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REVIEW

# Current Management Strategies of Chronic Kidney Disease in Resource-Limited Countries

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**Abstract:** The incidence and prevalence of chronic kidney disease (CKD) and kidney failure continues to increase worldwide, especially in resource-limited countries. Many countries in this category already have a massive burden of communicable diseases, as well as socio-economic and socio-demographic challenges. The rising CKD burden and exorbitant economic cost associated with treatment are mainly responsible for the alarming mortality rate associated with kidney disease in these regions. There is often poor risk factor (diabetes and hypertension) and CKD awareness in these countries and limited availability and affordability of treatment options. Given these observations, early disease detection and preventive measures remain the best options for disease management in resource-limited settings. Primary, secondary and tertiary preventive strategies need to be enhanced and should particularly include measures to increase awareness, regular assessment to detect hypertension, diabetes and albuminuria, options for early referral of identified patients to a nephrologist and options for conservative kidney management where kidney replacement therapies may not be available or indicated. Much is still needed to be done by governments in these regions, especially regarding healthcare funding, improving the primary healthcare systems and enhancing non-communicable disease detection and treatment programs as these will have effects on kidney care in these regions.

**Keywords:** chronic kidney disease, LMICs, kidney replacement therapy, non-communicable diseases, early detection and prevention, early referral

## Introduction

Over the past half century, there has been a steady and persistent increase in the global burden of chronic kidney disease (CKD), making it a significant public health issue.[1,2] This has been evidenced by the rise in global ranking of CKD as cause of mortality, rising from 17th in 1990 to 12th in 2017 and 16th as cause of years of life lost worldwide.[3,4] Analysis of the global burden of disease (GBD) data for the same period showed that the incidence of CKD increased by 89%, prevalence increased by 87%, death due to CKD increased by 98%, and disability-adjusted life years increased by 62%.[5] The global prevalence of CKD (stage 1–5) has been shown to be 13.4% (11.7%–15.1%) while the prevalence of CKD (stage 3–5) is 10.6% (9.2%–12.2%) (Figure 1).[6] Data from the International Society of Nephrology (ISN) Global Kidney Health Atlas (GKHA) support these prevalence values as it is seen that approximately 1 in 10 people worldwide have a lifetime risk of developing CKD, although large variations in proportion exists across countries and regions.[7] The GBD study also noted that the burden of CKD was much higher than expected for the level of development in several regions,

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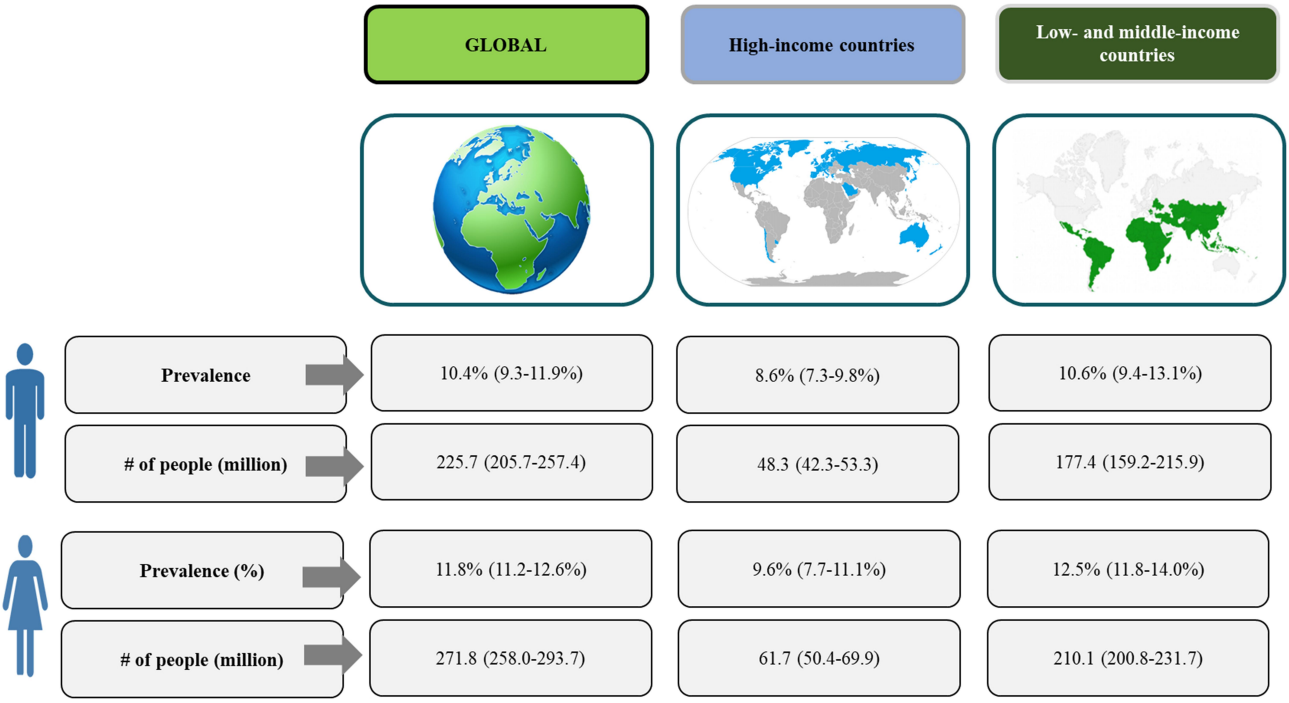


**Figure 1** Age-standardized prevalence of CKD (1–5) in adults (men and women).
**Notes:** Reprinted with permission from Hill NR, Fatoba ST, Oke JL, et al. Global prevalence of chronickidney disease - a systematic review and meta-analysis. *PLoS One*. 2016;11(7):e0158765.[6]

particularly Oceania, sub-Saharan Africa, and Latin America, whereas the disease burden was lower than expected in other regions.[3]

Differences in regional CKD prevalence may be attributed to causes of CKD, which varies by setting but is largely driven by the excessive burden of hypertension and diabetes mellitus, common in many developed countries, as well as other factors like human immunodeficiency virus (HIV) and exposure to various nephrotoxins in developing countries.[3] Reports from the ISN GKHA have also shown that there are significant gaps in CKD care structures and management with countries classified as low- and middle-income performing poorly.[8,9] The reasons for this relate to the absence of platforms for adequate funding, improving infrastructure, training, advocacy and lack of inclusion of CKD in several national noncommunicable disease (NCD) strategies.[10] This often leads to poor outcomes of CKD and kidney failure in many low-resource settings.[11,12] In this review, we will systematically and comprehensively discuss current management strategies for CKD in resource-limited countries. Although there is no clear agreement on how to define resource-limited countries, we used the World Bank country and lending groups classifications for low- and middle-income countries (LMICs) to represent resource-limited countries.[13]

## Definition and Classification of CKD

CKD is defined as presence and persistence of any of the following: estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 $m^2$, albuminuria ≥30 mg/24 hours, or markers of kidney damage (eg isolated proteinuria or isolated haematuria or structural abnormalities of the kidneys) for more than 3 months (Table 1).[14] CKD is classified based on levels of eGFR derived from an equation including serum creatinine and is divided into five stages, with stage 3 having two categories. As largely varied GFR estimates can be obtained from using different serum creatinine-based equations, it may be difficult to ascertain the best equation for that population, especially where population-wide eGFR validation studies have not been carried out for that population.[15] Hence, in many resource-limited countries, the accurate estimation of GFR may pose a challenge given that available equations may not have been validated for their setting. Also, given that the aetiology of CKD is heterogeneous in resource-limited countries, some causes of CKD also have inherent difficulties in GFR estimation. For example, HIV is

**Table 1** Definition and Classification of CKD[14]

| | | | Range (mL/min/1.73 $m^2$) | Persistent Albuminuria Categories Description and ACR Range | | |
|---|---|---|---|---|---|---|
| | | | | A1 | A2 | A3 |
| | | | | Normal to Mildly Increased (<30 mg/g) | Moderately Increased (30–300 mg/g) | Severely Increased (>300 mg/g) |
| eGFR categories (mL/min/1.73 $m^2$) Description and range | G1 | Normal or high | ≥90 | 1 if CKD | 1 | 2* |
| | G2 | Mildly decreased | 60–89 | 1 if CKD | 1 | 2* |
| | G3a | Mildly to moderately decreased | 45–59 | 1 | 2 | 3§ |
| | G3b | Moderately to severely decreased | 30–44 | 2 | 3 | 3§ |
| | G4 | Severely decreased | 15–29 | 3* | 3* | ≥4§ |
| | G5 | Kidney failure | <15 | ≥4§ | ≥4§ | ≥4§ |

**Notes:** *Clinical practice guidelines suggest that clinicians discuss these patients with their local specialist nephrology service. §Clinical practice guidelines suggest that people in these categories are referred for specialist nephrology opinion. Data from the KDIGO CKD Work Group clinical practice guidelines. Data from Kidney Disease: improving Global Outcomes (KDIGO) CKD Work Group.[14]
**Abbreviations:** CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ACR, albumin creatinine ratio.

a common cause of CKD in sub-Saharan Africa (SSA); however, the best method for estimating GFR in patients with HIV is yet to be determined.[16,17] Other reasons that include contentions about the use of "black ethnicity" in GFR equations[18] and relative paucity of laboratories producing isotope dilution mass spectroscopy traceable serum creatinine results[19] may contribute to inaccurate GFR reporting and misclassification of CKD in such settings whether in adults, pediatrics or in disease-specific subgroups. For these reasons, eGFR used in clinical practice in these settings are only a guide to kidney function and may not represent true level of function. Several patients in earlier stages of CKD (eg stage 3 CKD where early intervention makes a difference in disease progression) are more likely to be missed. Large population-wide validation studies or smaller studies in specific patient groups are needed to provide answers about the most accurate GFR estimating equations in different circumstances.

## Methods

To undertake this narrative review, we performed a systematic search of PubMed (MEDLINE) using relevant terms related to "Chronic kidney disease", "low- and middle-income countries" and "detection and management" (Table S1). Given that there is no standard definition for "resource-limited settings," we defined this in the context of capacity to provide adequate kidney care, as countries not having adequate capacity for kidney replacement therapy (KRT) and used LMICs as surrogate. We then screened the identified articles using titles and abstract before a full article screening (Figure S1). The bibliography of the studies selected for assessment of full articles was also examined to identify publications that would provide relevant data and information for the review. We focused on studies from LMICs that discussed methods of CKD definition, CKD prevention strategies (including population screening for CKD and its risk factors and other public health interventions), clinical management of CKD and its various risk factors and the suggestions on how to improve the health systems of LMICs to cope with the rising incidence of CKD and its major risk factors.

## Clinical Presentation and Diagnosis of CKD

Although the course of CKD is classically described as silent, it is by no means asymptomatic even in its early stages given the significant symptom burden[20,21] which requires a conscious enquiry of CKD symptomatology in the management of potential CKD patients, eg diabetics, hypertensives, and HIV patients. The clinical manifestations of early CKD are usually constitutional symptoms which occur subtly and insidiously and include symptoms such as chronic malaise, loss of appetite, poor sleep and

poor concentration; the number and severity of symptoms and signs manifested also tend to increase with worsening CKD stage.[21] For CKD patients in LMICs, the diagnosis of early CKD is more likely to be missed as the patients are more likely to be seen by non-specialists or sometimes non-physicians who do not have the requisite knowledge to make the connection between the rather constitutional symptoms of early CKD and the presence of chronic kidney dysfunction.[22] The overt, more commonly recognized symptoms of nausea and vomiting, muscle cramps, and physical signs of anemia, facial puffiness and limb edema usually manifest in the late stages of CKD; a point at which substantial ground has already been lost in preventing the progression of disease. CKD patients in LMICs are more likely to present for specialist care further along the spectrum of CKD, ie stages 4 and 5, due to a combination of health care system- and patient-related factors, such as delayed referrals of at-risk individuals from primary care physicians or other specialist physicians to nephrologists, low educational and socio-economic status and the increasingly competing role of complementary alternative medicine practitioners.[23] Indeed, "crash landing" presentation is more often a pattern of presentation; crash landing being a colloquial term used to describe CKD patients for whom maintenance dialysis is initiated in an unplanned, emergent manner.

# Management of Patients with CKD

## Principles of CKD Management in LMICs

The principles of the various aspects of CKD management are generally well known with extensive clinical practice guidelines being available from various professional societies and bodies for the care of the complex facets of CKD. Special mention must, however, be made about the challenges of health care delivery, and by inclusion CKD care delivery in LMICs. These must be appreciated in discussing the currently available CKD management strategies in LMICs as they have invariably influenced the cohesive, effective, and sustained delivery of CKD care. Scarcity of kidney care workforce[24] (eg nephrologists, renal nurses, dieticians and social workers), poorly structured health care delivery systems providing fragmented and interrupted care,[25] poor health care infrastructure as well as financial barriers to accessing care by the end-user patient are a number of the challenges mitigating against the effective CKD management in LMICs.

## CKD Detection and Prevention Strategies in LMICs

Compared to high-income countries, LMICs contribute less of their gross domestic product GDP) toward healthcare expenditures (12.5% vs 5.4%, respectively, in 2017),[26] and this often has implications on available funding for kidney care.[8] Thus, for compelling reasons, early CKD detection and prevention strategies should form the basis of CKD management in LMICs. The economic burden of treating advanced CKD in poor countries that already have dysfunctional health systems may be overwhelming. The failure of government driven treatment for kidney failure has led to out-of-pocket payment for dialysis and renal transplantation which causes catastrophic health expenditure and worsening poverty. The remarkably high mortality rates[11,27] among individuals with kidney failure in LMICs highlights the lack of facilities, personnel, medications and technologies required for optimal kidney care in such settings.[8,25] Furthermore, the main driver of the rising CKD prevalence in LMICs is an epidemiologic transition that has led to a significant increase in chronic NCDs (hypertension, type 2 diabetes mellitus, obesity) and an interplay with infectious diseases like HIV, malaria and schistosomiasis. While these risk factors are eminently modifiable, genetic predisposition to CKD like the apolipoprotein A1 (*APOL1*) renal risk variants in West Africa[28,29] are not modifiable and present another strong reason for prevention of CKD in this population.

CKD prevention programs include primary prevention, which aims to prevent the occurrence of CKD risk factors; secondary prevention, which employs screening to achieve early detection of CKD in at-risk groups; and tertiary prevention, which helps slow down or prevent CKD progression to kidney failure (Figure 2).[30] Strategies to increase disease awareness, eg mass media campaigns, are essential for primary and secondary prevention as they permit dissemination of information about CKD and its risk factors. Primary prevention strategies include lifestyle modifications like dietary salt restriction and consumption of healthy portions of fruits and vegetables for hypertension and obesity prevention, increased physical activity and low-fat and -calorie diet to reduce obesity, and avoidance of tobacco use (including passive smoking) and alcohol. With adequate awareness in LMICs, these measures could bring about population-level reduction in hypertension, type 2

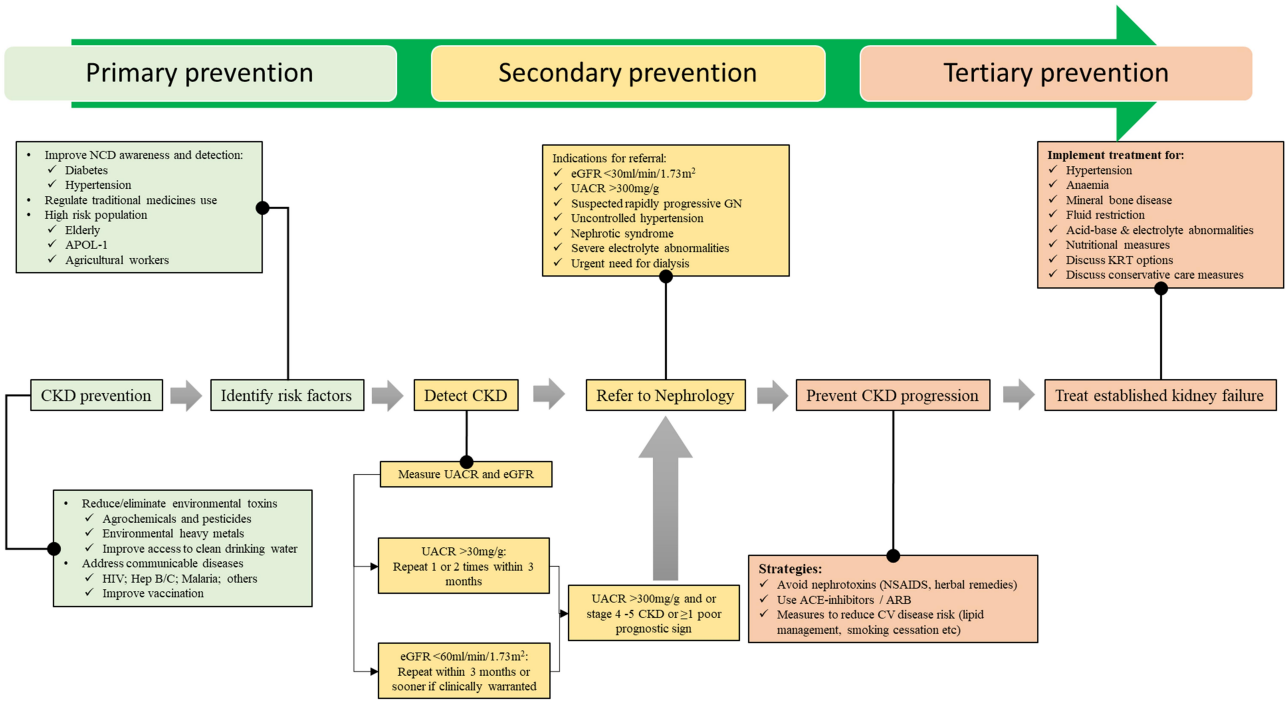


**Figure 2** Primary, secondary and tertiary prevention strategies for CKD in LMICs.
**Abbreviations:** eGFR, glomerular filtration rate; LMICs, low- to middle-income countries; UACR, urine protein creatinine ratio; GN, glomerulonephritis; CV, cardiovascular; CKD, chronic kidney disease; NCD, non-communicable disease; NSAIDs, non-steroidal anti-inflammatory drugs; HIV, human immunodeficiency virus; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; KRT, kidney replacement therapy; APOL-1, apolipoprotein- L1.

diabetes mellitus, obesity and dyslipidaemia prevalence, thereby reducing CKD incidence.

Secondary CKD prevention programs like screening for CKD are critical for the early detection of CKD. The cost-effectiveness of population screening in LMICs has not been ascertained, but data seem to point to targeted screening as a more feasible approach.[31] Due to low disease awareness in several LMICs,[32,33] using a screening strategy that involves, first, screening to identify CKD risk factors (eg hypertension, diabetes, etc) and then screening those with risk factors to ascertain CKD using biochemical methods (albuminuria and estimated GFR) may be beneficial. Such strategies have been utilized as national programs in a number of LMICs to achieve early CKD detection.[34–36] In many countries, health professionals continue to take advantage of commemorative days (eg World Kidney Day, May Measurement Month for hypertension, World Diabetes Day, etc.) to screen for CKD and risk factors and increase disease awareness in the community.[37–40]

Tertiary prevention strategies like ensuring blood pressure (BP) control in those diagnosed with hypertension, blood glucose control in diabetics, dyslipidaemia treatment, and reduction of proteinuria require medications which may be difficult to procure in LMICs because of the lack of functional health insurance systems. It is important to evolve mechanisms to provide angiotensin-converting enzyme inhibitors or angiotensin receptor blockers to delay CKD progression. The success of preventive strategies appears to be the only feasible management policy for CKD in LMICs.

## Using Integrated Approaches for Chronic Disease Management in LMICs

Health systems in developed countries have largely adopted integrated approaches for the management of chronic diseases, including CKD.[41] Such approaches, like the Innovative Care for Chronic Conditions (ICCC) proposed by the World Health Organization (WHO) in 2002 (Figure 3),[42] provide a model of health systems to help manage the increasing global epidemic of chronic diseases, including both communicable and non-communicable diseases. The different tiers of this model provide a unique platform for interaction, first between families/patients, health care teams and communities to provide information motivation and preparedness to manage chronic diseases; then a platform for interaction between health care organizations and the community to

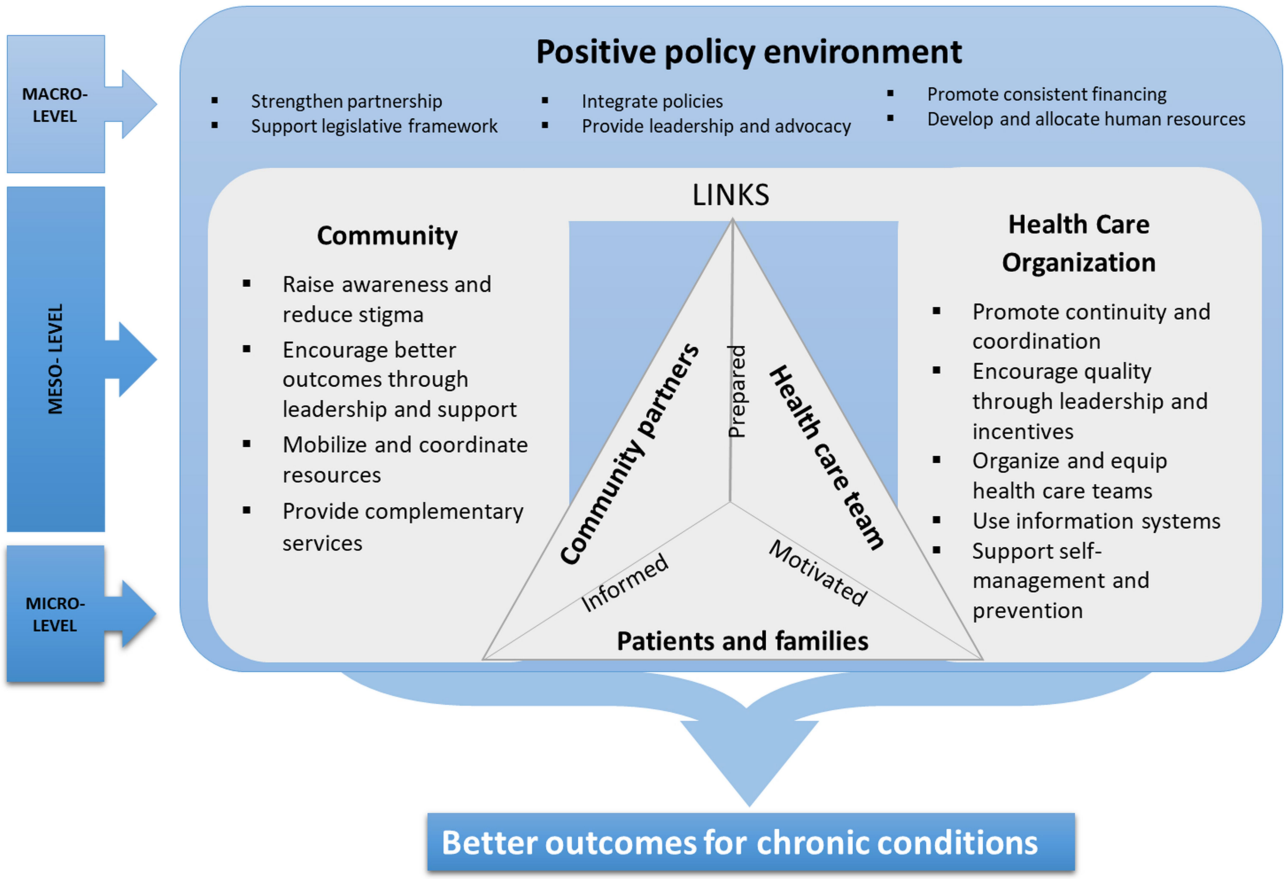


**Figure 3** The World Health Organization ICCC framework.
**Notes:** Adapted with permission from the WHO, Innovative care for chronic conditions: building blocks for action, Available from: http://www.who.int/chp/knowledge/publications/icccreport/en/. Copyright 2002.[42]

promote continuity; and lastly, a platform to engage policymakers and legislation in providing leadership and advocacy.[42] Given that many LMICs usually have dual burden of communicable diseases and NCDs, integrating care for detection, treatment and monitoring of these conditions reduces workload and workforce requirement and generally improves outcomes and can be cost-effective.[43,44] In the Effectiveness of Integrated Care on Delaying Progression of stage 3–4 CKD in Rural Communities of Thailand (ESCORT study), use of integrated care was associated with delayed CKD progression compared to usual care and suggests that such approaches can be leveraged by other LMICs for the management of CKD.[45] However, lack of rigorous care models for CKD have been identified in LMICs,[46] which if developed and used can improve care to slow CKD progression and inform national policies on CKD care. For these integrative approaches to become effective, there is a need for government involvement at all levels, especially with a focus on improving primary healthcare structures, funding and strengthening their NCD strategies.[47]

## Management of Hypertension

Hypertension is a major cause of CKD, particularly in LMICs. In 2010, it was estimated that 1.39 billion people had elevated BP worldwide (349 million in high-income countries versus 1.04 billion in LMICs).[48] Thus, measures to improve hypertension awareness, treatment and control including screening and use of recommended therapies such as diuretics with or without angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACE-I/ARB) or calcium channel blockers for specific populations will reduce the disease burden and reduce the associated target organ damage including CKD. As a recent large multi-centre study has shown that in black patients in SSA, amlodipine plus either hydrochlorothiazide or perindopril is more effective than perindopril plus hydrochlorothiazide at lowering BP.[49]

## Management of Diabetes Mellitus

Worldwide, diabetes mellitus is the leading cause of CKD, especially in developed countries, being driven by the high prevalence of obesity. Data from the IDF estimates the 2019 global prevalence of diabetes to be 9.3% (463 million people), projected to rise to 10.9% (700 million) by 2045. Although this will amount to a 51% global increase, the rise will be much higher in Africa (143%), the Middle East and North Africa (96%) and South East Asia (74%) compared to Europe (15%) and North America (33%).[50] The standard of care for diabetes management including targeting HbA1c of ~7.0% to delay or prevent microvascular complications and dose adjustments or discontinuation of oral agents such as metformin (if eGFR <30 mL/min/1.73 $m^2$) may be necessary.[14] Although newer agents such as SGLT-2 inhibitors have shown significant benefits in renal outcomes, cardiovascular outcomes and mortality,[51] cost and availability of drugs is a never-ending issue in many LMICs.[52] It is important that lifestyle measures (weight reduction, exercise, smoking cessation) and common pharmacological measures (eg insulin and ACE-I/ARB) continue to be available to patients.

## Management of Glomerular Diseases Including HIV and Other Infections

Although glomerular diseases are common in many LMICs and may significantly contribute to the burden of CKD from those regions, the diagnosis of glomerulonephritis (GN) is often limited by the lack of diagnostic tools, such as assessment of serum auto-antibodies, 24-hour protein estimation and kidney biopsy.[53] Even though the treatment of GN is cause-specific, the use of anti-proteinuric agents (eg ACE-I/ARB), BP control, treatment with diuretics, use of anti-lipid agents and reduction in salt intake may be useful.[54] However, it is important that steps are taken to reach diagnosis and institute appropriate immunotherapies where indicated. In Africa where HIV is common and may present with glomerular disease or where treatment with tenofovir may worsen kidney function, it is important that all HIV-positive patients be started on kidney-friendly anti-retroviral therapies (ART), which have been shown to reduce progression of disease and mortality.[55] Although some studies have evaluated and shown benefit when using corticosteroids in HIV patients, further studies are needed to assess the values of immunotherapies in such patients.[56] It is also relevant that appropriate therapies be instituted for infectious conditions (such as hepatitis B/C, schistosomiasis, syphilis, etc.) that can be associated with CKD in LMICs.

## Avoiding Nephrotoxins and Adjusting Drug Doses

Either due to high cost, unavailability of orthodox medicines or cultural acceptability of traditional medicine, herbal remedies are often resorted to for the treatment of acute infections such as malaria[57] and for many chronic health disorders including hypertension and diabetes in LMICs.[58] Herbal remedies have been associated with acute or chronic kidney damage[59,60] and it is important to raise awareness on the impact of unregulated herbal remedies on kidney disease in LMICs. Physicians should also routinely check patients' prescriptions for potential nephrotoxins and should encourage all patients to avoid taking them, including non-steroidal anti-inflammatory drugs (NSAIDs), which are often easily accessible, even to patients at high risk for CKD.[61] Preventive measures should be taken when using iodinated contrast media in CKD patients given that CKD is a major risk factor for contrast-induced nephropathy. Such measures can include the use of *N*-acetylcysteine, volume expansion with intravenous isotonic saline or bicarbonate, limiting the dose/volume of contrast medium and discontinuing any concomitant medications that increase the risk of acute kidney injury.[14,62] Local drug formularies should also be consulted regarding dose adjustments for commonly prescribed medicines (reviewed in detail elsewhere).[14]

## Nutritional and Dietary Management

Although guidelines[14] generally recommend that individuals with CKD should receive expert dietary advice tailored to severity of CKD and focused on intake of salt, phosphate, potassium, and protein, this is not often possible in many LMICs given that there is a shortage of workforce in nephrology, especially dietitians.[24] Practical approaches should, however, still be developed in the context of various factors including local diets, weather, literacy and cultural practices, to increase awareness and appropriately restrict intake of fluid, salt, phosphate, potassium and protein.[63]

## Management of Regional CKD Among Agricultural Workers

A regional type of CKD has been documented among agricultural workers, particularly in Central America[64]

and South Asia (Sri Lanka and India),[65,66] but there are also suggestive reports from Africa (Egypt and Sudan).[67] Although commonly referred to as CKD of unknown origin (CKDu), they are also referred to as "Meso-American nephropathy," "Uddanam nephropathy" and "Sri Lankan nephropathy." Common causes have been hypothesized to include excessive heat exposure and dehydration and exposure to various nephrotoxins including NSAIDs and other painkillers, pesticides, heavy metals, arsenic, and infections (malaria, hantavirus infections, leptospirosis, etc.). Given that CKDu is mainly an occupational and environmental health problem, primary and secondary prevention strategies should be directed toward preventing heat-associated health risks, avoiding nephrotoxin exposures, providing clean and safe drinking water, avoiding the use of pesticides, enhancing worker health and safety programs and conducting medical surveillance in at-risk populations for early detection of disease.[68] Temporary or permanent restrictions of work schedules may be implemented in those at high risk of disease progression.

## Treatment of Complications (Fluid Overload, Anemia, CKD-MBD)

Disorders of sodium handling in the kidney become more prominent as CKD stage advances and usually become associated with fluid overload. Fluid overload contributes significantly to cardiovascular morbidity (hypertension, left ventricular hypertrophy) and mortality in CKD.[69] Measures to address fluid overload are commonly available and inexpensive and are veritable strategies employed globally, including among LMICs. These strategies include restriction of fluid intake, reduction in dietary salt intake as well as the use of diuretics.

Anemia is an important and treatable complication of CKD with its prevalence increasing exponentially from 4.7% to 51.5% as eGFR declines from CKD stage 2 to stage 4.[70] Relative erythropoietin (EPO) deficiency as well as iron deficiency (true and relative) play key roles in the pathophysiology of anemia of CKD and exogenous replacements of iron and erythropoiesis-stimulating agents (ESAs) underpin anemia management in CKD. Current strategies for anemia management in LMICs are the same as for high-income countries (HICs) and are available from clinical practice guidelines that describe the use of ESAs and iron as well as the desired targets of hemoglobin and other indices of anemia to evaluate anticipated responses. A major problem with anemia management in many LMICs relates to the availability and affordability of intravenous iron, ESAs as well as the availability and costs of monitoring anemia beyond measuring hemoglobin alone.[71] More research is also needed in these regions to better define the peculiarities of CKD-related anemia as there might be other modifying and/or contributory prevalent factors other than EPO deficiency in LMICs such as parasitosis, hemoglobinopathies and nutritional deficiencies.

Mineral bone disease (MBD) is a complication of CKD that contributes significantly to cardiovascular morbidity and mortality.[72] Its management usually involves dietary and pharmaceutical approaches addressing phosphate, vitamin D and parathyroid hormone serum levels. There is a Kidney Disease Improving Global Outcomes (KDIGO) guideline available to provide a framework for CKD-MBD management which LMICs can adapt for use based on the local availability of phosphate binders, vitamin D and its analogues.

## Referral to a Nephrologist and Timing of Renal Replacement Therapy

KDIGO recommends specialist referral for all CKD patients with an eGFR <30 mL/min/1.73 $m^2$, or with significant albuminuria, or progression of disease demonstrable by a decline in eGFR category.[14] Late referral is the transfer of CKD patients to nephrologists less than 1–6 months to the time of initiation of dialysis therapies and is associated with increased morbidity and poor median survival rates.[73] Increased mortality has been attributed to the worse biochemical and nutritional profiles among lately referred patients. Early referral affords the opportunity to discuss KRT options, establish vascular or peritoneal access, enable use of appropriate treatment of uremic complications and can reduce mortality.[74,75] Identified barriers to early referral in developed countries include older age, non-black non-Caucasian race, the absence of comorbidities such as diabetes, coronary artery disease and hypertension, and initial CKD care by a general internist rather than by a general practitioner.[76] The role these barriers play in LMICs, and the presence of additional barriers unique to LMICs, remain difficult to ascertain due to the paucity of registry data. The late diagnosis of CKD is, however, likely to be a significant contributor to delayed nephrology referrals and unplanned initiation of dialysis as human and infrastructural capacity for

screening and detection and early management of CKD is poor, especially among LMICs. Timely referral is predicated on the early detection and monitoring of CKD, a situation that remains a challenge in LMICs as discussed earlier . Additionally, given that healthcare financing in low-income countries tends to be mostly out-of-pocket for affected patients, early referral might not guarantee early presentation for specialist care due to the economic impact of such specialized care on personal/family finances.

## Monitoring of Established CKD

Healthcare costs of CKD care increase exponentially as CKD stage advances, and thus the role of monitoring established CKD in LMICs cannot be overemphasized given the enormous economic burden CKD care imposes on individual and national finances as well as the inequitable access to, and coverage of, KRT for those who progress to kidney failure.[12,77] Therefore, strategies designed to promote the effective monitoring of established CKD in LMICs would not only be of clinical benefit but also economic advantage. Monitoring of established CKD is multidimensional involving the periodic assessment for eGFR decline, new-onset or worsening albuminuria (albuminuria and declining eGFR being indicators of progression of CKD), assessing for control of underlying disease causing CKD (which could also contribute to the progression of disease) such as diabetes, systemic hypertension, HIV, and vigilance for complications associated with worsening CKD stage, such as anemia, hyperphosphatemia and hyperkalemia.

KDIGO recommends the use of serum creatinine measurements and GFR determination utilizing the 2009 CKD-EPI estimating equation in the initial and subsequent assessments of GFR in CKD management.[14] There is a dearth of country-specific literature available to establish the degree to which both serum creatinine and eGFR determinations are currently being used for CKD follow-up in component countries of LMICs. The ISN-GKHA reported that 78% of countries in the LMICs never reported or used serum creatinine with eGFR in CKD monitoring at the secondary or tertiary care level of healthcare delivery, in contrast to 0% in HICs.[8] The inherent inaccuracies of eGFR equations among different ethnicities is likely to be a barrier to the widespread use of a universal estimating equation in these regions.[15] LMICs are made up of more heterogeneous ethnicities than HICs, thus necessitating the call for the development and validation of ethnicity-specific equations. It is more probable that serum creatinine measurements alone are the more commonly used parameters employed to monitor GFR trends. This is again reflected in the global kidney health care status survey which illustrated that serum creatinine without eGFR was usually used for monitoring at the secondary or tertiary level in 70% of low-income countries. KDIGO preferentially suggests the use of urine albumin-to-creatinine ratio (UACR) over manually read total protein urinalysis strips in assessing albuminuria in CKD diagnosis and follow-up.[14] This suggestion is however at variance with what truly obtains in LMICs. In low income countries, 0% of countries always use, UACR in albuminuria evaluation at the secondary or tertiary level of care while only 6% usually use UACR.[8] These figures forebode poor outcomes for CKD patients in these countries as the primary goal of slowing the progression of CKD by close monitoring is not attained.

## Conservative Care Options for Kidney Failure Treatment

Conservative kidney management (CKM) is an emerging sub-specialty in nephrology that refers to the application of palliative medicine principles and practices to patients with kidney disease. Although this often involves stopping dialysis (or not initiating dialysis in some patients with kidney failure), the term encompasses several domains that include symptom management (physical, psychological and spiritual), expert communication (prognosis sharing and shared decision making), interdisciplinary team support (nephrologist, palliative care specialist, nurse, dietitian, chaplain, social worker) and end-of-life care (use of hospice, maximize dignity and bereavement support).[78] Due to unavailability of various KRT modalities, various forms of CKM are often practiced in many LMICs with or without the appropriate professionals. It is important for kidney caregivers to be accustomed with CKM in order to provide total care for most patients who are unable to afford KRT.

## Future Directions: CKD Chronic Care Model as a Management Strategy

A more integrated, multidisciplinary, and sustainable approach to CKD management ought to be promoted in LMICs. As there is a dearth of specialized kidney care health professionals, an approach that co-opts other members of the health care team such as primary care physicians, nurses, and community health workers may be the way forward. There should also be a shift away from the

traditional/contemporary model of kidney and health care delivery which is provider-/organization-level-based to a patient-centered model of care.[79] This is particularly relevant to patients in culturally steeped communities for whom socio-cultural issues also play a prominent role in accessing health care. Chronic care models (CCM) in chronic diseases aim to promote cohesive, patient-centered, culturally competent, evidence-based, and cost-effective healthcare delivery.[80] The adoption of CCMs in CKD management is especially relevant in LMICs countries as a CCM provides a structure that harnesses, coordinates and integrates available human capacity (patient and health care teams), health care organizational capabilities, political/governmental resources and locally adapted clinical information systems with the aim of providing standard, reproducible, sustainable and cost-effective care to CKD patients while improving outcomes such as progression to kidney failure or death. The use of a CCM model in its entirety, or elements thereof, in the long-term care of patients with chronic diseases has been described in conditions such as diabetes, chronic respiratory diseases, mental health and HIV with varying benefits on care processes and/or patient outcomes.[81–85] While a more universal use of CCMs in CKD management in LMICs has the broad objective of improving CKD outcomes, a one-size-fits-all model might prove ineffective because CKD epidemiology is heterogeneous, local capacities are varied and healthcare financing priorities and budgets are different (given the local competing demands of acute and chronic infectious diseases). In SSA, for instance, HIV constitutes a major determinant of CKD epidemiology as opposed to diabetes in the Indian subcontinent. Each country would therefore have to identify domains of the model that would require emphasis based on local peculiarities.

## Conclusion

CKD continues to rise and is a major public health problem in LMICs. Due to economic challenges related to the cost of kidney care, unavailability and inaccessibility of various KRT modalities due to economic challenges, early disease detection, preventive measures and use of integrative approaches for chronic disease management remains the best options for management of CKD in these settings. There is need for the governments in LMICs to improve primary health care systems and to strengthen their NCD strategies in order for these preventive measures to become effective.

## Funding

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