Are your kidneys OK? Detect early to protect kidney health

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ABSTRACT

Early identification of kidney disease can protect kidney health, prevent disease progression and related complications, reduce cardiovascular risk, and decrease mortality. We must ask, "Are your kidneys OK?" by using serum creatinine to estimate kidney function and urine albumin to assess for kidney and endothelial damage. Evaluation of the causes and risk factors for chronic kidney disease includes testing for diabetes and measuring blood pressure and body mass index. This World Kidney Day, we assert that case-finding in high-risk populations—or even population-level screening—can decrease the global burden of kidney disease. Early-stage chronic kidney disease is asymptomatic, simple to test for, and recent paradigm-shifting treatments (eg, sodium-glucose co-transporter-2 inhibitors) dramatically improve outcomes and strengthen the cost–benefit case for screening or case-finding programmes. Despite these factors, numerous barriers exist, including resource allocation, healthcare funding, infrastructure, and healthcare professional and public awareness of kidney disease. Coordinated efforts by major kidney non-governmental organisations to prioritise the kidney health agenda for governments—and to align early detection efforts with existing programmes—will maximise efficiencies.

Introduction

Timely treatment is the primary strategy to protect kidney health, prevent disease progression and related complications, reduce cardiovascular risk, and prevent premature kidney-related and cardiovascular mortality.[1-3] International population assessments show low awareness and detection of kidney disease, along with substantial gaps in treatment.[2] People with kidney failure universally express a preference for having been diagnosed earlier in their disease trajectory, which would allow more time for educational, lifestyle, and pharmacological interventions.[4] Therefore, increasing knowledge and implementing sustainable solutions for the early detection of kidney disease to protect kidney health are public health priorities.[2,3]

Epidemiology and complications of kidney disease

Chronic kidney disease (CKD) is prevalent, affecting 10% of the global population—over 700 million people.[5] Nearly 80% of people with CKD live in low-

income countries (LICs) and lower-middle-income countries (LMICs), and approximately one-third of the known affected population resides in China and India alone.[5,6] The prevalence of CKD increased by 33% between 1990 and 2017.[5] This rising trend is driven by population growth, ageing, and the obesity epidemic, which contribute to higher rates of two major CKD risk factors: type 2 diabetes mellitus (T2DM) and hypertension. Additionally, risk factors beyond cardiometabolic conditions add to the growing burden of kidney disease. These include social deprivation, pregnancy-related acute kidney injury, preterm birth, and escalating environmental threats such as infections, toxins, climate change, and air pollution.[5,7] These threats disproportionately affect people in LICs and LMICs.[8]

Undetected and untreated CKD is more likely to progress to kidney failure and cause premature morbidity and mortality. Globally, more people died in 2019 of cardiovascular disease attributed to reduced kidney function (1.7 million people) than the number who died of kidney disease alone (1.4 million).[5] Chronic kidney disease is expected to become the fifth most common cause of years of life lost by 2040, surpassing T2DM, Alzheimer's disease, and road injuries.[9] The rising mortality associated with kidney disease is particularly remarkable compared with other non-communicable diseases—such as cardiovascular disease, stroke, and respiratory illness—which are projected to exhibit declining mortality rates.[8] Even in its early stages, CKD is associated with multi-system morbidity that diminishes quality of life. Notably, mild cognitive impairment is linked to early-stage CKD; early detection and treatment could slow cognitive decline and reduce the risk of dementia.[10] Chronic kidney disease in children has profound additional consequences, threatening growth and cognitive development, with lifelong health and quality of life implications.[11,12] The number of people requiring kidney failure replacement therapy—dialysis or transplantation—is anticipated to more than double from 2010 to 2030, reaching 5.4 million.[13,14] Kidney failure replacement therapy, particularly haemodialysis, remains unavailable or unaffordable for many in LICs and LMICs, contributing to millions of deaths annually. Although LICs and LMICs comprise 48% of the global population, they represent only 7% of the treated kidney failure population.[15]

Who is at risk of kidney disease?

Testing individuals at high risk for kidney disease (case-finding) minimises potential harms and false-positive results compared with general population screening, which should only be considered in high-income countries (HICs). Testing limited to those at increased risk of CKD would still encompass a large proportion of the global population. Moreover, targeted case-finding in patients at high risk of CKD is not optimally performed, even within HICs. Approximately one in three people globally have diabetes and/or hypertension. There is a bidirectional relationship between cardiovascular disease and CKD—each increases the risk of the other. Both the American Heart Association and the European Society of Cardiology recommend testing individuals with cardiovascular disease for CKD as part of routine cardiovascular assessments.[1,16]

Other CKD risk factors include a family history of kidney disease (eg, APOL1-mediated kidney disease, which is common among individuals of West African ancestry), prior acute kidney injury, pregnancy-related kidney conditions (eg, pre-eclampsia), malignancy, autoimmune disorders (such as systemic lupus erythematosus and vasculitis), low birth weight or preterm birth, obstructive uropathy, recurrent kidney stones, and congenital anomalies of the kidney and urinary tract (Fig 1).[3] Social determinants of health strongly influence CKD risk, both at individual and national levels. In LICs and LMICs, heat stress among agricultural workers is thought to contribute to CKD of unknown aetiology—an increasingly recognised and major global cause of kidney disease.[17] Additionally, envenomations, environmental toxins, traditional medicines, and infections (such as hepatitis B or C, HIV, and parasitic diseases) warrant attention as risk factors, particularly in endemic regions.[18,19]

How can we check kidney health?

Conceptually, there are three levels of CKD prevention. Primary prevention aims to reduce the incidence of CKD by treating risk factors; secondary prevention focuses on slowing disease progression and reducing complications in those with diagnosed CKD; and tertiary prevention seeks to improve outcomes in people with kidney failure by enhancing management, such as through improved vaccination coverage and optimised dialysis delivery.[20] Primary and secondary prevention strategies can incorporate the eight golden rules for promoting kidney health: maintaining a healthy diet, ensuring adequate hydration, engaging in physical activity, monitoring and controlling blood pressure, monitoring and controlling blood glucose levels, avoiding nicotine, avoiding regular use of non-steroidal anti-inflammatory drugs, and targeted testing for those with risk factors.[21] Five of these rules are identical to Life's Essential 8—guidelines for maintaining cardiovascular health—which also include achieving a healthy weight, getting adequate sleep, and managing lipid levels.[22] Early detection efforts are a form of secondary prevention that involves protecting kidney health and reducing cardiovascular risk.

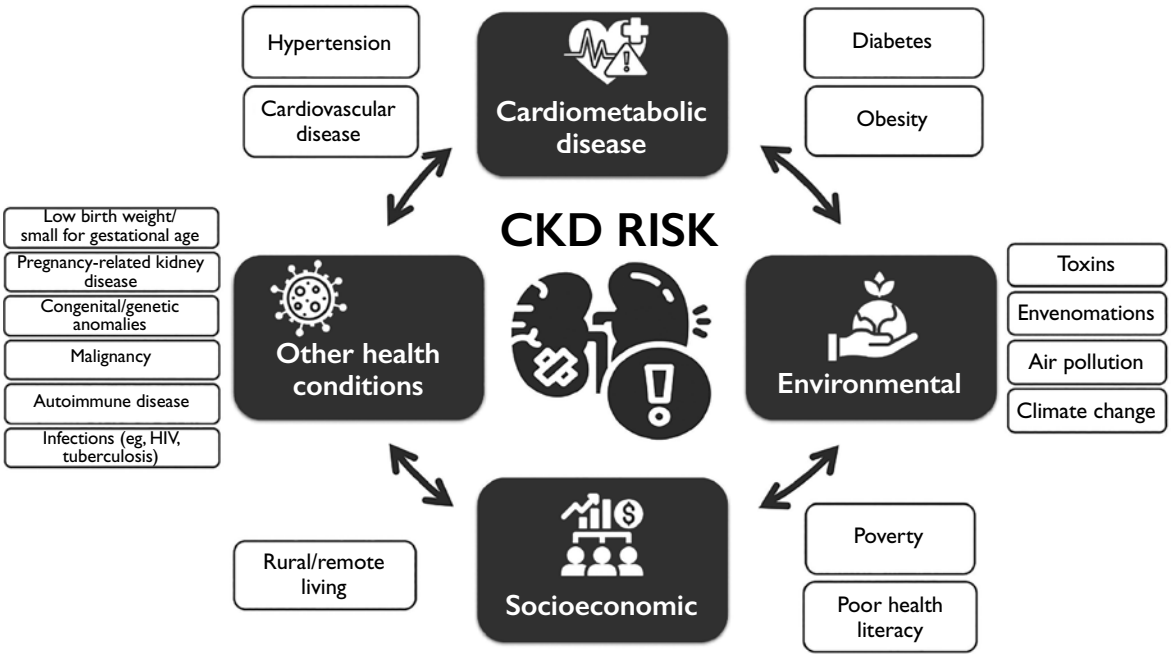

FIG 1. Risk factors for chronic kidney disease (CKD)[3]

Are your kidneys OK?

Globally, early detection of CKD remains rare, inconsistent, and less likely in LICs or LMICs. Currently, only three countries have a national programme for actively testing at-risk populations for CKD, and a further 17 countries perform such testing during routine healthcare encounters.[23] Even in HICs, albuminuria is not assessed in more than half of individuals with T2DM and/or hypertension.[24-26] Startlingly, a diagnosis of CKD is often absent even among those with documented reduced kidney function. A study conducted in HICs showed that 62% to 96% of individuals with laboratory evidence of CKD stage G3 had no recorded diagnosis of CKD.[27]

We recommend that healthcare professionals perform the following tests for all risk groups to assess kidney health (Fig 2[28]):

a) Blood pressure measurement: Hypertension is the most prevalent risk factor for kidney disease worldwide.[3,29,30]
b) Body mass index: Obesity is epidemiologically associated with CKD risk, both indirectly (via T2DM and hypertension) and directly, as an independent risk factor. Visceral adiposity contributes to monocyte-driven microinflammation and increased cardiometabolic kidney risk.[3,29,30]
c) Testing for diabetes: Assessment with glycosylated haemoglobin, fasting blood glucose, or random glucose should be part of kidney health screening because T2DM is a common risk factor.[3,29,30]
d) Evaluation of kidney function: Serum creatinine should be used to estimated glomerular filtration rate (eGFR) in all healthcare settings.[3] Glomerular filtration rate should be calculated using a validated, race-free equation appropriate for the specific country or region and age-group.[3] In general, eGFR <60 mL/min/1.73 m^2 is considered the threshold for CKD in adults and children; a threshold of <90 mL/min/1.73 m^2 can be regarded as 'low' in children and adolescents over the age of 2 years.[3] A limitation of creatinine-based eGFR is its sensitivity to nutritional status and muscle mass, which can lead to overestimation in states of malnutrition or frailty.[3,28] Thus, the use of both serum creatinine and cystatin C provides a more accurate estimate of eGFR in most clinical contexts. However, the feasibility of cystatin C testing is mainly limited to HICs because of assay availability and cost relative to creatinine testing.[3,28,31]
e) Testing for kidney damage (albuminuria): In both adults and children, a first morning urine sample is preferred for assessing albuminuria.[3] In adults, the quantitative urinary albumin–creatinine ratio (uACR) is the most sensitive and preferred test.[3] Analytical standardisation of urinary albumin is currently underway, which should eventually support global standardisation of uACR testing.[32] In children, both the protein–creatinine ratio and uACR should be tested to identify tubular proteinuria.[3] Semiquantitative albuminuria testing provides flexibility for point-of-care or home-based testing.[33] To be considered useful, semiquantitative or qualitative screening tests should correctly identify >85% of individuals with a quantitative uACR of ≥30 mg/g.[34] In

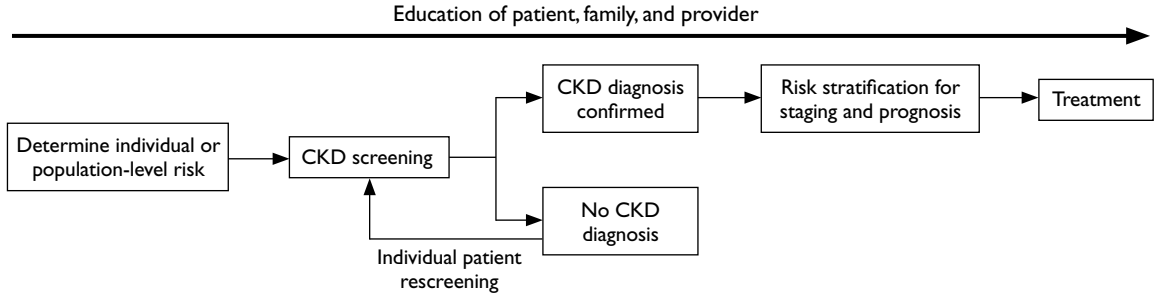

FIG 2. Conceptual framework for a chronic kidney disease (CKD) testing, risk stratification, and treatment programme[28]
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resource-limited settings, urine dipstick testing may be used, with a threshold of +2 proteinuria or greater to reduce false positives and guide repeat confirmatory testing.[35]

In specific populations, the following considerations may apply:

f) Testing for haematuria: Haematuria is often overlooked in recent clinical practice guidelines, despite its importance as a risk factor (particularly for individuals at risk of glomerular disease, such as immunoglobulin A nephropathy).[36]
g) Baseline imaging: Imaging should be performed in individuals presenting with signs or symptoms of structural abnormalities (eg, pain and haematuria) to identify kidney masses, cysts, stones, hydronephrosis, or urinary retention. Antenatal ultrasound can detect hydronephrosis and other congenital anomalies of the kidney and urinary tract.
h) Genetic testing: With increasing access to genetic diagnostics, family cascade testing for CKD is indicated where there is a known hereditary risk of kidney disease.[37]
i) Occupational health screening: Individuals with occupational risk of developing kidney disease should be offered kidney function testing as part of workplace health programmes.
j) Post-donation surveillance: Kidney donors should be included in long-term follow-up programmes to monitor kidney health after donation.[38]

Potential benefits of early detection

Screening for CKD aligns well with many of the World Health Organization (WHO)'s Wilson–Jungner principles.[39] Early-stage CKD is asymptomatic; effective interventions—including lifestyle modification, interdisciplinary care, and pharmacological treatments—are well established.[2,3,28,35] Several WHO Essential Medicines that improve CKD outcomes should be widely available, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, statins, and SGLT2is (sodium-glucose co-transporter-2 inhibitors).[2,40] Sodium glucose co-transporter-2 inhibitors alone are estimated to decrease the risk of CKD progression by 37% in individuals with and without diabetes.[41] For a 50-year-old individual with albuminuria and non-diabetic CKD, this treatment could extend their healthy kidney function period from 9.6 to 17 years.[42] These essential medicines slow progression to more advanced CKD stages and reduce cardiovascular hospitalisations, offering near-term cost-effectiveness—especially vital for LICs. Where available and affordable, the range of paradigm-shifting medications to slow CKD progression includes glucagon-like peptide-1 receptor antagonists, non-steroidal mineralocorticoid receptor antagonists, endothelin receptor antagonists, and specific disease-modifying drugs (eg, complement-inhibitors); these treatments herald an exciting new era for nephrology.

Considering the substantial healthcare costs associated with CKD—particularly those related to hospitalisation and kidney failure—effective preventive measures offer clear economic benefits for both HICs and LICs. Chronic kidney disease imposes enormous financial burdens on individuals, their families, healthcare systems, and governments worldwide. In the United States, CKD costs Medicare over US$85 billion annually.[13] In many HICs and middle-income countries, 2% to 4% of national health budgets are allocated to kidney failure care alone. In Europe, healthcare costs related to CKD exceed those associated with cancer or diabetes.[43] Reducing the global burden of kidney care would also yield important environmental benefits, including reductions in water usage and plastic waste, especially from dialysis.[44] On an individual level, CKD costs are frequently catastrophic, particularly in LICs and LMICs, where the individuals often

bear the majority of healthcare expenses. Only 13% of LICs and 19% of LMICs provide kidney failure replacement therapy coverage for adults.[15] Each year, CKD causes an estimated 188 million people in LICs and LMICs to incur catastrophic healthcare expenditures.[45]

The most widely cited and studied incremental cost effectiveness ratio threshold for assessing screening interventions is US$<50 000 per quality-adjusted life year.[46] When CKD prevalence is high, population-wide screening strategies may be considered in HICs.[33,47] For example, in the United States, a recent Markov simulation model assessed population-wide CKD screening in adults aged 35 to 75 years with albuminuria. The model included treatment with SGLT2is, in addition to standard care with ACE inhibitors or angiotensin receptor blockers. The analysis indicated that such a screening approach would be cost-effective.[47] Additionally, an evaluation of home-based, semiquantitative albuminuria screening in the general population in the Netherlands showed that it was cost-effective.[33] Case finding—targeting higher-risk groups for CKD detection—offers a more efficient and cost-effective approach than mass or general population screening. It reduces costs and potential harms while increasing the true positive rate of screening tests.[3,35,46] An alternative incremental cost-effectiveness ratio threshold, proposed by the WHO, suggests using a benchmark of less than 1 to 3 times the gross domestic product per capita per quality-adjusted life year to evaluate cost-effectiveness in LICs and LMICs.[46] The recommended tests for detecting kidney disease are low-cost and minimally invasive, making them feasible across diverse healthcare settings. Basic tests, such as eGFR and uACR, are widely available. In contexts where quantitative testing for proteinuria is unavailable or unaffordable, the use of urine dipstick testing can substantially reduce costs.[31]

When coupled with effective interventions, early identification of individuals with kidney disease would yield benefits for patients, healthcare systems, governments, and national economies.[45] Health and quality-of-life gains for individuals would lead to greater productivity—especially for younger people with more working years ahead—while improving developmental and educational outcomes in children and young adults. Individuals would also be less likely to face catastrophic healthcare expenses. Governments and healthcare systems would benefit from reduced CKD-related expenditures and lower cardiovascular disease costs. Economies would benefit from increased workforce participation. These benefits are especially crucial for lower-income countries, where the burden of CKD is greatest but the capacity to fund kidney care is most limited.

Challenges and solutions for implementation

Structural barriers to widespread CKD identification and treatment include high costs, limited test reliability, and lack of health information systems to monitor CKD burden. These challenges are compounded by a lack of relevant government and healthcare policy, low levels of CKD-related knowledge and implementation among healthcare professionals, and limited public awareness of CKD and low perceived risk among the general population. Solutions for implementing effective interventions include integrating CKD identification into existing screening programmes, educating both the public and primary care professionals, and leveraging joint advocacy efforts from non-governmental organisations to focus health policy agendas on kidney disease. Any proposed solution must carefully balance the potential benefits and harms of screening and case-finding initiatives. Ethical considerations encompass resource availability (such as trained healthcare workers and access to medicines), affordability of testing and treatment, and the psychological impact of false positives or negatives, including potential anxiety for patients and their families.[48]

Successful screening and case-finding programmes require adequate workforce capacity, robust health information systems, reliable testing equipment, and equitable access to medical care, essential medicines, vaccines, and medical technologies. Primary care plays a pivotal role in protecting kidney health, particularly in LICs and LMICs. The limited global nephrology workforce, with a median prevalence of only 11.8 nephrologists per million population, and an 80-fold disparity between LICs and HICs, is inadequate to detect and manage the vast majority of CKD.[23] As with other chronic diseases, primary care clinicians and frontline health workers are essential for the early detection and management of CKD.[49] Testing must be affordable, simple, and practical. In resource-limited settings, point-of-care creatinine testing and urine dipsticks are especially useful.[31] Educational efforts targeting primary care clinicians are crucial to integrating CKD detection into routine clinical practice, despite time and resource constraints.[50-52] Additionally, automated clinical decision support systems can leverage electronic health records to identify individuals with CKD or those at high risk, then prompt clinicians with appropriate actions (Fig 2[28]).

Currently, few countries have CKD registries, limiting the ability to accurately quantify disease burden and advocate for resources. Knowledge of the CKD burden is essential for prioritising kidney health and developing strategies that progressively expand to encompass the full spectrum of kidney

care.[53] A global survey revealed only one-quarter of countries (41/162) had a national CKD strategy, and fewer than one-third (48/162) recognised CKD as a public health priority.[23] Recognition by the WHO that CKD is a major contributor to non-communicable disease mortality would be a crucial step forward. It would help raise awareness, enhance local surveillance and monitoring, support the implementation of clinical practice guidelines, and improve allocation of healthcare resources.[2]

Programmes for the early detection of CKD will require extensive coordination and active engagement from a wide range of stakeholders, including governments, healthcare systems, and insurers. International and national kidney organisations—such as the International Society of Nephrology—are already advocating to the WHO and individual governments for greater prioritisation of kidney disease. We must continue this work through collaborative efforts to streamline the planning and implementation of early detection programmes. Integration with existing community interventions (eg, cardiovascular disease prevention initiatives) in both LICs and HICs can decrease costs and maximise efficiency by building on established infrastructures. Such programmes must be adapted to local contexts and can be delivered in a variety of settings, including general practice clinics, hospitals, regional or national healthcare facilities, and rural outreach initiatives. Depending on local regulations and available resources, screening and case-finding can also occur outside conventional medical environments, for example, in town halls, churches, or markets. Community volunteers can also assist with these outreach and screening efforts.

In conjunction with changes in clinical practice to promote earlier detection of CKD, we must also focus on increasing public awareness of kidney disease risk and promoting health education. Such campaigns should be aimed at both the general public and patients, with the goal of fostering greater awareness and self-empowerment. General population awareness of CKD is poor: nine of ten people with the condition are unaware that they are affected.[54] Furthermore, kidney disease is missing from mainstream media. One analysis of lay press coverage showed that kidney disease was discussed 11 times less frequently than would be expected based on its actual contribution to mortality.[55] A number of national and international organisations have developed public-facing quizzes to help individuals assess their risk of kidney disease. These initiatives are supported by regional studies showing that socially vulnerable patients with hypertension often do not understand their kidney health risks.[21,56-58] Online and direct education for healthcare professionals can also help improve consumer health literacy. Awareness leads to increased patient activation, engagement, and shared decision-making. However, education around CKD must be nuanced—balancing the need for detection and risk stratification with the importance of informing and empowering, rather than frightening, individuals about the timing and extent of potential interventions (Box).[4,58] Striking this balance will be critical for optimising self-efficacy and encouraging active involvement from patients, families and caregivers.

Conclusion: a call to action

We call on all healthcare professionals to assess the kidney health of patients at risk of CKD. Concurrently, we must partner with public health organisations to raise awareness among the general population about the risk of kidney disease and empower at-risk individuals to proactively seek kidney health checks. To make meaningful progress, collaboration with healthcare systems, governments, and the WHO is essential to prioritise kidney disease

BOX. Are your kidneys OK? Personal perspectives on chronic kidney disease (CKD) awareness, detection, and treatment[4,58]

I actually didn't fully understand, because nobody had ever given me the full information about what I had in a way that I could go, 'Well, this is what I've got [CKD], and this is why I've got it.'

[The clinicians] can answer those [kidney health] questions... but it's all very jargonistic.

I didn't know what it [CKD] meant, so I couldn't really share it with other people.

I may not know what my [kidney health] numbers are, but I do know what the tests are, and I do know that I've had them done before.

Well, let me put it this way: I'm well aware now of the significance of the kidneys and what the issues are. And I would definitely consider... When I go to the doctor, I would say to him, "Now listen, you did the blood tests—but how are my kidneys doing? What are the numbers?"

I know that they have done urine tests in the past, and I know there was protein and sugar in my urine.

I went from never taking a tablet to taking 22 tablets. What's going on here? I didn't know what they were. But I just numbered them, and that helped me a lot because I realised what was going on. Still, every time I went [to the doctor], I'd get another tablet. I knew that I had to take it because the doctors knew what they were doing.

This [CKD] was something new, so at first, I was like, just another thing to be concerned about. But then I felt kind of empowered, like I really do want to get ahead of this. I feel like I want to have a conversation with my primary care physician.

What I would be most interested in is: what is happening, why is it happening, and what can I do to slow it [CKD] down?

and develop effective, efficient early detection programmes. Only through these efforts can we ensure that the paradigm-shifting benefits of lifestyle changes and pharmacological treatments are fully realised, leading to better kidney and overall health outcomes for people around the world.

Author contributions

All authors contributed equally to the conception, preparation, and editing of the manuscript. All authors approved the final version for publication and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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