Time To Act: A New Review of Kidney Health Inequalities

Professor Shivani Sharma, Dr Bnar Talabani, Dr Gavin Dreyer, Faizan Awan, Professor Fergus Caskey
Disclaimer

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Note on terminology

Language is continually evolving. Since publication of Kidney Research UK’s 2018 report Kidney Health Inequalities in the United Kingdom: Reflecting on the Past, Reducing in the Future, there has been a move towards the use of ‘health inequity’ as a term to emphasise that some differences in health are unfair and reasonably avoidable. This recognises that not all health differences represent forms of injustice. For example, older adults might be expected to experience poorer general health compared to younger people, a health difference that is not inherently an inequity given the impact of aging. However, in the UK, it is widely acknowledged that many health differences are unfair, and so this report retains the use of health inequalities to describe patterns in kidney health while attributing a moral dimension.

The 2018 report, following convention at that time, also used the acronym of Black, Asian and Minority Ethnic (BAME) when describing broad trends affecting those who have an ethnicity other than white heritage. The current report refers to specific ethnic communities as far as possible. In some places, the term ‘minority ethnic’ is used to describe issues that more often impact people from a non-white ethnic background. In doing so, the intention is to highlight issues related to social justice stemming from being part of a minoritised community rather than emphasising attributes associated with cultural identity.
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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 £65 million into research.

We lobby governments and decision makers to change policy and practice to ensure that the estimated 7.2 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.
1. Foreword

Professor Bola Owolabi, Director of the National Healthcare Inequalities Improvement Programme, NHS England

UK data reveals people living in the most deprived regions are expected to live around one-third of their life in poor health and have around 20 fewer years of healthy life than those living in the least deprived regions.

Like me, anyone who works in the field of health inequalities spends a lot of time discussing data like this. But we must never forget that underlying these numbers are individual human stories, and these are our motivation to make change.

It is therefore important to note that this report – which brings together the latest evidence surrounding kidney health inequalities – has been created with the involvement of people affected by those inequalities. People who have their own stories of how hard it can be to access services and information designed without them in mind and who see how this impacts their own health and the communities around them.

Thanks to these contributions, and involvement of a host of other experts, this report has given focus to efforts to narrow the gaps in kidney health. It spotlights specific priorities that offer a starting point for action, in the same way that Core20PLUS5 – NHS England’s framework for tackling health inequalities – is helping to support a system-wide approach to mitigating avoidable disadvantage.

In the words of one of the report’s patient advisors, health inequalities are inherently complex. Solutions don’t come in an easy, one-size-fits-all package. Our best chances of improving patient experiences and outcomes lies in drawing the right people together to design and implement solutions.

As Kidney Research UK acknowledges, no single organisation, profession or sector can reduce kidney health inequalities. Agents of change must work together in their respective spheres of influence. The NHS, local and central government, third sector, academia and business must work together, and with vulnerable communities, to find the answers and make changes.

All of us can contribute something to the solution, and we must all embrace our agency to act.

“Health inequalities are complex because people and their lives are so different. To be able to respond to this in a meaningful way will require the right people teaming up to work on solutions together. One size will never fit all.”

Kola Ponnle, expert by experience

Bola Owolabi
Director of the National Healthcare Inequalities Improvement Programme, NHS England

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2. About this report

People’s experiences of kidney disease are not just determined by the condition itself, but a range of societal influences too.

Across public health services, charities and government departments, there is a national priority around the reduction of health inequalities. This recognises that not all people in society have the same opportunities for health and well-being. This is true when we think about kidney health too. People from certain demographic, social, and economic backgrounds are more disadvantaged in their likelihood of having kidney disease, progressing faster to the need for kidney replacement therapy, and experiencing worse outcomes.

As a charity, our aim is to prevent kidney disease by finding ways to see it coming and stop it happening. Our research is also focusing on slowing down kidney disease once detected and reducing its impact on people’s lives. In 2001, we first commissioned a report by Professor Liz Lightstone, Preventing Kidney Disease: The Ethnicity Challenge. This was an important step in recognising the disproportionate burden of kidney disease on people from minority ethnic communities in the UK, with a focus on genetic, environmental, and socio-economic factors.

In 2018, we again commissioned a report that was led by Professor Fergus Caskey, and Dr Gavin Dreyer, Kidney Health Inequalities in the United Kingdom. This was a comprehensive overview of the wide-reaching inequalities in occurrence, progression, and outcomes of kidney disease, resulting in 27 recommendations for the kidney research and clinical community. This signals the scale of issues affecting kidney patients.

It is time now, five years on, to take stock of what progress has been made to narrow kidney health gaps. This review is an important part of a wider strategic context, following on from our 2023 Health Economics of Kidney Disease, Mental Health Challenges of Kidney Disease and Chronic Kidney Disease and Prevention reports. Together, they emphasise that to reduce the personal and societal cost of kidney disease, we need to recognise the variable experiences of patients, understand its drivers, and do something about it, proportionate to need. In parallel, we must build trust with the communities most affected.

Kidney Research UK has acted as a catalyst for focusing attention on health inequalities. Based on the evidence in each of the reports we have commissioned, several changes have been made in our own approach and contribution towards addressing inequalities in kidney health. The main actions taken by the charity are highlighted overleaf.

This five-year review, led by an academic and clinical team working with patients, sets out revised recommendations that we hope will continue to inform researchers, health-policy makers, healthcare professionals and funders, of the ongoing challenges that limit kidney health being a reality for all.

Sandra Currie
Chief executive, Kidney Research UK
Kidney Research UK: taking action on health inequalities

First commissioned report on health inequalities: Preventing Kidney Disease: The Ethnicity Challenge.

Launch of our evidence based and multi award winning Peer Educator outreach initiative with ongoing work including early detection / prevention, home therapies, organ donation and under representation in research.

Kidney Health Inequalities in the UK – commissioned report on wide-reaching kidney health inequalities.

2006-2017
Partnered on UK Renal Research Strategy, emphasising the need for inclusive participation.

2018

- Changes made to funding applications to include a focus on centre health inequalities and their mitigation
- Partnership developed with the Northern Care Alliance NHS trust and NIHR’s Research For the Future’ to develop and deliver a pilot project to address under representation in renal research
- Report commissioned on the economic impact of kidney disease to 2033. This includes reference to risk factors for inequalities and makes recommendations for interventions
- Partnership working with Centre for Mental Health to commission a report into the mental health impact of kidney disease on patients. The report recognises inequalities and the intersectionality with poor mental health
- New grant funding announced with a focus on prescribing disparities of SGLT2-inhibitors.

2019-2023
New review of health inequalities commissioned five-years on to reposition emphasis on narrowing kidney health gaps.

2024
New review of health inequalities commissioned five-years on to reposition emphasis on narrowing kidney health gaps.

2001

2005 onwards
3. Introduction

Professor Shivani Sharma, Dr Bnar Talabani, Dr Gavin Dreyer, Professor Fergus Caskey

Chronic kidney disease (CKD) is a broad term that includes a range of problems that impact kidney function over several months or years. The kidneys are essential organs, often referred to as ‘master regulators’. Most people have two kidneys, one on each side of the body just below the rib cage. These bean-shaped organs filter blood, removing waste products and excess water that is cleared in urine. The kidneys also support bodily functions such as regulating blood pressure.

CKD is classified into five stages, with each stage describing a level of kidney damage ranging from mild to severe (stage 5). Most people living with CKD do not know about it in the early stages. This is because they may not experience any symptoms or because the symptoms are non-specific. The main risk factors that contribute to CKD in adults include diabetes, obesity, and hypertension. In children and young people, risk is more often related to factors present at birth or genetic disposition.

In the most severe stage of CKD, sometimes referred to as CKD stage 5 or kidney failure, kidney function is reduced to around 15% or less and kidney replacement therapy needs to be considered. This can take the form of dialysis or transplantation, both of which aim to restore the capacity to remove waste from the body. In the UK, there are around 30,000 people receiving dialysis and approximately 3,000 kidney transplants are carried out annually, of which 100 are for children. Not all patients choose to start kidney replacement therapy, particularly those at the extremes of age, frailty, or with multiple co-occurring conditions.

CKD is a long-term condition that usually develops over years but progresses more rapidly in some groups of people than others. Acute Kidney Injury (AKI) on the other hand refers to sudden decline or loss of kidney function that may occur over a few hours or days. AKI is usually brought about by other health conditions that impact the kidneys such as heart failure, infection, or dehydration. AKI is usually reversible, though evidence suggests that episodes may be related to a long-term risk of CKD.

CKD is not experienced in the same way by all people, even in countries such as the UK which aim to provide universal access to free, publicly funded healthcare services. Preventable differences in kidney health and outcomes are often referred to as forms of health inequalities. In the UK, for a measurable difference to represent a health inequality there needs to be a judgement that the difference is largely unfair and avoidable. As a charity, Kidney Research UK has a long-standing commitment to reducing kidney health inequalities, advocating that everyone should have equitable access to preventing and slowing down the impact of kidney disease, and where necessary, access to suitable treatment.

Kidney health inequalities

In 2018, Kidney Research UK commissioned a comprehensive review of health inequalities to inform future research priorities. This built on an earlier, ethnicity-focused report published by the charity in 2001. Together, these reports have acted as a stark reminder that kidney health and health care for kidney disease is unequal. In 2018, differences were described based on demographic factors such as sex, ethnicity, and age, and because of wider social determinants of health including living in deprivation. For example, although women were more likely to be diagnosed with kidney disease, they were less likely to commence kidney replacement therapy.
Introduction

Adults living in areas of high deprivation were also found to be more likely to develop kidney disease, progress faster to the need for intervention, and to experience worse outcomes such as early death. People of minority ethnic heritage were up to five times more likely to be diagnosed with kidney disease, progress faster to needing intervention, and to start dialysis rather than receive a transplant despite its added clinical and lifestyle advantages. Recent data from the UK Renal Registry suggests many of these inequalities persist.

Such findings focus attention on the broad spectrum of factors that affect kidney health alongside prompting a call to action to reduce kidney health inequalities. The 2018 report, based on an evidence synthesis across four thematic areas, resulted in ten broad recommendations and 17 recommendations aligned to specific domains. Five years on, it is time to evaluate progress towards addressing these recommendations, considering the extent to which the dial on kidney health inequalities has shifted.

Time To Act: A New Review of Kidney Health Inequalities is timely for a multitude of reasons. A 2023 report published by Kidney Research UK delineates the current and projected economic burden of kidney disease in the UK. With an estimated 7.2 million people living with kidney disease in 2023, (10% of the population), and this number projected to increase annually, the economic burden at that time was estimated to be around £7 billion per annum and could rise to as much as £13.9 billion by 2033. Efforts to prevent or slow down the progression of kidney disease in the most at risk patient groups are therefore essential to reduce the personal, societal, and economic burden of illness. The recent publication of Health Inequalities 2040 by the Health Foundation further underscores the need to reduce inequalities in conditions that are closely related to kidney disease such as diabetes, especially in those living in the most deprived areas. The same report predicts that more people living in areas of the highest deprivation will experience depression, anxiety and major physical major physical health conditions related to CKD during working age. This comes with far reaching personal and societal impact, a key reason why this review includes a chapter dedicated to the patient voice (chapter five). Written by patients this highlights the everyday physical, psychological, social, and economic impact of CKD.

At the time of evaluating progress on narrowing kidney health inequalities, there are several contextual factors that affect patients, care providers, commissioners, and policy makers that warrant mention. The Covid-19 pandemic impacted kidney health due to the rapid changes in care delivery necessitated. Some of these changes are likely to have resulted in new, innovative practices that may benefit patient care, whilst others have acted to amplify existing gaps in patient experience and outcomes. It is important to evaluate how the pandemic affected kidney care in the UK so that the recommendations of the current review inform equity orientated recovery plans (chapter six).

The cost of living crisis cannot be ignored, with its impact experienced differentially across social groups and geographies. At the same time, health providers have needed to balance lean delivery with increasing demand for holistic kidney services i.e. addressing physical and psychological well-being. Importantly, these factors not only impact adults, they also impact children. Much less is known about how inequalities are experienced in children. For this reason, as far as possible, the current review makes general and life-stage specific recommendations to address kidney health inequalities, recognising that disparity may be modifiable at each juncture.

Further, it is fair to say that understanding of health inequalities itself is becoming more sophisticated, recognising that disadvantage does not sit in isolation. There are several intersecting factors that make some people more likely to experience kidney health inequalities than others. For example, in the UK, people of specific, not all, minority ethnic communities are more likely to live in the highest areas of deprivation. Treating all minority ethnic people as a homogenous group therefore acts to limit the lens of understanding and potentially the impact of efforts to increase inclusion in research for patient benefit. The report recommendations therefore attempt, where possible, to highlight such intersectional disadvantages to support their mitigation.

In times where value-based healthcare is a necessity, policy as an enabler of fair health is important. Though NHS England has a firm commitment to health inequalities and their life-stage specific reduction, kidney disease is explicitly missing from many aspects of health policy prioritisation. This makes this five-year review even more important as a lever for change, especially given that challenges are matched with new horizons for innovative technologies transforming healthcare (e.g. AI, machine learning, digital health interventions).
Structure of the report

As an interim review on progress, this report is structured into a series of chapters that provide a narrative overview of evidence on:

- Covid-19 and kidney health inequalities in the UK
- Basic science insights into the development of kidney disease
- Development of kidney disease – acute kidney injury and chronic kidney disease
- Progression of kidney disease – acute kidney injury and chronic kidney disease
- Access to treatment and outcomes in people with kidney failure.

Each chapter includes a series of recommendations for addressing kidney health inequalities by reflecting on what progress has been made, and where effort is still needed to narrow kidney health inequalities. A patient-led chapter (chapter five) further highlights why the review is needed considering the ever-shifting societal backdrop against which kidney disease is experienced. The review is brought together in concluding remarks as we look towards a step change in reducing kidney health inequalities by 2030.

The following chapter outlines the approach towards ensuring transparency in conducting this review, including the processes involved in engaging patients, clinicians, researchers, and other stakeholders to ensure rigour and impact of recommendations.

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>Stage 1  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>Stage 2  Kidney damage with mild loss of kidney function</td>
<td>89-60%</td>
<td></td>
</tr>
<tr>
<td>Stage 3a 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>Stage 3b Moderate to severe loss of kidney function</td>
<td>44-30%</td>
<td></td>
</tr>
</tbody>
</table>
| Stage 4 Severe loss of kidney function | 29-15% | • Patients with kidney failure require dialysis\(^1\) or a kidney transplant to stay alive  
  • A proportion of people with kidney failure will not receive either dialysis or transplant, instead undergoing conservative care. |
| Stage 5 Kidney failure (end stage kidney disease) | Less than 15% | |

\(^1\) Dialysis is a type of kidney replacement therapy that replaces the blood-filtering function of the kidneys.
References


5 Raymond, A. et al. Health inequalities in 2040 - The Health Foundation.

4. Methods

Professor Shivani Sharma, Dr Bnar Talabani, Dr Gavin Dreyer, Professor Fergus Caskey,

This chapter outlines the actions undertaken by the core editorial team to ensure rigour, inclusion and transparency in reviewing kidney health inequalities five years on. The 2018 report editorial team (Fergus Caskey and Gavin Dreyer) met with Kidney Research UK in spring 2023 to re-convene a leadership team to oversee the review process. To broaden the lens of perspectives and expertise, Shivani Sharma and Bnar Talabani were invited to join the editorial team for this review. This ensured diversity in the range of clinical and research input. Additional scientific and logistical support was provided by existing and new members of the core team (Dr Emily Beadle, Professor Liz Lightstone and Kidney Research UK staff). Patients were invited to join as advisory members to the core editorial committee. A new patient sub-group was formed to input into the patient chapter and to guide the review approach overall, supported by Shivani Sharma. Scientific and clinical experts were identified to act as chapter leads for the new report.

An engagement event of patients, stakeholders, industry partners, report chapter leads, and scientific advisors was held in Birmingham, in November 2023. This was to review progress in reducing kidney health inequalities since 2018 and to begin deriving new recommendations for the five-year review. This process considered the extent to which existing recommendations had been realised, alongside considering the impact of the socio-political environment on kidney care experience and outcomes.

Representatives from UK national renal leadership positions, Kidney Research UK and chapter leads for the new report (adhering broadly to the chapter structure in the 2018 report), were asked to present a brief update on progress in kidney health inequalities in their area of focus, reflecting on the impact of the Covid-19 pandemic. Specific presentations were made relating to kidney health inequalities in paediatric services as well as a session dedicated to the patient voice and experience. Small group sessions were convened to discuss updates in the four main chapter areas to establish potential new research recommendations and consider which recommendations from the 2018 report remain valid and require additional resource.

Scientific chapter authors were provided with a framework to support their review. This involved reviewing progress on kidney health inequalities since the last report based on available evidence and practice, scoping the impact of the Covid-19 pandemic, revisiting previous recommendations from the 2018 report, and formulating new research recommendations based on knowledge gaps. New research recommendations were categorised based on where evidence synthesis, primary research, interventional approaches, or other methodologies are required to provide consistency in mapping onto the 2018 report format. The editorial team each reviewed and edited one of the four scientific chapters and took responsibility for the overall content of the report.

Two new chapters have been added to this review - a chapter authored by patients addressing lived experience and priorities for kidney health inequalities (chapter five) and a chapter addressing the impact of the Covid-19 pandemic on kidney health inequalities (chapter six). The latter draws on scoping review methods.
The editorial team used a combination of inductive and deductive methods to identify and review the key themes from the four scientific chapters. This enabled assessment of what progress has been made from the original 2018 recommendations, as well as supporting revision of future recommendations. Key research priorities arising from this analysis are presented as general recommendations for the wider kidney community.

A prioritisation exercise was undertaken by key stakeholder groups including report chapter authors, November 2023 workshop attendees, and patient charities to build consensus about the relative importance of areas of action. This was to address direct feedback from patients. New research recommendations, without associated priority, were categorised into four main groups - primary research required, evidence synthesis required, interventional studies necessary or other research technique indicated and further sub-divided into clinical strata. – AKI, CKD and end stage kidney disease (ESKD).

Review process overview

1. Planning
   Established editorial team, meeting regularly throughout the review process. Approached and assigned chapter leads.

2. Patient Advisory Group
   Recruited patients to form advisory group, applying lived experience lens to health inequalities and their mitigation.

3. Stakeholder involvement
   One day workshop with patients, clinicians, researchers, industry. Chapter leads used this as a platform to inform review of their designated theme.

4. Revising recommendations
   Emerging themes revised, further stakeholder involvement to support prioritisation.

5. Finalisation
   Final report agreed by editorial team and patient co-author.
Looking back to look forward: Patient perspectives on kidney health inequalities then, now and in the future

Patient Authors: Faizan Awan, Sanjay Mistry, Keith Bucknall, Tejal Amin, Kola Ponnle

Living with kidney disease can be frustrating, exhausting and potentially all-consuming, impacting across every part of someone’s life.

People living with and affected by kidney disease were an integral part of the creation of this review and both Kidney Research UK and the report authors are grateful for their insight, input and openness in their approach to writing this chapter.

Just a small window into their experiences is a vital reminder about why it is so important that patients and their voices remain at the heart of everything we do.

Why focus on kidney health inequalities?

There are countless stories from patients and carers about their CKD journey. What is apparent from this is that not all patients have the same or similar experience of developing and managing CKD. In the UK, some people have a much harder time staying healthy when it comes to their kidneys. This unfairness is often referred to as health inequality. It means that where you live, how much money you have, and factors such as your age, sex and ethnicity can affect how likely you are to have kidney disease and how it progresses. For example, people who are from deprived areas often have a harder time getting check-ups or seeing specialists. They might also struggle to afford healthy foods, live in poorer quality homes, and struggle to protect their health due to lack of access to information or knowing how to use or implement it.

All of this adds up and makes kidney problems more likely. People from minority ethnic backgrounds are also affected by kidney disease more often than the rest of the population. Sometimes this is due to genetics, or other life factors including the likelihood of living in deprivation. Minority ethnic people often face unfair treatment when they try to get help from services, which negatively impacts care experiences and outcomes. It is also true that living with a co-occurring mental health condition, including severe mental illness, adds to the already wide-reaching consequences of kidney disease, making keeping well despite CKD more challenging. We must change these realities. Everyone deserves a fair chance at a healthy life.
From the patient’s viewpoint, this is why the 2018 report on kidney health inequalities was an important step in acknowledging the deep-rooted disparities affecting our health outcomes, whether you are a child, young person, or adult with CKD. That report was not just about the statistics; it reflected the real struggles faced by many due to factors such as income, age, sex, ethnicity, and geographic location. The report challenged the kidney care and research community as well as patients to reflect on the question ‘are personal and life attributes affecting CKD experience and outcomes fair?’ Since this is a rhetorical question, the report placed an emphasis on what action needed to be taken to reduce these injustices. The report highlighted the need for focused advocacy, interventions, and policy reforms at a time when global health challenges were escalating.

“We can’t ignore that there are historic factors that mean that some people fall through the gaps. We need to plug those gaps before we just carry on trying to “fix” inequalities. A holistic view will help prevent them from happening in the first place.”

Fez Awan

“Living with kidney disease has shown me the critical need for equitable care. It is imperative that we address the health inequalities present in our system to ensure that every patient has access to the comprehensive and compassionate care they require. Additionally, we must provide targeted support to communities lacking digital resources, enabling them to leverage technology for improved health outcomes and equitable access to necessary care services.”

Sanjay Mistry

Life is not static: Societal factors and their impact on kidney patients

Living with CKD can be full of uncertainty and anxiety at the best of times. Layered on this is the impact of life more generally, which plays out in different ways for different people because of education, income or deprivation, sex, ethnicity, disability, and age as well as issues such as historical mistrust, community exclusion, low health literacy, and their experience of systemic racism. This means that major issues in society in the past five years have had a differential impact on kidney patients because of the way in which aspects of life circumstances come together:

- Covid-19: Though a virus does not discriminate, there is evidence that its impact acted to widen health inequalities. Patients have experienced these inequalities first-hand, from increased difficulties in accessing care to navigating overstretched health services. The pandemic underscored the necessity of resilient health systems capable of providing equitable care during crises, bringing to light the urgency of addressing health disparities more effectively.

One example of inequality is that people who already waited longer to access a kidney transplant now had an even greater delay, with geography making a difference to when transplants resumed and who was most likely to be treated. This all contributes to growing concerns over fair management, especially for those who already have reasons for mistrust in health services.

What this emphasises is that in times of crisis, those who are already disadvantaged or experience health disparities will be most impacted. So, looking to the future, we are hopeful that learning from this time will mean that policies and initiatives truly try to safeguard all patients fairly. This means recognising that doing the same for everyone might not reduce inequalities. For example, as the pandemic has placed a sharper focus on the advantages of home therapies, it will be important for agendas on this to work for people regardless of geography or postcode lottery, ethnicity, income/deprivation or a combination of these factors. Data already suggest that some patients are more likely to take up home therapies than others and efforts to increase this modality overall should equally benefit all patient communities. Some patients may need more support in making decisions.
**Cost of living crisis:** It’s not long since a UK patient charity described that for many with CKD, the current economic climate means that we are in a ‘cost of staying alive crisis’ (Kidney Care UK). The National Kidney Federation has also emphasised how the current economic climate is challenging patients. Transport costs for appointments and attending hospital-based dialysis, cost of managing a healthy, kidney-friendly diet, job security for those of working age, and heating costs are some of the everyday considerations that occupy the minds of patients and their families. The issue is that such worries do not sit in isolation, they complicate the whole experience of CKD and so where there are already difficulties in the care experience, co-occurring mental health or wider conditions, factors such as everyday costs and ability to sustain them adds further challenge to experience and outcomes. Scaling up support in such times is important, but making this a reality is a challenge when health systems, charities and other community organisations have the same challenge of meeting the demands on them under resource constraints. This will inevitably mean that some people continue to feel a greater toll of life with CKD unless there is more innovation in how support can reach those who need it most.

“Living with a mental health condition can change both your voice and its volume so that you blend into the background. The frustration may come across angry or stroppy and you may then be misjudged. The clock is always ticking in the kidney world on dialysis so there is no leeway. The health system flows and one’s own soul sighs again.”

Keith Bucknall

**Digital divide:** There is a pressing need to leverage digital technology to improve access to health data, empowering patients to take proactive roles in their care. Innovations such as telehealth services, mobile health apps and digital platforms can revolutionise patient engagement and health management, especially for marginalised groups. However, it is crucial to bridge digital divides and design inclusive technologies that cater to the diverse needs of the patient community, including children and young people not being excluded from such advances to care. Collaborative efforts between technology developers, healthcare providers, patients and families are essential in creating solutions that not only address health inequalities but also pave the way for a more equitable health future.

“It’s daunting that there are so many dimensions of injustices. Inequality of risk of development of CKD, access to care and treatment, how useful and relatable education and awareness campaigns are, equality of outcomes from treatments. It’s time to take a hard look at how well the initiatives to address these issues are working. And where they are not working, or not working fast enough, what else will make a difference?”

Tejal Amin
Equality, diversity and inclusion landscape: There has never been so much discussion in society about issues related to equality, diversity and inclusion. This has been driven by a number of high-profile and significant events.

The murder of George Floyd by police officers in the USA caused an international ripple effect and reignited important conversations about racism in policing. In the UK, the Windrush Scandal revealed systemic prejudice against a generation of people who thought the UK was their safe home, and government figures show that people from minority ethnic groups in the UK are over-represented at almost every point in the criminal justice system, compared to population levels. Meanwhile, multiple studies have researched racial bias in the investigation and treatment of pain and illness in healthcare systems, whilst Black women in the UK are four times more likely to die in pregnancy and childbirth than their white counterparts.

Structural issues were also brought into sharp focus in UK health services during the pandemic with stories about deaths amongst minority ethnic doctors and patients alike. In response, many organisations are looking more closely at what inclusion and equity means for them and how it is experienced. The same should be true for patient advocacy groups, care providers, and researchers. We see the past and current reality as a huge opportunity for the kidney community, patients included, to redesign a future that works better in all spheres for its patients, workforce, and society.

Health policy: Not all patients are engaged with developments in health policy and prioritisation. For those of us who are, it is disappointing that Core20PLUS5 – an NHS England initiative to target the reduction of health inequalities in specific patient groups – did not include CKD. Still, the focus on diabetes in young people and hypertension in adults are important to reducing inequalities in CKD prevention, which we hope the kidney community will be able to draw on as key policy enablers for actions that matter to prevent or slow down the impact of CKD for patients and their families.

“Health inequalities are complex because people and their lives are so different. To be able to respond to this in a meaningful way will require the right people teaming up to work on solutions together. One size will never fit all.”

Kola Ponnle

Looking forward

This five-year review is the first to include a chapter dedicated to the patient and family voice. Though those of us contributing are not representative of the entire kidney patient community, we have varied experiences (paediatrics and adult), varying ethnic heritage, different gender identities, faith backgrounds, geography, education and income. Some of us identify with disability, as well as multiple health conditions. Drawing on this collective experience, we have attempted to highlight why health inequalities matter, and some of the factors that are challenges of our time that will shape the future trajectory of health inequalities and their reduction.

The review encapsulates the ongoing journey towards addressing health inequalities and underscoring the progress made since the 2018 report whilst acknowledging the considerable work that remains. What we hope we have contributed is a lens that emphasises what difference the recommendations can make to people living with CKD at any age and stage of disease, calling for action that consistently centres health inequality reduction. We would finish by saying that prioritising patients and their families as equal partners in addressing what matters and how is essential. No one should be left behind in our pursuit of equitable health care, which itself is a collaborative task.
6. Covid-19

Professor Shivani Sharma, Dr Emily Beadle, Professor Fergus Caskey, Professor Ken Farrington

Introduction

This chapter draws on scoping review methodology to provide an overview of the type of evidence on the impact of Covid-19 on kidney health inequalities in the UK. Differences in occurrence, progression, and outcomes of kidney disease are well established. Factors such as deprivation, sex, ethnicity, age, education, and their intersection impact trajectories of kidney disease, reflecting forms of social injustice. Developing sustainable solutions to longstanding inequalities has been a challenge across health systems around the world.

Care for patients with CKD was complicated by the pandemic. Kidney disease is a risk factor for higher severity of Covid-symptoms and higher fatality rate, particularly amongst those receiving kidney replacement therapies. The disruption to health services impacted the specialised care involved with the provision of hospital-based dialysis, as well as severely reducing access to transplantation. Many patients described living in a state of heightened anxiety, worry, and social isolation, with evidence from research funded by Kidney Research UK and others suggesting that resources to offer psychological support are limited, including adaptation to the pandemic context.

Learning from previous public health crises has shown that those who already experience disadvantage are disproportionately impacted. This reflects broader issues in society such as access to good quality housing and employment having an impact on health and well-being. Being cognisant of this can help inform efforts to scale actions in future as services are restored and priorities refocused.

This review summarises the nature of research undertaken in the UK between March 2020 and November 2023 with a specific focus on the relationship between individual demographic and social factors with experience and outcomes of Covid-19 in CKD. It is not intended to summarise the broader pathopsychological dimensions of CKD and Covid infection.

Scoping review methodology was selected because the approach is designed to act as a tool to explore the nature of available evidence. This enables identification and mapping of what evidence exists. The approach is therefore well aligned to the review aims.

Method

The review was guided by Arksey and O’Malley’s framework. Broadly, this describes five stages that underpin scoping review methodology. This includes:

- Identifying the research question(s)
- Searching for relevant studies
- Screening studies for inclusion
- Charting the data
- Collating, summarising, and reporting the data

An initial search showed there were no existing reviews on kidney health inequalities during the Covid-19 pandemic specifically focused on the UK. Key words and phrases relevant to the review aims were identified aligned to the following domains of relevance and combined using OR / AND functions:

- **Population** – Patients with a diagnosis of kidney disease based in the UK [any stage]
- **Concept** – Health inequalities (especially related to the social determinants of health and protected characteristics [e.g., sex, age, race, disability])
- **Context and outcomes** – Covid-19 (including infection, vaccination, outcomes).
 Searching for literature

Searches were conducted in November 2023, and limited to the UK. Both peer reviewed and unpublished research from March 2020 onwards was reviewed. There were no restrictions on the types of research design included. The search strategy was implemented in PubMed, CENTRAL and the WHO Covid-19 Research Database which includes Scopus, Web of Science, Embase, ProQuest, europePMC, medRxiv / bioRxiv and various clinical trials registries. The search strategy, including all identified keywords and index terms, was adapted for each included database.

All identified citations were collated and uploaded into Rayyan software and duplicates removed. Titles and abstracts were screened against the inclusion criteria for the review. Potentially relevant sources were retrieved in full and assessed against the inclusion criteria. Reasons for exclusion were recorded.

Data was extracted from included studies using a data extraction tool developed by the authors. This included details such as the population, concept, context, design / methods and key findings relevant to the review question.

Outcomes of the review are thematically summarised in table 1 to provide an overview of the general nature of research on specific dimensions related to health inequality. A narrative overview of key findings is also given.

Results

Searches yielded 1336 articles for review. After screening titles and abstracts, 33 relevant studies were identified and included in the final summary. Collectively, the studies provided data on 1,092,359 participants. Geographically, a high proportion were localised to the London region (13 studies / 39%). The results were synthesised based on the main dimensions of inequality reported: age, sex, ethnicity, and deprivation.

Age

- Older patients experienced greater risk of infection and adverse outcomes
- Younger patients were less likely to be vaccinated
- Limited research emerged on children and young people and their experiences and outcomes during the pandemic.

Sex

- Women appeared to be more likely to engage in frequent Covid-19 testing
- Men who have received a transplant appeared more Covid-19 vaccine hesitant, though this observation was drawn from a limited evidence base
- Evidence does not imply sex differences in exposure and outcome of Covid-19 infection.

Ethnicity

- Though Covid-19 infection may have been more likely in specific minority ethnic communities, evidence is inconsistent about the scale of impact on outcomes such as death
- Evidence suggests vaccine hesitancy was more likely to occur in minority ethnic patients, though tailored uptake initiatives were promising, suggesting access rather than hesitancy as driving factors.

Deprivation

- High social deprivation was shown to be associated with CKD and Covid-19 infection risk, though evidence on increased mortality is mixed
- Though vaccine hesitancy may be frequent in those living in social deprivation, targeted support was promising to improve uptake in kidney patients. This likely signals issues in access to information than hesitancy in and of itself.
## Table 1: Scoping of UK-based research on dimensions of kidney health inequalities related to Covid-19

<table>
<thead>
<tr>
<th>Scope</th>
<th>Age</th>
<th>Sex</th>
<th>Ethnicity</th>
<th>Deprivation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reporting</td>
<td>All studies reported patient age</td>
<td>All studies reported patient sex</td>
<td>Ethnicity was reported in 81% of studies, with variation in the extent of precision. The majority of studies (33%) used white, Asian, Black, other, and unknown as categorisation schemes. Only one study reported on complete census categorisation</td>
<td>45% of studies included measurement of deprivation</td>
</tr>
<tr>
<td>Incidence / risk of Covid-19 infection</td>
<td>Patients with Covid-19 infection (with or without hospital admission) were older</td>
<td>No differences based on sex in most studies in rate of infection or severity of disease</td>
<td>Several studies reported no differences in infection rate (with / without admission) based on ethnicity or an association with severity of infection</td>
<td>CKD patients with Covid-19 were more likely to experience higher deprivation and more severe infection</td>
</tr>
<tr>
<td></td>
<td>A study specific to the first wave of the pandemic (March-May 2020) found that risk of infection increased with age, with those over 80 years being most vulnerable</td>
<td>There was no significant effect of sex on prolonged time to viral clearance</td>
<td>One study reported that during waves one and two (September 2020-April 2021) specifically, non-white heritage was more often associated with the incidence of Covid-19 infection, with larger differences present in wave one, especially in Black heritage patients</td>
<td>Increased deprivation was shown to be a predictor of breakthrough infections</td>
</tr>
<tr>
<td></td>
<td>Only one article reported on very low incidence of infection among children in all 13 paediatric renal sites</td>
<td>No effect of sex in two studies for antibody response but one study did report such differences</td>
<td>One study indicated that compared to white heritage patients, those from Black heritage and South Asian backgrounds were twice as likely to have CKD and severe Covid</td>
<td>No differences in antibody status were shown for differing levels of deprivation</td>
</tr>
<tr>
<td>Vaccination rates</td>
<td>Unvaccinated kidney patients were more likely to be younger than kidney patients who had received the vaccine</td>
<td>One study showed that unvaccinated patients were more likely to be men who have received a transplant</td>
<td>Uptake of the third dose of Covid-19 vaccine was slower in those from minority ethnic groups, with coverage ranging from 67% in the most deprived areas and 88% in the least deprived. In white heritage patient groups, it was only below 90% in those over the age of 70. Similarly, fourth dose uptake was slower in minority ethnic groups with a range of 35% to 71%, especially in 16–64-year-olds</td>
<td>Third and fourth vaccine dose uptake was slower in those experiencing deprivation, especially clustering with those reporting minority ethnic heritage, younger age and those receiving kidney replacement therapies (KRT)</td>
</tr>
<tr>
<td></td>
<td>Vaccination uptake was faster in older people at all doses, while four-dose coverage was below 75% in those under the age of 70</td>
<td>Sex was not a significant risk factor for non-uptake of vaccination in another study</td>
<td>In one study, kidney patients who refused the vaccine were more often of Black heritage (54.8%)</td>
<td>Vaccine programmes targeting vulnerable groups, including those affected by high deprivation showed promising results</td>
</tr>
<tr>
<td></td>
<td>Age was not a risk factor for non-uptake of the first dose of the vaccine in a study implementing a programme to improve uptake in those receiving kidney replacement therapies</td>
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| Time To Act: A New Review of Kidney Health Inequalities |

Covid-19
### Impact of vaccination on incidence / risk

<table>
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<th>Scope</th>
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| Infection after vaccination was predicted by older age but severity of illness was not. Two studies showed no association in antibody responses with one study showing a significant difference between antibody status by ethnicity. Ethnicity was shown to be associated with likelihood of seroconversion, with non-white patients having increased seroconversion especially when comparing white to Indian-heritage participants; additionally in the same study, white heritage patients were more likely to be infection naive. Longitudinal proteomic profiling of dialysis patients with Covid-19 revealed markers of severity and predictors of death which did not differ by ethnicity.

### Outcomes – hospitalisation, death, long Covid

<table>
<thead>
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| Covid-19 related hospital admission was significantly associated with older age. Though CKD in general was a factor in prolonged time to viral clearance in one study, this was unrelated to age. As well as the expected all-cause mortality increase with age, Covid-19 specific mortality was greater for those who were older, especially in the >80 age group. One study showed no significant associations with age and survival rate, while others showed no differences between fatalities in terms of age.

No differences were reported between men and women in all-cause or Covid-specific mortality rates for most studies with excess deaths slightly higher for men in one study. Associations with all-cause morbidity were shown with minority ethnic background, even when adjusted for age, comorbidity, deprivation, and frailty, specifically in Black and South Asian patients. Asian patients on in-centre haemodialysis had a 17% higher mortality risk than white heritage patients, with no differences between Black and white patients, while excess deaths were more prevalent in Black and Asian patients.

Evidence was mixed on deprivation and Covid-related mortality. One study found an increased likelihood of death, however in the other studies which looked at this, deprivation was not associated with mortality on in-centre haemodialysis.

### Impact of vaccination on outcomes - hospitalisation, death, long Covid

<table>
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</tr>
</thead>
</table>
| Age was significantly associated with vaccine antibody response in one study, however another showed no differences.

Evidence was mixed on deprivation and Covid-related mortality. One study found an increased likelihood of death, however in the other studies which looked at this, deprivation was not associated with mortality on in-centre haemodialysis.
Wider Impact

Reduction in dialysis frequency was more often initiated for patients who were significantly older, but this had no effect on whether this change in routine was successful or not. Children and young people were concerned about heightened vigilance about viral and kidney symptoms and the impact on education and work. Parents showed more fear than children and young people did in relation to the virus and had concerns of passing the virus to their children and its impact on other children in the family.

Children and young people were concerned about heightened vigilance about viral and kidney symptoms and the impact on education and work. Parents showed more fear than children and young people did in relation to the virus and had concerns of passing the virus to their children and its impact on other children in the family.

Suitability for dialysis reductions because of the Covid-19 pandemic did not differ by sex, and this had no effect on whether this change in routine was successful or not.

Covid-19 testing was more frequent in women than men, but the proportion of positive to negative tests were similar. Suitability for dialysis reductions because of the Covid-19 pandemic did not differ by sex, and this had no effect on whether this change in routine was successful or not.

Differences were shown in intervention type in patients being treated for Covid-19. Patients receiving molnupiravir were less likely to be white. The alternative treatment sotrovimab was associated with superior patient and transplant outcomes. Another study showed no effect modification for ethnicity in treatment.

Conclusion

This scoping review highlighted the range of research that has considered factors associated with CKD and Covid-19 experience and outcomes. Though this is not designed to be a systematic evidence synthesis, the mapping has helped to clarify that:

- In general, reporting on patient demographic and social factors in research on CKD and Covid-19 is more complete for age and sex, with some variation in whether or how ethnicity and deprivation are reported. Wider reporting on social determinants of health is limited.
- There is evidence that age, ethnicity, and deprivation continue to complicate the experience of CKD, including in the pandemic context. However, there are inconsistencies in the extent to which such variables are modifying factors in outcomes. This may be better suited to exploration through techniques such as meta-analysis.
- Evidence is mainly drawn from studies in adult patients with CKD, with fewer studies considering how children, young people, and their families have been impacted.
- Though the review has focused on dimensions of health inequality in patients who are known to have CKD, it is worth mentioning that separate evidence syntheses exist on the relationship between Covid-19 infection and AKI. These suggest that research on longer-term renal recovery would be beneficial.
- Although drawn from a limited pool, evidence suggests that health inequalities benefit from targeted approaches to address pandemic specific issues such as vaccine hesitancy. This reinforces the need for accessible and relevant interventions to narrow health gaps.
- The review did not identify studies focused on long Covid experience. This will be important to consider in future to understand the burden of post-Covid-19 conditions on patients with CKD, particularly in more advanced stages of disease.
- Though patients (see chapter 5) express that post-pandemic, initiatives aimed at improving uptake of home therapies should centre on equity, there is limited evidence to help guide interventions designed to support patient choice.
Recommendations

- A complete systematic review with embedded meta-analysis is recommended to fully consider the impact of age, sex, ethnicity, and deprivation on Covid-19 infection and outcomes amongst people with CKD.

- Evidence synthesis and primary research is recommended on the longer-term clinical relevance of Covid-19 infection, particularly amongst patients with ESKD.

- The research community will benefit from the use of a standardised framework for reporting on patient demographic and social circumstances. This will help contribute a fuller understanding of health inequalities and their mitigation.

- Learning from the pandemic, strategies to reduce inequalities should be progressed that focus on accessibility and relevance.

- In understanding health inequalities affecting those living with CKD, the experiences of children, young people, and their families should be prioritised. They are underrepresented in existing research, making awareness of health inequalities and their mitigation particularly challenging.

- This review focused on patients known to have CKD during the pandemic. It has not considered inequalities related to identification of CKD, and whether there has been loss of momentum in approaches aimed at improving detection in those with higher risk profiles. Such a review and primary research on this theme is recommended.

- Primary research on how dimensions of health inequality relate to access to home therapies is also recommended, particularly as the pandemic has underscored the need to accelerate action on diversifying uptake of different dialysis modalities.

- Primary research is recommended to understand recovery from AKI related to Covid-19 infection and the role of early identification of chronic kidney damage.
Covid-19

References


7. Basic science insights into the development of kidney disease

Dr Mohammed Al-Talib, Dr Andrew Chetwynd, Dr Laura Denby

Looking back – where has progress been made?

The 2018 Kidney Health Inequalities report’s chapter on basic science concluded that the increased levels of AKI and CKD in minority ethnic populations was multifactorial. There are some biological drivers for example, APOL1 gene variants, nephron endowment at birth, and an increased prevalence of co-morbidities such as diabetes. Socio-economic disadvantage adds an extra layer of complexity and may have a biological component e.g. altered microbiome. Key areas recognised in the previous report were:

1) Birth weight, kidney size, and nephron endowment
2) Progression of CKD and risk of AKI
3) Cohort and biobank studies

Reflecting on the recommendations, there has been progress made in understanding the relationship between birth weight, kidney size, and nephron endowment. However, much of this research has focussed on relatively homogenous populations at comparatively low risk of kidney disease. For example, a Norwegian retrospective study examining renal functional response (RFR) to an oral protein load in adults aged 41-52 who had been born with either low birth weight (LBW) or normal birth weight (NBW), found no relationship between birth weight and RFR. However, the entirely white heritage cohort and exclusion of individuals with an eGFR <60 ml/min/1.73 m² in this study may have biased findings and masked the renal consequences of LBW.

LBW is more common in people of South Asian heritage, with reduced foetal kidney size identified in the Born in Bradford birth cohort study. Longitudinal follow up of these children at ages 7-11 found no evidence of ethnic differences in kidney function despite differences in kidney volume at birth. Further follow up may reveal whether the renal consequences of presumed reduced nephron number at birth manifest later in life. Interestingly, maternal diet composition among an Australian Indigenous pregnancy cohort appeared to impact foetal growth, but not foetal kidney size. This study was conducted in the third trimester, and any nutritional intervention aiming to increase kidney size may need to be implemented earlier in gestation.

Paediatric kidney patients are a key population who are often neglected in basic science research. A recent study showed patients who develop kidney failure at the youngest age experience the greatest loss of life years even with kidney replacement therapy. The causes and drivers of this are poorly understood to date due to a relative lack of large longitudinal studies in paediatric patients.
Urinary epidermal growth factor (uEGF) was highlighted in the previous report as a translational research success in identifying a biomarker associated with renal tubular reserve. Investigations in Norwegian, Dutch, and North American cohorts have associated reduced uEGF / creatinine ratio with risk of rapid GFR loss and incident of CKD, and of major adverse kidney events. Furthermore, amongst Chinese children with IgA Nephropathy, higher baseline uEGF / creatinine ratio was associated with higher likelihood of complete remission of proteinuria, suggesting potential utility as a non-invasive tool for risk stratification and monitoring in glomerulonephritides. Again, data remains lacking regarding the utility of biomarkers such as uEGF in minority ethnic communities.

Animal models may provide key insights into understanding the pathophysiological relationship between low nephron endowment and kidney disease risk. A recent mouse model of reduced nephron number in utero identified compensatory post-natal renal hypertrophy, greater susceptibility to AKI and more rapid development of CKD associated with elevated inflammatory cytokines MCP-1 and CXCL-10. Biological aging is how old cells are and can be different from chronological age. Patients with CKD are often said to have accelerated biological aging. One way this can occur is by DNA methylation and has been implicated as a link between socio-economic status (SES) and health. A study of 1102 racially and ethnically diverse adults in the USA found that non-Hispanic Black participants, living in neighbourhoods with greater segregation of Black residents was associated with an accelerated GrimAge DNA methylation age of their immune cells, which was more pronounced in high poverty areas. Senescence occurs naturally as we age, but senescent tubular cells have been found to accumulate in injured kidneys and implicated in progression of kidney disease. Excitingly, targeting senescent tubular cells with senolytics improves repair post-AKI in pre-clinical models. As yet, whether minority ethnic patients have altered levels of senescence is not known.

**Specific examples of progress**

The recent rise of omics has increased our understanding of the molecular mechanisms driving CKD and risks for AKI. For example, single-cell RNA sequencing has been used to identify discrete tubular cell subtypes in mice and humans. The generation of accessible human datasets through the Kidney Precision Medicine Project (KPMP) has already driven an increase in publications revealing more molecular understanding of the mechanisms involved in human CKD and AKI. This includes understanding the participant experience with protocol research kidney biopsies. Promisingly, there have also been mechanistic and biomarker studies published utilising omics technologies investigating nephrotic syndrome, IgA vasculitis nephritis, ADPKD and lupus nephritis though compared to adult cohorts very few paediatric studies have been performed.

The building of the NURTuRE bioresource co-funded by Kidney Research UK was in response to the challenges faced by researchers studying (CKD) and idiopathic nephrotic syndrome (INS). Studies are now being published from these cohorts and this could improve risk prediction, including in minority ethnic populations. The Born in Bradford study cohort will also be useful in exploring interactions, associations and risk.

**Recommendations from the 2018 Kidney Health Inequalities report and status**

**Original recommendation 11:** To establish the utility of biomarkers to explain differences in AKI risk and outcomes between different ethnic groups - given the rapid evolution of the evidence base in this area, a review of published and grey literature is needed before deciding how primary research should proceed.

In 2020, a consensus statement was released on recommendations of AKI biomarkers and how these should be integrated in clinical practice. Conclusions were that substantial gaps still remain, and more research is necessary.

**Original recommendation 12:** To develop techniques that identify individuals at high life-time risk of CKD, early in life – this could include methods to assess nephron number and early life biomarkers that predict later life risk of developing CKD.

Methods have been generated and published but remain lacking in minority ethnic populations (see recommendations).
Original recommendation 13. To establish how high-risk alleles increase chance of developing CKD – there is strong evidence for the role of APOL1 across several renal diseases in those with Black heritage, but the mechanism of action has not been established and this is needed before interventions can be developed and tested. Primary research has yet to be undertaken to systematically search for similar candidate genes in people of South Asian heritage in the UK.

The use of basic science to unpick the role of the Apoll risk variants is a success story. Therapies are now being designed, such as the small molecule inhibitor on APOL1 channel called VX-147 or inaxaplin which demonstrated promising results in reducing proteinuria in patients with APOL1-associated FSGS in a recently published phase 2a study23. Recent (2022) genetic studies have been performed across ancestries which may help to identify candidate genes in the South Asian population in the UK24.

Original recommendation 14. To improve our understanding of biological and whole organism ageing – the full range of cellular age-related changes of normal and predisposed individuals from different ethnic groups needs to be better understood in relation to CKD. To define potential therapeutic targets, is a need to develop translationally relevant experimental models of CKD and AKI.

Human studies should ensure inclusion of individuals at high risk (particularly those with known barriers to research participation) versus low risk of CKD progression, and both males and females. This will require infrastructure support including sequencing costs, bioinformatics training and access to biobanking of relevant human samples for analysis.

Support the discovery and validation of novel, and ideally non-invasive, prognostic biomarkers e.g. microRNAs36,27 in minority ethnic populations and the replication of studies using imaging methods as discussed being funded and performed in ethnically diverse populations.

Specific recommendations

Acute kidney injury

Primary research

- Identify biomarkers and explore their utility in identifying at-risk populations who fail to recover from AKI and relate this back to genetic and epigenetic risk factors.

Mechanistic studies

- Leverage omics data to understand the role of genetic drivers, epigenetic drivers and other factors which contribute to increased risk of AKI in minority ethnic communities using APOL1 research as an exemplar.

Chronic kidney disease

Primary research

- Nutritional and / or pharmacological interventions to increase foetal kidney size and reduce long term risk among individuals with LBW or renal size. Advocating for concurrent qualitative studies and realistic evaluation to understand acceptability and applicability of such interventions

Mechanistic studies

- Biomarker studies: requirement to further characterise utility of biomarkers of renal tubular reserve (e.g. uEGF / creatinine ratio) in longitudinal studies including minority ethnic populations and relate these to birth weight and renal size.

Mechanistic studies

- Identify and explore mechanistic targets using omics data to understand the role of genetic drivers, epigenetic drivers and other factors which contribute to increased risk of CKD in minority ethnic populations using APOL1 research as an exemplar.

Research in this area is increasing with new knowledge around the drivers of healthy biological vs premature biological aging. We have a better molecular understanding of biological aging as discussed.

New research recommendations

General recommendations

Investment in training bioinformaticians: This is to support multi-omic studies in both animal models and humans

- To define and characterise renal development and composition
- To study the implication of nephron loss and response to injury
- To allow rapid analysis of the generated omics to study the molecular mechanisms / genetic causes underpinning premature biological aging, AKI, CKD
- To facilitate more rapid biomarker analysis in cohorts such as those contained within NURTuRE25.

Time To Act: A New Review of Kidney Health Inequalities

Basic science insights into the development of kidney disease
References


8. Development of AKI and CKD

Professor Simon Fraser, Dr Simon Sawhney, Dr Kristin Veighey

Looking back – where has progress been made?

The 2018 Kidney Health Inequalities report emphasised targeting modifiable health risk factors that are more prevalent among people who are socio-economically disadvantaged or living in certain ethnic groups: obesity, hypertension, diabetes and cardiovascular disease. Although progress has been made in several areas, the original recommendations still stand. Public health and collaborative health system approaches are likely to be the most effective in addressing them.

Evaluations of the Covid-19 pandemic have highlighted widening disparities within socio-economically disadvantaged and minority ethnic groups, with a loss of preventative and proactive care. Evaluations have also highlighted the long-term implications, which may include a wave of Covid-related complications (including cardiovascular and kidney diseases), burden on mental health and wellbeing, and exacerbation of gaps in long-term condition surveillance and monitoring. The NHS is under increasing strain, particularly in primary care, with long waiting lists for outpatient clinics, workforce issues, greater complexity for coordination and navigation of care, less in-person contact, a shift in the commissioning landscape in many regions of England and rising prevalence of multi-morbidity and associated inequalities. The cost of living crisis is disproportionately impacting the most disadvantaged in society and has led to substantially more people suffering the effects of poverty. New areas of inequality have emerged with a pronounced ‘coastal effect’ of CKD – a greater prevalence than can be explained by age and socio-economic factors alone.

Specific examples of progress

Since the 2018 Kidney Health Inequalities report, progress has been made and we highlight as examples three different types of clinical impact, and where this has led to further research:

• “Game changing” treatments are being introduced, such as SGLT2 inhibitors and new models of care incorporating kidney failure risk into decision making. These have the potential to improve kidney disease management and outcomes. However, timely identification of CKD remains an important issue and there is a need to avoid unintentionally widening inequities when applying new treatments and models. Emerging research describes substantial inequities in the delivery and outcomes of kidney care, particularly early in kidney disease.

• The NHS “Health Check” and the (discontinued) “Keep Well” in Scotland offered screening and education focusing on cardiovascular (though not specifically kidney) risk, with mixed findings. A 2022 rapid review found: “NHS Health Checks led to an overall increase in the detection of raised risk factors and morbidities including diabetes mellitus, hypertension, raised [blood pressure], cholesterol and CKD. Individuals most likely to attend the Health Check programme included women, persons aged ≥60 years and those from more socio-economically advantaged backgrounds.”

• There has been some progress on primary prevention of CKD through population-based strategies for blood pressure control in the ARIC study, with minor reduction in blood pressure associated with fewer incident CKD events.
AKI

Original recommendation 15: To identify the impact of shared risk factors for CKD on socio-economic and ethnic variation in the distribution of AKI incidence – this should include hypertension, diabetes, smoking, CVD and obesity.

There are now several studies showing an association between increased AKI risk and comorbidities/low socio-economic status (SES). For example, studies showing that lower SES, hypertension, diabetes, CKD, heart failure, cardiovascular disease, obesity and smoking are all independent risk factors for AKI, and that SES is particularly important in people under age 65. Ethnicity is also associated at an univariable level in some studies but missing data is a problem19, 20, 21, 22.

CKD

Original recommendation 16: To identify the barriers for people in different ethnic groups in accessing diagnosis and good quality care for both CKD and its risk factors – this could be a two-step process, first establishing where the barriers occur and second exploring what can be done to address them.

Ethnic and socio-economic health disparities have widened during the Covid-19 pandemic, including loss of preventative and proactive care1,2,3. As outlined above, the long-term implications of this are still uncertain4. As a result, the NHS is under unprecedented strain, particularly in primary care5,6. Added to this, the cost of living crisis is disproportionately impacting the most disadvantaged in society7, and new areas of inequality have emerged with a pronounced ‘coastal effect’ of CKD8. Although the original recommendation focused on ethnicity, intersectionality has emerged as an important concept in which individual experience of health and healthcare is influenced by multiple overlapping contexts such as gender, sex, ethnicity, education, finances, health literacy, freedoms, social support, geography, culture, and beliefs that interact with each other as well as systems and wider societal factors to influence inequalities and inequities23,24. On a positive note, new risk-based models of care have been developed and are being implemented, as outlined above, and these may improve equity of access to diagnosis and quality of care.

Original recommendation 17: To establish whether there is sufficient evidence to take forward an intervention targeting early life risk factors for life-time risk of CKD – this should look at targeting acquisition of early life risk factors as well as protecting kidney function in those who acquire those early life risk factors.

Some progress has been made but there is insufficient evidence at this stage for intervention development. The Born in Bradford studies on kidney size suggested a relationship with eGFR in childhood but no evidence of ethnic differences in kidney function in prepubertal children despite differences in kidney volume at birth25. Childhood modifiable risk factors may contribute to the CKD risk in adulthood, particularly adiposity, type 2 diabetes, and low socio-economic position and cardiorespiratory fitness in females26. The development of CKD cohorts and improving links with paediatric colleagues aligned with a life course approach to CKD could allow for the development of an intervention to reduce the lifetime risk of CKD.

Original recommendation 18: To summarise the most promising population level interventions to address later life shared risk factors for CKD – this could inform models of the impact of interventions and hence decisions about where to most effectively and efficiently focus efforts to reduce kidney health inequalities.

Screening and health promotion may play a role in identifying and addressing CKD risk27,28. Current international consensus supports screening among those with high-risk medical conditions (e.g. diabetes, hypertension)29. It may also be appropriate for other under-served or high-risk groups, although further evidence is needed29. As outlined above, new evidence from the ARIC Study suggests primary prevention of CKD is possible through population-based strategies for blood pressure control30.
Poor general awareness of kidney disease in society continues, along with uncertainty among clinicians about disclosing CKD to patients and suboptimal CKD detection and risk-assessment (e.g. urinary albumin measurement) 29,30,31,32.

As mentioned above, a 2022 rapid review of NHS Health Checks found evidence of an overall increase in the detection of risk factors for CKD and its complications – diabetes mellitus, hypertension, raised blood pressure, cholesterol, and CKD. Women, people aged 60 years and over, and those socially advantaged were most likely to attend these health checks17. More work is needed to assess whether it is possible to target those at greatest risk more effectively. Further, to inform future population level interventions, more evidence is needed to understand the context, mechanisms and outcomes underpinning interventions targeted at obesity, salt consumption, smoking and health literacy as contributors to the inequitable development of CKD and AKI.

New research recommendations

These recommendations aim to enhance kidney health literacy, identification, primary and secondary prevention, and equity of care. They should involve co-production with patients and members of the public and active consideration of intersectionality:

1. **CKD**

   **Evidence synthesis followed by primary research**

   To identify, develop and test accessible methods to improve kidney health literacy among members of the public, patients and health professionals.

2. **CKD and AKI**

   **Primary research**

   To develop and test communication methods for healthcare professionals that build confidence in interactions with patients and the public about kidney disease risk, implementing lifestyle changes, and communicating the meaning and implications of a CKD or AKI diagnosis.

3. **CKD**

   **Evidence synthesis and primary research**

   To improve understanding of the population-level impact of obesity, salt consumption, smoking, physical inactivity and limited health literacy on CKD incidence and prevalence to inform future population level interventions.

4. **CKD**

   **Evidence synthesis and primary research**

   To identify ways to address the needs of those at greatest CKD risk more effectively, more evidence is needed on not only inequality and variation but on fairness and equity, considering both horizontal (equal care for equal need) and vertical (unequal care for unequal need).

5. **CKD**

   **Evidence synthesis**

   To re-evaluate the role of screening for CKD both at population level and among existing and emerging underserved and high-risk groups.
References


2. Office for Health Improvement and Disparities. Excess mortality in England (2024). Available from: https://app.powerbi.com/view?r=eyJrIjoiYmUwNmFhMjYtNGZhYS00NDb2ZWFiMTA1OTq0OGNnNmFínGMOliwiciEiLCJyVlNGUxNDk5LTRhMzlINGlgyZSIhZDQ3LTVMmM2NmOWRiODY2NilslmMjOLh9


9. Progression of AKI and CKD

Dr Rupert Major, Dr Hilda Hounkpatin, Dr Jennifer Lees

Looking back – where has progress been made?

There continues to be a significant association of increased risk of serious adverse outcomes for people living with CKD and those who have experienced an episode of AKI. The increased risk of hospitalisation and premature death was particularly highlighted during the Covid-19 pandemic when mortality and morbidity related to Covid and non-Covid causes were substantially worse for these groups1,2,3, even compared to other major long-term conditions such as cancer, diabetes and CVD. Many other outcomes, particularly those highlighted by patient reported outcome measures (PROMs) related to quality of life, continue to be less well studied. Such examples include rates of employment and job security, effects on relationships, infertility for both women and men, poverty, and mental illness.

Age continues to be strongly associated with higher absolute risk of poor outcomes with CKD and AKI. Women remain more likely to be diagnosed with CKD but men more likely to progress to end-stage kidney disease. This may relate to women being more likely to attend for chronic disease health checks such NHS “Health Check”4. This is also likely to be related to worse outcomes for CKD associated cardiovascular disease. The association of deprivation, including the intersection of its parts5, and CKD has recently (2023) been summarised demonstrating a strong relationship with CKD development, progression and late presentation (and its associated worse outcomes for dialysis and transplantation)5.

The interaction between ethnicity and social disadvantage is complex, but generally individuals of South Asian, Black African and Black Caribbean heritage continue to be more likely to develop CKD and have progressive disease leading to ESKD7,8,9.

People living with severe mental illness face shorter life expectancy and are more likely to develop multiple long-term conditions such as CKD. This continues to be related to difficulties managing physical health conditions in the context of poor mental health, as well as certain medications such as lithium10,11,12.

Specific examples of progress

Since the 2018 Kidney Research UK Health Inequalities report, progress has been made and we highlight as examples three different types of clinical impact, and where this has led to further research:

• Identification and treatment of people with the APOL1 risk polymorphisms, which is more likely to occur in people of African ancestry and is associated with progressive kidney disease13. At the time of writing, larger trials are in progress, and recruiting participants in the UK, for a drug which showed a near 50% reduction in urine protein in an initial, small trial14.

• National guidelines15 in relation to kidney disease and pregnancy, which will start to address inequalities and inconsistencies in care where outcomes remain poor for both mother and child. There is ongoing work to personalise risk assessment in this area16.

• A UK-based collaboration is performing validation of the updated “race-free” eGFR formula in minority ethnic populations. People of South Asian heritage have again been highlighted as being more likely to progress to kidney replacement therapy (KRT) at a younger age17 and the UK-calibrated KFRE possibly underpredicting risk18. This has led to further primary care led NIHR funded research to address different outcomes for CKD in ethnic minority populations (NIHR156488)19.
General areas of progress which are likely to impact inequalities in CKD and AKI

- Evidence generation – eGFR slope and change in urine ACR is now established as a surrogate marker for KRT in clinical trials. This will expedite results of clinical trials in CKD

- Clinical monitoring – The Kidney Failure Risk Equation (KFRE) has been recommended for use by NICE to improve personalised care for CKD stages 3a to 5. Its utility in people of different ethnicities, socio-economic groups and with multiple long-term conditions is being studied. Tools for risk prediction in earlier stages of disease have not undergone thorough validation studies in UK-based populations.

- PROMs, including under-recognised symptoms such as itch and tiredness, for clinical and research use are being utilised. Whether the experience of outcomes important to patients varies across patient groups is unclear.

Recommendations from the 2018 Kidney Health Inequalities report and status

Acute kidney injury

Evidence synthesis is recommended

Original recommendation 19. To evaluate access to care and adverse outcomes (e.g., incidence of or progression of CKD) following an episode of AKI with respect to age, socio-economic deprivation and ethnicity. This review could lead to either more primary research or an interventional study investigating outcomes after an episode of AKI in groups where inequalities in outcomes may have been identified or predicted.

Sawhney et al. have demonstrated that both incident AKI and CKD were managed in less proactive fashion (fewer blood tests and monitoring visits, fewer outpatient attendances) and observed more emergency presentations and hospital admissions among people who lived in socio-economically deprived areas. The authors proposed that considering non-medical factors using qualitative approaches (such as social needs, health literacy, behaviour and / or access) would be the next steps to understand and narrow these gaps.

Chronic kidney disease

Primary research is recommended

Original recommendation 20. To investigate health inequalities in rates of CKD, referral to renal services with CKD, rates of KRT and competing mortality. This should look at all potentially disadvantaged populations, how they overlap and interact and whether there are signals about mechanism from trends over time.

In a study using data from the UK Biobank cohort, Sullivan et al. indicated that members of Asian or other ethnic groups were more likely than white individuals to be rated as at high risk of kidney disease progression (indicated by a KFRE score >5% at five years). This represents a favourable change in the guidelines for referral to nephrology services, suggesting that more high-risk members of minority ethnic groups will be identified using this updated approach.

In a primary care cohort from Wales, females were less likely than males to receive albuminuria testing in the context of CKD. Since albuminuria is essential for calculation of KFRE, this may partially explain the higher likelihood of males meeting criteria for referral to nephrology by KFRE criteria.

Recent studies have found poorer diagnosis and management of CKD for older people and people of Black African ethnicity, and an association between socio-economic deprivation / low health literacy and mortality. Suboptimal delivery of SGLT2 inhibitor therapy is a particular concern, where treatment is lower among the highest-risk individuals, and particularly among older people, women, those of Black ethnicity and those who live in socio-economically deprived areas. In 2024, Kidney Research UK awarded a grant to identify disparities in prescribing rates in this area.
Evidence synthesis is recommended

Original recommendation 21. To summarise traditional (e.g. mortality, cardiovascular events) and non-traditional outcomes (e.g. employment status and mental health) in different ethnic groups. This will need to be conducted with due consideration of how previous studies were designed and adjusted for.

We are not aware of any evidence synthesis in this area, but have identified some new original research. Mathur et al. described ethnic differences in progression of CKD and mortality for a diabetic population30. Major et al. again found people with CKD of South Asian heritage are more likely to progress to KRT at a younger age17 and Mayer et al identified that the UK-calibrated KFRE possibly underpredicted risk18. In contrast, Ling et al identified across all ranges of the general population, that rates of ESKD were similar between white and South Asian ethnicities31. Further work is required to test this association with adjustment for proteinuria measurement and linked to national ESKD registry data.

Original recommendation 22. To establish whether there is sufficient evidence to take forward an intervention to improve the outcomes of people from disadvantaged groups of working age living with CKD. Any such intervention is likely to be complex and outcomes would need to be culturally and medically relevant.

Complex interventions have been and are being tested in clinical trials settings for people living with CKD. Of particular note, Kidney BEAM in a randomised controlled trial setting has shown improvement in quality of life for people living with kidney disease32. However, access to digitalised interventions may be more limited for those with lower socio-economic status, without English as a first language and should be culturally competent in their approach33. A recent scoping review has identified that most interventions are feasible and acceptable to patients but require further clinical trial evidence34.

New research recommendations

Acute kidney injury

Primary research is recommended

- To undertake qualitative research work to understand and overcome the barriers to proactive diagnosis, monitoring and treatment after AKI, particularly in areas of high socio-economic deprivation, but also to include the perspective of older individuals and those from minority ethnic groups.

Chronic kidney disease

Evidence synthesis is recommended

- To summarise the current evidence for clinical implementation trials of urine ACR measurement for the UK’s general population, particularly high-risk groups facing inequalities.
- To summarise the current evidence for barriers in delivering evidence-based CKD care for underserved populations, including prescription of RAASi blockers and SGLT2 inhibitors, to inform future implementation work.

Primary research is recommended

- To design and develop trials of novel primary care and integrated care-based management of CKD for high-risk populations, focusing on earlier detection (including through increased ACR measurement), which will allow:
  - Improved personalised risk prediction for KRT (through KFRE) and cardiovascular disease
  - Improved personalised management of CKD such as with blood pressure targets and the use of specific therapies
- To collect non-traditional data in AKI and CKD related studies such as:
  - Further exploration of PROMs that are specific to the lived experience of different ethnic groups and / or according to varied socio-economic factors will be important, and could be informed by patient engagement and qualitative work
  - Underreported risk factors related to inequalities such as employment history, education status, air and noise pollution, housing, immigration status and English as a first language
- To develop clinical trials of lifestyle and education interventions tailored to people from disadvantaged backgrounds to empower them to manage their kidney condition and other related long-term conditions
- To include people with CKD in clinical trials, whether commercial or investigator-led, as default, learning from the success of studies such as the Covid RECOVERY trial35.
References


19. Search - NIHR Funding and Awards. NIHR https://fundingawards.nihr.ac.uk/award/NIHR156488.


10. Access to treatment and adverse outcomes with end stage kidney disease

Dr Michael Sullivan, Dr Sivakumar Sridharan, Professor Paddy Mark

Looking back – where has progress been made?

When reflecting on issues related to access to treatment and adverse outcomes over the last five years, the impact of the Covid-19 pandemic on kidney patients cannot be ignored. People with kidney failure faced numerous challenges, including an extremely high risk of death from Covid-19 infection. This risk has broadly been mitigated by vaccination, though differences have been observed in rates of hesitancy towards uptake. Renal services across the UK had to react to evolving infection rates and regulations. Many centres paused their transplant programmes, while dialysis units had to adapt their practices to address the impact of Covid-19.

Late presentation with kidney failure

The pandemic reduced the capacity of primary care to identify and monitor chronic diseases including CKD. In 2021, 18% of people starting KRT were referred within 90 days, an increase from 16% in 2020. Reduced capacity to recognise and refer high-risk CKD patients from primary care is likely to have contributed. Although evidence has emerged that children from areas of high deprivation are not the most likely to be referred late to renal services, the cost of living crisis is likely to have ongoing impacts on health inequalities for deprived and rural communities.

Access to kidney transplantation and outcomes

The UK wide ATTOM study demonstrated variation in transplant listing by centre and ethnicity. Adults from socio-economically deprived areas were less likely to be pre-emptively listed than those from less deprived areas, and the same has been found in children. Although efforts have been made to eliminate barriers to living kidney donation through education and outreach initiatives, a large cluster randomised controlled trial from Canada indicates that these efforts do not necessarily improve access to transplantation.

It is too early to ascertain if changes to the Kidney Offering Scheme made in 2019 will improve equity of access to transplantation as is intended or if it will introduce unanticipated new biases. Similarly, it will take time to see what impact recent implementation of ‘opt out’ legislation across the UK has on the number of kidneys available for transplantation from deceased donors. With the introduction of the medication ilmidase to prevent antibody-mediated rejection amongst “highly sensitised” transplant recipients, equitable access to this treatment will be key.
More than 80% of kidney transplant recipients have a functioning transplant at five years in all UK transplant centres (>90% for transplants from living donors)\(^{12,13}\). Graft survival in people of different ethnicities appears similar\(^{14}\). National Health Service Blood and Transplant (NHSBT) data demonstrate differences in the time to observe a survival benefit following successful kidney transplantation across different ethnicities, with a longer time to benefit in people from ethnic minorities. Nevertheless, kidney transplantation broadly improves survival in transplant candidates of all ethnicities compared to dialysis\(^{15}\). Further work is needed to understand these differences and describe access to transplantation and transplant outcomes in other underserved groups, including by immigration status, sexuality, gender identity, rurality, and disability.

**Access to dialysis and outcomes**

Use of home-based therapies continues to vary across the UK. The Getting It Right First Time (GIRFT) report in England highlighted the importance of home therapies with a target of >20% of patients\(^{16}\). However, there is variation between <5% and >40% in different centres\(^2\). The Inter-CEPt study may explain these variations and help develop interventions to promote the use of home therapies\(^17\).

For patients receiving in-centre haemodialysis, transport is a key issue. In 2021, NHS England improved equity of access to dialysis by providing free transport for all patients\(^{18}\).

Cardiovascular disease remains the leading cause of death amongst people on dialysis\(^3\). The interaction between modifiable risk factors (like smoking and diet) and outcomes in underserved groups remains poorly understood.

**Access to renal supportive care**

There has been an expansion of renal supportive care services in the UK, with nurse specialists in some units supporting people to be cared for in the community with reductions in medical interventions\(^4\). Ethnicity and socio-economic deprivation do not appear to affect the choice of renal supportive care\(^5\), but there needs to be equity of access. The results of the ongoing Prepare study\(^6\), which aims to consider practice in preparing patients for dialysis versus conservative care, will be important to inform further priorities about unbiased supportive decision making for patients and their families and whether inequities exist based on social drivers of health experience and outcomes.

**Recommendations from the 2018 report and status**

**Dialysis**

Primary research is recommended

- Original recommendation 23: To study the interaction between environmental, socio-economic and patient specific factors which drive premature CVD in patients with ESKD treated with dialysis. This could lead to clinical phenotyping studies of identified high risk groups or studies to understand the fundamental drivers of the inflammatory process.

This is an ongoing process, potentially best addressed by subgroup analysis of large UK based randomised controlled trials in this population such as PIVOTAL or BISTRO\(^{22,23}\).

An interventional study is recommended

- Original recommendation 24: To enhance the use of home therapies in groups that are traditionally low users of this service, as identified by pre-existing data. The intervention is likely to be complex and will need to be developed according to the various stages of the Medical Research Council complex intervention development guidance. It will need to take into account ongoing quality improvement work in this area.

Currently this has not been progressed, although the pandemic has highlighted additional benefits with home therapies whereby patients can maintain autonomy in being able to deliver dialysis with independence from health care staff. There are national campaigns that underscore the need for accelerated action such as the National Kidney Federation Home Dialysis campaign and the Dialysis at Yours: Life Fulfilled (DayLife) initiative, which is part of the Kidney Quality Improvement Partnership (KQuIP). Kidney Research UK’s Acceptance, Choice and Empowerment (ACE) pilot project demonstrated how peer education can make a positive impact but is yet to be rolled out further\(^{24}\). Monitoring of the impact of these initiatives for take up in patients least likely to adopt home therapies will be important.
Transplantation
Primary research is recommended

- Original recommendation 25: To identify if there is variation by transplant centre in the listing of patients from groups where health inequalities are likely to be prevalent, for example, minority ethnic heritage, migrant and elderly populations.

Much of this has been addressed by the publications from the AT TOM study, although these results must inform interventions to reduce variations in access to transplantation for all.

- Original recommendation 26: To establish whether there are inequalities in kidney transplant outcomes in the UK. Where these have been demonstrated in other countries, they often reflect health system or indigenous populations that do not apply to the other populations. A comprehensive UK assessment has recently been published.

Kidney transplantation broadly improves survival in transplant candidates when considering factors such as ethnic heritage. However, there is limited understanding of how wider disadvantages impact transplant equality of outcome.

Conservative care
Primary research is recommended

- Original recommendation 27: To understand how the documented variation in provision of conservative care affects disadvantaged populations. This will need to look beyond the traditional clinical factors to include the communication of risk and benefit and culturally specific issues such as religious beliefs.

This remains an unaddressed area with more research required. Primary research focusing on cultural attitudes to end of life care among patients, carers and health care staff, structural barriers in access to conservative care pathways and patient/carer experiences of these services will be required.

New research recommendations

Dialysis
Primary research is recommended

- To understand ongoing barriers and approaches to supporting informed decision making about home therapies, addressing disadvantage arising from factors such as income, education, ethnicity, disability, geography, housing or health literacy.

Transplantation
Primary research is recommended

- To develop further interventions to mitigate disadvantage in pre-emptive transplant listing. Exploring what has worked, why or why not from existing efforts will be important.
- To understand delays in survival advantage in transplantation considering factors such as susceptibility to complications and reasons for their occurrence.

Conservative care
Primary research is recommended

- To understand ongoing barriers and approaches to supporting informed decision making about kidney failure treatment options for frail older people with multi-morbidity, addressing disadvantages arising from factors such as income, education, ethnicity, disability, geography and or health literacy.
References


2. Adults starting kidney replacement therapy (KRT) for end-stage kidney disease (ESKD) in the UK in 2021. Chapter 2 Adults starting kidney replacement therapy (KRT) for end-stage kidney disease (ESKD) in the UK in 2020.


12. Adults with a kidney transplant (Tx) in the UK at the end of 2021 Chapter 4 Adults with a kidney transplant (Tx) in the UK at the end of 2020.


11. Recommendations

Professor Shivani Sharma, Dr Bnar Talabani, Dr Gavin Dreyer, Professor Fergus Caskey, Dr Emily Beadle

This chapter presents an overarching synthesis of key themes evidenced in relation to kidney health inequalities throughout this five-year review. Following a consensus building exercise, the outcomes of prioritisation informed by patients, healthcare professionals, and wider stakeholders are also shared with a focus on AKI, dimensions of CKD, and ESKD.

As an aid to the kidney research community, the recommendations within the 2018 report are revisited, summarising where progress has been made and where existing and new actions have been identified in the mapping of disparities. It is intended that by summarising the report and its recommendations in this way, researchers, funders, health policy makers and commissioners will be able to use the chapter as a tool to support planning to accelerate the pace and scale of action aimed at mitigating inequalities. It is intended that by summarising the report and its recommendations in this way, researchers, funders, health policy makers and commissioners will be able to use the chapter as a tool to support planning to accelerate the pace and scale of action aimed at mitigating inequalities. A full list of recommendations can be found on the Kidney Research UK website.

Overarching thematic synthesis

Reflecting on the evidence presented within this review, there are several overarching themes. As the patients most vulnerable to kidney health inequalities often experience greater burden of societal issues, it is recognised that the kidney care and research community have a role to play within a wider, whole systems approach to advancing health and wellbeing for all. The themes identified include:

- Genetic risk factors and the social determinants of health: Though there is greater awareness of risk factors stemming from genetic variables, and appreciation of the societal inequalities that shape kidney health and outcomes, there is a need for this knowledge to frame action more consistently. Further, drawing on knowledge of risk and modifiable factors, research could help embrace a life course perspective to kidney health outcomes, something which appears to be explicitly missing from collective efforts. This recognises how knowledge on genetic, environmental, and social exposures over an individual’s lifetime impacts CKD and its outcomes, offering multiple, coordinated junctures to target the prevention and intervention effort. This may also facilitate further collaboration between public health, primary, and specialist healthcare services, which is highly relevant in the context of changing public demography. Notably, the bidirectional relationship between mental health and kidney disease was missing from thematic syntheses in this review but forms part of understanding the clustering of disadvantages that complicate prevention, identification, and intervention.

- Access to meaningful kidney health communication: Disparities persist that mean some patients do not have access to the right information, at the right time, and in a way that is accessible as per individual need and or preference. This makes it difficult to make informed decisions to guide health behaviour and engagement with interventions. Across the kidney care continuum, from prevention to intervention and management, further evidence is needed about effective public health communication aimed at stopping CKD or communicating the meaning of a CKD or AKI diagnosis and associated care.
• **Reach of therapies and interventions:** Major health innovations, from forms of kidney replacement therapies to behavioural science informed approaches to slow down or reduce the impact of CKD or AKI, have limited reach into the most disadvantaged communities. Paediatric patients are under-served in reference to the majority of research cited within this review, and much of the evidence for inequalities has not translated into suitably adapted, scalable and sustainable interventions to mitigate disadvantage from factors such as ethnicity e.g. inequalities in pre-emptive transplant listing, access to donor organs. There is a huge opportunity to build capacity in research to allow meaningful engagement in priority setting, research management, and participation from patients with diverse personal demographics and life experiences. Notably, such disadvantages rarely sit in isolation. Their intersecting nature and impact on therapeutic and intervention engagement should be considered.

• **Leveraging research, and technological advances:** Scientific methods and technology underpinning digital health innovation is rapidly evolving. The benefits are far reaching for prevention, management, patient experience, cost reduction in public health and care delivery, and ultimately, for kidney health. The extent to which such solutions are being optimised to reduce kidney health inequalities remains unclear though an area where opportunity is likely extensive, and action welcomed by patients.

**Prioritising action**

This review continues to call for action to address kidney health inequalities from basic science to behavioural sciences. This is to promote a whole community approach to mitigating disadvantage. Following a prioritisation exercise of the new recommendations within this review by a community of stakeholders (see methods – chapter four), the following areas emerge as the most highly ranked within the categories of AKI, CKD prevention, CKD intervention and ESKD.

**Acute kidney injury**

1) To undertake qualitative research work to understand and overcome the barriers to proactive diagnosis, monitoring and treatment after AKI, particularly in areas of high socio-economic deprivation, but also to include the perspective of older individuals and those from minority ethnic groups.

2) To develop and test communication methods for healthcare professionals that build confidence in interactions with patients and the public about kidney disease risk, implementing lifestyle changes, and communicating the meaning and implications of an AKI diagnosis.

3) To identify biomarkers and explore their utility in identifying at risk populations who fail to recover from AKI and relate this back to genetic and epigenetic risk factors.

**Chronic kidney disease**

**Prevention**

1) To identify ways to address the needs of those at greatest CKD risk more effectively, more evidence is needed on not only inequality and variation but on fairness and equity, considering both horizontal (equal care for equal need) and vertical (unequal care for unequal need).

2) To develop and test communication methods for healthcare professionals that build confidence in interactions with patients and the public about kidney disease risk, implementing lifestyle changes and communicating the meaning and implications of a CKD diagnosis.

3) To identify, develop and test accessible methods to improve kidney disease health literacy among members of the public, patients, and health professionals.
Intervention

1) To include people with CKD in clinical trials, whether commercial or investigator-led, as default. The Covid RECOVERY trial was an excellent example of inclusivity and probably reduced inequalities for people with CKD being treated during the pandemic.

2) To re-evaluate the role of screening for CKD both at population level and among existing and emerging underserved and high-risk groups.

3) To design and develop trials of novel primary care and integrated care-based management of CKD for high-risk populations, focusing on earlier detection (including through increased ACR measurement), which will allow: 1) Improved personalised risk prediction for KRT (through KFRE) and cardiovascular disease, 2) Improved personalised management of CKD such as with blood pressure targets and the use of specific therapies.

End stage kidney disease

1) To understand ongoing barriers and approaches to supporting informed decision making about home therapies, addressing disadvantage arising from factors such as income, education, ethnicity, disability, geography, housing and / or health literacy.

2) To understand ongoing barriers and approaches to supporting informed decision making about kidney failure treatment options for frail older people with multi-morbidity, addressing disadvantage arising from factors such as income, education, ethnicity, disability, geography and or health literacy.

3) To develop further interventions to mitigate disadvantage in pre-emptive transplant listing. Exploring what has worked, why, or why not from existing efforts will be important.

Acute kidney injury

1) To undertake qualitative research work to understand and overcome the barriers to proactive diagnosis, monitoring and treatment after AKI, particularly in areas of high socio-economic deprivation, but also to include the perspective of older individuals and those from minority ethnic groups.

2) To develop and test communication methods for healthcare professionals that build confidence in interactions with patients and the public about kidney disease risk, implementing lifestyle changes, and communicating the meaning and implications of an AKI diagnosis.

3) To identify biomarkers and explore their utility in identifying at risk populations who fail to recover from AKI and relate this back to genetic and epigenetic risk factors.

4) Leverage omics data to understand the role of genetic drivers, epigenetic drivers and other factors which contribute to increased risk of AKI in minority ethnic populations using APOL1 research as an exemplar.

5) To collect non-traditional data in AKI related studies such as:
   a) Further exploration of PROMs that are specific to the lived experience of different ethnic groups and / or according to varied socio-economic factors will be important, and could be informed by patient engagement and qualitative work
   b) Underreported risk factors related to inequalities such as employment history, education status, air and noise pollution, housing, immigration status, and English as a first language.

Chronic kidney disease

Prevention

1) To identify ways to address the needs of those at greatest CKD risk more effectively, more evidence is needed on not only inequality and variation but on fairness and equity, considering both horizontal (equal care for equal need) and vertical (unequal care for unequal need). For this, consistent data collection centred on social and wider determinants of health is necessary.

2) To develop and test communication methods for healthcare professionals that build confidence in interactions with patients and the public about kidney disease risk, implementing lifestyle changes and communicating the meaning and implications of a CKD diagnosis.

Overall recommendations summarised thematically

The complete list of recommendations within each chapter of this review have been further summarised below under the headings of AKI, CKD prevention, CKD intervention, and ESKD. The top three in each are the top ranked as detailed above, while the others are numbered but not necessarily in ranked order. This is primarily to enable the research community to respond to the challenges facing patients within themed dimensions. Recommendations related to the scoping review of health inequalities during the Covid-19 pandemic are not duplicated where they overlap with theme specific priorities. Any new recommendations from this chapter are otherwise detailed under general recommendations.
To identify, develop and test accessible methods to improve kidney disease health literacy among members of the public, patients, and health professionals.

To collect non-traditional data in CKD related studies such as:

- Further exploration of PROMs that are specific to the lived experience of different ethnic groups and / or according to varied socio-economic factors will be important, and could be informed by patient engagement and qualitative work
- Underreported risk factors related to inequalities such as employment history, education status, air and noise pollution, housing, immigration status, and English as a first language.

Nutritional and / or pharmacological interventions to increase foetal kidney size and reduce long term risk among individuals with LBW or renal size. Advocating for concurrent qualitative studies and realistic evaluation to understand acceptability and applicability of such interventions.

Biomarker studies: requirement to further characterise utility of biomarkers of renal tubular reserve (e.g. uEGF / creatinine ratio) in longitudinal studies including minority ethnic populations and relate these to birth weight and renal size.

Identify and explore mechanistic targets using omics data to understand the role of genetic drivers, epigenetic drivers and other factors which contribute to increased risk of CKD in minority ethnic populations using APOL1 research as an exemplar.

To improve understanding of the population-level impact of obesity, salt consumption, smoking, physical inactivity and limited health literacy on CKD incidence and prevalence to inform future population level interventions.

Intervention

To include people with CKD in clinical trials, whether commercial or investigator-led, as default. The Covid RECOVERY trial was an excellent example of inclusivity and probably reduced inequalities for people with CKD being treated during the pandemic.

To re-evaluate the role of screening for CKD both at population level and among existing and emerging underserved and high-risk groups.

To design and develop trials of novel primary care and integrated care-based management of CKD for high-risk populations, focusing on earlier detection (including through increased ACR measurement), which will allow:

- Improved personalised risk prediction for KRT (through KFRE) and cardiovascular disease
- Improved personalised management of CKD such as with blood pressure targets and the use of specific therapies.

To summarise the current evidence for clinical implementation trials of urine ACR measurement for the UK’s general population, particularly high-risk groups facing inequalities.

To summarise the current evidence for barriers in delivering evidence-based CKD care for underserved populations, including prescription of RAASI blockers and SGLT2 inhibitors, to inform future implementation work.

To develop clinical trials of lifestyle and education interventions tailored to people from underserved communities to empower them to manage their kidney condition and other related long-term conditions.

End stage kidney disease

To understand ongoing barriers and approaches to supporting informed decision making about home therapies, addressing disadvantage arising from factors such as income, education, ethnicity, disability, geography, housing and / or health literacy.

To understand ongoing barriers and approaches to supporting informed decision making about kidney failure treatment options for frail older people with multi-morbidity, addressing disadvantage arising from factors such as income, education, ethnicity, disability, geography and or health literacy.

To develop further interventions to mitigate disadvantage in pre-emptive transplant listing. Exploring what has worked, why, or why not from existing efforts will be important.

To understand delays in survival advantage in transplantation considering factors such as susceptibility to complications and reasons for their occurrence.

To collect non-traditional data in ESKD related studies such as further exploration of PROMs that are specific to the lived experience of different ethnic groups and / or according to varied socio-economic factors will be important, and could be informed by patient engagement and qualitative work.
Review of progress made on the recommendations from the 2018 report

Significant progress has been made in areas of both the 17 topic specific recommendations from the 2018 Kidney Health Inequalities report and the ten broad research recommendations. The 17 topic specific recommendations have been reviewed by and comments on previous chapters in this report. However, there are ongoing areas where additional consideration of previous broad recommendations in 2018 is warranted.

The editorial team have highlighted two of the original broad recommendations which are considered of particular importance.

**Original recommendation 7:** Change research recruitment practice and infrastructure to enhance the inclusion of disadvantaged populations in primary research – Kidney Research UK must find efficient ways to make the inclusion of disadvantaged populations in primary research studies the default position.

The actions associated with this recommendation – translated research materials, studies powered to detect differences in underserved populations and peer educators or community connectors to increase recruitment – need to be normalised as part of research practice in kidney care. Exemplars of good practice need to be established and promoted. Researchers should also be encouraged to draw on the range of research tools that have evolved to support equality impact assessments in their methodological decision making.

**Original recommendation 9:** Assess the impact of all clinical research and service development on kidney health inequalities.

A mapping funded by NHS England as part of the Research Engagement Network has enabled members of the editorial team (Shivani Sharma, Emily Beadle and Fergus Caskey) to consider access to kidney research in primary and secondary care across three Integrated Care Board regions. Data from the past five years showed that out of 142 studies, only 6% included adaptations such as non-English language inclusion. There was limited consideration of the wider barriers to engagement in kidney research also, for example, disability inclusion. These findings will yield recommendations that can help support infrastructure development and capacity building. For example, by detailing how barriers to kidney research involvement can be mitigated using a whole systems approach.

It has been challenging to quantify progress on reducing health inequalities. Some new tools at national level including the Renal Services Transformation Programme (RSTP) dashboard will provide data and insights into the changing landscape of health inequalities but are limited by the lack of contemporary data. A sustainable system for data collection and impact assessment from research into kidney health inequalities both funded internally by Kidney Research UK and external organisations is required to ensure value from and impact of research funding is prospectively collected.
Additional research recommendations

Further to the chapter and topic specific recommendations, the members of the editorial team have identified additional recommendations for ongoing research activity by the UK kidney community and partners. These are numbered for reference but not ranked in order of importance or priority.

1) Engage with clinicians, academics, patients, families and carers to include children and young adults in research activity for health inequalities in paediatric kidney care. The recently announced, new investment in a research centre for rare disease may, for example, support this aim.

2) Build consensus to determine optimum methodology for patient focussed research into kidney health inequalities – co-creation compared to co-production with patients.

3) For funders of research to address the mismatch of research funds relative to patient care cost for inequalities in kidney disease.

4) Broaden the research community for kidney health inequalities to actively engage multi-disciplinary research expertise.

5) Take action to mitigate the potential risks that the use of artificial intelligence (AI) within research and healthcare will increase kidney health inequalities.

6) Explore ways to utilise AI to reduce kidney health inequalities.

7) Strengthen reporting of patient demographic and social factors and the intersection between these variables and their relationship to kidney health inequalities. For example, a standardised framework for reporting on patient demographic and social circumstances. This will help contribute to a fuller understanding of health inequalities and their mitigation.

8) Address the lack of evidence on the intersection of mental health and wider social determinants in relation to kidney health inequalities and their mitigation.

9) A systematic review with embedded meta-analysis is recommended to fully consider the impact of age, sex, ethnicity, and deprivation on Covid infection and outcomes amongst CKD patients.

10) Evidence is lacking on the longer-term clinical relevance of Covid infection in CKD. Partnership with patients should help shape specific research priorities, ensuring that care is responsive to need.

11) Primary research is recommended to understand recovery from AKI related to Covid infection. This is to enable early identification of kidney damage.

12) Deliver implementation research for kidney health inequalities in clinical kidney networks to enhance adoption and implementation of research evidence beyond pilot or small scale, time limited support.

13) Leverage the report and expertise in the kidney community to maximise sustained funding for research into kidney health inequalities.

14) Work with other medical / disease specific organisations and networks, beyond the kidney community, to identify intersectionality in health inequalities research to build sustainable academic and funding partnerships.

Included within the basic science chapter were three general recommendations:

15) Investment in training bioinformaticians: This is to support multi-omic studies in both animal models and humans.
   - To define and characterise renal development and composition
   - To study the implication of nephron loss and response to injury
   - To allow rapid analysis of the generated omics to study the molecular mechanisms / genetic causes underpinning premature biological aging, AKI, CKD
   - To facilitate more rapid biomarker analysis in cohorts such as those contained within NURTuRE

16) Human studies should ensure inclusion of individuals at high risk (particularly those with known barriers to research participation) versus low risk of CKD progression, and both males and females. This will require infrastructure support including sequencing costs, bioinformatics training and access to biobanking of relevant human samples for analysis.

17) Support the discovery and validation of novel, and ideally non-invasive, prognostic biomarkers e.g. microRNAs26,27 in minority ethnic populations and the replication of studies using imaging methods as discussed being funded and performed in ethnically diverse populations.
12. Conclusions

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This five-year review on kidney health inequalities serves as a resource for health policy makers, national and local leaders, research funders, clinicians, researchers, and patients. It is a guide to understanding the scale of kidney health inequalities and the specific themes within which further research is necessary to reduce disadvantage. Whilst there is increasing awareness of inequalities and how they impact CKD and AKI occurrence, progression and outcomes, this knowledge inconsistently shapes everyday care and research to serve the diverse needs and preferences of people affected by CKD at any stage of life. It is hoped the report will contribute to the larger body of evidence, both from the Kidney Research UK, and wider forums, that signposts the far-reaching consequences of not taking enough, the right, or any action.

There are opportunities and risks arising from the shift in responsibility for commissioning of care for kidney failure from (regional) specialised services to the (local) system level. Awareness of local issues and the ability to innovate in response are now more feasible than they were, but the kidney community, clinical and academic, must ensure that health inequalities are not exacerbated in less mature and less innovative Integrated Care Systems.

There are significant opportunities to ensure that all patients and their families have access to participation in research and derive benefit from its outcomes, and that their contributions drive meaningful, scalable and sustainable change. Opportunity needs to be met by resource investment.

Emerging from the Covid-19 pandemic, there is a very welcome political drive to encourage commercial research in the UK and attract industry partners wishing to evaluate their emerging disease modifying therapies; we must ensure that people with kidney disease – adults and children – have equal access to the clinical trials of these breakthrough treatments.

Against the backdrop of fragmented health policy support for kidney disease, there is a strong case for more co-ordinated strategies regionally and nationally to reduce kidney health disparities, particularly by embracing a life-course approach to bring different agencies together in a shared endeavour – identifying when AKI and CKD are coming and stopping them or reducing their impact on people and society at large. Advances in research methods and health innovations are yet to be maximised to support this effort. Patients rightly call for moving from short-term fixes to a unified, sustainable approach to mitigating kidney health disparities to rebuild trust in health systems.

As a charity, Kidney Research UK hopes to play a pivotal role by shaping research agendas with a stronger focus on translation and implementation sciences, alongside continuing to push primary and secondary prevention of CKD and AKI that equitably serves the UK population.
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