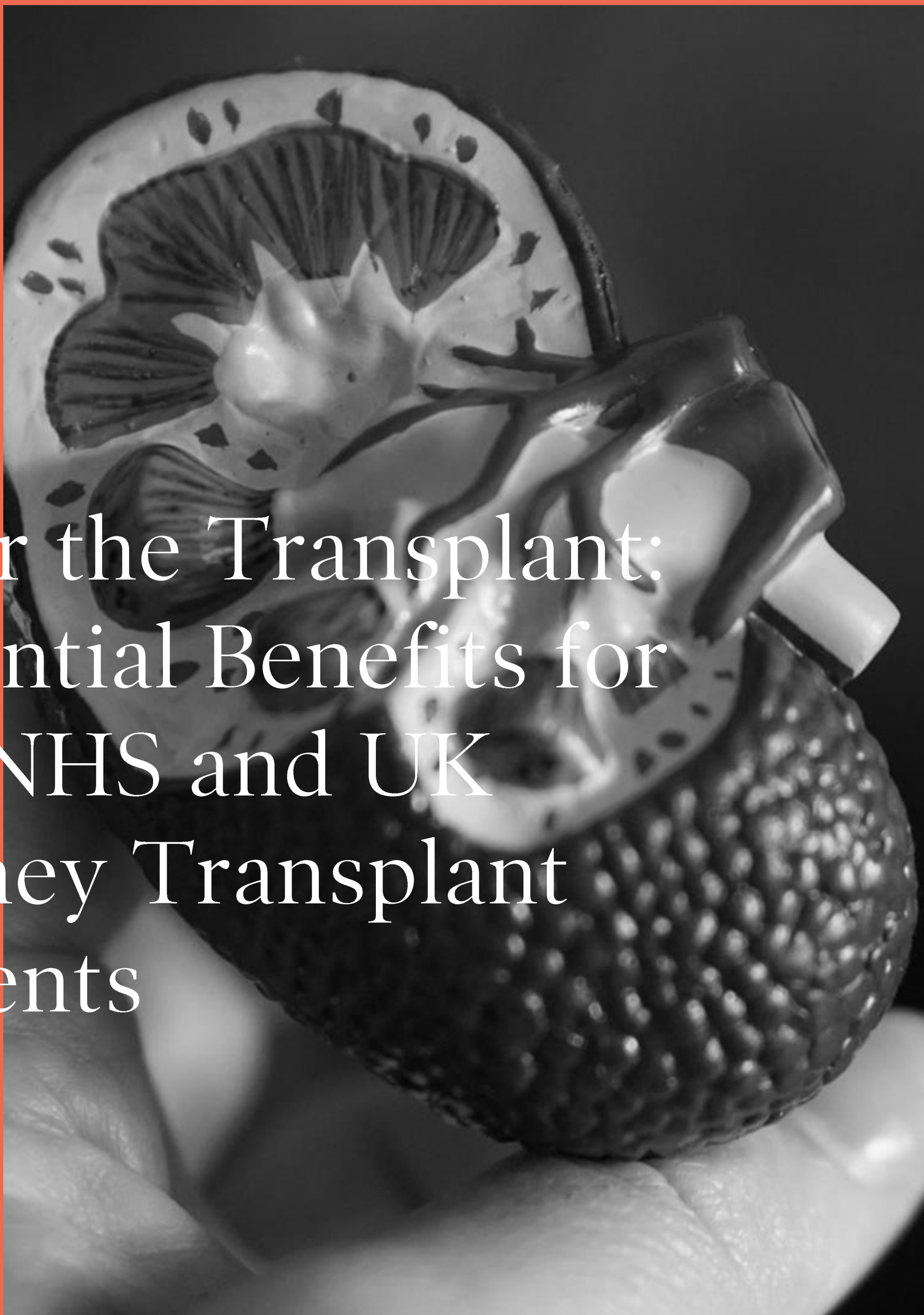


After the Transplant: Potential Benefits for the NHS and UK Kidney Transplant Patients

CONSULTING REPORT
NOVEMBER 2021

Chris Skedgel
Mehmet Bulut
Lotte Steuten

ohe.org

NOVEMBER 2021

After the Transplant: Potential Benefits for the NHS and UK Kidney Transplant Patients

Chris Skedgel
Office of Health Economics, London

Mehmet Bulut
Office of Health Economics, London

Lotte Steuten
Office of Health Economics, London

OFFICE OF HEALTH ECONOMICS
CONSULTING

Please cite this report as:
Skedgel C, Bulut M, Steuten L. (2021) After the Transplant: Potential Benefits for the NHS and UK Kidney Transplant Patients. London: Office of Health Economics. Available at: https://www.ohe.org/publications/after-the-transplant-potential-benefits-kidney-transplant

Corresponding Author:
Chris Skedgel
cskedgel@ohe.org

This consulting report was commissioned and funded by Novartis Pharmaceuticals. Novartis Pharmaceuticals were consulted throughout the development of this report and had editorial input to the final draft. Novartis had no input into the structure or the parameters of the model on which this report is based.

For further information please contact:

Professor Lotte Steuten
Vice-president and Head of Consulting, OHE
Honorary Visiting Professor in Economics at City, University of London

Tel +44 (0)207 747 1441
Email lsteuten@ohe.org

About OHE Consulting Reports

Many of the studies OHE Consulting performs are proprietary and the results are not released publicly. Studies of interest to a wide audience, however, may be made available, in whole or in part, with the client's permission. They may be published by OHE alone, jointly with the client, or externally in scholarly publications. Publication is at the client's discretion.

Studies published by OHE as OHE Consulting Reports are subject to internal quality assurance and undergo external review, usually by a member of OHE's Editorial Panel. Any views expressed are those of the authors and do not necessarily reflect the views of OHE as an organisation.

Funding and Acknowledgements

This consulting report was commissioned and funded by Novartis Pharmaceuticals. Novartis Pharmaceuticals were consulted throughout the development of this report and had editorial input to the final draft. Novartis had no input into the structure or the parameters of the model on which this report is based.

Table of Contents

Forewords

National Kidney Federation

Chronic kidney disease (CKD) affects around 3 million people in the UK. The situation for Black, Asian, mixed race and other ethnic minority (BAME) groups is particularly acute, as they are five times more likely to develop CKD. As the disease advances toward kidney failure, there are two main options faced by patients – to undergo a pre-emptive transplant or dialysis until a transplant becomes available.

Dialysis, while life-extending, can also be exhausting and severely impacts patients' quality of life. Dialysis occurs at least three times a week, lasting for hours with patients abiding by rigid fluid and dietary restrictions. Some patients are able to cope well with the routine and treatment demands, whereas for others, the loss of independence is difficult, with families and carers often needing to step in. Patients often reduce their working hours or leave work altogether, resulting in reduced financial capabilities and compounding their loss of independence. Promoting the benefits of home dialysis is a priority of the National Kidney Federation and is becoming increasingly popular as it offers greater flexibility that can improve quality of life.

While average waiting times have improved over the past decade, the average wait for a kidney transplant remains 2-3 years. Reducing the waiting list for transplant patients is a complex issue but can be supported by increasing organ supply or reducing the need for repeat transplants. However, things are getting better thanks to recent opt-out laws and organ donation awareness campaigns. NHS Blood and Transplant (NHSBT) and the National BAME Transplant Alliance (NBTA) have made great strides in raising awareness around the need for increased organ donation in BAME communities.

While recognising these gains is important, it's right that we recognise areas for improvement in post-transplant outcomes. While the average lifespan of a transplanted kidney ranges between 15-25 years, some patients can experience 40+ years, whereas others find themselves back on the waiting list after a few short years. Initiatives to help patients better understand the reasons why transplanted kidneys fail and extend kidney transplant survival is welcome and important to increase kidney donor numbers.

We're pleased that this research is shining a light on these issues and hope that the ensuing dialogue translates into meaningful change for post-kidney transplant patients. The National Kidney Federation is keen to work with all stakeholders to get people off the waiting list and back to the life experiences that matter to them.

David Coyle

Trustee, National Kidney Federation

Recipient of 2 kidney transplants

Kidney Care UK: Kidney Transplants – room for improvement?

8 out of every 10 people waiting for the gift of a transplant are waiting for a kidney. The difficulties of kidney failure should not be underestimated; it is emotionally, physically and financially demanding. A kidney transplant is the gold star treatment and is sought by many, but for some, the wait becomes too long. They become too poorly to benefit from a transplant and then, sadly, die.

The recent changes in the law in England and Scotland, following that in Wales, to an opt out donation system, are an excellent step towards increasing the numbers of transplants. However, it is not only about increasing transplantation. A successful transplant system will support people to maintain their transplant too. Back in 2013, I co-authored the Kidney Health Delivering Excellence report (cited in the 2021 GIRFT report), which highlights 'Living Well with a Transplant' as one of its ambitions to improve kidney care in the UK, so that "a person who receives a transplant is supported to achieve the greatest possible benefit from it". This is as fundamental now as it was then; right now, when the mental health burden of isolation from and fear of Covid is high, and innovations in technology are moving on, it is apt to draw attention to what we can do to increase the time people live well with their kidney transplant.

Whether that is clear education and advice, dietary or exercise help, being supported to understand rapidly changing medications, employment support, peer support or counselling, we can welcome a focus on post-transplant care which is not just about the medicines the patient goes home with, vital though that is. People from South Asian and Black communities wait longer, so their needs, experiences and views must be included in the work this initiative may generate. Good kidney healthcare is a team effort in which we as people with transplants, kidney charities, policymakers and our multiprofessional excellent healthcare teams can all take part.

Fiona Loud

Policy Director (and transplant recipient), Kidney Care UK

To read about the advocacy, counselling, financial and emotional support Kidney Care UK gives to kidney patients and their families, please see https://www.kidneycareuk.org/get-support/

Executive Summary

Kidney Care UK (2021) suggests that around 10% of people in the United Kingdom (UK) have chronic kidney disease (CKD). For most people, CKD can be managed through diet and lifestyle changes, but around 10% of those with CKD will reach **renal failure**, where their kidneys no longer function well enough to support a normal, healthy life. If left untreated, renal failure will ultimately lead to death.

For most patients, **kidney transplant** is the next step after renal failure, as it improves expected survival and quality-of-life and frees them from ongoing dialysis. It is also associated with lower long-term costs to the NHS relative to dialysis. The current cost of a kidney transplant is roughly £50,000 per patient, with annual follow-up care of £6,000 per year, compared to ongoing dialysis costs of almost £35,000 per patient per year (Jones-Hughes et al., 2016). Based on these figures, the cumulative cost of dialysis over ten years would be £350,000, compared to £104,000 with transplant.

Kidney Research UK (2017) estimated that although up to 5,000 people in the UK require a kidney transplant each year, only about 3,000 transplants can be performed each year, and around 250 people die each year while waiting for a transplant. A key limitation to the number of people transplanted each year is a shortage of donated organs relative to need. People from a BAME background are disproportionately affected by shortages and longer wait times for a suitable kidney for transplantation, in part due to lower rates of organ donation amongst these communities (NHS Blood and Transplant, 2020c).

Legislative changes such as 'presumed consent' (which requires individuals to 'opt out' of automatic organ donation) (NHS Blood and Transplant, 2021) seek to increase the number of organs donated and transplanted, but it is equally important to continue to find ways to make better use of the organs currently available. This includes improving post-transplant care to increase the likelihood of a successful transplant and extending the duration of graft survival. Extending graft survival reduces – or even eliminates – the number of re-transplants performed, freeing-up organs for first-time patients and reducing the burden of repeat transplantation on patients. Improved post-transplant care could also improve patient quality-of-life, reduce costs to the NHS, and allow more patients to return to work and other valuable activities more quickly.

There are two objectives for this report:

i. To describe the potential impact of improved post-transplant care for kidney recipients in terms of patient quality-of-life and psychosocial impacts, direct costs to the NHS, and indirect costs to patients and society in terms of foregone productivity and other valuable activities.

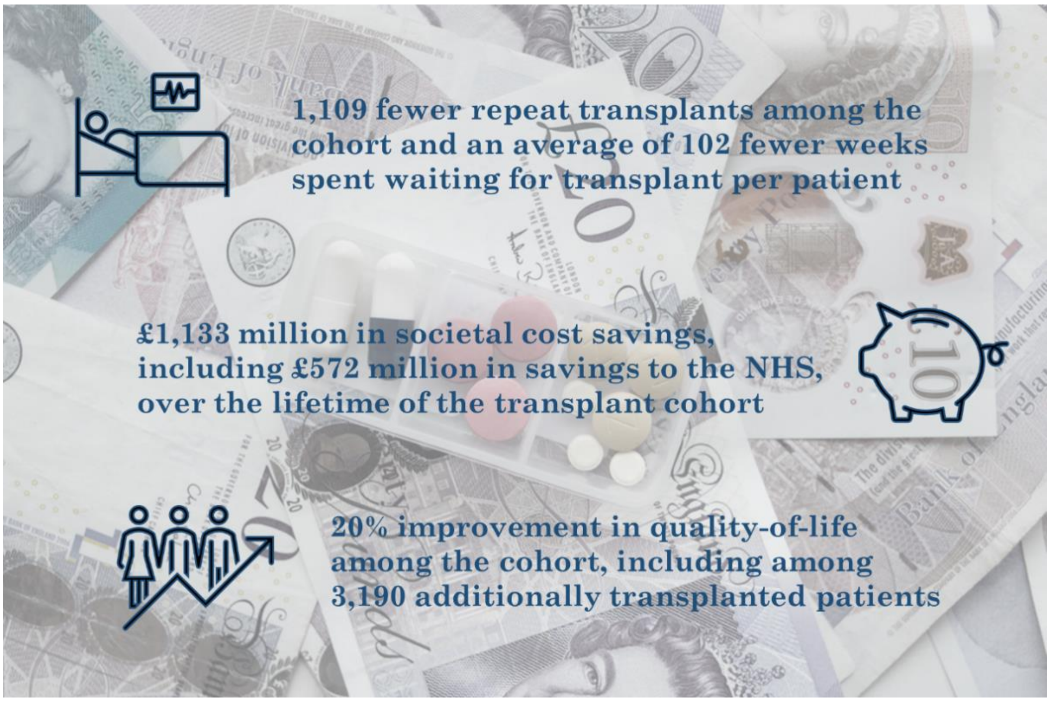
ii. To highlight potential policy priorities that could help achieve these impacts, focusing on the key drivers of cost and patient burden identified in objective 1.

i. What do we all stand to gain from improved post-kidney transplant care?

To address objective 1, we developed an economic model that combines information from different sources, including patient, National Health Service (NHS), and societal costs and burdens before, during, and after transplant.

OHE

Our primary results are based on a hypothetical cohort of 3,190 renal failure patients representative of United Kingdom patients transplanted in 2019 (NHS Blood and Transplant, 2019), assuming maximum or 'best case' effects. The model suggests that over the lifetime of the hypothetical cohort, optimal post-transplant care could avoid more than 1,100 repeat transplants; avoid more than 100 weeks of dialysis per patient; reduce the quality-of-life burden amongst the cohort by 20%; allow more than 3,000 additional patients to be transplanted in the short-term; reduce societal costs, including the value of lost productivity time, by almost £1.13 billion; and allow the NHS to reallocate more than £570 million to other programmes.



Improved ability of patients to make valuable use of their time in paid, voluntary, or leisure activities; reduced wait times; and an increase in the supply of organs have the greatest impacts on combined NHS and societal cost savings. From the patient perspective, reducing the incidence of serious complications (also known as serious sequelae) has the greatest single impact on quality-of-life, followed by improvements in transplant or recovery that can reduce the burden on patients, an increased supply of organs so that more patients can be transplanted, and reduced wait times so that patients can move off of dialysis more quickly.

ii. How can we realise these benefits?

Based on the key drivers of cost and quality-of-life in the economic model, **we believe that the following objectives should be key policy priorities:**

1. Improving the ability of post-transplant patients to restart activities;
2. Reducing wait times, including through increasing the supply of organs;
3. Reducing the incidence of serious complications post-transplant, especially depression

Policy recommendation 1: Improve the ability of patients to restart the activities that matter to them

Fewer than 1 in 4 patients with renal failure are able to engage in work or other valuable activities whilst they are waiting for a kidney transplant (Erickson et al., 2018), and even one year post-transplant, up to 15% of recipients are still unable to engage in productive activities (Miyake et al., 2019). Valuable activities outside the workplace can include volunteer or social work, contributing to the 'third sector', caregiving, or personal leisure. The economic model suggests that **supporting post-transplant patients in making productive use of their time** would provide the greatest societal benefits.

We recommend **an initial consultation among patient groups, professional groups, policymakers and trade bodies** to discuss the specific needs, challenges and capabilities of post-transplant patients and how best they can be supported to re-enter the workplace where able and wanting or to engage in other valuable activities in the community outside of traditional workplaces. Another suggestion is allowing patients post-transplant, who often feel immediately more energised after successful surgery, to engage in **voluntary education initiatives** that can support their transition back into society.

Policy recommendation 2: Focus on reducing wait times for kidney transplant, including by increasing the supply of organs

Over the last decade, there has been a 21% reduction in the number of people on the transplant wait list. Despite this progress, however, the average time on the kidney transplant waiting list is still more than 600 days (NHS Blood and Transplant, 2019). This extended wait is driven primarily by a shortage of organs relative to need and is often substantially higher for BAME patients given lower organ donation rates amongst this population. This situation will likely be made worse by the Covid-19 pandemic. The economic model suggests that **reduced wait times are the single most important source of cost savings and a key contributor to patient quality-of-life**. Therefore, this aspect should be a key focus of improved post-transplant care.

Efforts to **increase the supply of organs** through public awareness campaigns and 'presumed consent' legislation are central to increasing the supply of organs and reducing wait times, **particularly amongst ethnic minority populations,** to eliminate inequalities in wait times between patient groups. Additionally**, increased application of medical perfusion to sustain organs prior to transplant** can mean more successful transplants. Together, these can increase the supply of organs and reduce the number of re-transplants performed, free-up organs for patients on the waiting list, and indirectly reduce wait times.

Sharing capacity and learnings between transplant centres could also reduce wait times and decrease variation in outcomes between centres. Reduced variation in outcomes is a primary objective of the Getting It Right First Time (GIRFT) programme, which aims to improve care and patient outcomes, and promote efficiencies, such as a reduction in unnecessary procedures (GIRFT, 2021).

Policy recommendation 3: Reduce the incidence of serious post-transplant complications, especially depression and other mental health aspects

Kidney transplant patients are at increased risk of a number of serious complications, including serious infection, deep vein thrombosis, malignancies, diabetes, hypertension, obesity, and, notably, depression. The economic model suggests that these complications account for more than £126 million in direct costs to the NHS and a further £114 million in lost productive time and impose a substantial quality-of-life burden on patients. Kidney patients report significant impacts on their mental health both before and after transplant, and the prevalence of mental health issues is higher than in the general population.

Advances in surgical techniques and immunosuppressive medicines can contribute to a reduction in infections and malignancies, but **greater mental health support** is also required to address depression and anxiety amongst this population. In market research conducted by Portland, patients reported that **peer-to-peer support programmes** were effective in connecting patients who could then offer comfort to one another and explain the process of transplantation**. Digital technologies** offer the opportunity to expand peer-to-peer support to remote areas using virtual networks. Other digital technologies could support improved patient self-management, including remote blood tests, blood pressure monitoring, and glucose monitoring for patients with diabetes or pre-diabetes. Such technologies could improve outcomes as well as reduce the number of hospital visits for routine monitoring, saving patient and health system time and costs. **Personalised predictive systems that can monitor and predict graft condition** without hospital visits would also improve outcomes and potentially ease patient anxiety (Loupy et al., 2019; Vaulet et al., 2021).

iii. Conclusions

Kidney transplantation offers the greatest hope for patients with renal failure, but there is a substantial gap between the number of patients in need of a transplant and the number that can be performed each year. Much of this gap is the result of a shortage of donated organs relative to need, particularly amongst people from a BAME background. This shortfall is made worse by the fact that the time a transplanted organ can survive is limited, and a patient will often need more than one transplant over their lifetime.

NHS initiatives and legislative changes are seeking to increase the number of organs donated and transplanted. We welcome the renewed focus by the health system on finding ways to make better use of the organs currently available, particularly through improved post-transplant care that can increase the likelihood of a successful transplant and extend the duration of graft survival. Improved post-transplant care could reduce the number of re-transplants required, freeing-up organs for first-time patients and reducing the burden of repeat transplantation on patients, as well as improve patient quality-of-life, reduce costs to the NHS, and allow more patients to return to work and other valuable activities more quickly.

1 Why do we need to improve post-transplant care for kidney recipients?

Kidney Care UK (2021) suggest that around 10% of people in the United Kingdom (UK) have chronic kidney disease (CKD). Diabetes, hypertension (high blood pressure), heart disease, and other factors, including inherited causes, all increase the risk of CKD. For most people, CKD can be managed through diet and lifestyle changes. Around 10% of those with CKD, though, will reach **renal failure**, where their kidneys no longer function well enough to support a normal, healthy life. If left untreated, renal failure will ultimately lead to death.

Renal failure can be managed with dialysis, which functions as an 'artificial kidney', removing waste and toxins from a patient's blood. Peritoneal dialysis passes fluid through the abdomen to flush out toxins, whilst haemodialysis filters blood through a mechanical filter. Both approaches impose substantial physical, mental, and social burdens on patients and considerable costs on the National Health Service (NHS).

For most patients, **kidney transplant** is the next step after renal failure, as it improves expected survival and quality-of-life, and frees them from ongoing dialysis. It is also associated with lower long-term costs to the NHS relative to dialysis. The current cost of a kidney transplant is roughly £50,000 per patient, with annual follow-up care of £6,000 per year, compared to ongoing dialysis costs of almost £35,000 per patient per year (Jones-Hughes et al., 2016). Based on these figures, the cumulative cost of dialysis over 10 years would be £350,000, compared to £104,000 with transplant.

Kidney Research UK (2017) estimate that although up to 5,000 people in the UK require a kidney transplant each year, only about 3,000 transplants can be performed each year, and around 250 people die each year while waiting for a transplant. A key limitation to the number of people transplanted each year is a shortage of donated organs relative to need. People from a BAME background are disproportionately affected by shortages and longer wait times for a suitable kidney for transplantation, in part due to lower rates of organ donation amongst these communities (NHS Blood and Transplant, 2020c). Transplanted kidneys can come from living or deceased (cadaveric) donors. Transplants ("grafts") from living donors offer the greatest chance of a successful transplant, but currently, only 1 in 3 transplanted kidneys come from a living donor. This shortfall in available organs is made worse by the fact that the time a transplanted organ can survive is limited, and a patient will often need more than one transplant over their lifetime. Up to 9% of kidney grafts fail within five years of transplant (NHS Blood and Transplant, 2019), and 75% are likely to fail within 20 years of transplant (McCaughan and Courtney, 2015). This is exacerbated by the fact that kidneys from deceased donors – by far the larger source of organs – have shorter survival and a greater risk of complications than those from living donors (NHS Blood and Transplant, 2020b). This means that younger transplant recipients, particularly from deceased donors, may undergo the risk, stress and cost of transplantation multiple times over their lifetime. There is also a small but serious risk of fatal infection following transplant (Ying et al., 2020, p.2893), and reducing the need for re-transplant avoids some of this risk.

Legislative changes such as 'presumed consent' (requiring individuals to 'opt out' of automatic organ donation) (NHS Blood and Transplant, 2021) seek to increase the number of organs donated and transplanted. It is equally important, though, to continue to find ways to make better use of the organs currently available. This includes making use of higher risk donors (Heilman et al., 2016), as well as improving post-transplant care to increase the likelihood of a successful transplant and extending the duration of graft survival. Extending graft survival reduces – or even eliminates – the number of re-transplants performed, freeing-up organs for first-time patients and reducing the burden of repeat transplantation on patients. Improved post-transplant care could also improve patient quality-of-life, reduce costs to the NHS, and allow more patients to return to work and other valuable activities more quickly.

1.1 Objectives for this research

There are two objectives for this report:

1. To describe the potential impact of improved post-transplant care for kidney recipients in terms of patient quality-of-life and psychosocial impacts, direct costs to the NHS, and indirect costs to patients and society in terms of foregone productivity and other valuable activities.

2. To highlight potential policy priorities that could help achieve these impacts, focusing on the key drivers of cost and patient burden identified in Objective 1.

The first objective will be addressed through a combination of economic modelling and descriptive patient case studies. The highlights of these results are presented in the next section, and the detailed methods and full results are included in Appendix 1.

For the second objective, we suggest priority areas of policy focus based on the key drivers of cost and patient burden identified in the economic model. For each suggested focus area, we make specific policy suggestions based on evidence from the literature to reduce costs to the NHS and broader society and improve the wellbeing of patients.

2 What do we all stand to gain from improved post-kidney transplant care?

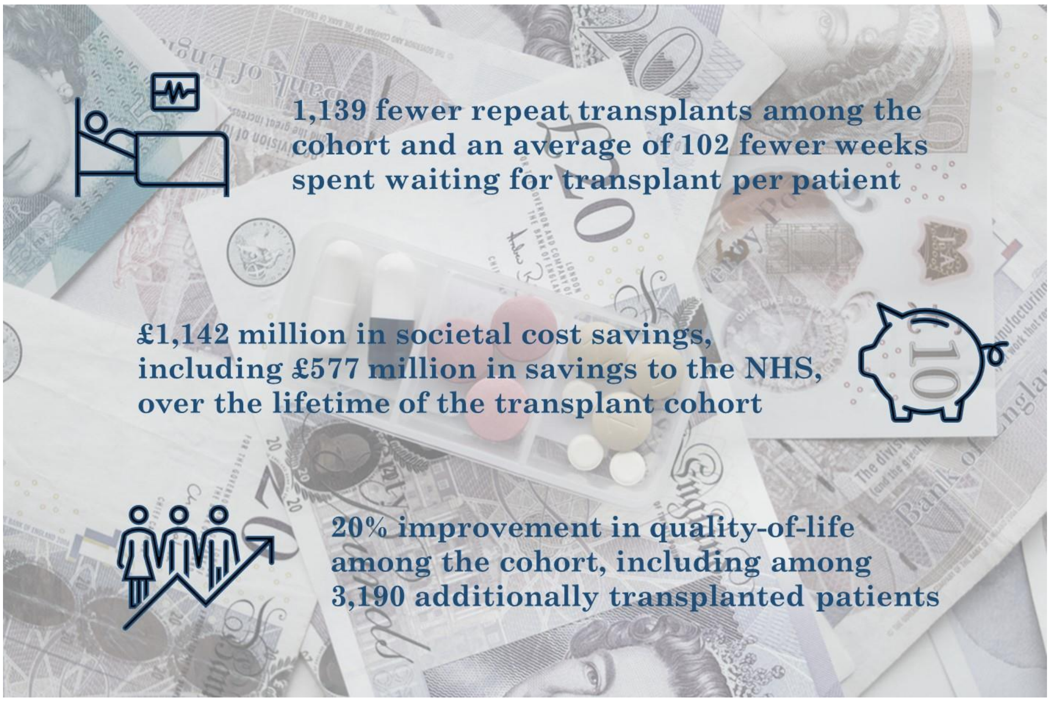
Improved post-transplant care has the potential to improve patient quality-of-life, reduce costs to the NHS, and allow more patients to return to work and other valuable activities more quickly. In this section, we quantify some of those impacts based on results from an economic model developed specifically for this report. The model combines information from different sources, including NHS costs before, during, and after transplant, the probability, or incidence, of short- and long-term complications associated with transplant, and the costs of treating those complications. All costs are adjusted to 2020 prices. From the patient's perspective, it includes information on the proportion able to engage in paid employment or other productive activities whilst on the waitlist or post-transplant and an estimate of the value of that time. Finally, it includes the characteristics of kidney transplant recipients, including their age at first transplant and the expected survival of the patient and the graft. This model and its inputs are described in detail in Appendix 1.

Our estimates of impact are based on maximum or 'best case' effects. These reflect what is *logically possible* (e.g., the maximum possible effect on wait times is a 100% reduction) without judging the technical, biological or policy limits to these effects (e.g., it is unlikely that it will be possible to fully eliminate wait times, i.e., 'instant' transplant). This means that what is *realistically achievable* in the short- to medium-term will be less than the maximum possible effect, but an understanding of the relative magnitude of the potential benefits associated with different effects can help to inform priorities for public policy, investment, and care.

The model estimates cumulative cost and quality-of-life impacts over the lifetime of a hypothetical cohort of patients. The number of individuals in the current hypothetical cohort reflects the number of kidney transplants performed in the UK in 2018/19 (NHS Blood and Transplant, 2019), and we make the simplifying assumption that all patients in this cohort are receiving their first transplant. We use a 'microsimulation' approach, described in more detail in Appendix 1, to estimate the lifetime costs and quality-of-life impacts for each individual in the cohort. In generating our baseline estimates, we use the current level of factors, including kidney transplant wait times, expected graft survival, the incidence of adverse events, post-transplant quality-of-life, lost productivity, and the proportion of living kidney donors. We compare these simulated individual results to a 'best case' alternative for the same individuals where outcomes are estimated with each factor set to its optimal level (e.g., no wait time for transplant; no quality-of-life penalty following transplant). As a conservative estimate, we impose an arbitrary limit on potentially 'open ended' effects such as increased graft survival and the supply of organs. For example, we assume the maximum change in the duration of graft survival is 100% or a doubling of the current duration. To the extent that greater extensions in graft survival are possible, we may underestimate potential gains, although we note that graft survival is inevitably constrained by the patient's survival.

Our estimates of the 'best case' potential gains for a UK cohort of 3,190 hypothetical renal failure patients are summarised below in Figure 1. The model suggests that over the lifetime of the hypothetical cohort, optimal post-transplant care could avoid more than 1,100 repeat transplants; avoid more than 100 weeks of dialysis per patient; reduce the quality-of-life burden amongst the cohort by 20%; allow more than 3,000 additional patients to be transplanted in the short-term; reduce societal costs, including the value of lost productivity time, by almost £1.14 billion; and allow the NHS to reallocate £577 million to other programmes. This represents a societal saving of almost £85 million per year over the average lifetime of the cohort (13.5 years).

FIGURE 1: SUMMARY OF 'BEST CASE' PATIENT AND NHS IMPACTS



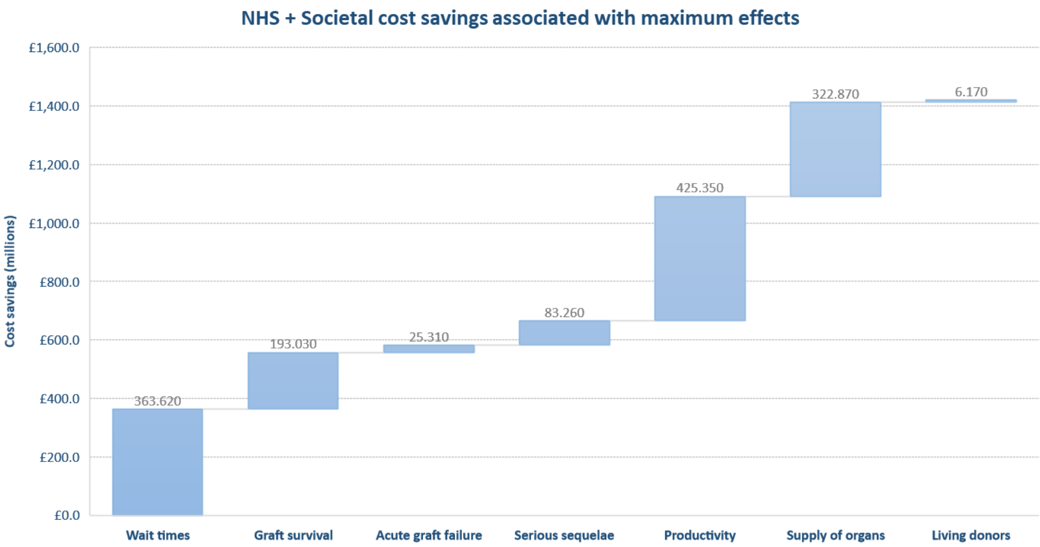
Relative to baseline aggregate societal costs of £1.6 billion, this 'best case' scenario represents societal savings of more than 90%, and relative to baseline NHS cost of £833 million, savings of almost 70%. The 'best case' impacts by UK nation are shown in Table 1. More detailed national results are shown in Appendix 2. Results by nation represent the overall savings scaled by relative share of the UK population.

TABLE 1: 'BEST CASE' IMPACTS BY UK NATION

				
Societal savings	£1.04 billion	£97 million	£55 million	£34 million
NHS savings	£545 million	£52 million	£31 million	£19 million
Transplants avoided	964	93	59	38

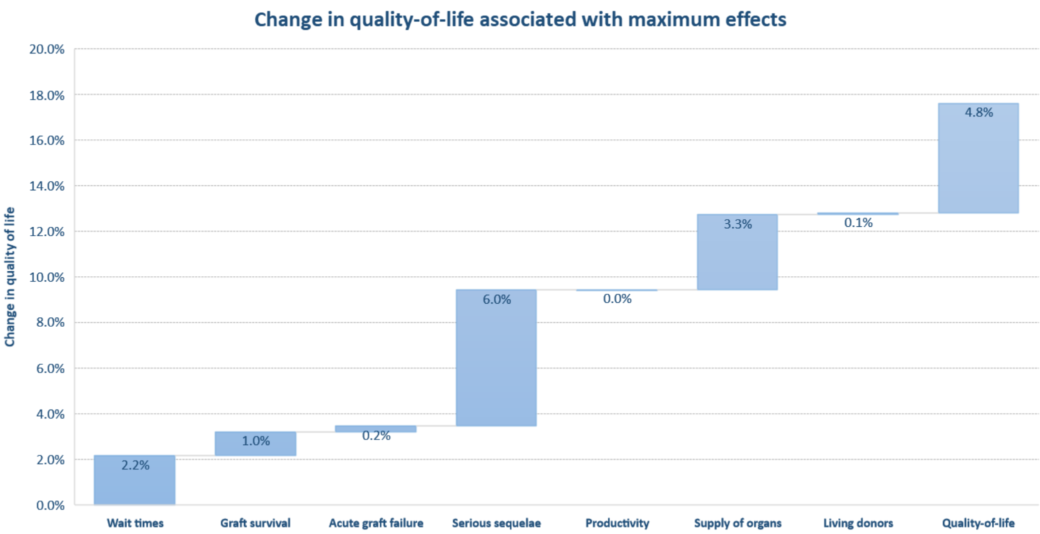
When we consider the contribution of each effect in the model to these overall gains, illustrated in Figure 2 below, we see that improved ability of patients to make valuable use of their time in paid, voluntary, or leisure activities; reduced wait times; and an increase in the supply of organs have the greatest impacts on combined NHS and societal cost savings.

FIGURE 2: COMBINED NHS AND SOCIETAL COST SAVINGS BY EFFECT



When we consider impacts on patient quality-of-life, the key drivers are slightly different, as illustrated in Figure 3. Reducing the incidence of serious complications has the greatest single impact on quality-of-life, followed by improvements in transplant or recovery that can reduce the burden on patients, an increased supply of organs so that more patients can be transplanted, and reduced waiting times so that patients can move off of dialysis more quickly.

FIGURE 3: CHANGE IN PATIENT QUALITY-OF-LIFE BY EFFECT



Given the high incidence of depression and anxiety amongst transplant patients – a systematic review (Palmer et al., 2013) suggested that up to 1 in 4 kidney transplant patients experience depression – we tracked the specific impact of depression on costs and patient quality-of-life. We find that **post-transplant depression is associated with avoidable costs to the NHS of £8.4 million**

and a loss of more than 1,000 quality-adjusted life years (QALYs)[1] within the UK cohort, accounting for almost half of the total burden of all serious long-term complications following transplant.

2.1 Longer graft survival is associated with fewer repeat transplants and quicker first transplants for patients in need

Improvements in graft survival reduce the expected number of transplants per person over their lifetime, avoiding the costs, quality-of-life impacts, and lost productive time associated with a return to dialysis, transplantation surgery and recovery. Reducing the number of transplants a patient can expect to require over their lifetime also frees up more organs for other patients in need.

Doubling current graft survival, from an average of 9.3 years (McCaughan and Courtney, 2015) to more than 18 years, would save society £189 million over the lifetime of the cohort, including £129 million in direct savings to the NHS through dialysis and re-transplants avoided. Reduced dialysis and re-transplants would also avoid some quality-of-life burden on patients by avoiding aspects such as the discomfort and anxiety of dialysis and recovery from transplant surgery.

2.2 Improved post-transplant care can free up hundreds of millions to the NHS and save at least as much to broader society

The aggregate benefits of improved post-transplant care could total more than a billion GBP when considering savings to the NHS and the value of patient time.

Patient case-study: Daniel

For some patients, life after transplant holds a range of opportunities – not always inside formal workplaces. For Daniel, the peer support he received while on dialysis was so immeasurably valuable; once he was well enough, he sought a job in the hospital to offer patients similar support.

Daniel suffered from Alport's Syndrome, a genetic condition characterised by kidney disease, hearing loss and eye abnormalities, from the age of 12, leading to kidney failure at age 28. After being on the transplant waitlist for six years, he had been given months to live. In the months leading up to the transplant, his health had deteriorated, and a transplant was considered his last hope.

The transplant 11 years ago saved his life, and he talks openly about the joy of returning to a life of potential after "expecting to die in a couple of months". Prior to his transplant, Daniel spent almost all his time in the dialysis ward, receiving dialysis three times a week.

"In the end, I got a full-time job in sterile services. So, I used to go to work for the day, finish work, go on dialysis. Come back the next day, work, day after; work and dialysis. I spent pretty much all my time at the hospital I dialysed at."

[1] QALYs are a summary measure that combine information on the length of life and quality of life. Each year lived is weighted by the health-related quality of that year, measured on a 0 to 100% scale, where 100% is the best health state imaginable and 0 is equivalent to dead. Ten years lived at a quality of 60% would be represented as 10 years x 60% = 6 QALYs. An intervention that improved quality from 60% to 80% without changing the number of years lived would represent a gain of 2 QALYs, i.e. (10 x 80%) – (10 x 60%) = 2.0.

He describes the change as drastic and acknowledges that although his graft has a finite life span, he feels it is important to remain optimistic. He enjoys being able to take a bath after six years, going out to restaurants stress-free and being able to travel. The transplant gives him more energy to put into developing ways to help other renal patients, including patient support groups, diet books and sharing his experience at conferences.

"Because three days a week I was occupied with going to the hospital, to stay alive. Trying to fit everything around that lifestyle isn't easy. It gets stressful and depressing, and sometimes it gets you down."

He focuses particularly on how important the peer-to-peer patient experience is in supporting other transplant patients. If there was one thing he could add to patient support programmes, it would be Government-sponsored Meet and Greets.

Ten months after the operation, Daniel was diagnosed with multiple sclerosis (MS), and besides positing that it may have been caused by trauma, his doctors remain unsure why. Daniel also experienced minor infections and currently takes 21 tablets a day for MS and his transplant combined.

3 How can we realise these benefits?

Based on the key drivers of cost and quality-of-life in the economic model, **the following objectives represent key policy priorities:**

1. Improving the ability of post-transplant patients to make valuable use of their time

2. Reducing wait times, including through increasing the supply of organs

3. Reducing the incidence of serious complications post-transplant, especially depression

In the following sections, we outline our rationale for these areas of emphasis and suggest some potential approaches to promote these improvements.

3.1 Policy recommendation 1: Improve the ability of people with transplants to restart activities that matter to them

For those waiting for a kidney transplant, health and energy levels are extremely low, and the ability to engage in any kind of activity can be totally diminished, with their efforts focused on adhering to treatment. Less than 1 in 4 people with renal failure are able to engage in work whilst they are waiting for a kidney transplant (Erickson et al., 2018), and even a year post-transplant, up to 15% of recipients are still unable to engage in productive activities (Miyake et al., 2019). For many post-kidney transplant patients, resuming any kind of activity that matters to them can feel like a victory, whether it's volunteer or social work, education, contributing to the third sector, caregiving, exercise or other personal leisure. For those able to return to work, the median time to return is three months (Miyake et al., 2019). Kidney disease is also associated with high risks of absenteeism and presenteeism (low productivity whilst at work), limiting the productivity of transplant recipients able to return to work or other productive activities (Savira et al., 2021).

The economic model indicates that **supporting post-transplant recipients in returning to normal activities** would provide the greatest societal benefits. This support could include surgical developments that speed recovery time, educating employers that the long-term productivity of a patient who is able to return to work is comparable to non-transplanted individuals, or supporting patients in being rehabilitated post-transplant to restart the activities that matter to them and promote their mental health. As a NICE consultation on quality standards in the workplace details, it is currently difficult for patients to return to the workplace after a long-term illness. These barriers need to be removed for post-transplant recipients to feel empowered to return to the workplace.

It will be important to distinguish between two types of patients, and initiatives will need to be tailored to each group:

- those who receive pre-emptive transplants or transplants after a short period on dialysis

- the majority of patients who will have been on dialysis for years and may not have been able to take part in the activities that matter to them for a considerable time.

We recommend **an initial consultation among patient groups, professional groups, policymakers and trade bodies** to discuss the specific needs, challenges and capabilities of post-transplant recipients and how best they can be supported to re-enter the workplace where able and wanting, or to restart or engage in other activities in the community outside of traditional workplaces.

Another suggestion is allowing patients post-transplant, who often feel immediately more energised after successful surgery, to engage in **voluntary education initiatives** that can support their transition back into society. Similarly, dialysis patients, who are often extremely unwell and can spend multiple days at hospital undergoing dialysis – combining this with voluntary support initiatives such as low-energy expenditure art or entertainment initiatives could reduce the anxiety of treatment and expand their skill sets.

3.2 Policy recommendation 2: Focus on reducing wait times for kidney transplant, including by increasing the supply of organs

In the decade between 2010/11 and 2019/20, there was a 21% fall in the number of people on the transplant waiting list in England. Despite a fall in the number of *people* on the kidney transplant waiting list, however, the average *time* on the waiting list is still more than 600 days (NHS Blood and Transplant, 2019). This wait is driven primarily by a shortage of organs relative to need and can often be much higher for ethnic minority patients given lower organ donation rates amongst many of these communities. This situation will likely be made worse by the Covid-19 pandemic. Researchers have estimated that 1,670 transplant opportunities in the UK were missed over a 6-month period from March 2020 (Sharma et al., 2020), leaving more patients on the waitlist for a longer time. Once normal service returns, it will be important to ensure that the NHS is able to keep pace with transplant requirements whilst also reducing the backlog of missed transplants. This challenge cannot be underestimated.

The economic model indicates that reduced waiting times are the single most important source of cost savings and a key contributor to patient quality-of-life. Therefore, this aspect should be a key focus of improved post-transplant care.

Efforts to **increase organ donations** through public awareness campaigns and 'presumed consent' legislation are central to increasing the supply of organs and reducing waiting times. As noted in *Organ Donation and Transplantation 2030: Meeting the Need* (NHS Blood and Transplant, 2020b), it will be particularly important to **encourage organ donation amongst ethnic minority populations**, especially Black and South Asian communities, to eliminate inequalities in wait times between patients.

As noted earlier, it will be equally important to find ways to **make better use of the organs currently available** through accepting higher risk donors and improved post-transplant care that can increase the likelihood of a successful transplant and extend the duration of graft survival. Additionally, increased application of medical perfusion to sustain organs to transplant means more can be transplanted, a key pillar of NHSBT's new strategy. Together these can reduce the number of re-transplants performed, freeing-up organs for those on the waiting list.

A review of the current waiting list and decision-making organ distribution processes and **increasing sharing capacity and learnings between transplant centres** could also reduce waiting times and decrease variation in outcomes between centres. Reduced variation in outcomes is a primary objective of the Getting It Right First Time (GIRFT) programme, which aims to improve care and patient outcomes and promote efficiencies, such as the reduction of unnecessary procedures and cost savings (GIRFT, 2021). The long-term ambition of this policy is to reduce variation of transplant quantity and quality across the UK and elevate lower tier centres to improve local care and decrease pressure on high tier centres.

3.3 Policy recommendation 3: Reduce the incidence of serious post-transplant complications, especially depression and other mental health aspects

Kidney transplant recipients are at increased risk of a number of serious complications, including serious infection, deep vein thrombosis, malignancies, diabetes, hypertension, obesity, and, notably, depression. The economic model suggests that these complications account for more than £126 million in direct costs to the NHS and a further £114 million in lost productive time amongst our hypothetical UK cohort and impose a substantial quality-of-life burden on patients. Kidney patients report particularly significant impacts on their mental health both before and after transplant, and the prevalence of mental health issues is higher than in the general population. For those who are able to work, these mental health issues are closely linked to increased absenteeism and presenteeism at work (Veater and East, 2016).

Advances in surgical techniques and immunosuppressive medicines can contribute to a reduction in infections and malignancies, but **greater mental health support** is also required to address depression and anxiety amongst this population. In market research conducted by Portland, patients reported that **peer-to-peer support programmes** were effective in connecting patients who could then offer comfort to one another and explain the process of transplantation. **Digital technologies** offer the opportunity to expand peer-to-peer support to remote areas using virtual networks and similarly increase the capacity in traditional care settings or touchpoints for those patients who can't or don't want to use digital solutions. Other digital technologies could support improved patient self-management, including remote blood tests, blood pressure monitoring, and glucose monitoring for patients with diabetes or pre-diabetes. Such technologies could improve outcomes as well as reduce the number of hospital visits for routine monitoring, saving patient and health system time and costs. **Personalised predictive systems that can monitor and predict graft condition** without hospital visits would also improve outcomes and potentially ease patient anxiety (Loupy et al., 2019; Vaulet et al., 2021).

Finally, as also noted earlier, sharing learnings between transplant centres and **national audits of transplant outcomes** associated with different therapeutic choices and approaches could improve treatment and optimise outcomes.

4 Conclusions

Kidney transplants offer the greatest hope for patients with renal failure, but there is a substantial gap between the number of patients in need of a transplant and the number that can be performed each year. Much of this gap is the result of a shortage of donated organs relative to need. People from ethnic minority backgrounds are particularly affected, in part due to lower rates of organ donation amongst these communities (NHS Blood and Transplant, 2020c). The shortfall in available organs is made worse by the fact that the time a transplanted organ can survive is limited, and a patient will often need more than one transplant over their lifetime.

NHS initiatives and legislative changes are seeking to increase the number of organs donated and transplanted, but it is equally important to find ways to make better use of the organs currently available, particularly through improved post-transplant care that can increase the likelihood of a successful transplant and extend the duration of graft survival. Improved post-transplant care could reduce the number of re-transplants required, freeing-up organs for first-time patients and reducing the burden of repeat transplantation on patients, as well as improve patient quality-of-life, reduce costs to the NHS, and allow more patients to return to work and other valuable activities more quickly.

The 'best case' modelling scenario, based on a hypothetical UK cohort of 3,190 patients, suggests that optimal post-transplant care could avoid more than 1,100 repeat transplants; avoid more than 100 weeks of dialysis per patient; reduce the quality-of-life burden amongst the cohort by 20%; allow more than 3,000 additional patients to be transplanted immediately; reduce societal costs, including the value of lost productivity time, by almost £1.17 billion; and allow the NHS to reallocate more than £600 million to other programmes. We find that improved availability of productive time, reduced wait times, and an increase in the supply of organs have the greatest impacts on combined NHS and societal cost savings. Notably, we also find that post-transplant depression is associated with avoidable costs to the NHS of £8.4 million and a loss of more than 1,000 quality-adjusted life years (QALYs) within the UK cohort, accounting for almost half of the total burden of all serious long-term complications following transplant.

On the basis of these results, we suggest that interventions that could improve the ability of post-transplant patients to make valuable use of their time, reduce wait times, including through increasing the supply of organs, and reduce the incidence of serious complications post-transplant, especially depression, should be key policy objectives.

References

1. Erickson, K.F., Zhao, B., Ho, V. and Winkelmayer, W.C., 2018. Employment among Patients Starting Dialysis in the United States. *Clinical Journal of the American Society of Nephrology*, 13(2), pp.265–273. 10.2215/CJN.06470617.

2. GIRFT, 2021. Getting It Right First Time. *Getting It Right First Time - GIRFT*. Available at: https://www.gettingitrightfirsttime.co.uk/what-we-do/ [Accessed 21 May 2021].

3. Heilman, R.L., Mathur, A., Smith, M.L., Kaplan, B. and Reddy, K.S., 2016. Increasing the Use of Kidneys From Unconventional and High-Risk Deceased Donors. *American Journal of Transplantation: Official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons*, 16(11), pp.3086–3092. 10.1111/ajt.13867.

4. Jones-Hughes, T., Snowsill, T., Haasova, M., Coelho, H., Crathorne, L., Cooper, C., Mujica-Mota, R., Peters, J., Varley-Campbell, J., Huxley, N., Moore, J., Allwood, M., Lowe, J., Hyde, C., Hoyle, M., Bond, M. and Anderson, R., 2016. Immunosuppressive therapy for kidney transplantation in adults: a systematic review and economic model. *Health Technology Assessment*, 20(62), pp.1–594. 10.3310/hta20620.

5. Kidney Care UK, 2021. *Chronic kidney disease (CKD)*. [online] Kidney Care UK. Available at: https://www.kidneycareuk.org/documents/526/Chronic_Kidney_Disease_CKD.pdf [Accessed 14 May 2021].

6. Kidney Research UK, 2017. *Statement on organ donation*. [online] Kidney Research UK. Available at: https://kidneyresearchuk.org/about-us/position-statements/statement-on-organ-donation/ [Accessed 14 May 2021].

7. Loupy, A., Aubert, O., Orandi, B.J., Naesens, M., Bouatou, Y., Raynaud, M., Divard, G., Jackson, A.M., Viglietti, D., Giral, M., Kamar, N., Thaunat, O., Morelon, E., Delahousse, M., Kuypers, D., Hertig, A., Rondeau, E., Bailly, E., Eskandary, F., Böhmig, G., Gupta, G., Glotz, D., Legendre, C., Montgomery, R.A., Stegall, M.D., Empana, J.-P., Jouven, X., Segev, D.L. and Lefaucheur, C., 2019. Prediction system for risk of allograft loss in patients receiving kidney transplants: international derivation and validation study. *BMJ*, 366, p.l4923. 10.1136/bmj.l4923.

8. McCaughan, J.A. and Courtney, A.E., 2015. The Clinical Course of Kidney Transplant Recipients After 20 Years of Graft Function: Outcome After 20 Years of Transplant Function. *American Journal of Transplantation*, 15(3), pp.734–740. 10.1111/ajt.13041.

9. Miyake, K., Endo, M., Okumi, M., Unagami, K., Kakuta, Y., Furusawa, M., Shimizu, T., Omoto, K., Shirakawa, H., Ishida, H. and Tanabe, K., 2019. Predictors of return to work after kidney transplantation: a 12-month cohort of the Japan Academic Consortium of Kidney Transplantation study. *BMJ Open*, 9(10), p.e031231. 10.1136/bmjopen-2019-031231.

10. NHS Blood and Transplant, 2019. *Annual report on kidney transplantation*. [online] Available at: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/16778/nhsbt-kidney-transplantation-annual-report-2018-19.pdf [Accessed 28 Jan. 2021].

11. NHS Blood and Transplant, 2020a. *Annual report on liver transplantation 2019/2020*. [online] Available at: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19867/nhsbt-liver-transplant-report-1920.pdf [Accessed 28 Jan. 2021].

12. NHS Blood and Transplant, 2020b. *Organ Donation and Transplantation 2030: Meeting the Need*. [online] Available at: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/20790/7b-nhsbt-board-nov-2020-organ-donation-and-transplantation-2030-meeting-the-need-20-92b.pdf [Accessed 14 May 2021].

13. NHS Blood and Transplant, 2020c. *Organ Donation and Transplantation data for Black, Asian and Minority Ethnic (BAME) communities, 2019/2020*. [online] Available at: https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19753/bame-report-201920.pdf [Accessed 14 May 2021].

14. NHS Blood and Transplant, 2021. *Organ donation law in England*. [online] NHS Organ Donation. Available at: /uk-laws/organ-donation-law-in-england/ [Accessed 14 May 2021].

15. Palmer, S., Vecchio, M., Craig, J.C., Tonelli, M., Johnson, D.W., Nicolucci, A., Pellegrini, F., Saglimbene, V., Logroscino, G., Fishbane, S. and Strippoli, G.F.M., 2013. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. *Kidney International*, 84(1), pp.179–191. 10.1038/ki.2013.77.

16. Savira, F., Ademi, Z., Wang, B.H., Kompa, A.R., Owen, A.J., Liew, D. and Zomer, E., 2021. The Preventable Productivity Burden of Kidney Disease in Australia. *Journal of the American Society of Nephrology*, 32(4), pp.938–949. 10.1681/ASN.2020081148.

17. Sharma, V., Shaw, A., Lowe, M., Summers, A., van Dellen, D. and Augustine, T., 2020. The impact of the COVID-19 pandemic on renal transplantation in the UK. *Clinical Medicine*, 20(4), pp.e82–e86. 10.7861/clinmed.2020-0183.

18. Vaulet, T., Divard, G., Thaunat, O., Lerut, E., Senev, A., Aubert, O., Loon, E.V., Callemeyn, J., Emonds, M.-P., Craenenbroeck, A.V., Vusser, K.D., Sprangers, B., Rabeyrin, M., Dubois, V., Kuypers, D., Vos, M.D., Loupy, A., Moor, B.D. and Naesens, M., 2021. Data-driven Derivation and Validation of Novel Phenotypes for Acute Kidney Transplant Rejection using Semi-supervised Clustering. *Journal of the American Society of Nephrology*, 32(5), pp.1084–1096. 10.1681/ASN.2020101418.

19. Veater, N.L. and East, L., 2016. Exploring Depression Amongst Kidney Transplant Recipients: A Literature Review. *Journal of Renal Care*, 42(3), pp.172–184. https://doi.org/10.1111/jorc.12162.

20. Ying, T., Shi, B., Kelly, P.J., Pilmore, H., Clayton, P.A. and Chadban, S.J., 2020. Death after Kidney Transplantation: An Analysis by Era and Time Post-Transplant. *Journal of the American Society of Nephrology*, 31(12), pp.2887–2899. 10.1681/ASN.2020050566.

Appendix 1: How did we estimate this?

To understand the potential impact of changes in post-transplant care on NHS spending and patient productivity, and quality-of-life, we built an economic model to combine different types and sources of information.

As we describe in more detail below, the information in the model included information on NHS costs before, during, and after transplant, as well as the probability, or incidence, of short- and long-term complications associated with transplant and the costs of treating those complications. From the patient's perspective, it includes information on the proportion able to engage in paid employment or other productive activities whilst on the waitlist or post-transplant and an estimate of the value of that time. Finally, it includes estimates of the average age of transplant recipients and the expected length of graft survival with the current standard of care to understand how long these different costs and quality-of-life benefits will last.

4.1 Model structure

The structure and logic flow of the model is represented in Figure 4 below.

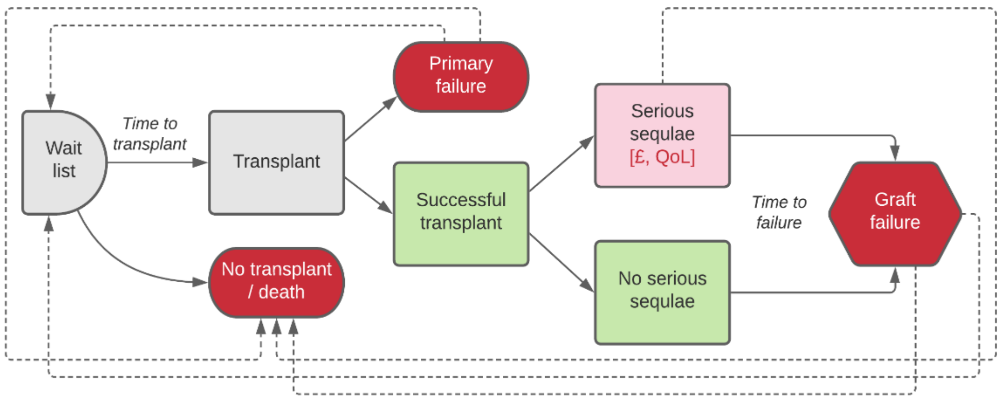


FIGURE 4: MODEL LOGIC FLOW

The model starts with all patients on the waitlist for transplant following initial organ failure. The size of the cohort is based on the number of patients receiving a transplant in a given year, but as the model allows accounts for the impact of waiting time for the initial transplant, we begin following these patients from the time of their entry to the waiting list. Once a patient receives a transplant, there is a chance that the transplanted organ fails within a year, known as primary or acute failure, in which case the patient returns to the waitlist and waits for another transplant. In the more likely event that the transplant is successful, patients can experience short- and long-term complications or serious sequelae. Short-term complications resolve within weeks or months, and long-term sequelae are assumed to persist for the entire time that the graft survives, also known as time-to-failure. Following graft failure, the patient returns to the waitlist and begins the process again. The model allows for up to three transplants: an initial transplant and up to two re-transplants. If and when the third transplant fails, the model assumes that patients spend their remaining life expectancy on end-of-life dialysis. Patients can die at any point in the model logic.

The model is a **microsimulation**, meaning that it 'simulates' different experiences to represent individual patients rather than representing the 'average' experience of a cohort of identical patients as in state-transition or "Markov" models. A microsimulation is more complicated than a state-transition model, but the variety of outcomes and time-to-failures that are possible after each transplant means a more complicated microsimulation approach was necessary to produce credible estimates of the expected outcomes. The concept of the microsimulation is illustrated in Figure 5.

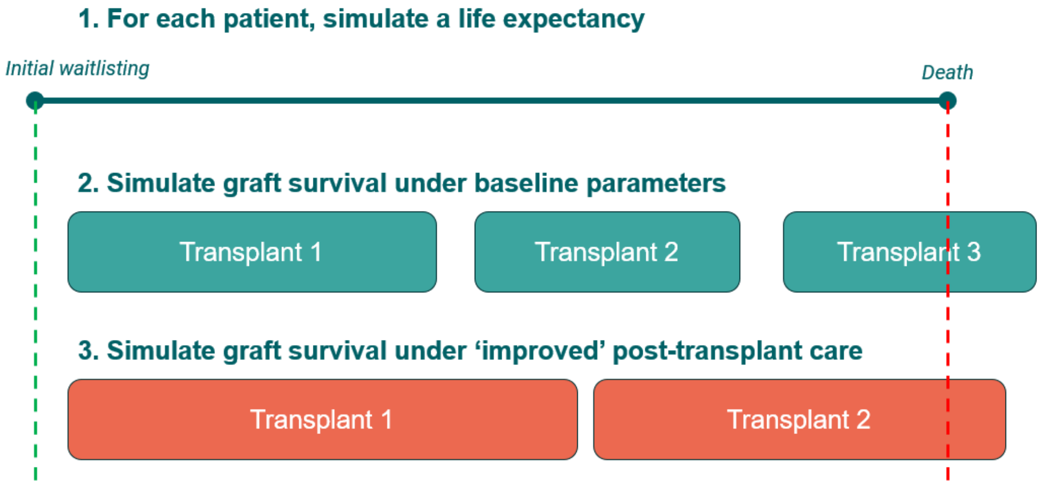


FIGURE 5: MICROSIMULATION CONCEPTION

Each simulated patient is represented by a set of characteristics. Broadly speaking, the key characteristics are life expectancy and the survival or time-to-failure of up to three transplants. The value of each characteristic for each simulated patient is randomly drawn from a probability distribution around a mean or expected value based on data from the literature. The shape of the probability distribution determines how far away and the direction each simulated value will be from the expected value. A normal distribution means that some simulated values may be much larger or much smaller than the expected value, but most values will be reasonably close to the expected value. A gamma distribution, on the other hand, has a very long 'tail', and therefore some values will be much larger than the expected value, but there will not be many values much smaller than the expected value.

The model first simulates a life expectancy for each patient, drawing from a normal distribution (constrained to be greater than zero). The means that some patients will live a very short time (e.g. dying whilst on the waitlist for their first transplant) whilst others will live a very long time (i.e. outliving all three transplanted organs). Most, though, live around the average life expectancy of all transplanted patients reported in the literature.

In the second step, the model simulates a series of times on the waitlist and times-to-failure for up to three transplants, depending on life expectancy and cumulative graft survival. Figure 5 represents a combination of wait times and time-to-failure for one simulated patient under the current standard of care (step 2) and an alternative state of the world where the probabilities or durations of different events have been adjusted (step 3). Under standard-of-care, the simulated patient requires three transplants over their life and dies with a functioning third graft. Under the alternative state of the world, with improved graft survival and shorter wait times, the same patient would require only two transplants in their lifetime, avoiding the costs and quality-of-life impacts of the third transplant. The microsimulation allows us to simulate identical sets of patients and see how a specific change in one parameter would affect costs and patient outcomes between the two states of the world.

4.2 Model effects

Impacts in the model are driven by 11 independent effects and a scaling factor, as illustrated in Figure 6. Each of the effects, with the exception of immunosuppression adherence, adjusts the probability or duration of different states in the model. Adherence proportionally scales the impact of the other effects according to the proportion of patients that are expected to comply with their immunosuppression protocol. We also include an adjustment for the distribution of standard and higher-risk organs.

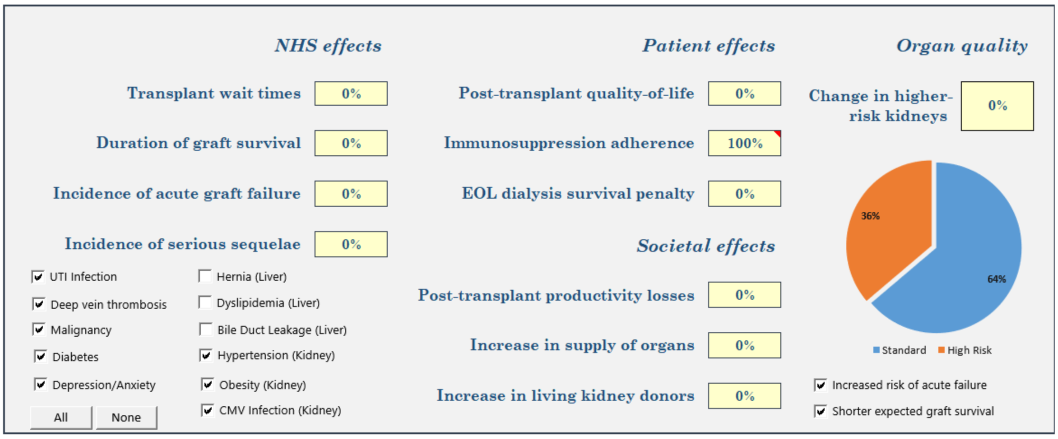


FIGURE 6: MODEL EFFECTS

The interpretation of the different effects is briefly described below. In all cases, 0% means no change from baseline.

- The **transplant wait times effect** reduces average time on the wait list. -100% means there is no wait time and transplant is effectively 'instantaneous'.
- The **duration of graft survival effect** increases time to graft failure. +100% means a doubling of average graft survival.
- The **incidence of acute graft failure effect** reduces the incidence (probability) of graft failure within 1 year of transplant. -100% mean no acute graft failures.
- The **incidence of serious sequelae effect** reduces the incidence (probability) of short- and long-term complications. The effect is the same for short- and long-term complications. -100% means no complications.

- The **post-transplant quality-of-life effect** reduces the quality-of-life penalty (also known as *disutility*) associated with the post-transplant health state. -100% means this penalty is eliminated and post-transplant quality of life is 'full health'.

- The **end-of-life (EOL) dialysis survival penalty effect** only applies to patients who have received the maximum of three transplants allowed by the model, and whose third transplant has failed before their simulated life expectancy. The model imposes an additional mortality risk on patients receiving EOL dialysis relative to those with a functioning graft. This effect reduces the risk of mortality for these patients. -100% means no mortality penalty relative to a functioning graft (i.e. full life expectancy regardless of dialysis or functioning graft).

- The **post-transplant productivity losses effect** reduces productivity losses post-transplant. -100% means no productivity losses, or all patients return to valuable activities.

- The **(relative) increase in supply of organs effect** increases the number of transplants performed. +100% doubles the baseline supply of organs and transplants. The impact of additional transplants is limited to time avoided on the waitlist. By default, the model assumes any increased supply or organs is driven by expanding the pool of donors and does not change the distribution of organ quality. This assumption can be changed using the proportion of higher-risk organs factor, described below.

- The **(relative) increase in living kidney donors effect** increases the proportion of living kidney donors. Living donor transplants have a lower probability of acute failure, independent of the incidence of acute graft failure effect.

- The **(relative) change in higher-risk organs** allows users to adjust the mix of standard and higher-risk kidneys. Users have the option to allow a greater proportion of higher-risk organs to increase the risk of acute graft failure (within 1 year) and/or reduce expected graft survival. +100% doubles the current proportion of higher-risk organs.

There is evidence that higher-risk organs are associated with a relatively higher risk of acute failure and a shorter expected duration of graft function (Lehner et al., 2018). Therefore, a greater proportion of higher-risk organs reduces expected health outcomes and increases costs, holding all other effects constant. We note, though, that there can be trade-offs between the risk of implanting a lower-quality organ and risks associated with waiting for a higher-quality organ (Massie et al., 2014). The current functionality of the model allows users to test trade-offs between this proportion and other effects such as an increased supply of organs and consequently reduced wait times, holding other effects constant. At present, however, the model does not define a formal relationship between the proportion of higher-risk organs and other outcomes such as graft survival or wait times. These trade-offs must be defined by the user and, therefore, should be seen as a sensitivity analysis rather than a primary outcome of the model.

4.3 Cohort definition and time horizon

In the model, we simulate a cohort of patients who receive their first transplant in the same calendar year, and we follow the outcomes of that cohort until the last patient dies. To the greatest extent possible, the parameters in the model are based on 2020 values, so the **cohort** represents everyone who received a transplant in 2020. The cohort only represents people who *received* a transplant, not those on the waitlist in 2020 who did not receive a transplant.

There is no fixed **time horizon** in the model – the simulation continues until the last patient 'dies' – and because life expectancy is probabilistic, not fixed, this horizon changes with each simulation. Therefore, the results should be interpreted as the cumulative costs and benefits over the (variable) lifetime of the cohort. For context, the model reports the survival of the longest-surviving patient in each simulation as the model horizon and the average survival of the full cohort as the denominator in calculating annualised outcomes.

4.4 Perspective

The model takes a **societal perspective**, considering direct costs to the NHS, patients and donors, as well as indirect costs to patients and donors in the form of lost productive time.

Lost productive time is estimated by the proportion of patients unable to work whilst on the waitlist or post-transplant, but we extend the interpretation of 'productive time' to include any activity of value to the patient or society. Limiting productive time to 'employment' ignores the value of improved post-transplant outcomes to retired persons, the unemployed, and any other members of society who are not in paid work, such as full-time parents or informal caregivers. This approach overestimates the direct impact of productivity gains on government tax revenues but is a broader measure of societal wellbeing, where time has value to patients regardless of their employment status.

4.5 Analytic methods

As described earlier, we take a prospective cohort approach to the analysis. We aggregate costs and quality-of-life impacts over the lifetime of the cohort and do not discount costs or effects.

For simplicity, we assume that the number of transplants performed in each region is proportional to the region's share of the UK population. Likewise, costs and patient impacts are a function of the total number of transplants. With the exception of population, all other regional characteristics and model inputs are identical across regions based on UK averages.

Our estimates of impact are based on maximum or 'best case' effects. These reflect what is *logically possible* (e.g. the maximum possible effect on wait times is a 100% reduction) without judging the technical, biological or policy limits to these effects (e.g. it is unlikely that it will be possible to fully eliminate wait times, i.e. 'instant' transplant). This means that what is *realistically achievable* in the short- to medium-term will be less than the maximum possible effect, but an understanding of the relative magnitude of the potential benefits associated with different effects can help to inform priorities for public policy, investment, and care.

4.5.1 Sensitivity analyses

The model includes a **one-way sensitivity analysis** to illustrate the cost and quality-of-life impacts associated with the full range of each individual parameter while keeping all other parameter inputs at their baseline level. This analysis shows the direction of effect (e.g. cost-increasing or cost-saving) and the specific cost/saving for each value between 0 and +/-100%.

The model also includes a **scenario analysis**. As some effects are cost-increasing and others are cost-saving, this analysis tests different combinations of maximum effect and zero effect to find the combination that maximises a selected outcome: aggregate cost savings (including productivity), NHS cost savings, patient quality-of-life, or the sum of percentage change in all attributes.

4.6 Key inputs and data sources

The model is based on the most recent and UK-representative clinical and cost data available. Key data sources included NHS Blood and Transplant (NHSBT) annual reports on kidney and liver transplants (NHS Blood and Transplant, 2019, 2020a), and a systematic review and economic model of immunosuppressive therapy for kidney transplantation commissioned by NICE (Jones-Hughes et al., 2016). Other kidney and liver transplant data sources are detailed in the following summary tables.

4.6.1 Kidney inputs

Parameter	Source value	Adjusted value	Alternative	Source
Kidney Transplants performed	3190	3190		ANNUAL REPORT ON KIDNEY TRANSPLANTATION REPORT FOR 2019/2020 (1 APRIL 2010 – 31 MARCH 2020)
Median Waiting Time (days)	603	603		ANNUAL REPORT ON KIDNEY TRANSPLANTATION REPORT FOR 2019/2020 (1 APRIL 2010 – 31 MARCH 2020)
Deceased Donors	2241	2241		ANNUAL REPORT ON KIDNEY TRANSPLANTATION REPORT FOR 2019/2020 (1 APRIL 2010 – 31 MARCH 2020)
Living Donors	949	949		ANNUAL REPORT ON KIDNEY TRANSPLANTATION REPORT FOR 2019/2020 (1 APRIL 2010 – 31 MARCH 2020)
% Deceased donors	70%	70%	70%	Calculated
% Living donors	30%	30%	30%	Adjusted by Effect_LiveDonors
1 year graft survival from Deceased Donor (1-AcuteFailure)	94.0%	94.0%	94.0%	ANNUAL REPORT ON KIDNEY TRANSPLANTATION REPORT FOR 2019/2020 (1 APRIL 2010 – 31 MARCH 2020)
1 year graft survival from Living Donor	98.0%	98.0%	98.0%	ANNUAL REPORT ON KIDNEY TRANSPLANTATION REPORT FOR 2019/2020 (1 APRIL 2010 – 31 MARCH 2020)
1 year graft survival	**95.2%**	**95.2%**	**95.2%**	ANNUAL REPORT ON KIDNEY TRANSPLANTATION REPORT FOR 2019/2020 (1 APRIL 2010 – 31 MARCH 2020)
Relative risk of 1-year graft failure		**1.0000**	**1.0000**	Calculated
Median patient survival (years)	13.3	13.3		https://onlinelibrary.wiley.com/doi/pdf/10.1111/ajt.13041
Median graft survival (years)	9.3	9.3		https://onlinelibrary.wiley.com/doi/pdf/10.1111/ajt.13041

	Raw	Adjusted	Alternative	
Dialysis Cost per patient per year (2014/15 prices)	£30,800	£34,568	£34,568	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22

Kidney Transplant Surgery cost £ (2013/14 prices)	£15,772	£18,184	£18,184	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Initial post transplant care cost (2017)	£17,000	£17,860	£17,860	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22

Deceased Donor Costs (2013 prices), retrieval	£10,142	£11,693	£13,480	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Living Donor Costs (2013 prices), retrieval	£8,771	£10,111	£11,657	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Probability-weighted donor costs	£9,734	**£11,222**	**£12,938**	

Cost of acute rejection - per episode (14/15 price)	£3,557	£3,992		https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22

Follow-up/maintenance costs

Patient Transport annual per patient cost (2019 prices)	£1,000	£1,000		https://www.healthwatch.co.uk/report/2019-10-02/there-and-back-what-people-tell-us-about-their-experiences-travelling-and-nhs
Post transplant care cost - subsquent years (2017)	£5,000	£5,253		https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Annual combined follow-up costs		**£6,253**		

	Raw	Adjusted	Alternative	
Utility decrement for functioning kidney graft from baseline	0.053	0.053	0.04823	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Utility decrement on kidney transplant waitlist	0.23	0.23	0.23	https://researchonline.lshtm.ac.uk/id/eprint/4259117/1/Estimating%20Health-State%20Utility%20Values%20in%20Kidney%20Transplant.pdf

Short-term sequelae	*Raw*	*Adjusted*	*Alternative*	
1 year UTI Infection incidence rate post transplant	28.2%	28.2%	21.2%	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6136109/#:~:text=Incidence%20of%20all%2Dcause%20infection,and%2067%25%20at%202%20years.
Incidence of CMV Infection	10.7%	10.7%	8.0%	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Incidence of Deep Vein Thrombosis	1.0%	1.0%	0.8%	https://www.nhs.uk/conditions/kidney-transplant/risks/#:~:text=Blood%20clots%20can%20develop%20in,the%20blood%20supply%20is%20blocked.

Duration (weeks) with infection	2	2	2
Duration (weeks) with CMV	5	5	5
Duration (weeks) with Deep Vein Thrombosis	8	8	8

Infection utility decrement	0.0100	0.0004	0.0004	https://www.nice.org.uk/guidance/ta348/documents/organ-rejection-liver-transplantation-prevention-everolimus-committee-papers
CMV utility decrement	0.0800	0.0077	0.0077	https://pubmed.ncbi.nlm.nih.gov/29025787/
Deep Vein Thrombosis utility decrement	0.1100	0.0169	0.0169	https://pubmed.ncbi.nlm.nih.gov/30578462/
Probability-weighted short-term utility decrement	**0.012**	**0.001**	**0.001**	

Cost of UTI Infection (2010 prices)	£31.00	£38.96	£38.96	https://www.bmj.com/content/340/bmj.c346
Cost of CMV infection treatment per patient (CMV) 2014/15 prices	£3,009.00	£3,377.07	£3,377.07	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Cost of treating Deep Vein Thrombosis (2004 prices)	£6,153.85	£9,205.69	£9,205.69	https://publications.parliament.uk/pa/cm200405/cmselect/cmhealth/99/99we07.htm
Probability-weighted short-term cost per patient	**£392.85**	**£465.07**	**£348.80**	

Long-term sequelae	*Raw*	*Adjusted*	*Alternative*	
5 year Incidence of malignancy post transplant	7.2%	7%	6%	https://journals.lww.com/transplantjournal/Abstract/2018/07001/Long_term_Cancer_Incidence_in_Kidney_Transplant.822.aspx
1 year Incidence of New onset diabetes after transplantation	13.0%	13%	10%	https://reader.elsevier.com/reader/sd/pii/S0085253815507333?token=EC554EF12FD26D67DBCB70B888D7AF3197FD0D5D07BF83087BDC2A757DC286923F59845128A664E48A2BA27F1D0947B5
1 year post transplant incidence of hypertension (above 140mm HG)	45.0%	45%	35%	https://www.sciencedirect.com/science/article/abs/pii/S0272638604003786
Incidence of post transplant Obesity (within 4 years)	34.0%	34%	26%	https://www.frontiersin.org/articles/10.3389/fpsyt.2020.00399/full#:~:text=The%20prevalence%20rates%20of%20obesity,diabetes%20mellitus%20and%20of%20NODAT.
Incidence of Depression post transplant	26.6%	27%	21%	https://www.kidney-international.org/article/S0085-2538(15)55927-9/fulltext
Malignancy utility decrement	0.02	0.02	0.02	https://pubmed.ncbi.nlm.nih.gov/15970790/
New onset diabetes utility decrement	0.06	0.06	0.06	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Hypertension disutility decrement	0.01	0.01	0.01	https://www.nice.org.uk/guidance/ta481/documents/kidney-transplantation-adults-immunosuppressive-therapy-review-of-ta-85-committee-papers-part-22
Obesity utility decrement	0.06	0.06	0.06	https://www.sciencedirect.com/science/article/pii/S109830151101401X
Depression utility decrement	0.12	0.12	0.12	https://www.researchgate.net/publication/316900515_Estimating_Health-State_Utility_Values_in_Kidney_Transplant_Recipients_and_Waiting-List_Patients_Using_the_EQ-5D-5L/link/59173f77aca27200fe51b74b/download
Probability-weighted long-term utility decrement	**0.07**	**0.07**	**0.05**	
Unit Cost of Malignancy Treatment (2010 prices)	£30,000	£37,705	£37,705	https://www.nhs.uk/news/cancer/cancer-survival-rates-threatened-by-rising-cost/#:~:text=What%20does%20the%20report%20say%20about%20costs%20of%20cancer%20treatment,30%2C000%20per%20person%20with%20cancer.
Cost of treating for new onset diabetes -per year (2014/15 prices)	£1,352.00	£1,517.38	£1,517	https://www.nice.org.uk/guidance/ta348/documents/organ-rejection-liver-transplantation-prevention-everolimus-committee-papers
Unit cost of hypertension treatment (2013)	£769.00	£886.56	£887	https://www.nice.org.uk/guidance/ta348/documents/organ-rejection-liver-transplantation-prevention-everolimus-committee-papers
Cost of obesity per patient (2015)	£517.00	£569.22	£569	https://iea.org.uk/wp-content/uploads/2017/01/Obesity-and-the-Public-Purse-PDF.pdf

OFFICE OF HEALTH ECONOMICS **CONSULTING**

Cost of depression treatment (2009 prices)	£741	£958	£958	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3552476/
Probability-weighted cost per patient	**£3,063 .63**	**£3,770. 78**	**£2,92 2.35**	

Productivity	***Raw***	***Adjuste d***	***Altern ative***	
Out of work (days) short term	90.00	90.00	49.50	https://www.royalfree.nhs.uk/services/services-a-z/kidney-services/kidney-transplants/after-my-kidney-transplant/
Median (days) time to return to work after kidney transplant	120.00	120.00	66.00	https://bmjopen.bmj.com/content/9/10/e031231
Probability of returning to work within 2 months	22.3%	22.3%	57.3%	https://bmjopen.bmj.com/content/9/10/e031231
Probability of returning to work within 4 months	59.0%	59.0%	77.5%	https://bmjopen.bmj.com/content/9/10/e031231
Probability of returning to work within 6 months	77.1%	77.1%	87.4%	https://bmjopen.bmj.com/content/9/10/e031231
Probability of returning to work within 12 months	85.0%	85.0%	91.8%	https://bmjopen.bmj.com/content/9/10/e031231
Probability of employment whilst on waitlist	23.5%	23.5%	57.9%	https://cjasn.asnjournals.org/content/13/2/265

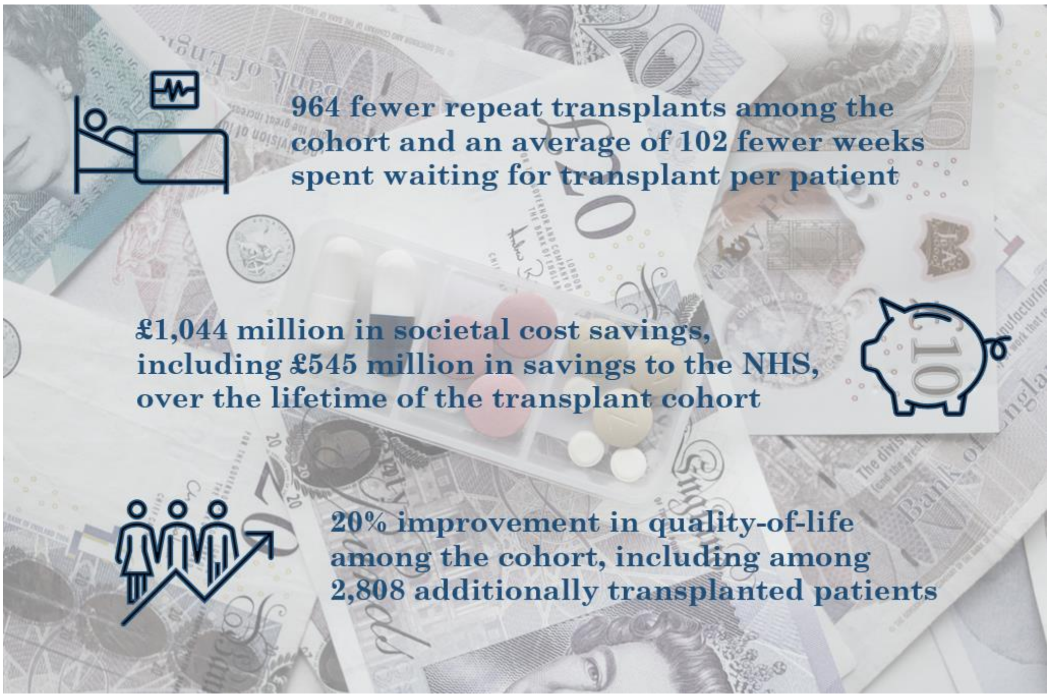
Financial impact on living donors			
Donor time off work (weeks)	12	0.231	https://journals.lww.com/transplantjournal/Fulltext/2004/07271/Eight_years_experience_of_reimbursement_costs.19.aspx

Appendix 2: Regional results

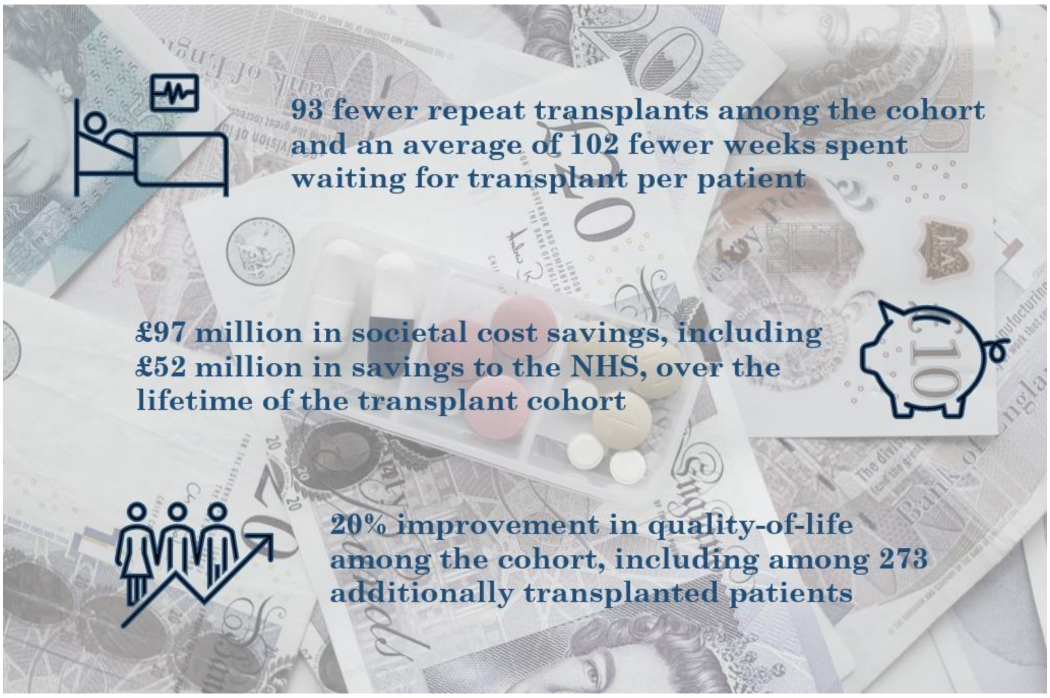
The following results report outcomes for each of the nations of the UK: England, Scotland, Wales, and Northern Ireland. Please note that these results are generated by scaling the overall UK results by the relative population of each region. This means that the absolute outcomes of the model change in proportion to the population of the nation, but the relative relationship between the different outcomes stays the same. That is, as in the overall UK results, productivity, supply of organs, and wait times are the key drivers in each nation, but the absolute impact of each aspect will differ.

We find that even in the smaller nations of Wales and Northern Ireland, the potential benefits of improved post-transplant care are substantial, including £55 million in potential societal cost savings in Wales and £34 million in Northern Ireland.

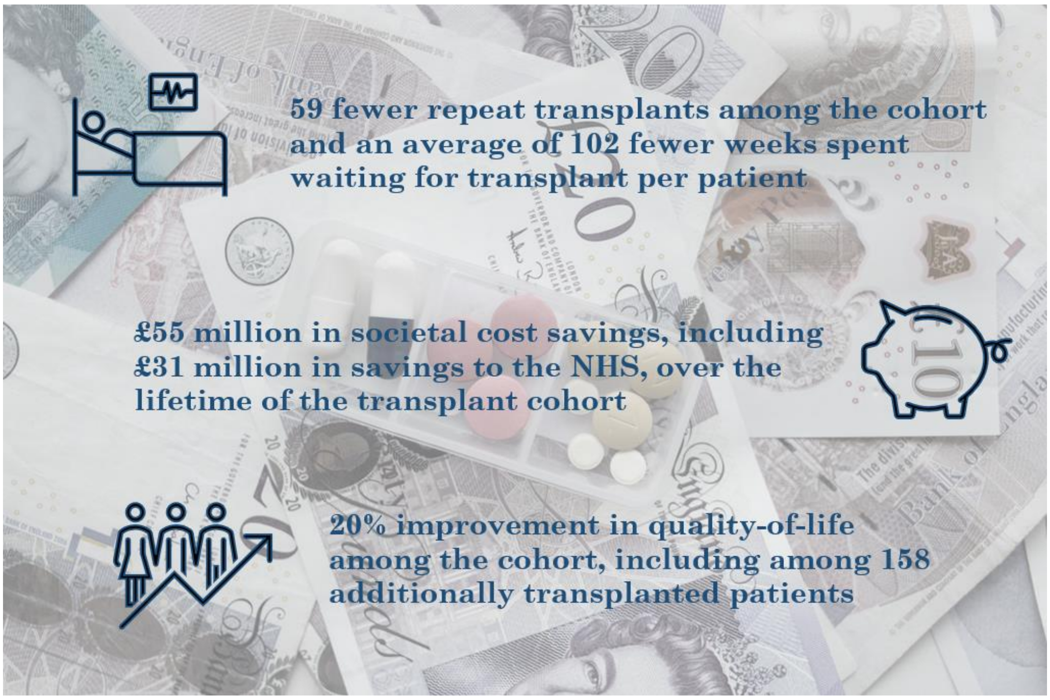
England results



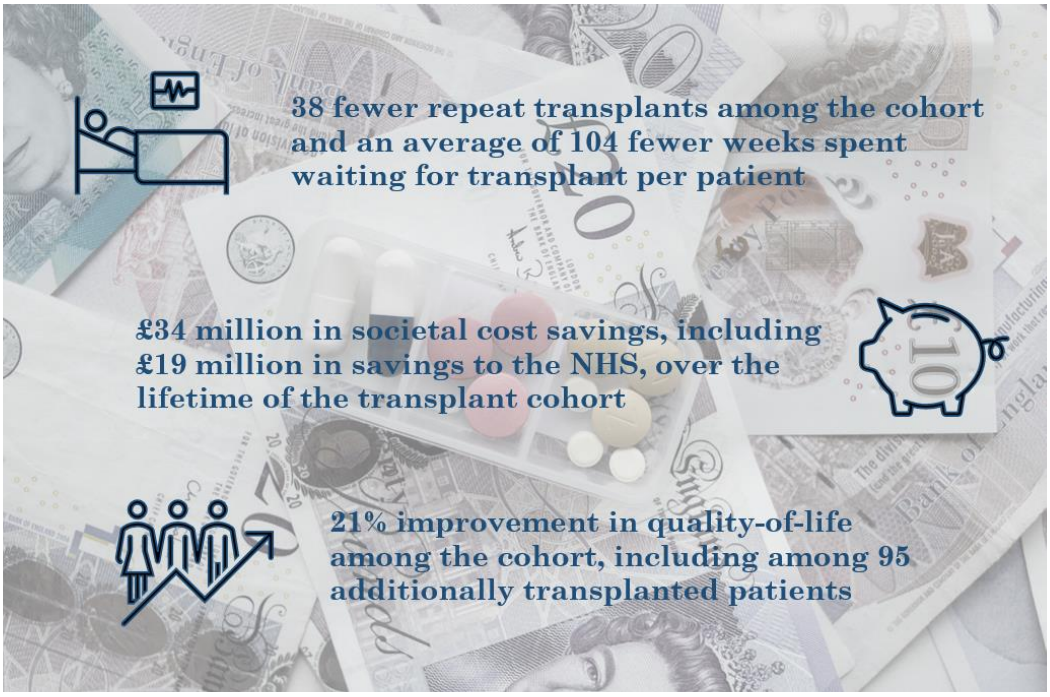
Scotland results



Wales results



Northern Ireland results



OHE

About us
Founded in 1962 by the Association of the British Pharmaceutical Society, the Office of Health Economics (OHE) is not only the world's oldest health economics research group, but also one of the most prestigious and influential.

OHE provides market-leading insights and in-depth analyses into health economics & health policy. Our pioneering work informs health care and pharmaceutical decision-making across the globe, enabling clients to think differently and to find alternative solutions to the industry's most complex problems.

Our mission is to guide and inform the healthcare industry through today's era of unprecedented change and evolution. We are dedicated to helping policy makers and the pharmaceutical industry make better decisions that ultimately benefit patients, the industry and society as a whole.

OHE. For better healthcare decisions.

Areas of expertise
- Evaluation of health care policy
- The economics of health care systems
- Health technology assessment (HTA) methodology and approaches
- HTA's impact on decision making, health care spending and the delivery of care
- Pricing and reimbursement for biologics and pharmaceuticals, including value-based pricing, risk sharing and biosimilars market competition
- The costs of treating, or failing to treat, specific diseases and conditions
- Drivers of, and incentives for, the uptake of pharmaceuticals and prescription medicines
- Competition and incentives for improving the quality and efficiency of health care
- Incentives, disincentives, regulation and the costs of R&D for pharmaceuticals and innovation in medicine
- Capturing preferences using patient-reported outcomes measures (PROMs) and time trade-off (TTO) methodology
- Roles of the private and charity sectors in health care and research
- Health and health care statistics

CONSULTING | REPORT
MAY 2021

ohe.org

The Office of Health Economics A Company Limited by Guarantee of Registered No. 09848965
OHE Consulting Ltd Registered Company No. 09853113
OHE is a Charity Registration No. 1170829
Registration Office Southside, 105 Victoria Street, London SW1E 6QT