Kidney disease: A UK public health emergency

The health economics of kidney disease to 2033

June 2023

Kidney Research UK

ZS
Disclaimer

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* These stakeholders were members of the steering committee, a smaller group of ten clinicians, academics and patients who met regularly between February 2023 and April 2023 to guide the project and validate the key findings.
About this report
Kidney Research UK commissioned ZS Associates to prepare an independent report on the health economics of kidney disease and associated factors in the UK in 2022. The report includes modelling of some illustrative interventions for adults with chronic kidney disease, risk factors associated with chronic kidney disease and changes in the health economic burden of treatment of kidney disease over the next ten years. Kidney disease is a major challenge for health care systems around the world, and its prevalence is increasing. There have been various papers prepared on the health economics of kidney disease in the UK, although there has not been a comprehensive report prepared since 2012. This report was prepared by ZS Associates in collaboration with Kidney Research UK and the expert advisory steering group in 2023.

About Kidney Research UK
Kidney Research UK is the leading charity in the UK focused on funding research into the prevention, treatment and management of kidney disease.

Our vision is the day when everyone lives free from kidney disease and for more than 60 years the research we fund has been making an impact.

But kidney disease is increasing as are the factors contributing to it, such as diabetes, cardiovascular disease and obesity, making our work more essential than ever.

At Kidney Research UK we work with clinicians and scientists across the UK, funding and facilitating research into all areas of kidney disease. We collaborate with partners across the public, private and third sectors to prevent kidney disease and drive innovation to transform treatments.

Over the last ten years we have invested more than £58 million into research. We lobby governments and decision makers to change policy and practice to ensure that more than 3 million people living with kidney disease in the UK have access to the most effective care and treatment, and to make kidney disease a priority.

Most importantly, we also work closely with patients, ensuring their voice is heard and is at the centre of everything we do, from deciding which research to invest in to how we plan our priorities and our work across the charity.

Those patient contributions are vital, always helping us and our partners to understand what life is like with kidney disease, always ensuring we see the patient behind the treatment and always reminding us that behind every statistic and every number is a person – the patients and the carers who inspire our mission and push us forward to make a difference and change the future of kidney disease.
Foreword

Professor Sir Stephen Powis
National Medical Director of NHS England
Professor of Renal Medicine at University College London

This is the most comprehensive review of the health economics of kidney disease in the UK for more than ten years. At a time of unprecedented health system pressures, and an ageing population, this report is timely and welcome. Kidney disease is on the increase and there is no cure. It is a life changing disease that can put a significant strain on the body, often referred to as the silent killer, and yet it is not as widely recognised or acknowledged as other long-term conditions.

Globally, kidney disease is forecast to be the fifth leading cause of premature death by 2040, and often progresses undiagnosed, until its later stages, due to a lack of symptoms. It can affect anyone. In the UK, more than three million people are living with kidney disease and this is increasing rapidly. Factors contributing to kidney disease are also growing, such as diabetes, cardiovascular disease and obesity, and people with kidney disease are also at increased risk of heart attack or stroke. The case for action is more urgent than ever. The later the diagnosis, the greater the impact on the patient.

In its late stages, kidney disease is life changing for patients, with few treatment options available. There is an enormous impact on quality of life for patients and for their families and carers, in addition to significant emotional and financial burdens.

Until a cure for kidney disease is developed, only early diagnosis, new and effective prevention strategies and better management of kidney disease can reduce its incidence and slow progression.

This report estimates that the current economic burden of kidney disease to the UK is £7bn with £6.4bn of this related to direct NHS costs; these figures could grow to as much as £13.9bn and £10.9bn, respectively by 2033.

This report serves as a stark call to action for stakeholders across the public, private, academic and health sectors to come together to implement its recommendations, improve prevention, management and treatment, and drive the research and innovation that could end kidney disease.

Professor Sir Stephen Powis
Key Findings

1. In the UK, there are approximately 3.25 million people living with chronic kidney disease (CKD) stages 3-5. A further 3.9 million people are estimated to have CKD stages 1-2. Together reaching a total of 7.2 million – more than 10% of the entire population.

2. By 2033, the number of people with CKD stages 3-5 is projected to reach 3.9 million. This is mainly driven by an ageing population, as well as risk factors such as diabetes, hypertension and cardiovascular disease and other important factors such as health and economic inequalities.

3. Around 615,000 episodes of acute kidney injury occur each year; mainly among people who are already unwell or hospitalised for another reason.

4. A total of 30,000 adults and children are on dialysis due to kidney failure and lose at least 12 hours per week of work and leisure time (dialysing three sessions a week, 4 hours per session). The number of patients requiring dialysis could rise to 143,000, while the demand for transplantation could be as high as 12,000 per year by 2033.

5. Dialysis is a key driver of the economic burden of kidney disease, estimated to cost the NHS £34,000 per year per patient in 2023 – more than three times the annual value of a state pension.

6. The total annual economic burden of kidney disease in the UK is £7.0 billion, with £6.4 billion being direct costs to the NHS – about 3.2% of NHS budgets.

7. People living with CKD and those who support them experience a dramatic impact in their daily lives, with £372 million in productivity loss to the UK economy annually from missed work due to dialysis alone. This could rise to £2.0 billion by 2033.

8. Kidney disease is currently the tenth biggest killer worldwide and is projected to be the fifth highest cause of life years lost by 2040.

9. Despite the large and rapidly growing burden of kidney disease, it received only 1.4% of relevant public healthcare research funding – just £17.7 million – in financial year 2021/2022.

10. Modelling suggests that improved implementation of four illustrative kidney-related healthcare interventions alone could save more than 10,000 lives between 2023 and 2033 in the UK and would be cost effective.
Executive Summary

Background

The kidneys are master regulators and essential for life, when they fail, the result is devastating. Responsible for a multitude of functions, kidneys are vital organs, yet Kidney Research UK’s own research has found that 80% of people don’t know where they are or what they do. The kidneys are located on either side of the spine, and they are responsible for hormone secretion into the bloodstream, removing waste, toxins and excess fluids from the blood.

The term “kidney disease” encompasses a broad range of conditions that leads to poor kidney function. Since the kidneys are necessary for many bodily functions, kidney disease increases the risk of developing other diseases, and conversely other diseases are risk factors for kidney disease. There is no cure for kidney disease, and managing it is a complex task, as kidney abnormalities exist across every age group, gender and ethnicity and can appear without warning.

Kidney disease is often labelled as a silent killer due to its frequent lack of physical symptoms, and as this report demonstrates is fast becoming a crisis. Even when symptoms are present, they are often overlooked or attributed to a differential diagnosis or other health issues. Since early diagnosis is key to managing and slowing progression to kidney failure, patients face devastating consequences if symptoms go undiagnosed. The majority of kidney diseases can be characterised as acute kidney injury, chronic kidney disease or end-stage kidney disease.

Acute kidney injury is a rapid deterioration in kidney function and typically occurs in people who are hospitalised, especially those who require treatment in intensive care units. Acute kidney injury causes a build-up of waste products in the blood, affecting other organs such as the brain, heart, and lungs. Acute kidney injury requires most patients to be hospitalised for kidney function to recover and in most cases is reversible. However, it is recognised as an important risk factor for progression of chronic kidney disease.

Chronic kidney disease is usually categorised into five stages (Table E1).
### Table E1. Stages of chronic kidney disease

<table>
<thead>
<tr>
<th>Stages of chronic kidney disease</th>
<th>% of kidney function</th>
<th>Symptom/implication</th>
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</thead>
<tbody>
<tr>
<td><strong>STAGE 1</strong></td>
<td></td>
<td></td>
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<tr>
<td>Kidney damage with normal kidney function</td>
<td>100-90%</td>
<td>• People in early-stage CKD may not know they have CKD as they often feel well and show no symptoms</td>
</tr>
<tr>
<td>Kidney damage with mild loss of kidney function</td>
<td>89-60%</td>
<td></td>
</tr>
<tr>
<td><strong>STAGE 2</strong></td>
<td></td>
<td></td>
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<tr>
<td>Mild to moderate loss of kidney function</td>
<td>59-45%</td>
<td>• People are often diagnosed with kidney disease in the mid-stage, with many people still asymptomatic as waste in the body builds and blood pressure rises</td>
</tr>
<tr>
<td><strong>STAGE 3a</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate to severe loss of kidney function</td>
<td>44-30%</td>
<td></td>
</tr>
<tr>
<td><strong>STAGE 3b</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe loss of kidney function</td>
<td>29-15%</td>
<td>• Patients with kidney failure require dialysis* or a kidney transplant to stay alive</td>
</tr>
<tr>
<td><strong>STAGE 4</strong></td>
<td></td>
<td>• A proportion of people with kidney failure will not receive either dialysis or transplant, instead undergoing conservative care</td>
</tr>
<tr>
<td><strong>STAGE 5</strong></td>
<td></td>
<td></td>
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<tr>
<td>Kidney failure</td>
<td>Less than 15%</td>
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*Dialysis is a type of kidney replacement therapy that replaces the blood-filtering function of the kidneys.

Chronic kidney disease affects more than 10% of the UK population and is rapidly becoming more common as the population ages. Despite its high prevalence, early detection and awareness are low, in part because of an absence of early symptoms.

Many health conditions can contribute to chronic kidney disease, but two primary risk factors are diabetes and high blood pressure. Diabetes and the accompanying high levels of blood sugar can damage various organs in the body, including the kidneys and heart. High blood pressure, or hypertension, damages blood vessels throughout the body, including those in the kidneys. When these blood vessels are damaged, the kidneys are less effective at removing waste and excess fluid from the body.
In addition to clinical risk factors, there are environmental and social factors that contribute to an increased risk of developing chronic kidney disease. These factors include access to healthcare, societal inequalities, and biological, genetic and cultural factors. Rare and genetic forms of kidney disease collectively affect a large number of people, while health inequalities make it challenging for people to receive the medical attention, access to care and support they need. In the UK, some groups are particularly at a disadvantage when it comes to kidney care. It is well established that people from lower socio-economic groups, in some instances ethnic minority groups, are more likely to develop chronic kidney disease, progress faster towards kidney failure and die earlier. People from some ethnic minority groups are three to five times more likely to require dialysis and wait much longer for a kidney transplant on average than people from a white background.

Complications associated with kidney disease can accelerate progression and increase the risk of cardiovascular-related events. As chronic kidney disease worsens and becomes kidney failure (end-stage kidney disease), dialysis or kidney transplantation is required to survive.

End-stage kidney disease is defined by permanent kidney damage, and kidney function is reduced to 15% or less. Patients may experience a variety of symptoms which include fatigue, drowsiness, reduction or absence of urine production, itchy skin, headache, weight loss, nausea, bone pain, skin and nail changes and easy bruising. This stage is ultimately fatal and requires either dialysis or a kidney transplant. The number of people with end-stage kidney disease requiring kidney replacement therapy is increasing worldwide and is predicted to double by 2030.

To date in 2023, there are 30,000 people in the UK who rely on dialysis to stay alive. There are two main types of dialysis to manage end-stage kidney disease – haemodialysis and peritoneal dialysis. In the UK, the majority (72%) of the 7,500 adults a year starting kidney replacement therapy begin with haemodialysis, where an artificial kidney machine is used to clean the blood. Most people receiving haemodialysis dialyse three times a week for four hours at a time. The other main form of dialysis, peritoneal dialysis, uses the lining of the abdomen (peritoneum) to filter the blood. In 2020, around 3,800 patients in the UK were on peritoneal dialysis.

An alternative treatment for patients with kidney failure is a kidney transplant. In the UK, over 2,900 adult transplants and 100 paediatric transplants are performed annually. For adult patients waiting for a kidney transplant, the average time frame is 2-3 years, with about 4,600 patients on the waiting list in 2022. On average, a transplant from a deceased donor lasts 15-20 years and a transplant from a living donor around 20-25 years, with the longevity affected by a variety of factors including age, health and other multi-morbid risk factors including diabetes and cardiovascular complications.

Despite the high prevalence and burden of kidney disease, research spending is relatively low, at just 1.4% (£17.7 million) of relevant publicly funded research budgets in the financial year 2021/22. A systematic analysis of the economic burden of kidney disease has not been undertaken in the UK, since 2012.
Scope of this report

Kidney Research UK commissioned ZS Associates to prepare a report investigating the following topics:

- The current kidney disease landscape in the UK, including acute, chronic and end-stage kidney disease, as well as rare and paediatric kidney diseases
- The current management strategies, risk factors, health of people from socially deprived communities, and the impact of Covid-19 on the kidney patient population
- The current incidence and prevalence of acute, chronic and end-stage kidney disease in the UK
- The current and projected (2033) economic burden of kidney disease, for both NHS and the wider UK economy

Approach

The diagram below shows the key steps taken to develop this report (Figure E1).

Figure E1. Project approach

1. 30 contributing stakeholders with a steering committee of ten
2. Targeted literature review of 11,000 UK articles from the last 5 years
3. Epidemiological modelling
4. Health economic modelling for CKD using a population-level Markov model
1. **Over 30 stakeholders** contributed to the development of this report. Stakeholders were recruited from various backgrounds, including nephrologists, cardio-renal specialists, kidney transplant specialists, paediatric nephrologists, primary care physicians, nephrology clinical service directors, academics, data specialists and patients. Stakeholder engagement played a pivotal role in shaping the inputs of this report and validating the outputs. Stakeholder engagement began with a series of scoping meetings from December 2022 to January 2023. A smaller steering group of ten clinicians, academics and patients met regularly between February 2023 and April 2023 to guide the project and validate the key findings.

2. **A targeted literature review** was conducted to comprehensively gather the most up-to-date, publicly available evidence. The targeted literature review search strategy aligned with previously defined standards and was based on predefined reproducible search strings for epidemiology and economic literature reviews. The search identified approximately 11,000 UK-based articles published in the last 5 years. In some cases, additional targeted searches were performed to find model parameters. Additional evidence was provided through stakeholders in the scoping meetings and steering committee meetings.

3. The purpose of **epidemiological modelling** was to understand the historic trends in incidence and prevalence of the various conditions under the banner of kidney disease, and to calculate estimates of future demand and disease burden. The approach taken was to analyse several years of historic trends and changes in patient demographics. The modelling also examined the known impact of Covid-19 on these patient populations from 2020 to 2022. Because it is based on historical activity data, the projections from the epidemiological modelling will incorporate any existing capacity constraints – they will not factor in any unmet need. This is a particular risk for projections of transplantation and dialysis as they may underestimate the true level of future need, and for that reason additional unconstrained projections were produced using the health economic model.

4. **A population-level health economic model** (Markov model) was used to estimate the current and future incidence/prevalence and economic burden of chronic kidney disease across all stages and show the directional impact of illustrative interventions based on costs and outcomes. The model was developed to capture both NHS (direct cost) and UK economy (wider economic cost) perspectives. The time horizon for the model was set to 10 years. In addition to this baseline, the model was used to estimate the impact of four potential public health interventions: earlier diagnosis, better adherence to clinical guidelines, increased uptake of new medicines and increased rates of transplantation.
Findings

Epidemiology of kidney disease
The prevalence of the various types and stages of kidney disease has grown considerably in recent years and will continue to do so. Factoring in the ageing population and excess deaths in high-risk populations during the Covid-19 pandemic, an estimated 7.19 million people in the UK have chronic kidney disease in 2023, more than 10% of the UK population. By 2033, this will increase to 7.61 million people. While the overall prevalence as a proportion of the age 16+ population is expected to remain constant, among the people with chronic kidney disease, the proportion of patients with later-stage chronic kidney disease is expected to increase from 45% to 51% (Figure E2).

Figure E2. Epidemiology of chronic kidney disease stages 1-5 (excluding transplantation and dialysis)
Rates of acute kidney injury will also continue to grow, although more slowly than chronic kidney disease. Based on historic trends, the incidence of acute kidney injury will increase from an estimated 615,000 episodes in 2022 to 637,000 by 2033.

For dialysis and transplantation, a broad range of potential future demand was calculated. The constrained view assumes NHS capacity continues to grow at current rates based on the actual numbers of patients treated over the past 10 years, while the unconstrained view estimates the number of people who may need dialysis based on how quickly people progress through the stages of kidney disease. In the unconstrained view of demand, which factors in all potential unmet need, the number of patients requiring dialysis could rise to 143,000, while the demand for transplantation could be as high as 12,000 per year by 2033 (Figure E3).

Figure E3. Constrained vs. unconstrained projections of adults receiving kidney transplants in the UK (2033)
Current and future economic burden of kidney disease

In 2023, the total cost of kidney disease to the UK economy is estimated at £7.0 billion. This includes £6.4 billion in direct costs to the NHS, approximately 3.2% of the £197 billion of total NHS spending across the four nations. The £7.0 billion estimate also includes £372 million in productivity loss for people living with end-stage kidney disease and those who support them, in addition to £225 million of transport costs for patients receiving dialysis.

With the assumption that the current system is at its maximum capacity for expensive end-stage kidney care such as dialysis and transplantation, the cost of kidney disease will rise to £7.5 billion by 2033 (11% increase from 2023), with the biggest increase in cost due to the increasing prevalence and associated costs of chronic kidney disease stages 3-5. However, when modelling unconstrained need, the health economic model projected that in 2033 the cost could be as high as £13.9 billion, with the biggest driver being the growth in demand for dialysis (Figure E4).

Figure E4. Economic burden of kidney disease in the UK
Modelling of interventions to manage the burden of chronic kidney disease

There is a growing body of evidence indicating that the burden of chronic kidney disease can be reduced through early detection, pharmacological intervention and outreach. A key objective for this report was to assess whether a basket of potential population-level interventions for managing chronic kidney disease, including end-stage kidney disease, could be cost-saving or cost-effective.

Through the stakeholder engagement process, several interventions were cited as having the potential to improve clinical outcomes associated with chronic kidney disease. The following interventions were applied to the model:

- **Intervention 1. Early/improved diagnosis**: This intervention targets underserved populations through outreach programmes to improve screening opportunities and increase early diagnosis and is illustrative of the benefits which can be achieved through well-targeted early/improved diagnosis in general.

- **Intervention 2. Improved CKD management**: This intervention targets eligible patients with chronic kidney disease who are either untreated or not receiving standard care according to clinical guidelines (e.g. adequate blood pressure management).

- **Intervention 3. Use of SGLT-2 inhibitors**: This intervention aims to increase uptake of new medications such as sodium-glucose transport protein 2 (SGLT-2) inhibitors to reduce cardiovascular events and slow progression to end-stage kidney disease.

- **Intervention 4. Increased rates of transplantation**: This intervention models the impact of increased outreach and awareness to increase pre-emptive live donor transplants. It is illustrative of the benefits of improving transplantation rates more generally.

The combined impact of these interventions was to prevent more than 10,000 deaths over the 10-year time horizon, with 49,574 quality-adjusted life years saved (Table E2). This is predicted to cost £7,688 per quality-adjusted life years – significantly below the National Institute for Health and Care Excellence willingness-to-pay threshold of £20,000-£30,000 per quality-adjusted life year (QALY), meaning these interventions would be deemed cost effective. The modelling also predicts that the reduction in indirect costs (travel and lost economic productivity) of £445.7 million would more than offset the total increase in NHS costs of £381.1 million. All of the interventions individually or combined show a cost-effective or cost-saving Incremental Cost-Effectiveness Ratio (ICER) (Figure E5).
Table E2. Economic impact of combined interventions in the unconstrained view

<table>
<thead>
<tr>
<th>Scenario (Years 1-10)</th>
<th>Direct costs (£)</th>
<th>Indirect costs (£)</th>
<th>Total costs (£)</th>
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<td>91,018,278,811</td>
<td>71,662,137</td>
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<td>Combined Interventions</td>
<td>71,064,652,248</td>
<td>19,889,062,335</td>
<td>90,953,714,583</td>
<td>71,711,711</td>
</tr>
<tr>
<td>Difference</td>
<td>381,118,041</td>
<td>(445,682,268)</td>
<td>(64,564,228)</td>
<td>49,574</td>
</tr>
<tr>
<td>% change</td>
<td>0.5%</td>
<td>-2.2%</td>
<td>-0.1%</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

Figure E5. Summary of incremental cost-effectiveness ratios (ICERs) in the unconstrained view
Conclusions

The evidence presented in this report suggests that kidney disease leads to thousands of premature deaths each year, reduces quality of life and places a significant economic burden on the NHS, patients with kidney disease, the people who support them and the wider economy:

1. Chronic kidney disease affects 13% of the global population and is predicted to be the fifth leading cause of premature death* by 2040.
2. In the UK, approximately 3.25 million adults are living with chronic kidney disease stages 3-5, and a total of 7.2 million adults have chronic kidney disease (all stages), more than 10% of the entire population.
3. By 2033, the number of people living with all-stage chronic kidney disease is projected to reach 7.6 million. This is mainly driven by an ageing population as well as risk factors such as diabetes, hypertension and cardiovascular disease, as well as other important factors such as health and economic inequalities.
4. Amongst those with chronic kidney disease, the proportion with later-stage chronic kidney disease (3-5) is expected to increase from 45% (3.25 million) to 51% (3.9 million).
5. Around 615,000 episodes of acute kidney injury occur each year, mainly among those who are already unwell or hospitalised for another reason. By 2033, the number of acute kidney injury episodes is projected to rise by 4% to 637,000.
6. The total economic burden of kidney disease in the UK is £7.0 billion, with £6.4 billion attributable to direct costs to the NHS – about 3.2% of NHS budgets across the four nations. The total burden of kidney disease could rise to £13.9 billion by 2033.
7. There is a further estimated £372 million in productivity loss to the UK economy from missed work due to dialysis alone. Productivity loss in the UK could reach up to £2.0 billion by 2033, as a higher proportion of patients continue living with end-stage kidney disease.
8. In 2023, the cost of dialysis for people with end-stage kidney disease is £1.05 billion annually, or 0.53% of the NHS budget. In addition to the direct cost of dialysis, transport for patients on in-centre dialysis costs approximately £225 million per year. The cost to the NHS of dialysis to manage kidney disease (per person) is £34,000 per year – more than three times the annual value of a state pension.
9. Despite its substantial and increasing cost to the NHS, and the urgent need for new and better treatments driven by research, kidney disease received only 1.4% of relevant public healthcare research funding – just £17.7 million in financial year 2021/2022.
10. Economic modelling suggests that improved implementation of four illustrative healthcare interventions could save more than 10,000 lives by 2033. These interventions individually and collectively are shown to be cost-effective or cost-saving, where costs to the NHS are offset by quality-adjusted life years gained.

* Premature death can be measured by life years lost, which takes into account frequency of death and age at which it occurs. It is calculated by multiplying the number of deaths by a global standard life expectancy at which death occurs.
Recommendations

Strategic
Modelling indicates that significant, cost-effective patient benefits can be achieved through better implementation of existing technologies and guidelines for the prevention, management and treatment of kidney disease. Across the health and care system, a national effort should be made to improve uptake of these interventions.

Paediatric kidney disease is relatively rare and historically has not received the attention it deserves. Establishing some oversight of paediatric kidney care from kidney policymakers, in particular to establish better transition management for young adults, has been highlighted by stakeholders as important.

The population with chronic kidney disease and end-stage kidney disease is varied in terms of age, gender, ethnicity and the root causes of illness, and therefore the same diagnostic techniques, management strategies and treatments are not effective for all groups. For example, eGFR tests have been shown to be less sensitive at predicting outcomes in people who are of South Asian descent. There should be efforts made to personalise the care of patients with, or at risk of, kidney disease across the disease pathway. These should include:

- Use of the best possible diagnostic tests based on proven effectiveness for the demographics of the specific patient
- Genetic testing followed by appropriate management for those at risk of inherited kidney disease
- Patient choice in treatment, e.g. support with home dialysis for patients who feel this would better enable them to continue working and undertaking their usual activities
- Access to new and proven therapies to manage and slow disease progression in a timely manner
- Creating an environment fostering innovation and its implementation in real-world settings

Kidney disease is complex and is intertwined with other chronic/serious health conditions. The NHS and voluntary sector organisations should seek to break down silos between organisations and teams working on kidney disease and related conditions such as diabetes, hypertension, cardiovascular disease and inherited genetic conditions.

Modelling suggests that more proactive engagement with people who are at risk or have kidney disease would be clinically and cost effective, e.g.:

- Peer engagement to improve adherence to disease management strategies
- Engaging in proactive discussions around living donor transplants
- Community outreach to engage underserved groups
However, given the frequent multi-morbidity of people with kidney disease, this engagement could be even more cost effective if it addressed multiple health conditions relevant to these populations at the same time. The NHS and voluntary sector should consider how to pool resources and efforts to collaborate across multiple programmes of engagement.

Current research funding for kidney disease is just 1.4% of relevant healthcare budgets, while kidney disease represents 3.2% of NHS budgets, with a risk of significant growth in this burden. Kidney disease research funding should be increased in line with the clinical and financial burden of disease.

**Clinical**

In this report, kidney disease has been referred to as a silent killer, because many patients are undiagnosed or asymptomatic until they reach a later stage of disease. Stakeholder interviews have revealed opportunities to improve adherence to best practice guidelines by making them simpler and more accessible, especially for primary care, where the huge breadth of conditions general practitioners treat is a challenge. In addition, measures should be taken to monitor local adherence to guidelines and intervene where necessary.

To address barriers to implementation, focus is required on how best to provide knowledge transfer and pathway/process development. This could include closer collaboration between secondary and primary care, e.g. with regular virtual consultations between general practitioners and kidney specialists.

A broader transformation of renal services is needed to improve care through standardisation and knowledge sharing. In England, the Renal Services Transformation Programme (RSTP) is currently reviewing adult renal services and recommending areas where improvements should be made. The recommendations for service improvement in the areas of early detection, dialysis and transplantation are in alignment with the findings of this report, which also addresses the scale of the challenge across the whole of the UK and the requirements of paediatric services to meet future needs.

Severe kidney disease in children can have a similar impact in terms of mortality and lifelong disease to cancer. Because chronic kidney disease is a lifelong, gradually deteriorating condition, children with mild chronic kidney disease are likely to develop severe chronic kidney disease later in life, and therefore early intervention and ongoing management is important. Currently, however, poor infrastructure exists for children with kidney disease transitioning to adult services. Until recently, services were overseen nationally by a clinical reference group that included several other paediatric sub-specialties, which may be a cause for this disconnect. There is now a separate clinical reference group in place for paediatric renal services, and one of the focus areas should be establishing a more effective transition to adult services.
Research
In the development of this report, several evidence gaps were identified, and further research should be considered to address them:

- Understanding the rate at which patients progress through the stages of chronic kidney disease is essential to predicting future demand for services. However, much of the data currently in the public domain is out of date, and up-to-date transition probabilities/relative risks of progression of chronic kidney disease for the whole population and subgroups are needed.

- Understanding the relative risk/rate of progression for undiagnosed populations is essential for assessing the cost effectiveness of early diagnosis and treatment interventions, but there is very little published literature relevant to the UK. Studies, potentially using real-world data, comparing the relative rates of progression in diagnosed vs undiagnosed populations are required.

- Sources such as the renal registries provide data on the numbers of patients receiving dialysis. However, there is limited data on unmet need or delays in meeting need, and as more patients progress to later-stage kidney disease, having real-time data which allows monitoring of any potential capacity pressures will become increasingly important.

- This report utilises evidence from other European countries to estimate the economic burden of kidney disease for the UK. UK-specific studies on the impact of kidney disease on economic productivity are necessary.

- There is evidence of a strong and complex relationship between kidney disease and mental health. UK-specific studies on this relationship, including the impact of poor mental health on adherence to treatment, are needed.

- The evidence base relating to rare forms of kidney disease is scarce. Further research in this area is required to understand the natural history, determinants (including genetic), treatment effectiveness and burden of rare forms of kidney disease.

- Paediatric kidney disease is relatively rare and often complex. Better data and evidence are required to understand the needs of these patients, e.g. studies characterising their epidemiology, demographics and broader health needs.

- This report has highlighted the multitude of risk factors for kidney disease, but evidence on the causal link between diabetes, hypertension, chronic kidney disease and other risk factors at a population level is scarce. Studies investigating the relationships between these conditions in a predictive manner would provide a powerful tool for population health planning.

- There are still large evidence gaps on how Covid-19 has affected and will continue to affect people with or at risk of kidney disease. At the time of writing this report, work in this area is ongoing using the OpenSAFELY platform, and it is important that it continues to be supported.

- There is an opportunity for the four nations of the UK to learn from each other on the management of kidney disease, but inconsistent data is a barrier to this. Introducing more consistent data, e.g. extending the Healthcare England Survey methodology to Scotland, Wales and Northern Ireland, could be an important enabler for driving better health outcomes for the entire UK population.
Background

Introduction: kidney disease, the silent crisis

The kidneys are vital, life-sustaining organs, whose primary function is to filter the blood to remove wastes, poisons and excess fluid from the body. The kidneys are located just below the rib cage, one on each side of the spine. Each kidney is made up of units called nephrons, and their function is to remove waste while returning needed components back into the blood. The kidneys are also responsible for controlling blood pressure, stimulating red blood cell production, keeping bones healthy, regulating blood chemicals and secreting essential hormones. When the kidneys are not working properly, harmful toxins and excess fluids build up in the body, which may lead to kidney failure. These symptoms can include extreme tiredness or lethargy, persistent headaches, swelling in the face and ankles, fluid retention, lower back pain and death.

The term kidney disease encompasses a broad range of conditions that lead to issues with kidney function. Since the kidneys are vital to many bodily functions, kidney disease increases the risk of developing other diseases, and, conversely, other diseases are risk factors for kidney disease. There is no cure for the majority of kidney diseases, and managing them is a complex task as kidney abnormalities exist across every age group, gender and ethnicity and can occur without any warning, often without symptoms.

Persistent and progressive damage to the kidneys leads to chronic kidney disease (CKD). CKD is a major public health issue. It affects 13% of the global population and is predicted to be the fifth leading cause of life years lost (LYL)* worldwide by the year 2040. In 2016, the UK prevalence of all-stage CKD was estimated at 12.7% of the adult (16+) population, and 5.1% of the population had CKD stages 3-5. This data was based on a comprehensive population survey of the UK and includes both diagnosed and undiagnosed kidney diseases in the population.

CKD is defined as abnormalities of either the kidney structure or its function that are present for more than 3 months. CKD is a long-term condition in which kidney function declines over time, and it is grouped and characterised into five stages (Table 1), each of which is associated with progressive damage. As CKD stages 1-2 are not well diagnosed or reported, the majority of patients are diagnosed between stages 3 and 5; however, there are many variables and risk factors that influence diagnosis, including age, gender, ethnicity and co-morbidities (e.g. diabetes, hypertension, and cardiovascular disease).

* Life years lost is a measure of premature mortality which takes into account frequency of death and age at which it occurs. LYL is calculated by multiplying the number of deaths by a global standard life expectancy at which death occurs.
Table 1. Stages of chronic kidney disease

<table>
<thead>
<tr>
<th>Stages of chronic kidney disease</th>
<th>% of kidney function</th>
<th>Symptom/implication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STAGE 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney damage with normal kidney function</td>
<td>100-90%</td>
<td>• People in early-stage CKD may not know they have CKD as they often feel well and show no symptoms</td>
</tr>
<tr>
<td>Kidney damage with mild loss of kidney function</td>
<td>89-60%</td>
<td></td>
</tr>
<tr>
<td><strong>STAGE 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild to moderate loss of kidney function</td>
<td>59-45%</td>
<td>• People are often diagnosed with kidney disease in the mid-stage, with many people still asymptomatic as waste in the body builds and blood pressure rises</td>
</tr>
<tr>
<td>Moderate to severe loss of kidney function</td>
<td>44-30%</td>
<td></td>
</tr>
<tr>
<td><strong>STAGE 3a</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe loss of kidney function</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>STAGE 3b</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe loss of kidney function</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>STAGE 4</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe loss of kidney function</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>STAGE 5</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney failure</td>
<td>Less than 15%</td>
<td>• Patients with kidney failure require dialysis* or a kidney transplant to stay alive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• A proportion of people with kidney failure will not receive either dialysis or transplant, instead undergoing conservative care</td>
</tr>
</tbody>
</table>

*Dialysis is a type of kidney replacement therapy that replaces the blood-filtering function of the kidneys.

In early-stage CKD (stages 1-2), patients are often asymptomatic, but as the stage of CKD increases, non-specific symptoms develop and include tiredness, nausea, sleep disturbance, more frequent urination (including at night) and muscle cramps. When kidney disease is advanced (CKD stage 5) and kidney function is less than 15%, typically patients rely on dialysis or kidney transplantation where appropriate. Untreated kidney failure is fatal.8
Detection and diagnosis of CKD is a challenge. A 2020 study estimated that approximately half of people with CKD were undiagnosed. Most people with CKD are typically asymptomatic in the early and late stages and only diagnosed as a result of routine blood or urine tests, including those for other conditions, or once the disease has progressed. Uncoded CKD, where the disease is not formally diagnosed, is associated with lower quality of care, as well as greater numbers of co-morbidities and adverse outcomes.

These estimates, from 2016, are likely to significantly underestimate the current and future burden of CKD, since the prevalence of CKD was much higher in the older population, e.g. the all-stage CKD rate was 46% for the population aged 75 years or older. This means that as the UK’s population is ageing, the prevalence of CKD is also increasing. Estimates of current prevalence along with projections to 2033 are provided later in this report.

These dual challenges of increasing prevalence and low detection are the reason kidney disease can be considered a silent crisis.

Without detection and treatment, kidney disease progresses more rapidly to end stage (ESKD), at which point the burden on the individual, the National Health Service (NHS) and the UK economy increases significantly. When on haemodialysis, patients will spend several hours a week receiving treatment, preventing them from participating in their usual activities and reducing their ability to work. A year of in-centre haemodialysis has previously been estimated to cost the NHS approximately £30,000 per patient.

Productivity losses due to dialysis are not well characterised in the UK, but assuming similar losses to those observed in other European countries, patients and the people who support them will on average lose 20 days of work per year, an estimated cost to the economy of £2,940 per person per year. This average is relatively low, since most patients on dialysis are of retirement age, although there are some dialysis patients of working age (55 years and younger), in particular many using home dialysis. Assuming similar losses to other European countries, employed people on dialysis on average will miss 30 days of work due to absenteeism and will lose an additional 56 days of work due to presenteeism (showing up to work but lacking productivity due to illness). In total, the productivity loss per annum for an employed person on dialysis is estimated to cost the economy approximately £12,600, and many people on dialysis are unable to work at all. A Dutch study estimated that only 20% of people on dialysis were in full employment. In addition, a person caring for a loved one on dialysis provides on average 9 hours of informal care per week, equivalent to an additional £9,200 in lost productivity per year.
Kidney disease policy and research

Despite its high prevalence and burden, kidney disease has not received the same level of priority as other long-term conditions. The 2019 NHS Long Term Plan called out the need for better care of other major health conditions such as cardiovascular disease, diabetes and stroke but was silent on kidney disease.\textsuperscript{15}

Paediatric kidney disease populations are often neglected from a policy perspective due to small patient numbers and the complexity of the disease in children, since they do not fall under the same national leadership structures as the adult population with kidney disease. This can result in a lack of focus and structure, in which case, some challenges surrounding the paediatric kidney population might not be clearly understood.\textsuperscript{16}

The last significant review describing the burden of kidney disease in the UK (which focused on England) was published in 2012. This review was focused on estimates based on 2010 NHS data.\textsuperscript{17} The financial burden of CKD and ESKD estimated by that report was £1.45bn (1.3% of NHS budgets) and is still used in policy documents despite the increasing prevalence of CKD due to the ageing population, the impact of additional risk factors and increasing costs to the NHS.\textsuperscript{17,19}

Research funding for kidney disease is also disproportionately low compared with the current economic burden. As set out below (Table 2), kidney disease received only 1.4% of relevant public sector research budgets in 2021-2022, in line with the cost to the NHS of CKD in 2010, but likely far below the equivalent share of the current economic burden of kidney disease in 2023, estimated at 3.2% of the total NHS budget in this report.

Table 2. NHS funding and research cost for kidney disease

<table>
<thead>
<tr>
<th>Year</th>
<th>UKRI/ MRC funding for KD (£m)</th>
<th>NIHR funding for KD (£m)</th>
<th>Total KD research funding (£m)</th>
<th>UKRI Medical research budget (£m)</th>
<th>NIHR spent research programmes Budget 2022 (excluding Covid-19) (£m)</th>
<th>Total estimated relevant research budget (£m)</th>
<th>KD % of budget</th>
</tr>
</thead>
<tbody>
<tr>
<td>19/20</td>
<td>7.7</td>
<td>14</td>
<td>21.7</td>
<td>800</td>
<td>426</td>
<td>1,226</td>
<td>1.8</td>
</tr>
<tr>
<td>20/21</td>
<td>7.8</td>
<td>8</td>
<td>15.8</td>
<td>800</td>
<td>426</td>
<td>1,226</td>
<td>1.3</td>
</tr>
<tr>
<td>21/22</td>
<td>6.7</td>
<td>11</td>
<td>17.7</td>
<td>800</td>
<td>426</td>
<td>1,226</td>
<td>1.4</td>
</tr>
</tbody>
</table>
Scope of this report

The purpose of this report is to consolidate and build on the existing evidence regarding the burden of kidney disease in the UK. It has a broader scope than the 2012 report, as it covers multiple types of kidney disease:
- CKD
- Acute kidney injury (AKI)
- ESKD
- Rare kidney diseases
- Paediatric kidney disease

It also takes a broader perspective on economic burden, measuring this in terms of both cost to the NHS and cost to the wider economy. The following sections of this report cover:
- A more detailed overview of each group of patients with kidney disease
- Risk factors and inequalities
- The epidemiology (incidence and prevalence) of kidney disease in the UK, now and projected to 2033
- The economic burden of kidney disease, for both the NHS and the wider economy, now and projected to 2033
- Interventions to reduce this burden, with a focus on CKD
- Recommendations
Overview of kidney disease

Chronic kidney disease

CKD is a progressive condition and is usually asymptomatic in the early stages. For kidney disease to be considered chronic, damage must be evident for at least 3 months. As the disease progresses, the kidneys become increasingly damaged, leading to a range of symptoms such as fatigue, weakness, difficulty concentrating and loss of appetite. In advanced stages of CKD, patients may experience serious complications such as high blood pressure, anaemia, bone disease, and increased risk of cardiovascular disease (CVD). Over time, CKD can cause renal dysfunction and progression to ESKD.

Detection and diagnosis of CKD at early stages is crucial, as the right treatment can slow disease progression and prevent complications. CKD stages are traditionally categorised based on estimated glomerular filtration rate (eGFR; G categories, G1-G5), which is a measure of how well the kidneys filter the blood. The risk of progression is assessed based on a combination of eGFR and presence of the protein albumin (albuminuria; A categories, A1-A3). As per the table below (Table 3), risk level is scored between 1 and 4+, and this score helps determine the method and intensity of monitoring and treatment of patients. As these scores increase, so does the risk of CKD progression, death from all causes, cardiovascular death and AKI.
Table 3. Guide to frequency of monitoring (number of times per year) by eGFR and albuminuria

<table>
<thead>
<tr>
<th>GFR categories (ml/min per 1.73m²)</th>
<th>Persistent albuminuria categories</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal to mildly increased</td>
<td>Normal to mildly increased</td>
<td>≥90</td>
<td>1CKD</td>
<td>1</td>
</tr>
<tr>
<td>G1</td>
<td>G1</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Mildly decreased</td>
<td>Mildly decreased</td>
<td>60-89</td>
<td>1CKD</td>
<td>1</td>
</tr>
<tr>
<td>G2</td>
<td>G2</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Mildly to moderately decreased</td>
<td>Mildly to moderately decreased</td>
<td>45-59</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>G3a</td>
<td>G3a</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Moderately to severely decreased</td>
<td>Moderately to severely decreased</td>
<td>30-44</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>G3b</td>
<td>G3b</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Severely decreased</td>
<td>Severely decreased</td>
<td>15-29</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>G4</td>
<td>G4</td>
<td></td>
<td></td>
<td>4+</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td></td>
<td>4+</td>
</tr>
</tbody>
</table>

GFR and albuminuria grid to reflect the risk of progression by intensity of colouring (green=low risk, yellow=moderate risk, orange=high risk, pink and red = very high risk.)
As CKD is a long-term condition, management of kidney disease relies on treatment to prevent CKD progression and avoidance of risk factors such as smoking, diabetes, hypertension and CVD.\(^3\) It is important for a patient to be properly staged in order to carry out accurate assessments of the severity of the disease, which helps to inform decisions associated with their management and monitoring.\(^3\) Since there is an association between CKD and increased risk of CVD, well-managed patients can reduce the risk of disease progression by monitoring their eGFR and associated risk factors such as cardiovascular events, hospitalisation and blood sugar, as these risk factors are associated with poor outcomes.\(^22\)

In the UK, managing CKD prior to ESKD primarily involves the use of medications to control blood pressure and glucose levels, medications to manage CKD complications (e.g. metabolic bone disease anaemia, etc) and lifestyle changes such as dietary adjustments and exercise.\(^21\) While effective medications such as angiotensin-converting enzyme inhibitors (ACEs) and angiotensin receptor blockers (ARBs) have been available since the 1980s, there is evidence that not all patients who could be receiving them, based on the National Institute for Health and Care Excellence (NICE) guidelines, are receiving them.\(^16, 23-25\) Absence of treatment can lead to faster progression to ESKD, along with increased risk of cardiovascular events such as heart attack and stroke.\(^26\)

Sodium-glucose transport protein 2 (SGLT-2) inhibitors are also known to slow progression towards ESKD and reduce the risk of cardiovascular events.\(^27\) These medicines have been available for patients with conditions such as diabetes since 2013, and NICE has now approved the use of SGLT-2 inhibitors for CKD.\(^24\) Given these treatments are new to CKD, NICE estimates that approximately 19% of patients with CKD will be eligible. In England, this is equivalent to about 340,000 people.\(^24\)

**Acute kidney injury**

AKI is a common health problem,\(^28\) typically occurring in patients who are hospitalised, especially those who require treatment in an intensive care unit (ICU).\(^29\) AKI is characterised by an abrupt loss of kidney function and is strongly associated with high morbidity and mortality.\(^30\) AKI is complex due to multiple risk factors, including age, heart failure, liver failure, CKD, anaemia and exposure to nephrotoxic agents such as antibiotics.\(^29\) Patients who experience AKI are at higher risk of developing CKD in the future.\(^31\) In one study, CKD developed in approximately 25% of hospitalised patients with AKI after 3 years.\(^32\)

AKI is associated with poor patient outcomes, increased length of hospital stay and high mortality.\(^31\) Based on a national study in the UK, up to 30% of deaths attributed to AKI could have been prevented with early recognition and treatment.\(^31\)

A significant proportion of patients with AKI require management in a hospital setting, which involves fluid resuscitation, avoidance of nephrotoxic medications and correction of electrolyte imbalances.\(^33\) Optimal management of AKI requires close collaboration with a multi-disciplinary team including primary care physicians, nephrologists, allied health professionals and other subspecialists participating in the care of the patient.\(^33\)
End-stage kidney disease

In ESKD, permanent kidney damage has occurred to the point where the kidneys are unable to support life. Patients may experience a wide variety of symptoms, including fatigue, drowsiness, decrease in urination or inability to urinate, dry skin, itchy skin, headache, weight loss, nausea, bone pain, skin and nail changes and easy bruising. This stage is ultimately fatal and requires either dialysis – a kidney replacement therapy that replaces the normal blood filtering function of the kidneys – or a kidney transplant. Currently, there are 30,000 people in the UK who rely on dialysis to stay alive, and every year, around 3,000 people receive a kidney transplant. The number of people with ESKD requiring kidney replacement therapy (KRT) has been increasing worldwide and is predicted to double by 2030.

Management: dialysis

Two major types of dialysis exist to manage ESKD – haemodialysis and peritoneal dialysis. In the UK, the majority (72%) of the 7,500 adults a year starting KRT begin with haemodialysis, where an artificial kidney machine is used to clean the blood. The average number of sessions for a patient on haemodialysis is three times a week, for an average of 4 hours per session, both at home and in-centre. In 2019, cost estimates for in-centre haemodialysis were approximately £30,000, representing a huge cost burden to the NHS and a huge impact on patients’ lives. Beyond allowing greater flexibility in a patient’s schedule, as they can dialyse overnight, home-based haemodialysis was significantly cheaper, with an annual estimate of over £20,000 compared with in-centre dialysis, and these more regular sessions at home can lower restrictions on dietary and fluid consumption. In 2020, 1,400 patients were on home-based haemodialysis.

The second form of dialysis, peritoneal dialysis, uses the lining of the abdomen (peritoneum) to filter the blood through a daily routine at home. Around 3,800 patients in the UK were on peritoneal dialysis in 2020. Peritoneal dialysis is classified into two types: continuous ambulatory peritoneal dialysis, which uses a portable machine for at least 2 hours a day, and automated peritoneal dialysis, which uses a home-based machine overnight.

* Kidney replacement therapy (KRT) is a term used to encompass treatments used for kidney failure. These treatments include dialysis and transplantation.
Management: transplantation

In the UK, over 2,900 adult kidney transplants and 100 paediatric kidney transplants are performed annually.\(^{35}\) For adult patients waiting for a kidney transplant, the average time frame is 2-3 years, with about 4,600 active patients on the waiting list in 2022.\(^{35}\) For patients, the typical time frame from when they start on dialysis to transplantation is on average 3 years.\(^{35}\) Among those on the waiting list, some receive a transplant, but others die waiting or are removed, typically from becoming too unwell for transplantation (Figure 1).\(^{35}, 41\) The majority of adult transplant recipients (>70%) receive deceased donor kidneys, while the opposite is true for children – the majority (>65%) receive living donor kidneys.\(^{35}\) Patient survival at 5 years is 88% for adult patients who received deceased donor kidneys and 94-95% for adult patients who received living donor kidneys.\(^{34}, 35\) On average, deceased donor kidneys last 15-20 years, while living donor kidneys last 20-25 years.\(^{35}\)

Figure 1. Representation of transplant waiting list over 5-year period

Footnote: From years 1-3, 2% (92 people) will be ineligible to receive a kidney and 2% (92 people) will die. From years 3-5, 5% (143 people) will be ineligible to receive a kidney and 5% (143 people) will die. Following being on a waiting list for 5 years, 8% (50 people) will be ineligible to receive a kidney and 7% (44 people) will die.
Management: conservative care as an alternative

Conservative care is an important therapeutic option for patients with advanced kidney disease who believe that the burdens of dialysis are not outweighed by its potential benefits. Individuals who neither plan for nor initiate KRT when they reach kidney failure receive conservative kidney management. Conservative care is an option patients may choose over dialysis, with the objectives including slowing down the progression of kidney dysfunction and treating complications (anaemia, bone diseases, cardiovascular diseases). While there are noted survival benefits of dialysis, many patients are willing to forgo lengthy hospital stays and dialysis as it means a better quality of life for them; however, it may also be a precursor to KRT. This may be particularly appropriate for patients in circumstances where they may not increase their life expectancy by receiving dialysis in any case, e.g. where they have substantial co-morbidities.

Because conservative care is more focused on maintaining remaining kidney function and preventing or treating symptoms, cost to the NHS is substantially lower than dialysis (on average £5,600 for conservative care compared to the £15,000+ for dialysis).

Conservative care can also be less burdensome than dialysis for carers. When looking at the carer experience and caregiver quality of life (QoL), carers for patients on conservative care rate their experience higher than those caring for patients on dialysis (15 points higher on a 100-point scale). QoL is a concept which aims to capture the well-being, whether of a population or individual, regarding both positive and negative elements. For example, common facets of QoL include personal health (physical, mental, and spiritual), relationships, education status, work environment, social status, wealth, a sense of security and safety, freedom, autonomy in decision-making, social-belonging, and their physical surroundings. Fatigue and mental health scores were worse for dialysis carers than conservative carers, but both had low scores for “assistance from organisations and government.”
Rare kidney diseases

Rare kidney diseases encompass at least 150 different conditions, most of which are inherited. Although individual rare kidney diseases raise specific issues, as a group these rare diseases can present challenges in differential diagnosis, which include small numbers of affected patients, unidentified causes of disease, lack of biomarkers for monitoring disease progression, and need for complex care. Patients often spend years visiting multiple healthcare providers before receiving an accurate diagnosis. In the UK, according to the UK Kidney Association (UKKA) there are 20 rare renal conditions that are well characterised and diagnosed (Table 4).

Table 4. Top 20 rare kidney conditions in the UK

<table>
<thead>
<tr>
<th>Rare kidney condition</th>
<th>Disease description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alport Syndrome</td>
<td>• Alport syndrome is a genetic condition that occurs due to an abnormality in part of the kidneys’ filtering system and affects around 1 in 5,000 people</td>
</tr>
<tr>
<td></td>
<td>• Diagnosed by a kidney biopsy and genetic testing</td>
</tr>
<tr>
<td></td>
<td>• Blood pressure medication can help maintain kidney function, although dialysis and/or transplant may eventually be needed</td>
</tr>
<tr>
<td>Atypical Haemolytic Uraemic Syndrome (aHUS)</td>
<td>• aHUS occurs due to an abnormality in the immune system, with about 20 new cases a year in the UK</td>
</tr>
<tr>
<td></td>
<td>• Symptoms include tiredness, breathlessness and feeling extremely unwell</td>
</tr>
<tr>
<td></td>
<td>• aHUS is diagnosed via a blood test</td>
</tr>
<tr>
<td></td>
<td>• Treatment may include an infusion of a medication called eculizumab</td>
</tr>
<tr>
<td>Autosomal dominant polycystic kidney disease (ADPKD)</td>
<td>• ADPKD is a genetic condition that causes cysts in the kidneys and affects around 1 in 2,000 people (equally common in men and women)</td>
</tr>
<tr>
<td></td>
<td>• Common symptoms include high blood pressure and urinary tract infections (UTIs)</td>
</tr>
<tr>
<td></td>
<td>• Diagnosed in adulthood by a scan (ultrasound, computed tomography or magnetic resonance imaging)</td>
</tr>
<tr>
<td></td>
<td>• Blood pressure medication can help maintain kidney function, although dialysis and/or transplant may eventually be needed</td>
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</table>
### Rare kidney condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>Disease description</th>
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</table>
| **Autosomal recessive polycystic kidney disease (ARPKD)** | - ARPKD is a severe genetic condition causing cysts in the kidneys affecting around 1 in 20,000 people (equally common in boys and girls)  
  - The main symptom is large kidneys  
  - Diagnosed by an ultrasound scan during pregnancy  
  - By the age of ten, most children with ARPKD will have developed kidney failure and need dialysis or a kidney transplant |
| **Bartter syndrome**                           | - Bartter syndromes are very rare types of inherited kidney conditions that cause excess salts and water to be lost from the body in the urine, affecting around 1 in 1 million people (boys and girls are affected equally)  
  - Symptoms include vomiting, muscle weakness, persistent thirst and a general failure to thrive in children  
  - Diagnosed in childhood by blood tests  
  - Treatment focuses on ‘topping up’ the levels of potassium, magnesium and salt by dietary changes and supplements |
| **C3 glomerulopathy (C3G)**                   | - C3G occurs due to immune system dysfunction and affects around 1 in 500,000 people (men and women are affected equally)  
  - Symptoms include blood and protein in the urine  
  - Diagnosed by kidney biopsy  
  - Dietary changes, immunosuppressant drugs and blood pressure medication can help with kidney function, although dialysis and/or transplantation may eventually be needed |
| **Cystinosis**                                | - Cystinosis is a rare inherited condition caused by a build-up of an amino acid called cystine; it affects 1 in 200,000 people (equally common in men and women)  
  - Symptoms include difficulty feeding, increased thirst, slow growth and muscle weakness  
  - Diagnosed in early childhood by a blood test  
  - Cysteamine is used to control the build-up of cystine |
| **Cystinuria**                                | - Cystinuria is an inherited condition that causes an amino acid called cystine to build up in the urine and form crystals, which can eventually turn into kidney stones, and affects around 1 in 10,000 people  
  - Symptoms include lower back or groin pain and UTIs  
  - Treatment aims to keep the urine diluted to prevent stones from forming |
<table>
<thead>
<tr>
<th>Rare kidney condition</th>
<th>Disease description</th>
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</thead>
</table>
| Dense deposit disease (DDD)              | • DDD occurs when part of the immune system called complement is deposited in the kidneys and affects 1 in 500,000 people (men and women are affected equally)  
• Symptoms include blood and protein in the urine, swelling around the eyes and ankles and high blood pressure  
• The precise diagnosis depends on the appearance of the kidneys by biopsy  
• Dietary changes, immunosuppressants and blood pressure medication can help with kidney function, although dialysis and/or transplant may eventually be needed |
| Gitelman Syndrome                        | • Gitelman syndrome is a rare inherited condition that causes salt to be lost from the kidneys in the urine and that affects around 1 in 40,000 people (men and women are affected equally)  
• Symptoms include extreme tiredness, muscle cramps, cravings for salty food and excessive thirst  
• Diagnosed by blood tests  
• Treatment focuses on ‘topping up’ the levels of potassium, magnesium and salt by dietary changes and supplements |
| IgA nephropathy (IgAN)                   | • IgAN occurs when immunoglobulin A damages the kidneys, reducing their ability to clear waste from the body; it affects around 1 in 50,000 people (men are more likely to be affected)  
• Some people with IgAN do not have any symptoms  
• Diagnosed in late teens to early adulthood by a kidney biopsy  
• Blood pressure medication and/or immunosuppressants such as steroids may be prescribed to help the immune system |
| Lowe Syndrome                            | • Lowe syndrome is a very rare genetic condition that causes severe physical and cognitive disabilities; it affects around 1 in 500,000 people (only affects boys)  
• All babies with Lowe syndrome have cataracts over their eyes  
• Diagnosed shortly after birth  
• Treatment focuses on symptom management |
| Membranous Nephropathy (MN)              | • MN occurs when the immune system causes the tiny filters in the kidney to malfunction; it affects around 1 in 100,000 people (twice as common in men than women)  
• Symptoms include foamy, frothy urine (like the head on a pint of beer), high blood pressure, puffiness around the eyes and swollen ankles  
• Diagnosed between the ages of 40 and 70 by a kidney biopsy  
• Around one in three people with MN recover without the need for any treatment |
<table>
<thead>
<tr>
<th>Rare kidney condition</th>
<th>Disease description</th>
</tr>
</thead>
</table>
| Membranoproliferative glomerulonephritis (MPGN) | • MPGN occurs when antibodies are deposited in the kidneys, affecting 1 in 100,000 people (men and women are affected equally)  
• Common symptoms include blood and protein in the urine, swelling around the eyes and ankles, high blood pressure, hives and anaemia  
• Diagnosed by a kidney biopsy  
• Dietary changes, immunosuppressants, and blood pressure medication can help with kidney function, although dialysis and/or transplant may be needed |
| Nephronophthisis (NPHP)               | • NPHP is an inherited condition that affects the cilia, affecting 1 in 75,000 people  
• Symptoms include excessive thirst, repeated urination, anaemia, high blood pressure and reduced growth  
• Diagnosed in babies and young children by an ultrasound scan  
• Regular blood and urine tests are needed to monitor kidney function, along with dietary changes, immunosuppressants and blood pressure medication, although dialysis and/or transplant may eventually be needed |
| Primary Hyperoxaluria (PH, also known as Oxalosis) | • PH is a genetic condition where excess oxalate is excreted by the kidneys. This can lead to kidney stones, affecting 1 in 1 million people (men and women are affected equally)  
• Symptoms include blood in the urine, reduced growth, anaemia and severe pain in the stomach or back  
• Diagnosis is often delayed as the condition is so rare. Genetic testing is available in the UK to identify some types of PH  
• Treatment aims to keep the urine diluted to prevent stones from forming. PH can eventually lead to kidney failure and the need for dialysis and/or transplant |
| Steroid Resistant Nephrotic Syndrome (SRNS) | • SRNS occurs when the tiny filters in the kidney are damaged, causing them to leak protein and retain excess water, affecting 1 in 30,000 people  
• Symptoms include protein in the urine, swelling around the eyes and ankles, increased risk of infection, anaemia and low blood pressure  
• Diagnosed in childhood by a blood or urine test  
• The first course of treatment is usually steroids which are effective in the majority of people |
<table>
<thead>
<tr>
<th>Rare kidney condition</th>
<th>Disease description</th>
</tr>
</thead>
</table>
| Steroid Sensitive Nephrotic Syndrome (SSNS) | • SSNS occurs when the tiny filters in the kidney are damaged, causing them to leak protein and retain excess water, affecting around 1 in 30,000 people  
• Symptoms include protein in the urine, swelling around the eyes and ankles, increased risk of infection, anaemia and low blood pressure  
• Diagnosed in childhood by a blood or urine test  
• The first course of treatment is usually steroids, which are effective, but the condition may reoccur |
| Tuberous Sclerosis (TSC)                     | • TSC is a genetic condition that causes non-cancerous growths in various parts of the body, including the brain and kidneys, affecting between 4,000 and 11,000 people in the UK  
• Symptoms include epilepsy, autism and learning and/or behavioural difficulties  
• Diagnosis is by physical examination and imaging scans  
• Medication is prescribed to reduce blood pressure and for epilepsy |
| Vasculitis                                   | • Vasculitis is an immune system disorder that causes an inflammation of the blood vessels, affecting 2,000 people a year  
• Symptoms include muscle weakness, tiredness, joint pains and rashes  
• Some types of vasculitis do not need any treatment as the symptoms resolve over time by themselves |
Paediatric kidney disease

Although relatively uncommon in children, kidney disease can be a devastating illness with many long-term consequences, including reduced life expectancy. Kidney disease in children can be caused by birth defects, hereditary diseases, infection and systemic disease. Alongside CKD disease complications seen at any age, such as anaemia, high blood pressure and mineral bone disorder, CKD can affect growth in children. Beyond clinical complications, children with advanced CKD lose many hours of education through hospital attendances and illness and have a greater incidence of problems relating to behaviour, relationships and self-esteem.

Treatment decisions can be complicated by the rarity of the paediatric kidney disease, meaning there are few specialist centres to help manage the complexity of these diseases in the paediatric patient population. In the UK, there are approximately 1,000 children living with CKD.

Management

Managing kidney disease in children is particularly challenging. Developing best practices for the management of paediatric kidney diseases is complicated due to a limited number of studies, which are often single centre or reflect a selected cohort of children with access to specialist care. Some children with ESKD may need dialysis if they present late or are unsuitable for pre-emptive transplantation for medical or psychosocial reasons, but for virtually all children, the ultimate aim is kidney transplantation. Children with kidney disease currently have an average waiting time (including dialysis and suspension) of 2 years for a kidney transplant, based on children who were first put onto the national kidney transplant waiting list between April 2015 and March 2019.

In general, the care of children with kidney disease requires a multidisciplinary approach to a much greater extent than adult care.
Table 5. Support needed for children with CKD

<table>
<thead>
<tr>
<th>Multidisciplinary team</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatric nephrologist</td>
<td>• Manage children and young people with chronic and acute kidney disease, including through provision of dialysis and kidney transplantation.</td>
</tr>
<tr>
<td>Social workers</td>
<td>• Essential workers that provide support in dealing with the emotional, practical and financial impacts of kidney disease for the patient and their family. Social workers understand the difficulties of managing kidney disease in a child, and they provide resources for patients, carers and family members to help balance health-related commitments.</td>
</tr>
<tr>
<td>Specialist nurses</td>
<td>• Professional nurses who work with patients with kidney disease that requires treatment or surgery. They assist in dialysis treatments and often work in a surgical setting with kidney transplant patients.</td>
</tr>
<tr>
<td>Dietitians</td>
<td>• Provide advice on feeding, as well as support for nutritional and dietary alterations required for certain kidney diseases.</td>
</tr>
<tr>
<td>Play specialists</td>
<td>• Professional caregivers who advocate for children and help them manage painful procedures or a forthcoming operation.</td>
</tr>
<tr>
<td>Psychologists</td>
<td>• Licensed professionals who specialise in helping children cope and adjust to the emotional stresses of living with a kidney disease.</td>
</tr>
<tr>
<td>Youth workers</td>
<td>• Provide tools and information that will help young people learn to take on the responsibility for their own kidney disease and treatment. Help young people develop skills and support them in building their confidence and self-esteem, which can so often be a problem.</td>
</tr>
</tbody>
</table>
Risk factors

Clinical risk factors for kidney disease

CKD is associated with a range of co-morbid conditions, particularly, diabetes, hypertension, CVD, and obesity. These conditions are closely linked, with each one contributing to the development and progression of CKD. Risk of death in people with CKD rises exponentially as kidney function deteriorates, largely attributable to CVD. Some studies have suggested that diabetes and hypertension are the leading causes of CKD and are risk factors for the progression of both CKD and CVD. Targeting modifiable risk factors can therefore improve survival and quality of life by reducing CVD in those with CKD and slowing progression of CKD to ESKD.

Diabetes

Figure 2. Prevalence of diabetes in the UK (2014-2019)
Type 2 diabetes is a complex chronic condition characterised by increased blood glucose levels and is associated with vascular complications.\textsuperscript{18} Diabetes damages the blood vessels in the kidneys and impairs their function, leading to the development and progression of CKD\textsuperscript{18, 63}.

Diabetes is also a leading cause of ESKD.\textsuperscript{18} Almost one in three people who need dialysis or a transplant have diabetes, and one in five people with diabetes will need treatment for kidney disease during their lifetime.\textsuperscript{64} In the UK, the prevalence of diabetes varies across the four nations, England, Scotland, Wales, and Northern Ireland over a six-year period (Figure 2).\textsuperscript{65}

Management
Early screening and detection is important, as diabetes is a risk factor for developing CKD and requires early treatment, which can stop or slow disease progression. SGLT-2 inhibitors are commonly used to treat type 2 diabetes in patients with CKD, as they have shown positive effects on diabetic kidney disease in clinical trials.\textsuperscript{66}

Hypertension
Blood pressure is the force of the blood against the walls of blood vessels as the heart pumps blood around the body. If this pressure becomes too high, patients typically are diagnosed with high blood pressure, or hypertension. Hypertension is a major risk factor for the development and progression of CKD, and it is also a common consequence of CVD, leading towards ESKD.\textsuperscript{67, 68} Hypertension can damage the blood vessels in the kidneys, leading to reduced blood flow and impaired kidney function.\textsuperscript{67}

Management
Hypertension in patients with CKD can be managed through a combination of lifestyle interventions, including diet modification, and pharmacological interventions.\textsuperscript{69} Based on NICE guidelines, calcium-channel blockers are recommended as first-line pharmacological therapy to manage hypertension and also have a demonstrated effect on reducing proteinuria (protein levels in the urine), a key component of CKD. ACEs and ARBs are recommended for those with proteinuria.\textsuperscript{69} Management and monitoring of blood pressure is important for reducing CKD progression and cardiovascular events such as heart attack or stroke.

Cardiovascular disease
Cardiovascular disease is a general term for conditions affecting the heart or blood vessels. CVD is the most common co-morbidity associated with CKD, and it is a major contributor to morbidity and mortality in patients with CKD.\textsuperscript{19} Patients with CKD have an elevated risk for cardiovascular events; 50% of all patients with CKD stages 4-5 have CVD, and cardiovascular mortality accounts for approximately 40% to 50% of all deaths in patients with advanced CKD (stage 4) as well as ESKD (stage 5), compared with 26% in controls with normal kidney function.\textsuperscript{63} People
with CKD are at an increased risk of developing CVD, and those with established CVD are at increased risk of developing CKD. The reasons for this overlap are complex and not fully understood, but it is believed that shared risk factors such as diabetes, inflammation, oxidative stress and endothelial dysfunction all play a role in the development and progression of both CKD and CVD.

Management
Control of traditional risk factors, such as diabetes, hypertension and dyslipidaemia (also known as high cholesterol), is essential to reduce CVD. The substantial morbidity and mortality from coronary artery disease in patients with CKD or ESKD make the effective management of CVD critical. Risk factors for CVD and acute cardiovascular events can be managed in patients with CKD through lifestyle modification and drugs such as ACEs and ARBs. SGLT-2 inhibitors have also shown beneficial effects in reducing cardiovascular events such as heart failure, stroke and heart attack in patients with CKD.

Multi-morbidity
Patients with kidney disease often have more than one co-morbidity, including diabetes, arterial hypertension, hyperlipidaemia, anaemia and malnutrition. The presence of these co-morbidities can complicate the management of CKD and make it more difficult to slow or stop the progression of the disease. Patients with co-morbidities such as CVD, hypertension and diabetes are at increased risk of AKI, particularly if they have pre-existing CKD. The management of AKI in patients with co-morbidities can be complex, and it requires a coordinated approach that takes into account the patient’s underlying conditions. Treatment may involve addressing the underlying cause of the AKI, such as dehydration or medication toxicity, as well as managing the patient’s co-morbidities to prevent further damage to the kidneys. In some cases, patients may require dialysis to support their kidney function and prevent further complications.

In addition, these co-morbidities can increase the risk of complications such as heart attack, stroke and infections, particularly in patients with advanced CKD or ESKD.

Kidney disease and mental health
While a number of other health conditions are risk factors for CKD, long-term conditions (including CKD) are associated with a greater risk of mental health problems and cognitive impairment. For example, patients who have both CKD and diabetes have a two-fold increase in the rate of cognitive disorders when compared with patients who do not have diabetes or CKD. Mental health problems are associated with a much greater cost to the health service. For example, the NHS, in England alone, spends £8-13 billion per annum on co-morbid mental health problems in patients with chronic disease. Those with long-term conditions are two to three times more likely to experience mental health problems, which is associated with high socio-economic deprivation. Beyond the problems associated with their management, co-morbid mental health problems are associated with poorer clinical outcomes, a lower quality of life, and reduced ability to manage physical symptoms.
Kidney disease has a significant negative impact on the quality of life and mental health of children and young people.\textsuperscript{78-82} This impact is seen across their emotional, social, physical and educational well-being and functioning.\textsuperscript{83-85} Additionally, as in adults, there is evidence that psychosocial issues have a negative impact on the medical outcomes of children and young people.\textsuperscript{86,87}

**Demographic and inequality risk factors**

In addition to clinical risk factors, there are environmental and social factors that contribute to an increased risk of developing CKD and poor CKD outcomes. These factors include access to care, social inequalities and biological factors; biological factors include socio-demographic, biological, genetic and cultural factors.\textsuperscript{10,11} Health inequalities make it challenging for people to receive the medical attention, access to care and support they need.\textsuperscript{10,11} In the UK, some groups are particularly at a disadvantage when it comes to kidney care.\textsuperscript{10} It is well established that people from lower socio-economic groups and people from ethnic minority groups (previously referred to as Black, Asian and minority ethnic [BAME] in a previous study) are more likely to develop CKD, progress faster towards kidney failure and die earlier with CKD.\textsuperscript{10,11} As the UK population as a whole grows older, the demographics within it are changing.\textsuperscript{88} Today, most ethnic minorities have younger populations than the majority white British population; however, by 2051, those ethnic groups, particularly, South Asian, will have the highest proportion of people aged 50 and older, shifting the demographics and needs of patients.\textsuperscript{88}

**Age and frailty**

Kidney disease can develop at any time, but older people are at greater risk due to risk factors that increase with age.\textsuperscript{58} Based on 2016 data, 12% of adults aged 65-74 were diagnosed and staged with CKD.\textsuperscript{7} In the 2016 Health Survey for England (HSE), 34% of adults aged 75 or older had CKD stages 3-5.\textsuperscript{7}

Frailty, a syndrome of physiological decline, is associated with an increased vulnerability to adverse health outcomes and annually costs the UK £5.8 billion.\textsuperscript{89} Patients with CKD are more frail than the general population because they lose biological reserves and become more vulnerable to conditions such as inflammation, physical inactivity, reduced energy intake and metabolic acidosis.\textsuperscript{89} Estimating frailty prevalence in CKD is challenging because of the different criteria used in each study.\textsuperscript{89} There are studies that demonstrate the association between frailty trajectories and cardiovascular, kidney and mortality outcomes in CKD,\textsuperscript{89} showing that frailty is associated with increased mortality and rate of dialysis in patients and suggesting that patients who are more frail have an increased rate of requiring dialysis.\textsuperscript{89}

**Ethnic inequalities**

Individuals of Black and Asian descent are more likely to progress faster towards kidney failure and are less likely than white people to receive a kidney transplant.\textsuperscript{10,11} These communities are also disproportionately affected by inequalities in transplant services in the UK, as they are at greater risk of developing organ failure, are less likely to be organ donors and wait longer
Thirty-five percent of patients waiting for a kidney are from ethnic minority groups, while only 7.2% of people from these communities are on the NHS organ donor register. Investigating inequalities in kidney care and their impact on these communities is not only necessary for reducing inequalities in the UK but also likely to improve the understanding of access to care barriers for other groups with ESKD globally, as well.

eGFR is a measure of kidney function and has been used to predict outcomes with varied success. For patients of European descent, eGFR is inversely related to mortality and CVD but is not a good predictor of outcomes in South Asians with similar eGFR levels. Albumin-to-creatinine ratio (ACR) has been suggested to be more predictive of outcomes in South Asians than eGFR, as high levels of ACR was correlated with the increased rates of CVD and cardiovascular death in South Asian ethnic patients.

**Gender inequality**
AKI is more common in men than women after accounting for socio-economic status, ethnicity, alcohol intake and smoking history. This contrasts with current guidelines and clinical scoring systems which place a higher risk on females, mostly based on older, smaller observational studies.

**Economic inequality**
Socio-economic deprivation is a measure of individual and area indicators that may have a direct link to healthcare and outcomes, often correlated with poor survival outcomes. Patients with CKD who are socio-economically deprived have faster rates of disease progression, higher risk of CVD and premature mortality. Patients with CKD and an annual income of £12,500 had a two-fold increased risk of having adverse cardiovascular outcomes compared with patients with CKD who had a higher income.

Socio-economic deprivation is also associated with an increased length of time on the transplant waiting list and more limited access to living donor transplants, leading to higher rates of mortality and long-term kidney failure. Analysis of survival post-transplant also showed that deprivation was associated with increased mortality at 1 and 5 years post-transplant, and patients from deprived areas were less likely to have a functioning transplant at 5 years. Patients in the UK living with kidney disease also report that the cost of living impacts both their physical and mental health.

Just as economic circumstances can impact kidney disease, living with kidney disease can negatively impact individuals’ financial wellbeing. Increasing costs are driving patients to choose between food, electricity and their health. Managing kidney health often requires special diets that can increase food costs, which are further impacted by inflation, and therefore more likely to affect people from low-income households or who are economically inactive. Since CKD is known as a silent disease, most patients only treat symptoms when they arise and may neglect daily maintenance of risk factors such as diabetes or hypertension that may prevent progression of kidney disease.
Transport costs can also be a barrier to patients receiving treatment. Recently, the cost of travel to appointments has been a focus for the NHS, and as of May 2022, transport eligibility for people on dialysis was confirmed for in-centre dialysis in England; however, there are variations in policies around the UK that impact reimbursement of health-associated travel.86

As with other paediatric conditions, kidney disease can create severe financial hardship for children and their families. Out-of-pocket expenses such as transportation (travel and parking for appointments), food and drink, and household bills can all be increased. Additionally, a critically ill child may mean that one or both parents are unable to work, or are working less to care for the child, putting a further strain on household finances and impacting the wider UK economy.86

Health literacy
Health literacy is the degree to which individuals have the ability to find, understand and use information and services to inform health-related decisions and actions for themselves and others.100, 101 Health literacy, often associated with other inequalities, can also have an impact on health outcomes. In the UK, approximately 80% of people did not know the location or the function of the kidneys.102 More than half believe, incorrectly, that kidney transplants last a lifetime and are a cure for kidney disease.102 In the general public, these inaccurate assumptions lead to reduced uptake of prevention services and adherence to medical advice, which may lead to increased morbidity and mortality.103 A systematic review found that people with lower literacy had less appropriate patterns of health service use and were not always able to secure appropriate treatment.101, 103 When compared with people with adequate health literacy, people with limited health literacy generally enter the health system when they are sicker.103 Twenty-five percent of people with CKD have limited health literacy, and this disproportionally affects ethnic minorities and other underserved communities.104

Covid-19–associated risk factors

The Covid-19 pandemic had a significant impact on kidney disease, through:

• Creating new incidence of kidney disease
• Disrupting the care of people with existing kidney disease
• Increasing mortality for people with kidney disease
• Delaying/reducing the diagnosis of diabetic kidney disease (due to testing not taking place)

Kidney disease incidence and Covid-19

Covid-19 patients had a high risk of developing AKI, and those who did were more likely to become critically ill. Hospitalised patients with Covid-19 had a one in four chance of developing early AKI and a further 8% chance of developing late AKI.105-107 Early AKI was defined by Kidney Disease: Improving Global Outcomes (KDIGO) creatinine criteria within 7 days of admission, and late AKI was defined as AKI occurring only after day 7.107 The risk factors for developing AKI during a Covid-19 infection were similar to those for pre-pandemic AKI, such as diabetes, cardiovascular disease and multi-
morbidity. In turn, patients with AKI had an ICU admission rate of 39.4% as compared to 18.4% for those without AKI. In the ICU, AKI and renal impairment were associated with an increased need of respiratory support and mechanical ventilation for critical disease.

Retrospective studies have also associated increased risk of developing AKI during hospital admission for Covid-19 in ethnic minority groups (previously referred to as BAME), potentially further demonstrating inequities in those communities as noted above. Beyond developing AKI, patients with Asian ethnicity were found to have a higher rate of persistent AKI or relapsing AKI while hospitalised.

The risk of developing CKD was also high in patients hospitalised with Covid-19 particularly if they did not recover kidney function by discharge – 44.8% of patients who had not recovered kidney function developed CKD, as compared to 10.1% who had.

Disruption to kidney services and Covid-19
During the pandemic, the UK was forced to rapidly evolve existing care models in preparation for significant front-line service pressures, and this created a number of dilemmas, contributing to poor outcomes in patients with kidney disease.

A suspension of all non-urgent elective surgery to create hospital capacity for Covid-19–related activity meant most UK transplant centres suspended kidney transplant activity, although there were geographic variations across the UK based on the availability of ICU capacity and emergency personnel.

Mortality in Covid-19 patients during the pandemic
Renal impairment in the ICU was correlated with increased requirement of KRT, which was further associated with increased mortality. The mortality rate was 20–30% in kidney transplant recipients during the first wave of the pandemic, with a reduction in mortality during the second wave and a disproportionate impact on ethnic minority groups and socio-economically disadvantaged individuals. Although living donation came to a nearly complete stop early on during the pandemic, it has resumed since then but does not appear to have reached pre-pandemic levels.

Patients on dialysis were amongst those at highest risk of death, not just because of the propensity for serious illness but also because of missed treatments. Data from universal screening of a single dialysis unit in the UK showed that patients experienced a spike in infection following a spike in infection of health care workers, implying potential transmission from health care worker to patient.

Overall, patients with CKD experienced significant excess mortality during the Covid-19 pandemic. A retrospective analysis of data in England found that there were 34,000 observed excess deaths in the CKD population from March 2020 to March 2021.
Limitations and ongoing research

In the modelling process, significant gaps were found in the evidence base, specifically the relationship between Covid-19 and kidney disease, e.g. uncertainties regarding the incidence of Covid-19 infections in the CKD prevalent population and the impact of Covid-19 on the paediatric kidney disease population. At the time of writing, there is ongoing research investigating the impacts of Covid-19 on kidney disease, in particular work utilising the OpenSAFELY database, which covers the primary care records of about 24 million patients in England. This data was not included in this report. A limitation of current research is that it often does not take a systematic approach (e.g. there is a need to consider patient outcomes, patient experiences, workforce capacity and capability, as well as inclusion/diversity of research participation). 117
Methodology

Overview of approach

The ambitious scope of this report necessitates a multifaceted methodology, with elements of evidence synthesis and modelling (Figure 3). It has been underpinned by broad stakeholder engagement from the outset. Early engagement was undertaken via workshops with expert clinicians, academics, data experts within the field of kidney disease and patient representatives. A subset of these stakeholders was subsequently consulted on a regular basis as part of a project steering group to review and challenge preliminary and final project outputs, suggest refinements and provide subject matter expertise. Representatives from industry were also convened to provide insights into innovations which other stakeholders may not yet be aware of and challenges they face in bringing them to market. Input from additional experts was sought where particular gaps or uncertainties in the data emerged.

A targeted literature review (TLR) of economic and epidemiological research related to kidney disease in the UK was undertaken. It focused on literature published over the last 5 years, including published systematic literature reviews (SLRs) and TLRs which summarised older evidence.

Outputs from the TLR were combined with additional data and grey literature, e.g. from government websites, where required. These were the key inputs to epidemiological and health economic (cost-effectiveness) modelling.

The epidemiological modelling focused on understanding the current number of people with CKD, dialysis, transplantation and AKI and the associated costs. These were projected forward to 2033.

The health economic model focused on the CKD pathway, understanding the costs and outcomes associated with the current state of clinical care, and testing the impact and cost-effectiveness of potential interventions at a population level. Included interventions were chosen based on recommendations from stakeholders and availability of evidence.

Figure 3. Diagram of flowchart methodology

1. STAKEHOLDER ENGAGEMENT
2. TARGETED LITERATURE REVIEW
3. EPIDEMIOLOGY MODELLING
4. COST-EFFECTIVENESS MODELLING

SCOPING MEETINGS
(December 2022–January 2023)

STEERING GROUP
(February–April 2023)
The ultimate output metrics of the modelling are prevalence, incidence, costs, quality-adjusted life years (QALYs)*, deaths and productivity losses associated with kidney disease in the UK. Not all of these metrics could be calculated for all types and stages of kidney disease. The availability of outputs is summarised in the table below (Table 6).

Table 6. Outcomes captured within each health state for CKD

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
<th>Prevalence</th>
<th>Cost to the NHS</th>
<th>QALYs</th>
<th>Deaths</th>
<th>Cost to the UK economy†</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD 3-5</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>CKD 1-2</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Dialysis</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Transplant</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Paediatric kidney disease‡</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>AKI</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rare/inherited kidney disease</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Quality-adjusted life years (QALYs) is a commonly used measure in health economic evaluations to quantify the effect of medical intervention or prevention programme. QALYs are calculated by multiplying the years of life by the utility value. In a cost-effectiveness exercise, the current standard of care is taken as the baseline, and QALYs gained from the new intervention or prevention programme are counted in addition.
† Cost to UK inclusive of productivity costs and transport costs.
‡ Paediatric kidney disease outputs only related to transplantation and dialysis in paediatric kidney disease.
Detailed method: stakeholder engagement

Stakeholder engagement played a pivotal role in shaping the inputs of this report and validating the outputs. Given the complexity of kidney disease, it was essential to engage a range of stakeholders across the care pathway. The stakeholders helped to shape the areas of focus for the TLR, identifying key evidence, providing updates on ongoing unpublished research and reviewing the modelling and report itself (Figure 4).

For the modelling, where published literature did not exist, stakeholders provided rationale for assumptions based on clinical practice and experience.

Figure 4. Diagram of stakeholder engagement process

Who: Thirty stakeholders including patients, senior NHS clinicians and UK academics.

Objectives: Understand the current and future care of people with kidney diseases, identify priority topics for the targeted literature review, and advise on key elements for this report.

In total, 30 stakeholders were involved in the project, including senior NHS clinicians, academic professors, general practitioners, and senior academics in kidney disease (many of whom were also clinicians), who were consulted on data availability, modelling assumptions and ongoing research. These included:

- Secondary care nephrology
- Cardio-renal
- Kidney transplantation
- Paediatric nephrology
- Primary care
- Nephrology clinical service directors
- Epidemiologists
- Registry operators (e.g. Scottish Renal Registry, UK Renal Registry and OpenSAFELY)
- Public health specialists
- Health inequalities specialists
- Patient representatives with kidney disease were also consulted through this project
Stakeholder engagement began with a series of scoping meetings from December 2022 to January 2023. A smaller steering group of ten with clinicians, academics and patients met regularly between February 2023 and April 2023 to guide the project and validate the key findings. With clinicians and patients, the objectives of these scoping meetings were to understand the current state and future state of care for people with kidney disease in the UK: this included probes on clinical guidelines, changing epidemiology and patient demographics, opportunities for innovation, and evidence gaps which could be addressed in this report or future research. With academics and data specialists, the focus was on identifying, interpreting and understanding the limitations of data sets currently available in the public domain.

Meetings with the steering group focused on refining the modelling approach, defining the key interventions for the cost-effectiveness model and pressure testing the outputs contained within this report. In total, the steering group met three times from February to April 2023. This was supplemented by ad hoc meetings with individual steering group members.

In addition to the above, on three occasions, the project team met with Kidney Research UK industry affiliates, life science companies focused on kidney health to provide their perspectives on advancements in treatments for people with kidney disease. They also provided insights on research and operational challenges their organisations faced with regards to their pipeline therapeutics for kidney disease in the UK.
Detailed method: targeted literature review

The TLR was conducted as a comprehensive way to gather the most up-to-date, publicly available evidence to inform this report. The TLR informed the content in this report as well as provided evidence for the epidemiology and cost-effectiveness models.

The TLR search strategy aligned with standards developed by the Centre of Reviews and Dissemination at the University of York and was based on predefined reproducible search strings for epidemiology and economic literature reviews. The stakeholder engagement scoping meetings helped refine the search string. Search eligibility criteria followed the population, interventions, comparators, outcomes, timeframe and study design (PICOTS) framework as per Cochrane guidelines (Appendix A). This search strategy covered AKI, CKD, ESKD and other rare and inherited kidney diseases. It included epidemiological evidence from cohort studies, cross-sectional studies and registry studies and economic evidence that reported cost and resource use.

The search identified approximately 11,000 UK-based articles, published in the last 5 years, on the epidemiology and economic impact of kidney disease (Figure 5). Articles were screened in two rounds: first pass title and abstract review, second pass full text review.
In some cases, additional targeted searches were performed to find model parameters and other supplementary evidence outside the search parameters. Additional evidence was provided through stakeholders in the scoping meetings and steering committee meetings. These additional searches used articles outside of the original search criteria (e.g. articles from before 2017).
Detailed method: epidemiological modelling

The purpose of epidemiological modelling is to understand the historic trends in prevalence and incidence in the various conditions under the banner of kidney disease, to calculate estimates of future demand and disease burden.

The approach taken was to analyse several years of historic trends and changes in patient age demographics to project the burden of CKD stages 3-5, transplantation, dialysis and AKI from 2023 to 2033. It also examines the known impact Covid-19 has had on these patient populations from 2020 to 2022 (CKD stages 1-2 were projected using the health economic modelling approach only, due to constraints of the data, as set out below).

The epidemiological model uses historical incidence rates of dialysis and transplantation to project rates for 2033. Historical rates have been relatively flat over the last 10 years, indicating that current capacity for dialysis and transplantation is most likely maximised. Discussions with stakeholders have indicated that current needs for dialysis and transplantation are being met; however, there are ongoing stressors to the health system with staffing and resource challenges (e.g. nurses and techs take on extra hours to meet current demand for dialysis or availability of live and deceased donor organs for transplants). An alternative approach to projecting future demand of dialysis uses historical transition probabilities to estimate the potential number of people on dialysis based on disease progression rates (described in greater detail below).

Method for CKD Stages 3-5

The prevalence of CKD stages 3-5 in the UK was calculated based on the prevalence reported in the 2016 Health Survey for England (HSE), the most recent HSE report to examine the prevalence of kidney disease. Analysis was undertaken at a whole UK population level, with population numbers taken from the 2020 Office for National Statistics (ONS) projection in 2020. The benefit of the HSE is that it is designed to be representative of the whole English population and used a form of random population sampling. Similar data was not available for Wales, Scotland and Northern Ireland, necessitating the assumption that this sample from England is representative of the UK and applied to the entire UK population.

The patient burden of CKD stages 3-5 was projected forward to 2033 using three methodologies to arrive at a final base-case projection (Figure 6).

Method 1: The prevalence of CKD stages 3-5 was calculated by applying the average expected prevalence of CKD stages 3-5 in the over-45 population (~10.1%) to ONS forecasts of the over-45 population. It should be noted that the under-45 population had very low recorded prevalence of CKD in the 2016 HSE.

Method 2: The prevalence of CKD stages 3-5 for this projection is based on the average prevalence recorded in each age cohort in the 2016 HSE (Table 7).
The populations in these age cohorts were projected forward by applying them to the ONS population forecast for each age group. This approach is consistent with approaches used by other bodies to project CKD 3-5 prevalence, e.g. UK Health Security Agency (formerly Public Health England).

Method 3: This method uses the output of method 2 but adjusts the projection for the estimated excess deaths due to Covid-19 in 2020. This method provides the base case presented in this report.

Table 7. Prevalence of CKD stage 3-5 by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Prevalence of CKD 3-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-34</td>
<td>-</td>
</tr>
<tr>
<td>35-44</td>
<td>-</td>
</tr>
<tr>
<td>45-54</td>
<td>0.7%</td>
</tr>
<tr>
<td>55-64</td>
<td>2.6%</td>
</tr>
<tr>
<td>65-75</td>
<td>12.3%</td>
</tr>
<tr>
<td>75+</td>
<td>34.1%</td>
</tr>
</tbody>
</table>

For CKD stages 3-5 there was no data available for ages 16-34 and 35-44.

Figure 6. Growth in CKD (stages 3-5) prevalence in the UK

Additional explanatory variables to account for risk factors other than age were explored, in particular diabetes. However, it was found that UK studies forecasting diabetes growth used age-stratified population growth as the basis of their projections, which is already accounted for in methods 2 and 3 (base case).
Stages 1-2
To understand the costs associated with CKD stages 1-2, estimates from the cost-effectiveness model were used (see methodology for cost-effectiveness model below). As stages 1-2 are not well diagnosed or reported, insufficient data prevented forecasting using the epidemiological model methodology. In the cost-effectiveness model, prevalence of CKD stages 1-2 was estimated through the 2016 HSE and literature. The cost-effectiveness model utilised transition probabilities to move patients between states. Patients in stages 1-2 can transition to stages 3-5 over time or remain in the same health state.

Method for dialysis
The starting point for modelling of dialysis is current prevalence based on the 2020 UKKA CKD annual report. The number of patients on dialysis was projected forward using the historical compound annual growth rate (CAGR) in dialysis prevalence from 2015-2019 (pre–Covid-19) and applied to current 2020 figures. As this projection is based on historical dialysis activity which has stayed relatively flat over the last 10 years, it implicitly assumes that despite CKD stages 3-5 and ESKD population growing, the current health system is maximised with limited ability to accommodate a growth in demand.

The “unconstrained view” of dialysis is an alternative projection of the dialysis population numbers from the cost-effectiveness Markov model. Growth in the dialysis population in the unconstrained view is based on historical transition probabilities of patients in ESKD starting on dialysis. The unconstrained view represents the predicted need for dialysis taking into account the historical probability of a patient in ESKD receiving dialysis. It does not account for future constraints in the delivery of dialysis to a growing ESKD population.

Method for transplantation
The starting incidence of kidney transplantation is based on the number of single-organ kidney transplants recorded in the NHS Blood and Transplant Reports on Kidney Transplant. The incidence of transplantation has been projected forward using the historical CAGR in transplant incidence from 2015-2019 (pre–Covid-19) applied to the most recent data on transplant incidence (December 2021). This projection is the “constrained view” of transplant and assumes that despite the CKD stage 3-5 population and ESKD population growing, there is limited growth in the supply of living and deceased donor organs.

The unconstrained view of kidney transplant is an alternative projection of the incidence of transplant projected in the cost-effectiveness Markov model. Growth in transplant incidence is based on historical transition probabilities of patients in ESKD receiving a kidney transplant and demonstrates the “need” for kidney transplant in the population but does not consider the ability for the healthcare system to deliver transplants.

Method for paediatric dialysis and transplantation
Paediatric dialysis and transplant populations were derived from UKKA CKD and NHS Blood and Transplant data, respectively. These populations were projected forward using the same CAGR methodology as the adult populations. It was assumed similar costs and productivity losses (for carers) would be incurred to patients’ families, the NHS and the UK economy in the absence of data specific to this age group.
Method for acute kidney injury

Previous reports have estimated that AKI accounts for approximately 1% of the NHS budget. The approach to estimating the burden of AKI for this report is to provide a simplified update to these previous studies based on more recent data. Starting incidence rates were derived from the 2018 UKKA AKI report for England and ongoing monitoring dashboard of AKI alerts in England. Given the dashboard only reports AKI alerts and not episodes, the number of AKI episodes was estimated based on the ratio of alerts to episodes from the 2018 report.

Where data was incomplete on AKI alerts, it was assumed that missing data on AKI episodes would be proportional to recorded episodes within that integrated care board and quarter. A CAGR was calculated based on the 2016-2019 AKI alert data, which enabled a projection of AKI forward to 2033 in England. It was assumed the number of AKI episodes in the UK would be proportional to the rate of AKI in England as equivalent data was not available for Scotland, Wales and Northern Ireland. The cost to the NHS of an AKI episode was assumed to be £5,065. In most cases, AKI may have been part of an admission for a different primary diagnosis and caused excess bed days; however, for the purposes of this estimate, each AKI episode was considered as its own admission.

Method for rare/inherited kidney disease

There is limited publicly available information on the epidemiology of rare/inherited kidney diseases in the UK. The National Registry of Rare Kidney Diseases is an informed consent register that recruits from a large number of hospitals and may not be optimal to support the understanding of the epidemiology of rare kidney diseases. The methodology assumes that a majority of the cost and care burden of patients with rare/inherited kidney diseases are already captured in the CKD, transplantation and dialysis modelling.

Detailed method: health economic modelling for CKD (all stages)

A population-level Markov model was used to estimate the current and future incidence/prevalence and economic burden of CKD across all stages and show the directional impact of current interventions used based on costs and outcomes. The model was developed to capture both NHS (direct cost) and UK economy (wider economic cost) perspectives. The model schematic was adapted from Wong et al. (2018) to make it possible to explore disease progression between undiagnosed and diagnosed people with CKD, and this was the only study identified with a suitable model structure (Figure 7). The schematic was modified to include additional health states for transplantation (acute event), post-transplant, cardiovascular disease (acute event) and post-CVD. Based on the availability and quality of data, stages 1 and 2 within the model were disaggregated, and stages 3a and 3b were combined. Each cycle length was defined as quarterly (every 3 months) and the time horizon for the model was set to 10 years.
The starting point for the model includes adults (18+) in the UK population, with an average starting age of 49 and a CKD prevalent population based on the same datasets utilised in the epidemiological modelling. People enter the model at undiagnosed CKD stage 1 based on the estimated incidence rate and can transition to the next stage using transition probabilities. To determine the probabilities in the diagnosed pathway, values sourced from the literature were used. Based on key opinion leaders (clinicians, data experts, etc) feedback and external validation, the model assumes that approximately half of the patients in the diagnosed pathway were appropriately managed by ACEs and ARBs, and their effects were already accounted for within the probability values. Transition probabilities were adjusted for the undiagnosed pathway based on the relative risk reduction ACEs and ARBs have on CKD progression in patients with proteinuria.

In the model, patients can only transition forward or remain in the same state in the next cycle. Patients who are in undiagnosed CKD 4 transition to diagnosed CKD 4 or diagnosed CKD 5. Transplantation (acute) and CVD (acute) are tunnel states – all patients who enter this state transition out in the next cycle. Underlying population mortality was sourced from life tables. CKD-specific mortality rates were calculated using hazard ratios sourced from literature and applied to the UK life tables.

Unit costs were sourced from NICE, NHS, UK Personal Social Services Research Unit (PSSRU) and publicly available literature. Costs were adjusted to 2022 sterling using the UK consumer price index for medical/health inflation factor. Annual or monthly costs were adjusted to be a quarterly cost for inclusion into the model. A micro-costing approach was not considered as this would not be generalisable to the whole UK population. Instead, the model leveraged peer-reviewed literature to source costs.
Outputs reported are QALYs, direct costs to the NHS, indirect costs (UK economy) and total costs. Utility values are sourced from literature.\textsuperscript{127, 128}

A base case provides a snapshot of the current burden of CKD for the adult population in the UK. The model projects the outcomes and costs of the future burden of CKD to 2033 with an unconstrained view.

An intervention case estimates the impact of potential interventions on the base case. Through stakeholder engagement and examination of available evidence, four interventions were identified with the potential for patient and system benefits and selected for modelling.

Interventions were modelled by adjusting values such as transition probabilities and costs used in the base case to quantify the impact of each intervention individually and combined. The interventions chosen are representative examples affecting unique sections of the disease pathway (Figure 8). In order to prevent any confounding effects of combining interventions, the model assumes that no two interventions will affect the same transition probability or costs within the pathway. The interventions modelled are:

1. Earlier/improved diagnosis (focused on addressing health inequalities)
2. Improved CKD management (through better adherence to guidelines on ACEs and ARBs)
3. Use of SGLT-2 inhibitors (to reduce CVD events and progression to ESKD)
4. Increased rate of transplantation (through pre-emptive transplantation)

**Figure 8. Health model to capture interventions affecting the disease pathway**

1. Earlier/improved diagnosis
2. Improved CKD management
3. SGLT-2 inhibitors
4. Increased rate of transplantation
Two additional interventions – CKD prevention and conservative care – were also considered based on stakeholders’ recommendations and insights but ultimately were not modelled due to a lack of evidence upon which to base assumptions.

**Intervention 1: earlier/improved diagnosis**

Based on feedback from stakeholders, earlier and improved diagnosis has been cited as an important strategy for reducing the economic burden of CKD. Unlike for other chronic conditions with established screening strategies, there has been limited consensus by governments and health systems to prioritise early screening and interventions for CKD. The burden of CKD falls disproportionately on people with lower socio-economic status, as they have a higher prevalence for CKD, greater difficulty accessing treatment and poorer outcomes. Prioritising earlier and improved CKD diagnosis is a health equity imperative.

Based on clinical stakeholder engagement, the largest gap in early diagnosis is among Black, Asian and other minority populations. In the economic model, the targeted population for the intervention was Black and Asian adults aged 65 years and older. The intervention would primarily involve an outreach initiative (e.g. screening programmes) within the community. An example of a current outreach initiative is the Scottish peer educator programme, which works with different faiths from the South Asian community based in either Edinburgh or Glasgow to discuss and answer questions on kidney health, disease and organ donation (living or deceased) and educate audiences on new policies related to kidney disease and treatment.

Approximately 15% of adults with CKD are from Black and Asian communities, and 54% of people within those communities are uncoded. To model the intervention, it was assumed that 25% of the uncoded Black and Asian population were undiagnosed or not receiving the correct treatment. Under the intervention, they received an earlier diagnosis, which increased the number of people in the undiagnosed CKD 1, 2 and 3 stages moving into the diagnosed pathway, where they can be managed through treatment options recommended by NICE. Costs for the intervention include outreach efforts (£2 million per year fixed cost), cost of the test and a general practitioner appointment.

**Intervention 2: improved CKD management**

Optimal CKD management can reduce the progression of CKD to ESKD. Controlling high blood pressure (hypertension) in people with proteinuria* through the use of renin-angiotensin system (RAS) antagonists (e.g. ACEs or ARBs) have shown benefits in reducing cardiovascular events, CKD progression and mortality. ACEs and ARBs are recommended as a first-line (standard of care) therapy option for people with CKD who have hypertension, diabetes or proteinuria (ACR >30 or protein-to-creatinine ratio [PCR] >50), which equates to approximately 83.3% of the CKD population. Discussions with clinical stakeholders and additional external expert validation have revealed that only 53.3% of the eligible CKD population are receiving the standard care with ACEs or ARBs.

* Proteinuria is defined as protein in the urine with an ACR level of greater than 30 mg/g.
The model assumes that the intervention will proactively identify the appropriate patients who may be unmanaged or untreated. People who received the intervention would experience the benefit of reducing CKD progression to ESKD.26 Costs of the intervention included the annual cost of the medications and additional testing and monitoring.24

Intervention 3: use of SGLT-2 inhibitors to reduce CVD events and progression to ESKD

SGLT-2 inhibitors have demonstrated significant benefits and an even greater benefit in people with proteinuria24 in delaying progression of kidney disease and reducing cardiovascular events in people with CKD with or without diabetes. While SGLT-2 inhibitors have been approved for use in treating type 2 diabetes since 2013, dapagliflozin was approved in 2022 for use in CKD patients with or without diabetes.24 These new medications help the kidneys to lower blood glucose levels by removing glucose in the urine.24 The promising outcomes from studies involving SGLT-2 inhibitor use in CKD have shown the importance of incorporating this intervention in cost-effectiveness modelling.

The eligible population to receive this intervention is approximately 18.8%.24 The modelling assumption is that 100% of the eligible population will receive this intervention. The benefit of this intervention is applied in the model by slowing the progression to ESKD and reducing cardiovascular events. Dapagliflozin is indicated for use in CKD patients in eGFR stage 3. Costs for the intervention include annual cost of dapagliflozin and additional testing and monitoring.24

Intervention 4: increased rates of transplantation

For patients with advanced kidney disease, transplants have been shown to be the best form of kidney replacement therapy, as they are associated with lower costs and better outcomes in the long term.34 Current waiting time for a deceased donor kidney is 2.5-3 years in the UK. Waiting times for a kidney transplant are long due to a gap in the supply and demand for kidneys.132 Discussions with clinical stakeholders have recommended increased rates of transplantation as a viable intervention to improve clinical outcomes. To demonstrate the benefits of increasing transplantation rates, one illustrative example identified for the health economic modelling was pre-emptive transplants.

Pre-emptive transplants before dialysis have several benefits, such as lower risk of rejection of the donor kidney, improved survival rates, improved quality of life, lower treatment costs and avoidance of dialysis.133 The benefits of pre-emptive transplants are particularly significant in children and adolescents with ESKD.133

Currently, only 18% of transplants are pre-emptive.35 To model the benefits of this intervention, a 100% increase in pre-emptive transplants is assumed, and this benefit is applied to patients in CKD stage 5 who may be transitioning to KRT. The cost of this intervention is a fixed cost for outreach within the community to promote the benefits of pre-emptive transplants.
Epidemiology of kidney disease

Prevalence of the various types and stages of kidney disease has grown considerably in recent years, and will continue to grow, although growth rates are likely to vary considerably. This is due to the varying risk factors driving growth (e.g. changing demographics for CKD vs number of acute hospital admissions for AKI). For dialysis and transplantation prevalence, where actual historic activity data represent a constrained view showing a system that is most likely at maximum capacity, scenarios of constrained vs unconstrained demand (e.g. including potential unmet demand) are provided and vary significantly.

CKD

Factoring in the ageing population and excess deaths in the prevalent population during the Covid-19 pandemic, an estimated 7.19 million people in the UK have CKD (all stages) in 2023 – 12.8% of the population aged 16 years or older (Figure 9). By 2033 this will increase to 7.61 million people. While the overall prevalence as a proportion of the 16+ population is expected to remain constant, among the people with CKD, the proportion of later-stage CKD patients is expected to increase from 45% to 51%. Patients with later-stage CKD are more likely to be diagnosed; therefore, the recorded prevalence is likely to increase from the current level.

Figure 9. Epidemiology of CKD stages 1-5 (excluding transplantation and dialysis)

<table>
<thead>
<tr>
<th>Year</th>
<th>CKD 1-2 (in millions)</th>
<th>CKD 3-5 (in millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2023</td>
<td>3.9M (55%)</td>
<td>3.25M (45%)</td>
</tr>
<tr>
<td>2033</td>
<td>3.8M (49%)</td>
<td>3.9M (51%)</td>
</tr>
</tbody>
</table>
CKD stages 3-5
It is estimated that as of 2023, 3.25 million people are living with CKD stages 3-5 in the UK (Figure 10). The prevalence of CKD stages 3-5 is expected to increase to 3.85 million over the next 10 years. This increase is primarily driven by an ageing population. The ageing population also captures a majority of CKD risk factors that include diabetes and hypertension.

A study estimated 34,000 excess Covid-19 deaths based on two electronic medical record databases containing patients with CKD in England. After scaling the estimate to the predicted CKD population in UK in 2020, the Covid-19 pandemic is estimated to have led to an additional 55,000 deaths in people with CKD in the UK. No adjustment has been made for the growth trajectory of the CKD stage 3-5 population due to Covid-19, as insufficient evidence is available to make such an assumption at present.

Figure 10. Growth in CKD prevalence in the UK

The changing age structure of the UK population is the key driver of historic CKD growth and the projections presented here. Accounting only population growth in the over-45 population, by 2033, the estimated population of CKD stages 3-5 would be 3.41 million people (see Method 1 – black line), but anticipated demographic changes revise this to 3.91 million people by 2033 (see Method 2 – purple line).

The final projection of 3.85 million incorporating Covid-19 excess deaths is the most likely case based on the evidence available, if risk factors such as diabetes continue to grow at a faster rate than demographic risk factors.
CKD stages 1-2
Counts for CKD stage 1-2 populations were estimated using the cost-effectiveness model. Using prevalence estimates from the 2016 HSE as a starting point, the model predicted that there were approximately 3.9 million people in CKD stages 1-2 in 2023. At the end of the 10-year time horizon, the count of patients in CKD stages 1-2 in 2033 declines by 4.6% to 3.8 million. The decline in CKD stages 1-2 would be driven by the population ageing and transitioning into CKD stages 3-5.

Dialysis (adult and paediatric)
In 2020, there were 29,354 adults and 226 children and young people receiving dialysis for ESKD in the UK (Figure 11). If the historic trend in dialysis numbers, constrained by a maximised health system, continues, then those needing dialysis will rise to 33,845 adults and 330 children by 2033.

Figure 11. Current and future projections of dialysis in adults with ESKD in the UK

The alternative approach using historical transition probabilities predicted that the increasing prevalence of CKD stages 3-5 would exponentially increase the number of adults needing dialysis for ESKD to 142,920 in 2033 (Figure 12). When comparing the estimates from the two approaches, there is a significant gap indicating that the current system does not have capacity to handle the potential increase in demand. To address this gap, investments should be made for advanced action to reduce progression to ESKD, and corrective measures should be taken to address future potential staffing challenges.
While the Covid-19 pandemic disproportionately increased the risk of morbidities and mortality among patients on dialysis, current data suggests that it did not substantially change the total number of people receiving dialysis for ESKD in the UK.

As of 2020, in-centre dialysis was the most common form of dialysis delivered in the UK (24,155 adults), followed by peritoneal dialysis (3,822 adults) and home haemodialysis (1,377 adults) (Figure 13).

Figure 13. Adults with ESKD on dialysis (UK population, 2020)
Transplantation (adult and paediatric)

In 2021, there were 2,863 adults and 148 children who received a kidney transplant in the UK (Figure 14). By 2033, based on current projections and due to limited availability of kidneys, the number of kidney transplants will rise in adults and remain about even in children, with 3,615 adults and 135 children expected to receive a kidney transplant. In 2020, there was a significant drop in the number of kidney transplants performed, likely due to the Covid-19 pandemic; however, rates of kidney transplants resumed closer towards historical levels in 2021.

Figure 14. Constrained vs unconstrained projection of adults receiving kidney transplants in the UK (2033)

If the supply of available kidneys and capacity constraints in NHS services were not limiting factors, the cost-effectiveness model estimates that 11,665 kidney transplants would be needed by 2033.
Impact of Covid-19: Prior to the Covid-19 pandemic, the increased rate of transplantation could at least partially be attributed to the opt-out consent system. While the access and rate of transplantation was increasing prior to the pandemic, there was still a long waiting period for transplant, averaging around 1.5 years. Before 2020, the waiting list size for kidney-only transplant (excluding multi-organ transplant patients) was on a decline. As the pandemic began, resources were diverted away from non-emergency medical care and surgeries were delayed when there was a perceived risk for the patient from Covid-19, which had a dramatic impact on surgeries, such as kidney transplants. Early models suggested a loss of approximately 1,600 opportunities for adult and paediatric kidney transplants over 6 months due to the limited transplantation schedule, driving an increase in the waiting list size. The delay in transplantation further compounds the problem of a limited number of organs, as all deceased organs that could have been utilised are lost. Beyond the waiting list impact, since many patients are on dialysis while they wait for transplants, the proportion of adults starting dialysis as their first method of KRT increased from 91.7% to 94.1%.
Acute kidney injury

Most cases of AKI involve hospitalisation. The 2018 UKKA report for England found that 18% of people with an AKI episode died within 30 days of their first AKI alert.\(^{[21]}\)

In 2022, an estimated 615,000 episodes of AKI occurred in the UK (Figure 15). If trends in AKI continue, it is projected that by 2033 the number of AKI episodes will rise by 4% to 637,000.

Figure 15. Current and future projections of AKI episodes in the UK
Paediatric kidney disease

As of 2020, there were 226 children and young people with CKD on dialysis and a further 148 children who received a kidney transplant. In the 13 British Association for Paediatric Nephrology (BAPN) centres across the UK, there were also 619 children and young people living with kidney transplants and 199 CKD children and young people with advanced kidney disease (stage 4 and 5) living without KRT. This is only the population known to paediatric specialist services. Epidemiological evidence from other countries if applied to the UK population suggest this could be an underestimate of the true extent of CKD in children and young people; however, more detailed epidemiological studies in this population are needed.

Rare kidney disease

In the UK, there are 20 rare kidney conditions that are well characterised and diagnosed. Though individually rare, their collective prevalence is relatively high (Table 8). The three most common rare diseases are ADPKD, Alport syndrome and TSC, which have a combined prevalent population of approximately 58,000. By contrast, among the least common rare kidney diseases are Bartter syndrome and PH.

Table 8. Estimated prevalence of rare kidney disease in the UK

<table>
<thead>
<tr>
<th>#</th>
<th>Rare kidney disease</th>
<th>Estimated UK Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ADPKD</td>
<td>1 in 2,000=33,700</td>
</tr>
<tr>
<td>2</td>
<td>Alport syndrome</td>
<td>1 in 5,000=13,466</td>
</tr>
<tr>
<td>3</td>
<td>TSC</td>
<td>1 in 6,100-16,750=4,000-11,000</td>
</tr>
<tr>
<td>...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Bartters Syndrome</td>
<td>1 in 1,000,000=67</td>
</tr>
<tr>
<td>20</td>
<td>PH</td>
<td>1 in 1,000,000=67</td>
</tr>
</tbody>
</table>

There is insufficient evidence on the trends in the prevalent population for these conditions, and as such a projection of future prevalence has not been possible for this report.
The current and future economic burden of kidney disease

Overview

In 2023, the total cost of kidney disease to the UK economy is estimated at £7 billion (Figure 16). This includes £6.4 billion in direct costs to the NHS; approximately 3.2% of the £197 billion total NHS spending across the four nations. It also includes £372 million productivity loss for people living with ESKD and the people who care for them, and £225 million in dialysis transport costs. It does not include non-monetary costs such as the utility of lost leisure time for patients and carers who do not work, and as such can be viewed as an underestimate in welfarist* terms.

Assuming that the current capacity for the health system to provide expensive end-stage kidney care such as dialysis and transplantation remains at maximum capacity, the cost of kidney disease will rise to £7.8 billion by 2033 (11% increase from 2023), with the biggest increase in cost due to the increasing prevalence and associated costs of CKD stages 3-5.

However, when modelling unconstrained need using the health economic model, the 2033 cost could be over £13.9 billion, with the biggest driver being the growth in demand for dialysis.

It should be noted that the constrained view is likely to be an underestimate, as a significant unmet need for dialysis and transplantation would likely result in further complications for patients, with increased costs and mortality either in the CKD pathway or other parts of the system. Modelling this, however, has not been possible with the currently available data and evidence.

* Welfare economics seeks to maximise the social welfare or utility across all individuals in society and may include factors not counted in current NHS Health Technology Assessment evaluation such as leisure or unpaid volunteering time.
The economic burden of rare/inherited diseases is excluded from these estimates due to the epidemiology of these patient populations being poorly defined. It is anticipated that a majority of these patients’ costs are already captured in transplantation and dialysis activity costs, which tend to be the most expensive costs of managing these patients.

Comparison to other research on the cost of CKD

Previous estimates of the economic burden of kidney disease in the UK had a significantly narrower scope to this report. The most similar in scope was a 2012 report focusing on all-stage CKD based on 2010 data. The total burden of CKD presented in that report was significantly smaller to the estimate presented in this report for the equivalent conditions and disease stages. Figure 17 reconciles the key drivers of that difference – both in terms of true changes to the cost base and methodological differences.
Figure 17. Bridge reconciling differences in key drivers of total costs in this 2023 report and the 2012 NHS report

<table>
<thead>
<tr>
<th>Category</th>
<th>2023 report (total)</th>
<th>2012 report (total)</th>
<th>Differences</th>
<th>Additional factors</th>
</tr>
</thead>
<tbody>
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<td>Societal costs</td>
<td>£7,016,645,670</td>
<td>£1,450,217,265</td>
<td>£5,566,428,405</td>
<td></td>
</tr>
<tr>
<td>AKI</td>
<td></td>
<td></td>
<td>£3,127,330,925</td>
<td></td>
</tr>
<tr>
<td>CKD 1-2</td>
<td></td>
<td></td>
<td>£167,858,960</td>
<td></td>
</tr>
<tr>
<td>Pediatrics</td>
<td></td>
<td></td>
<td>£11,815,706</td>
<td></td>
</tr>
<tr>
<td>Inflation</td>
<td></td>
<td></td>
<td>£809,249,402</td>
<td></td>
</tr>
<tr>
<td>Incidence/prevalence</td>
<td></td>
<td></td>
<td>£462,501,460</td>
<td></td>
</tr>
<tr>
<td>(dialysis and transplant)</td>
<td></td>
<td></td>
<td>£389,900,379</td>
<td></td>
</tr>
<tr>
<td>CKD 3-5</td>
<td></td>
<td></td>
<td>£173,973,197</td>
<td></td>
</tr>
<tr>
<td>Anti-hypertensive non-excess</td>
<td></td>
<td></td>
<td>£49,081,001</td>
<td></td>
</tr>
<tr>
<td>CVD</td>
<td></td>
<td></td>
<td>£125,548,194</td>
<td></td>
</tr>
<tr>
<td>Other variation</td>
<td></td>
<td></td>
<td>£462,501,460</td>
<td></td>
</tr>
<tr>
<td>Differences in methodology</td>
<td></td>
<td></td>
<td>£3,127,330,925</td>
<td></td>
</tr>
<tr>
<td>Additional factors</td>
<td></td>
<td></td>
<td>£167,858,960</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>£462,501,460</td>
<td></td>
</tr>
</tbody>
</table>
The cost of CKD

In 2023, CKD stages 1-5 (excluding ESKD treatments like dialysis and transplantation) will cost the NHS £1.95 billion, with 91% (£1.79 billion) of these costs attributable to CKD stages 3-5 and 9% (£167 million) attributable to CKD stages 1-2 based on a cost-per-diagnosed case basis reported in Kent et al. (2015). This alone represents approximately 1% of the total NHS budget.

By 2033, the cost of CKD stages 1-5 is expected to increase by 19% to £2.32 billion annually. The increase in cost is primarily driven by the increasing prevalence of both CKD stages 1-2 and CKD stages 3-5 described in the Epidemiology of CKD section and have not accounted for inflation. These costs are also not inclusive of the KRT costs, which have been modelled separately, and do not include the cost of innovative treatments that may become more common in these populations by 2033.

The cost of dialysis

In 2023, the cost of dialysis for people with ESKD is £1.05 billion, or 0.53% of the NHS budget. A majority of these costs are due to the adult patient population rather than the paediatric population. In addition to the direct cost of dialysis, transport for patients on in-centre dialysis costs approximately £225 million per year. The cost of transport is sometimes incurred by the NHS (e.g. a 2022 study of dialysis in Wales reported that 60% of patients relied on NHS-provided transport), but for the purposes of this report, the cost of transport is included as a separate indirect societal cost.

By 2033, based on the constrained model, the cost of dialysis is expected to increase by 11.5% to £1.16 billion annually, and the cost of transport for dialysis is expected to increase to £251 million. The increase in cost for dialysis in the constrained model is due to a modest increase in the ability of the NHS to deliver dialysis to patients with ESKD and based on the historical CAGR of dialysis from 2015 to 2019 as noted above.

In the unconstrained model, the cost of dialysis is expected to increase by 370% to £4.91 billion annually and the cost of transport for dialysis is expected to increase to £1.05 billion annually. The substantial increase in cost is due to the rapid rise in the population with ESKD who require dialysis in the model. These unconstrained costs represent the upper bound of the cost of dialysis to the NHS based on the projected future demand.

The cost of kidney transplantation

In 2023, kidney transplants will cost the UK £293 million. Most of these costs are attributable to the transplant procedure itself (including hospitalisation, medicines, etc), while a small proportion of the costs are attributable to care following transplantation. These costs are also inclusive of the cost of adverse events due to transplantation and organ rejection. The cost of newer immunosuppression medicines involved in kidney transplants has not been considered in this report.
By 2033, based on the constrained model, the cost of kidney transplants is expected to increase by 43% to £418 million annually. The increase in cost for transplantation in the constrained model is due to the increase in the historical CAGR of kidney transplantation from 2015 to 2019, as noted above, and is contingent on the availability of organs for transplantation. If organs are not available, it is expected that patients who would have received kidney transplants would need to undergo dialysis, which is more expensive per annum and would increase NHS costs further.

In the unconstrained model, the cost of kidney transplants is expected to increase by 105% to £600 million annually. The increase in cost is driven by the increase in people with ESKD and the historical probability of a patient with ESKD receiving a transplant.

The cost of dialysis and transplantation to the UK economy

In 2023, it is estimated that dialysis and transplantation will cost the UK economy a further £372 million due to lost patient and carer productivity. By 2033, it is expected this will increase to £417 million to £2.0 billion in the constrained and unconstrained models, respectively. These productivity losses already account for many patients and carers being unemployed due to retirement. As mentioned in the Methods section, there has been limited research on productivity loss due to dialysis and kidney transplantation in the UK context, so research from other countries such as the Netherlands has been relied upon to produce these estimates.

Additionally, it is expected that people with CKD stages 4-5 not on KRT would also experience some productivity loss; however, these costs have not been included in the results above. A 2020 study reported that productivity loss in people with CKD stages 4-5 ranged from £489 to £19,951 per year.127

The cost of AKI

In 2023, AKI will cost the NHS £3.13 billion per year, or approximately 1.6% of the total NHS budget. This is inclusive of costs due to AKI hospital episodes and post-AKI discharge care. By 2033, the cost of AKI is expected to increase to £3.24 billion per year. This increase in costs and AKI cases is based on historical CAGR of AKI pre-Covid-19 (from 2016 to 2019).

The cost of paediatric kidney diseases

In 2023, dialysis and transplantation for paediatric kidney diseases will cost the NHS £3.3 million and £8.5 million, respectively. The cost to the UK economy due to lost carer productivity is £2.7 million, with transport costing a further £1.8 million.

Based on historical CAGR in the paediatric population with ESKD, in 2033, the direct NHS costs of dialysis and transplantation are expected to increase in the dialysis population to £11.4 million and slightly decrease in the transplant population to £3.1 million. Productivity loss will increase to £3.4 million, while transport costs will increase to £2.4 million. The costs presented for paediatrics have already been included in the costs enumerated in the cost of dialysis and transplantation sections, so they have not been called out separately to avoid double counting costs.
Since the burden of kidney disease for paediatric patients who are not receiving dialysis or transplantation is poorly defined, the associated costs of their treatment are not included in these estimates. It is expected that these patients would contribute additional care costs to the NHS.

The cost of rare kidney diseases

The prognosis of many rare kidney diseases is kidney failure, which ultimately requires KRT. It is anticipated that for many people living with rare kidney diseases, the economic burden of kidney disease is primarily driven by the need for dialysis or transplants. The economic burden of dialysis and transplantation has already been accounted for in previous sections on the cost of dialysis and the cost of transplantation. To avoid double-counting costs, costs for rare kidney diseases have not been enumerated in this section of the report. In addition to KRT costs, there may be additional resource utilisation for specialised medicines for rare kidney diseases and additional resource utilisation for those patients in secondary care services without ESKD. At the time of this report, there is limited economic literature around the cost of rare kidney diseases in the UK, and this should be an area of focus for future research.
Interventions to manage the burden of CKD

There is a growing body of evidence that the cost of managing CKD can be reduced through early detection, pharmacological intervention and outreach.\textsuperscript{136}

A key objective for this report was to assess whether a basket of potential population-level interventions for managing CKD including ESKD would be cost-saving or cost-effective. Cost-saving means an intervention reduces costs of care in addition to benefiting patients clinically. Cost-effective means that the intervention creates clinical benefits for an additional cost, but that cost is within a threshold that represents good value (willingness-to-pay threshold). The most common metric used to evaluate cost-effectiveness is the incremental cost-effectiveness ratio (ICER), a summary measure representing the economic value of the intervention compared to the alternative (base case). The ICER is the ratio of the difference of costs (direct costs) between the two scenarios to the difference of effectiveness (QALYs). An ICER helps to determine if the intervention is cost-effective or even cost-saving. In the UK, NICE determines an intervention as cost-effective if the ICER is below a threshold range of £20,000-£30,000. A cost-saving intervention has an ICER of less than 0 when compared to the base case, which means the intervention has negative net costs and greater benefits.

Through the stakeholder interviews, several interventions were cited as having the potential to improve clinical outcomes associated with CKD. The following interventions were applied to the model:

- **Early/improved diagnosis**: This intervention targets ethnic minority groups and other underserved populations through outreach programmes to improve screening opportunities and increase early diagnosis
- **Improved CKD management**: This intervention targets eligible patients with chronic kidney disease who are either untreated or not receiving standard care according to clinical guidelines (e.g. adequate blood pressure management)
- **Use of SGLT-2 inhibitors**: This intervention aims to increase uptake of new medications such as SGLT-2 inhibitors (e.g. dapagliflozin) to reduce CVD events and slow progression to ESKD
- **Increased rates of transplantation**: This intervention models the impact of increased outreach and awareness to increase pre-emptive live donor transplants. It is illustrative of the benefits of improving transplantation rates more generally.

To estimate the true impact of the intervention, the interventions were modelled using the health economics model (cost-effectiveness model) with the unconstrained perspective, since several of these interventions affect ESKD and KRT.
The base case of the model estimated the combined direct costs to the NHS at £70.7 billion and indirect costs at £20.3 billion (total burden = £91.0 billion) from 2023 to 2033 within the unconstrained perspective. The model showed that the combined effect of all four interventions generated a cost-effective ICER of 7,688 and reduced the total burden of CKD by £64.6 million when compared to the base case. Implementing all four interventions would increase direct costs to the NHS by £381.1 million; however, the biggest impact was estimated to be the reduction in indirect costs by £445.7 million. These cost-savings are primarily driven by the reduction in transportation costs and lost productivity, as these interventions would reduce the number of patients receiving dialysis or having a CVD event.

Combined impact

The combined effect of implementing all four interventions is greater than looking at each intervention individually. The combined interventions had an ICER of £7,688, which means that as modelled, the combined basket of interventions was cost-effective (£7,688<£20,000).

As described in greater detail below, when applied to the unconstrained demand forecast, over the 10 years modelled:

- Collectively, the interventions reduced total deaths by more than 10,000
- Approximately 50,000 QALYs were gained
- They came at a direct cost of approximately £381 million
- These direct costs were more than offset by savings to the UK economy from increased economic activity and decreased transport costs of approximately £446 million
- Intervention 4, increased rates of transplantation, was the only intervention found to be cost-saving as well as clinically beneficial
- Over time, early diagnosis had an increasingly positive impact, and projecting findings beyond the 10-year time horizon showed that the early/improved diagnosis intervention would also become cost-saving by year 13
- For all the interventions, the biggest benefits clinically and in terms of cost offsets came from reducing the number of patients progressing to dialysis
- When applied to the constrained model, the basket of interventions is still cost-effective with an ICER of £21,890, which falls within the NICE threshold range
Combined clinical impact
The model estimated that the combined impact of the interventions reduced deaths by 10,495 over the 10-year period (Table 9). Additionally, 5,465 people avoided dialysis and over 2,500 people avoided CVD events. The increase in people with CKD stages 3-5 (3,444,060 vs 3,467,156) and transplants (11,663 vs 11,725) compared to the base case would primarily be driven by interventions 1 and 4, respectively.

Table 9. Clinical impact of combined interventions

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Prevalence (year 10)</th>
<th>Incidence (year 10)</th>
<th>Total (years 1-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CKD 1-2</td>
<td>CKD 3-5</td>
<td>Dialysis</td>
</tr>
<tr>
<td>Base case</td>
<td>3,742,425</td>
<td>3,444,060</td>
<td>142,918</td>
</tr>
<tr>
<td>Combined interventions</td>
<td>3,743,058</td>
<td>3,467,156</td>
<td>137,453</td>
</tr>
<tr>
<td>Difference</td>
<td>633</td>
<td>23,096</td>
<td>-5,535</td>
</tr>
<tr>
<td>% change</td>
<td>0.02%</td>
<td>0.7%</td>
<td>-3.8%</td>
</tr>
</tbody>
</table>

Combined economic impact
The model estimated that in the base case the cumulative burden of CKD was £91.0 billion over the 10-year period (Table 10). Implementing all four interventions would decrease the burden of CKD by £64.6 million (0.07% difference) and would increase the total QALYs in the population by 49,574. While direct costs to the NHS would increase by £381.1 million, the burden would be offset by savings of £445.7 million in dialysis transportation costs and patient and carer productivity.

Table 10. Economic impact of combined interventions

<table>
<thead>
<tr>
<th>Scenario (Year 1-10)</th>
<th>Direct costs (£)</th>
<th>Indirect costs (£)</th>
<th>Total costs (£)</th>
<th>QALYs</th>
<th>ICER (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>70,683,534,208</td>
<td>20,334,744,603</td>
<td>91,018,278,811</td>
<td>71,662,137</td>
<td></td>
</tr>
<tr>
<td>Combined interventions</td>
<td>71,064,652,248</td>
<td>19,889,062,335</td>
<td>90,953,714,583</td>
<td>71,711,711</td>
<td>7,688</td>
</tr>
<tr>
<td>Difference</td>
<td>381,118,041</td>
<td>(445,682,268)</td>
<td>(64,564,228)</td>
<td>49,574</td>
<td></td>
</tr>
<tr>
<td>% change</td>
<td>0.5%</td>
<td>-2.2%</td>
<td>-0.1%</td>
<td>0.1%</td>
<td></td>
</tr>
</tbody>
</table>
The QALYs gained from combining the interventions are greater than looking at each intervention alone (Figure 18). The sum of the QALYs gained from the four interventions individually (71,711,171) is less than the total effect of combining the interventions together (71,711,711), a difference of an additional 540 QALYs.

Figure 18. QALYs gained by intervention
For the direct costs to the NHS, interventions 1, 2 and 3 are cost generating (Figure 19). However, intervention 4 is cost-saving at £51.8 million pounds, since pre-emptive transplants reduce the probability of patients transitioning to dialysis, which is a more expensive health state. The combination of the four interventions generates an additional £12.6 million in direct costs to the NHS.

Figure 19. Incremental direct costs by intervention

- **Base case**: £71,064,652,248
- **Intervention 1**: Earlier/improved diagnosis
  - £74,753,141
- **Intervention 2**: Improved CKD management
  - £228,769,763
- **Intervention 3**: Use of SGLT-2 inhibitors
  - £116,789,545
- **Intervention 4**: Increased rates of transplantation
  - (£51,766,866)
- **Interaction factor**: £12,572,459
- **Combined**: £71,064,652,248
All of the interventions individually or combined show a cost-effective or cost-saving ICER (Figure 20).

Figure 20. Summary of ICERs in the unconstrained view
Intervention 1: early/improved diagnosis

Based on feedback from stakeholders, earlier and improved diagnosis has been cited as an important strategy for reducing the economic burden of CKD. Some forms of screening for CKD have previously been found to be cost-effective, as early detection can prevent the progression of the disease and the need for more expensive interventions. In addition, interventions such as lifestyle modifications and medication can reduce the risk of complications associated with CKD, such as CVD. Unlike for other chronic conditions with established screening strategies, there has been limited consensus by governments and health systems to prioritise early screenings and interventions for CKD. The burden of CKD falls disproportionately on people with lower socio-economic status as they have a higher prevalence for CKD, more limited access to treatment and poorer outcomes. Prioritising earlier and improved CKD diagnosis becomes a health equity imperative.

The earlier/improved diagnosis intervention speeds up the transition of patients from the undiagnosed pathway to the diagnosed pathway (Figure 21). Compared to the base case, earlier/improved diagnosis led to a reduction in the number of people who received transplants (33), needed dialysis (389) or had a CVD event (28), and it avoided 581 deaths by 2033. The modest results were primarily driven by a small number of people affected by the intervention and relatively short time horizon. As a result of an earlier diagnosis, more people remained in CKD stages 1-2 (771) and CKD stages 3-5 (464) by year 10 (Table 11). The primary impact of the intervention led to approximately 17,000 patients diagnosed earlier, on average per year, compared to the base case. By 2033, the intervention had an ICER of £17,954, which is below the NHS threshold for cost-effectiveness.

Figure 21. Intervention 1 schematic: early/improved diagnosis
Table 11. Clinical impact of intervention 1

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Prevalence (year 10)</th>
<th>Incidence (year 10)</th>
<th>Total (years 1-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CKD 1-2</td>
<td>CKD 3-5</td>
<td>Dialysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Transplant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CVD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Death</td>
</tr>
<tr>
<td>Base case</td>
<td>3,742,425</td>
<td>3,444,060</td>
<td>142,918</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11,663</td>
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<td></td>
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<td></td>
<td>192,970</td>
</tr>
<tr>
<td>Intervention 1</td>
<td>3,743,196</td>
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<td></td>
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<td></td>
<td>192,942</td>
</tr>
<tr>
<td>Difference</td>
<td>771</td>
<td>464</td>
<td>(389)</td>
</tr>
<tr>
<td>% change</td>
<td>0.02%</td>
<td>0.0%</td>
<td>-0.3%</td>
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<td>-0.3%</td>
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<tr>
<td></td>
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<td></td>
<td>-0.0%</td>
</tr>
</tbody>
</table>

The model estimated the implementation of intervention 1 would increase the burden of CKD by £43.5 million, primarily driven by the cost of additional testing and general practitioner appointments. Earlier diagnosis was estimated to save patients and carers approximately £31.3 million. Overall, 4,164 QALYs would be gained over 10 years (Table 12).

Table 12. Economic impact of intervention 1

<table>
<thead>
<tr>
<th>Scenario (Year 1-10)</th>
<th>Direct costs (£)</th>
<th>Indirect costs (£)</th>
<th>Total costs (£)</th>
<th>QALYs</th>
<th>ICER (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>70,683,534,208</td>
<td>20,334,744,603</td>
<td>91,018,278,811</td>
<td>71,662,137</td>
<td></td>
</tr>
<tr>
<td>Intervention 1</td>
<td>70,758,287,348</td>
<td>20,303,477,074</td>
<td>91,061,764,422</td>
<td>71,666,302</td>
<td>17,954</td>
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<tr>
<td>Difference</td>
<td>74,753,141</td>
<td>(31,267,529)</td>
<td>43,485,612</td>
<td>4164</td>
<td></td>
</tr>
<tr>
<td>% change</td>
<td>0.1%</td>
<td>-0.2%</td>
<td>0.05%</td>
<td>0.01%</td>
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</tbody>
</table>

Screening programmes and better diagnosis technologies may take longer to generate benefits than the modelled time horizon since patients take time to progress through the various cost-generating stages of disease progression. As such, cost-savings for intervention 1 may not be realised until a couple years after the modelled time horizon. To demonstrate when the intervention becomes cost-effective and eventually cost-saving, the ICER was forecast using a logarithmic regression formula. The modelled ICERs showed the intervention was increasingly cost-effective across the 10-year time horizon (Figure 22). At year 10, the intervention was below the NICE cost-effectiveness threshold range of £20,000–£30,000, with an ICER of £17,954. The forecast estimated the intervention becoming cost-saving in year 13 (ICER of -£3,864).
Figure 22. Projected ICER for intervention 1

Intervention 2: improved CKD management

Optimal CKD management can reduce the progression of CKD. Controlling blood pressure (hypertension) through the use of RAS antagonist drugs (e.g. ACEs or ARBs) has shown benefits in reducing cardiovascular events, CKD progression and mortality.\textsuperscript{13} ACEs and ARBs are recommended as a first-line (standard of care) therapy option for people with CKD who have hypertension, diabetes or proteinuria (ACR >30 or PCR >50), which equates to approximately 83.3\% of the CKD population.\textsuperscript{23, 24} Discussions with clinical stakeholders and additional external expert validation have shown that only 53.3\% of the eligible CKD population is receiving the standard care with ACEs or ARBs.\textsuperscript{24}

Implementation of intervention 2 aimed to capture patients with unmanaged CKD or those who were untreated with standard-of-care treatments. This was implemented within the model by reducing the transition probabilities between the health states in the diagnosed pathway to demonstrate a reduction in CKD progression (Figure 23).
Improved CKD management led to more people remaining in CKD stages 3-5 (6,524) compared to the base case, since people progress through the model slower (Table 13). With slower progression, further downstream effects include fewer transplants (173) and CVD events (155). Additionally, 2,048 people avoided dialysis by year 10 and 3,491 avoided death over the 10-year time period.

Table 13. Clinical impact of intervention 2

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Prevalence (year 10)</th>
<th>Incidence (year 10)</th>
<th>Total years (1-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CKD 1-2</td>
<td>CKD 3-5</td>
<td>Dialysis</td>
</tr>
<tr>
<td>Base case</td>
<td>3,742,425</td>
<td>3,444,060</td>
<td>142,918</td>
</tr>
<tr>
<td>Intervention 2</td>
<td>3,742,373</td>
<td>3,450,583</td>
<td>140,870</td>
</tr>
<tr>
<td>Difference</td>
<td>-</td>
<td>6524</td>
<td>(2048)</td>
</tr>
<tr>
<td>% change</td>
<td>0.0%</td>
<td>0.2%</td>
<td>-1.4%</td>
</tr>
</tbody>
</table>

The model estimated that implementing intervention 2 would increase the direct cost to the NHS by £228.8 million at the end of the time horizon (Table 14). However, costs would be offset by savings due to dialysis transportation and productivity costs of £188.2 million. Overall, 20,374 QALYs would be gained over 10 years. Having improved CKD management as an intervention is cost-effective, with an ICER of £11,229.
Table 14. Economic impact of intervention 2

<table>
<thead>
<tr>
<th>Scenario (Year 1-10)</th>
<th>Direct costs (£)</th>
<th>Indirect costs (£)</th>
<th>Total costs (£)</th>
<th>QALYs</th>
<th>ICER (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>70,683,534,208</td>
<td>20,334,744,603</td>
<td>91,018,278,811</td>
<td>71,662,137</td>
<td></td>
</tr>
<tr>
<td>Intervention 2</td>
<td>70,912,303,970</td>
<td>20,146,524,173</td>
<td>91,058,828,144</td>
<td>71,682,511</td>
<td>11,229</td>
</tr>
<tr>
<td>Difference</td>
<td>228,769,763</td>
<td>(188,220,430)</td>
<td>40,549,333</td>
<td>20,374</td>
<td></td>
</tr>
<tr>
<td>% change</td>
<td>0.3%</td>
<td>-0.9%</td>
<td>0.04%</td>
<td>0.03%</td>
<td></td>
</tr>
</tbody>
</table>

Intervention 3: use of SGLT-2 inhibitors

SGLT-2 inhibitors have demonstrated significant benefits in delaying progression of kidney disease and reducing cardiovascular events in people with CKD with or without diabetes. While SGLT-2 inhibitors have been approved for use in treating type 2 diabetes since 2013, dapagliflozin was approved in 2022 for use in CKD patients with or without diabetes.\(^{24}\) Dapagliflozin is indicated for CKD stage 3. The benefit of this intervention was applied in the model by adjusting the transition probabilities to represent a reduction in the progression to ESKD and cardiovascular events (Figure 24).

Figure 24. Intervention 3 schematic: use of SGLT-2 inhibitors

The model showed that increasing the use of SGLT-2 inhibitors in people with CKD and slowing the progression of ESKD increased the number of people remaining in CKD stages 3-5 by year 10 compared to the base case (Table 15). However, in turn, fewer transplants (164) and CVD events (2,397) occurred by year 10. Additionally, 1,960 people avoided dialysis at the end of the time horizon. Increased SGLT-2 inhibitor use also led to 5,611 deaths avoided over the time horizon.
Table 15. Clinical impact of intervention 3

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Prevalence (year 10)</th>
<th>Incidence (year 10)</th>
<th>Total (years 1-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CKD 1-2</td>
<td>CKD 3-5</td>
<td>Dialysis</td>
</tr>
<tr>
<td>Base case</td>
<td>3,742,425</td>
<td>3,444,060</td>
<td>142,918</td>
</tr>
<tr>
<td>Intervention 3</td>
<td>3,742,349</td>
<td>3,461,157</td>
<td>140,958</td>
</tr>
<tr>
<td>Difference</td>
<td>-</td>
<td>17,097</td>
<td>(1,960)</td>
</tr>
<tr>
<td>% change</td>
<td>0.0%</td>
<td>0.5%</td>
<td>-1.4%</td>
</tr>
</tbody>
</table>

Increasing uptake of SGLT-2 inhibitors in people with CKD decreased the overall cost of CKD by £70.9 million over the next 10 years (Table 16). The increase in direct costs (£116.8 million) to the NHS was primarily driven by the annual drug costs of dapagliflozin. However, the added benefit of reducing transplants, CVD events and the number of patients on dialysis decreased indirect costs by £187.7 million. Overall, 23,343 QALYs were estimated to be gained over the 10-year period. Increasing the use of SGLT-2 inhibitors is a cost-effective intervention with an ICER of £5,003.

Table 16. Economic impact of intervention 3

<table>
<thead>
<tr>
<th>Scenario (Year 1-10)</th>
<th>Direct costs (£)</th>
<th>Indirect costs (£)</th>
<th>Total costs (£)</th>
<th>QALYs</th>
<th>ICER (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>70,683,534,208</td>
<td>20,334,744,603</td>
<td>91,018,278,811</td>
<td>71,662,137</td>
<td></td>
</tr>
<tr>
<td>Intervention 3</td>
<td>70,800,323,752</td>
<td>20,147,087,994</td>
<td>90,947,411,746</td>
<td>71,685,480</td>
<td>5,003</td>
</tr>
<tr>
<td>Difference</td>
<td>116,789,545</td>
<td>(187,656,609)</td>
<td>(70,867,064)</td>
<td>23,343</td>
<td></td>
</tr>
<tr>
<td>% change</td>
<td>0.2%</td>
<td>-0.9%</td>
<td>-0.08%</td>
<td>0.03%</td>
<td></td>
</tr>
</tbody>
</table>

Intervention 4: increased rates of transplantation

For patients with advanced renal disease, transplantation is the best form of renal replacement therapy as it is associated with lower costs and better outcomes in the long term. Currently, waiting time for a deceased donor kidney transplant is 2.5-3 years in the UK. Waiting times for a kidney transplant are long due to a gap in the supply and demand for kidneys. Discussions with clinical stakeholders have recommended increased rates of transplantation as a viable intervention to improve clinical outcomes. To demonstrate the benefits of increasing transplantation rates, one illustrative example identified for the health economic modelling was pre-emptive transplants.
Pre-emptive transplants (before dialysis is initiated) have several benefits, such as lower risk of rejection of the donor kidney, improved survival rates, improved quality of life, lower treatment costs and avoidance of dialysis.\textsuperscript{133} The benefits of pre-emptive transplants are particularly significant in children and adolescents with ESKD.\textsuperscript{133} To model the benefits of pre-emptive transplants, the transition probabilities were adjusted to illustrate an increased number of transplants per cycle (Figure 25). Additional fixed costs associated with outreach programmes within the community were incorporated when calculating the costs.

Figure 25. Intervention 4 schematic: increased rate of transplantation

In the UK, guidelines recommend all patients with CKD stage 5 be assessed and placed on the kidney transplant waiting list if determined to be within 6 months of their anticipated dialysis start date.\textsuperscript{139} Studies have found improved patient and graft survival in pre-emptive transplants compared to transplants occurring after dialysis.\textsuperscript{140} Other benefits include reduced overall cost of care and improved employment status for the patient.\textsuperscript{140}
Pre-emptive transplants increased the total number of transplants across the time horizon compared to the base case (11,663 vs 12,108, respectively). This will lead to an 0.8% reduction in dialysis at year 10 and avoid 614 deaths over 10 years (Table 17).

Table 17. Clinical impact of intervention 4

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Prevalence (year 10)</th>
<th>Incidence (year 10)</th>
<th>Total (years 1-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CKD 1-2</td>
<td>CKD 3-5</td>
<td>Dialysis</td>
</tr>
<tr>
<td>Base case</td>
<td>3,742,425</td>
<td>3,444,060</td>
<td>142,918</td>
</tr>
<tr>
<td>Intervention 4</td>
<td>3,742,417</td>
<td>3,442,797</td>
<td>141,783</td>
</tr>
<tr>
<td>Difference</td>
<td>-</td>
<td>(1,262)</td>
<td>(1135)</td>
</tr>
<tr>
<td>% change</td>
<td>0.0%</td>
<td>0.0%</td>
<td>-0.8%</td>
</tr>
</tbody>
</table>

While unit costs do not change by increasing transplants, outreach programmes to increase awareness of transplants will have a fixed cost applied for each year. Increasing pre-emptive transplants will save the NHS £51.8 million (Table 18). Indirect costs will also reduce by £41.6 million. The overall financial burden of CKD will reduce by £93.4 million to £90.9 billion compared to the base case (£91.0 billion). Overall, 1,154 QALYs will be gained over the 10 years. Implementing the intervention for increasing pre-emptive transplants is cost-saving, with an ICER of -£44,850.

Table 18. Economic impact of intervention 4

<table>
<thead>
<tr>
<th>Scenario (Year 1-10)</th>
<th>Direct costs (£)</th>
<th>Indirect costs (£)</th>
<th>Total costs (£)</th>
<th>QALYs</th>
<th>ICER (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>70,683,534,208</td>
<td>20,334,744,603</td>
<td>91,018,278,811</td>
<td>71,662,137</td>
<td></td>
</tr>
<tr>
<td>Intervention 4</td>
<td>70,631,767,341</td>
<td>20,293,107,052</td>
<td>90,924,874,393</td>
<td>71,663,291</td>
<td>-44,850</td>
</tr>
<tr>
<td>Difference</td>
<td>(51,766,866)</td>
<td>(41,637,551)</td>
<td>(93,404,418)</td>
<td>1,154</td>
<td></td>
</tr>
<tr>
<td>% change</td>
<td>-0.1%</td>
<td>-0.2%</td>
<td>-0.10%</td>
<td>0.00%</td>
<td></td>
</tr>
</tbody>
</table>
Scenario and sensitivity analysis

Models always have uncertainty, and it is important to understand the degree of uncertainty influenced by the inputs chosen in the model. To quantify the impact each input has on the results, it is standard to run sensitivity analyses and scenarios in the model. To test the sensitivity of the inputs within the model, a scenario analysis and one-way sensitivity analysis was conducted. The scenario analysis tests the interventions in the constrained view where the current health system’s ability to provide dialysis and transplants is maximised. The one-way sensitivity analysis tests the impact that changes within a certain input will have on output results. The one-way sensitivity analysis adjusts select parameters by ± 20%. One input is adjusted at a time to determine the degree to which the overall results change. Results for the scenario analysis and one-way sensitivity analysis are presented by showing the change in ICER for the combined basket of interventions and assessing whether the interventions collectively or individually are still cost-effective.

Scenario – constrained view

Within the constrained view, the transition probabilities in the health economic (cost-effectiveness) model for dialysis and transplants needed to be adjusted to illustrate the slower transition to stage 5 of CKD. Using the 10 year estimates for dialysis and transplantation from the epidemiological model, the goal-seek function in Excel was used to determine the approximate transition probabilities. The same inputs used in the unconstrained view to model the interventions were then applied.

People who remain in CKD stage 5 without moving to KRT due to high waiting times would continue to get sicker. Currently, the model does not capture the decline in health and the added costs that people with CKD stage 5 are experiencing due to the restriction of transitioning to dialysis or transplantation states. Within the constrained view, the transition probability from ESKD to KRT is low and the true benefit of diverting patients from the dialysis health state through the modelled interventions is not experienced.

Figure 26 shows the results of the ICER of the constrained view and the unconstrained view of the combined basket of interventions. The scenario analysis confirms that the combined interventions fall within the NICE threshold of £20,000-£30,000. Additionally, interventions 1-3 in the constrained view are also cost-effective; however, intervention 4 (increased rate of transplantation) is not cost-effective. Within the constrained view, the benefits of increasing transplantation are not realised within the health economic model since there is a minimal reduction in the number of patients moving to dialysis. Dialysis is a very costly health state. The number of patients who avoid dialysis through pre-emptive transplants does not offset the magnitude of patients who remain in CKD stage 5 or move to dialysis, both of which are health states with high costs and lower economic benefits (QALYs).
People who remain in CKD stage 5 without moving to KRT due to high waiting times would continue to get sicker. Currently, the model does not capture the decline in health and the added costs that people with CKD stage 5 are experiencing due to the restriction of transitioning to dialysis or transplantation states. Within the constrained view, the transition probability from ESKD to KRT is low and the true benefit of diverting patients from the dialysis health state through the modelled interventions is not experienced.

**Figure 26. Comparison of ICERs for the combined interventions, constrained vs unconstrained view**
One-way sensitivity analysis
The sensitivity analysis was conducted on select input parameters:
- Dialysis transition probability
- Transplant transition probability
- Incidence
- Assumption of the undiagnosed population in intervention 1 who get diagnosed
- Effectiveness of intervention 2 from diagnosed CKD stage 2 to CKD stage 3
- Quarterly cost of SGLT-2 inhibitors in intervention 3
- Assumption of the proposed state of increasing transplants in intervention 4

Figure 27 shows the results of the one-way sensitivity analysis on the ICER for the combined set of interventions. Effectiveness of intervention 2 from diagnosed CKD 2 to CKD stage 3 had the largest impact on the combined ICER, followed by the quarterly cost of SGLT-2 inhibitors in intervention 3, and the dialysis transition probability. Adjusting the assumption of the undiagnosed population in intervention 1 who get diagnosed by ± 20% had the lowest impact on the combined ICER. Overall, the analysis shows that the ICER for the combined interventions remains cost-effective when changing the inputs. The changes are marginal.

Figure 27. One-way sensitivity analysis
Conclusions and recommendations

Conclusions

The evidence presented in this report suggests that kidney disease leads to thousands of premature deaths each year, reduces quality of life and places a significant economic burden on the NHS, patients with kidney disease, the people who support them and the wider economy:

1. Chronic kidney disease affects 13% of the global population and is predicted to be the fifth leading cause of premature death* by 2040.
2. In the UK, approximately 3.25 million adults are living with chronic kidney disease stages 3-5, and a total of 7.2 million adults have chronic kidney disease (all stages), more than 10% of the entire population.
3. By 2033, the number of people living with all-stage chronic kidney disease is projected to reach 7.6 million. This is mainly driven by an ageing population as well as risk factors such as diabetes, hypertension and cardiovascular disease, as well as other important factors such as health and economic inequalities.
4. Amongst those with chronic kidney disease, the proportion with later-stage chronic kidney disease (3-5) is expected to increase from 45% (3.25 million) to 51% (3.9 million).
5. Around 615,000 episodes of acute kidney injury occur each year, mainly among those who are already unwell or hospitalised for another reason. By 2033, the number of acute kidney injury episodes is projected to rise by 4% to 637,000.
6. The total economic burden of kidney disease in the UK is £7.0 billion, with £6.4 billion attributable to direct costs to the NHS – about 3.2% of NHS budgets across the four nations. The total burden of kidney disease could rise to £13.9 billion by 2033.
7. There is a further estimated £372 million in productivity loss to the UK economy from missed work due to dialysis alone. Productivity loss in the UK could reach up to £2.0 billion by 2033, as a higher proportion of patients continue living with end-stage kidney disease.
8. In 2023, the cost of dialysis for people with end-stage kidney disease is £1.05 billion annually, or 0.53% of the NHS budget. In addition to the direct cost of dialysis, transport for patients on in-centre dialysis costs approximately £225 million per year. The cost to the NHS of dialysis to manage kidney disease (per person) is £34,000 per year – more than three times the annual value of a state pension.

* Premature death can be measured by life years lost, which takes into account frequency of death and age at which it occurs. It is calculated by multiplying the number of deaths by a global standard life expectancy at which death occurs.
9. Despite its substantial and increasing cost to the NHS, and the urgent need for new and better treatments driven by research, kidney disease received only 1.4% of relevant public healthcare research funding – just £17.7 million in financial year 2021/2022.

10. Economic modelling suggests that improved implementation of four illustrative healthcare interventions could save more than 10,000 lives by 2033. These interventions individually and collectively are shown to be cost-effective or cost-saving, where costs to the NHS are offset by quality-adjusted life years gained.

Recommendations

Strategic
Modelling indicates that significant, cost-effective patient benefits can be achieved through better implementation of existing technologies and guidelines for the prevention, management and treatment of kidney disease. Across the health and care system, a national effort should be made to improve uptake of these interventions.

Paediatric kidney disease is relatively rare and historically has not received the attention it deserves. Establishing some oversight of paediatric kidney care from kidney policymakers, in particular to establish better transition management for young adults, has been highlighted by stakeholders as important.

The population with chronic kidney disease and end-stage kidney disease is varied in terms of age, gender, ethnicity and the root causes of illness, and therefore the same diagnostic techniques, management strategies and treatments are not effective for all groups. For example, eGFR tests have been shown to be less sensitive at predicting outcomes in people who are of South Asian descent. There should be efforts made to personalise the care of patients with, or at risk of, kidney disease across the disease pathway. These should include:

- Use of the best possible diagnostic tests based on proven effectiveness for the demographics of the specific patient
- Genetic testing followed by appropriate management for those at risk of inherited kidney disease
- Patient choice in treatment, e.g. support with home dialysis for patients who feel this would better enable them to continue working and undertaking their usual activities
- Access to new and proven therapies to manage and slow disease progression in a timely manner
- Creating an environment fostering innovation and its implementation in real-world settings

Kidney disease is complex and is intertwined with other chronic/serious health conditions. The NHS and voluntary sector organisations should seek to break down silos between organisations and teams working on kidney disease and related conditions such as diabetes, hypertension, cardiovascular disease and inherited genetic conditions.
Modelling suggests that more proactive engagement with people who are at risk or have kidney disease would be clinically and cost effective, e.g.:

- Peer engagement to improve adherence to disease management strategies
- Engaging in proactive discussions around living donor transplants
- Community outreach to engage underserved groups

However, given the frequent multi-morbidity of people with kidney disease, this engagement could be even more cost effective if it addressed multiple health conditions relevant to these populations at the same time. The NHS and voluntary sector should consider how to pool resources and efforts to collaborate across multiple programmes of engagement.

Current research funding for kidney disease is just 1.4% of relevant healthcare budgets, while kidney disease represents 3.2% of NHS budgets, with a risk of significant growth in this burden. Kidney disease research funding should be increased in line with the clinical and financial burden of disease.

Clinical

In this report, kidney disease has been referred to as a silent killer, because many patients are undiagnosed or asymptomatic until they reach a later stage of disease. Stakeholder interviews have revealed opportunities to improve adherence to best practice guidelines by making them simpler and more accessible, especially for primary care, where the huge breadth of conditions general practitioners treat is a challenge. In addition, measures should be taken to monitor local adherence to guidelines and intervene where necessary.

To address barriers to implementation, focus is required on how best to provide knowledge transfer and pathway/process development. This could include closer collaboration between secondary and primary care, e.g. with regular virtual consultations between general practitioners and kidney specialists.

A broader transformation of renal services is needed to improve care through standardisation and knowledge sharing. At the time of writing, in England the Renal Services Transformation Programme (RSTP) was reviewing adult renal services and recommending areas where improvements should be made. The recommendations for service improvement in the areas of early detection, dialysis and transplantation are in alignment with the findings of this report, which also addresses the scale of the challenge across the whole of the UK and the requirements of paediatric services to meet future needs.

Severe kidney disease in children can have a similar impact in terms of mortality and lifelong disease to cancer. Because chronic kidney disease is a lifelong, gradually deteriorating condition, children with mild chronic kidney disease are likely to develop severe chronic kidney disease later in life, and therefore early intervention and ongoing management is important. At the time of writing, however, poor infrastructure exists for children with kidney disease transitioning to adult services. Until recently, services were overseen nationally by a clinical reference group that included several other paediatric sub-specialties, which may be a cause for this disconnect. There is now a separate clinical reference group in place for paediatric renal services, and one of the focus areas should be establishing a more effective transition to adult services.
Research
In the development of this report, several evidence gaps were identified, and further research should be considered to address them:

• Understanding the rate at which patients progress through the stages of chronic kidney disease is essential to predicting future demand for services. However, much of the data currently in the public domain is out of date, and up-to-date transition probabilities/relative risks of progression of chronic kidney disease for the whole population and subgroups are needed.

• Understanding the relative risk/rate of progression for undiagnosed populations is essential for assessing the cost effectiveness of early diagnosis and treatment interventions, but there is very little published literature relevant to the UK. Studies, potentially using real-world data, comparing the relative rates of progression in diagnosed vs undiagnosed populations are required.

• Sources such as the renal registries provide data on the numbers of patients receiving dialysis. However, there is limited data on unmet need or delays in meeting need, and as more patients progress to later-stage kidney disease, having real-time data which allows monitoring of any potential capacity pressures will become increasingly important.

• This report utilises evidence from other European countries to estimate the economic burden of kidney disease for the UK. UK-specific studies on the impact of kidney disease on economic productivity are necessary.

• There is evidence of a strong and complex relationship between kidney disease and mental health. UK-specific studies on this relationship, including the impact of poor mental health on adherence to treatment, are needed.

• The evidence base relating to rare forms of kidney disease is scarce. Further research in this area is required to understand the natural history, determinants (including genetic), treatment effectiveness and burden of rare forms of kidney disease.

• Paediatric kidney disease is relatively rare and often complex. Better data and evidence are required to understand the needs of these patients, e.g. studies characterising their epidemiology, demographics and broader health needs.

• This report has highlighted the multitude of risk factors for kidney disease, but evidence on the causal link between diabetes, hypertension, chronic kidney disease and other risk factors at a population level is scarce. Studies investigating the relationships between these conditions in a predictive manner would provide a powerful tool for population health planning.

• There are still large evidence gaps on how Covid-19 has affected and will continue to affect people with or at risk of kidney disease. At the time of writing this report, work in this area is ongoing using the OpenSAFELY platform, and it is important that it continues to be supported.

• There is an opportunity for the four nations of the UK to learn from each other on the management of kidney disease, but inconsistent data is a barrier to this. Introducing more consistent data, e.g. extending the Healthcare England Survey methodology to Scotland, Wales and Northern Ireland, could be an important enabler for driving better health outcomes for the entire UK population.
Acronyms

ACE, angiotensin-converting enzyme
ACR, albumin-to-creatinine ratio
ADPKD, autosomal dominant polycystic kidney disease
aHUS, atypical haemolytic uraemic syndrome
AKI, acute kidney injury
ARB, angiotensin receptor blocker
ARPKD, autosomal recessive polycystic kidney disease
BAPN, british association for paediatric nephrology
C3G, C3 glomerulopathy
CAGR, compound annual growth rate
CKD, chronic kidney disease
Covid-19, coronavirus disease-19
CRG, clinical reference group
CVD, cardiovascular disease
DDD, dense deposit disease
eGFR, estimated glomerular filtration rate
ESKD, end-stage kidney disease
GFR, glomerular filtration rate
HSE, Health Survey for England
ICER, incremental cost-effectiveness ratio
ICU, intensive care unit
IgAN, IgA neuropathy
KD, kidney disease
KRT, kidney replacement therapy
LYL, life years lost

MN, membranous nephropathy

MPGN, membranoproliferative glomerulonephritis

MRC, Medical Research Council

NHS, National Health Service

NICE, National Institute for Health and Care Excellence

NIHR, National Institute for Health and Care Research

NPHP, nephronophthisis

ONS, Office for National Statistics

PCR, protein-to-creatinine ratio

PH, primary hyperoxaluria

PICOTS, population, interventions, comparators, outcomes, timeframe, and study design

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PSSRU, personal social services research unit

QALY, quality-adjusted life year

RAS, renin-angiotensin system

RSTP, renal service transformation programme

SGLT-2, sodium-glucose transport protein 2

SLR, systematic literature review

SRNS, steroid-resistant nephrotic syndrome

SSNS, steroid-sensitive nephrotic syndrome

TLR, targeted literature review

TSC, tuberous sclerosis

UK, United Kingdom

UKKA, UK Kidney Association

UKRI, United Kingdom Research and Innovation

UTI, urinary tract infection
Definitions

1. **Constrained view**: Scenario of modelling where growth for dialysis and transplantation is estimated based on NHS historical rates.
2. **Co-morbidity**: The simultaneous presence of two or more diseases or medical conditions in a patient.
3. **Dialysis**: A type of kidney replacement therapy that replaces the blood-filtering function of the kidneys.
4. **Dyslipidaemia**: Abnormally elevated cholesterol or fats (lipids) in the blood.
5. **Endothelial dysfunction**: A type of non-obstructive coronary artery disease in which there are no heart artery blockages.
6. **Epidemiology**: The method used to find the causes of health outcomes and diseases in populations. In epidemiology, the patient is the community and individuals are viewed collectively.
7. **Evidence synthesis**: The process of bringing together information from a range of sources and disciplines to inform debates and decisions on specific issues.
8. **Grey literature**: Materials and research produced by organisations outside of the traditional commercial or academic publishing and distribution channels.
9. **Hazard ratio**: A measure of how often a particular event happens in one group compared to how often it happens in another group, over time.
10. **Health state**: A clinical event/stage used in models. All events in a disease pathway are represented as transitions from one state to another.
11. **Hyperlipidaemia**: Abnormally elevated levels of any or all lipid in the blood.
12. **Kidney replacement therapy**: A term used to encompass treatments used for renal failure. These treatments include dialysis and transplantation.
13. **Nephrotoxic agents**: All drugs with the potential to generate kidney damage and to reduce renal function.
14. **Oxalate**: Another term for salt.
15. **Oxidative stress**: Oxidative stress reflects an imbalance between the systemic manifestation of reactive oxygen species and a biological system’s ability to readily detoxify the reactive intermediates or to repair the resulting damage.
16. **Schematic**: Representation of a drawing or diagram.
17. **Search string**: A combination of keywords, truncation symbols and Boolean operators you enter into the search box of a library database or search engine.
18. **Tunnel state**: All patients transition out of the health state at the next cycle.
19. **Unconstrained view**: Scenario of modelling where growth for dialysis and transplantation is estimated based on transition probabilities for disease progression. This represents future potential unmet need.
20. **Underserved**: This may include people from ethnic minority and deprived communities, those with severe mental health conditions and those with low levels of health literacy.
References


51. Kidney Care UK. Rare conditions. https://www.kidneycareuk.org/about-kidney-health/conditions/rare-conditions/


100. What is Health Literacy? https://www.cdc.gov/healthliteracy/learn/index.html


121. UKKA. Data from: AKI ICB data portal. 2018.


Appendices

Appendix A - TLR protocol summary

<table>
<thead>
<tr>
<th>Topic</th>
<th>Inclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study population (P)</td>
<td>Patients with:</td>
</tr>
<tr>
<td></td>
<td>• Acute kidney disease</td>
</tr>
<tr>
<td></td>
<td>• Chronic kidney disease</td>
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<tr>
<td></td>
<td>• End-stage kidney disease</td>
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<tr>
<td></td>
<td>• Other kidney diseases such as rare and inherited kidney disease (e.g. as Fabry disease, cystinosis, and polycystic kidney disease)</td>
</tr>
<tr>
<td></td>
<td><strong>Age, race, and gender</strong>: No restriction</td>
</tr>
<tr>
<td>Intervention (I)</td>
<td>No restriction on intervention</td>
</tr>
<tr>
<td>Comparator (C)</td>
<td>No restriction on comparator</td>
</tr>
<tr>
<td>Outcome (O)</td>
<td><strong>Epidemiology evidence</strong></td>
</tr>
<tr>
<td></td>
<td>• Incidence and incidence rates of kidney disease and comorbidities</td>
</tr>
<tr>
<td></td>
<td>• Prevalence and prevalence rates of kidney disease and comorbidities</td>
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<tr>
<td></td>
<td>• Incidence/prevalence over time</td>
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<td></td>
<td>• Mortality</td>
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<tr>
<td></td>
<td>• The evidence will be categorized and detailed by country and Integrated Care System/health system geographies</td>
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<tr>
<td></td>
<td>• Impact of Covid-19 infection/long Covid-19 on symptoms, complications (arterial and thromboembolic)</td>
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<tr>
<td></td>
<td>• Impact of Covid-19 on the incidence, prevalence, mortality among patients with kidney disease/CKD/ESKD/kidney transplant recipients/on haemodialysis</td>
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<tr>
<td></td>
<td><strong>Economic evidence</strong></td>
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<tr>
<td></td>
<td>• Direct costs of kidney disease, including direct medical pharmacy healthcare costs for complications and comorbidities (such as for cardiovascular disease and dyslipidaemia, anaemia, malnutrition, mineral and bone disorders, pruritus, decreased functional status, etc.), cost of dialysis (home based, in centre), transplantation, end-of-life care for kidney disease, admission/hospitalisation costs</td>
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<td></td>
<td>• Resource use: Hospitalisation, length of ICU stays, intervention usage, increased admission rate, home care</td>
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<td></td>
<td>• Indirect costs: Disease-related production losses due to patient and caregiver absenteeism/presenteeism from work, loss of employment, productivity, out-of-pocket costs to attend hospital clinics, insurance premiums</td>
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<td></td>
<td>• Patients and family/caregiver costs: Travel, annual loss of income, formal and informal care, loss of disposable income</td>
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<tr>
<td></td>
<td>• Evaluation details (perspective, time horizon, source of cost, resource use data, cost effectiveness, cost year, model, model description and justification)</td>
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<td></td>
<td>• Cost analysis: Assumptions, hypothesis, type of cost, year of cost, budget impact details, resource use</td>
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<tr>
<td></td>
<td>• CEA: Cost effectiveness or cost utility, ICER, QALY</td>
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<tr>
<td></td>
<td>• Impact of Covid-19 infection/long Covid-19 on the economic and resource use burden of patients and their caregivers</td>
</tr>
<tr>
<td>Topic</td>
<td>Inclusion Criteria</td>
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<tr>
<td>-------------------------------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Study design (S)</td>
<td><strong>Epidemiology evidence</strong>&lt;br&gt;Any study reporting epidemiology data, including cohort studies, cross-sectional, registry studies&lt;br&gt;<strong>Economic evidence</strong>&lt;br&gt;Any studies reporting original cost and/or resource use data&lt;br&gt;Economic evaluations for cost/resource use input data</td>
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<tr>
<td>Language of full text article (L)</td>
<td>English-language publications and English-language abstracts of foreign language</td>
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<tr>
<td>Year of publication (Y)</td>
<td><strong>Databases</strong>&lt;br&gt;• Epidemiological review: 2017-2022&lt;br&gt;• Economic review: 2017-2022&lt;br&gt;• Conferences: 2019-2022</td>
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<tr>
<td>Country of study</td>
<td>UK</td>
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</tbody>
</table>
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