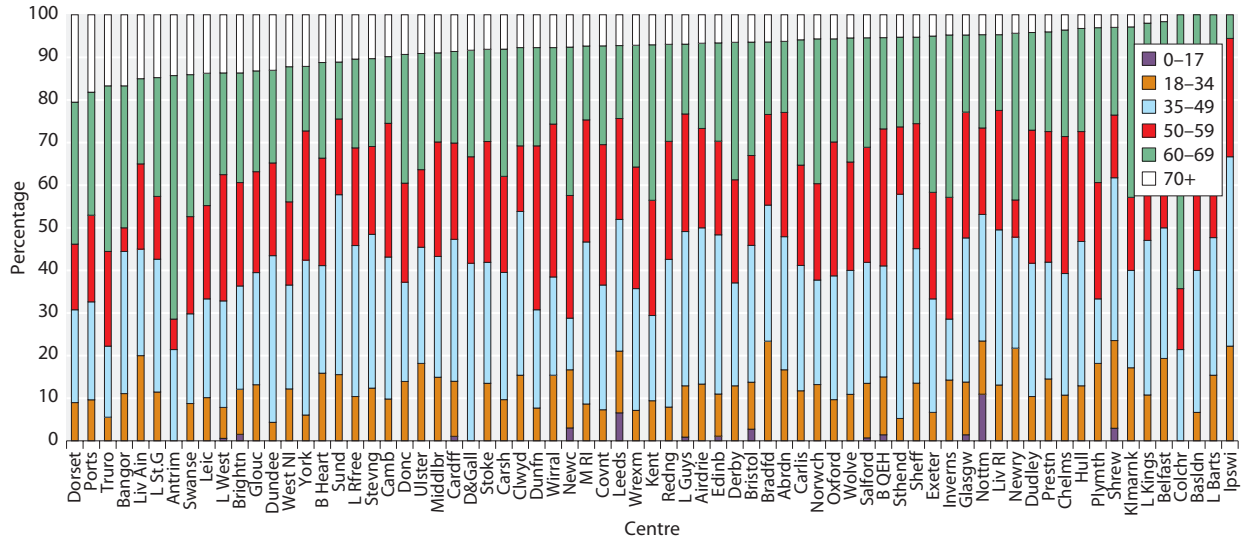

Fig. 4.5. Percentage of listed patients in each age group on 01/01/2011 by centre

to Dorset, Portsmouth, Truro and Bangor, where more than a sixth of their listed patients were aged 70 or more (figure 4.5). These differences may be due to variation in local listing practices, although could also reflect variation in the ethnic make-up of the catchment population and the social deprivation index of the local population.

Primary renal diagnosis

Data for primary renal diagnosis (PRD) were not complete for 3% of patients (table 4.7) and there remained a marked inter-centre difference in completeness of data returns for PRD to the UKRR. Glomerulonephritis (GN) was the most common PRD amongst patients listed for transplantation on 1st January 2011 at 22% (table 4.7), whilst hypertension only accounted for 7% and renovascular disease only 2%. This may be explained by the fact that younger patients (age <65 years) who are more likely to be listed are more likely to have GN or pyelonephritis and less likely to have renovascular disease or hypertension as the cause of their renal failure which are more prominent in older age.

Diabetes accounted for just 10% of listed patients, lower than the 15% seen in prevalent patients.

Amongst patients pre-emptively listed the most common diagnosis was polycystic kidney disease (PKD), which is probably a reflection of the fact that these patients are often known to renal services for many

Table 4.7. Number and percentage of prevalent listed patients and their modalities by primary renal diagnosis on 01/01/2011

	Modality							
	HD		PD		Pre-emptive		Total	
Primary renal diagnosis	*N*	%	*N*	%	*N*	%	*N*	%
Diabetes	463	11	114	9	41	6	618	10
Glomerulonephritis	926	22	323	24	124	20	1,373	22
Hypertension	311	7	83	6	26	4	420	7
Missing	127	3	40	3	47	7	214	3
Other	709	17	212	16	84	13	1,005	16
Polycystic kidney disease	493	11	189	14	131	21	813	13
Pyelonephritis	489	11	126	10	72	11	687	11
Renovascular	89	2	21	2	8	1	118	2
Uncertain	684	16	218	16	103	16	1,005	16

Table 4.8. Number and percentage of prevalent listed patients and their modalities by blood group, match grade and cRF group on 01/01/2011

		Modality							
		HD		PD		Pre-emptive		Total	
		N	%	*N*	%	*N*	%	*N*	%
Blood group	O	2,189	51	639	48	517	48	3,345	50
	A	1,290	30	475	36	373	35	2,138	32
	B	684	16	181	14	154	14	1,019	15
	AB	128	3	31	2	37	3	196	3
Match grade	Easy	1,175	27	482	36	422	39	2,079	31
	Moderate	1,684	39	601	45	492	46	2,777	41
	Difficult	1,432	33	243	18	167	15	1,842	28
cRF group	0 to <10	2,191	51	833	63	767	71	3,791	57
	10 to <30	172	4	75	6	57	5	304	5
	30 to <85	644	15	229	17	174	16	1,047	16
	85 to 100	1,284	30	189	14	83	8	1,556	23

years prior to starting dialysis allowing their timely work up to be pre-emptively listed.

Blood group

Table 4.8 shows that 50% of patients listed had blood group type O, whilst blood group AB was the least common accounting for just 3% of listed patients. The percentage of patients listed with blood group B (who are known to have the longest median waiting times) showed inter-centre variation (see table 4.9, figure 4.6) with some centres having more than a quarter of patients listed with blood group B (London St George's 31% and London West 26%) whilst four centres had none (Antrim, Basildon, Colchester, Truro). This may partly be due to the ethnic make-up of the catchment population with both London West and St George's having a large non-White prevalent dialysis population. Additionally the actual number of patients listed in Antrim, Basildon, Colchester and Truro were quite small, which may explain why all blood groups were not represented in their listed patients.

Calculated HLA antibody reaction frequency (cRF) and match grade

Table 4.8 shows that 43% of all patients listed for kidney transplantation on the 1st January 2011 were sensitised (cRF $\geqslant$10). Patients on haemodialysis had the largest proportion of sensitised patients with 49% having a cRF $\geqslant$10, whilst only 29% of patients listed pre-emptively were sensitised. This is likely a reflection of haemodialysis patients having an increased risk of exposure to sensitising events (e.g. blood transfusions) relating to dialysis complications and access procedures as compared to those listed pre-emptively and also selective enrichment of the HD population with patients with previous failed transplants (due to longer RRT vintage). Similar reasons are also likely to account for the disparity seen in distribution of highly sensitised patients (cRF $\geqslant$85) which constitute nearly a quarter (23%) of all patients listed for transplantation. Patients listed on haemodialysis had the largest proportion of highly sensitised patients with 30% having a cRF $\geqslant$85, whilst only 8% of patients listed pre-emptively were highly sensitised.

Centre analysis highlighted wide variation in the proportion of highly sensitised patients listed (table 4.10, figure 4.7) ranging from 50% of patients or more in Ipswich and Liverpool Aintree, to only 9% in Wolverhampton.

Similar trends were also noted when analysing match scores by modality (table 4.8) with those listed on haemodialysis having the greatest proportion of patients that were difficult to match (33%) as compared to those who were pre-emptively listed (15%). Centre variation was also seen in the proportion of patients that were difficult to match ranging from 48% of patients at London Royal Free, to only 13% at Wolverhampton (table 4.10, figure 4.8).

Table 4.9. Number and percentage of prevalent listed patients in each blood group by centre on 01/01/2011

	Blood group							
	O		A		B		AB	
Centre	*N*	%	*N*	%	*N*	%	*N*	%
England								
Basldn	9	60	6	40				
B Heart	44	41	33	31	24	22	6	6
B QEH	116	41	94	34	63	23	7	3
Bradfd	26	55	11	23	10	21		
Brightn	31	47	24	36	9	14	2	3
Bristol	54	50	37	34	16	15	2	2
Camb	29	57	16	31	4	8	2	4
Carlis	11	65	3	18	3	18		
Carsh	73	59	31	25	18	15	2	2
Chelms	13	46	13	46	2	7		
Colchr	7	50	7	50				
Covnt	36	44	28	34	13	16	5	6
Derby	29	47	20	32	13	21		
Donc	22	51	17	40	4	9		
Dorset	48	62	27	35	2	3	1	1
Dudley	25	52	15	31	8	17		
Exeter	27	45	28	47	4	7	1	2
Glouc	18	47	18	47	2	5		
Hull	30	48	23	37	3	5	6	10
Ipswi	11	61	5	28	2	11		
Kent	47	55	25	29	12	14	1	1
Leeds	82	54	42	28	23	15	5	3
Leic	148	48	89	29	53	17	16	5
Liv Ain	13	65	5	25	1	5	1	5
Liv RI	55	51	40	37	8	7	4	4
L Barts	90	46	58	30	44	23	3	2
L Guys	58	50	40	34	13	11	5	4
L Kings	48	47	30	29	17	17	7	7
L Rfree	92	48	49	26	46	24	5	3
L St.G	23	38	17	28	19	31	2	3
L West	171	50	71	21	89	26	13	4
M RI	80	53	46	31	21	14	3	2
Middlbr	39	58	23	34	2	3	3	4
Newc	32	48	18	27	15	23	1	2
Norwch	28	53	22	42	3	6		
Nottm	80	63	38	30	10	8		
Oxford	54	44	47	38	19	15	4	3
Plymth	21	64	10	30	2	6		
Ports	80	43	79	42	20	11	8	4
Prestn	67	54	28	23	23	19	6	5
Redng	49	49	36	36	13	13	3	3
Salford	71	48	49	33	25	17	3	2
Sheff	60	45	59	44	10	8	4	3
Shrew	17	50	13	38	3	9	1	3
Sthend	11	58	4	21	4	21		
Stevng	50	52	29	30	16	16	2	2
Stoke	34	46	29	39	8	11	3	4
Sund	31	69	10	22	4	9		
Truro	17	47	19	53				
Wirral	16	41	16	41	7	18		
Wolve	31	56	17	31	7	13		
York	17	52	9	27	5	15	2	6

Table 4.9. Continued

	Blood group							
	O		A		B		AB	
Centre	*N*	%	*N*	%	*N*	%	*N*	%
N Ireland								
Antrim	6	43	8	57				
Belfast	34	55	17	27	10	16	1	2
Newry	15	65	4	17	2	9	2	9
Ulster	5	45	5	45	1	9		
West NI	23	56	15	37	3	7		
Scotland								
Abrdn	29	60	12	25	7	15		
Airdrie	17	57	8	27	5	17		
D&Gall	6	50	2	17	3	25	1	8
Dundee	11	48	7	30	4	17	1	4
Dunfn	21	81	4	15	1	4		
Edinb	51	56	23	25	16	18	1	1
Glasgw	116	55	48	23	39	19	7	3
Inverns	15	71	4	19	2	10		
Klmarnk	19	54	10	29	4	11	2	6
Wales								
Bangor	10	56	7	39	1	6		
Cardff	38	41	38	41	13	14	4	4
Clwyd	6	46	4	31	3	23		
Swanse	28	49	20	35	8	14	1	2
Wrexm	7	50	6	43	1	7		
England	**2,371**	**50**	**1,523**	**32**	**742**	**16**	**139**	**3**
Northern Ireland	**83**	**55**	**49**	**32**	**16**	**11**	**3**	**2**
Scotland	**285**	**57**	**118**	**24**	**81**	**16**	**12**	**2**
Wales	**89**	**46**	**75**	**38**	**26**	**13**	**5**	**3**
UK	**2,828**	**50**	**1,765**	**31**	**865**	**15**	**159**	**3**

Blank cells denote no patients listed for that blood group within corresponding centre

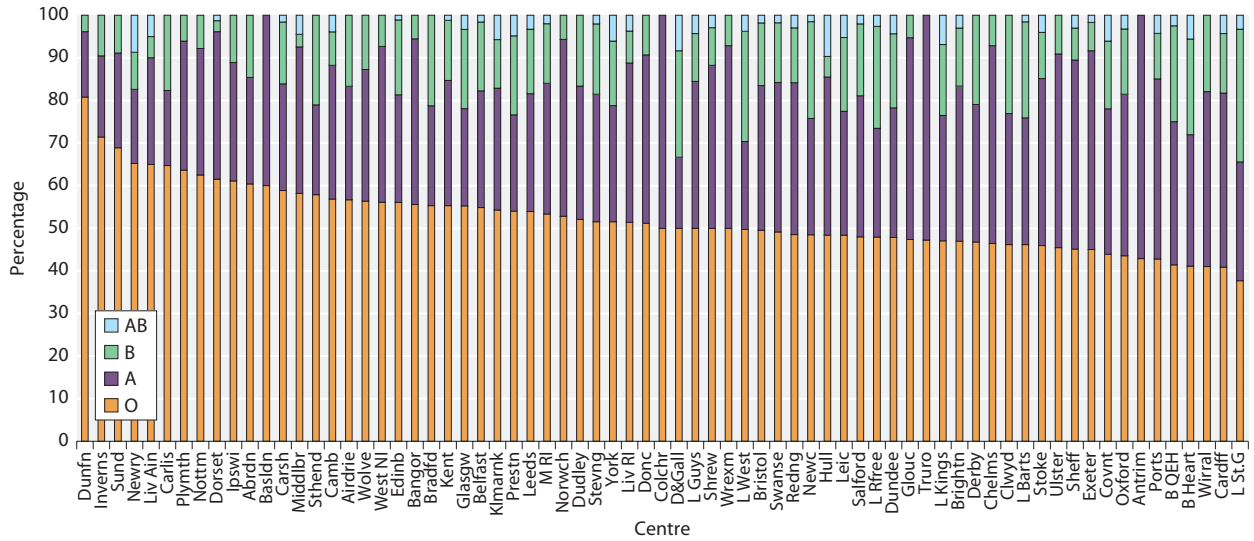

Fig. 4.6. Percentage of listed patients by blood group on 01/01/2011 by centre

Table 4.10. Centre analysis of number and percentage of prevalent listed patients by cRF and match score on 01/01/2011

	cRF Group								Match score					
	0 to <10		10 to <30		30 to <85		85 to 100		Easy		Moderate		Difficult	
Centre	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
England														
Basldn	9	60			4	27	2	13	5	33	7	47	3	20
B Heart	63	59	8	7	13	12	23	22	23	22	54	50	30	28
B QEH	137	49	12	4	46	16	85	30	70	25	119	43	91	33
Bradfd	23	49	2	4	10	21	12	26	11	23	23	49	13	28
Brightn	47	71	2	3	9	14	8	12	24	36	27	41	15	23
Bristol	66	61	3	3	14	13	26	24	29	27	50	46	30	28
Camb	20	39	7	14	7	14	17	33	12	24	20	39	19	37
Carlis	7	41			7	41	3	18	7	41	5	29	5	29
Carsh	60	48	6	5	20	16	38	31	32	26	46	37	46	37
Chelms	14	50	2	7	6	21	6	21	7	25	13	46	8	29
Colchr	8	57			4	29	2	14	4	29	6	43	4	29
Covnt	41	50	2	2	15	18	24	29	28	34	23	28	31	38
Derby	33	53	7	11	10	16	12	19	18	29	29	47	15	24
Donc	27	63	3	7	4	9	9	21	18	42	16	37	9	21
Dorset	40	51	6	8	10	13	22	28	36	46	22	28	20	26
Dudley	25	52	2	4	8	17	13	27	16	33	19	40	13	27
Exeter	30	50	1	2	11	18	18	30	20	33	22	37	18	30
Glouc	23	61	1	3	6	16	8	21	16	42	16	42	6	16
Hull	33	53	2	3	11	18	16	26	20	32	20	32	22	35
Ipswi	5	28	2	11	2	11	9	50	6	33	6	33	6	33
Kent	53	62	3	4	13	15	16	19	31	36	37	44	17	20
Leeds	66	43	6	4	23	15	57	38	42	28	58	38	52	34
Leic	201	66	2	1	66	22	37	12	102	33	136	44	68	22
Liv Ain	7	35	1	5	1	5	11	55	7	35	5	25	8	40
Liv RI	52	49	3	3	22	21	30	28	38	36	37	35	32	30
L Barts	122	63	7	4	30	15	36	18	36	18	105	54	54	28
L Guys	57	49	10	9	14	12	35	30	19	16	53	46	44	38
L Kings	61	60	2	2	19	19	20	20	22	22	49	48	31	30
L Rfree	80	42	12	6	33	17	67	35	25	13	75	39	92	48
L St.G	35	57	6	10	7	11	13	21	10	16	24	39	27	44
L West	264	77	5	1	28	8	47	14	83	24	172	50	89	26
M RI	63	42	5	3	32	21	50	33	33	22	61	41	56	37
Middlbr	30	45	6	9	11	16	20	30	17	25	26	39	24	36
Newc	31	47	4	6	5	8	26	39	23	35	20	30	23	35
Norwch	23	43	6	11	9	17	15	28	22	42	12	23	19	36
Nottm	68	53	5	4	25	20	30	23	40	31	61	48	27	21
Oxford	58	47	8	6	14	11	44	35	32	26	50	40	42	34
Plymth	17	52	1	3	6	18	9	27	15	45	10	30	8	24
Ports	109	58	2	1	29	16	47	25	64	34	64	34	59	32
Prestn	52	42	7	6	29	23	36	29	40	32	41	33	43	35
Redng	53	52	7	7	12	12	29	29	29	29	40	40	32	32
Salford	59	40	3	2	39	26	47	32	42	28	56	38	50	34
Sheff	58	44	9	7	24	18	42	32	41	31	54	41	38	29
Shrew	16	47			7	21	11	32	10	29	13	38	11	32
Sthend	12	63			2	11	5	26	6	32	8	42	5	26
Stevng	54	56	4	4	12	12	27	28	29	30	40	41	28	29
Stoke	36	49	8	11	10	14	20	27	27	36	25	34	22	30
Sund	20	44	2	4	10	22	13	29	15	33	17	38	13	29
Truro	16	44	1	3	6	17	13	36	13	36	10	28	13	36
Wirral	20	51	4	10	4	10	11	28	10	26	17	44	12	31
Wolve	37	67	6	11	7	13	5	9	27	49	21	38	7	13
York	15	45	2	6	3	9	13	39	7	21	16	48	10	30

Table 4.10. Continued

	cRF Group								Match score					
	0 to <10		10 to <30		30 to <85		85 to 100		Easy		Moderate		Difficult	
Centre	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
N Ireland														
Antrim	9	64			1	7	4	29	6	43	5	36	3	21
Belfast	28	45			11	18	23	37	23	37	18	29	21	34
Newry	11	48			5	22	7	30	4	17	13	57	6	26
Ulster	7	64	2	18			2	18	6	55	3	27	2	18
West NI	25	61	3	7	8	20	5	12	13	32	21	51	7	17
Scotland														
Abrdn	33	69	2	4	3	6	10	21	15	31	21	44	12	25
Airdrie	20	67	1	3	4	13	5	17	10	33	12	40	8	27
D&Gall	6	50			1	8	5	42	4	33	4	33	4	33
Dundee	15	65	2	9			6	26	8	35	11	48	4	17
Dunfn	16	62			3	12	7	27	12	46	6	23	8	31
Edinb	46	51	5	5	9	10	31	34	33	36	31	34	27	30
Glasgw	112	53	6	3	27	13	65	31	71	34	86	41	53	25
Inverns	13	62			2	10	6	29	8	38	9	43	4	19
Klmarnk	15	43	2	6	2	6	16	46	9	26	12	34	14	40
Wales														
Bangor	9	50	2	11	4	22	3	17	8	44	7	39	3	17
Cardff	53	57	3	3	13	14	24	26	35	38	38	41	20	22
Clwyd	4	31			4	31	5	38	4	31	4	31	5	38
Swanse	41	72	2	4	5	9	9	16	26	46	23	40	8	14
Wrexm	5	36	2	14	2	14	5	36	3	21	5	36	6	43
England	**2,556**	**54**	**215**	**5**	**769**	**16**	**1,235**	**26**	**1,359**	**28**	**1,956**	**41**	**1,460**	**31**
Northern Ireland	**80**	**53**	**5**	**3**	**25**	**17**	**41**	**27**	**52**	**34**	**60**	**40**	**39**	**26**
Scotland	**276**	**56**	**18**	**4**	**51**	**10**	**151**	**30**	**170**	**34**	**192**	**39**	**134**	**27**
Wales	**112**	**57**	**9**	**5**	**28**	**14**	**46**	**24**	**76**	**39**	**77**	**39**	**42**	**22**
UK	**3,024**	**54**	**247**	**4**	**873**	**16**	**1,473**	**26**	**1,657**	**29**	**2,285**	**41**	**1,675**	**30**

Blank cells denote no patients listed for that category within corresponding centre

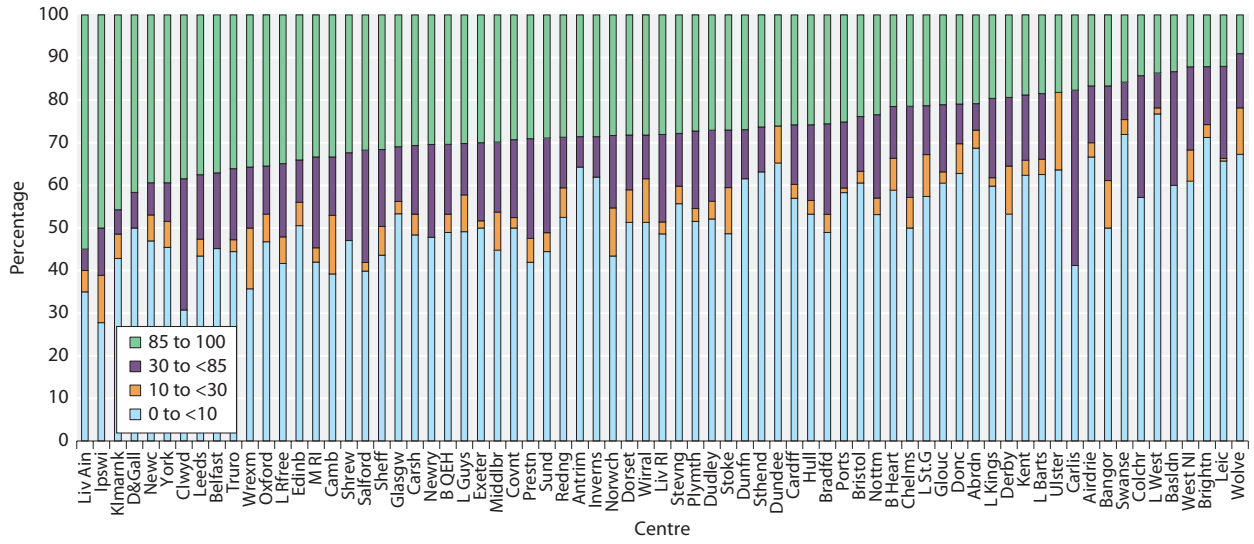

Fig. 4.7. Centre analysis of the percentage of patients listed by calculated reaction frequency group (cRF) on 01/01/2011

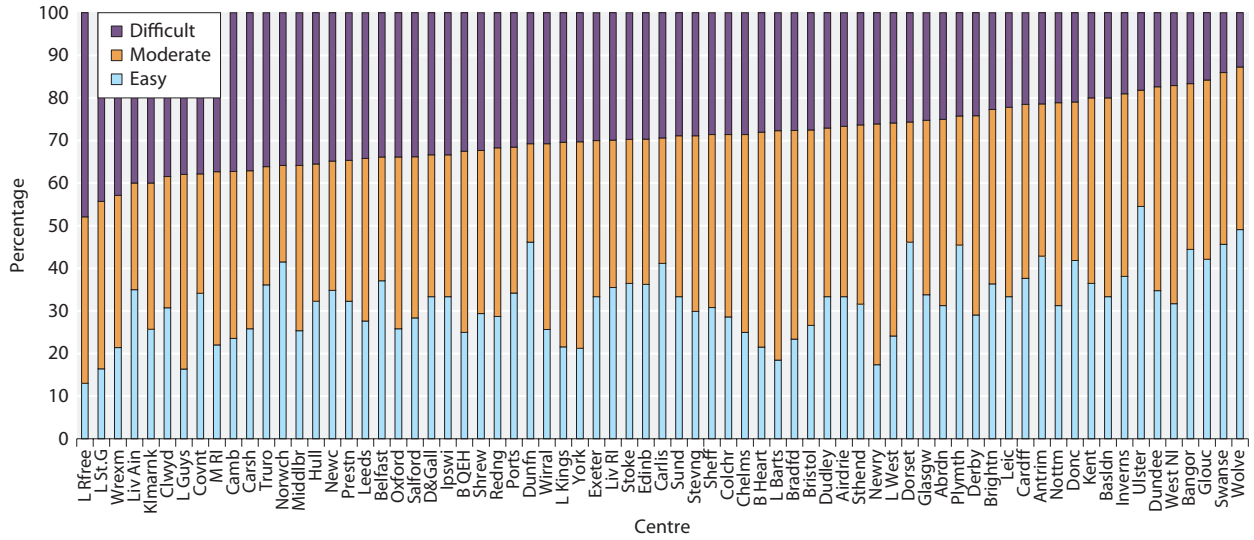

Fig. 4.8. Centre analysis of the percentage of patients listed by match score on 01/01/2011

Median waiting times

The median waiting times for receiving a deceased DBD kidney via the national allocation scheme are shown by ethnicity, blood group and cRF in tables 4.11, 4.12 and 4.13 respectively. These times were calculated using patients registered for kidney only transplants in the UK between 1st January 2006 and 31st December 2009. The overall median waiting time was 1,160 days for an adult (aged $\geqslant$18 years at time of registration) and 339 days for a paediatric patient (aged $<$18 years at time of registration). Due to the allocation algorithm stratifying patients on level of sensitisation and the need to match donor and recipient blood groups waiting times are seen to differ across ethnicity, blood groups and level of sensitisation. Adult White patients were seen to have significantly shorter waiting times (1,098 days, CI: 1,071–1,125) as compared to Black patients (1,396 days, CI: 1,301–1,491) or Asian patients (1,411 days, CI: 1,334–1,488) with similar trends seen across paediatric ethnic groups (table 4.11).

Across blood groups, adult patients with blood group O (1,373 days) and B (1,343 days) were seen to have significantly longer waiting times than those with blood group A (931 days) or AB (607 days). These differences were not seen to be significant across paediatric patients (table 4.12).

Table 4.11. Median waiting time to kidney only transplant in the UK by ethnicity, for patients registered 1st January 2006 to 31st December 2009

Ethnicity	Patients registered *N*	Waiting time (days) Median	95% CI
Adult			
White	6,899	1,098	(1,071–1,125)
South Asian	1,252	1,411	(1,334–1,488)
Black	667	1,396	(1,301–1,491)
Other	236	1,209	(1,046–1,372)
Total	**9,054**	**1,160**	**(1,136–1,184)**
Paediatric			
White	248	266	(212–320)
South Asian	73	542	(458–626)
Black	18	623	(361–885)
Other	11	276	(33–519)
Total	**350**	**339**	**(263–415)**

Table 4.12. Median waiting time to kidney only transplant in the UK by blood group, for patients registered 1st January 2006 to 31st December 2009

Blood group	Patients registered *N*	Waiting time (days) Median	95% CI
Adult			
O	4,066	1,373	(1,335–1,411)
A	3,364	931	(899–963)
B	1,259	1,343	(1,287–1,399)
AB	365	607	(521–693)
Total	**9,054**	**1,160**	**(1,136–1,184)**
Paediatric			
O	168	410	(294–526)
A	121	269	(161–377)
B	48	241	(128–354)
AB	13	504	(0–1,101)
Total	**350**	**339**	**(263–415)**

Table 4.13. Median waiting time to kidney only transplant in the UK by sensitisation at registration, for patients registered 1st January 2006 to 31st December 2009

Level of sensitisation	Patients registered *N*	Waiting time (days)	
		Median	95% CI
Adult			
0–9	6,731	1,063	(1,039–1,087)
10–29	308	1,148	(1,014–1,282)
30–84	1,297	1,475	(1,400–1,550)
85+	718	2,218	(1,958–2,478)
Total	**9,054**	**1,160**	**(1,136–1,184)**
Paediatric			
0–9	217	299	(212–386)
10–29	15	138	(2–274)
30–84	91	312	(215–409)
85+	27	1,241	(836–1,646)
Total	**350**	**339**	**(263–415)**

Table 4.13 shows that the level of sensitisation also has an impact on median waiting times with waiting times in highly sensitised patients (2,218 days CI: 1,958–2,478) being more than twice that seen in patients who were not sensitised (1,063 days CI: 1,039–1,087), which was highly significant $p \leqslant 0.0001$. This trend was also seen in paediatric listed patients with highly sensitised paediatric patients having a significantly longer median waiting time of 1,241 days as compared to 299 days in paediatric patients who were not sensitised.

Summary

Inter-centre variation exists in the number of patients wait-listed (both pre-emptively and after commencing dialysis) and in the proportion listed across different ethnic groups, age and blood groups. This may reflect differences in geography, local population density, age distribution, ethnic composition, prevalence of diseases predisposing to kidney disease and the social deprivation index of that population as well as individual centre practice patterns. Significant unexplained inter-centre variation was also seen in the proportion of patients listed that were highly sensitised.

Median waiting times are seen to differ significantly across blood groups, degree of sensitisation and ethnic groups, with differences in blood group being one probable factor in explaining the differences in median waiting times seen amongst the major ethnic groups.

Conflicts of interest: none

References

1 Renal Association Clinical Practice Guidelines Committee: Assessment of the Potential Kidney Transplant Recipient, 5th Edition. 2011. http://www.renal.org/Clinical/GuidelinesSection/AssessmentforRenalTransplantation.aspx
2 UK Kidney Transplantation: organ allocation policy. http://www.odt.nhs.uk/pdf/kidney_allocation_policy.pdf
3 http://www.odt.nhs.uk/pdf/kidney_allocation_policy.pdf
4 Office for National Statistics. www.statistics.gov.uk
5 National Records of Scotland. http://www.nrscotland.gov.uk/
6 Northern Ireland Statistics and Research Agency. http://www.nisra.gov.uk/

Appendix B: Details of Patient Level Data collected by ATTOM

ATTOM data sheet

DEMOGRAPHICS

Patient group:
Choose one of 3 options. Groups self explanatory

Cohort:
Choose from one of 2 options. 'Detailed PROMs cohort' will only be relevant to patients in certain centres + centres undertaking pancreas transplantation

Name/DOB/Sex:
Self explanatory. System limit – no later than 31/12/1994, no earlier than 01/01/1935

Ethnicity:
Choose one of 5 options.
White – patient appears or is recorded as being of white ethnicity
Black – patient appears black or is recorded as being of black ethnicity
Mixed – patient appears or is recorded as being of mixed (any combination) of ethnic parentage
Asian – patient appears or is recorded as being of Indian/Pakistani/Bangladeshi ethnicity
Chinese – patient appears or is recorded as being of Chinese ethnicity

Height:
Height in centimeters – system limit of 100 – 240 cms

Weight:
Weight in kilograms – dry weight/target weight as far as possible
System limit 30-220 kgs
Decimal places not allowed

Patient email id:
Entry only required if patient requests e-access for completing questionnaires.
Entering email id will generate an auto-email to patient with a password to enable access to the web site

Centre:
Transplant centre where nurse is employed. Not related to centre caring for patient

Renal unit:
Name of renal unit (transplanting or non-transplanting) to which patient belongs

Hospital number:
Unique id number (with or without alphabets) in the hospital with primary care for patient (hospital that undertakes the patient's dialysis treatment)
Other number – unique id number in secondary hospital (for ex: transplant centre) where the patient may have had tertiary care

NHS number (for patients in England, Wales and Northern Ireland only):
Invalid NHS numbers will not be accepted / saved (internal modulus 11 algorithm check)

CHI number (for patients in Scotland only)
Invalid CHI number will not be accepted / saved

Address/Post code:
Address as listed in the IT system of the hospital that provides primary care for the patient.

Date first seen by Nephrologist:
Date when first seen by Nephrologist (either in clinic or as an in-patient)
If information on all 3 variables day/month/year – enter exact date
If information on only month/year available – enter 15th of that month
If information on only year available – enter 30th June for that year

Date of data entry:
Date when you started filling in the demographics page for this patient for the first time (may or may not be the same date as obtaining consent from the patient for study participation)

Mandatory data items for the demographics page:
Patient group
Cohort
First name
Surname
DOB
Address & Post code

SOCIOECONOMIC DATA

(cannot save data on this page without entering details on demographic page first)

Language

Is English your first language? Self explanatory yes/no. If no chosen - pop up of 'what is your first language?' self explanatory – free text box for writing language
Pop up box of 'Please rate your fluency in English?' – ask patient to choose from 'basic/moderate/good fluency' as reported by the patient

Leading question ("How often do you need …..….") on help required for medical instructions – give patients the 5 choices and record patient preference

Place of birth
Self explanatory question. No follow up questions

Ethnicity
Record patient reported preferences from choices listed. If 'other' is chosen from any category – pop up free text box

Education
Record patient reported educational qualifications. More than 1 and a maximum of 5 options can be ticked. Highest achieved qualification must be selected.

Employment status
Record patient preference from list of 8 options. Patient must report status from the preceding 4 weeks

Car ownership
Self explanatory question. Only 3 or 4 wheeled motorised vehicles to be counted. If 'yes' ticked pop up question of 'How many vehicles'. No system limit to number of vehicles

Housing
Record patient preference for self explanatory question. If 'other' chosen pop up free text box

Civil status
Record patient preference for self explanatory question.

Dependants
Question implies number of people living in the same household and not necessarily dependant in financial or social terms. Children classified as <18years and adults as aged 18 or over. No system limits to number entered

Smoking
Record patient preference for self explanatory question. If 'yes' is ticked pop up question on number of cigarettes. If 'no' is ticked pop up question on previous smoking habit. If 'yes' ticked for previous smoker pop up question on duration since last smoked (aim to get the closest number of years unless it is <12 months since smoking cessation)

COMORBIDITY

(cannot save data on this page without entering details on demographic page first)

For the following data items, please read case notes (admission clerking notes, inter-specialty referral letters, discharge summaries are particularly useful), clinic letters, local renal IT systems or based on reports from patient/patient's named consultant. Record data items as per information gathered from above sources. If in doubt for any item check with the patient's named consultant nephrologist. For each item – if both month and year known, enter exact month/year. If only year known enter June as default month. Exact date of diagnosis for long term conditions (for ex: Diabetes, Asthma/COPD etc) is difficult to ascertain and in such situations ask patient how many years they have had this diagnosis and then choose that year in 'year' box and then choose default options of '15th' and 'June' for day and month respectively.
For each data item – if more than one entry is needed, please click on the 'add' button to the right of the 'Month/Year' tabs to open a new box. Up to a maximum of 3 boxes can be opened for each data item.

Primary Renal diagnosis

This data item indicates cause of kidney failure. Usually specified in clinic letters, local renal IT systems, patient reported cause etc. If 'other' is chosen, please fill pop up free text box Code numbers help link presumed diagnosis to registry records.

Diabetes

This data item indicates whether the patient has diabetes or not (irrespective of whether the diabetes caused kidney failure or not)

If 'yes' is checked pop up box of type I or II

Type I – diagnosis must be before age 30 years, must be on Insulin from day 1 of diabetes, may have had previous episodes of diabetic ketoacidosis. Type II – diagnosed after the age of 30, may have had diet/tablets/insulin as treatment for diabetes. This includes diabetes induced by drugs such as Ciclosporin/Tacrolimus, patients who developed diabetes after pancreatectomy/pancreatitis etc.

Ischaemic heart disease

This data item indicates whether the patient suffers from / has suffered from Ischaemic/coronary heart disease.

Angina – diagnosis of angina as recorded in case notes or reported by patient. Usually implies typical sounding cardiac chest pain, often on exertion, relieved by GTN/rest etc.

NSTEMI – diagnosis of non-ST segment elevation MI or acute coronary syndrome without ECG changes (i.e. raised troponin levels). Can only be diagnosed following blood test + ECG and therefore cannot be reported as an event by patient

STEMI/MI – diagnosis of ST elevation MI with obvious ECG changes. Can only be diagnosed with an ECG

Coronary intervention – patient has had an intervention for presumed ischaemic heart disease (with or without previous history of angina/NSTEMI/STEMI). Please choose between PCI (coronary angioplasty with or without stent insertion) or CABG (bypass operation)

Heart failure

This data item indicates whether the patient suffers from heart failure. Indicate 'yes' if any of the following items appear to have been diagnosed according to the case notes/clinic letters

Congestive cardiac failure or CCF

Left ventricular failure or LVF

Right ventricular failure of RVF

LV or RV dysfunction on ECHO

Ejection fraction or EF <30% on ECHO

Atrial Fibrillation

This data item indicates whether the patient is in atrial fibrillation currently. Do not choose 'yes' if patient had previous episodes of atrial fibrillation but is not in AF currently.

Cardiac valve replacement

This data item indicates whether the patient had a previous cardiac valve replacement or valve repair surgery. If 'yes' ticked, pop up box of which valve was replaced/repaired and month/year of procedure.

Permanent pacemaker
This data item indicates whether the patient currently has a permanent pacemaker in-situ. If 'yes' is ticked, pop up box of month/year of insertion
Cerebrovascular disease
This data item indicates whether the patient has had symptomatic cerebrovascular disease or cerebrovascular intervention. If 'yes' is ticked pop up box of type of event.
TIA – Indicate if TIA(transient ischaemic accident) /mini-stroke/transient stroke appears in case notes/letters
CVE/Stroke – Indicate if CVE or CVA (cerebro-vascular event or accident) /Stroke/hemiplegia/cerebral haemorrhage/sub-arachnoid haemorrhage/sub-dural haemorrhage appears in case notes/letters
Carotid intervention – indicate if carotid endartrectomy or carotid angioplasty or carotid operation appears in case notes

Peripheral vascular disease
This data item indicates whether the patient suffers from peripheral (usually lower limb) vascular disease. If 'yes' is ticked pop up box of type of event.
Claudication – indicate if claudication (lower limb pain on walking) appears in case notes
Radiological or surgical intervention – indicate if iliac or femoral or popliteal or profunda or anterior tibial or posterior tibial artery intervention (angioplasty, endartrectomy, bypass etc) appears in case notes
Amputation – indicate if any amputation of any part of any limb (except traumatic amputation or penile amputation) appears in case notes

Abdominal Aortic Aneurysm
This data item indicates whether the patient has ever been diagnosed as having or treated for a AAA. If AAA is indicated any where in case notes tick 'yes' and specify whether the AAA is just being monitored or whether radiological (EVAR) or open surgical procedure (AAA repair) has been undertaken.

Respiratory disease
This data item indicates whether the patient suffers from any form of respiratory disease. If any of the terms including 'Asthma', 'COPD', 'Emphysema' or 'Bronchiectasis' appears in the case notes tick 'yes' and specify which/how many of the 3 diagnoses is relevant to the patient. Emphysema can be coded as COPD.
Liver Disease
This data item indicates whether the patient suffers from any form of liver disease. If the term 'Cirrhosis', 'Non Alcoholic steato-hepatitis or NASH', 'Drug induced (for ex: paracetamol poisoning' liver disease and 'Alcoholic liver disease' appears in the case notes tick 'yes'. If the word cirrhosis is used in the case notes choose 'cirrhotic liver disease' from the drop down menu. If liver disease is mentioned without the term cirrhosis then choose 'non-cirrhotic liver disease'.
Note – cholecystitis / gall stones etc does not constitute liver disease

Blood Borne Viruses
This data item indicates whether the patient suffers/has suffered from BBV infection. If Hepatitis C/B/HIV infection (past or present) or Hep C/B PCR or antibody positive

or HIV PCR/antibody positive is recorded in case notes tick 'yes' and then indicate which/how many viral infections is relevant to the patient.

Malignancy

This data item indicates whether the patient has been diagnosed with one or more malignancies in the past. If any malignancy has been recorded in the case notes, tick 'yes' and then specify which type of malignancy from the drop down menu. Please note – tick 'yes' only for a malignancy. Benign tumours (such as breast adenoma, colon polyp, skin warts/actinic keratosis etc do not count as malignancy).

Mental illness

This data item indicates whether the patient has suffered from/suffers from any recorded mental illness in the case notes. Tick 'yes' if the term 'Depression', 'Psychosis/Psychotic disorder', 'Bipolar disorder', 'substance abuse' (usually indicates poisoning with one or more drugs – not alcohol or recreational drugs) and 'deliberate self harm' (usually indicates physical attempts at self harm – not chemical means which should be classified under 'substance abuse') or related terms such as 'Schizophrenia' (should be classified as a psychotic disorder) appears in the case notes. If in doubt ask the patient / consultant nephrologist/ named psychiatric nurse.

Dementia

This data item indicates whether the patient suffers from any form of dementia. Tick 'yes' if the term 'dementia', 'vascular dementia', 'Alzheimer's disease', 'memory loss' (short or long term) etc appears in the case notes. If in doubt, please check with the consultant Nephrologist.

Smoking

This data item captures whether the patient's smoking history is available in the case notes and therefore fill in the data item purely based on information available in the case notes. This may or may not contradict what the patient reports in the socio-economic questionnaire. If the term 'smoker', 'heavy smoker' etc is recorded in case notes indicate patient is a current smoker. If the case notes indicate that patient is an 'ex-smoker' , 'quit xx years ago' etc indicate patient is an ex-smoker. If the notes indicate that the patient has never smoked indicate 'non-smoker'. If there is no mention of smoking anywhere in the notes – indicate 'don't know'.

Other illness

3 x free text boxes to indicate any other illness that does not come under the above topic headings.

Incident dialysis

(cannot save data on this page without entering details on demographic page first)
(Demographic, comorbidity and socio-economic data same as for all patients)

Start date of dialysis

Indicated when the patient commenced long term / permanent dialysis treatment. For many patients it will be planned start on dialysis (for ex: after PD catheter insertion or AVF formation). This should be the date of the first ever dialysis session (PD or HD) even if the patient subsequently changed modalities. If the patient started dialysis as an 'acute patient' recovered renal function for a little while and then re-started dialysis, indicate date when dialysis was re-started. For patient crash landing on dialysis treatment (starting dialysis without prior planning – usually during an in-patient admission) record date of first dialysis session (usually HD session and rarely PD) as date of first dialysis. If in doubt check with local renal IT system or ask consultant nephrologist / dialysis unit sister.

Type of dialysis

This should be the dialysis modality that the patient started on when dialysis first commenced. The type of dialysis modality is self explanatory and if not clear please check with the HD unit sister to confirm between HD-v-HDF and PD unit sister between APD-v-CAPD.
If patient has been on more than one type of modality between start of treatment and time of consenting to participate in this research project, tick the modality that the patient has spent most time on.
If HD or HDF is chosen, pop up menu of type of dialysis access. This indicates the type of HD access at the start of HD/HDF (first ever HD/HDF session). The types of access are self explanatory. Non-tunnelled lines are also often referred to as 'Vascath' and tunnelled lines are often referred to as 'Permcath' or 'Tesio'.
If the patient has used more than one type of access between start of HD/HDF and time of consenting the patient for participation in the research project, tick the access type that was most used since starting HD/HDF. If patients were using one needle in AVF/AVG and one needle in tunnelled line/non-tunnelled line – tick tunnelled line/non-tunnelled line as access used.

Previous transplant

This data item indicates whether the patient has had a previous organ transplant (any solid organ and not just kidney only). The previous organ transplant may or may not be still working (for ex: working liver transplant as compared to failed kidney transplant). Indicate number of previous transplants and then indicate type of organ transplant. If exact day/month/year of previous transplant known, enter exact date. If only month/year known – enter 15th of the month/year. If only year known – enter 30th June of the year.

Incident transplant patient
Transplant work up

(cannot save data on this page without entering details on demographic page first)
(Demographic, comorbidity and socio-economic data same as for all patients)

Cardiac
Indicates whether the patient had any cardiac investigations were undertaken as part of the work up / declaration of fitness for kidney (or kidney + pancreas transplant). The investigations undertaken are likely to be listed in the case notes or described in clinic letters (either from the nephrologist or cardiologist). The result of the test is not relevant to this data item but just whether any tests were done or not done. Please include only tests done as part of work up for transplantation (usually done prior to transplant wait-listing or prior to transplant) and not include tests done in the past. If no tests are apparent then please tick 'none'.
More than one option can be ticked.

Pulmonary
Indicates whether the patient had any pulmonary function tests (includes lung function tests and CPEX or cardio-pulmonary exercise testing). If no tests are apparent then please tick 'none'.

Vascular
Indicates whether the patient had any vascular investigations (iliac/lower limb and carotid only – upper limb vascular investigations should not be included). Clinic letters from the vascular surgeons / transplant surgeons are likely to be the best sources of information. If no tests are apparent, then please click 'none'. More than one option can be ticked.

Other tests
If any other tests (for ex: genetic tests, CT/MRI scans of other organs, other radiological tests, blood tests such as Glucose Tolerance Tests etc) were undertaken exclusively for the purpose of confirming fitness for transplantation, please list then the free text box. Up to 3 items can be entered.

Incident transplant information

Date of transplant
Indicates date of renal (or renal + pancreas) transplant that triggered entry into the ATTOM study. Please enter exact date of transplant.

Transplanted organ
Indicates whether this was a kidney only or kidney + other organ transplant.

Transplant type
Indicates whether the organ/s came from a live donor or brain dead (DBD/HBD) or non-heart beating (DCD/NHBD) donor.

Treatment modality
Indicates what form of dialysis if any the patient was having just before the transplant.

If any modality (other than preemptive or failing transplant) is chosen please fill in date when the patient started dialysis for the first time. This helps calculate total time on dialysis before transplant. If HD/HDF was chosen, please also complete additional pop up menu of type of dialysis access.

Patient has had a previous transplant?
This data item indicates whether the patient has had any previous organ transplant (not just kidney). Please indicate type of transplant and date (using default options of 15th for the day and June for the month if either not known).

Induction immune suppression
Indicates the type of drug given just before the transplant operation. This is usually an IV drug and the common drugs used are listed. If 'other' is chosen – please fill in name of drug in the free text box

Maintenance CNI
CNI stands for 'Calcineurin inhibitor' and can only be Ciclosporin or Tacrolimus. Please indicate 'Tacrolimus' or 'ciclosporin' irrespective of whether the primary brand or generic brand of the drug is used. Maintenance therapy usually indicates that the patient is likely to remain on this drug for the foreseeable future.

Maintenance anti-proliferative
This data item captures whether the patient is likely to continue on any anti-proliferative agent for the foreseeable future. This is usually an oral medication and the common drugs are listed. Please pick from the drop down menu.

Maintenance steroid
This data item captures whether the patient is likely to be on short or long term steroid (usually Prednisolone) treatment. If unit policy is that for all/most patients to be weaned off steroids at 1 or 3 months, then please tick this option. If unit policy is for steroid continuation for >3 months but not indefinitely (say 6 or 12 months) please tick 'long term continuation'.

Maintenance other
This data item captures whether the patient is on any other long term immune suppression using drugs not in any of the above categories. This maybe a oral drug or IV/SC drug (Belatacept) and the common drugs are listed. Please tick any appropriate choice.

Matched control for transplant patient

(cannot save data on this page without entering details on demographic page first)
(Demographic, socio-economic info and comorbidity same as for all patients)
Transplant work up information – same as above

Wait-listing information

Date of activation on the waiting list
Please indicate the date of very first activation on the waiting list (irrespective of any subsequent suspensions etc). Data should normally be available with the transplant coordinators, renal IT system and less rarely in the notes.

Organ
The data item captures which organ/s the patient was first listed for. If the patient was listed for a kidney only and subsequently listed for a kidney + other organ – please tick 'kidney only' as this was the choice at time of first listing.

Dialysis modality at time of data collection
Data item captures type of dialysis at the time the patient was recruited to the ATTOM study. If HD/HDF chosen, please indicate type of access. Please leave blank if patient is currently not on any form of dialysis (preemptively listed or has a failing transplant but not yet back on dialysis)
Please do not fill in 'supervising hospital'. This data field is not required.

Patient had a previous transplant
This data item captures if the patient has had a previous organ (not kidney only) transplant. Please indicate exact date of transplant if known, and if not use default options of 15th if day not known and 30th June if month not known.

Appendix C: Interview Guide

Stakeholders

1. Consultant Nephrologists
2. Consultant Transplant Surgeons
3. Transplant Coordinator/Lead Transplant Nurse
4. AKCC/LCC Nurse
5. Living Donation Nurse

ATTOM: Qualitative Study Staff Topic Guide.

Briefing

1. Thank you for agreeing to take part.
2. Introduction researcher/ATTOM project.
3. If at any time during the interview you do not wish to answer a question that's fine. Feel free to answer only the questions you feel comfortable with.
4. I would like to digitally record our conversation. The interview will be typed out, but everything you say will be anonymous.
5. Your interview will remain confidential unless (as discussed and outlined in the consent form) it is possible that you or someone else is at risk, but this will be discussed with you first.
6. If at any stage you wish to stop the audio recorder, please let me know.
7. Do you have any questions?

Introduction: Topics to be covered

The purpose of this interview is to get a better understanding of the barriers and facilitators of accessing the national transplant list, by exploring your personal experience/involvement in the listing process. During the scope of this interview we hope to discuss:

a. Late presentation of renal disease and how referrals are managed
b. Managing Chronic Kidney disease
c. Co-morbidities and their implications on transplant listing
d. How transplantation is discussed
e. Transplant work up
f. Managing outcomes of the listing process
g. Conclusions and final thoughts

Diagnosis/Late Presentation

1. How do you receive referrals (modality), and where do they come from?
2. Can general renal advice be sought by referrers? If so how and how much is this service utilized?
3. How are your referrals processed?
4. Please describe the workforce constituting to your renal department, and what proportion of these are involved in seeing new referrals?
5. Could you describe any occasions where delays have occurred and any reasons for why this happened?

6. Do you interact much with primary care providers? If so could you describe your interactions
7. Does your unit have any direct linkage/unique initiatives with primary care providers/commissioner's?
8. How are biopsies arranged in your unit?
9. Do you feel well supported by your radiology department?
10. Can you describe any occasion where there has been an avoidable delay in making a diagnosis, if so what was the cause?
11. Has ineffective communication ever hindered diagnosis/treatment/management and what do you perceive to have been the cause? **Explore:** language, health literacy, education, religious beliefs, fear, socioeconomic status, cultural beliefs, Psychosocial status, lack of trust.

Managing Chronic Kidney Disease

12. Describe your chronic kidney disease service
13. Do you have a Low clearance clinic or Advanced Kidney Care Clinic, if so what is the criteria for entry/who has access?
14. Do patients have to travel to a centralized LCC/AKCC clinic, or do you travel to outreach hospitals/units? Is there significant variation in travel times amongst patients?
15. Briefly explain which aspects of chronic kidney disease management you focus on in each consultation, and whether you feel pressured/over burdened to cover all bases in the allocated time slot.(consider exploring time per patient consultation), Hep B
16. Are other professionals employed to assist in CKD management and share workload e.g anaemia nurse, dietician, access nurse/access surgeon? If so how many of each/any unfilled posts?
17. Have you tried to recruit allied health professionals and not been successful? If so why? Lack of support/funds/appropriate applicants
18. Do you see any non-compliance or frequent non-attendance, if so which groups of patients are particular prone to such behavior? Have you taken any measures to improve this, and if so what? Has it been effective?
19. Following national reporting of eGFR and CKD guidelines, have you noticed any increase in CKD referrals, how is your service coping with the increased burden, and what do you perceive as being the solution?
20. How confident/inspired do you feel in the willingness and ability of your local primary care providers in managing CKD
21. Do you think primary care could +/- should do more in managing CKD, if so what would you propose?

Comorbidities

22. Do you perceive CKD patients to have more co-morbidities, and if so whether other healthcare professionals appreciate this and does your current CKD clinic structure allow sufficient time to probe these additional co-morbidities
23. Whose responsibility do you think it is to manage co-morbidities particularly those which may affect possible future transplantation?

24. How successful is primary care in tackling CKD co-morbidities, by their own initiative, and following secondary care request? Has this led to a delay in transplantation work up? Any examples
25. Is the current non-interdepartmental referral system a hindrance/dis-incentive to investigate co-morbidities, and if you worked before it's introduction has it changed your practice/practice of others

Discussion of Transplantation

26. Do you believe all patients should be considered for transplantation, if not whom would you exclude?
27. What factors do you think should be considered in deciding if a person should be considered for transplantation, e.g life expectancy, eGFR, QoL, Access
28. Are there any specific renal diagnoses which would delay your decision to consider transplantation
29. Does your unit have a set protocol for listing patients
30. If you decide a patient is not appropriate for transplantation (before conducting any additional work-up) how is this decision reached and recorded, and is this decision always communicated to the patient, do you believe the later is important?
31. What method of appeal is in place (if any) if a patient is deemed unsuitable for transplantation? (MDM, 2nd opinion, alternative unit, none)
32. When (and whom) do you think one should broach/introduce the concept of transplantation?
33. When would you consider delaying discussing transplantation? e.g. in presence of co-morbidities requiring investigation
34. When discussing transplantation how is this done, and what information discussed, any documentation provided? How is the outcome followed up? E.g. waiting for next OPA/telephone..etc
35. Are all patients offered the option of pre-emptive or living donation? When is this first discussed? Do you have a designated healthcare professional/service? Explain their role

Transplant Work Up

36. Do you have a transplant work up protocol
37. Who initiates transplant work up?
38. Which investigations do you perform/require before listing a patient for transplantation?
39. Are all tests requested simultaneously or in a stepwise fashion? Do some tests require a mandatory review by another health professional? Before or after the test in question?
40. Where are these investigations performed?
41. Do all or any patients undergo psychological assessment, who conducts this, and is this formally recorded?
42. If additional review is required or an intervention, is this at an alternative site? How is review organized and the response dealt with?
43. If a comorbidity requires investigation, do you organise tests and review, or request the GP to take ownership?

44. How long does the work up usually take? Which tests take longest to happen, why?
45. Are there any frequent ambiguous results requiring a judgment call? Could you give any examples?
46. Is there anyone who overseas all transplant work up, could you explain how they achieve this?
47. Do you classify transplant work up tests as routine or urgent?
48. How are cancellation of tests dealt with/followed up?
49. Once all tests are complete, when is any action taken?
50. How are patients ultimately listed? MDM/Transplant Surgeon review etc
51. Do you hold any regular meetings to review listing progress of patients?
52. What processes are in place to review 'grey' or 'borderline' cases? Any available forum?
53. Which aspects of transplant work up do you find ambiguous? Could you explain why
54. If a patient is deemed fit tor transplantation, how are they activated on national list, how long does this process take, who is in charge/responsible for this?

Patient deemed unsuitable for transplantation

55. How is this communicated to patients/documented?
56. If this decision is based on an existing illness/comorbidity which could change, how is this reviewed/any mechanisms in place?
57. If there are addressable co-morbidities who do you allocate to manage them? What factors influence how aggressive you are in trying to tackle their co-morbidity if any?
58. Could discuss how units manage different co-morbidities, some more aggressively than others
59. Do you provide psychological support to those declined transplantation, how readily is this accessible/utilized?
60. Are there provisions for patients to seek a second opinion? Have you been asked to provide a second opinion, if so can you provide details and what was the outcome?

Patients activated on transplant list

61. If a patient is deactivated on list following an event eg intercurrent illness, what process is followed to get he/she reactivated? What timeframe does this take? Whose responsibility is it?
62. How is their continued suitability monitored?
63. Do you or your unit have any set guidelines on how frequently transplant workup components need to be repeated/reviewed? If so what are they?
64. How do you store completed transplant work up information? How accessible is this? How often is this reviewed? If a paper document, is this made available if your unit uses electronic notes?
65. How do you manage patients likely to be on list for long duration, e.g high immunological risk/high PRA etc. Do you have access to HLA incompatible/ABOi programmes etc
66. Any psychological support given to those waiting on list for long duration/expected to be on list for a while?

Conclusion/Thought Provoking & Further Theory Generation

67. Is there anything else that we have not spoken about today, that you feel is an important barrier or facilitator in accessing transplantation
68. Are there any questions you would like to ask me?

Thank you very much for taking time to speak with me. Your participation is very much appreciated. I want to remind you that although our conversation will be typed up, all identifying information will be removed from the typed up interview so that if someone heard or read your interview they would not know who you are.

Appendix D: The National Survey of Practice Patterns in UK Renal Centres for Listing Patients for Transplantation

UNIVERSITY OF Southampton
School of Medicine

Academic Unit of Primary Care and Population Sciences
Faculty of Medicine, University of Southampton,
Aldermoor Health Centre, Aldermoor Close, Southampton,
SO16 5ST

12th March 2014

Dear Dr {name}

ATTOM - A national study of practice patterns in UK renal units in listing patients for renal transplantation.

This is a paper version of the ATTOM survey. You have already received the web link for the same survey by email. If you have completed the web version, please ignore this postal survey as you do not have to complete both.

We are writing to you on behalf of the ATTOM group of investigators to request your participation in completing a national survey exploring practice patterns in listing patients for kidney transplantation in the UK. The ATTOM study is funded by the National Institute of Health Research (NIHR), and seeks to improve equity of access to kidney transplantation across the UK and is supported by the Department of Health, Renal Association, British Transplantation Society, UK Renal Registry, Scottish Renal registry and NHS Blood and Transplant.

A key objective of ATTOM is to identify centre specific factors that may influence access to transplantation. To address this, a questionnaire has been devised to explore practice patterns in listing patients for transplantation. This information will be valuable in its own right, and will be used to develop unit-variables for a multi-level hierarchical model of factors associated with transplant listing, and to inform a Delphi Consensus group meeting on the transplant work-up process to be undertaken next year.

This questionnaire has been developed following thematic analysis of semi-structured interviews with a variety of health professionals involved in transplant listing conducted in nine renal units across the UK and after reviewing existing national and international literature.

It is anticipated that this questionnaire will take no more than 40 minutes to complete and has been sent to the Clinical Directors / Service leads of all 71 renal units across the UK. Clinical directors are being approached to complete this questionnaire; however we acknowledge that individual units may have clinical leads in transplantation that may be better placed to complete it, if so we would be grateful if you could pass on this letter and the survey to them for completion. All responses provided will be anonymised.

We really hope that you will be able to participate in completing this survey at your earliest convenience so that all renal units across the UK are represented in what promises to provide a clearer understanding of listing practice patterns and shed a better light on our understanding on how the process can be made more equitable.

On behalf of the ATTOM group of investigators we would like to thank you for your kind consideration in taking part in this study. If you have any queries please contact Rishi or Sarah, contact details are below.

We would be very grateful if you could complete and return the questionnaire in the freepost envelope by **Friday 11th April.**

Yours sincerely,

Prof Paul Roderick
Professor of Public Health
University of Southampton

Dr Rommel Ravanan,
Consultant Nephrologist,
Southmead Hospital, Bristol

Dr Gabriel Oniscu,
Consultant Transplant Surgeon,
Royal Infirmary of Edinburgh

Dr Rishi Pruthi,
Clinical Research Fellow,
UK Renal Registry, Bristol

Contact details of Research Fellow:
Dr Sarah Tonkin-Crine, 02380 241080, S.K.Tonkin-Crine@soton.ac.uk

UNIVERSITY OF Southampton

ID

ATTOM Survey

A national survey of practice patterns in UK renal units in listing patients for renal transplantation

Transplant Units

Thank you for completing this survey

This questionnaire asks about the transplant listing process in your unit.

Some of the questions address practice patterns that may vary among staff members in your unit. Please try to give the answer that is most representative of the unit as a whole (i.e. the whole renal service including satellite units).

In order to complete this questionnaire, you may want to consult other members of the renal team or to delegate this task to a more appropriate person who has responsibility for such patients (e.g. you will be asked who participates in the decision-making process; how the decision is taken). The questionnaire will take about 45 minutes to fill in.

Instructions for completing the questionnaire

- Please answer each question by ticking the appropriate box(es).
- The survey can be completed by multiple respondents.
- Please return the survey in the FREEPOST envelope provided.

We would be very grateful if you could complete the survey as soon as possible.

Prof Paul Roderick, Professor of Public Health, University of Southampton
Dr Rommel Ravanan, Consultant Nephrologist, Southmead Hospital, Bristol
Dr Gabriel Oniscu, Consultant Transplant Surgeon, Royal Infirmary of Edinburgh, Edinburgh
Dr Rishi Pruthi, ATTOM Clinical Research Fellow, UK Renal Registry, Bristol

If you have any queries regarding this questionnaire, please contact:
Dr Sarah Tonkin-Crine on 023 8024 1080, S.K.Tonkin-Crine@soton.ac.uk

Before asking questions regarding your CKD service workforce and organisation in your unit, we would like to know the name of your unit and your occupation.

In order to supplement the data publicly available from the UK Renal Registry, please answer the following questions.

1 **Please state your role within the renal unit:**

Please tick one

- ☐ Clinical Director
- ☐ Consultant Nephrologist (other than Clinical Director)
- ☐ Consultant Transplant Surgeon
- ☐ Transplant Co-ordinator
- ☐ Other **(Please specify)**

2 **Please enter the name of your renal unit:**

1. Understanding your CKD Service Workforce and Organisation

3 **For each of the staff roles listed, please provide the number of Whole Time Equivalent (WTE) in your centre (e.g. Full-time=1.0 WTE, Half-time=0.5 WTE, Three Full-time staff = 3.0 WTE).**

Put 0 if you do not have any staff in a particular role or leave blank if you do not know the answer.

Please combine contributions across directorates if not all under one single directorate.

Consultant Nephrologists	
Consultant Transplant Surgeons	
Transplant Staff grade/Associate specialist	
Nephrology Staff grade/Associate specialist	
Transplant recipient Co-ordinators	
Living kidney Donor Nurses	

4 **How many neighbouring hospitals do you provide a service to?**

Enter number for all that apply

For managing patients with chronic kidney disease	
For transplantation	

5 **Which statement best describes how pre-dialysis patients are managed in your unit?**

- ☐ All pre-dialysis patients are seen in dedicated low clearance clinics
- ☐ Some pre-dialysis patients are seen in a low clearance clinic whilst some are seen as part of a general nephrology clinic
- ☐ All pre-dialysis patients are seen in a mixed general nephrology clinic alongside other CKD patients as there are no specific low clearance clinics **(go to question 14)**

6 **What are the entry criteria for being referred to your low clearance clinic?**

Tick and complete all that apply

- ☐ eGFR **(Please specify)** _____
- ☐ No defined criteria
- ☐ Expected/projected time frame before needing to commence renal replacement therapy **(Please specify in months)** _____
- ☐ Other criteria **(Please specify)** _____

continued over

7 **Who primarily leads the delivery of your low clearance service?**

(If jointly led, tick all that apply)

- ☐ Consultant Nephrologist
- ☐ Nurse
- ☐ Staff Grade nephrologist

8 **In how many of the neighbouring hospitals that you serve for chronic kidney disease do you have a dedicated low clearance clinic?**

(Please enter number) ☐

9 **Which statement most accurately describes your LCC service?**

- ☐ 'Single Hub and Spokes': CKD clinics present at all neighbouring hospitals feed into a single main LCC clinic based at Main renal unit/hospital
- ☐ LCC clinics present at >50% of neighbouring hospitals served by unit
- ☐ LCC clinics present at <50% of neighbouring hospitals served by unit

10 **Are all pre-dialysis patients referred to a LCC clinic?**

- ☐ Yes **(go to question 13)**
- ☐ No

11 **If No, please explain why a pre dialysis patient might not be referred to a low clearance clinic?**

Tick all that apply

- ☐ Consultant responsible wishes to maintain continuity
- ☐ To avoid longer travel times for patient
- ☐ Patient choice
- ☐ Consultant's belief it would not add any additional value
- ☐ Patient's belief it would not add any additional value
- ☐ Other

☐

12 **If you do not have a Low Clearance Clinic what are the reasons for this?**

continued over

2 Discussing Transplantation

13 **Is transplantation discussed with all pre dialysis patients under 75 years?**

- ☐ Yes **(go to question 15)**
- ☐ No

14 **If transplantation is not discussed with all patients, please explain how this decision is most commonly made:**

- ☐ Consultant nephrologist decides alone
- ☐ Consultant nephrologist decides in discussion with other consultants
- ☐ Consultant nephrologist decides with input from other professionals from an MDT meeting
- ☐ Clinical nurse specialist/consultant nurse decides alone
- ☐ Clinical nurse specialist/consultant nurse decides with input from other consultants
- ☐ Clinical nurse specialist/consultant nurse decides with input from other professionals from an MDT meeting
- ☐ Other **(Please specify)**

15 **When is transplantation most commonly first discussed with a patient?**

- ☐ When they are referred to the low clearance clinic
- ☐ When their eGFR reaches a certain level **(Please specify)**
- ☐ At a specific time point prior to the anticipated start of dialysis **(Please specify in months)**
- ☐ When symptoms start
- ☐ After being established on dialysis
- ☐ Other **(Please specify)**

16 **Who plays the lead/main role in the discussion of transplantation with a patient?**

- ☐ Consultant Nephrologist
- ☐ Consultant Surgeon
- ☐ Transplant Co-ordinator
- ☐ Nurse (Pre Dialysis Nurse/Low clearance Nurse/Education Nurse)
- ☐ Other **(Please specify)**

17 **Which of the following applies to how education about transplantation is delivered across the hospitals you serve?**

Tick all that apply

- ☐ One to One consultation
- ☐ DVD education material to take home
- ☐ Written material to take home
- ☐ Translated (if appropriate) written material to take home
- ☐ Computer-based education programme
- ☐ Group session with other pre-dialysis patients discussing all options of RRT
- ☐ Group session with other patients considering transplantation discussing just transplantation
- ☐ Talk from a patient with a functioning transplant
- ☐ Talk from a patient with failed transplant
- ☐ Cultural/language matched nurse educators
- ☐ Home visit education
- ☐ Education session (based only at main unit)
- ☐ Education session (based at local hospital)
- ☐ Other **(Please specify)**

continued over

3 Understanding Transplant listing processes

18 **Which type of clinic do patients undergoing transplant work up have their medical assessment e.g. tissue typing, cardiac work up?**

- ☐ In their usual general nephrology clinic **(go to question 24)**
- ☐ In a Low Clearance clinic **(go to question 24)**
- ☐ In Clinic run by nephrologist with interest in transplantation **(go to question 24)**
- ☐ In a specific transplant assessment clinic **(go to question 19)**
- ☐ Other (if none of the above accurately describe your unit's organisation please briefly describe here) **(go to question 24)**

19 **How frequently does the transplant assessment clinic take place?**

- ☐ More than once weekly
- ☐ Weekly
- ☐ Fortnightly
- ☐ Monthly
- ☐ Less than monthly
- ☐ Other **(Please specify)**

20 **At which point is a patient referred to the transplant unit?**

- ☐ Before undergoing any investigations
- ☐ After completing some baseline investigations
- ☐ After completing all necessary investigations
- ☐ Other **(Please specify)**

21 **Who is involved in the transplant assessment clinics?**

Tick all that apply

- ☐ Usual named consultant nephrologist
- ☐ Local Associate specialist/staff grade
- ☐ Transplant surgeon
- ☐ Transplant nephrologist
- ☐ Other **(Please specify)**

22 **Do any of the following allied health professionals attend transplant assessment clinics?**

Tick all that apply

- ☐ Education Nurse
- ☐ Living Donor Nurse
- ☐ Transplant Co-ordinator
- ☐ Other **(Please specify)**

23 **Which statement best describes the purpose of the transplant assessment clinic:**

- ☐ To assess medical suitability prior to referring patient for surgical review **(go to question 24)**
- ☐ To assess medical and surgical suitability prior to referring patient for surgical review **(go to question 27)**
- ☐ Other **(if none of the above are suitable, please specify)**

Surgical Review

24 **Are all patients seen by a transplant surgeon prior to being listed for transplantation?**

- ☐ Yes **(skip to question 26)**
- ☐ No

25 **If no, are all patients discussed with a transplant surgeon prior to being listed for transplantation?**

- ☐ Yes
- ☐ No

26 **Which statement best describes the timing of surgical involvement/referral?**

- ☐ Patients are referred for surgical assessment as soon as they agree to undergo assessment prior to completing any investigations
- ☐ Patients are referred for surgical assessment after completing their medical assessment
- ☐ Patients are referred for surgical assessment whilst medical assessment is on-going
- ☐ Medical and surgical assessment occurs concurrently at the same clinic appointment
- ☐ None of the above **(Please specify)**

continued over

4 The Assessment Process

27 **Please identify the lead/key healthcare professional(s) responsible for performing each of the following processes:**

Tick all that apply for each

	Consultant Nephrologist	Transplant Surgeon	Staff Grade	Transplant Co-ordinator	Pre-dialysis nurse	Other
Identifies patient for assessment	☐	☐	☐	☐	☐	☐
Refers patient for assessment	☐	☐	☐	☐	☐	☐
Requests investigations for assessment	☐	☐	☐	☐	☐	☐
Follows up investigation results	☐	☐	☐	☐	☐	☐
Organises additional reviews (if required)	☐	☐	☐	☐	☐	☐
Requests Surgical Review	☐	☐	☐	☐	☐	☐
Makes decision to activate patient onto list	☐	☐	☐	☐	☐	☐
Requests NHSBT to activate patient	☐	☐	☐	☐	☐	☐
In charge of overseeing entire process	☐	☐	☐	☐	☐	☐

28 **Does your unit have a written transplant work up protocol used for assessment?**

If yes, please could you return this in the stamped addressed envelope with this survey or email it to Rishi.Pruthi@nbt.nhs.uk

☐ Yes ☐ No

29 **Which of the following investigations are performed as part of routine assessment?**

	For all patients	Only for specific indications
Chest x ray	☐	☐
Pelvic X Ray	☐	☐
ECG	☐	☐
Hep B antigen	☐	☐
Hep C antibodies	☐	☐
CMV Serology	☐	☐
EBV	☐	☐
HIV	☐	☐
PSA	☐	☐
Herpes Zoster antibody	☐	☐
Tissue typing	☐	☐
Lung Function Tests	☐	☐
Upper GI Endoscopy	☐	☐
Sigmoidoscopy/Barium enema	☐	☐

	For all patients	Only for specific indications
CPEX Testing	☐	☐
Echo	☐	☐
ETT	☐	☐
Stress Echo	☐	☐
Thallium Stress Test	☐	☐
Coronary angiogram	☐	☐
Peripheral Doppler	☐	☐
Pelvic Doppler	☐	☐
Voiding Cystourethrogram	☐	☐
Abdo USS	☐	☐
Abdo CT	☐	☐
Other **(Please specify)**	☐	☐

30 **Does your unit have an upper age limit for listing for transplantation?**

☐ Yes **(Please specify the upper age limit)** ☐ No

31 **Amongst your prevalent CKD 5 and dialysis population which of the following age bands corresponds to the level at which you would not expect to see more than 5% listed?**

☐ 60-64 ☐ 70-75

☐ 65-69 ☐ >75

BMI

32 **Does your unit have a BMI exclusion criterion for listing?**

☐ Yes **(Please specify minimum and maximum criteria)**

Minimum Maximum

☐ No **(go to question 35)**

continued over

33 **Why does your unit consider a raised BMI a contraindication for transplantation?**

Tick all that apply

- ☐ Increased cardiovascular risk
- ☐ Lower Graft survival compared to a normal BMI
- ☐ Lower Graft survival compared to a normal BMI
- ☐ Increased technical difficulty in performing procedure
- ☐ Increased post-operative complication risk
- ☐ Other **(Please specify)**

34 **If obesity is deemed to rule a patient out for transplantation, which of the following actions are routinely employed to facilitate weight loss and subsequent listing of a patient?**

Tick all that apply

- ☐ Verbal motivation in clinic
- ☐ Provide written weight loss education
- ☐ Conservative 'wait and see' approach
- ☐ Refer to dietician
- ☐ Refer to physiotherapists/physical activity specialist
- ☐ Refer to specific weight loss clinic/services
- ☐ Refer to other specialists e.g endocrinologists
- ☐ Prescribe anti-obesity drugs
- ☐ Refer to surgeon specialized in bariatric surgery
- ☐ Other **(Please specify)**

Cardiac investigations

35 **Does your unit stratify patients to guide cardiac investigations?**

- ☐ Yes
- ☐ No **(go to question 37)**

36 **If Yes which factors are taken into account when stratifying risk**

- ☐ Age **(Please specify)** _____ years
- ☐ Known history of Diabetes
- ☐ BMI **(Please specify)** _____
- ☐ Smoking history
- ☐ BP (Hypertension/hypotension)
- ☐ Abnormal ECG
- ☐ Previous CVD
- ☐ Significant family history
- ☐ Other **(Please specify)**

_____

37 **What is the minimum cardiac work-up undertaken?**

Tick all that apply

- ☐ ECG
- ☐ ECHO
- ☐ Exercise tolerance test
- ☐ Thallium Stress Test
- ☐ Stress Echocardiography
- ☐ Dobutamine Stress Tc Scan
- ☐ Coronary Angiography
- ☐ CPEX Testing
- ☐ Other **(Please specify)**

_____

38 **What is your first line investigation for assessing possible underlying coronary artery disease in high risk patients if you risk stratify, or any patient if you do not risk stratify?**

- ☐ Exercise Tolerance test
- ☐ Thallium Stress Test
- ☐ Stress Echocardiography
- ☐ Dobutamine Stress Tc Scan
- ☐ Coronary Angiography
- ☐ CPEX Testing
- ☐ Other **(Please specify)**

_____

continued over

39 **Who primarily decides which cardiac investigations are required for a moderate to high risk patient before listing?**

Please tick one

- ☐ Consultant Nephrologist
- ☐ Consultant Transplant Surgeon
- ☐ Consultant Cardiologist
- ☐ Consultant Anaesthetist
- ☐ MDT approach
- ☐ Other **(Please specify)**

40 **What are the indications for performing coronary angiography at your unit?**

Tick all that apply. (Note: these are not mutually exclusive)

- ☐ All symptomatic patients
- ☐ Prior CVD
- ☐ Patients with a positive stress test
- ☐ All diabetics
- ☐ Asymptomatic patients with risk factors
- ☐ Asymptomatic older patients **(Please specify age)**
- ☐ No specific policy
- ☐ Other **(Please specify)**

41 **If a coronary angiogram is deemed necessary for listing in a low clearance patient, would your unit refrain from performing the test until they were on dialysis to avoid precipitating the need for dialysis?**

- ☐ Always
- ☐ Sometimes
- ☐ Never

42 **Logistics of cardiac investigations**

If cardiac investigations are required where are they performed and what are the approximate median waiting times in weeks

Test	Local acute hospital	Non-transplant renal unit hospital	Transplant renal unit hospital	Waiting time
ECHO				
Exercise Tolerance Test				
Thallium Stress Test				
Stress Echocardiography				
Dobutamine Stress Tc Scan				
Coronary Angiography				
CPEX Testing				
Other (**Please state**)				

43 **Does your unit have a named cardiologist to provide advice/review patients undergoing assessment for suitability for transplantation?**

☐ Yes ☐ No **(go to question 45)**

44 **Where are they based and what are the approximate waiting times for review?**

☐ Median waiting time **(in weeks)**

☐ Local acute hospital

☐ Non-transplant renal unit hospital

☐ Transplant renal unit hospital

continued over

45 **If cardiology investigations and/or a cardiology opinion have been performed by a referring non-transplanting unit are these ever repeated at your transplanting unit?**

- ☐ Often
- ☐ Sometimes
- ☐ Rarely
- ☐ Never **(go to question 47)**

46 **If you selected often/sometimes/rarely please describe why this tends to occur.**

Peripheral vascular disease assessment

47 **In the evaluation of lower limb peripheral vascular disease, peripheral doppler studies are obtained on which of the following?**

Note: these are not mutually exclusive

- ☐ Asymptomatic older patients
- ☐ All diabetics
- ☐ Symptomatic patients
- ☐ Asymptomatic patients with poor peripheral pulses
- ☐ Patients with asymptomatic bruit
- ☐ History of smoking
- ☐ Other **(Please specify)**

Malignancies

48 **Does your unit routinely screen for malignancies as part of transplant assessment work up?**

☐ Yes ☐ No **(go to question 50)**

49 **Which of the following malignancies are routinely screened for?**

☐ Prostate ☐ Bladder

☐ Breast ☐ Cervical

☐ Skin ☐ Colorectal

☐ Other **(Please specify)**

Urological evaluation

50 **Which statement best describes the urological service available to your unit in assessing patients for transplantation?**

☐ Designated urologist with interest in transplantation available on site within urology department

☐ In House trained urologist available as part of surgical transplant team

☐ No designated urologist with an interest in transplantation available

☐ Other **(Please specify urological support)**

Psychological assessment

51 **Do most patients undergoing assessment for transplant suitability undergo formal psychological assessment?**

☐ Yes ☐ No **(go to question 53)**

52 **If yes, could you briefly describe what psychological assessment they undergo:**

continued over

53 **Do most patients undergoing assessment for transplant suitability undergo formal cognitive assessment?**

☐ Yes ☐ No

54 **What psychological support is available at your unit?**

Tick all that apply

☐ Renal Counsellor

☐ Renal Psychologist

☐ Psychologist/Counsellor shared with other specialities

☐ Other **(Please specify)**

5 Decision Making Process to list patient

55 **How is the final decision to list a patient for transplantation most commonly reached?**

- ☐ By usual named consultant nephrologist
- ☐ By Consultant nephrologist at Transplant unit
- ☐ Jointly by usual Consultant nephrologist and Consultant Transplant surgeon
- ☐ Jointly by Consultant nephrologist (at transplanting unit) and Consultant Transplant Surgeon
- ☐ By Consultant Transplant Surgeon
- ☐ At MDT meeting at transplanting unit
- ☐ Other **(Please specify)**

56 **How is the final decision to list a patient for transplantation, whose CKD/dialysis care is under a non-transplant renal unit, most commonly reached?**

- ☐ By usual named consultant nephrologist
- ☐ By Consultant nephrologist at Transplant unit
- ☐ Jointly by usual Consultant nephrologist and Consultant Transplant surgeon
- ☐ Jointly by Consultant nephrologist (at transplanting unit) and Consultant Transplant Surgeon
- ☐ By Consultant Transplant Surgeon
- ☐ At local MDT at non-transplanting unit (without representation present from transplanting unit)
- ☐ At local MDT at non-transplanting unit (with representation present from transplanting unit)
- ☐ At MDT meeting at transplanting unit (without representation present from non-transplanting unit)
- ☐ At MDT meeting at transplanting unit (with representation present from non-transplanting unit)
- ☐ Other **(Please specify)**

57 **Do you utilise an MDT approach in listing patients for transplantation?**

☐ Yes ☐ No **(go to question 61)**

continued over

58 **If yes, what purpose does it serve?**

Tick all that apply

- ☐ To discuss ALL patients prior to them being listed
- ☐ To discuss complex/borderline patients prior to deciding whether to list or not
- ☐ Other **(Please specify)**

59 **How frequently is your MDT held?**

(Please specify) every _____ weeks

60 **Who attends your MDT (either in person or via teleconference/video link up)?**

- ☐ Consultant nephrologist from non-transplanting unit
- ☐ Consultant nephrologist from transplant unit
- ☐ Consultant surgeon
- ☐ Transplant co-ordinator from non-transplanting unit
- ☐ Transplant co-ordinator from transplanting unit
- ☐ Living Kidney Donor Nurse from non-transplanting unit
- ☐ Living Kidney Donor Nurse from transplanting unit
- ☐ Other **(Please specify)**

61 **Please indicate your views on whether the following factors influence the decision to list a patient**

Please indicate how strongly you agree or disagree with each of the following

	Not at all					Very Strongly
Being employed	☐	☐	☐	☐	☐	☐
High patient enthusiasm towards transplantation	☐	☐	☐	☐	☐	☐
High level of education	☐	☐	☐	☐	☐	☐
English as first language	☐	☐	☐	☐	☐	☐
Having a potential living donor	☐	☐	☐	☐	☐	☐
Having a potential pre-emptive living donor	☐	☐	☐	☐	☐	☐

62 **If a patient is not suitable for deceased donor transplantation but has a potential living donor, would you consider transplantation with a living donor acceptable?**

☐ Yes ☐ No

63 **What proportion of CKD stage 5 patients and dialysis patients under age 75 are informed of the decision to list or not?**

☐ All ☐ Most

☐ Some ☐ Few

☐ None

64 **Do you routinely record all decisions made on the suitability of a patient for transplantation on their electronic patient record?**

☐ Yes ☐ No **(go to question 67)**

65 **If yes, do you audit this?**

☐ Yes ☐ No **(go to question 67)**

66 **If yes, how frequently do your audit this?**

(Please specify) every ☐ months

67 **How long on average does the overall assessment process take from beginning transplant work up to being listed in your unit?**

(Please give median answer in months) ☐

continued over

6 Post Assessment/Re-evaluation on the waiting list

68 **Do you have a unit protocol for the monitoring of patients activated on the transplant list?**

If yes, please could you return this in the stamped addressed envelope with this survey or email it to Rishi.Pruthi@nbt.nhs.uk

- ☐ Yes
- ☐ No

69 **Once activated on the transplant list how frequently are patients usually monitored for continued suitability?**

- ☐ Never
- ☐ 3 Monthly
- ☐ 6 Monthly
- ☐ Annually
- ☐ Other **(Please specify)**

70 **Who reviews/monitors the continued suitability of patients activated on the list?**

- ☐ Usual dialysis nephrologist at a routine follow up appointment
- ☐ Transplant nephrologist in a transplant assessment review clinic
- ☐ Transplant surgeon in a transplant assessment review clinic
- ☐ Both nephrologist and transplant surgeon in a transplant assessment review clinic
- ☐ Other **(Please specify)**

71 **Do you have a specific transplant review clinic for listed patients?**

- ☐ Yes
- ☐ No **(go to question 83)**

72 **If yes, how frequently are patients seen in this review clinic?**

- ☐ 6 months
- ☐ Annually
- ☐ Every two years
- ☐ Other **(Please specify in months)**
- ☐ N/A

73 **Which of the following investigations are routinely performed when patients are reviewed?**

Tick all that apply

- ☐ HIV & Hepatitis Serology
- ☐ DRE
- ☐ Pap smear
- ☐ Mammography
- ☐ Cognitive assessment
- ☐ PSA
- ☐ Pelvic examination
- ☐ Breast examination
- ☐ Colonoscopy/sigmoidoscopy
- ☐ None of the above

74 **Which of the following cardiac investigations (if any) are repeated?**

- ☐ ECG
- ☐ Exercise tolerance test
- ☐ Stress Echocardiography
- ☐ Coronary Angiography
- ☐ ECHO
- ☐ Thallium Stress Test
- ☐ Dobutamine Stress Tc Scan
- ☐ CPEX Testing
- ☐ Other **(Please specify)**

75 **How often are these cardiac investigations repeated?**

Provide answers in months

ECG

ECHO

Exercise tolerance test

Thallium Stress Test

Stress Echocardiography

Dobutamine Stress Tc Scan

Coronary Angiography

CPEX Testing

Other (Please state)

continued over

76 **Which of the following accurately describes your local practice in continued surveillance of cardiac disease in asymptomatic patients on the waiting list?**

- ☐ No routine surveillance if asymptomatic
- ☐ All patients screened irrespective of remaining asymptomatic
- ☐ Surveillance only in high risk groups
- ☐ Variable , no specific policy
- ☐ Other **(Please specify)**

77 **Is psychological support offered routinely to patients listed?**

- ☐ Yes **(go to question 79)**
- ☐ No

78 **If No, what is the main reason for this?**

- ☐ Not perceived to be an area where patients require support
- ☐ Lack of resources/overburdened counselling service
- ☐ Do not think that patients' would make use of this service if offered
- ☐ Other **(Please specify)**

79 **How are patients deemed unsuitable for transplantation in their current state, but with the potential to be listed in the future (depending on changing circumstances/factors) re-assessed?**

- ☐ At routine outpatient appointment with regular nephrologist
- ☐ At a follow up transplant assessment clinic appointment
- ☐ At a MDT
- ☐ Other **(Please specify)**

7 Working relationships, attitudes and other allied health professionals & services involved in transplant listing

80 **How would you describe your relationship with your local non-transplanting units?**

- ☐ Excellent
- ☐ Very Good
- ☐ Good
- ☐ Fair
- ☐ Poor

81 **What is your view of the following statements regarding your unit's interaction with local non-transplanting units?**

Please indicate how strongly you agree or disagree with each of the following

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
Little communication exists with non-transplanting units	☐	☐	☐	☐	☐
Non-Transplanting units always refer patients with complete investigations	☐	☐	☐	☐	☐
Non-Transplanting units adhere to agreed work up protocol	☐	☐	☐	☐	☐
Non- transplanting units do not have access to adequate cardiology investigations/opinions	☐	☐	☐	☐	☐

82 **Which statement best describes the attitude of your unit staff towards pre-emptive transplant listing?**

- ☐ Everyone has a positive attitude towards listing patients pre-emptively with no exceptions
- ☐ The majority of individuals have a positive attitude towards pre-emptive listing
- ☐ The unit is split roughly 50 50
- ☐ The majority have a negative attitude towards pre-emptive transplantation
- ☐ Everyone has a negative attitude towards pre-emptive transplantation

continued over

83 **What is your opinion on the following statements as to the reason behind why certain individuals may have a negative attitude towards pre-emptive listing?**

Please indicate how strongly you agree or disagree with each of the following

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
There is limited evidence that listing patients pre-emptively is more beneficial as compared to listing after starting dialysis	☐	☐	☐	☐	☐
There is strong evidence to support pre-emptive listing, though there is a lack of appreciation of this evidence amongst those who are less keen to list pre-emptively	☐	☐	☐	☐	☐
The experience of dialysis before transplantation is better for patients as it improves their post-transplantation adherence and patients value their transplant more	☐	☐	☐	☐	☐
It is unfair to allocate an organ to a patient who has not been on dialysis when there are many on the waiting list who have been waiting for many years.	☐	☐	☐	☐	☐

84 **What is your opinion on the following statements regarding living donation within your unit?**

Please indicate how strongly you agree or disagree with each of the following

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
The work up required to assess suitability of living donors for kidney donation is well defined	☐	☐	☐	☐	☐
Living donor work up commences only once potential recipient has been assessed as being suitable and activated on the transplant list	☐	☐	☐	☐	☐
Potential donors can self-refer for assessment	☐	☐	☐	☐	☐
Potential donors need to be referred by a health professional	☐	☐	☐	☐	☐
Transplant opportunities have been delayed/missed due to failure to identify existing potential donor early in process	☐	☐	☐	☐	☐
Donation from young female donors often poses moral dilemmas for health professionals involved in transplantation	☐	☐	☐	☐	☐
High cost of living donation work up is a hindrance to working up multiple donors simultaneously	☐	☐	☐	☐	☐

85 **What level of administrative support is provided to the living donor nurse/transplant co-ordinator?**

- ☐ Nil
- ☐ Designated specific secretary
- ☐ Shared secretary
- ☐ Other **(Please specify)**

86 **Do you have an on-site tissue typing service?**

- ☐ Yes
- ☐ No

87 **How long does it usually take for tissue typing to process final samples and request NHSBT to activate a patient once decision taken to list?**

- ☐ **(Please specify number of weeks)**

88 **Has processing of tissue typing samples ever been the source of significant delays in listing patient for transplantation?**

- ☐ Yes
- ☐ No

continued over

8 Improving transplant listing

89 **Does your unit undertake any regular audit of whether CKD 5 patients and or those on dialysis have been listed?**

- ☐ Yes, 1 to 2 per year
- ☐ Yes, 3 to 4 per year
- ☐ Yes, 5 or more per year
- ☐ No
- ☐ Other **(Please specify)**

90 **Has there been any significant improvement in the time taken to complete the overall assessment process in your unit over the last year?**

- ☐ Yes
- ☐ No **(go to question 92)**

91 **If yes, please describe briefly what improvement there has been and how it was achieved.**

92 **What is your opinion on whether more funding for the following resources would improve overall listing and time to listing in your unit?**

Please indicate how strongly you agree or disagree with each of the following

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
Cardiac service	☐	☐	☐	☐	☐
Tissue typing service	☐	☐	☐	☐	☐
Education service	☐	☐	☐	☐	☐
Transplant co-ordinators	☐	☐	☐	☐	☐
Living donor nurses	☐	☐	☐	☐	☐
Urology service within transplantation	☐	☐	☐	☐	☐
Consultant nephrologists with interest in transplantation	☐	☐	☐	☐	☐
Consultant surgeons	☐	☐	☐	☐	☐
Interpreter service and developing pathways to improve language barriers amongst ethnic minorities	☐	☐	☐	☐	☐
Administrative support for allied health professionals e.g. transplant co-ordinators, living donor nurses	☐	☐	☐	☐	☐
Better renal IT systems	☐	☐	☐	☐	☐
Psychological assessment and counselling service	☐	☐	☐	☐	☐
Increasing operation time slots for transplantation service	☐	☐	☐	☐	☐
Other **(Please specify and rate)**	☐	☐	☐	☐	☐

continued over

93 **What is your opinion on the following statements about whether they would improve listing of patients for transplantation?**

Please indicate how strongly you agree or disagree with each of the following

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
National consensus on cardiac work up	☐	☐	☐	☐	☐
National consensus on entire work up (not just cardiac)	☐	☐	☐	☐	☐
Improvements in commissioning of transplant work up	☐	☐	☐	☐	☐
Ensuring MDT approach utilised systematically in making all decisions to list patients or not	☐	☐	☐	☐	☐
Introducing time target for tissue typing processing	☐	☐	☐	☐	☐
Better evidence base behind necessary assessment work up	☐	☐	☐	☐	☐

Further comments on transplant listing

94 **If you would like to make any further comments on listing for transplantation, please use the space below:**

9 Details of person completing the questionnaire

95 **If someone else helped you complete this questionnaire, please give their role in renal unit.**

96 **Please provide your contact details in case we need to contact you. This information is confidential and will not be used in any research reports.**

Name

Your role in the renal unit

Email

Tel

If you previously indicated that your unit has a written transplant work up protocol and/or a protocol for monitoring patients on the transplant list please could you post these back with this survey.

Appendix E: Multiple Imputation Tables

Table A – Multivariable logistic regression model for the probability of being pre-emptively listed adjusted for patient and centre level factors with imputed data for missing variables

Variable	N	Odds Ratio	95% Wald Confidence Limits		p-value
Age					
18-29	2980	1	-	-	
30-39	4700	0.9	0.51	1.57	0.71
40-49	9100	0.79	0.47	1.32	0.36
50-59	13140	0.57	0.34	0.97	0.037
60-64	7440	0.47	0.26	0.87	0.015
65-75	16160	0.19	0.1	0.37	<0.0001
Ethnic Group					
White	43540	1	-	-	
Asian	5860	0.49	0.33	0.72	0.0003
Black	3540	0.43	0.26	0.71	0.0009
Other	580	0.23	0.07	0.8	0.021
Time Since First Seen by Nephrologist					
<1 Year					
	14028	1	-	-	
1-3 Years	12387	8.12	5.44	12.1	<0.0001
>3 Years	27105	11.55	8.05	16.55	<0.0001
BMI					
Less than 20	3681	0.66	0.4	1.09	0.11
20<=bmi<25	15967	1	-	-	
25<=bmi<30	16898	1.31	0.99	1.73	0.059
30<=bmi<35	9646	0.97	0.69	1.38	0.89
35<=bmi<40	4452	0.31	0.18	0.54	<0.0001
>= 40	2876	0.12	0.05	0.28	<0.0001
Education					
GCSE, A-level or NVQ 1-3	22302	1.26	0.96	1.67	0.098
Degree, Higher or NVQ 4-5	9539	1.06	0.74	1.51	0.75
No Qualifications	21679	1	-	-	
Car ownership		1	-	-	
No	14024				
Yes	39496	1.98	1.41	2.76	<0.0001

Variable	N	Odds Ratio	95% Wald Confidence Limits		p-value
Accommodation					
Owned by you (Outright or with a Mortgage)	30657	1	-	-	
Other	3315	0.58	0.34	1	0.051
Part rent, Part owned (shared ownership)	1181	0.32	0.13	0.74	0.0084
Rented Privately from Council / Housing Association	18367	0.55	0.41	0.75	0.0002
Employment					
Working full time/ part time	13341	1	-	-	
Long term sick/disabled	14927	0.42	0.3	0.58	<0.0001
Retired from paid work	18950	0.55	0.37	0.82	0.0037
Unemployed	3702	0.51	0.31	0.85	0.0095
Other	2600	0.93	0.54	1.6	0.8
Malignancy					
No	46804	1	-	-	
Yes	6716	0.33	0.2	0.53	<0.0001
Smoking					
No	22958	1	-	-	
Current	7652	0.53	0.36	0.78	0.0011
Ex-smoker	15376	0.95	0.72	1.25	0.69
Don’t know	7534	0.75	0.52	1.07	0.11
Vascular Disease					
No	49116	1	-	-	
Yes	4404	0.29	0.13	0.61	0.0013
Heart Disease					
No	43408	1	-	-	
Yes	10112	0.55	0.36	0.82	0.004
Heart Failure					
No	49796	1	-	-	
Yes	3724	0.25	0.08	0.77	0.016
Diabetes					
No	32522	1	-	-	
Type 1	5318	1.12	0.76	1.64	0.58
Type 2	15680	0.37	0.26	0.52	<0.0001
Cerebrovascular Disease					
No	48966	1	-	-	
Yes	4554	0.53	0.3	0.92	0.025

Variable	N	Odds Ratio	95% Wald Confidence Limits		p-value
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

Table B – Multivariable Cox Regression model for time to listing within 2 years of starting dialysis, adjusted for patient and centre level factors with imputed data for missing variables

Effect	N	Hazard Ratio	95% Wald Confidence Limits		p-value
Age					
18-29	1720	1	-	-	
30-39	2740	0.8	0.56	1.12	0.2
40-49	5600	0.64	0.46	0.89	0.0077
50-59	9240	0.35	0.25	0.49	<0.0001
60-64	5800	0.27	0.18	0.41	<0.0001
65-75	14300	0.15	0.1	0.23	<0.0001
Gender					
Male	25700	1	-	-	
Female	13700	0.82	0.68	0.99	0.035
Ethnic Group					
White	31320	1	-	-	
Asian	4660	1.42	1.12	1.79	0.004
Black	2920	1.04	0.76	1.43	0.8
Other	500	1.56	0.85	2.87	0.15
BMI					
Less than 20	2850	0.85	0.6	1.21	0.37
20<=bmi<25	11210	1	-	-	
25<=bmi<30	11150	1.15	0.93	1.42	0.19
30<=bmi<35	7378	0.88	0.67	1.14	0.33
35<=bmi<40	3995	0.48	0.33	0.7	0.0002
>= 40	2817	0.15	0.08	0.3	<0.0001

Effect	N	Hazard Ratio	95% Wald Confidence Limits		p-value
Dialysis Modality					
Haemodialysis	32060	1	-	-	1
Peritoneal dialysis	7340	1.34	1.1	1.64	0.004
Smoking					
No	15675	1	-	-	
Current	6323	0.76	0.58	1	0.049
Ex-smoker	11630	1.17	0.95	1.45	0.13
Don't know	5772	1.06	0.82	1.36	0.65
Education					
GCSE, A-level or NVQ 1-3	14972	1.05	0.85	1.3	0.63
Degree, Higher or NVQ 4-5	6100	1.38	1.07	1.79	0.013
No Qualifications	18328	1	-	-	
Car ownership					
No	12377	0.73	0.6	0.9	0.0026
Yes	27023	1	-	-	
Accommodation					
Owned by you (Outright or with a Mortgage)	20693	1	-	-	
Other	2529	0.81	0.58	1.13	0.22
Part rent, Part owned (shared ownership)	937	1.07	0.64	1.8	0.79
Rented Privately from Council / Housing Association	15241	0.76	0.61	0.94	0.012
Employment					
Working full time/ part time	6619	1	-	-	
Long term sick/disabled	12112	0.54	0.43	0.68	<0.0001
Retired from paid work	16286	0.58	0.42	0.8	0.0009
Unemployed	284	0.77	0.56	1.06	0.11
Other	1499	0.74	0.5	1.1	0.13
Malignancy					
No	33537	1	-	-	
Yes	5863	0.33	0.2	0.53	<0.0001
Vascular Disease					
No	35280	1	-	-	
Yes	4120	0.6	0.37	0.96	0.035
Heart Disease					
No	30390	1	-	-	
Yes	9010	0.8	0.59	1.09	0.16

Effect	N	Hazard Ratio	95% Wald Confidence Limits		p-value
Heart Failure					
No	35946	1	-	-	
Yes	3454	0.58	0.36	0.93	0.025
Blood Borne Viruses					
No	38124	1	-	-	
Yes	1276	0.36	0.18	0.71	0.0035
Diabetes					
No	21700	1	-	-	
Type 1	3520	0.76	0.57	1.02	0.064
Type 2	14180	0.62	0.49	0.79	<0.0001
Centre Level Variables					
Consultant Nephrologists					
<=6	30	1	-	-	
>6	41	1.26	1	1.59	0.054
MDT					
No	17	1	-	-	
Yes	54	1.23	0.99	1.52	0.57
Written Protocol for listing					
No	21	1	-	-	
Yes	50	1.72	1.58	1.9	0.0033

References

1. https://www.gov.uk/government/publications/the-nhs-constitution-for-england
2. Kawachi I, Subramanian SV, Almeida-Filho N. A glossary for health inequalities. J epidemiol Community Health 2002;56(9):647-52.
3. Braveman P, Gruskin S. Defining equity in health. J Epidemiol Community Health 2003;57(4):254-8.
4. 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;341:1725–30.
5. Oniscu GC, Brown H, Forsythe JLR Impact of cadaveric renal transplantation on survival in patients listed for transplantation. J Am Soc Nephrol 2005;16:1859–65.
6. Neipp M, Karavul B, Jackobs S et al. Quality of life in adult transplant recipients more than 15 years after kidney transplantation. Transplantation 2006;81:1640–4.
7. Abecassis M, Bartlett ST, Collins AJ et al. Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQITM) conference. Clin J Am Soc Nephrol 2008;3: 471–80.
8. Terasaki PI, Cecka JM, Gjertson DW, Takemoto S. High survival rates of kidney transplants from spousal and living unrelated donors. N Engl J Med 1995;**333**(6):333-6.
9. Gjertson DW, Cecka JM. Living unrelated donor kidney transplantation. Kidney Int 2000;**58**(2):491-9.
10. Pruthi R, Casula A, MacPhee I, UK Renal Registry 17th Annual Report: Chapter 3 Demographic and Biochemistry Profile of Kidney Transplant Recipients in the UK in 2013: National and Centre-specific Analyses. Nephron 2015;129(suppl 1):57-86

11. 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*.
12. Ravanan R, Udayaraj U, Ansell D, Collett D, Johnson R, O'Neill J, Tomson CR, Dudley CR. Variation between centres in access to renal transplantation in UK: longitudinal cohort study. BMJ. 2010 Jul 20;341:c3451. doi: 10.1136/bmj.c3451.
13. 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.
14. Fored CM, Ejerblad E , Fryzek JP, Lambe M, et al. Socio-economic status and chronic renal failure: a population-based case-control study in Sweden. Nephrol. Dial. Transplant. (2003) 18 (1): 82-88
15. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End stage renal disease in African Amercian and White Men. 16-year MRFIT findings. JAMA 1997;277(16):1293-8
16. Volkova N, McClellan W, Klein M, Flanders D, Kleinbaum D, Soucie JM, et al. Neighbourhood poverty and racial differences in ESRD incidence. J Am Soc Nephol 2008;19(2):356-64
17. Narva AS. Kidney disease in Native Americans. J Natl Med Assoc 2002;94(8):738-42.
18. Lightstone L, Rees AJ, Tomson C, Walls J, Winearls CG, Feehally J. High incidence of end-stage renal disease in Indo-asians in the UK. Q J Med 195;88(3):191-5.
19. Xue JL, Eggers PW, Agodoa LY, Foley RN, Collins AJ. Longitudinal study of racial and ethnic differences in developing end-stage renal disease among aged medicare beneficiaries. J Am Soc Nephrol 2007;18(4):1299-306.
20. Roderick PJ, Jones I, Raleigh VS, McGeown M, Mallick N. Population need for renal replacement therapy in Thames regions: ethnic dimension. BMJ 1994;309(6962):1111-4.

21. Cass A, Cunningham J, Hoy W. The relationship between the incidence of end stage renal disease and markers of socioeconomic disadvantage. N S W Public health Bull 2002;13(7):147-51.
22. Ward MM. Socioeconmic status and the incidence of ESRD. Am J Kidney Dis 2008;51(4):563-72.
23. Young EW, Mauger EA, Jiang KH, Port FK, Wolfe RA. Socioeconmic status and end-stage renal disease in the United Status. Kidney Int 1994;45(3):907-11.
24. Kasiske BL, Snyder JJ, Matas AJ, Ellison MD, Gill JS, Kausz AT. Preemptive kidney transplantation: the advantage and the advantaged. J Am Soc Nephrol 2002;13(5):1358-64.
25. Held PJ, Pauly MV, Bovbjerg RR, Newmann J, Salvatierra O. Access to kidney transplantation. Has the United States eliminated income and racial differences? Arch Intern Med 1988;148(12):2594-600.
26. Alexander GC, Sehgal AR. Barriers to cadaveric transplantation among blacks, women and the poor. JAMA 1998;280(13):1148-52.
27. 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.
28. Eggers PW. Racial differences in access to transplantation. Health Care Financ Rev 1995;17(2):89-103.
29. Kjellstrand CM. Age, sex, and race inequality in renal transplantation. Arch intern Med 1988;148(6):1305-9.
30. Ozminkowski RJ, White AJ, Hassol A, Murphy M. Minimising racial disparity regarding receipt of a cadaver kidney transplant. Am J Kidney Dis 1997;30(6):749-59.
31. Garg PP, Diener-West M, Powe NR. Reducing racial disparities in transplant activation whom should we target? Am J Kidney Dis 2001;37(5):921-31
32. 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.

33. Keith D, Ashby VB, Port FK, Leichtman AB. Insurance type and minority status associated with large disparities in prelisting dialysis among candidates for kidney transplantation. Clin J Am Soc Nephrol 2008;3(2):463-70.
34. 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.
35. Tonelli M, Hemmelgarn B, Gill JS, Chou S, Culleton B, Klarenbach S, et al. Patient and allograft survival of Indo Asian dialysis patients treated in Canada. Kidney Int 2007;72(4):499-504.
36. Epstein AM, Ayanian JZ, Keogh JH, Noonan SJ, Armistead N, Cleary PD, et al. Racial disparities in access to renal transplantation-clinically appropriate or due to underuse or overuse? N Engl J Med 2000;343(21):1537-44.
37. https://www.nice.org.uk/guidance/cg182/chapter/1-recommendations?unlid=995980121201582220544 7
38. Levey A, Andreoli S, DuBose T, Provenzano R, Collins A. Chronic kidney disease: common, harmful, and treatable-World Kidney Day 2007. J am Soc Nephrol 2007;18(2):374-78
39. Coresh J, Selvin E, Stevens LA, Manzi J, kusek JW, Eggers P, et al. Prevalence of chronic kidney disease in the United States. JAMA 2007;298(17):2038-47.
40. Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Welborn TA, Zimmet PZ, et al. Prevalence of kidney damage in Australian adults: The AusDiab kidney Study. J Am Soc nephrol 2003; 14(7 Suppl 2):S131-8.
41. Lusignan S, Chan T., Stevens PE, et al. Identifying patients with chronic kidney disease from general practice computer records. Family Practice, 22 (2005), pp. 234–241
42. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis 2003;41(1):1-12.
43. Drey N, Roderick P, Mullee M, Rogerson M. A population-based study of the incidence and outcomes of diagnosed chronic kidney disease. Am J kidney Dis 2003;42(42):677-84.

44. Roderick P, Clements S, Stone N, Martin D, Diamond I. What determines geographical variation in rates of acceptance onto renal replacement therapy in England? J Health Serv Res Policy 1999;4(3):139-46.
45. Shoham DA, Vupputuri S, Kshirsagar AV. Chronic kidney disease and life course socioeconomic status: a review. Adv Chronic Kidney Dis 2005;12(1):56-63
46. Norris K, Nissenson AR. Race, gender and socioeconomic disparities in CKD in the United States. J Am Soc Nephrol 2008;19(7):1261-70.
47. Nzerue CM, Demissochew H, Tucker JK. Race and kidney disease: role of social and environmental factors. J Natl Med Assoc 2002;94(8 Suppl):28S-38S.
48. USRDS 2006 Annual report: Atlas of End-Stage Renal Disease in the United States. Bethesda: National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, 2006.
49. Roderick PJ, Raleigh VS, Hallam L, Mallick NP. The need and demand for renal replacement therapy in ethnic minorities in England. J Epidemiol Community Health 1996;50(3):334-9.
50. Stevens PE, O'Donoghue DJ, de Lusignan S, Van Vlymen J, Klebe B, Middleton R, et al. Chronic kidney disease management in the United Kingdom: NEOERICA project results. Kidney int 2007;72():92-9.
51. Keith DS, Nichols GA, Gullion CM, et al. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization
Arch Intern Med, 164 (2004), pp. 659–663
52. Ishani A, Granditis GA, Grimm RH, Svendsen KH, Collins AJ, Prineas RJ, et al. Association of single measurements of dipstick proteinuria, estimated glomerular filtration rate, and haematocrit with 28-year incidence of end-stage renal disease in the multiple risk factor intervention trial. J Am Soc Nephrol 2006;17(5):1444-52.
53. Rahman M, Pressel s, davis BR, Nwachuku C, Wright JT Jr, Whelton PK, et al. cardiovascular outcomes in high risk hypertensive patients stratified by baseline glomerular filtration rate. Ann Intern Med 2006;144(144(3):172-80.

54. Brancati FL, Whelton PK, Randall BL, Neaton JD, Stamler J, klag MJ. Risk of end-stage renal disease in diabetes mellitus: a prospective cohort study of men screened for MRFIT. Multiple Risk Factor Intervention Trial. JAMA 1997;278(23):2069-74.

55. John RI, Webb MC, Young A, et al. Unreferred chronic kidney disease: a longitudinal study. Am J Kidney Dis, 43 (2004), pp. 825–835

56. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalisation. N Engl J Med, 351 (2004), pp. 1296–1305

57. Foley RN, Murray AM, Li S, et al. Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare Population, 1998–1999. J Am Soc Nephrol, 16 (2005), pp. 489–495

58. Chandna SM, Da Silva-Gane M, Marshall C, Warwicker P, Greenwood RN, Farrington K. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. Nephrol Dial Transplant. 2011 May;26(5):1608-14.

59. Renal Physicians Association (2010). Clinical Practice Guideline on Shared Decision Making in the Appropriate Initiation of and Withdrawal from Dialysis, 2nd Ed. October 2010 [on-line]. Available at www.renalmd.org/ end-stage-renal-disease/ Accessed June 21, 2016.

60. Charlson ME, Pompei P, Ales KL, et al. . A new method of classifying prognostic comorbidity in longitudinal studies: development and validation, *J Chronic Dis* , 1987, vol. 40 5(pg. 373-383).

61. Hude Quan, Bing Li, Chantal M. Couris, Kiyohide Fushimi, Patrick Graham, Phil Hider, Jean-Marie Januel, Vijaya Sundararajan; Updating and Validating the Charlson Comorbidity Index and Score for Risk Adjustment in Hospital Discharge Abstracts Using Data From 6 Countries. Am J Epidemiol 2011; 173 (6): 676-682. doi: 10.1093/aje/kwq433.

62. MacNeill S, J, Casula A, Shaw C, Castledine C, UK Renal Registry 18th Annual Report: Chapter 2 UK Renal Replacement Therapy Prevalence in 2014: National and Centre-specific Analyses. Nephron 2016;132(suppl 1):41-68

63. De Vecchi A, Dratwa M, Wiedemann M. Healthcare systems and end-stage renal disease (ESRD) therapies-an international review: costs and reimbursement/funding of ESRD therapies. Nephrol Dial Transplant 1999;14(Suppl 6):31-41.
64. Chugh KS, Jha V. Differences in the care of ESRD patients wordwide: required resources and future outlook. Kidney Int Suppl 1995;50:S7-13.
65. Pruthi R, Casula A, MacPhee I, UK Renal Registry 18th Annual Report: Chapter 3 Demographic and Biochemistry Profile of Kidney Transplant Recipients in the UK in 2014: National and Centre-specific Analyses. Nephron 2016;132(suppl 1):69-98
66. http://nhsbtmediaservices.blob.core.windows.net/organ-donation-assets/pdfs/kidney_activity.pdf
67. Nicholson ML, Metcalfe MS, White SA, Waller JR, Doughman TM, Horsburgh T, et al. A comparison of the results of renal transplantation from non-heart beating, conventional cadaveric, and living donors. Kidney Int 2000;58(6):2585-91.
68. Alonso A, Fernandez-Rivera C, Villaverde P, Oliver J, Cillero S, Lorenzo D, et al. Renal transplantation from non-heart beating donors: a single-centre 10-year experience. Transplant Proc 2005;37(9):3658-60.
69. Sanchez-Fructuoso AI, marques M, Prats D, Cornesa J, Calvo N, Perez-Contin MJ et al. Victims of cardiac arrest occurring outside the hospital: a source of transplantable kidneys. Ann Intern Med 2006;145(3)157-64.
70. Pinson CW, Feurer ID, Payne JL, Wise PE, Shockley S, Speroff T. Health-related quality of life after different types of solid organ transplantation. Ann Surg 2000;232(4):597-607.
71. Sureshkumar KK, Patel BM, Markatos A, Nghiem DD, Marcus RJ. Quality of life after organ transplantation in type 1 diabetes with end stage renal disease. Clin Transplant 2006;20(1):19-25.
72. Gross CR, Limwattananon C, Matthees B, Zehrer JL, savik K. Impact of transplantation on quality of life in patients with diabetes and renal dysfunction. Transplantation 2000;70(12):1736-46.

73. Balaska A, Moustafellos P, Gourgiotis S, Pistolas D, Hadjiyannakis E, Vougas V, et al. Changes in health-related quality of life in Greek adult patients 1 year after successful renal transplantation. Exp Clin Transplant 2006;4(2):521-4.
74. https://nhsbtmediaservices.blob.core.windows.net/organ-donation-assets/pdfs/activity_report_2010_11.pdf
75. Cecka JM. Living donor transplants. Clin Transpl 1995:363-77.
76. Roodnat JL, Riemsdijk IC, Mulder PG, Doxiadis I, Claas FH, et al. The superior results of living-donor renal transplantation are not completely caused by selection or short cold ischaemia time: a single-center, multivariate analysis. Transplantation 2003;75(12):2014-8.
77. Kasiske BL, Snyder JJ, Matas AJ, Ellison MD, Gill JS, Kausz AT. Preemptive kidney transplantation: the advantage and the advantaged. J Am Soc Nephrol 2002;13(5):1358-64.
78. Asderakis A, Augustine T, Dyer P, Short C, Campbell B, Parrott NR, et al. Pre-emptive kidney transplantation: the attractive alternative. Nephrol Dial Transplant 1998;13(7):1799-803.
79. UK Kidney Transplantation: organ allocation policy. http://www.odt.nhs.uk/pdf/kidney_allocation_policy.pdf
80. Opelz G. Correlation of HLA matching with kidney graft survival in patients with or without cyclosporine treatment. Transplantation 1985; 40:240.
81. Opelz, G. Collaborative Transplant Study Newsletter 1988; number 3.
82. Gilks WR, Bradley BA, Gore SM, Klouda PT. Substantial benefits of tissue matching in renal transplantation. Transplantation 1987; 43:669.
83. Doxiadis II, de Fijter JW, Mallat MJ, et al. Simpler and equitable allocation of kidneys from postmortem donors primarily based on full HLA-DR compatibility. Transplantation 2007; 83:1207.
84. Coupel S, Giral-Classe M, Karam G, et al. Ten-year survival of second kidney transplants: impact of immunologic factors and renal function at 12 months. Kidney Int 2003; 64:674.
85. http://www.nhsbt.nhs.uk (Accessed June 25, 2016).

86. Shaw C, Pruthi R, Pitcher D, Fogarty D. UK Renal Registry 15th annual report: Chapter 2 UK RRT prevalence in 2011: national and centre-specific analyses. Nephron Clin Pract. 2013;123 Suppl 1:29-54. doi: 10.1159/000353321.

87. Office for National Statistics. www.statistics.gov.uk

88. Dudley et al; Renal association Guidelines: Assessment of the potential kidney transplant recipient http://www.renal.org/guidelines/modules/assessment-of-the-potential-kidney-transplant-recipient#sthash.Y8hVkX1q.dpbs

89. Douglas DD. Should everyone have equal access to organ transplantation? An argument in favor. *Arch Intern Med* 2003; 163: 1883.

90. Kasiske BL, Cangro CB, Hariharan S, Hricik DE, Kerman RH, Roth D, Rush DN, Vazquez MA, Weir MR*; The evaluation of renal transplantation candidates*: *clinical practice guidelines* Am J *Transplant*. 2001;1 Suppl 2:3-95.

91. Campbell S, Pilmore H, Gracey D, Mulley W, Russell C, McTaggart S, et al; KHA-CARI guideline: recipient assessment for transplantation, Nephrology (Carlton). 2013 Jun;18(6):455-62. doi: 10.1111/nep.12068.

92. Berthoux F, Abramowicz D, Bradlet B, et al. European best practice guidelines for renal transplantation (Part 1). Nephrol Dial Transplant 2000;15:Suppl 7

93. EBPG. Section I: evaluation, selection and preparation of the potential renal transplant candidate. Nephrol Dial Transplant 2000; 15: 3.

94. Bhagani S, Sweny P, Brook G. Guidelines for kidney transplantation in patients with HIV disease. HIV Med 2006; 7: 133.

95. MMOH. Renal Replacement Therapy—Clinical Practice Guidelines. 3rd ed. Kuala Lumpur, Malaysia: Malaysian Ministry of Health; 2009.

96. Steinman TI, Becker BN, Frost AE, et al.. Guidelines for the referral and management of patients eligible for solid organ transplantation. Transplantation 2001; 71: 1189.

97. Kasiske BL, Cangro CB, Hariharan S, et al.. The evaluation of renal transplantation candidates: clinical practice guidelines. Am J Transplant 2001; 1: 3.

98. Knoll G, Cockfield S, Blydt-Hansen T, et al.. Canadian Society of Transplantation: consensus guidelines on eligibility for kidney transplantation. CMAJ 2005; 173: S1.

99. Kalble T, Alcaraz A, Buddle K, et al.. Guidelines on renal transplantation. European Association of Urology 2010. Available at http://www.uroweb.org/fileadmin/tx_eauguidelines/2009/Full/Renal_Transplant.pdf.
Accessed June 25, 2016

100. Scientific Registry of Transplant Recipients (SRTR) 2012 Annual Data Report http://srtr.transplant.hrsa.gov/annual_reports/2012/ (Accessed on June 25, 2016).

101. Bunnapradist S, Danovitch GM. Evaluation of adult kidney transplant candidates. Am J Kidney Dis 2007; 50: 890.

102. Gill JS, Ma I, Landsberg D et al. Cardiovascular events and investigation in patients who are awaiting cadaveric kidney transplantation. J Am Soc Nephrol 2005; 16: 808–816.

103. Rostand S, Rutsky E. Coronary artery disease in end-stage renal disease. In: Principles and Practice of Dialysis, Henrich WL (Ed), Williams & Wilkins, Baltimore 1994.

104. Collins A. US renal data system 2012 annual report. Am J Kidney Dis 2013; 6: A7.

105. Raggi P, Boulay A, Chasan-Taber S et al. Cardiac calcification in adult hemodialysis patients. J Am Coll Cardiol 2002; 39: 695–701.

106. Gowdak LH, de Paula FJ, Ce´sar LA et al. Screening for significant coronary artery disease in high-risk renal transplant candidates. Coron Artery Dis 2007; 18: 553–558.

107. Ohtake T, Kobayashi S, Moriya H et al. High prevalence of occult coronary artery stenosis in patients with chronic kidney disease at the initiation of renal replacement therapy: an angiographic examination. J Am Soc Nephrol 2005; 16: 1141–1148.

108. Charytan D, Kuntz RE, Mauri L et al. Distribution of coronary artery disease and relation to mortality in asymptomatic hemodialysis patients. Am J Kidney Dis 2007; 49: 409–416.

109. Hayashi T, Obi Y, Kimura T et al. Cardiac troponin T predicts occult coronary artery stenosis in patients with chronic kidney disease at the start of renal replacement therapy. Nephrol Dial Transplant 2008; 23: 2936–2942.
110. Gill J, Marcello T, Nathan J et al. The impact of waiting time and comorbid conditions on the survival benefit of kidney transplantation. Kidney Int 2005; 68: 2345–2351.
111. Kasiske BL, Maclean JR, Snyder JJ. Acute myocardial infarction and kidney transplantation. J Am Soc Nephrol 2006; 17: 900–907.
112. Kiberd B, Panek R. Cardiovascular outcomes in the outpatient kidney transplant clinic: the Framingham risk score revisited. Clin J Am Soc Nephrol 2008; 3: 822–828.
113. Lentine KL, Brennan DC, Schnitzler MA. Incidence and predictors of myocardial infarction after kidney transplantation. J Am Soc Nephrol 2005; 16: 496–506.
114. Aalten J, Hoogeveen EK, Roodnat JI et al. Associations between pre- kidney-transplant risk factors and post-transplant cardiovascular events and death. Transplant Int 2008; 21: 985–991.
115. Hart A, Weir MR, Kasiske BL. Cardiovascular risk assessment in kidney transplantation. Kidney Int. 2015 Mar;87(3):527-34.
116. Boden W, O'Rourke R, Teo K et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med 2007; 356: 1503–1516.
117. Pilmore H. Cardiac assessment for renal transplantation. Am J Transplant 2006; 6:659.
118. Wang LW, Fahim MA, Hayen A, et al. Cardiac testing for coronary artery disease in potential kidney transplant recipients. Cochrane Database Syst Rev 2011; :CD008691.
119. Ramos EL. The evaluation of candidates for renal transplantation: the current practice of US transplant centers. Transplantation 1994; 57: 490.
120. Danovitch GM, Hariharan S, Pirsch JD et al. Management of the waiting list for cadaveric kidney transplants: report of a survey and recommendations by

the clinical practice guidelines committee of the American Society of Transplantation. J Am Soc Nephrol 2002; 13: 528–535.

121. Brunkhorst R, Lufft V, Dannenberg B *et al*. Improved survival in patients with type 1 diabetes mellitus after renal transplantation compared with hemodialysis: A case-control study. *Transplantation* 2003; 76: 115–19.

122. Cecka JM. The UNOS Scientific Renal Transplant Registry. *Clin. Transpl.* 1996; 1–14.

123. Waki K. Impact of diabetes mellitus on transplantation. *Clin. Transpl.* 2004; 357–77.

124. Tonelli M, Wiebe N, Knoll G *et al*. Systematic review: Kidney transplantation compared with dialysis in clinically relevant outcomes. *Am. J. Transplant.* 2011; 11: 2093–109.

125. Holley JL, Fenton RA, Arthur RS. Thallium stress testing does not predict cardiovascular risk in diabetic patients with end-stage renal disease undergoing cadaveric renal transplantation. Am J Med 1991; 90:563.

126. Abbott KC, Swanson SJ, Agodoa LY, Kimmel PL. Human immunodeficiency virus infection and kidney transplantation in the era of highly active antiretroviral therapy and modern immunosuppression. J Am Soc Nephrol 2004;15:1633-9

127. Gathogo EN, Hamzah , Hilton R, et al. Kidney transplantation in HIV-positive adults: the UK experience. Int J STD AIDS. 2014 Jan;25(1):57-66.

128. Pereira BJ, Natov SN, Bouthot BA, et al. Effects of hepatitis C infection and renal transplantation on survival in end-stage renal disease. Kidney Int 1998;53:1374-81

129. Patel HV, Kute VB, Vanikar AV et al. Clinical outcome of renal transplantation in end-stage renal disease patients with positive pretransplantation hepatitis B surface antigen. Transplant Proc. 2012 Jan;44(1):72-4.

130. Friedman AN, Miskulin DC, Rosenberg IH et al. Demographics and trends in overweight and obesity in patients at time of kidney transplantation. Am. J. Kidney Dis. 2003; 41: 480–87.

131. Modlin CS, Flechner SM, Goormastic M, et al. Should obese patients lose weight before receiving a kidney transplant? Transplantation. 1997;64:599-604.
132. Lynch RJ, Ranney DN, Shijie C, Lee DS, Samala N, Englesbe MJ. Obesity, surgical site infection, and outcome following renal transplantation. Annals of Surgery. 2009; 250:1014-1020.
133. Gore JL, Pham PT, Danovitch GM, et al. Obesity and outcome following renal transplantation. Am J Transplant. 2006;6:357-363.
134. Glanton CW, Kao TC, Cruess D, Agodoa LY, Abbott KC. Impact of renal transplantation on survival in end-stage renal disease patients with elevated body mass index. Kidney Int. 2003;63(2):647-653.
135. Meier-Kriesche H-U, Arndorfer JA, and Kaplan B. The impact of body mass index on renal transplant outcomes: a significant independent risk factor for graft failure and patient death. Transplantation. 2002;73:70-74.
136. Aalten J, Christiaans MH, de Fijter H, et al. The influence of obesity on short- and long-term graft and patient survival after renal transplantation. Transpl Int. 2006;19: 901-907.
137. Howard RJ, Thai VB, Patton PR, et al. Obesity does not portend a bad outcome for kidney transplant recipients. Transplantation. 2002;73:53-55.
138. Chang SH, Coates PTH, McDonald SP. Effects of body mass index at transplant on outcomes of kidney transplantation. Transplantation. 2007;84:981-987.
139. Batabyal P, Chapman JR, Wong G, et al. Clinical practice guidelines on wait-listing for kidney transplantation: consistent and equitable? Transplantation 2012; 94:703.
140. Chapman JR, Sheil AG, Disney AP. Recurrence of cancer after renal transplantation. Transplant Proc 2001; 33:1830.
141. Penn I. Evaluation of transplant candidates with pre-existing malignancies. Ann. Transplant. 1997; 2: 14–17.
142. Maisonneuvre P, Agodoa L, Gellert R, et al. Cancer in patients on dialysis for end-stage renal disease: An international collaborative study. Lancet 1999;10:93-9

143. Kiberd BA, Keough-Ryan T, Clase CM. Screening for prostate, breast and colorectal cancer in renal transplant recipients. Am J Transplant 2003; 3: 619-25

144. Kasiske B and Klinger D. Cigarette smoking in renal transplant recipients. J Am Med Assoc 2000;11:753-59

145. Sung RS, Althoen M, Howell TA, et al. Excess risk of renal allograft loss associated with cigarette smoking. Transplantation 2001;71(12):1752-57

146. Sekhri N, Timmis A, Chen R, Junghans C, Walsh N, Zaman J, et al. Inequity of access to investigation and effect on clinical outcomes: prognostic study of coronary angiography for syspected stable angina pectoris. BMJ. 2008 May 10, 2008;336(7652):1058-61.

147. Wood DJ, Clark D, Gatrell AC. Equity of access to adult hospice inpatient care within north-west England. Palliative Medicine. 2004;18(6):543

148. Ward PR, Noyce PR, St Leger AS. Are GP practice prescribing rates for coronary heart disease drugs equitable? A cross sectional analysis in four primary care trusts in England. Journal of Epidemiology and Community Health. 2004;58:89-96.

149. Szczepura A, Price C, Gumber A. Breast and bowel cancer screening uptake patterns over 15 years for UK south Asian ethnic minority populations, corrected for differences in socio-demographic characteristics. BMC Public Health. 2008;8:346. doi:10.1186/1471-2458-8-346.

150. Majeed FA, Cook DG, Given-Wilson R, Vecchi P, Poloniecki J. Do general practitioners influence the uptake of breast cancer screening?. J Med Screen. 1995;2(3):119-24.

151. Judge A, Welton NJ, Sandhu J, Ben-Shlomo Y. Equity in access to total joint replacement of the hip and knee in England: cross sectional study. The BMJ. 2010;341:c4092. doi:10.1136/bmj.c4092.

152. Judge A, Welton NJ, Sandhu J, and Ben-Shlomo Y. Geographical variation in the provision of elective primary hip and knee replacement: the role of socio-demographic, hospital and distance variables. J Public Health (2009) 31 (3): 413-422.

153. Dudley CR, Johnson RJ, Thomas HL et al. Factors that influence access to the national renal transplant waiting list. Transplantation 2009;88:96–102.
154. Ravanan R, Udayaraj U, Steenkamp R, Ansell D, Tomson C. The tenth annual report. Chapter 11. Measures of care in adult renal transplant recipients in the UK. Bristol: UK Renal registry, 2007.
155. MacMillan MA, Briggs JD. Survey of patient selection for cadaveric renal transplantation in the United Kingdom. Nephrol Dial Transplant 1995;10(6): 855-8
156. Wolfe RA, Ashby VB, Milford EL, et al. Differences in access to cadaveric renal transplantation in the United States. Am J Kidney Dis. 2000 Nov;36(5):1025-33.
157. Gaylin DS, Held PJ, Port FK, Hunsicker LG, Wolfe RA, Kahan BD, Jones CA, Agodoa LY. The impact of comorbid and socio-demographic factors on access to renal transplantation. JAMA. 1993;269:603-8.
158. Satayathum S, Pisoni RL, McCullough KP, et al. Kidney transplantation and wait-listing rates from the international Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int. 2005 Jul;68(1):330-7.
159. A multicentre study of registration on renal transplantation waiting list of the elderly and patients with type 2 diabetes. Nephrol. Dial. Transplant. (2004) 19 (1): 207-214
160. Bayat S, Frimat L, Thilly N, et al. Medical and non-medical determinants of access to renal transplant waiting list in a French community-based network of care. Nephrol Dial Transplant 2006; 21: 2900.
161. Bloembergen WE, Mauger EA, Wolfe RA, Port FK. Association of gender and access to cadaveric renal transplantation. Am J Kidney Dis 1997;30: 733-8
162. Abbott KC, Glanton CW, Agodoa LY. Body mass index and enrollment on the renal transplant waiting list in the United States. Nephrol. 2003 Jan-Feb;16(1):40-8.
163. http://www.ons.gov.uk/ons/guide-method/census/2011/census-data/index.html (Accessed June 25, 2016)

164. Li S, McAlpine DD, Liu J, Li S, Collins AJ. Differences between blacks and whites in the incidence of end-stage renal disease and associated risk factors. Adv Ren Replace Ther 11 : 5 –13, 2004

165. Hostetter TH: Research opportunities for reducing racial disparities in kidney disease. Adv Ren Replace Ther 11 : 59 –65, 2004

166. Tzur S, Rosset S, Shermer R et al. Missense mutations in the APOL1 gene are highly associated with end stage kid- ney disease risk previously attributed to the MYH9 gene. Hum Genet 2010: 128: 345.

167. Hsu CY, Lin F, Vittinghoff E, et al. Racial differences in the progression from chronic renal insufficiency to end-stage renal disease in the United States. J Am Soc Nephrol 2003;14:2902–7.

168. Peralta CA, Ziv E, Katz R, et al. African ancestry, socioeconomic status, and kidney function in elderly African–Americans: a genetic admixture analysis. J Am Soc Nephrol 2006;17:3491–6.

169. Udayaraj U, Pruthi R, Casula A, Roderick P. UK Renal Registry 16th annual report: chapter 6 demographics and outcomes of patients from different ethnic groups on renal replacement therapy in the UK. Nephron Clin Pract. 2013;125(1-4):111

170. Tarver-Carr ME, Powe NR, Eberhardt MS, LaVeist TA, Kington RS, Coresh J, Brancati FL. Excess risk of chronic kidney disease among African-American versus white subjects in the United States: a population-based study of potential explanatory factors. J Am Soc Nephrol. 2002 Sep;13(9):2363-70.

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

172. Castledine et al. How much of the regional variation in RRT incidence rates within the UK is explained by the health needs of the general population? Nephrol Dial Transplant 2012 Oct;27(10):3943–3950

173. Wohland P et al. Life Expectancy variation across England's local areas by ethnic group in 2001. Journal of Maps; 6(1):354–359

174. Pei YP, Greenwood CM, Chery AL, Wu GG. Racial differences in survival of patients on dialysis. Kidney Int 2000;58(3):1293-9.

175. Roderick P, Byrne C, Casula A, Steenkamp R, Ansell D, Burden R, Nitsch D, Feest T. Survival of patients from South Asian and Black populations starting renal replacement therapy in England and Wales. Nephrol Dial Transplant. 2009 Dec;24(12):3774-82.

176. Rudge C, Johnson RJ, Fuggle SV, Forsythe JL. Renal transplantation in the United Kingdom for patients from ethnic minorities. Transplantation 2007;83 (9):1169-73.

177. 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.

178. Udayaraj U, Ben-Shlomo Y, Roderick P, Casula A, Dudley C, Johnson R, Collett D, Ansell D, Tomson C, Caskey F. Social deprivation, ethnicity, and access to the deceased donor kidney transplant waiting list in England and Wales.Transplantation. 2010 Aug 15;90(3):279-85.

179. Udayaraj U, Ben-Shlomo Y, Roderick P, Casula A, Dudley C, Collett D, Ansell D, Tomson C, Caskey F. Social deprivation, ethnicity, and uptake of living kidney donor transplantation in the United Kingdom. Transplantation. 2012 Mar 27;93(6):610-6.

180. Minniefield WJ, Yang J, Muti P. Differences in attitudes toward organ donation among African Americans and whites in the United States. J Natl Med Assoc 2001;**93**(10):372-79.

181. 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.

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

183. 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.

184. Lentine KL, Schnitzler MA, Xiao H, et al. Racial variation in medical outcomes among living kidney donors. N Engl J Med 2010;**363**(8):724-32.

185. Segev DL, Muzaale AD, Caffo BS, et al. Perioperative mortality and long-term survival following live kidney donation. JAMA 2010;**303**(10):959-66.

186. Weng FL, Reese PP, Mulgaonkar S, Patel AM. Barriers to Living Donor Kidney Transplantation among Black or Older Transplant Candidates. Clinical Journal of the American Society of Nephrology : CJASN 2010;**5**(12):2338-47.
187. Townsend, P. (1979) Poverty in the United Kingdom, London, Allen Lane and Penguin Books
188. Townsend P, Phillimore P, Beattie A. Health and Deprivation: Inequality and the North. Croom Helm, 1988
189. Carstairs V, Morris R. Deprivation and health in Scotland. Aberdeen: Aberdeen University Press, 1991
190. Jarman B. Identification of underprivileged areas. Br Med J (Clin Res Ed). 1983 May 28;286(6379):1705-9.
191. Noble M, Wright G, Dibben C, et al. Indices of Deprivation 2004. Report to the Office of the Deputy Prime Minister. London: Neighbourhood Renewal Unit, 2004.
192. McLoone P. Targeting deprived areas within small areas in Scotland: population study. BMJ 2001;323:374–5.
193. Blakely T, Pearce N. Socio-economic position is more than just NZDep. N Z Med J 2002;115:109–11.
194. Davey Smith G, Hart C, Watt G, et al. Individual social class, area-based deprivation, cardiovascular disease risk factors, and mortality: the Renfrew and Paisley study. J Epidemiol Community Health 1998;52:399–405.
195. Shoham DA, Vupputuri S, Kaufman JS, et al. Kidney disease and the cumulative burden of life course socioeconomic conditions: the Atherosclerosis Risk in Communities (ARIC) study. Soc Sci Med. 2008 Oct;67(8):1311-20.
196. Krop JS, Coresh J, Chambless LE, et al. A community-based study of explanatory factors for the excess risk for early renal function decline in blacks vs whites with diabetes: the Atherosclerosis Risk in Communities study. Arch Intern Med. 1999 Aug 9-23;159(15):1777-83.
197. Merkin SS, Coresh J, Diez Roux AV, et al. Area socioeconomic status and progressive CKD: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Kidney Dis. 2005 Aug;46(2):203-13.

198. Caskey FJ, Roderick P, Steenkamp R, et al. Social deprivation and survival on renal replacement therapy in England and Wales. Kidney Int. 2006 Dec;70(12):2134-40.
199. Obialo CI, Ofili EO, Quarshie A, Martin PC. Ultralate referral and presentation for renal replacement therapy: socioeconomic implications. Am J Kidney Dis. 2005 Nov;46(5):881-6.
200. Bello AK, Peters J, Rigby J, Rahman AA, El Nahas M. Socioeconomic status and chronic kidney disease at presentation to a renal service in the United Kingdom. Clin J Am Soc Nephrol. 2008 Sep;3(5):1316-23.
201. Port FK, Wolfe RA, Levin NW, Guire KE, Ferguson CW. Income and survival in chronic dialysis patients. ASAIO Trans. 1990 Jul-Sep;36(3):M154-7.
202. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. Circulation 1993;88(4 Pt 1):1973-98.
203. Rovelli M, Palmeri D, Vossler E, Bartus S, Hull D, Schweizer R. Non-compliance in renal transplant recipients: evaluation by socioeconomic groups. Transplant Proc 1989;21(6):3979-81.
204. Garg PP, Diener-WestM, Powe NR. Income-based disparities in outcomes for patients with chronic kidney disease. Semin Nephrol 2001;(4):377-85.
205. Roodnat JI, Laging M, Massey EK et al. Accumulation of unfavorable clinical and socioeconomic factors precludes living donor kidney transplantation. Transplantation 2012;93:518–23.
206. Gore JL, Danovitch GM, Litwin MS et al. Disparities in the utilization of live donor renal transplantation. Am J Transplant 2009;9:1124–33.
207. Axelrod DA, Dzebisashvili N, Schnitzler MA et al. The interplay of socioeconomic status, distance to center, and interdonor service area travel on kidney transplant access and outcomes. Clin J Am Soc Nephrol 2010;5:2276–88.
208. Schold JD, Heaphy ELG, Buccini LD et al. Prominent impact of community risk factors on kidney transplant candidate processes and outcomes. Am J Transplant 2013;13:2374–83.

209. Grace BS, Clayton PA, Cass A et al. Transplantation rates for living- but not deceased-donor kidneys vary with socioeconomic status in Australia. Kidney Int 2013;83:138–45.

210. 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.

211. 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.

212. Coulter A, McPherson K, Vessey M. Do British women undergo too many or too few hysterectomies?. Soc Sci Med. 1988;27(9):987-94.

213. Bradley EH, Herrin J, Wang Y, et al. Strategies for reducing the door-to-balloon time in acute myocardial infarction. N Engl J Med. 2006 Nov 30;355(22):2308-20.

214. Bradley EH, Curry LA, Webster TR, et al. Achieving rapid door-to-balloon times: how top hospitals improve complex clinical systems. Circulation. 2006 Feb 28;113(8):1079-85.

215. Majeed A, Eliahoo J, Bardsley M, Morgan D, Bindman AB. Variation in coronary artery bypass grafting, angioplasty, cataract surgery, and hip replacement rates among primary care groups in London: association with population and practice characteristics. J Public Health Med. 2002 Mar;24(1):21-6.

216. Geller SE, Burns LR, Brailer DJ. The impact of nonclinical factors on practice variations: the case of hysterectomies. Health Serv Res. 1996 Feb;30(6):729-50

217. Plantinga LC, Fink NE, Jaar BG, et al. Frequency of sit-down patient care rounds, attainment of clinical performance targets, hospitalization, and mortality in hemodialysis patients. J Am Soc Nephrol. 2004 Dec;15(12):3144-53

218. Plantinga LC, Jaar BG, Fink NE, et al. Frequency of patient-physician contact in chronic kidney disease care and achievement of clinical performance targets. Int J Qual Health Care. 2005 Apr;17(2):115-21. Epub 2005 Feb 21.

219. Spiegel B, Bolus R, Desai AA, et al. Dialysis practices that distinguish facilities with below- versus above-expected mortality. Clin J Am Soc Nephrol. 2010 Nov;5(11):2024-33.
220. Castledine CI, Gilg JA, Rogers C, Ben-Shlomo Y, Caskey FJ. Renal centre characteristics and physician practice patterns associated with home dialysis use. Nephrol Dial Transplant. 2013 Aug;28(8):2169-80.
221. http://www.renal.org/docs/default-source/clinical-service/clinical-service/Timely_Listing.pdf?sfvrsn=0
222. Pruthi R, Ravanan R, O'Neill J, Roderick P, Pankhurst P, Udayaraj U. UK Renal Registry 15th Annual Report: Chapter 9 Centre Variation in Access to Renal Transplantation in the UK (2006–2008). Nephron Clin Pract 2013;123(suppl1):183–193 DOI: 10.1159/000353328
223. Herdman M, Gudex C, Lloyd A, *et al*. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011;**10**:1727–36.
224. Riazi A, Bradley C, Barendse S, *et al*. Development of the Well-being questionnaire short-form in Japanese: the W-BQ12. *Health Qual Life Outcomes* 2006;**4**:40.
225. Bradley C. The 12-item Well-Being Questionnaire. Origins, current stage of development, and availability. *Diabetes Care* 2000;**23**:875. http://bmjopen.bmj.com/cgi/ijlink?linkType=PDF&journalCode=diacare&resid=23/6/875
226. McMillan CV, Bradley C, Gibney J, *et al*. Psychometric properties of two measures of psychological well-being in adult growth hormone deficiency. *Health Qual Life Outcomes* 2006;**4**:16.
227. Mitchell J, Bradley C. Psychometric evaluation of the 12-item Well-being Questionnaire for use with people with macular disease. *Qual Life Res* 2001;**10**:465–73.
228. Ansell D, Tomson C, R, V, UK Renal Registry 11th Annual Report (December 2008): Chapter 15 The UK Renal Registry, UKRR database, validation and methodology. Nephron Clin Pract 2009;111(suppl 1):c277-c285

229. UK Renal Registry 17th Annual Report: Appendix A The UK Renal Registry Statement of Purpose. Nephron 2015;129(suppl 1):267-271

230. Pruthi R, Hilton R, Pankhurst L, Mamode N, Hudson A, Roderick P, Ravanan R, UK Renal Registry 16th Annual Report: Chapter 4 Demography of Patients Waitlisted for Renal Transplantation in the UK: National and Centre-specific Analyses. Nephron Clin Pract 2013;125:81-98

231. Hall YN, Choi AI, Xu P, O'Hare AM, Chertow GM. Racial Ethnic Differences in Rates and Determinants of Deceased Donor Kidney Transplantation. Journal of the American Society of Nephrology : JASN. 2011;22(4):743-751. doi:10.1681/ASN.2010080819.

232. Tong A, Chapman JR, Wong G, Kanellis J, McCarthy G, Craig JC. The motivations and experiences of living kidney donors: a thematic synthesis. Am J Kidney Dis. 2012 Jul;60(1):15-26. doi: 10.1053/j.ajkd.2011.11.043. Epub 2012 Feb 4.

233. Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Ralph AF, Tong A. The expectations and attitudes of patients with chronic kidney disease toward living kidney donor transplantation: a thematic synthesis of qualitative studies. Transplantation. 2015 Mar;99(3):540-54. doi:10.1097/TP.0000000000000433.

234. Ralph AF, Butow P, Hanson CS, Chadban SJ, Chapman JR, Craig JC, Kanellis J, Luxton G, Tong A. Donor and Recipient Views on Their Relationship in Living Kidney Donation: Thematic Synthesis of Qualitative Studies. Am J Kidney Dis. 2017 May;69(5):602-616. doi: 10.1053/j.ajkd.2016.09.017. Epub 2016 Nov 23.

235. Roodnat JI, van de Wetering J, Zuidema W, van Noord MA, Kal-van Gestel JA, Ijzermans JN, Weimar W.Ethnically diverse populations and their participation in living kidney donation programs. Transplantation 2010: 89: 1263.

236. Cooper M, Kramer A, Barth R, Phelan M. Living kidney donor relationship in caucasian and African American populations and implications for targeted donor education programs. Clin Transplant 2013: 27: 32.

237. http://www.usrds.org/2015/view/v2_07.aspx (accessed March 2016)

238. Thiel GT, Nolte C, Tsinalis D. Gender imbalance in living kidney donation in Switzerland. Transplant Proc. 2005;37:592–4.
239. Davis CL, Cooper M. The State of U.S. Living Kidney Donors. Clinical Journal of the American Society of Nephrology : CJASN. 2010;5(10):1873-1880. doi:10.2215/CJN.01510210.
240. https://www.organdonation.nhs.uk
241. Bailey PK, Tomson CRV, Ben-Shlomo Y. Study of living kidney donor–recipient relationships: variation with socioeconomic deprivation in the white population of England. Clin Transplant 2013: 27: E327–E331 DOI: 10.1111/ctr.12120.
242. Yardley, L. & Marks, D. F. (2004). Introduction to research methods in clinical and health psychology. In Marks, D.F. & Yardley, L. (Eds). Research Methods for Clinical and Health Psychology. Sage Publications; London, UK.
243. Eisner, E.W. (2003). On the art and science of qualitative research in psychology. In Camic, P.M., Rhodes, J.E. & Yardley, L. (Eds). Qualitative research in psychology: expanding perspectives in methodology and design. American Psychological Association; Washington DC, USA.
244. Judith Green and Nicki Thorogood. Qualitative methods for health research, 3rd Edition. SAGE Publications Ltd. 2014.
245. Bloch, M. (2004). A discourse that disciplines, governs, and regulates: On scientific research in education. Qualitative Inquiry, 10(2), 235-245.
246. Morgan D L. The focus group guide book. London: Sage Publications, 1998.
247. Clive Seale (2004). Quality in Qualitative Research in Qualitative Research Practice. Sage Publications; London, UK.
248. Ritchie J, Lewis J. Qualitative research practice: a guide for social science students and researchers. London: Sage; 2003.
249. Heath G, Cameron E, Cummins C, Greenfield S, Pattison H, Kelly D, Redwood S. Paediatric 'care closer to home': stake-holder views and barriers to implementation. Health Place. 2012;18(5):1068–1073. doi: 10.1016/j.healthplace.2012.05.003.

250. Elkington H, White P, Addington-Hall J, Higgs R, Petternari C. The last year of life of COPD: a qualitative study of symptoms and services. Respir Med. 2004;98(5):439–445. doi: 10.1016/j.rmed.2003.11.006.

251. Murtagh J, Dixey R, Rudolf M. A qualitative investigation into the levers and barriers to weight loss in children: opinions of obese children. Archives Dis Child. 2006;91(11):920–923. doi: 10.1136/adc.2005.085712.

252. Ellis J, Wagland R, Tishelman C, Williams ML, Bailey CD, Haines J, Caress A, Lorigan P, Smith JA, Booton R. et al. Considerations in developing and delivering a nonpharmacological intervention for symptom management in lung cancer: the views of patients and informal caregivers. J Pain Symptom Manag (0) 2012;44(6):831–842.

253. Gale NK, Heath G, Cameron E, Rashid S, Redwood S. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Medical Research Methodology. 2013;13:117. doi:10.1186/1471-2288-13-117.

254. Joffe, H. & Yardley, L. (2004). Content and thematic analysis. In Marks, D. F. & Yardley, L. (Eds). Research Methods for Clinical and Health Psychology. Sage publications: London UK.

255. Braun, V. & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative research in psychology,* 3, 77-101.

256. Guest, Gregg (2012). Applied thematic analysis. Thousand Oaks, California: Sage. p. 17.

257. Jane Ritchie et al (2013) Qualitative Research Practice, London: SAGE.

258. Feminist Qualitative Research and Grounded Theory: Complexities, Criticisms, and Opportunities. (2007). In A. Bryant, & K. Charmaz (Eds.), The SAGE Handbook of Grounded Theory. (pp. 417-436). London, England: SAGE Publications Ltd.

259. Michael Quinn Patton, (2002) Qualitative Research & Evaluation Methods, Sage Publications.

260. Planning, Initiating and Withdrawal of Renal Replacement Therapy. http://www.renal.org/guidelines/modules/planning-initiating-and-

withdrawal-of-renal-replacement-therapy#sthash.zl7vrDXg.dpbs. Accessed December 10, 2015.

261. Akolekar D, Oniscu GC, Forsythe JL. Variations in the assessment practice for renal transplantation across the United Kingdom. Transplantation. 2008 Feb 15;85(3):407-410.

262. Renal Physicians Association. Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis, 2nd ed, Rockville, MD, Renal Physicians Association, 2010

263. AH Moss. Revised dialysis clinical practice guideline promotes more informed decision-making. Clin J Am Soc Nephrol 2010;5:2380-3.

264. National Kidney Foundation, Inc. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. 2002.

265. Patient and caregiver values, beliefs and experiences when considering home dialysis as a treatment option: a semi-structured interview study. Walker RC, Howard K, Morton RL, Palmer SC, Marshall MR, Tong A. Nephrol Dial Transplant. 2016 Jan;31(1):133-41.

266. Nephrologists' Perspectives on Recipient Eligibility and Access to Living Kidney Donor Transplantation. Hanson CS, Chadban SJ, Chapman JR, Craig JC, Wong G, Tong A. Transplantation. 2016 Apr;100(4):943-53.

267. Calestani M, Tonkin-Crine S, Pruthi R, et al; ATTOM Investigators. Patient attitudes towards kidney transplant listing: qualitative findings from the ATTOM study. Nephrol Dial Transplant. 2014 Nov;29(11):2144-2150.

268. The views of patients and carers in treatment decision making for chronic kidney disease: systematic review and thematic synthesis of qualitative studies. Morton RL, Tong A, Howard K, Snelling P, Webster AC. BMJ. 2010 Jan 19;340:c112. doi: 10.1136/bmj.c112.

269. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/216980/Liberating-the-NHS-No-decision-about-me-without-me-Government-response.pdf

270. Lunsford SL, Simpson KS, Chavin KD, et al. Racial differences in coping with the need for kidney transplantation and willingness to ask for live organ donation. Am J Kidney Dis. 2006; 47: 324–331.

271. Ayanian JZ, Cleary PD, Weissman JS, Epstein AM. The effect of patients' preferences on racial differences in access to renal transplantation. N Engl J Med. 1999 Nov 25;341(22):1661-9.

272. Mistrust, misperceptions, and miscommunication: a qualitative study of preferences about kidney transplantation among African Americans. Wachterman MW, McCarthy EP, Marcantonio ER, Ersek M. Transplant Proc. 2015 Mar;47(2):240-6. doi: 10.1016/j.transproceed.2015.01.016.

273. Kidney transplant referral guide – OPTN Minority affairs committee http://optn.transplant.hrsa.gov/ContentDocuments/Guidance_Kidney_Transplant_Referral.pdf. Accessed December 10, 2015.

274. Abramowicz D, Cochat P, Claas FH, et al. European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care. Nephrol Dial Transplant. 2015 Nov;30(11):1790-1797.

275. British Transplantation Society. Standards for solid organ transplantation in the United Kingdom. Available at: http://www.bts.org.uk/BTS/Guidelines_Standards/Current/BTS/Guidelines_Standards/Current_Guidelines.aspx?hkey=e285ca32-5920-4613-ac08-fa9fd90915b5. Accessed December 10, 2015.

276. Fritsche L, Vanrenterghem Y, Nordal KP, et al. Practice variations in the evaluation of adult candidates for cadaveric kidney transplantation: A survey of the European Transplant Centers. Transplantation. 2000;70:1492-1497.

277. Pruthi R, Calestani M, Leydon G, et al. Access to transplantation and transplant outcome measures (ATTOM): Exploring healthcare professionals' perspectives on access to renal transplantation in the UK. Nephrology Dialysis Transplantation. Conference: 50th ERA-EDTA Congress Istanbul Turkey. http://www.abstracts2view.com/era_archive/view.php?nu=ERA13L_453038. Accessed November 5, 2015.

278. Office of National Statistics. http://www.ons.gov.uk. Accessed December 10, 2015.

279. Recommendations of the National Renal Workforce Planning Group 2002. http://www.britishrenal.org/BritishRenalSociety/files/24/24f2096f-442e-44c3-9ae0-51d9382b5292.pdf. Accessed December 10, 2015.

280. Levin A, Lewis M, Mortiboy P, et al. Multidisciplinary predialysis programs: quantification and limitations of their impact on patient outcomes in two Canadian settings. Am J Kidney Dis. 1997;29:533-540.
281. Ravani P, Marinangeli G, Stacchiotti L, Malberti F. Structured pre-dialysis programs: More than just timely referral? J Nephrology. 2003;16:862-869.
282. Ravani P, Marinangeli G, Tancredi M, Malberti F. Multidisciplinary chronic disease management improves survival on dialysis. J Nephrology. 2003;16:870-877.
283. Buck J, Baker R, Cannaby A-M, Nicholson S, Peters J, Warwick J. Why do patients known to renal services still undergo urgent dialysis initiation? A cross-sectional survey. Nephrol Dial Transplant. 2007;22:3240-3245.
284. Renal Transplantation – NHS England. https://www.england.nhs.uk/wp-content/uploads/2014/04/a07-renal-transpl-ad-0414.pdf. Accessed December 10, 2015.
285. Lamb BW, Brown KF, Nagpal K, Vincent C, Green JS, Sevdalis N. Quality of care management decisions by multidisciplinary cancer teams: a systematic review. Ann Surg Oncol. 2011 Aug;18(8):2116-2125.
286. Bosch M, Faber M, Voerman G, et al. Quest for Quality and Improved Performance: Quality Enhancing Interventions Patient Care Teams. (2009). Available online at http://www.health.org.uk/sites/default/files/QuestForQualityAndImprovedPerformanceQualityEnhancingInterventions_PatientCareTeams.pdf. Accessed December 10, 2015.
287. Raine R, Wallace I, Bhaird C, et al. Improving the effectiveness of multidisciplinary team meetings for patients with chronic diseases: a prospective observational study.http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0011/131420/ScientificSummary-hsdr02370.pdf. Accessed December 15, 2015.
288. Matas AJ, Kasiske B, Miller L. Proposed guidelines for re-evaluation of patients on the waiting list for renal cadaver transplantation. Transplantation. 2002;73:811-812.

289. Browne, W. and Rasbash, J. (2004). 'Multilevel Modelling', in Hardy, M. and Bryman, A. (eds.), Handbook of data analysis, Sage Publications, pp 459-78.
290. Pinheiro, J.C. and Bates, D.M. (2000). Mixed-Effects Models in S and S-PLUS, Springer.
291. Raudensbush, S.W. and Bryk, A.S. (2002). Hierarchical Linear Models, Sage Publications.
292. Marinovich S, Lavorato C, Rosa-Diez G, Bisigniano L, Fernández V, Hansen-Krogh D. The lack of income is associated with reduced survival in chronic haemodialysis. Nefrologia. 2012; 32:79–88.
293. Kimmel PL, Fwu CW, Eggers PW. Segregation, income disparities, and survival in hemodialysis patients. J Am Soc Nephrol. 2013; 24:293–301.
294. Xu R, Han QF, Zhu TY, et al. Impact of individual and environmental socioeconomic status on peritoneal dialysis outcomes: A retrospective multicenter cohort study. PLoS ONE. 2012; 7:e50766.
295. Rovelli M, Palmeri D, Vossler E, Bartus S, Hull D, Schweizer R. Noncompliance in renal transplant recipients: evaluation by socioeconomic groups. Transplant Proc. 1989 Dec;21(6):3979-81.
296. Cass A, Cunningham J, Snelling P, Ayanian JZ. Late referral to a nephrologist reduces access to renal transplantation. Am J Kidney Dis. 2003 Nov;42(5):1043-9.
297. Udayaraj UP, Ben-Shlomo Y, Roderick P, Casula A, Ansell D, Tomson CR, Caskey FJ. Socio-economic status, ethnicity and geographical variations in acceptance rates for renal replacement therapy in England and Wales: an ecological study. J Epidemiol Community Health. 2010 Jun;64(6):535-41. doi: 10.1136/jech.2009.093518. Epub 2009 Oct 23.
298. Bailey PK, Ben-Shlomo Y, Tomson CR, Owen-Smith A. Socioeconomic deprivation and barriers to live-donor kidney transplantation: a qualitative study of deceased-donor kidney transplant recipients. BMJ Open. 2016 Mar 2;6(3):e010605. doi: 10.1136/bmjopen-2015-010605.
299. Zimmerman D, Albert S, Llewellyn-Thomas H, Hawker GA. The influence of socio-demographic factors, treatment perceptions and attitudes to living donation on willingness to consider living kidney donor among kidney

transplant candidates. Nephrol Dial Transplant. 2006 Sep;21(9):2569-76. Epub 2006 May 15. PMID: 16702204

300. Hiller J, Sroka M, Weber R, Morrison AS, Ratner LE. Identifying donor concerns to increase live organ donation. J Transpl Coord. 1998 Mar;8(1):51-4. PMID: 9726221

301. Schaeffner ES, Mehta J, Winkelmayer WC. Educational level as a determinant of access to and outcomes after kidney transplantation in the United States. Am J Kidney Dis. 2008 May;51(5):811-8. doi: 10.1053/j.ajkd.2008.01.019. Epub 2008 Apr 3.

302. Goldfarb-Rumyantzev, A. S., Sandhu, G. S., Baird, B., Barenbaum, A., Yoon, J. H., Dimitri, N., Koford, J. K. and Shihab, F. (2012), Effect of education on racial disparities in access to kidney transplantation. Clinical Transplantation, 26: 74–81. doi:10.1111/j.1399-0012.2010.01390.x

303. Taylor DM, Bradley JA, Bradley C, Draper H, Johnson R, 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.

304. Morony S, Flynn M, McCaffery KJ, Jansen J, Webster AC. Readability of Written Materials for CKD Patients: A Systematic Review. Am J Kidney Dis. 2015 Jun;65(6):842-50. doi: 10.1053/j.ajkd.2014.11.025. Epub 2015 Feb 4.

305. Patel CR, Sanghvi S, Cherla DV, Baredes S, Eloy JA. Readability assessment of Internet-based patient education materials related to parathyroid surgery. Ann Otol Rhinol Laryngol. 2015;124:523-527.

306. 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

307. L.A. Dageforde, A.W. Petersen, I.D. Feurer, et al. Health literacy of living kidney donors and kidney transplant recipients. Transplantation, 98 (2014), pp. 88-93

308. Rodrigue, J. R., Cornell, D. L., Lin, J. K., Kaplan, B. and Howard, R. J. (2007), Increasing Live Donor Kidney Transplantation: A Randomized Controlled Trial of a Home-Based Educational Intervention. American Journal of Transplantation, 7: 394–401. doi:10.1111/j.1600-6143.2006.01623.x

309. Tong A, Hanson CS, Chapman JR, Halleck F, Budde K, Papachristou C, Craig JC. The preferences and perspectives of nephrologists on patients' access to kidney transplantation: a systematic review. Transplantation. 2014 Oct 15;98(7):682-91. doi: 10.1097/TP.0000000000000336.

310. Ghahramani N, Karparvar ZY, Ghahramani M, et al. Nephrologists' perceptions of renal transplant as treatment of choice for end-stage renal disease, preemptive transplant, and transplanting older patients: an international survey. Exp Clin Transplant 2011; 9: 223.

311. The Israel Penn International Transplant Tumour Registry www.ipittr.uc.edu/Home.cfm

312. Segev DL, Simpkins CE, Thompson RE, Locke JE, Warren DS, Montgomery RA. Obesity impacts access to kidney transplantation. J Am Soc Nephrol. 2008 Feb; 19(2):349-55.

313. Huml AM, Sehgal AR. BMI, Sex, and Access to Transplantation. Clinical Journal of the American Society of Nephrology : CJASN. 2014;9(5):843-844. doi:10.2215/CJN.02610314.

314. Johansen KL. Obesity and body composition for transplant wait-list candidacy – challenging or maintaining the BMI limits? Journal of renal nutrition : the official journal of the Council on Renal Nutrition of the National Kidney Foundation. 2013;23(3):207-209. doi:10.1053/j.jrn.2013.02.005.

315. Gill JS, Hendren E, Dong J, Johnston O, Gill J. Differential Association of Body Mass Index with Access to Kidney Transplantation in Men and Women. Clinical Journal of the American Society of Nephrology : CJASN. 2014;9(5):951-959. doi:10.2215/CJN.08310813.

316. Ojo A, Wolfe RA, Agodoa LY, et al. Prognosis after primary renal transplant failure and the beneficial effects of repeat transplantation: multivariate analyses from the United States Renal Data System. Transplantation 1998; 66: 1651-9.

317. Fuquay R, Teitelbaum I. Care of the patient after renal allograft failure: managing the present and planning for the future. Am J Nephrol 2012; 36: 348-54.

318. Weiner DE, Carpenter MA, Levey AS, et al. Kidney function and risk of cardiovascular disease and mortality in kidney transplant recipients: the FAVORIT trial. Am J Transplant 2012; 12: 2437-45.

319. Maduell F, Moreso F, Pons M, Ramos R, Mora-Macia J, Carreras J, et al. High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. J Am Soc Nephrol. 2013;24(3):487–97. doi: 10.1681/ASN.2012080875.

320. Schiffl H, Lang SM, Fischer R. Effects of high efficiency post-dilution on-line hemodiafiltration or conventional hemodialysis on residual renal function and left ventricular hypertrophy. Int Urol Nephrol. 2013;45(5):1389–96. doi: 10.1007/s11255-012-0336-4.

321. Knight RJ, Teeter LD, Graviss EA, Patel SJ, DeVos JM, Moore LW, Gaber AO. Barriers to preemptive renal transplantation: a single center questionnaire study. Transplantation. 2015 Mar;99(3):576-9.

322. Pruthi R, Casula A, Inward C, Roderick P, Sinha MD; British Association for Paediatric Nephrology. Early Requirement for RRT in Children at Presentation in the United Kingdom: Association with Transplantation and Survival. Clin J Am Soc Nephrol. 2016 May 6;11(5):795-802. doi: 10.2215/CJN.08190815. Epub 2016 Feb 15.

323. Levin A. Consequences of late referral on patient outcomes. Nephrol Dial Transplant. 2000;15 Suppl 3:8-13.

324. Boehm M, Winkelmayer WC, Arbeiter K, Mueller T, Aufricht C. Late referral to paediatric renal failure service impairs access to pre-emptive kidney transplantation in children. Arch Dis Child. 2010 Aug;95(8):634-8. doi: 10.1136/adc.2009.174581. Epub 2010 Jun 3.

325. Kurella Tamura M, Li S, Chen SC, Cavanaugh KL, Whaley-Connell AT, McCullough PA, Mehrotra RL. Educational programs improve the preparation for dialysis and survival of patients with chronic kidney disease. Kidney Int. 2014 Mar;85(3):686-92. doi: 10.1038/ki.2013.369. Epub 2013 Sep 25.

326. Mehrotra R, Marsh D, Vonesh E, Peters V, Nissenson A. Patient education and access of ESRD patients to renal replacement therapies beyond in-center hemodialysis. Kidney Int. 2005 Jul;68(1):378-90.