**Manuscript version: Author’s Accepted Manuscript**
The version presented in WRAP is the author’s accepted manuscript and may differ from the published version or Version of Record.

**Persistent WRAP URL:**
http://wrap.warwick.ac.uk/122785

**How to cite:**
Please refer to published version for the most recent bibliographic citation information. If a published version is known of, the repository item page linked to above, will contain details on accessing it.

**Copyright and reuse:**
The Warwick Research Archive Portal (WRAP) makes this work by researchers of the University of Warwick available open access under the following conditions.

Copyright © and all moral rights to the version of the paper presented here belong to the individual author(s) and/or other copyright owners. To the extent reasonable and practicable the material made available in WRAP has been checked for eligibility before being made available.

Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge. Provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way.

**Publisher’s statement:**
Please refer to the repository item page, publisher’s statement section, for further information.

For more information, please contact the WRAP Team at: wrap@warwick.ac.uk.
Equity-efficiency trade-offs associated with alternative approaches to deceased donor kidney allocation: a cost-effectiveness patient-level simulation

Bernadette Li, PhD
Department of Health Services Research and Policy
London School of Hygiene and Tropical Medicine
London, UK

John A. Cairns, MPhil
Department of Health Services Research and Policy
London School of Hygiene and Tropical Medicine
London, UK

Rachel J. Johnson, MSc
NHS Blood and Transplant
Bristol, UK

Christopher J. E. Watson, MD
Department of Surgery
University of Cambridge and the NIHR Cambridge Biomedical Research Centre
Cambridge, UK

Paul Roderick, MD
Primary Care and Population Sciences
Faculty of Medicine
University of Southampton
Southampton, UK

Gabriel C. Oniscu, MD
Transplant Unit
Royal Infirmary of Edinburgh
Edinburgh, UK

Wendy Metcalfe, MD
Scottish Renal Registry
Glasgow, UK
J. Andrew Bradley, PhD
Department of Surgery
University of Cambridge and the NIHR Cambridge Biomedical Research Centre
Cambridge, UK

Charles R. Tomson, DM
Department of Renal Medicine
Freeman Hospital
Newcastle upon Tyne, UK

Heather Draper, PhD
Division of Health Sciences
Warwick Medical School
University of Warwick
Coventry, UK

John L. Forsythe, MD
Transplant Unit
Royal Infirmary of Edinburgh
Edinburgh, UK

Christopher Dudley, MD
Richard Bright Renal Unit
Southmead Hospital
Bristol, UK

Rommel Ravanana, MD
Richard Bright Renal Unit
Southmead Hospital
Bristol, UK

CORRESPONDENCE TO:
Bernadette Li
Department of Health Services Research and Policy
London School of Hygiene and Tropical Medicine
15-17 Tavistock Place, London WC1H 9SH, UK
E-mail: bernadette.li@lshtm.ac.uk
AUTHORSHIP

BL and JAC participated in the development of the simulation model and analyses of data inputs. RJJ facilitated acquisition and interpretation of data from the UK Transplant Registry. All authors participated in the research design, performance of the research and writing of the article.

Disclosure: The authors declare no conflicts of interests.

Funding: This work was funded by a National Institute for Health Research (NIHR) Programme Grant for Applied Research (RP-PG-0109-10116).
ABSTRACT

Background: The number of patients waiting to receive a kidney transplant outstrips the supply of donor organs. We sought to quantify trade-offs associated with different approaches to deceased donor kidney allocation in terms of quality-adjusted life years (QALYs), costs and access to transplantation.

Methods: An individual patient simulation model was developed to compare five different approaches to kidney allocation, including the 2006 UK National Kidney Allocation Scheme (NKAS) and a QALY-maximisation approach designed to maximise health gains from a limited supply of donor organs. We used various sources of patient-level data to develop multivariable regression models to predict survival, health-state utilities and costs. We simulated the allocation of kidneys from 2200 deceased donors to a waiting list of 5500 patients and produced estimates of total lifetime costs and QALYs for each allocation scheme.

Results: Among patients who received a transplant, the QALY-maximisation approach generated 48,045 QALYs and cost £681 million while the 2006 NKAS generated 44,040 QALYs and cost £625 million. When also taking into consideration outcomes for patients who were not prioritised to receive a transplant, the 2006 NKAS produced higher total QALYs and costs and an incremental cost-effectiveness ratio of £110,741/QALY compared to the QALY-maximisation approach.

Conclusions: Compared to the 2006 NKAS, a QALY-maximisation approach makes more efficient use of deceased donor a limited supply of kidneys but reduces access to transplantation for older patients and results in greater inequity in the distribution of health gains between patients who receive a transplant and patients who remain on the waiting list.
ABBREVIATIONS

EPTS, expected post-transplant survival

HLA, human leukocyte antigen

ICER, incremental cost-effectiveness ratio

LYFT, life years from transplant

NKAS, national kidney allocation scheme

QALY, quality-adjusted life year

UKDRI, UK kidney donor risk index
INTRODUCTION

In 2017, there were approximately 5200 patients waiting to receive a kidney transplant in the UK.\(^1\) Because the number of patients waiting to receive a transplant far outstrips the supply of organs from deceased donors, many countries have put in place allocation systems that make the criteria for prioritising potential recipients transparent and explicit.\(^1\)

Some form of rationing is inevitable. In many countries, the approach to rationing is made explicit through the design of a national kidney allocation scheme. In the UK, a matching system between recipients and deceased donors has been in place since 1972.\(^2\) The approach to kidney allocation in the UK is subject to continuous audit and review and over the decades, the national scheme has undergone a number of revisions to address and balance considerations of both improving transplant outcomes and promoting equity in access to transplantation.\(^3\)\(^-\)\(^4\)

Simulation modelling is a practical tool that can be used to evaluate or prospectively test the impact of potential changes to kidney allocation schemes.\(^5\)\(^-\)\(^7\) As part of the Access to Transplantation and Transplant Outcomes Measure (ATTOM) study, we conducted a simulation exercise to explore and compare alternative approaches to allocating kidneys from deceased donors in the UK context. We approached the development of the simulation model with three key objectives in mind:

1. To simulate different approaches to kidney allocation that reflect varying degrees of emphasis on the competing objectives of efficiency (maximising health gains from scarce resources) and promoting equity in access to transplantation.

2. To report outcomes for each kidney allocation scheme in terms of both quality-adjusted life years (QALYs) and costs.
3. To maximise use of information on individual patient and donor characteristics to inform the allocation process and to account for between-patient variability in the estimation of outcomes.

**Kidney allocation concepts of interest**

The last major revision to the UK kidney allocation scheme took place in 2006. In this simulation exercise, we compared the 2006 national kidney allocation scheme (NKAS) to several alternative approaches, with a particular interest in exploring the feasibility of designing an allocation scheme that maximises health gains, expressed in terms of QALYs, among transplant recipients from a fixed supply of donor kidneys. The design of a QALY-maximisation allocation scheme was predicated on the following assumptions:

1. For patients awaiting a transplant, there is a treatment alternative, namely dialysis.
2. Not all donor kidneys will result in equally good survival outcomes.
3. Not all potential recipients will derive the same survival benefit from a given donor kidney.

In the QALY-maximisation scheme, for each donor kidney that becomes available, the simulation model estimates expected QALYs following transplant for each patient on the waiting list given the characteristics of both the patient and the donor kidney to be allocated. Next, the simulation model estimates expected QALYs for each patient on the waiting list if the patient were to remain on dialysis. After calculating the difference between expected QALYs following transplant and expected QALYs on dialysis, each kidney is allocated to the patient who is expected to gain the most as a result of receiving the transplant. Over the population of transplant recipients, this approach to allocation should yield the maximum total QALY gains for a fixed number of donor kidneys. This QALY-
maximisation scheme is conceptually similar to the Life Years from Transplant (LYFT) calculation previously described by Wolfe et al., but in the current simulation exercise we used UK data sources and adopted a different method to extrapolate survival using flexible parametric survival analysis in order to calculate QALYs. A new kidney allocation scheme based on the concept of longevity matching was introduced in the US in 2014. Under this concept, donor kidneys are risk-stratified using a scoring system in order to identify which kidneys are associated with better post-transplant survival. Similarly, potential recipients on the waiting list are risk-stratified based on estimates of their expected post-transplant survival (EPTS) score. The allocation policy then prioritises candidates in the top 20\textsuperscript{th} percentile of EPTS scores to receive kidneys from the top 20\% of donor kidneys. The cost implications of this new allocation policy in the US have been estimated. To test the concept of longevity matching in the UK context, we used a UK-specific kidney donor risk index (UKKDRI) and developed a multivariable parametric model to estimate mean post-transplant survival for potential recipients based on an analysis of historical UK Transplant Registry data. A key difference between our approach to estimating recipient post-transplant survival and the EPTS score used in the US kidney allocation scheme is that our survival predictions also take into account two donor characteristics: age and history of hypertension. Thus, in our simulation exercise, recipient post-transplant survival estimates for both the QALY-maximisation and longevity matching allocation schemes are recalculated for each potential donor-recipient combination. In addition to exploring the concepts of QALY-maximisation and longevity matching, we included two other allocation concepts in our simulation exercise that were intended to reflect greater emphasis on the principle of equity in access to transplant: random allocation
and allocation based on waiting time. Table 1 provides an overview of all five allocation
concepts explored in our simulation exercise.

METHODS

Characteristics of waiting list patients and donor kidneys

To simulate the composition of the transplant waiting list, we obtained data on 1948
prevalent listed patients who were recruited into the ATTOM study between November
2011 and September 2013. Of these patients, 513 had received a previous transplant. In
the absence of predictive survival models that would allow us to account for prior
transplants, we excluded these patients from the simulation exercise leaving a sample of
1435 patients, whose characteristics were replicated to make up a total waiting list of 5500
patients, which reflected the size of the waiting list at the time the simulation model was
designed (Table 2). During the simulation exercise, each time a patient received a
transplant, a replacement was added to the waiting list to keep it constant at 5500 patients.

For the donor dataset, we obtained characteristics of 2200 donors (4400 kidneys) from NHS
Blood and Transplant based on a representative historical cohort reflecting the time period
between January 2010 and December 2011 from NHS Blood and Transplant (Table 3).

Characteristics of individual patients and donors were assigned at the point of entry into the
model so that these characteristics could be used throughout the simulation to inform the
allocation process as well as to estimate survival, costs and health-state utilities. Most
patient characteristics, including comorbidities, were kept constant throughout the
simulation, however three characteristics were updated as simulation time progressed;
waiting time and time on dialysis were incremented on a daily basis, while patient age was
incremented annually.

Model structure and assumptions

The simulation model was constructed using the software package SIMUL8 2015
Professional version (SIMUL8 Corporation, Boston, MA, USA). At the start of the simulation,
prevalent waiting list patients are loaded and held in a queue while donor kidneys are
assumed to arrive at a fixed rate equivalent to 1200 deceased donors per year (Figure 1).
The allocation process is triggered by the arrival of each donor kidney. Using Visual Logic,
SIMUL8’s internal programming language, we are able to loop through patients on the
waiting list to evaluate blood group and tissue compatibility for each potential donor-
recipient combination and perform the necessary calculations and scoring algorithms
relevant to each allocation scheme of interest. In the model, we allowed for the possibility
that no appropriate match is identified for a kidney from a donor with a rare blood or tissue
type. This is unlikely to happen in practice but could occur in a small proportion of cases in
our simulation because the composition of the waiting list was based on a limited sample of
patients who were recruited into the ATTOM study. In the current UK allocation scheme,
tissue matching between the donor and recipient is determined on the basis of human
leukocyte antigens (HLA); patients are separated into one of four possible HLA mismatch
levels from level 1 (000-mismatched) to level 4 (poorly matched). In current practice,
patients with a level 4 HLA mismatch are not eligible to receive the donor kidney through
the national allocation scheme. In order to maintain comparability between allocation
schemes, we applied the same minimum criteria for blood group and HLA matching to all
allocation schemes in the simulation exercise.
Once a match has been identified, the recipient and donor kidney are assembled into a
single entity to simulate the transplantation event and moved to the next step in the
simulation process to determine post-transplant survival and to estimate lifetime QALYs and
costs. The model assumes only two events are possible following transplantation: graft
failure, in which the transplanted kidney stops working, or patient death. These events are
modelled as competing risks in which we randomly sample from the survival curve for each
event and move the patient to the event with the earliest sampled time. If a patient
experiences graft failure, we have assumed the patient returns to dialysis and faces the
same mortality risk as a patient who has been on the waiting list and receiving dialysis for >3
years. However, if the sampled value for time to death following graft failure is longer than
the time the patient would have survived based on the previously sampled value to
determine initial post-transplant outcomes, we replaced it with the lower value. We did not
attempt to model repeat transplants in the simulation.

The model was built by developing separate sections of Visual Logic code for each step in
the allocation process so that, for example, the same procedure to evaluate blood group
compatibility could be called at any point in the simulation for any of the five allocation
schemes. Internal spreadsheets were used extensively to perform interim calculations at the
patient level, which also facilitated model checks and step-by-step verification of the
simulation process.

Estimating life years, QALYs and costs

Survival models
There are three survival models underpinning time-to-event calculations to estimate post-
transplant patient survival, post-transplant graft failure and waiting list survival at various
points in the simulation. Each of these models was developed based on analysis of historical
UK Transplant Registry data. Data on dialysis start dates were additionally obtained through
linkage to the UK Renal Registry to inform the waiting list survival model. Models were fitted
using flexible parametric survival analysis in order to facilitate:

1. Extrapolation of survival curves to allow calculation of mean survival in years.
2. Inclusion of relevant patient and donor characteristics as covariates to capture variability
   in our predictions of survival and by extension in our estimates of costs and QALYs.

A more detailed description of the method used to fit the post-transplant patient survival
model is described elsewhere.\textsuperscript{11,12} A summary of the patient and donor characteristics that
were included as covariates in each of the final models is provided in Table S1. When the
survival models were used as part of the allocation process to match recipients and donor
kidneys (longevity matching and QALY-maximisation), they were applied deterministically to
produce mean survival estimates. When the survival models were used to inform competing
risks following transplantation in order to estimate lifetime QALYs and costs, we allowed for
stochastic variation.

\textit{Health-state utility estimates}

Health-state utility estimates for transplant recipient and patients on the waiting list were
captured in the ATTOM study using the EQ-5D-5L questionnaire. We developed
multivariable regression models to identify patient characteristics that led to variations in
utility scores to inform quality-adjustment of survival estimates in the simulation model (see
Table S2 for a list of characteristics included in the final models).\textsuperscript{16,17}
**Costs**

The costs of maintenance dialysis and transplant surgery were estimated in the simulation by applying fixed national tariffs.\(^{12,18}\) We estimated annual hospital costs using two-part regression models that were developed by analysing patient-level data from linkage of the Hospital Episode Statistics dataset to UK Renal Registry data.\(^{18,19}\) Hospital costs were captured by treatment modality (dialysis vs. transplantation) and by hospital setting (inpatient vs. outpatient) and regression models included a number of patient characteristics as covariates (Table S3a and Table S3b). For transplant recipients, the annual cost of maintenance immunosuppression assumed that patients received a combination of corticosteroids, a calcineurin inhibitor (ciclosporin or tacrolimus) and an antiproliferative agent (mycophenolate mofetil or azathioprine)\(^{20,20}\).

**Running the simulation**

For each allocation scheme, we performed three runs using a separate random number stream for each run. A single run ends when all 4400 donor kidneys have been allocated or removed from further consideration if no match has been identified. The proportion of donor kidneys for which no match was identified was approximately 1% across all simulation runs and therefore the number of patients who received a transplant was similar across allocation schemes.

Although we are primarily interested in comparing total costs and QALYs across all transplant recipients resulting from the different allocation schemes, it is also important to consider the outcomes of those patients who did not receive a transplant within the time frame of the simulation. For these patients, we made a simplifying assumption that they
face a mortality risk equivalent to remaining on the waiting list until death and used this as the basis for projecting their lifetime costs and QALYs at the end of the simulation. QALYs and costs were both discounted at an annual rate of 3.5%.

For each allocation scheme, we report the characteristics of patients who received a transplant, the distribution of life years and QALYs for transplant recipients by age group and the total discounted costs and QALYs for patients who received a transplant, for patients who remained on the waiting list and for the overall cohort. To highlight the magnitude of trade-offs between efficiency and equity in access to transplantation, we also compare several key characteristics of patients who received a transplant under each scheme.

RESULTS

Cost-effectiveness results

The motivation behind the QALY maximisation approach is to allocate each donor organ in a way that maximises the potential gain in health among transplant recipients, in other words to make the most efficient use of a scarce supply of kidneys. Table 2 shows that for patients who received a transplant, this approach generated the most QALYs (48,045) and also led to the highest costs (£681 million). However, Table 2 also shows that patients who were not prioritised to receive a transplant and who remained on the waiting list had worse health outcomes and generated fewer total QALYs (20,504) compared to other allocation schemes. Taking into account total costs and QALYs for both transplant recipients and patients who remained on the waiting list, longevity matching produced the fewest QALYs (65,665) and the lowest costs (£1,473 million), while the 2006 NKAS produced the most QALYs (70,569)
and the highest costs (£1,722 million). While the longevity matching and QALY maximisation schemes both generated more QALYs for transplant recipients than the 2006 NKAS, they generated far fewer QALYs for those patients who were assumed to remain on the waiting list. In incremental cost-effectiveness analysis, random allocation and waiting time allocation were both dominated; that is to say, they were both less effective and more costly than at least one of the other allocation approaches. The comparison of the QALY maximisation approach to longevity matching generated an incremental cost-effectiveness ratio (ICER) of £8,751/QALY while the comparison of the 2006 NKAS to the QALY maximisation approach generated an ICER of £110,741/QALY (Figure 2).

Access to transplantation

To understand the impact of the different allocation schemes on access to transplantation, Table 3-4 reports the age, sex and diabetes status of patients who received a transplant. Moving along the equity-efficiency spectrum from random allocation towards allocation based on QALY-maximisation, there is a notable decrease in the average age of transplant recipients. Under random allocation, which preserves the composition of the original waiting list at the start of the simulation, 31% of transplant recipients were aged ≥60 years and above; under the QALY-maximisation approach, this proportion fell to just 4%.

Allocation schemes that emphasised greater efficiency also resulted in a higher proportion of female transplant recipients and a lower proportion of transplant recipients with diabetes.

Distribution of life years and QALYs
Table 5 shows mean survival (life years) and mean QALYs for each allocation scheme. The QALY-maximisation scheme resulted in the highest mean life years and QALYs for each transplant recipient (23.6 life years, 19.3 QALYs) but correspondingly the lowest mean life years and QALYs for patients who were not prioritised to receive a transplant (6.5 life years, 5.1 QALYs). The waiting time allocation scheme resulted in the lowest mean life years and QALYs for each transplant recipient (17.1 life years, 13.9 QALYs) and also resulted in the smallest difference in survival for those who received a transplant compared to those who did not.

Although the QALY-maximisation scheme resulted in the lowest proportion of patients aged ≥60 years receiving a transplant (4%), those who did receive a transplant survived longer on average than patients aged ≥60 years under any of the other allocation schemes. This is because the QALY-maximisation scheme is selecting patients who are expected to live long enough to derive the biggest survival benefit from each donor kidney compared to remaining on dialysis.

**Cost-effectiveness results**

The motivation behind the QALY-maximisation approach is to allocate each donor organ in a way that maximises the potential gain in health among transplant recipients, in other words to make the most efficient use of a scarce supply of kidneys. Table 26 shows total QALYs and costs for the entire cohort of patients in the simulation. For patients who received a transplant, the QALY-maximisation approach generated the highest total QALYs (48,045) and also led to the highest costs (£681 million). However, Table 26 also shows that patients who were not prioritised to receive a transplant and who remained on the waiting
list had worse health outcomes and generated fewer total QALYs (20,504) compared to other allocation schemes.

Taking into account total costs and QALYs for both transplant recipients and patients who remained on the waiting list, longevity matching produced the fewest QALYs (65,665) and the lowest costs (£1,473 million), while the 2006 NKAS produced the most QALYs (70,569) and the highest costs (£1,722 million). While the longevity matching and QALY-maximisation schemes both generated more QALYs for transplant recipients than the 2006 NKAS, they generated far fewer QALYs for those patients who were assumed to remain on the waiting list. In incremental cost-effectiveness analysis, random allocation and waiting-time allocation were both dominated; that is to say, they were both less effective and more costly than at least one of the other allocation approaches. The comparison of the QALY-maximisation approach to longevity matching generated an incremental cost-effectiveness ratio (ICER) of £8,751/QALY while the comparison of the 2006 NKAS to the QALY-maximisation approach generated an ICER of £110,741/QALY (Figure 2).
DISCUSSION

The allocation of deceased donor kidneys to patients who are awaiting a transplant is
constrained not only by a limited supply of kidneys but also, like all resource allocation
decisions in healthcare, by a limited budget. The emphasis of the literature and the debate
about kidney allocation has historically focussed on donor organs as the only constraint, and
in particular on the trade-off between maximising survival and ensuring equity in access to
transplantation. In this research, we have explored a wider range of potential objectives in
the design of a kidney allocation scheme and used simulation modelling to quantify the
magnitude of trade-offs associated with moving from one allocation approach to another. In
particular, this is the first patient-level simulation exercise to consider the costs associated
with different approaches to kidney allocation in the UK and to report outcomes in terms of
QALYs.

The motivation for the simulation exercise described in this paper was not only to explore
different allocation concepts from across the equity-efficiency spectrum, but also to
improve our ability to estimate variability in outcomes resulting from different approaches
to allocation using patient-level data. If alternative approaches to kidney allocation result in
different patients receiving transplants, then an accurate comparison of the consequences
of alternative allocation schemes depends on our ability to predict variability in outcomes
dependent on individual patient characteristics. This simulation exercise relied on a number
of rich sources of patient-level data including the ATTOM study, the UK Transplant Registry
(held by NHS Blood and Transplant), Hospital Episode Statistics and the UK Renal Registry in
order to develop predictive regression models to estimate survival, health-state utilities and
costs. These predictive models were used not only to estimate QALYs and costs for
transplant recipients in all five allocation schemes but also as part of the criteria to inform the kidney allocation process for the longevity matching and QALY-maximisation schemes.

Our research demonstrates the richness of information that can be generated from a patient-level simulation but we are cognisant that there are limitations to any modelling exercise. In particular, we made a number of assumptions with respect to the model structure, such as only considering first-time transplants and excluding paediatric patients as the latter group fell outside of the scope of the ATTOM study. The characteristics of the donors were based on a contemporaneous cohort with the waiting list patients in the ATTOM study but we have not attempted to model the consequences of the different allocation schemes if the composition of either the donor pool or the waiting list were to change significantly over time. Another important simplifying assumption was that patients who were on the waiting list at the end of the simulation would not receive a transplant in the future. This assumption is unlikely to be met in practice. Survival on the waiting list is on average poorer than survival following transplant, so the likely effect of this assumption is that we have underestimated total QALYs for all allocation schemes. It is difficult to anticipate the net impact of this assumption on the cost-effectiveness results. Different allocation criteria will result in different types of patients receiving transplants and by corollary, the composition of patients who remain on the waiting list will also differ between schemes. Under the waiting-time allocation scheme, patients who remain on the waiting list at the end of the simulation would in practice still have a reasonable prospect of receiving a future transplant as their likelihood of being prioritised for transplant increases with time. In contrast, under the QALY-maximisation scheme, patients who remain on the waiting list at the end of the simulation may be less likely to receive a future transplant if their expected
QALY gains from transplant decrease over time relative to new patients joining the waiting list. Rather than attempt to apply different assumptions to each allocation scheme to project what proportion or which types of patients on the waiting list are likely to receive a future transplant at the end of the simulation, we chose to implement a standardised assumption so as not to confound our ability to observe and compare the effect of the different allocation schemes themselves. Given the importance of this assumption on estimates of QALYs and costs for the total patient population, future research should focus on testing alternative assumptions, for example by exploring if a non-terminating model could achieve a steady-state outcome that can be compared across allocation schemes over a long enough period of time. As with all simulation exercises, the need to make simplifying assumptions may limit the generalisability of the results to the real world context. With these caveats in mind, simulation modelling is still an important tool that can help increase our understanding of the potential consequences of different approaches to kidney allocation under the same set of conditions in comparison to each other.

Although we chose to report lifetime QALYs and costs as the main outcomes of interest, this simulation exercise was not specifically designed with standard methods for cost-effectiveness modelling at the forefront of our approach. There were both technical and philosophical reasons that contributed to this decision. During development of the simulation model, primary emphasis was placed on the design, feasibility and coding of the different allocation schemes. Each scheme requires the simulation model to loop through all patients on the waiting list in order to evaluate donor-recipient compatibility. In the case of the QALY-maximisation and longevity matching schemes, survival predictions take into account both recipient and donor characteristics and therefore need to be recalculated for
all 5500 patients on the waiting list each time a donor kidney enters the simulation. The
computational burden of the allocation process itself led to long model running times even
in the absence of introducing parameter uncertainty and therefore we were unable to
perform full probabilistic sensitivity analysis. On a more philosophical note, kidney
allocation represents a somewhat unique particular resource allocation problem constrained
not only by a finite healthcare budget but also by a limited supply of donor organs.
Conventional cost-effectiveness methods focus on maximising health gains, but in the
case of kidney allocation it is clear from current policy that maximising health gains is not
the only objective. For this reason, we presented incremental cost-effectiveness results of
all for the five allocation schemes and but refrained from evaluating ICERs with respect to a
specific threshold value. The results of this simulation exercise cannot answer the question
about what the objectives of a national kidney allocation scheme should be, but nonetheless
provide insight into the magnitude of QALY and cost differences to inform the discussion
about trade-offs associated with alternative allocation concepts from across the equity-
efficiency spectrum.

The QALY-maximisation approach to kidney allocation was designed to maximise health
gains from a limited supply of donor kidneys. This approach yielded the most QALYs for
transplant recipients but also resulted in a notable decrease in access to transplantation for
older patients. Although the QALY-maximisation approach made more efficient use of a
limited number of kidneys, it resulted in greater inequity in terms of both access to
transplantation and the distribution of QALYs between transplant recipients and patients
who remained on the waiting list.
A different kind of trade-off was evident when we considered the costs associated with each of the approaches to kidney allocation. The 2006 NKAS resulted in a modest increase in total QALYs across all patients compared to the QALY-maximisation approach but also incurred much higher total costs. If the 2006 NKAS is viewed as a compromise between equity and efficiency, then the results of this simulation provide an estimate of the additional cost to the NHS of maintaining greater equity in the allocation of deceased donor kidneys.
ACKNOWLEDGMENTS

This article presents independent research commissioned by the National Institute for Health Research (NIHR) under the Programme Grant for Applied Research (RP-PG-0109-10116) entitled Access to Transplantation and Transplant Outcome Measures (AT TOM). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR, NHS Blood and Transplant, the UK Renal Registry or the Department of Health.

The authors thank all transplant centres who contributed data to the UK Transplant Registry and all renal centres for providing data to the UK Renal Registry upon which parts of this simulation model are based. We would like to acknowledge Lisa Mumford at NHS Blood and Transplant for facilitating access to data on donor characteristics. We are grateful to SIMUL8 Corporation (www.SIMUL8.com) for providing access to use the software under the PhD Research Scheme and to Tom Stephenson for his support during model development. We would also like to thank Matt Stevenson for providing comments on a draft version of this manuscript.
REFERENCES


<table>
<thead>
<tr>
<th>Allocation concept</th>
<th>Description of allocation criteria considered in each scheme</th>
</tr>
</thead>
</table>
| Random               | • Blood group compatibility and HLA match  
                        • Priority for HLA mismatch level 1 (000)  
                        • Taking the above criteria into account, allocate the kidney randomly                                             |
| Waiting time         | • Blood group compatibility and HLA match  
                        • Priority for HLA mismatch level 1 (000)  
                        • Taking the above criteria into account, allocate the kidney to the patient with the longest waiting time       |
| 2006 NKAS            | • Priority for HLA mismatch level 1 (000), taking into account whether or not patients are highly sensitised or HLA-DR homozygous  
                        • Within tiers, prioritise patients according to a points-based system based on:  
                          - waiting time  
                          - HLA match and age combined  
                          - donor-recipient age difference  
                          - location of patient relative to donor  
                          - HLA-DR homozygosity  
                          - HLA-B homozygosity  
                          - blood group match |
| Longevity matching   | • For each donor kidney, estimate expected post-transplant survival for each patient on the waiting list  
                        • If the donor kidney has a UKKDRI score in the top 20%, then 20% of patients with the longest expected post-transplant survival are prioritised to receive the kidney  
                        • Taking the above criteria into account, allocate the kidney according to the 2006 NKAS |
| QALY-maximisation    | • Blood group compatibility and HLA match  
                        • Priority for HLA mismatch level 1 (000)  
                        • For each donor kidney, estimate expected post-transplant QALYs for each patient and expected QALYs if each patient were to remain on the waiting list (on dialysis)  
                        • Taking the above criteria into account, allocate the kidney to the patient with the biggest expected QALY gain from transplant |
Table 2. Characteristics of the recipient cohort (n=5500) used in the simulation model

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
</tr>
<tr>
<td>18-29</td>
<td>369 (6.7%)</td>
</tr>
<tr>
<td>30-39</td>
<td>708 (12.9%)</td>
</tr>
<tr>
<td>40-49</td>
<td>1,245 (22.6%)</td>
</tr>
<tr>
<td>50-59</td>
<td>1,576 (28.7%)</td>
</tr>
<tr>
<td>≥60</td>
<td>1,602 (29.1%)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2,320 (42.2%)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4,017 (73.0%)</td>
</tr>
<tr>
<td>Asian</td>
<td>727 (13.2%)</td>
</tr>
<tr>
<td>Black</td>
<td>626 (11.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>140 (2.6%)</td>
</tr>
<tr>
<td><strong>Blood group</strong></td>
<td></td>
</tr>
<tr>
<td>O</td>
<td>3,135 (57.0%)</td>
</tr>
<tr>
<td>A</td>
<td>1,590 (28.9%)</td>
</tr>
<tr>
<td>B</td>
<td>684 (12.4%)</td>
</tr>
<tr>
<td>AB</td>
<td>91 (1.7%)</td>
</tr>
<tr>
<td><strong>Highly sensitised</strong></td>
<td>468 (8.5%)</td>
</tr>
<tr>
<td><strong>Primary renal diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>826 (15.0%)</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>82 (1.5%)</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>475 (8.6%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>178 (3.2%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>199 (3.6%)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>293 (5.3%)</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>447 (8.1%)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>74 (1.4%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>262 (4.8%)</td>
</tr>
<tr>
<td>Mental illness</td>
<td>403 (7.3%)</td>
</tr>
<tr>
<td>Years on dialysis at time of listing</td>
<td>Pre-dialysis</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Smoker</td>
<td>730 (13.3%)</td>
</tr>
</tbody>
</table>
Table 3. Characteristics of the donor cohort (n=2200) used in the simulation model

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>394 (17.9%)</td>
</tr>
<tr>
<td>30-39</td>
<td>283 (12.9%)</td>
</tr>
<tr>
<td>40-49</td>
<td>503 (22.9%)</td>
</tr>
<tr>
<td>50-59</td>
<td>548 (24.9%)</td>
</tr>
<tr>
<td>≥60</td>
<td>472 (21.5%)</td>
</tr>
<tr>
<td><strong>Blood group</strong></td>
<td></td>
</tr>
<tr>
<td>O</td>
<td>1,024 (46.5%)</td>
</tr>
<tr>
<td>A</td>
<td>892 (40.5%)</td>
</tr>
<tr>
<td>B</td>
<td>197 (9.0%)</td>
</tr>
<tr>
<td>AB</td>
<td>87 (4.0%)</td>
</tr>
<tr>
<td><strong>History of hypertension</strong></td>
<td>499 (22.7%)</td>
</tr>
<tr>
<td><strong>UK kidney donor risk index</strong></td>
<td></td>
</tr>
<tr>
<td>High risk (≥ 1.35)</td>
<td>582 (26.5%)</td>
</tr>
</tbody>
</table>
Table 4. Summary of characteristics of patients who received a transplant under each allocation scheme

<table>
<thead>
<tr>
<th>Age group - years</th>
<th>Mean age - years (SD)</th>
<th>Random</th>
<th>Waiting time</th>
<th>2006 NKAS</th>
<th>Longevity matching</th>
<th>QALY-maximisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-29</td>
<td>51.4 (12.8)</td>
<td>52.5 (12.3)</td>
<td>46.6 (12.5)</td>
<td>46.3 (12.6)</td>
<td>41.8 (10.7)</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>52%</td>
<td>11%</td>
<td>19%</td>
<td>20%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>22%</td>
<td>21%</td>
<td>28%</td>
<td>29%</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>28%</td>
<td>30%</td>
<td>25%</td>
<td>23%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>31%</td>
<td>33%</td>
<td>18%</td>
<td>18%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>42%</td>
<td>43%</td>
<td>44%</td>
<td>44%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>15%</td>
<td>15%</td>
<td>14%</td>
<td>14%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Life years</td>
<td>Random allocation</td>
<td>Waiting time</td>
<td>2006 NKAS</td>
<td>Longevity matching</td>
<td>QALY-maximising</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>-------------------</td>
<td>--------------</td>
<td>-----------</td>
<td>-------------------</td>
<td>-----------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Transplant recipients (by age group)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29</td>
<td>27.2 (24.7, 29.7)</td>
<td>27.2 (24.0, 30.3)</td>
<td>32.8 (30.3, 35.3)</td>
<td>31.5 (29.3, 33.7)</td>
<td>29.2 (27.3, 31.2)</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>26.5 (24.6, 28.4)</td>
<td>25.4 (23.5, 27.3)</td>
<td>29.2 (27.7, 30.8)</td>
<td>30.1 (28.6, 31.7)</td>
<td>27.5 (26.2, 28.8)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>23.4 (22.3, 24.6)</td>
<td>22.2 (21.0, 23.3)</td>
<td>23.4 (22.4, 24.5)</td>
<td>22.6 (21.6, 23.6)</td>
<td>23.4 (22.5, 24.4)</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>15.2 (14.5, 15.9)</td>
<td>15.0 (14.3, 15.7)</td>
<td>14.5 (13.8, 15.2)</td>
<td>14.5 (13.7, 15.2)</td>
<td>15.6 (14.7, 16.6)</td>
<td></td>
</tr>
<tr>
<td>&gt;60</td>
<td>11.2 (10.7, 11.6)</td>
<td>11.4 (11.0, 11.9)</td>
<td>10.7 (10.2, 11.3)</td>
<td>11.0 (10.4, 11.6)</td>
<td>13.2 (11.5, 14.8)</td>
<td></td>
</tr>
<tr>
<td>Transplant recipients (all)</td>
<td>18.0 (17.5, 18.5)</td>
<td>17.1 (16.7, 17.6)</td>
<td>21.1 (20.5, 21.7)</td>
<td>21.2 (20.7, 21.8)</td>
<td>23.6 (23.0, 24.2)</td>
<td></td>
</tr>
<tr>
<td>No transplant (all)</td>
<td>8.9 (8.8, 9.1)</td>
<td>9.0 (8.9, 9.1)</td>
<td>9.0 (8.9, 9.1)</td>
<td>6.8 (6.7, 6.9)</td>
<td>6.5 (6.4, 6.6)</td>
<td></td>
</tr>
<tr>
<td>Transplant recipients (by age group)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29</td>
<td>22.4 (20.4, 24.5)</td>
<td>22.4 (19.8, 24.9)</td>
<td>27.1 (25.0, 29.2)</td>
<td>26.0 (24.1, 27.8)</td>
<td>24.1 (22.5, 25.7)</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>21.4 (19.9, 22.9)</td>
<td>20.6 (19.1, 22.2)</td>
<td>23.8 (22.5, 25.1)</td>
<td>24.5 (23.2, 25.8)</td>
<td>22.4 (21.3, 23.5)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>18.9 (18.0, 19.9)</td>
<td>17.9 (17.0, 18.8)</td>
<td>18.9 (18.0, 19.8)</td>
<td>18.3 (17.5, 19.1)</td>
<td>19.1 (18.3, 19.9)</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>12.3 (11.7, 12.9)</td>
<td>12.1 (11.6, 12.7)</td>
<td>11.7 (11.1, 12.3)</td>
<td>11.7 (11.1, 12.3)</td>
<td>12.7 (12.0, 13.5)</td>
<td></td>
</tr>
<tr>
<td>&gt;60</td>
<td>9.0 (8.7, 9.4)</td>
<td>9.2 (8.8, 9.6)</td>
<td>8.7 (8.2, 9.1)</td>
<td>8.9 (8.4, 9.4)</td>
<td>10.7 (9.3, 12.0)</td>
<td></td>
</tr>
<tr>
<td>Transplant recipients (all)</td>
<td>14.6 (14.2, 15.0)</td>
<td>13.9 (13.5, 14.2)</td>
<td>17.1 (16.6, 17.6)</td>
<td>17.2 (16.8, 17.7)</td>
<td>19.3 (18.8, 19.8)</td>
<td></td>
</tr>
<tr>
<td>No transplant (all)</td>
<td>6.9 (6.8, 7.0)</td>
<td>6.9 (6.9, 7.0)</td>
<td>7.0 (6.9, 7.1)</td>
<td>5.2 (5.1, 5.3)</td>
<td>5.1 (5.0, 5.1)</td>
<td></td>
</tr>
</tbody>
</table>
Table 26. Cost-effectiveness results for transplant recipients, patients who remained on the waiting list, patients who did not receive a transplant and all patients combined

<table>
<thead>
<tr>
<th></th>
<th>Transplant recipients</th>
<th>Waiting-list patients</th>
<th>No transplant</th>
<th>All patients</th>
<th>Incremental costs</th>
<th>Incremental QALYs</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absolute c Costs</td>
<td>Absolute QALYs</td>
<td>Absolute c Costs</td>
<td>Absolute QALYs</td>
<td>Absolute c Costs</td>
<td>Absolute QALYs</td>
<td></td>
</tr>
<tr>
<td>Longevity matching</td>
<td>£632,382,864</td>
<td>44,704</td>
<td>£841,064,018</td>
<td>20,961</td>
<td>£1,473,446,881</td>
<td>65,665</td>
<td></td>
</tr>
<tr>
<td>QALY-maximisation</td>
<td>£680,552,945</td>
<td>48,045</td>
<td>£818,130,717</td>
<td>20,504</td>
<td>£1,498,683,661</td>
<td>68,549</td>
<td>£25,236,780</td>
</tr>
<tr>
<td>Random</td>
<td>£590,657,199</td>
<td>40,236</td>
<td>£1,088,809,775</td>
<td>26,328</td>
<td>£1,679,466,974</td>
<td>66,563</td>
<td>£180,783,313</td>
</tr>
<tr>
<td>Waiting time</td>
<td>£584,489,615</td>
<td>39,496</td>
<td>£1,099,379,875</td>
<td>26,572</td>
<td>£1,683,869,490</td>
<td>66,068</td>
<td>£185,185,829</td>
</tr>
<tr>
<td>2006 NKAS</td>
<td>£624,864,970</td>
<td>44,040</td>
<td>£1,097,473,021</td>
<td>26,529</td>
<td>£1,722,337,991</td>
<td>70,569</td>
<td>£223,654,330</td>
</tr>
</tbody>
</table>

|                   |                       |                       |               |              |                   |                   |       |
|                   |                       |                       |               |              |                   |                   |       |
|                   |                       |                       |               |              |                   |                   |       |
|                   |                       |                       |               |              |                   |                   |       |
|                   |                       |                       |               |              |                   |                   |       |
|                   |                       |                       |               |              |                   |                   |       |
|                   |                       |                       |               |              |                   |                   |       |
|                   |                       |                       |               |              |                   |                   |       |

ICER = Incremental Cost-Effectiveness Ratio
Table 3. Summary of characteristics of patients who received a transplant under each allocation scheme

<table>
<thead>
<tr>
<th></th>
<th>Random</th>
<th>Waiting-time</th>
<th>2006.NKAS</th>
<th>Longevity matching</th>
<th>QALY-maximisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age—years (SD)</td>
<td>51.4</td>
<td>52.5</td>
<td>46.6</td>
<td>46.3</td>
<td>41.8</td>
</tr>
<tr>
<td>Age-group—years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29</td>
<td>7%</td>
<td>5%</td>
<td>10%</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>30-39</td>
<td>12%</td>
<td>11%</td>
<td>19%</td>
<td>20%</td>
<td>27%</td>
</tr>
<tr>
<td>40-49</td>
<td>22%</td>
<td>21%</td>
<td>28%</td>
<td>29%</td>
<td>36%</td>
</tr>
<tr>
<td>50-59</td>
<td>28%</td>
<td>30%</td>
<td>25%</td>
<td>23%</td>
<td>18%</td>
</tr>
<tr>
<td>≥60</td>
<td>31%</td>
<td>33%</td>
<td>18%</td>
<td>18%</td>
<td>4%</td>
</tr>
<tr>
<td>Female</td>
<td>42%</td>
<td>43%</td>
<td>44%</td>
<td>44%</td>
<td>50%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15%</td>
<td>15%</td>
<td>14%</td>
<td>14%</td>
<td>11%</td>
</tr>
</tbody>
</table>
**Figure 1.** Structure of the simulation model

**Figure 2.** Cost-effectiveness plane showing the relative positions of the 5 allocation schemes in terms of both total costs (vertical axis) and total QALYs (horizontal axis) for all patients
Figure 1.

Add new patient each time someone on the waiting list receives a transplant

Load prevalent patients at start of run

Transplant waiting list

Allocation process

Donor kidney arrivals

Kidney for allocation

No match identified

Graft failure (return to dialysis)

Determine post-transplant outcome (competing risk)

Survival with functioning graft

Death
Figure 2.

- Waiting time
- Random
- £110,741/QALY
- £8,751/QALY
- QALY maximisation
- 2006 NKAS

Cost (Million £) vs. QALYs
Click here to access/download
Supplemental Digital Content to Be Published (cited in text)
Supplemental digital content.docx