In response to an enquiry from NHS National Services Scotland as the commissioners for kidney transplant services in NHSScotland

An economic evaluation of living donor kidney transplantation in Scotland

Key messages

Living donor kidney transplantation (LDKT) occurs when a person with established renal failure (ERF) receives a kidney from a living relative, friend or stranger who has agreed to donate one of their kidneys. This is possible because most of the general population has two kidneys and can lead a normal, healthy life with just one kidney.

LDKT offers advantages over deceased donor kidney transplantation (DDKT), including reduced time to donation, increased opportunity for suitability testing and potentially, a healthier donated kidney which may contribute to living donor kidneys lasting longer and therefore improved survival rates.

Our economic modelling, based on data from Public Health Scotland, found that LDKT was cost-effective compared with DDKT and kidney dialysis.

- LDKT and DDKT are both less costly and more effective than kidney dialysis for the treatment of patients with ERF.
- LDKT is less costly and more effective than DDKT for patients with ERF.

What were we asked to look at?

We were asked by NHS National Services Scotland's National Services Division (NSD) to undertake an economic evaluation of living donor kidney transplantation to inform the future commissioning of transplant services in Scotland.

Why is this important?

Living donation offers people with end stage kidney disease a greater chance of a successful transplant compared with deceased donation.[1] Living donation adds to the overall supply of available organs for those who are waiting for transplant.

In recent years several awareness raising initiatives have been implemented to increase the number of living donor kidney transplants, to improve equity of access, and to support those with end stage renal failure to receive a kidney transplant before requiring dialysis. Living donor transplantation currently contributes 35% of overall transplant activity in the UK.[1, 2]

What was our approach?

We developed an economic model to determine the cost effectiveness of living donor transplantation compared with both deceased donor transplantation and kidney dialysis. The model simulates future costs and outcomes associated with the three interventions, based on ten years of data from patients records available from the Scottish Renal Registry.

What next?

This economic evaluation will inform service planning.

Contents

Definitions

Fistula   An abnormal passage that leads from an abscess or hollow organ (or part) to the body surface or from one hollow organ (or part) to another and that may be surgically created to permit passage of fluids or secretions.[3]

In patients needing dialysis, a fistula is surgically created by connecting a vein to an artery, usually in the wrist or upper arm. This strengthens the blood vessel to allow fast following blood to be pumped through a dialysis machine. The fistula is strong enough to withstand regular dialysis.[4]

Haemodialysis   The process of removing blood from an artery (as of a patient affected with kidney failure), purifying it by dialysis (the separation of substances in solution by means of their unequal diffusion through semipermeable membranes), adding vital substances, and returning it to a vein.[5]

In patients needing dialysis a haemodialysis machine replaces some functions of the kidney. The machine is attached to the patient and works like an artificial kidney by processing the patient's blood to remove waste and extra fluids. It maintain safe levels of minerals in the blood and regulates blood pressure.[6]

Hyperparathryroidism   The presence of excess parathyroid hormone in the body resulting in disturbance of calcium metabolism with increase in serum calcium and decrease in inorganic phosphorus, loss of calcium from bone, and renal damage with frequent kidney-stone formation.[7] Almost everyone who needs dialysis will develop some degree of hyperparathyroidism.[8]

Parathyroid glands   Four small endocrine glands that are adjacent to or embedded in the thyroid gland and produce parathyroid hormone[9]. Parathyroid hormone controls the level of calcium in the blood.[10]

Peritoneal dialysis   A procedure performed in the peritoneal cavity in which the peritoneum acts as the semipermeable membrane needed for dialysis (see haemodialysis above).[5] The peritoneum (inside lining of the abdomen) filters the blood and remove waste products. A fluid called dialysate flows through the abdomen absorbing waste products and excess water. It is then drained out of the body taking the toxins and excess water with it.[11]

Abbreviations are listed in *Appendix 1*.

Introduction

The main role of the kidneys in the human body is to filter waste products from the blood and produce urine. Chronic kidney disease (CKD) occurs when one or both kidneys do not work as well as they should.[12] CKD is most often caused by damage to the kidneys from other conditions including diabetes and high blood pressure.

The risk of CKD increases with age and having CKD leads to an increased risk of other adverse health events. For example, people with CKD may be at an increased risk of a heart attack because of circulatory system changes as a result of CKD. CKD may lead to established kidney failure, also known as ERF(established renal failure) or end stage renal disease (ESRD).[12] During ERF, a person's kidneys are no longer functioning adequately and renal replacement therapy (RRT) is required for longer term survival.

RRT, which includes dialysis or kidney transplantation, has been in routine clinical practice since 1960.[13] Kidney transplantation is regarded as the optimal treatment for the management of people with ERF and increases life expectancy and improves quality of life compared with people who receive dialysis alone.[14-16]

Pre-emptive transplantation is preferred at the onset of RRT, as opposed to dialysis followed by transplantation, particularly for children because dialysis adversely affects their growth and development.[14] Despite this, the average waiting time for an active kidney transplant from a deceased organ donor is 706 for adults and 287 days for children.[17] Living donation of kidneys provides an important contribution to the organ donor pool by offering more people the possibility of an earlier successful transplant.

Research question

SHTG was asked to assess the cost effectiveness of living donation within the Scottish healthcare setting. SHTG was asked to model the anticipated costs and health benefits of living kidney donation compared with deceased donor transplantation and kidney dialysis.

Health technology description

LDKT occurs when a person with ERF receives a kidney from a living donor.[12] This is possible because most of the general population has two kidneys and can lead a normal, healthy life with just one kidney.

LDKT involves the removal of a donor's kidney for transplantation into someone with ERF who needs a kidney. The donor does not need to be the same age, blood group or tissue type as the recipient.

The UK Living Kidney Sharing Scheme facilitates matching between donor and recipient.[18] The legal lower age limit for donating in Scotland is 16 years old.

LDKT offers advantages over DDKT.[19] LDKT can occur quickly if the patient has somebody willing to donate a kidney to them. It usually takes between 3 to 6 months to arrange and carry out the donation. It is also possible to do more suitability testing in advance of the transplant compared with a DDKT, where a suitable recipient must be found at short notice. In addition, because the kidney has come from someone who is fit and well, rather than someone who has died, there are higher chances of the kidney working straight away and of prolonged survival of the allograft. The option to better plan LDKTs increases the likelihood of patients undergoing a transplant before requiring dialysis, which could lead to reduced hospital visits and inpatient stays for patients if the need for dialysis can be avoided.

A transplanted kidney from a living donor lasts for an average time of 27 years and can last for over 40 years [20] In comparison, kidneys from DDKTs are functional for 15 years on average and patients are more likely to require several transplants during their lifetime.[19] LDKT offers the best long-term graft and patient survival, with a 10-year survival rate of 89% after transplant, compared with 77% for DDKT recipients and 44% for dialysis patients.[1]

Epidemiology

CKD is an increasing global health issue with over 5 million people requiring RRT in the form of dialysis or transplantation worldwide.[21] There are 24 kidney transplant centres in the UK and two in Scotland. In 2023/24, across the UK, 3,361 people received a kidney (2,300 from deceased donors and 913 from a living donor, a further 148 were multi-organ transplants and the type of kidney transplant is not known). As of March 2024, there were 6,212 people waiting for a kidney in the UK.[1, 22]

In Scotland, the number of new patients starting RRT in 2023 was 635.[2] This compares with 597 new patients in 2022, and 602 the year before (2021).[23, 24] The incident rate per 100,000 population was 11.7 compared with a rate of 10.9 per 100,000 population in 2022 and 11.0 per 100,000 population the year before (2021).[2, 23, 24] There were 5,732 patients who were not new cases that year but were still receiving RRT by 31 December 2023, of whom 61% had a functioning transplanted kidney.[2] This makes kidney transplantation the most common treatment among patients receiving RRT (36% received haemodialysis and a further 4% were receiving peritoneal dialysis).[2]

Eighty-nine patients (37.2%) received a living donor transplant in 2023 compared with 176 patients (62.8%) who received a deceased donor transplant.[2] Forty-eight of the transplants were pre-emptive (that is, performed before the patient had required any other form of RRT). Of those 48 pre-emptive transplants, 34 were from living donors and 14 were from deceased donors. Across Scotland in December 2023 there was 460 patients actively waiting for a transplant.[2] There is expected to be a considerable psychological impact over time for patients waiting for a transplant, in some cases this

could be for many years, and patients simply do not know when a suitable kidney may become available. In some cases, a patient could be called for a transplant but the procedure may not go ahead and this also be very difficult for patients emotionally.[25]

Methods for economic analysis

Discrete event simulation (DES) is a method of simulating a real-life process or system. DES models a system as a series of events that occur over time. In this scenario events might be a living donor transplant, an intensive care unit (ICU) stay because of complications, a transfer or a discharge from a waiting list. In DES, patients are modelled as independent entities and can be given associated attribute information. Unlike cohort Markov models, in DES, movements between patients' health states are usually driven by events which occur at varying times rather than during cycles of a fixed length of time. DES requires time-to-event distributions for each event.

DES was chosen for the analysis because it can incorporate variation in time between events that occur for each simulated patient. This makes the DES approach particularly suited to RRT pathways. The pathway, that is the events and outcomes, for a patient with RRT can vary considerably from person to person and depend on many factors, from a patient's age to the cause of their ERF. DES timings are based on observed data and can be extrapolated to determine what is likely to happen in the longer term to the patients who are still alive at the end of the observed timeframe.

Datasets

To populate the DES, national data containing information on all patients receiving RRT between 2009 and 2019 were provided by Public Health Scotland (N Cameron, Senior Information Analyst, Public Health Scotland. Information request IR:2021-00907. Personal communication). The data were provided across four datasets relating to patients over the observation period between January 2009 to December 2019.

The first dataset contained patient level information about the type of transplant received from 1 January 2009 to 31 March 2019 for all participants who had received a transplant.

The second dataset contained patient level biopsy information including the rationale for undertaking the biopsy, whether the native or transplanted organ was biopsied, the subsequent biopsy result and any complications that occurred. These data are only available between 1 January 2014 and 31 March 2019.

The third dataset contained hospital episode level data for patients in the cohort, including transplant and dialysis patients, the Primary Renal Diagnostic group (PRD 1–5), age, sex, date and cause of death for deceased patients. These data were subsequently added to patients' operation dates.

The fourth dataset contained all the variables as for the third dataset except hospital episode data. In other words, these were patients where no hospital episode data were available.

Patient attributes and event data included:

- time to death
- time to living donor transplant
- time to deceased donor transplant
- time to events that occur before transplant
- time to events that occur after transplant (living and deceased donor cohorts only)
- current health state utility
- time since last event
- time to next event
- age
- sex
- PRD group
- modality of treatment (dialysis, transplant or post-transplant states).

Data were analysed and modelled using the statistical software programs R and R Studio (R version 4.2.3 and R Studio version 2023.03.0.386).

Simulating event data

Event data were simulated in the DES based on observed probabilities of an event occurring, the time to the event occurring for the first time, and time to the same event occurring for a subsequent time. In some cases, events were not observed to recur and so the time to a subsequent event was not possible to simulate. For the events that did happen more than once, the model makes a simplifying assumption that these subsequent events would occur only once.

Events were modelled separately before and after transplant to account for how transplantation may affect the rate of occurrence for any of the adverse events. Distributions were fitted to the adverse events that occur for the first and subsequent time (where required) *before* transplant, and to the adverse events that occur for the first (where required) and subsequent time (where required) *after* transplant. For both the living and deceased donor simulations, time to transplant was modelled which informed the shift between health state from dialysis to transplant.

Time to death was included for all simulated patients. For the purpose of the model, it was necessary to predict timing of death for all patients who survived at the end of the observed data period in 2019. This was done by using the midpoint between a) National Records of Scotland (NRS) estimates of general population life expectancy based on average patient age at the end of the observation period,[26] and b) matching the life expectancy of surviving patients to that observed survival of deceased patients who were within the observed dataset but started their RRT prior to 2009. Based

on the available data, using the midpoint between these two values was deemed to be the most appropriate way to predict deaths within the model, recognising that general population life expectancy may overestimate survival but that matching surviving patients to deceased patients may underestimate survival.

Events included

All simulated patients start the model receiving dialysis only for ERF. Events that could then occur within the model are:

- living donor transplant (living donor cohort only)
- deceased donor transplant (deceased donor cohort only)
- all other event(s) that occur before transplant based on the observed data provided by PHS. Events can occur for all simulated patients including those who remain in the dialysis group and do not go on to have a transplant and were categorised as:

  - cardiovascular
  - catheter related
  - compensation renal failure
  - central venous catheter
  - dialysis catheter
  - examination of abdomen/kidney
  - exchange of plasma
  - excision of parathyroid
  - fistula
  - hernia related
  - rejected donor kidney (can still occur before transplant for anyone who had a transplant prior to the start of the observation period)
  - skin related
  - topical anaesthesia
  - transplant-related (for dialysis patients only affects those who previously had a transplant prior to the start of the observation period)
  - other (costed)

- event(s) that occur after transplant were identical to the list of events before transplant but were applied to the LDKT and DDKT cohorts only
- death, which can occur at any time before or after transplant (based on deaths in the observed dataset and modelled using population mortality, adjusted for age and gender).

Attached to each event in the model is:

- the number of patients in the simulation (1,000) and the proportion of patients experiencing each event based on the observed data
- the number of days since the diagnosis of ERF to each event based on the distribution of days since diagnosis to each event (for those who experienced the event) in the observed data
- costs for each type of transplant
- costs for all other events
- baseline utility (to estimate quality of life at the time of diagnosis), taken from the published literature that has researched health state utility values in groups of ERF patients (this was necessary as the Scottish Renal Registry does not collect any health state utility data directly)
- utility data for all relevant events to estimate changes in quality of life associated with each event that occurs after baseline that may change the quality of life of the patient
- discounting factors (3.5% for both costs and benefits). Discounting costs and benefits that occur beyond the first year of the model allows greater value to be assigned to outcomes that occur sooner rather than those occurring much later in the longer term
- total costs (discounted and undiscounted)
- total quality-adjusted life-years (QALYs), discounted and undiscounted.

A summary of the model structure is shown in *Figure 1.*

Figure 1: Model structure
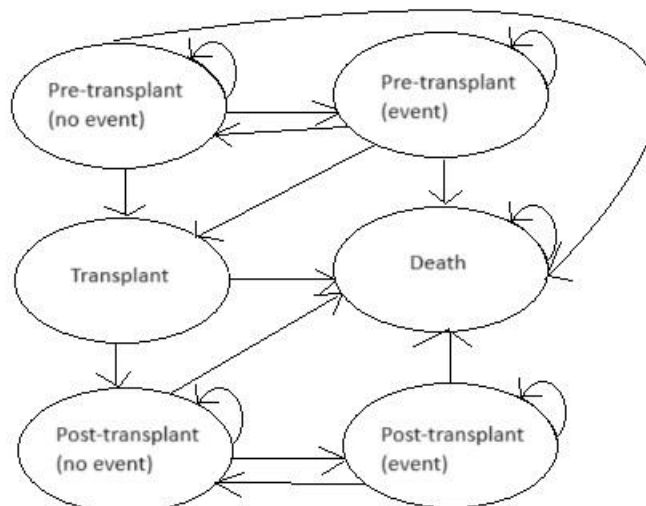
Event distributions

To run the simulation, probability distributions were fitted to observed times to each event. Distributions were fitted, as standard, according to visual fit and Akaike's Information Criterion (AIC) AIC is a commonly used measure to compare potential distributions in terms of their fit with the observed data. Distributions used in the model are presented in Appendix 2.

Costs

To estimate the cost of events in the model, procedures of relevance to kidney transplantation were grouped by clinicians according to their operation code. For each procedure, a unit cost for the most recent year was provided by Public Health Scotland (M Aldhous, Panel Manager, NHS Scotland Public Benefit and Privacy Panel for Health and Social Care, Public Health Scotland. eDRIS/PBPP reference 2021-0036. Personal communication) as shown in *Table 1*.

In most cases, modelled events incurred a one-off cost applied at the time of the event, but some events required a continuous cost for the remaining lifetime of the patient in the model, for example in the case of a rejected donor kidney where ongoing dialysis costs would be applied. Costs per patient and overall treatment (that is, LDKT, DDKT or dialysis only) costs were estimated within the model.

Table 1: Estimated annual costs of treating events (inflated from 2020 price year to 2022).

Event item	Cost of treating event 2022 GBP (£)
Living donor transplant	£8,789
Deceased donor transplant	£9,942
Dialysis	£28,899
Catheter related	£3,215
Cardiovascular	£3,977
Exchange of plasma	£2,081
Excision of parathyroid event	£3,635
Examination of abdomen/kidney	£5,819
Central venous catheter	£7,759
Compensation renal failure	£5,377
Skin related	£4,221
Hernia related	£5,732
Topical anaesthesia	£1,655
Fistula	£3,842
Rejected donor kidney	£9,042
Dialysis catheter	£3,731
Transplant kidney related	£24,422
Other treatment events	£8,090
Death	£1,110
Cost of not being on RRT (outwith cost of death itself)	£638

Utilities

Health state elicitation methods provide a way to understand patients' quality of life over time. The outputs can be used to calculate quality-adjusted life years (QALYs) that incorporate both quality and length of life. Quality of life (or 'utility') scores are anchored at 0 (death) and 1 (full health), but negative values are possible (a value less than zero would denote a health state considered by someone to be 'worse than death').

A review of the literature was undertaken for utility scores associated with different stages in the CKD pathway, the results of which were applied to the health states within the model (*Table 2*).

Table 2: Utility applied in the model

Utility value	NHS specific value	Source
Before transplant haemodialysis	0.75	Briggs (2016)[27]
Before transplant haemodialysis with adverse event	0.62	Davison (2009)[28]
Transplant	0.74	Ortega 2007[29]
Transplant with adverse event	0.71	Lee 2005[30]
After transplant (transplant follow-up)	0.86	Ortega 2009[31]
After transplant with adverse event	0.827	Li 2017[32]

The model makes a simplifying assumption that all patients remain receiving either a transplant or dialysis until the end of their life. This was based on the observed data which indicated very few instances of a patient receiving no RRT.

Results

There were 9,922 patients for who we have data. Of these:

- 754 received a living donor transplant
- 1,741 received a deceased donor transplant
- 7,352 patients received dialysis alone
- in 75 cases, the type of transplant was not known, but as a transplant was known to have occurred it was assumed in the base case to be deceased donor
- there were 5,094 people still alive at the time of data cut off.

The base case analysis used a subgroup of patients that included only those for whom we have all data about their RRT, from start of RRT to the end of the follow up period. These data were chosen for the base case because otherwise we cannot be sure whether reported events represent first or subsequent events for those with RRT prior to the start of the data observation period. The base case subgroup therefore includes 5,669 patients, of which 3,970 were dialysis patients, 1,100 were deceased donor recipients and 599 were living donor patients.

The total costs and QALYs for the different RRT treatment groups after running a simulation of 1,000 patients are shown in *Table 3*.

Based on our model, living and deceased donor transplants are less costly and more effective than dialysis. When comparing both the transplantation types, living donor transplantation is less costly and more effective compared with deceased donor transplantation. This indicates that living donor transplantation is the most cost-efficient strategy for ERF patients.

Table 3: Base case results

	Living donor	Deceased donor	Dialysis	Living donor versus dialysis	Deceased donor versus dialysis	Living donor versus deceased donor
Costs	£52,555,104	£85,694,634	£147,444,313	-£94,889,209	-£61,749,679	-£33,139,530
QALYs	4,942	4,262	1,186	3,756	3,076	680
ICER[+]	-	-	-	Dialysis is dominated (LD transplantation is less costly and more effective in terms of QALYs)	Dialysis is dominated (DD transplantation is less costly and more effective in terms of QALYs)	Deceased donor is dominated (LD transplantation is less costly and more effective in terms of QALYs)

[+] Incremental cost-effectiveness ratio (ICER) values have not been calculated due to the fact that treatments dominated each other, that is, were more effective and less costly. ICER values do not make sense when one treatment dominates another.

Sensitivity analysis

We tested the sensitivity of the results across a 20% increase and 20% decrease in the cost of each event and a 20% increase and 20% decrease in the utilities associated with each event. We also varied the discount rate to 0%, 1.5% and 6%, from the base case rate of 3.5%. It was important to test a 1.5% discount rate given the longer term benefit associated with transplantation.

Conclusions were not sensitive to any of the changes and were therefore considered to be robust.

Discussion

Time-to-event data

A DES model was used to allow differences in the timings of events and to extrapolate data beyond the observed study period. However, patient data are censored, meaning we only have follow up data up to 2019. A patient could, for example, incur additional costs and/or health related quality of life benefits beyond 2019 that have not been accounted for in the model.

Although we have data on survivors of transplants that occurred before the start of follow-up in 2009 (that is, they were still in receipt of NHS care at the start of our follow up period), we have no data on patients who may have received a transplant who did not survive into the start of the trial follow up period, even if they received their transplant in the same year as some of the survivors. This is a limitation of the data.

We do not have early hospital episode data for those who survived into the follow up period, which means we could be underestimating the full costs of their transplants, and we only have survival data for those who survived until at least 2009, which means we could overestimate the benefits of transplants. That said, people can receive RRT for a long time, and attempting to take our dataset back to the diagnosis of the person in the cohort who had been on RRT for the longest would a) pre-date the Scottish Renal Registry and b) potentially underestimate the benefits of renal transplantation since techniques have developed since it was first used in Scotland.

Costs and effects beyond the person receiving a transplant

The perspective of the economic analysis focused on the patient and health system, as standard. Costs and effects may also be incurred by (living) donors and potentially recipients' family members, friends and/or carers. Transport costs may also be considerable, given the transplant service is centralised across Scotland. For patients receiving dialysis, additional costs and effects may also be borne by family members, friends and/or carers, including regular transport costs for hospital-based dialysis or energy costs associated with home-based dialysis. A wider perspective would encapsulate these costs but would not be expected to affect the overall conclusions of the analysis.

Regardless of the perspective of the analysis, a limitation of the model was not including a donor cohort. It is reasonable to assume that the costs associated with removal of a kidney from a living donor may be lower than removal of a kidney from a deceased donor[33], yet there are potential quality of life impacts for living donors. Future analysis may wish to explore:

- recovery times and quality of life associated with patients undergoing the removal of a kidney. The surgical procedure itself may be debilitating, although patients who have been successfully screened to donate a kidney would most likely recover quickly
- longer term quality of life impacts associated with having donated a kidney, potentially to a loved one, which would require making assumptions about the value of the relationships between living donors and those receiving a kidney from them
- longer term risks associated with LDKT, where over time, donors themselves require treatment for kidney problems, including potentially needing a transplant themselves. We consider these risks to be low otherwise the clinical effectiveness of living donation would be called into question.

Distributions

For some events, it was not possible to fit an appropriate probability distribution due to a lack of observed data. This is to be expected because some events - particularly subsequent events - may only occur once for people within an RRT pathway. Where it was not possible to fit distribution data, events were excluded from the model. Where distributions are possible but based on a low number of observed events, there is a risk of type 1 error (false positive attribution of a significant effect identified by chance).

For many events there was no statistically significant difference in the times to events by treatment group. The exceptions were times to excision of parathyroid, which occurred more rapidly in living and deceased donor patients compared to dialysis patients, time to first hernia-related event, and dialysis catheter events. Fistula events consistently occurred later in living donor patients compared to deceased donor patients both before and after transplant.

Model structure

The first iteration of the model excluded dialysis patients on the basis that their treatment (that is, no transplant) meant some of the events would not apply to them and would make comparison of the types of transplantation less relevant. The model was revised to more accurately reflect the patient pathway. Dialysis patients are included in the model prior to transplant, but it is important to note we do not know from the data whether they were awaiting a transplant (and if so what type of transplant) at the end of their last follow-up (or at the time of their death if they did not survive until the end of follow-up). This may have implications for the relative costs and effects within the modelled dialysis group.

It remains unclear whether survival benefit associated with LDKT stems from patients receiving a transplant more quickly, by the choice of a living donor transplant regardless of time to transplant, or both. This was beyond the scope of this work.

We are also unable to model the impact of any recent changes to the eligibility of donors and recipients because the analysis is based on prior observed data. We recognise that eligibility decisions will change over time as clinicians gain knowledge and experience in conducting successful LDKT.

Conclusion

Living donor transplantation is estimated to be less costly and more effective than deceased donor transplantation. Both living donor transplantation and deceased donor transplantation are less costly and more effective than dialysis treatment.

Identified research gaps

A broader analytical perspective may be valuable to capture costs and benefits incurred by patients' families and carers, thus capturing the overall value of different RRT strategies.

The demographics of ERF are well described from a clinical perspective, but the demographic details of living and deceased donors and the motivations of living donors to donate a kidney, were beyond the scope of this analysis. This means that it was not possible to consider the resulting impact of these issues on health inequalities in Scotland.

Acknowledgements

References

1. NHS Blood and Transplant. Organ donation and transplantation: activity report 2019/20. 2020 [cited 2024 Nov 25]; Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19481/activity-report-2019-2020.pdf.

2. Public Health Scotland. Scottish renal registry: annual report 2024. 2024 [cited 2024 Nov 25]; Available from: https://publichealthscotland.scot/media/29206/final-srr-report-2024-1.pdf.

3. Merriam-Webster Inc. Fistula. 2024 [cited 2024 Dec 18]; Available from: https://www.merriam-webster.com/dictionary/fistula.

4. National Kidney Federation. Having a fistula for dialysis. 2022 [cited 2024 Nov 22]; Available from: https://www.kidney.org.uk/having-a-fistula-for-dialysis.

5. Merriam-Webster Inc. Dialysis. 2024 [cited 2024 Dec 18]; Available from: https://www.merriam-webster.com/dictionary/dialysis.

6. National Kidney Foundation. Haemodialysis. 2024 [cited 2024 Nov 22]; Available from: https://www.kidney.org/kidney-topics/hemodialysis.

7. Merriam-Webster Inc. Hyperparathyroidism. 2024 [cited 2024 Dec 18]; Available from: https://www.merriam-webster.com/dictionary/hyperparathyroidism.

8. Kidney Research UK. Secondary hyperparathyroidism. 2024 [cited 2024 Nov 22]; Available from: https://www.kidneyresearchuk.org/conditions-symptoms/secondary-hyperparathyroidism/.

9. Merriam-Webster Inc. Parathyroid gland. 2024 [cited cited 2024 Dec 18; Available from: https://www.merriam-webster.com/dictionary/parathyroid%20gland.

10. You and Your Hormones, Society for Endocrinology. Parathyroid glands. 2021 [cited 2024 Nov 22]; Available from: https://www.yourhormones.info/glands/parathyroid-glands/.

11. Kidney Care UK. Peritoneal dialysis. 2023 [cited 2024 Nov 22]; Available from: https://kidneycareuk.org/kidney-disease-information/treatments/peritoneal-dialysis-pd/.

12. NHS Inform. Chronic kidney disease. 2022 [cited 2024 Nov 25]; Available from: https://www.nhsinform.scot/illnesses-and-conditions/kidneys-bladder-and-prostate/chronic-kidney-disease.

13. Boyd J, Mackinnon MWB, Severn A, Traynor JP, Whitworth CE. The delivery of renal replacement therapy in Scotland: why the geographic variation? QJM. 2013;106(12):1077-85.

14. Kramer A, Stel VS, Geskus RB, Tizard J, Verrina E, Schaefer F, et al. The effect of timing of the first kidney transplantation on survival in children initiating renal replacement therapy. Nephrol Dial Transplant. 2012;27(3):1256-64.

15. National Institute for Health and Care Excellence (NICE). Renal replacement therapy and conservative management. 2018 [cited 2024 Nov 25]; Available from: https://www.nice.org.uk/guidance/ng107.

16. Oniscu GC, Ravenan R, Wu D, Gibbons A, Li B, Tomson C, et al. Access to transplantation and transplant outcome measures (ATTOM): study protocol of a UK wide, in-depth, prospective cohort analysis. BMJ Open. 2016;6(2):e010377.

17. NHS Blood and Transplant. Organ donation and transplantation: activity report 2018/19. 2019 [cited 2024 Nov 25]; Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/16537/organ-donation-and-transplantation-activity-report-2018-2019.pdf.

18. NHS Blood and Transplant. UK living kidney sharing scheme: your questions answered. [cited 2024 Nov 25]; Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/26186/31204-0766mp-living-kidney-sharing-olc2173-web.pdf.

19. NHS Blood and Transplant. Organ transplantation: living donor kidney transplant. c2024 [cited 2024 Nov 25]; Available from: https://www.nhsbt.nhs.uk/organ-transplantation/kidney/receiving-a-kidney/living-donor-kidney-transplant/.

20. Bellini MI, Courtneu AE, McCaughan JA. Living donor kidney transplantation improves graft and recipient survival in patients with multiple kidney transplants. J Clin Med. 2020;9(7):2118.

21. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. Bull World Health Organ. 2018;96(6):414-22D.

22. NHS Blood and Transplant. Annual report on kidney transplantation: report for 2023/2024. 2024 [cited 2024 Dec 18]; Available from: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/34295/nhsbt-kidney-transplantation-report-2324.pdf.

23. Public Health Scotland. Scottish renal registry: annual report 2023. 2023 [cited 2024 Dec 18]; Available from: https://publichealthscotland.scot/publications/scottish-renal-registry/scottish-renal-registry-annual-report-2023//.

24. Public Health Scotland. Scottish renal registry: annual report 2022. 2022 [cited 2024 Dec 18]; Available from: https://publichealthscotland.scot/publications/scottish-renal-registry/scottish-renal-registry-reporting-on-2021/.

25. Kidney Care UK. Transplant care in the UK: a patient perspective. 2024 [cited 2024 Dec 18]; Available from: https://kcuk.cdn.ngo/media/documents/Kidney_Care_UK_Transplant_report_2024.pdf.

26. National Records of Scotland. Life expectancy in Scotland 2021-2023. 2024 [cited 2024 Nov 25]; Available from: https://www.nrscotland.gov.uk/files//statistics/life-expectancy-in-scotland/21-23/life-expectancy-21-23-report.pdf.

27. Briggs AH, Parfrey PS, Khan N, Tseng S, Dehmel B, Kubo Y, et al. Analyzing health-related quality of life in the EVOLVE trial: the joint impact of treatment and clinical events. Med Decis Making. 2016;36(8):965-72.

28. Davison SN, Jhangri GS, Feeny DH. Comparing the health utilities index mark 3 (HUI3) with the short form-36 preference-based SF-6D in chronic kidney disease. Value Health. 2009;12(2):340-5.

29. Ortega T, Valdes C, Rebollo P, Ortega F. Evaluation of reliability and validity of Spanish version of the end-stage renal disease symptom checklist-transplantation module. Transplantation. 2007;84(11):1428-35.

30. Lee Aj, Morgan CLI, Conway P, Currie CJ. Characterisation and comparison of health-related qulaity of life for patients with renal failure. Curr Med Res Opin. 2005;21(11):1777-83.

31. Ortega T, Deulofeu R, Salamero P, Lauzurica R, Casanovas T, Cofan F, et al. Perceived state of health is worse in kidney recipients younger than 60 years vs older than 60 years. Transplant Proc. 2009;41(6):2118-21.

32. Li B, Cairns JA, Draper H, Dudley C, Forsythe JL, Johnson RJ, et al. Estimating health-state utility values in kidney transplant recipients and waiting-list patients using the EQ-5D-5L. Value Health. 2017;20(976-84).

33. NHS England. National cost collection for the NHS: national schedule of NHS costs 2022/23. 2023 [cited 2024 Nov 25]; Available from: https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection/.

Appendix 1: Abbreviations

AFT	accelerated failure times
AIC	Akaike's Information Criterion
CI	confidence interval
CKD	chronic kidney disease
DD	deceased donor
DDKT	deceased donor kidney transplantation
DES	discrete event simulation
ERF	established renal failure
ESRD	end stage renal disease
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
LD	living donor
LDKT	living donor kidney transplantation
NA	not available
NHS	National Health Service
NRS	National Records of Scotland
NSD	NHS National Services Scotland's National Services Division
PRD	primary renal diagnostic
QALY	Quality-adjusted life years
RRT	renal replacement therapy
SD	standard deviation
SHTG	Scottish Health Technologies Group
UK	United Kingdom

Appendix 2: Event distributions in the model

In some cases, there were so few events that a distribution could not be fitted to the observed data and is reported as 'NA' (not available). The AIC data are available upon request. Accelerated failure times (AFT) below one indicate that the event happens more quickly for that group. AFT for groups that are equal to or exceed one indicate that the event happens at the same time or takes longer for that group.

Event	Transplant status at time of event	Event type	Dialysis Distribution	Deceased donor (DD) Distribution	Living donor (LD) Distribution
Catheter related	Before	1st	Lognormal (12.7, 6.2)	Weibull (0.362, 9,010). AFT LD 1.59 (95% CI 0.652 to 3.86)	
		2nd or subsequent	Lognormal (13.1655, 3.8103) AFT DD 2.062 (95% CI 1.0615 to 4.0053) AFT LD 1.7599 (95% CI 0.6196 to 4.9986)		
	After	1st	NA	Log logistic (1.06, 1500)	Log logistic (0.826, 712)
		2nd or subsequent	NA	Lognormal (12.611, 3.254) AFT LD 1.495 (95% CI 0.832 to 2.688)	
Cardiovascular	Before	1st	Gamma (0.539, 0.0000301)	Lognormal (8.847, 2.375)	Lognormal (9.64, 3)
		2nd or subsequent	Lognormal (10.7889, 2.4863)	Lognormal (9.2887, 1.6209) AFT LD 0.7411 (95% CI 0.497 to 1.1047)	
	After	1st	NA	Lognormal (12.206, 2.56)	Lognormal (12.5, 2.88)
		2nd or subsequent	NA	Lognormal (14.838, 2.625) AFT LD 0.64 (95% CI 0.222 to 1.84)	
Exchange of plasma	Before	1st	Lognormal (57, 16.9)	Lognormal (23.2, 6.52)	Weibull (0.502, 1,470,000)
		2nd or subsequent	Gamma (0.471, 1.14E-10) AFT DD 17.3 (95% CI 0.347 to 867) AFT LD 308 (95% CI 45.2 to 210,000)		
	After	1st	NA	Lognormal (19.5278, 4.1841) AFT LD 0.1377 (95% CI 0.0182 to 1.041)	
		2nd or subsequent	NA	Lognormal (19.005, 3.9915) AFT LD 0.1874 (95% CI 0.0272 to 1.2889)	
Excision of parathyroid	Before	1st	Weibull (1.2, 196,000) AFT DD 0.157 (95% CI 0.0844 to 0.291) AFT LD 0.102 (95% CI 0.0466 to 0.225)		

Event	Transplant status at time of event	Event type	Dialysis Distribution	Deceased donor (DD) Distribution	Living donor (LD) Distribution
		2nd or subsequent	NA		
	After	1st	NA	Lognormal (20.629, 4.848) AFT DD 0.201 (95% CI 0.027 to 1.489)	
		2nd or subsequent	NA		
Exam of abdomen/ kidney	Before	1st	Log Logistic (0.414, 86,900,000).= AFT DD 0.28 (95% CI 0.0615 to 1.27) AFT LD 0.239 (95% CI 0.0251 to 2.27)		
		2nd or subsequent	NA		
	After	1st	NA	Lognormal (19.156, 6.212) AFT LD 2.766 (95% CI 0.599 to 12.783)	
		2nd or subsequent	NA		
Central venous catheter	Before	1st	Lognormal (9.05, 5.83)	Lognormal (9.42, 4.91)	Lognormal (8.77, 4.56)
		2nd or subsequent	Lognormal (10.7, 4.14)	Lognormal (9.47, 2.76)	Lognormal (10.8, 3.21)
	After	1st	NA	Lognormal (16.07, 4.44) AFT LD 0.331 (95%CI: 0.133, 0.827)	
		2nd or subsequent	NA	Lognormal (16.76, 3.4827) AFT LD 0.314 (95%CI: 0.0868, 1.136)	
Compensation renal failure	Before	1st	Lognormal (17.62, 5.519) AFT DD 0.439 (95% CI 0.17 to 1.134) AFT LD 0.407 (95% CI 0.098 to 1.691)		
		2nd or subsequent	Lognormal (18.9, 4.42)	Lognormal (13.8, 2.58)	Lognormal (16.9, 4.95)
	After	1st	NA	Lognormal (25.24, 5.42) AFT LD 0.04855 (95%CI: 0.0004, 4.9971)	
		2nd or subsequent	NA		
Skin related	Before	1st	Log logistic (0.497, 6,510,000)	Lognormal (14.3, 3.12)	Log logistic (144, 25,200)
		2nd or subsequent	NA		
	After	1st	NA	Lognormal (15.218, 2.64) AFT LD 0.646 (95% CI 0.191 to 2.19)	

Event	Transplant status at time of event	Event type	Dialysis Distribution	Deceased donor (DD) Distribution	Living donor (LD) Distribution
		2nd or subsequent	NA		
Hernia related	Before	1st	Lognormal (18.1534, 4.6471) AFT DD 0.095 (95% CI 0.0348 to 0.2595) AFT LD 0.1877 (95%CI 0.0378 to 0.9332)		
		2nd or subsequent	NA		
	After	1st	Lognormal (15.444, 3.568) AFT LD 2.38 (95% CI 0.736 to 7.704)		
		2nd or subsequent	NA		
Topical anaesthesia	Before	1st	Lognormal (20.4, 5.21)	Log logistic (68.7, 386000)	Log logistic (144, 25,200)
		2nd or subsequent	NA		
	After	1st	NA	Gamma (0.638, 2.01E-08)	NA
		2nd or subsequent	NA		
Fistula	Before	1st	Lognormal (7.13, 3.14)	Log logistic (0.649, 1020) AFT LD 2.04 (95% CI 1.37 to 3.03)	
		2nd or subsequent	Lognormal (8.93, 2.52)	Lognormal (8.16, 1.774) AFT LD 1.74 (95% CI 1.21 to 2.504)	
	After	1st	NA	Lognormal (11.3632, 2.5301) AFT LD 1.6186 (95% CI 1.0426 to 2.513)	
		2nd or subsequent	NA	Lognormal (13.4979, 2.6866) AFT LD 2.7344 (95% CI 1.0705 to 6.9845)	
Rejected donor kidney	Before	1st	Log logistic (0.435, 2.92E+11) AFT DD 0.0187 (95% CI 0.0000182 to 19.2) AFT LD 0.000349 (95% CI 0.000000124 to 0.985)		
		2nd or subsequent	NA		
	After	1st	NA	Lognormal (15, 3.29)	Lognormal (21.9, 6.32)
		2nd or subsequent	NA		
Dialysis catheter	Before	1st	Lognormal (13, 6.41)	Lognormal (10.745, 4.385) AFT LD 0.37 (95% CI 0.185 to 0.741)	

Event	Transplant status at time of event	Event type	Dialysis Distribution	Deceased donor (DD) Distribution	Living donor (LD) Distribution
		2nd or subsequent	Lognormal (14.4211, 3.8187) AFT DD 0.2178 (95% CI 0.1206 to 0.3932) AFT LD 0.1484 (95% CI 0.0639 to 0.3445)		
	After	1st	NA	Lognormal (13.785, 3.917). AFT LD 0.75 (95% CI 0.38 to 1.48)	
		2nd or subsequent	NA	Lognormal (17.098, 3.5397) AFT LD 0.2807 (95% CI 0.0709 to 1.1112).	
Transplant related	Before	1st	Lognormal (24.309351, 5.211988) AFT DD 0.005031 (95% CI 0.000272 to 0.09289) AFT LD 0.001276 (95% CI 0.000048 to 0.033904)		
		2nd or subsequent	NA		
	After	1st	NA	Lognormal (21.9597, 5.9837) AFT LD 0.4226 (95% CI 0.0597 to 2.9927)	
		2nd or subsequent	NA		
Other costed events	Before	1st	Lognormal (16.3252, 5.307) AFT DD 0.069 (95% CI 0.0343 to 0.1389) AFT LD 0.0693 (95% CI 0.0258 to 0.1864)		
		2nd or subsequent	Lognormal (19.2767, 4.9177) AFT DD 0.8747 (95% CI 0.1789 to 4.2779) AFT LD 0.1052 (95% CI 0.0189 to 0.5862)		
	After	1st	NA	Lognormal (15.706, 4.629) AFT LD 3.652 (95% CI 1.219 to 10.938)	
		2nd or subsequent	NA	Lognormal (20.6142, 4.5714) AFT LD 0.3384 (95% CI 0.0356 to 3.2199)	
Transplant	NA	NA	NA	Gamma (1.36, 0.00187)	Gamma (0.59, 0.00159)
Death	NA	NA	Weibull (0.832, 2000)	Weibull (2.05, 8690)	Weibull (2.18, 10,200)
Abbreviations: NA = not available, CI = confidence interval, AFT = accelerated failure time					