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Climate Health Emergency: Medicine 2050

The future of nephrology in 2050

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ABSTRACT

As medicine advances at an unprecedented pace, the field of nephrology is poised for transformative change. By 2050, breakthroughs in kidney disease prevention, dialysis, transplantation, and omics-driven precision medicine could redefine patient care and outcomes. Here, we share our perspectives on the challenges faced and how changes in health policy, emerging technologies, novel therapies, and data-driven approaches might shape the future of nephrology. From innovative dialysis solutions to xenotransplantation and AI-powered diagnostics, we explore the possibilities that could revolutionise kidney health in the decades to come.

Prevention of kidney disease

In 2025, policy makers realised that unless there was an early intervention for the 30% overweight or obese school children, there would be a tsunami of middle-aged adults with multimorbidity overwhelming the NHS, including insulin-resistant diabetes and kidney disease (Fig. 1). This is why in 2050 it is considered most cost-effective to treat obesity in young people with school-based screening / early interventions including weight loss drugs,[1] and to have a population-wide screening and intervention programme to find and reverse type 2 diabetes with moderate calorie restriction, exercise and SLGT2i treatment.[2]

In 2050, the government has invested in more health education at schools and fully funded healthy school meals for all children to prevent chronic disease later in life. Tobacco products are illegal, and tobacco companies are still paying out for smoking-related health damage. Tobacco products have lost appeal for young people, similar to what happened decades ago with regards to alcohol, which was seen as 'uncool'. Alcohol-containing products are more difficult to sell compared to healthier alcohol-free versions, as those have less impact on body weight. Young obese women are aware that they need to optimise their overall health before getting pregnant, reducing the risk of pre-eclampsia and gestational diabetes. All women will have access to health visitors and social support during pregnancy, similar to the type of support that families with young children receive, and the burden of births with congenital disease related to diabetes in pregnancy, premature births, and low birth weight has halved compared to 2025.

Working-age staff will be an increasingly scarce resource and staff recruitment costs a driver of inflation. Hence, policy makers will have rolled out aggressive prevention programmes, and childcare support to keep people working. People with learning disabilities and severe mental health problems are most likely to have cardiovascular and kidney problems, and receive access to workplace coaching, adequate adjustments for their needs at work, and personalised exercise coaching that is integrated with their mental health support. Because the economic output is measured in a circular fashion, the economic contribution of caring jobs is appropriately remunerated, now representing a significant part of the UK's GDP, and being a sector that artificial intelligence (AI) cannot effectively replace. There are fewer 'nursing homes' and more 'care at home' facilities in large co-housing communities of older residents sharing with students near hospital facilities. Older people who cannot cook for themselves receive 'meals on wheels', which are tailored to their needs in terms of diabetes, heart failure and chronic kidney disease (CKD) with known carbohydrate load (to allow dosing of medication) and low salt content to prevent nutrition-related admissions.

In 2050, the one-third of middle-aged adults who had grown up in significant poverty may unfortunately struggle with their mental health, accessing the diabetes treatment reversal programme, and maintaining weight loss, which means that many require permanent GLP-1 agonist therapy to prevent worsening of their established multimorbidity. Because of aggressive prevention and treatment of kidney disease, dialysis rates in 2050 are similar to 2025. Approximately 20% of the population live with CKD, with 10% being GLP-1 agonist-dependent patients whose

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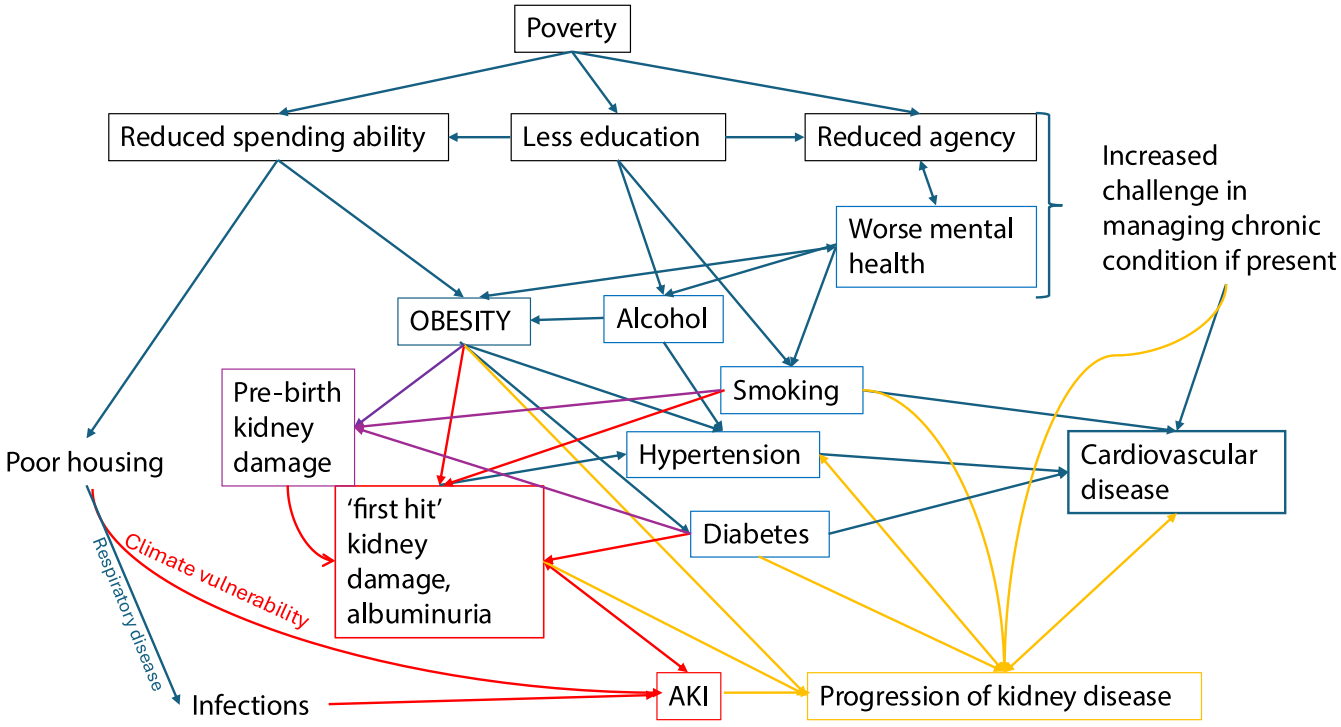

Fig. 1. Conceptual diagram of common population-based risk factors for initial kidney damage and contributors for kidney disease progression. Purple arrows (risk factors for pre-birth kidney damage) and red arrows (risk factors for kidney damage in later life) highlight primary prevention pathways; secondary prevention of delaying kidney disease progression is highlighted by orange arrows.

progression of kidney disease has been halted but not reversed, and the other 10% frail older community-dwelling adults who have opted against dialysis. Both groups are at significant risk of acute kidney injury, and are prioritised for vaccination to prevent seasonal infections and against all pandemic strain viruses, which tend to occur every few years. There will be extra housing support for homes, with adequate cooling/heating facilities and adequate ventilation for people with advanced CKD to prevent climate-related hospital admissions.

Many of the working-age CKD patients will have many practical challenges to solve: apart from maintaining their job, supporting their children who cannot afford to leave the parental home due to high housing costs in urban areas, they need to organise care and support for their older family members with CKD, many of whom live in coastal areas. This is why in 2050, after decade-long campaigning by patient charities, there is a social service support bursary for affected families to receive timely social care support.

Dialysis

The number of people with CKD continues to increase worldwide, and although newer treatments and targeted health policies may help retard the progression to end-stage kidney disease (ESKD), it is expected that the number of patients requiring treatment for ESKD will continue to increase. Although kidney transplantation would be the most preferable treatment, unless alternatives to cadaveric or living-donor solid organ transplantation can be developed as discussed below, then due to cultural and religious mores, the majority of patients with ESKD will require some form of dialysis treatment. Although dialysis using exchange with the gastrointestinal tract has been tried, patients are currently treated with peritoneal dialysis (PD) using exchanges between dialysate instilled into the peritoneal cavity and the gastrointestinal and peritoneal vasculature, and haemodialysis (HD) with clearance of waste products of metabolism as blood is passed through an extracorporeal circuit.

Both PD and HD require single passage of dialysates and generate large amounts of medical plastic wastes that currently cannot be recycled. As such, the first key question is whether the amount of water required for dialysis can be reduced, as the environmental impact of excessive water consumption has been highlighted. To reduce the amount of water required to produce dialysate, then recycling of the dialysate is required. Several groups are currently working on dialysis treatments using sorbents, which could refresh waste dialysate, and allow recycling of dialysate. These include both portable wearable haemodialysis and peritoneal treatments, designed to be worn continuously. These devices including the WAK and AWAK have currently undergone proof of concept clinical trials and are expected to be developed into devices available for routine clinical practice for suitable patients. Although these devices would have a major impact on reducing the carbon footprint of dialysis treatments, and require fewer trained staff to support patients, these newer developments will not be suitable for all patients.

Currently PD patients require delivery of litres of fresh dialysate packaged in plastic bags. Developments have led to the possibility of PD patients generating fresh dialysate in their own homes from the domestic water supply, so reducing carbon emissions in terms of the manufacture of plastics, transport and waste disposal. Haemodialysis utilises domestic water, which is then passed through water softeners, carbon filtration and reverse osmosis systems to provide dialysate-quality water. As such, a substantial volume of water is rejected and not used for the dialysis treatment. Improvements in water treatment technology and recycling the water initially rejected will reduce the amount of water discarded for dialysis treatments. Similarly, improvements in the design of dialysers improving the respective counter current flow of blood and dialysate, and so maximising diffusional clearance, has reduced the necessary dialysate flow to achieve the effective clearance of uraemic solutes, so dialysate flows of 700 mL/min are no longer required. Advances in dialysis machine technology have led to a newer generation of machines which link dialysate flow to blood flow, so that flows of 1.5:1.0 in HD mode and 1.2:1.0 in haemodiafiltration (HDF) mode are

now in clinical practice, and over time even lower dialysate flows are anticipated. HD treatments mix dialysis-quality water, acid concentrate and bicarbonate. Although dialysis centres produce dialysis-quality water on site, most centres then rely on external deliveries of plastic cannisters containing acid concentrate and bags of bicarbonate powder, which are then mixed by the dialysis machine. Newer developments allow the production of the final dialysate in the dialysis centre by mixing powdered acid concentrate and bicarbonate with water, so reducing plastic packaging, transport and waste disposal. Unless there are substantial advances in polymer technology, it is unlikely that biodegradable plastics would be suitable for dialysis treatments, as these would have to withstand sterilisation processes and yet retain sufficient tensile strength to withstand the pressures generated within the dialysis circuit.

Currently dialysis treatments are targeted at removing water-soluble uraemic toxins. However, experimental data suggest that protein-bound toxins increase the risk of cardiovascular disease, the major cause of mortality for patients with ESKD. As such, there has been interest in developing sorbent technology to increase the removal of these protein-bound toxins. All the prototype wearable PD and HD devices include sorbents and so are effective in removing these toxins. As for standard HD and HDF treatments, there are two options: firstly adding a sorbent into the dialyser membrane or including an additional sorbent monolith into the HD or PD circuit. However, as most of these toxins are produced by metabolism from colonic bacteria, then alternative approaches include using oral sorbents to bind these toxins in the gastrointestinal tract or to change the colonic microbiome by changes in diet and the use of probiotics. In terms of healthcare economics, the combinations of dietary modification, use of oral sorbents and probiotics would be expected to play a greater additional role in reducing the amounts of protein-bound toxic solutes required to be cleared by either PD or HD/HDF.

Transplantation

Transplant volume and recipient characteristics

Predominantly due to an aging and comorbid population, the prevalence of ESKD is predicted to rise sharply over the coming decade. A recent report from Kidney Research UK framing kidney disease as a 'public health emergency' suggests that the demand for transplantation could be as high as 12,000 per year by 2033.[3] This represents a four-fold increase on current transplant activity,[4] and if this rate of rise continues, around 200,000 kidney transplants per year will be needed to meet demand by 2050. Trends in recipient demographics will likely continue, with increasingly older patients transplanted, and novel infrastructure will need to be developed to cope with the increased demand. Transplant nephrology will become its own specialty separate from general nephrology, and dedicated transplant hospitals will need to be built.

Donor characteristics

Given this increased demand, every effort will be needed to expand the donor pool. Transplantation will be at the forefront of the political healthcare agenda, and national awareness schemes will result in a rise in donation rates. In the setting of a worsening climate crisis, healthcare systems will incentivise transplantation given its environmental benefit, and reimbursement will be significantly greater than that received for dialysis. Novel interventions, primarily targeting donor cardiometabolic risk, will facilitate living donation, and interventions pre- and post-retrieval will permit the use of kidneys from older and more comorbid deceased donors. These interventions, and subsequent organ retrieval, will occur in dedicated organ recovery centres, as already happens in some US states.[5] Use of machine perfusion technology will become routine, and post-retrieval organ modification will be undertaken, as has recently been shown possible to alter blood group.[6]

Xenotransplantation

However, other species will be needed to cope with the surge in transplant demand. Significant advances have recently been made in the field of xenotransplantation, with gene editing technology permitting the use of pig kidneys in human recipients. This was initially undertaken in brain-dead recipients,[7–10] but more recently a porcine kidney was transplanted into a living human recipient in a landmark moment for kidney transplantation in the USA.[11] Histological guidelines for rejection in xenotransplantation are under consideration and research remains active in the field. Xenotransplantation will become a realistic option for patients who are difficult to transplant, albeit longer-term outcomes using porcine kidneys will likely remain inferior to their human counterparts.

Organ allocation, immunosuppression and cell therapies

While short-term outcomes in kidney transplantation have significantly improved, largely the result of calcineurin inhibitor use and reduced acute rejection rates, there have been more modest advances in longer-term graft outcomes. Chronic alloimmune injury is the major contributor to graft loss, with current immunosuppression ineffective in its prevention and treatment. Mismatches in human leucocyte antigens (HLAs) are important drivers of this alloimmune response, and current allocation algorithms include points for HLA matching at a crude level. HLA matching is now possible at the molecular level[12] and HLA epitope matching will be incorporated into allocation schemes. HLA-incompatible transplantation will be facilitated by drugs targeting preformed circulating HLA antibodies (already in routine use in other countries)[13] alongside novel agents to target the underlying B and NK cell response.[14] However, increasingly patients will be able to rid themselves of immunosuppression altogether and the unwanted pill burden and side effects associated with traditional regimens. This will be made possible through the development of cell therapies, with non-specific[15,16] and antigen-specific[17] regulatory cell therapies already tested in clinical trials.

Precision medicine techniques post-transplant

Transplant follow-up will become predominantly patient initiated with wearable healthcare devices and point-of-care home testing becoming the norm. Clinical variables will be fed into centralised computer systems and AI-enabled algorithms will alert patients and clinicians of need for intervention. Standard biomarkers such as creatinine and proteinuria will be supported by more novel biomarkers, such as donor-derived cell-free DNA, urinary chemokines and gene expression profiles, already recommended by European guidelines.[18,19] Graft prediction systems, such as the iBox,[20] will be increasingly used in routine clinical practice and current histological analyses of transplant biopsies will be supported by transcriptomic analyses, already adopted by the Banff classification system for antibody-mediated rejection.[21] Ultimately, earlier detection of graft inflammation with more precise diagnosis of graft injury alongside better treatments will mean transplants may routinely last over 30 years.

Personalised kidney medicine

Early detection and risk stratification

By 2050, whole genome sequencing (WGS) is expected to become a routine part of neonatal care with a pilot study screening newborn babies for rare inherited disorders, including Alport syndrome, already underway.[22] WGS will expand to pre-implantation embryo and antenatal settings, enabling the identification (and potential correction) of rare monogenic kidney diseases (eg autosomal dominant polycystic kidney disease; ADPKD) *in utero*. In addition, whole-genome risk predic-

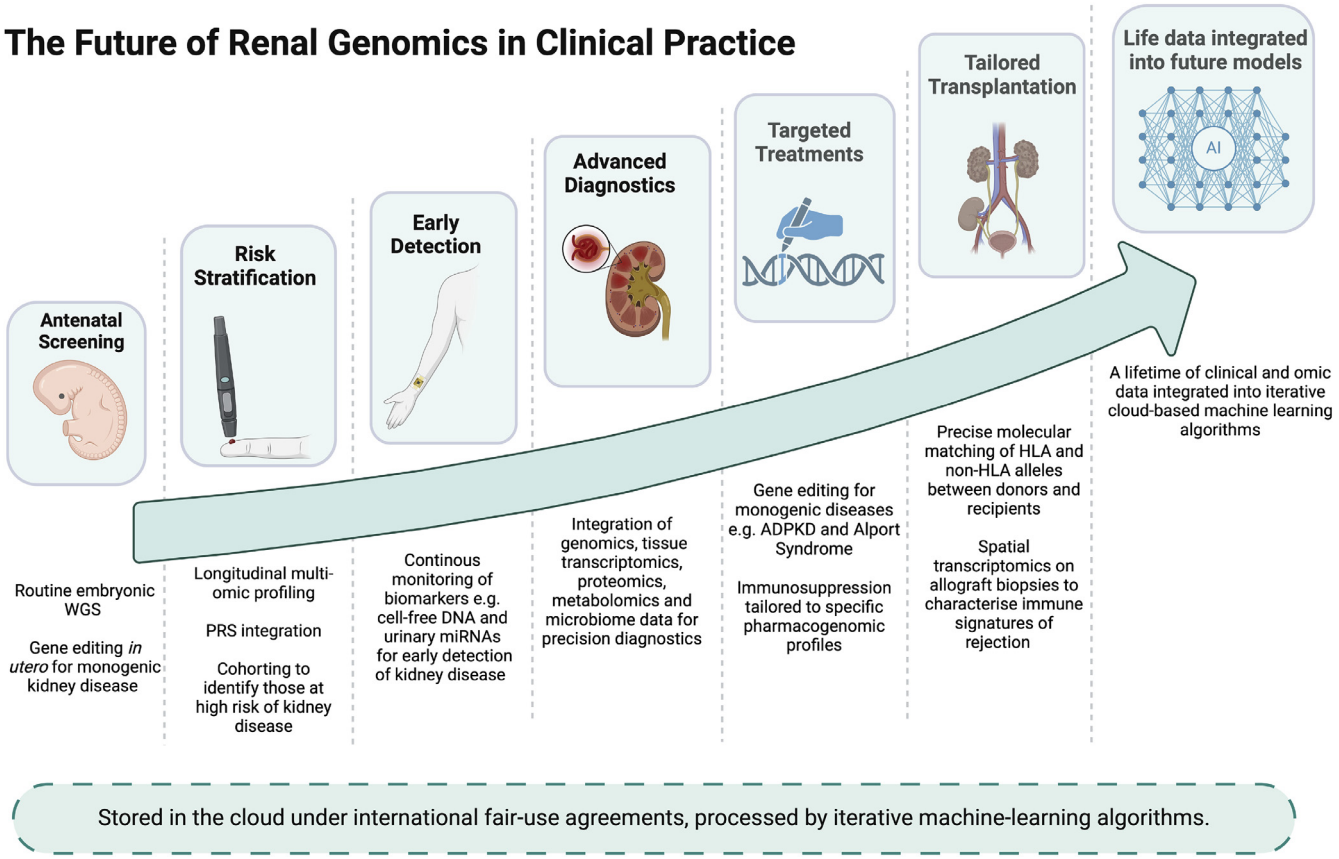

Fig. 2. The future of renal genomics and precision medicine across the life course. WGS, whole genome sequencing; PRS, polygenic risk score; miRNAs, micro RNAs; ADPKD, autosomal dominant polycystic kidney disease; HLA, human leucocyte antigen. Created in BioRender https://BioRender.com/k41l084.

tion using polygenic scores[23] for common kidney diseases, such as IgA nephropathy, and incorporating *APOL1* renal risk variants would identify those at highest risk of developing kidney disease and guide targeted screening and early intervention from birth (Fig. 2). A robust and comprehensive regulatory framework will, however, be essential to address the myriad of ethical issues raised including the use of predictive genomic information to inform reproductive decision-making (so called 'designer babies') and to ensure equitable access to these new technologies to prevent worsening health disparities.

Driven by the boom in wearable health technology, the ease of multi-omic profiling and the ability for molecular signatures to improve prediction of common and rare disease;[24] continuous biomarker monitoring through wearable devices will integrate multiple molecular outputs, such as the entire circulating proteome or metabolome, to monitor for early signs of kidney disease.[25] This will enable better understanding of the role that one's environment has on genetic risk and disease physiology.

Advanced diagnostics and targeted treatments

High-resolution spatial transcriptomics and proteomics (mapping genes and proteins within the spatial context of a tissue) will become integrated into digital pathology workflows. Identification of inflammatory or fibrotic microenvironments with specific molecular signatures will improve prognostication[26] and enable therapies targeted at the underlying disease mechanism, leveraging pharmacogenomics to optimise drug therapy, minimise adverse effects and maximise efficacy. In transplantation, spatial omics will enhance the detection of subclinical rejection or chronic allograft dysfunction, enabling timely interventions and improving graft survival.

Gene therapy, targeted specifically at the kidney cell type of interest, will be used to treat genetic diseases such as congenital nephrotic syndrome.[27] The scope of therapeutic small interfering RNAs (siRNAs) and antisense oligonucleotides (which modulate gene expression) will expand beyond hereditary transthyretin-mediated amyloidosis and primary hyperoxaluria to APOL1-mediated kidney disease, IgA nephropathy and other complement-mediated kidney diseases. Meanwhile, breakthroughs in CRISPR-based gene editing therapies, such as the recently approved Casgevy for sickle-cell disease and beta thalassaemia,[28] will open avenues for the development of curative therapies for monogenic disorders like ADPKD and Alport syndrome by 2050.

Big data

Central to these advances will be advanced AI algorithms to analyse generated data as well as cloud-based storage solutions allowing rapid data access globally. Iterative machine learning algorithms will 'churn' over the data, refining and customising prediction models as new information is added.[29] Personalised models will incorporate each patient's unique genomic and biomarker profiles, alongside lifestyle and environmental factors, enabling precise, proactive management strategies.

The sheer volume of personal data from genomics, multi-omics and digital health technologies has made true anonymity impossible. Even deidentified data can be reidentified through cross-referencing.[30] This necessitates international collaboration to establish unified regulations on the permissible uses of individual-level data. Legislators must balance innovation with ethical safeguards, defining clear limitations on data sharing, robust consent mechanisms, and protection against discrimination. Transparency is key – individuals should have control over their data and understand its use. A global framework is essential to

protect privacy, foster trust, and responsibly harness data for scientific advancement and preventative medicine.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Melanie MY Chan: Writing – review & editing, Writing – original draft. **Omid Sadeghi-Alavijeh:** Writing – review & editing, Writing – original draft. **Rhys DR Evans:** Writing – review & editing, Writing – original draft. **Andrew Davenport:** Writing – review & editing, Writing – original draft. **Dorothea Nitsch:** Writing – review & editing, Writing – original draft.

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