

Perspectives on early detection of chronic kidney disease: the facts, the questions, and a proposed framework for 2023 and beyond



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Chronic kidney disease (CKD) is a growing global health burden, as measured by financial cost, mortality, morbidity, or other indicators.¹ In 2017, the Global Burden of Disease (GBD) study found 697.5 million cases of CKD, indicating a global prevalence of 9.1%.² CKD is currently the third-fastest growing cause of death worldwide and is expected to become the world's fifth-leading cause of death by 2040.^{S1} A World Bank analysis showed that about 188 million people experience catastrophic health expenditure annually because of kidney diseases across low- and lower middle-income countries (LLMICs), the highest of any disease group.^{S2}

CKD is asymptomatic in its early stages, but it can be identified with simple tests, and its progression can be influenced by public health measures, lifestyle interventions, and inexpensive drug treatments. Many of the drivers of kidney disease can be assessed in the context of addressing the fundamental issues of obesity, hypertension, and diabetes. The costs of anti-hypertensive agents, angiotensin-pathway blockers, and statins have been reduced markedly in many LLMICs, due to availability of generics, often locally manufactured. Some newer agents (e.g., sodium–glucose transport protein-2 [SGLT2] inhibitors) will come off patent in the next 2–4 years, making them more affordable. Therefore, calls have been made for including CKD early-detection programs among national public health priorities.

However, uncertainty remains regarding whether the cost of early-detection programs for CKD is balanced out by the expenditure on medical care, and the incremental benefits and resource requirements associated with early detection. Further, the potential exists for moral hazard in case-finding if those identified as having CKD cannot get appropriate treatment for want of resources.

Thus, debate surrounds 3 related issues. First, does early detection of CKD represent a wise use of resources? Second, what are the

circumstances under which early detection of CKD is an appropriate policy option, and finally, what is the optimal way to maximize benefit and reduce harm?

To guide stakeholders (especially in those parts of the world that are putting together chronic disease–screening programs) to decide whether or not to establish early-detection and intervention programs for CKD, the International Society of Nephrology (ISN) assembled a diverse working group to examine this issue through a scoping review of evidence² and a case-study series³ that gives examples of CKD detection and treatment strategies in a range of communities. The current article presents both the distillation of that information and arguments to facilitate a set of systematic considerations and directions based on current knowledge and gaps.

The facts

Progress has been made in reducing the mortality and morbidity due to noncommunicable diseases, with the global age-standardized mortality rates between 2007 and 2017 for ischemic heart disease, stroke, and chronic obstructive pulmonary disease coming down by 9.7%, 13.6%, and 13.6%, respectively.¹ However, the mortality rate due to CKD went up by 1.5% during the same period.¹ Most of the future increase in CKD burden is projected to occur in LLMICs and among disadvantaged and indigenous communities.^{1,S3} Although the increasing prevalence of diabetes and hypertension does explain a significant proportion of the rise in CKD burden in high-income countries (where the preexisting kidney testing rates may be high already), the contribution of these conditions is lower in LLMICs, and country-specific data suggest that unique risk factors play a role (e.g., infections and environment change),⁴ for which no existing programs are in place. For example, a high burden of CKD has been described in agricultural workers who work outdoors in hot and humid conditions for long hours and in

farmers exposed to pesticides.⁵³ In a community-based study,⁵ a CKD prevalence of 22% was described in such a high-prevalence area, with 90% of patients unaware that they had CKD. Other studies have shown a rapid rate of kidney function decline in these populations.⁵³ CKD commonly develops in patients at younger ages in LLMICs, with kidney failure setting in a couple of decades earlier than it does in high-income countries, with greater socioeconomic consequences.⁵⁴ Finally, although kidney failure is the best recognized consequence of CKD, most people with CKD will die before developing kidney failure, due to cardiovascular disease. Identification of CKD may allow early institution and aggressive implementation of effective therapies for cardiovascular disease prevention.

If used over the long-term, certain medications and other strategies can reduce the risk of adverse outcomes in CKD. Many of these treatments are part of the care of diabetes and hypertension, and the presence of early CKD may not significantly alter management in people with these conditions.⁵⁵ New evidence that use of sodium–glucose transport protein-2 inhibitors can improve kidney and cardiovascular outcomes in patients with CKD, irrespective of the presence of these risk factors, is presenting new opportunities for people with CKD.

CKD can be detected using blood-based and/or urine-based tests.⁴ Both are commonly ordered in routine clinical practice, especially in high-income countries. What are the best testing methods is a subject of debate (serum creatinine, cystatin C, urine dipstick and urine protein- or albumin-to-creatinine ratios, and urine sediment testing). Variability in accuracy of some of these tests, in particular glomerular filtration rate (GFR) estimation equations, complicate their use in all populations. Full discussion about these issues is beyond the scope of the current paper, but a point to note is that even the cheapest of these tests are not universally available in LLMICs.⁵⁶ Even when such tests are available, CKD is not always recognized or acknowledged by the ordering provider.

Health economic analyses from high-income countries suggest that population-based screening for CKD is not cost-effective.^{57,58} However, under some circumstances, case-finding to identify and treat CKD in individuals at increased risk may lead to benefits at reasonable cost.⁵⁶ Experience from LLMICs

suggests that a large undiagnosed population creates a burden of a range of non-communicable diseases, including diabetes, hypertension, and CKD.⁵ Population-level screening might therefore allow identification of more than one chronic condition. Programs for early detection also enhance public awareness, facilitate advocacy efforts, and help secure additional resources for effective non-communicable disease and CKD care.

The benefits of early detection should be balanced against the costs of investigations, treatment, and follow-up, as well as opportunity costs (potential benefits resulting from other programs that may be foregone because of the investment in early CKD detection). The greater the resource constraints at baseline, the more carefully decision makers must evaluate the opportunity costs associated with early detection of CKD, as compared to other health programs.

The questions

Although there is interest in implementation science to achieve evidence-based policy, existing CKD detection programs often are not evidence-based. In part, this may be because the existing evidence is limited, or is not accessible or comprehensible to decision makers. Evidence is combined with heuristics—both rational (based on trusted sources) and irrational (such as beliefs, emotions, familiarity, and availability bias). For example, despite the overwhelming evidence that preventing CKD is preferable to treating the most advanced disease, governments, especially in LLMICs, may opt to do the latter by funding dialysis programs. Although such programs promote universal health coverage and enhance financial risk protection, especially to the worst off, they alone are not enough, especially in the context of limited resources, unless combined with a comprehensive health package that also includes upstream disease prevention, including addressing obesity, diabetes, and hypertension.

To evaluate the potential risks and benefits of implementing an early CKD detection program, in a specific region or country, several important questions must be asked of society members, including patients, care providers, and payers (Box 1).

Potential solutions

High-quality research using participatory methodologies that incorporate patient preferences is needed. We need to better understand a

Box 1 | Questions to be asked to evaluate the potential risks and benefits of implementing an early detection program for CKD

1. Is the society committed to addressing the basic social and health needs, including primary prevention, for the most important causes of premature death and disability?
2. Is there a good understanding of the population that is at risk for developing CKD?
3. Do the baseline conditions favor case-finding (for example, a lower preexisting rate of kidney testing in at-risk groups; a higher population prevalence of CKD; faster loss of kidney function; higher capacity to treat newly identified cases of CKD; and lower baseline use of effective treatments for CKD in those at risk)?
4. Would the people with newly identified CKD have access to the sustainable care required to realize clinical benefit?
5. Are resources (human, technological) sufficient to allow successful implementation of an early-detection program?
6. Should early detection of CKD be conducted as a standalone program or integrated with the management of other major noncommunicable diseases, perhaps as a care bundle?
7. Should early CKD-detection programs be a priority, given the competing demands on limited resources?
8. Are there societal and political considerations that make CKD more or less important to address than its prevalence, health outcomes, or economic costs might suggest?

CKD, chronic kidney disease.

society's values, preferences, and views about allocating resources to early CKD detection and treatment strategies, and the kind of evidence needed to make such decisions. The circle of stakeholders involved in the generation of evidence to answer these questions must be expanded, along with the evidence-to-policy process. Several national and international professional organizations have established patient advisory groups, consult regularly with them, and facilitate interaction with other stakeholders through policy and research meetings. Solutions must be responsive to local needs and use locally available resources. For example, primary frontline health workers can be trained in the use of decision tools to identify at-risk populations to efficiently prescribe and tailor

treatments needed to mitigate risk in areas with a shortage of physicians.^{S9}

From an advocacy perspective, we should consider how best to communicate the answers to patients, communities, and policy makers. Conveying uncertainty is not easy, such as the strengths and weaknesses of research or models that estimate the harms and benefits of different policy options. Policy and its implementation should be responsive to changing local needs and resources. This broader context should consider early detection of CKD not as an end, but as a starting point for the continuum of care required by people with kidney diseases and their major risk factors.

The ISN recognizes that operationalization of the principles outlined here will require

Box 2 | Suggested evidence-based, resource-sensitive framework that can be adjusted to suit local context

1. Case-finding programs for CKD will represent an appropriate choice for some jurisdictions. However, overt acknowledgement of how, in whom, when, and why these programs are considered important is critical to success and building the trust of the community.
2. If early-detection programs are adopted, they must be adapted to the local circumstances, including health system capacity and integration with other NCD detection programs.
3. Community engagement is needed to understand societal values and preferences about the potential value of early detection—including lived experience—while including other considerations, such as stigma, and the possibility of catastrophic expenditure.
4. CKD detection programs should be approached with an equity lens—for example, the most vulnerable may stand to lose out the most by the nonavailability of a case-finding and treatment program.
5. The tests and methods used for early detection and follow-up of detected cases should maximize benefit and value, while reducing harms, misuse, and overtesting.
6. Any early-detection program should be accompanied by an embedded evaluation of effectiveness in real time, with a commitment to provide feedback on results to communities and develop a learning health system.
7. Early-detection programs and interventions that are provided to newly detected cases (choice of at-risk population, screening tests, and treatment options) must be customized to local circumstances and may evolve over time.

CKD, chronic kidney disease; NCD, noncommunicable disease.

The essential components (key principles, processes, and building blocks) to inform those interested in launching and sustaining early CKD detection and intervention programs

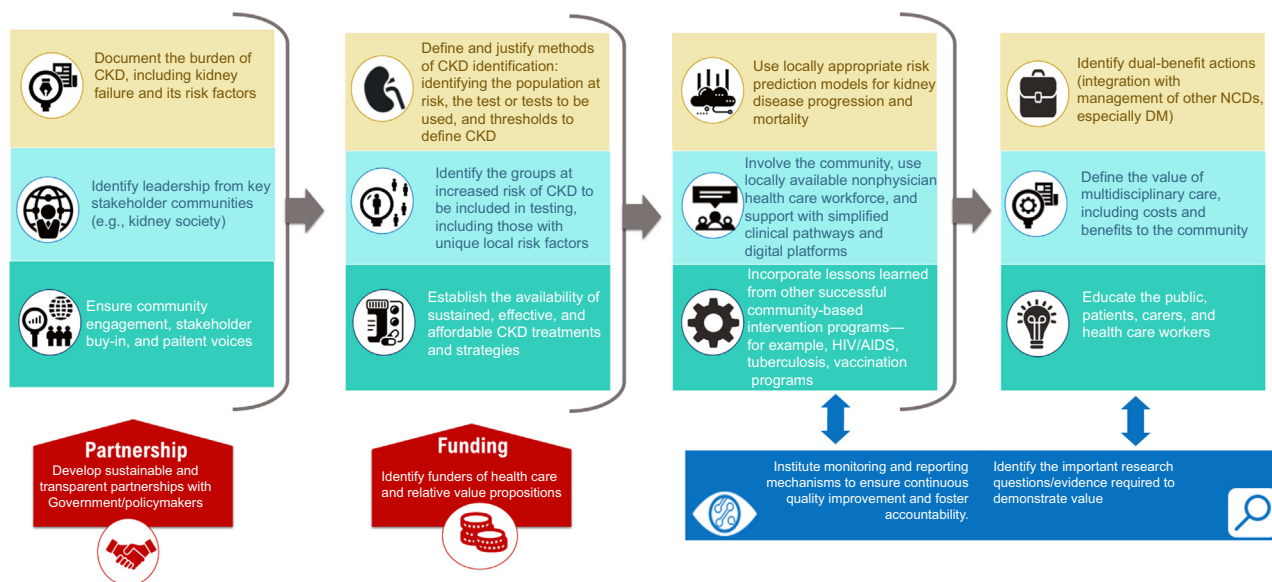


Figure 1 | The essential components (key principles, processes, and building blocks) to inform those interested in launching and sustaining early chronic kidney disease (CKD) detection and intervention programs. DM, diabetes mellitus; NCD, noncommunicable disease,

flexibility, coordination and cooperation. With its 10 regional boards, Advocacy Working Group, and Patient Liaison Advisory Group, the ISN can facilitate linkages among specific activities directed toward early CKD detection and treatment, and toward increasing awareness. The ISN-Global Kidney Health Atlas offers an ongoing assessment of the current state and progress being made in specific regions as regards registries, workforce capacity, access to medications, and research.

We acknowledge that in some situations, a focus on CKD may not be possible due to a multitude of sociopolitical reasons. In these instances, ongoing liaison with ISN regional boards and champions, along with education and advocacy, are the first steps in an arduous journey that can still be undertaken.

Considering the above complexity, and the multiplicity of organizations and resources potentially available, we suggest an accessible, evidence-based, resource-sensitive framework that stakeholders can apply to their own context. The basic tenets are shown in [Box 2](#). [Figure 1](#) addresses the complex question of relative value of early detection for a given community and process to be followed. This framework will need to be refined and adapted across jurisdictions, and over time.

Summary and recommendations

Responsible use of limited healthcare and community resources to improve the kidney health of communities is critical. We encourage the thoughtful use of a comprehensive framework directed at achieving change, and incorporating robust research principles, patient and community engagement strategies, enhanced understanding of the political landscape, and targeted communication strategies.

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SUPPLEMENTARY MATERIAL

[Supplementary File \(Word\)](#)

Supplementary References.

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