Mind the gap in kidney care: translating what we know into what we do

Valerie A Luyckx[1,2,3 # *], MD, Katherine R Tuttle[4,5 #], MD, Dina Abdellatif[6 †], MD, Ricardo Correa-Rotter[7 †], MD, Winston WS Fung[8], MBBChir (Cantab), FRCP (Lond), Agnès Haris[9 †], MD, PhD, LL Hsiao[2 †], MD, Makram Khalife[10 ‡], BA, Latha A Kumaraswami[11 †], BA, Fiona Loud[10 ‡], BA, Vasundhara Raghavan[10 ‡], BA, Stefanos Roumeliotis[12], MD, Marianella Sierra[10 ‡], BA, Ifeoma Ulasi[13 †], MD, Bill Wang[10 ‡], BA, SF Lui[14 †], MD, Vassilios Liakopoulos[12 †], MD, PhD, Alessandro Balducci[15 †], MD; for the World Kidney Day Joint Steering Committee

[1] Department of Public and Global Health, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland
[2] Renal Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, United States
[3] Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa
[4] Providence Medical Research Center, Providence Inland Northwest Health, Spokane, United States
[5] Nephrology Division, Department of Medicine, University of Washington, Seattle, United States
[6] Department of Nephrology, Cairo University Hospital, Cairo, Egypt
[7] Department of Nephrology and Mineral Metabolism, National Medical Science and Nutrition Institute Salvador Zubiran, Mexico City, Mexico
[8] Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong SAR, China
[9] Nephrology Department, Péterfy Hospital, Budapest, Hungary
[10] International Society of Nephrology Patient Liaison Advisory Group
[11] Tamilnad Kidney Research Foundation, Chennai, India
[12] 2nd Department of Nephrology, AHEPA University Hospital Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece
[13] Department of Medicine, College of Medicine, University of Nigeria, Ituku-Ozalla, Enugu, Nigeria
[14] Division of Health System, Policy and Management, The Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong SAR, China
[15] Italian Kidney Foundation, Rome, Italy

[#] Equal contribution

[†] Members of the World Kidney Day Joint Steering Committee

[‡] Patient representatives of the Patient Liaison Advisory Group of the International Society of Nephrology

* Corresponding author: valerie.luyckx@uzh.ch

Hong Kong Med J 2024;30:200-1.e1-12
https://doi.org/10.12809/hkmj245162

ABSTRACT

Historically, it takes an average of 17 years to move new treatments from clinical evidence to daily practice. Given the highly effective treatments now available to prevent or delay kidney disease onset and progression, this is far too long. The time is now to narrow the gap between what we know and what we do. Clear guidelines exist for the prevention and management of common risk factors for kidney disease, such as hypertension and diabetes, but only a fraction of people worldwide with these conditions are diagnosed, and even fewer receive appropriate treatment. Similarly, the vast majority of people living with kidney disease are unaware of their condition, because in the early stages it is often silent. Even among diagnosed patients, many do not receive appropriate treatment for kidney disease. Considering the serious consequences of kidney disease progression, kidney failure, or death, it is imperative to initiate treatments early and appropriately. Opportunities to diagnose and treat kidney disease early must be maximised, starting at the primary care level. Many systematic barriers exist, encompassing patient, clinician, health system, and societal factors. To preserve and improve kidney health for everyone everywhere, each of these barriers must be acknowledged so that sustainable solutions are developed and implemented without further delay.

At least 1 in 10 people worldwide is living with a kidney disease.[1] According to the Global Burden of Disease study, >3.1 million deaths were attributed to kidney dysfunction in 2019, making it the seventh leading risk factor for mortality worldwide (Fig 1 and online supplementary Fig).[2] However, global mortality from all kidney diseases may actually range from 5 to 11 million per year if the mortality rate also includes estimated lives lost from acute kidney injury and lack of access to renal replacement therapy for kidney failure (KF), especially in lower-resource settings.[3] These high global mortality rates

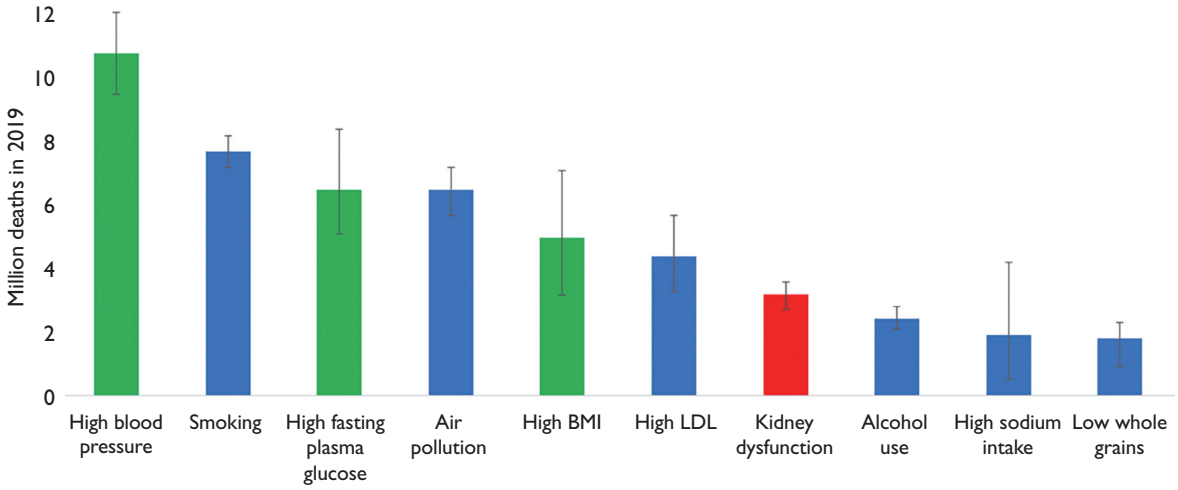

FIG 1. Top 10 global risk factors for mortality, all ages, 2019. Kidney dysfunction (defined as estimated glomerular filtration rate <60 mL/min per 1.73 m^2 or albumin-to-creatinine ratio ≥30 mg/g) was the seventh-highest global level 3 risk factor for death in 2019 (red). The three leading global risk factors for kidney diseases, including hypertension, diabetes, and overweight/obesity, are also leading global risk factors for mortality (green); therefore, holistic strategies are required to simultaneously address all risk factors. Rankings are based on millions of deaths attributed to each risk factor. Error bars depict confidence intervals. Global rankings of kidney dysfunction stratified by World Bank income category and sex are presented in online supplementary Figure. Data in this figure were obtained from the Global Burden of Disease Study[2]
Abbreviations: BMI = body mass index; LDL = low-density lipoprotein

reflect disparities in prevention, early detection, diagnosis, and treatment of chronic kidney disease (CKD).[4] Mortality rates from CKD are especially high in some regions, particularly Central Latin America and Oceania (islands of the South Pacific Ocean), highlighting the need for urgent action.[5]

Chronic kidney disease also represents a substantial global economic burden, with exponentially increasing costs as CKD progresses, due to the costs of dialysis and transplantation, as well as multiple co-morbidities and complications that accumulate over time.[6,7] In the United States, Medicare fee-for-service spending for all beneficiaries with CKD was US$86.1 billion in 2021 (22.6% of total expenditures).[8] Data from many lower-resource settings, where most healthcare spending comprises out-of-pocket costs, are absent. A recent study in Vietnam showed that the per-patient cost of CKD was higher than the gross domestic product per capita.[7] In Australia, it has been estimated that early diagnosis and prevention of CKD could save the health system AU$10.2 billion over 20 years.[9]

Although there is regional variation in the causes of CKD, the risk factors with the highest population-attributable factors for age-standardised CKD-related disease-adjusted life years are hypertension (51.4%), a high fasting plasma glucose level (30.9%), and a high body mass index (26.5%).[10] These risk factors are also leading risk factors for mortality worldwide (Fig 1). Only 40% and 60% of people with hypertension and diabetes, respectively, are aware of their diagnosis; considerably smaller proportions of these individuals are receiving treatment and reaching therapeutic targets.[11,12] Moreover, at least 1 in 5 people with hypertension and 1 in 3 people with diabetes also have CKD.[13]

Most cases of CKD can be prevented through healthy lifestyles, prevention and management of risk factors, avoidance of acute kidney injury, optimisation of maternal and child health, mitigation of climate change, and efforts to address social and structural determinants of health.[3] Nevertheless, the benefits of some of these measures may only be evident in future generations. Until then, early diagnosis and risk stratification create opportunities to introduce therapies that can slow, halt, or even reverse CKD.[14] It is concerning that CKD awareness is particularly low among individuals with kidney dysfunction, such that approximately 80% to 95% of such patients worldwide are unaware of their diagnosis (Fig 2).[15-20] Therefore, people are dying because of missed opportunities to detect CKD early and deliver optimal care.

Furthermore, CKD is a major risk factor for cardiovascular disease; during kidney disease progression, cardiovascular death and KF become competing risks.[21] Indeed, data from the 2019 Global Burden of Disease Study showed that more deaths were caused by kidney dysfunction–related cardiovascular disease (1.7 million deaths) than by CKD itself (1.4 million deaths).[2] Therefore,

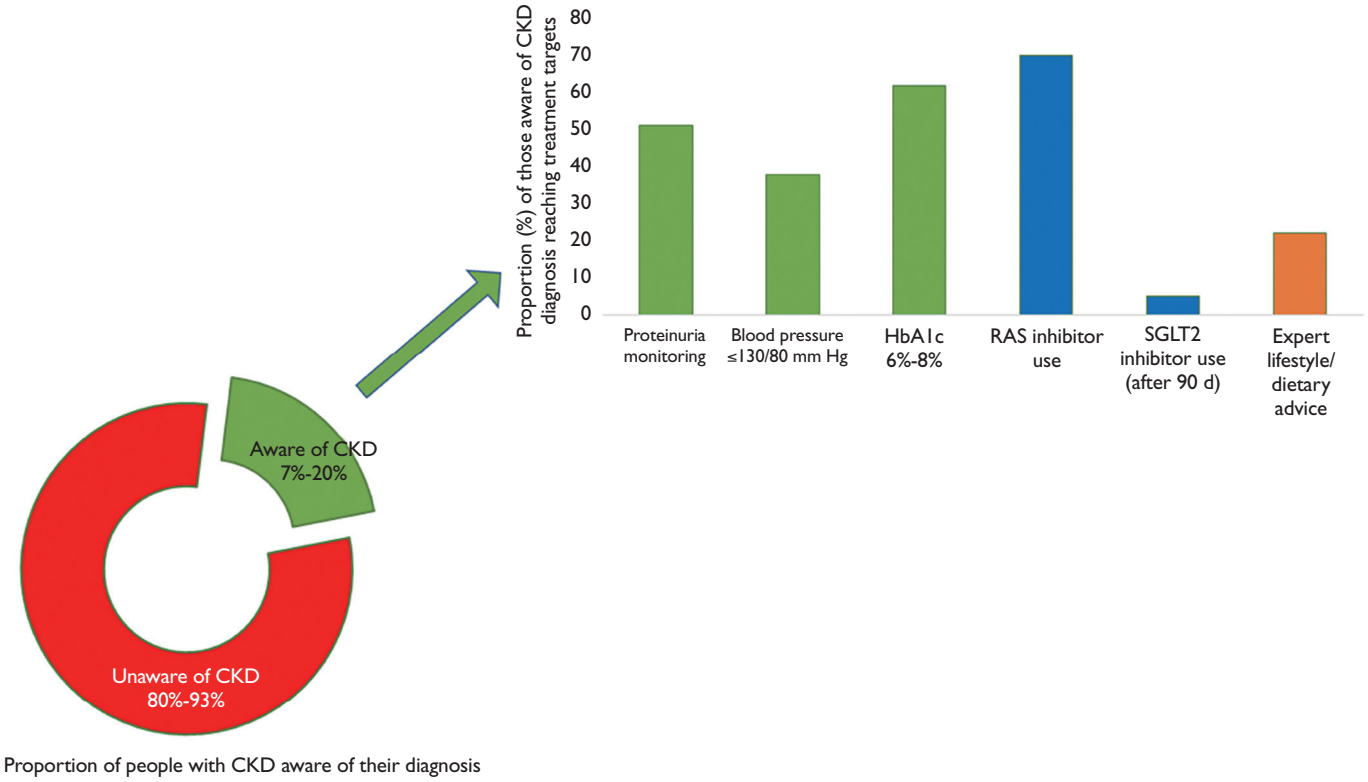

FIG 2. Proportion of people with chronic kidney disease (CKD) who are aware of their diagnosis and receiving guideline-recommended care. The proportion of people with CKD who are aware of their diagnosis varies from 7% to 20% worldwide. Knowledge of CKD increases as CKD stage worsens. Among those with a diagnosis of CKD, the average proportion of patients receiving appropriate medication to delay CKD progression (renin-angiotensin-aldosterone system [RAS] inhibitors and sodium-glucose cotransporter 2 [SGLT2] inhibitors) is suboptimal, as are the average proportions of patients achieving target blood pressure, maintaining diabetes control, and receiving nutrition advice. Treatment targets depicted in the figure follow the 2012 Kidney Disease: Improving Global Outcomes guidelines.[15] Most data are from higher-resource settings; the corresponding proportions are likely to be lower in lower-resource settings. Data represent the proportions of patients reaching blood pressure <130/80 mm Hg. Data compiled from previous studies[15-20]
Abbreviation: HbA1c = haemoglobin A1c

cardiovascular disease management should also be prioritised for people with CKD.

Gaps between knowledge and implementation in kidney care

Strategies to prevent and treat CKD have been established on the basis of strong evidence collected over the past three decades (Fig 3).[19,22] Clinical practice guidelines for CKD are clear; however, adherence to these guidelines is suboptimal (Fig 2).[15,19,20]

Regardless of aetiology, management of major risk factors, particularly diabetes and hypertension, forms the basis of optimal care for people with CKD.[19,23] In addition to lifestyle changes and risk factor control, the earliest pharmacological agents to demonstrate kidney protection were renin-angiotensin-aldosterone system inhibitors in the form of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers.[14,19] Despite decades of knowledge that these medications have substantial protective effects on renal and cardiovascular function in people with CKD, real-world data from electronic health records show that their use remains low (Fig 2). For example, in the United States, ACEI and angiotensin receptor blocker utilisation rates ranging from 20% to 40% were reported ≥15 years after the most recent approval of these agents for patients with CKD and/or type 2 diabetes.[24] Although more recent data show that prescribing rates in this population have improved to 70%, only 40% of such patients continue taking an ACEI or angiotensin receptor blocker for at least 90 days.[20] These data indicate gaps in prescribing nephroprotective medication and continuity of care over time, potentially related to cost, lack of patient education, polypharmacy, and adverse effects.[25]

Although the initial enthusiasm for sodium-glucose cotransporter 2 (SGLT2) inhibitors focused

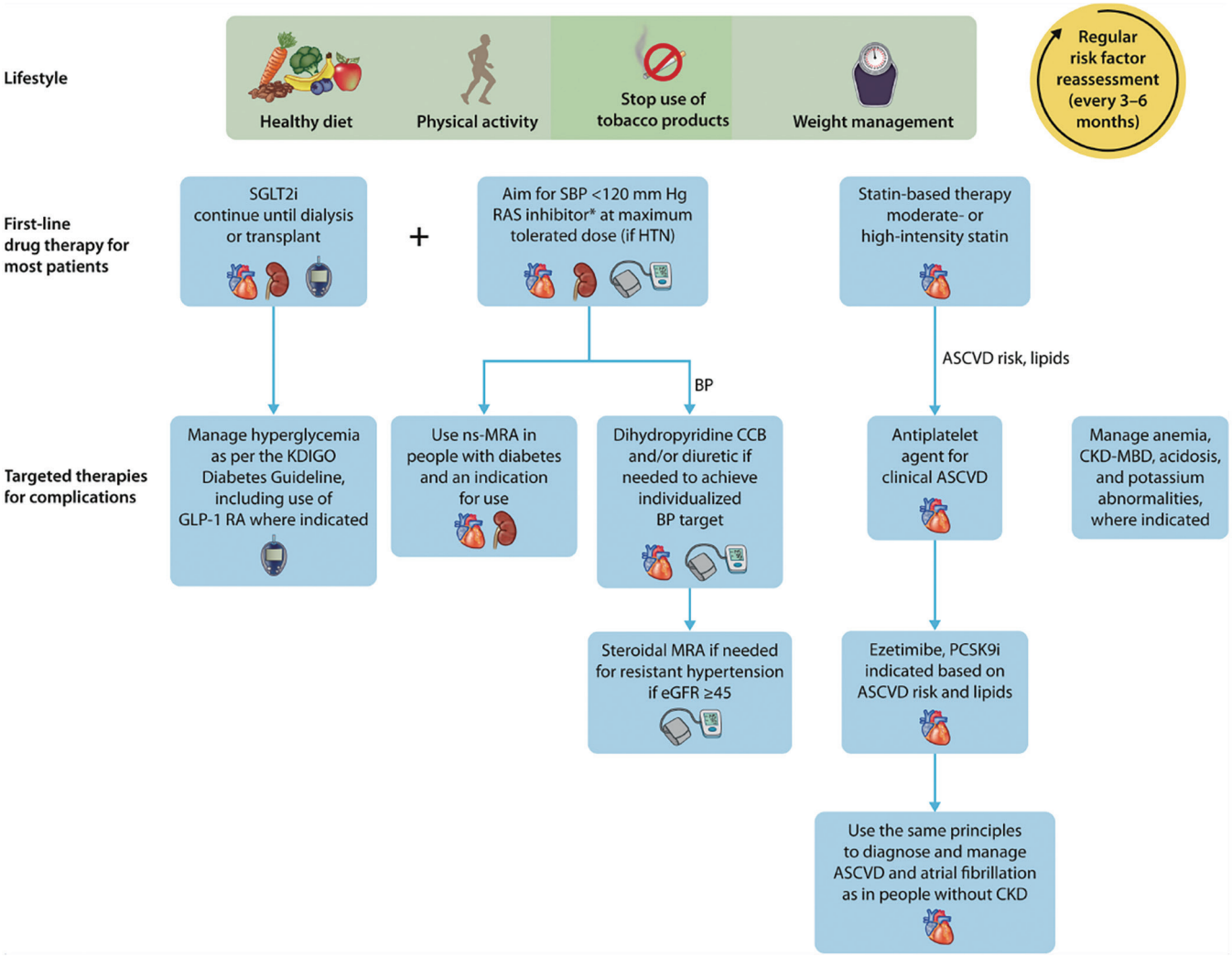

FIG 3. Recommended optimal lifestyle and therapeutic management for chronic kidney disease (CKD) in people with diabetes. Illustration of a comprehensive and holistic approach to optimising kidney health in people with CKD. In addition to key lifestyle adjustments, attention to diabetes, blood pressure (BP), and cardiovascular risk factors is important for kidney care

Abbreviations: ASCVD = atherosclerotic cardiovascular disease; CCB = calcium-channel blocker; CKD-MBD = chronic kidney disease–mineral and bone disorder; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HTN = hypertension; MRA = mineralocorticoid receptor antagonist; ns-MRA = nonsteroidal mineralocorticoid receptor antagonist; PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor; RAS = renin-angiotensin-aldosterone system; SBP = systolic blood pressure; SGLT2-i = sodium-glucose cotransporter 2 inhibitor

*Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker therapy should be first-line treatment for BP control when albuminuria is present; otherwise, dihydropyridine CCB or diuretic treatment can be considered

Figure reproduced from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. https://doi.org/10.1016/j.kint.2023.10.018[22]

on their benefits for diabetes and cardiovascular disease, unprecedented therapeutic benefits have also been observed regarding CKD. Relative risk reduction levels with SGLT2 inhibitors approach 40% for substantial decreases in estimated glomerular filtration rate, KF, and mortality among populations with several types of CKD, heart failure, or elevated cardiovascular disease risk.[26,27] These decreases were observed in addition to benefits from standard-of-care risk factor management and renin-angiotensin-aldosterone system inhibitors. The risks of heart failure, cardiovascular death, and all-cause mortality were also reduced in patients with CKD during SGLT2 inhibitor treatment.[26] The addition of SGLT2 inhibitors to renin-angiotensin-aldosterone system inhibitor–based treatment was able to delay

the need for renal replacement therapy by several years, depending on the initial timing of combined treatment.[28] Moreover, for every 1000 patients with CKD who received an SGLT2 inhibitor in addition to standard therapy, 83 deaths, 19 heart failure–related hospitalisations, 51 instances of dialysis initiation, and 39 episodes of acute renal function worsening were prevented.[29]

The persistent underuse of these and other guideline-recommended therapies involving SGLT2 inhibitors is concerning (Fig 2).[20,24] In the CURE-CKD (Center for Kidney Disease Research, Education and Hope–CKD) Registry, only 5% and 6.3% of eligible patients with CKD and diabetes, respectively, continued to receive SGLT2 inhibitor and glucagon-like peptide-1 receptor agonist therapy at 90 days.[18] Notably, a lack of commercial health insurance and the receipt of treatment in community-based (versus academic) institutions were associated with lower likelihoods of SGLT2 inhibitor, ACEI, or angiotensin receptor blocker prescriptions among patients with CKD and diabetes.[20] In low- or middle-income countries (LMICs), the gap between evidence and implementation is even wider, considering the high cost and inconsistent availability of these medications, although generics are available.[30] Such gaps in delivering optimal care for CKD are unacceptable.

In addition to SGLT2 inhibitors, nonsteroidal mineralocorticoid receptor antagonists have been demonstrated to reduce the risks of CKD progression, KF, cardiovascular events, and mortality, when used in addition to standard-of-care treatment involving renin-angiotensin-aldosterone system inhibitors, among people with type 2 diabetes.[31] There is a growing portfolio of promising therapeutic options, including glucagon-like peptide-1 receptor agonists (NCT03819153, NCT04865770), aldosterone synthase inhibitors (NCT05182840), and dual-to-triple incretins (online supplementary Table 1).[26,32] Furthermore, there is clear evidence that in patients with CKD and/or type 2 diabetes, glucagon-like peptide-1 receptor agonists reduce cardiovascular events, constitute safe and effective glucose-lowering therapies, and aid in weight loss.[32]

Historically, it has taken an average of 17 years for new treatments to move from clinical evidence to routine practice.[33] Considering that millions of people with CKD die each year, this waiting period is far too long.

Closing the 'gap' between what we know and what we do

Lack of policy and presence of global inequity

Health policy

Since the launch of the World Health Organization Global Action Plan for the prevention and control of non-communicable diseases (NCDs) in 2013, there has been global progress in the proportion of countries with a national NCD action plan and dedicated NCD units.[34] However, CKD is incorporated into NCD strategies in approximately one-half of countries.[4] Policies are required to integrate kidney care within essential health packages under universal health coverage (Fig 4).[30] Multisectoral policies must also address social determinants of health, which are major amplifiers of CKD risk and severity that limit people's opportunities to improve their health.[3] A lack of investment in kidney health promotion, along with primary and secondary prevention of kidney diseases, hinders progress.[14]

Health systems

Two major goals of universal health coverage are to achieve coverage for essential health services and to reduce financial hardship imposed by healthcare. However, universal health coverage alone is insufficient to ensure adequate access to kidney care.[3] Health systems must be strengthened, and quality of care must be prioritised, because poor quality care contributes to more deaths than lack of access in low-resource settings.[35] Quality care requires a well-trained healthcare workforce, sustainable availability of accurate diagnostics, reliable infrastructure, and medication supplies; it should be monitored through a continuous quality improvement process (Fig 4). Medication quality, especially in LMICs, may be an additional barrier to successful management of CKD.[36] Regulation and monitoring of drug manufacturing and quality standards are important to ensure safe and effective therapies. Strategies to support regulation and quality assurance should be developed according to local circumstances and guidelines, as outlined elsewhere.[37]

The establishment of a credible case for CKD detection and management based on real-world data regarding risks, interventions, outcomes, and costs will help translate theoretical cost-effectiveness (currently established primarily in high-income countries with minimal data from other countries) into economic reality.[30,38] Screening should include evaluation of risk factors for CKD; identification of family history; recognition of potential symptoms (usually advanced, such as fatigue, poor appetite, oedema, and itching); and measurements of blood pressure, serum creatinine, urine components (ie, urinalysis), and urine albumin/protein to creatinine ratio, as outlined in established guidelines.[19,39] Early identification of CKD in primary care is expected to lower costs over time by reducing CKD complications and KF. Medications required for kidney care are already included in the World Health Organization Model List of Essential Medicines (Table 1). These medications should be provided at the national level

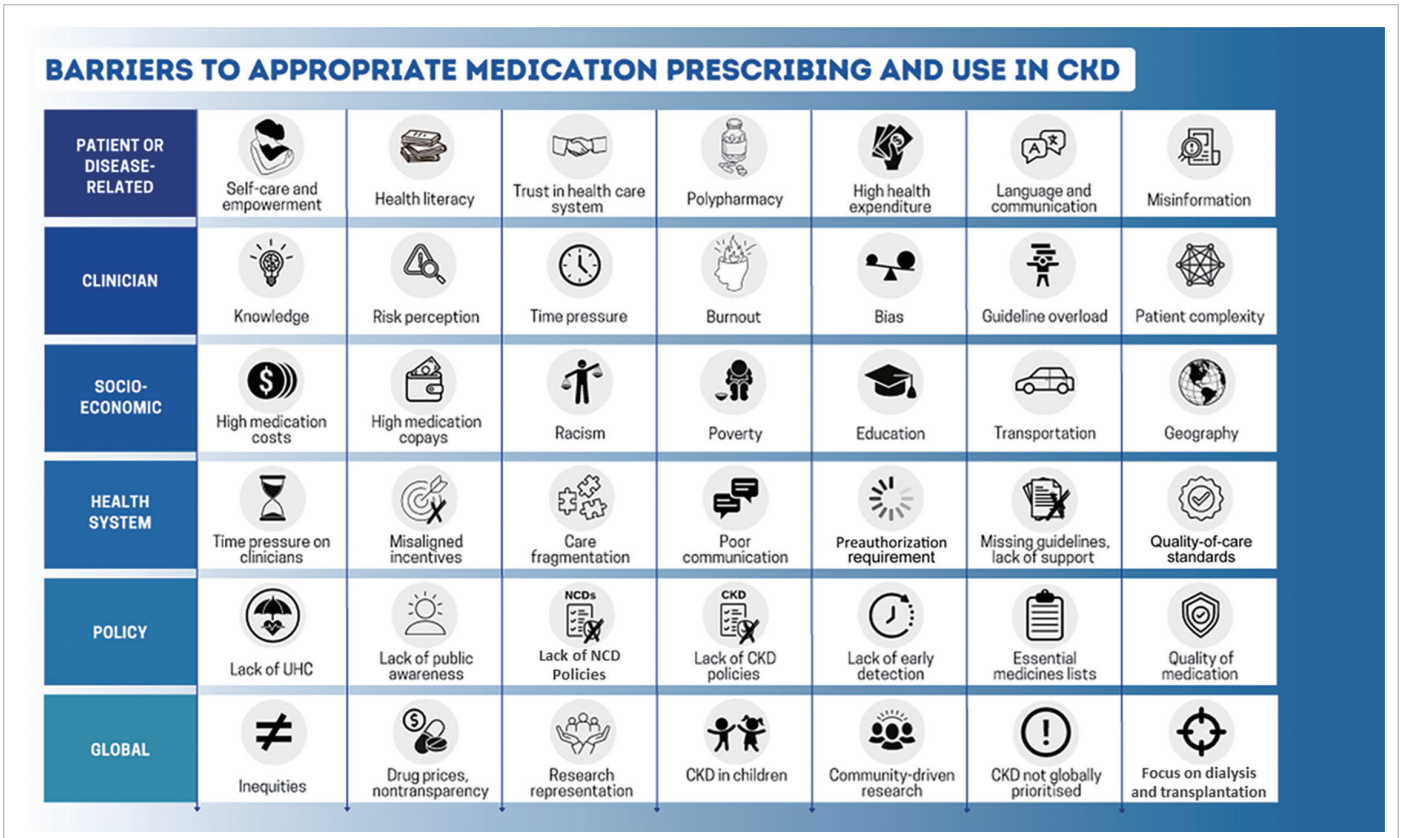

FIG 4. Depiction of factors impacting the implementation of timely, high-quality kidney care
Abbreviations: CKD = chronic kidney disease; NCD = non-communicable disease; UHC = universal health coverage

under universal health coverage.[40] Additionally, pharmaceutical companies should provide these medications at affordable prices.

Challenges in primary care and clinical inertia

Healthcare professionals

The shortage of primary care professionals is exacerbated by inconsistent access to specialists and allied health professionals in both high-income countries and LMICs. It is essential to define roles and responsibilities for kidney care. Solutions may include multidisciplinary team care (primary care physicians, pharmacists, specialists, nurses, therapists, educators, nutritionists, and mental health professionals), well-established mechanisms for collaboration among all elements, and rapid communication technologies (both within health systems and among health professionals) to support care and decision-making.[41,42] Brain drain in low-resource settings is a complex issue that must be addressed.

The mobilisation of community health workers yields cost-savings in infectious disease programmes within LMICs; it may facilitate early detection, diagnosis, and management of NCDs.[43] Protocolised CKD management, possibly assisted by electronic decision-support systems, may be appropriate for interventions at the community level, with the integration of primary care physicians and aid from nephrologists and other professionals.[44,45] For example, in some settings, pharmacists could identify people with diabetes or hypertension exhibiting CKD risk, based on their prescriptions, then offer on-site testing and referral as needed.[46] Pharmacists could also provide medication reconciliation and advice regarding safety, effectiveness, and adherence. Social workers and pharmacists can help patients with medications to access suitable programmes.[46]

Clinical inertia

Clinical 'inertia', commonly regarded as a causative factor in low prescribing rates, has many facets (Fig 4).[47] Many knowledge gaps regarding CKD exist among primary care physicians.[48] Such gaps can be remedied with focused public and professional education. Additional factors include fear of adverse effects from medication, misaligned incentives within

TABLE 1. Essential medicines for patients with kidney disease

Medication/technology	Example	Reason	On WHO Model List of Essential Medicines
ACE inhibitor	Enalapril, lisinopril	Delays CKD progression; prevents cardiovascular disease and stroke	Yes
Angiotensin receptor blocker	Losartan, telmisartan	Delays CKD progression, cardiovascular disease, and stroke	Yes
Calcium channel blocker	Amlodipine, verapamil	BP control	Yes
Loop diuretic	Furosemide, torsemide	Useful when GFR is low, good for heart failure	Yes
Thiazide diuretic	Hydrochlorothiazide, metolazone, indapamide	Good for BP, especially in Black individuals	Yes
SGLT2 inhibitor	Empagliflozin, canagliflozin, dapagliflozin	Diabetes control; delays CKD progression, cardiovascular disease, and death	Yes
GLP-1 agonist	Semaglutide	Diabetes control, weight loss	No
Mineralocorticoid inhibitor	Spironolactone, finerenone	Delays CKD progression, reduces heart failure risk Caution: risk of hyperkalaemia in patients with kidney diseases	Yes/no
β-blocker	Bisoprolol	Prevention and treatment of ischemic heart disease	Yes
Statin	Simvastatin	Prevention of CAD in patients with CKD, patients with kidney transplant	Yes
Aspirin		Secondary prevention of MI in patients with CKD, patients with kidney transplant	Yes
Fixed-dose combinations (polypill)	Aspirin + atorvastatin + ramipril	Simultaneous management of CKD, cardiovascular disease, and risk factors where indicated*	Yes
	Aspirin + simvastatin + ramipril + atenolol + hydrochlorothiazide		Yes
	Aspirin + perindopril + amlodipine		Yes
Oral hypoglycaemic medication	Gliclazide, metformin, SGLT2 inhibitors	DM management Caution with dosing and GFR	Yes
Insulin	Long- and short-acting	DM management	Yes

Abbreviations: ACE = angiotensin-converting enzyme; BP = blood pressure; CAD = coronary artery disease; CKD = chronic kidney disease; DM = diabetes mellitus; GFR = glomerular filtration rate; GLP-1 = glucagon-like peptide-1; MI = myocardial infarction; SGLT2 = sodium-glucose cotransporter 2; WHO = World Health Organization

* Polypills containing aspirin may not be appropriate for patients with early CKD who lack other cardiovascular indications

the health system, excessive workload, formulary restrictions, and clinician burnout.[47] Furthermore, inconsistent recommendations in guidelines from different professional organisations may enhance confusion. A major barrier to optimal care is the time constraints imposed on individual clinicians. A typical primary care physician in the United States would require approximately 26.7 hours per day to implement guideline-recommended care for a panel of 2500 patients.[49] Innovation is required to support guideline implementation, especially for primary care physicians who must follow multiple guidelines to meet the diverse needs of their patients. Electronic health records, reminders, team-based nudges, and decision-support tools offer potentially valuable assistance for quality kidney care in busy clinical practices.[50] However, the additional time and effort involved in negotiating pre-authorisations or completing medication assistance programme requests, as well as the need for frequent monitoring of multiple medications, also hinder appropriate prescribing.[25] Many primary care physicians only have a few minutes allocated for each patient because of institutional pressure or patient volume. The term 'inertia' can hardly be applied to clinicians working at this pace. The number of health professionals worldwide must increase.

Visits for patients with CKD are complex

because multimorbidity is common. Such patients are often managed by multiple specialists, leading to fragmentation of care, lack of holistic oversight, and diffusion of responsibility for treatment. Single and combined outcomes analyses have shown that multidisciplinary care improves transition to renal replacement therapy and reduces mortality.[51] Novel 'combined clinic' models with on-site collaboration and joint participation (eg, with nephrologists, cardiologists, and endocrinologists) may provide substantial benefits for patients in terms of reduced fragmentation of care, logistics, and cost savings.

Patient centeredness

Health literacy

Self-management is the most important aspect of kidney care. A patient's ability to understand his/her health needs, make healthy choices, feel safe and respected in the health system, and obtain psychosocial support are important for promoting health decision-making (Fig 4). Good communication should begin with quality information and confirmation of 'understanding' by the patient (and family members, as applicable). Electronic apps and reminders can serve as useful tools that support patients by improving disease knowledge, promoting patient empowerment, and improving self-efficacy; however, a one-size-fits-all approach is unlikely to be successful.[52] Important barriers include a lack of patient health information, poor communication, and mistrust, especially in the marginalised and minoritised communities where CKD is common.[30] Patients may also be confused by contradictory recommendations among healthcare professionals, as well as conflicting messages in mainstream media. Innovative platforms that improve CKD-related communication between patients and clinicians represent a promising approach to promote optimal prescribing and adherence.[53,54]

Patient perspectives are essential when designing and testing health strategies to overcome barriers and promote equity. Collaborative care models must include patients, families, and community groups, as well as various types of healthcare professionals, health systems, government agencies, and payers.[38] Advocacy organisations, local community groups, and peer navigators with trusted voices and relationships can serve as conduits for education while providing input regarding the development of patient tools and outreach programmes.[55] Most importantly, patients must be the focus of their own care.

Medication cost and availability

In high-income countries, people without health insurance and people with high copays paradoxically pay the highest amounts for essential and non-essential medications.[38] Across LMICs, kidney diseases represent the leading cause of catastrophic health expenditures due to reliance on out-of-pocket payments.[56] In 18 countries, four cardiovascular disease medications frequently indicated in CKD (statins, ACEIs, aspirin, and β-blockers) had greater availability in private settings than in public settings; they were mostly unavailable in rural communities, and they were unaffordable for 25% of people in upper middle-income countries and 60% of people in low-income countries.[57] Newer therapies may be prohibitively expensive worldwide, especially where generics are not yet available. In the United States, the retail price for a 1-month supply of an SGLT2 inhibitor or finerenone is approximately US$500 to $700; for glucagon-like peptide-1 receptor agonists, the retail price is approximately US$800 to $1200 per month.[38] This reliance on out-of-pocket payments for vital, life-saving essential medications is unacceptable (Fig 4).

Special considerations

Not all kidney diseases are equal. Much of what has been discussed here applies to the most common forms of CKD (eg, diabetes-related and hypertension-related). Some incompletely understood forms of CKD have different risk profiles, including environmental exposures, genetic predisposition, and autoimmune or other systemic disorders. Highly specialised therapies may be required. Pharmaceutical companies should be responsible for ensuring that research studies include disease-representative participants with appropriate representation (eg, race, ethnicity, sex, and gender), that effective drugs are made available after studies, and that the balance between profits and prices is fair and transparent. Many novel therapies are offering new hope for various kidney diseases; once these therapies are approved, there must be no delay in extending benefits to all affected patients (online supplementary Table 1).

An important but often overlooked group consists of children with kidney diseases. This group is especially vulnerable in LMICs, where nephrology services and resources are limited; families must often decide whether to pay for one child's treatment or support the rest of the family.[58] Children with CKD also have a high risk of cardiovascular disease, even in high-income settings, and they require more attention to control risk factors and achieve treatment targets.[59]

Fostering innovation

Implementation science and knowledge translation

Considering that rigorous evidence-based treatments for CKD have been established, implementation

must be optimised.[60] Implementation research aims to identify effective solutions by understanding how evidence-based practices, often developed in high-income countries, can be integrated into care pathways in lower-resource settings. The management of CKD is suitable for implementation research: optimal therapeutic strategies are known, outcomes are easily measurable, and essential diagnostics and medications already are in place. Crucial components of such research are the identification of local patient preferences and elucidation of challenges. Ministries of health should commit to overcoming identified barriers and scaling up successful and sustainable programmes.

Polypills as an example of simple innovation

Polypills are attractive on multiple levels: fixed doses of several guideline-recommended medications are present within a single tablet (Table 1), the price is low, the pill burden is reduced, and the regimen is simple.[61] Polypills can prevent cardiovascular disease and are cost-effective for patients with CKD.[62] More studies are needed, but considering the alternatives of costly renal replacement therapy or premature death, it is likely that polypills will be a cost-effective approach for reducing CKD progression.

Harnessing digital technologies

The integration of telehealth and other types of remotely delivered care can improve efficiency and reduce costs.[63] Electronic health records and registries can support monitoring of quality of care and identify gaps to guide implementation and improve outcomes within an evolving health system that is capable of learning. Artificial intelligence may also be harnessed to stratify risk, personalise medication prescribing, and facilitate adherence.[64] The use of telenephrology for communication between primary care physicians and specialists may also be beneficial for patient care.[65]

Patient perspectives

Multiple methods can support the identification of patient preferences for CKD care, including interviews, focus groups, surveys, discrete choice experiments, structured tools, and simple conversations.[66,67] Many of these methods are currently in the research phase. Clinical translation will require contextualisation and assessments of local and individual acceptability.

The journey of each person living with CKD is unique; however, common challenges and barriers exist. As examples of lived experiences, comments collected from patients about their medications and care are detailed in online supplementary Table 2. These voices must be heard and acknowledged to close gaps and improve the quality of kidney care worldwide.

Call to action

The current lack of progress in kidney care has been tolerated for far too long. New therapeutic advances offer real hope that many people with CKD can survive without developing KF. The evidence for clinical benefit is overwhelming and unequivocal. These patients cannot wait another 17 years for this evidence to be translated into clinical practice.[33] It is time to ensure that all who are eligible for CKD treatment receive this care in an equitable manner.

Known barriers and global disparities in access to diagnosis and treatment must be urgently addressed (Fig 4). To achieve health equity for people with kidney diseases and those at risk of developing kidney diseases, we must raise awareness among policy makers, patients, and the general population; harness innovative strategies to support all cadres of healthcare workers; and balance profits with reasonable prices (Table 2). If we narrow the gap between what we know and what we do, kidney health will become a reality worldwide.

Author contributions

All authors contributed equally to the conception, preparation, and drafting of the manuscript.

Conflicts of interest

VA Luyckx is chair of the Advocacy Working Group of the International Society of Nephrology and has no financial disclosures. KR Tuttle has received research grants from the National Institutes of Health (National Institute of Diabetes and Digestive and Kidney Diseases, National Heart, Lung, and Blood Institute, National Center for Advancing Translational Sciences, National Institute on Minority Health and Health Disparities, director's office), the United States Centers for Disease Control and Prevention, and Travere Therapeutics; and consultancy fees from AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, and Novo Nordisk. She is also chair of the Diabetic Kidney Disease Collaborative for the American Society of Nephrology. R Correa-Rotter is a member of the Steering Committee for World Kidney Day, a member of the Diabetes Committee of the Latin American Society of Nephrology and Hypertension, and a member of the Latin American Regional Board of the International Society of Nephrology. He is also a member of the Steering Committees for the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial (AstraZeneca), the Study Of diabetic Nephropathy with AtRasentan (SONAR) [AbbVie], A Non-interventional Study Providing Insights Into the Use of Finerenone in a Routine Clinical Setting (FINE-REAL) [Bayer], and CKD-ASI (Boehringer Ingelheim). He has received research grants from AstraZeneca, GlaxoSmithKline, Roche, Boehringer Ingelheim, and Novo Nordisk, as well as speaker honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, and Amgen. All other authors have declared no competing interests.

Funding/support

This editorial received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

TABLE 2. Examples of strategies to improve implementation of appropriate chronic kidney disease care

Domain	Potential solutions
Health policy	Include NCDs and CKD as healthcare priorities; ensure sustainable financing; monitor disease burdens and outcomes; establish registries; implement multisectoral action; promote kidney health through public health measures; achieve SDGs
Health systems	Integrate CKD care into primary care under UHC; establish quality standards; include necessary diagnostics and medications in national essential medication/diagnostic lists; conduct monitoring and evaluation; reduce brain drain; monitor equity; simplify and streamline guidelines
Quality assurance	Regulate and monitor medication quality, especially that of generics; monitor health outcomes and care processes to permit iterative improvement
Healthcare professionals	Reduce time pressure; improve knowledge; broaden scope of practice (eg, pharmacists); engage community health workers
Patient empowerment	Promote health literacy, education, community engagement, and involvement in research design and conduct
Medication cost	Ensure quality generics; reduce prices; utilise UHC for essential medications
Implementation research	Identify barriers within local contexts; test solutions to overcome barriers
Polypills	Reduce cost; lower pill burden
Digital technologies	Utilise electronic pill boxes, bags, bottles; blister pack technology; ingestible sensors; electronic medication management systems; patient self-report technology; video-based technology; motion sensor technology; telemedicine; smartphone apps; and/or electronic health records

Abbreviations: CKD = chronic kidney disease; NCDs = non-communicable diseases; SDGs = sustainable development goals; UHC = universal health coverage

Declaration

This article was published in *Kidney International* (Luyckx VA, Tuttle KR, Abdellatif D, et al. Mind the gap in kidney care: translating what we know into what we do. Kidney Int 2024;105:406-17. https://doi.org/10.1016/j.kint.2023.12.003), and was reprinted concurrently in several journals. The articles cover identical concepts and wording, but vary in minor stylistic and spelling changes, detail, and length of manuscript in keeping with each journal's style. Any of these versions may be used in citing this article.

Supplementary material

The supplementary material was provided by the authors and some information may not have been peer-reviewed. Accepted supplementary material will be published as submitted by the authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (https://doi.org/10.12809/hkmj245162).

References

1. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. Kidney Int 2019;96:1048-50.
2. Institute for Health Metrics and Evaluation (IHME). GBD compare data visualization. Available from: http://vizhub.healthdata.org/gbd-compare. Accessed 18 Nov 2023.
3. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. Bull World Health Organ 2018;96:414-22D.
4. International Society of Nephrology. ISN Global Kidney Health Atlas, 3rd ed. Available from: https://www.theisn.org/initiatives/global-kidney-health-atlas/. Accessed 18 Nov 2023.
5. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020;395:709-33.
6. Vanholder R, Annemans L, Brown E, et al. Reducing the costs of chronic kidney disease while delivering quality health care: a call to action. Nat Rev Nephrol 2017;13:393-409.
7. Nguyen-Thi HY, Le-Phuoc TN, Tri Phat N, et al. The economic burden of chronic kidney disease in Vietnam. Health Serv Insights 2021;14:11786329211036011.
8. United States Renal Data System. Healthcare expenditures for persons with CKD. Available from: https://usrds-adr.niddk.nih.gov/2023/chronic-kidney-disease/6-healthcare-expenditures-for-persons-with-ckd. Accessed 18 Nov 2023.
9. Kidney Health Australia. Changing the chronic kidney disease landscape: the economic benefits of early detection and treatment. Available from: https://kidney.org.au/uploads/resources/Changing-the-CKD-landscape-Economic-benefits-of-early-detection-and-treatment.pdf. Accessed 16 Jan 2024.
10. Ke C, Liang J, Liu M, Liu S, Wang C. Burden of chronic kidney disease and its risk-attributable burden in 137 low-and middle-income countries, 1990-2019: results from the Global Burden of Disease Study 2019. BMC Nephrol 2022;23:17.
11. Gregg EW, Buckley J, Ali MK, et al. Improving health

outcomes of people with diabetes: target setting for the WHO Global Diabetes Compact. Lancet 2023;401:1302-12.
12. Geldsetzer P, Manne-Goehler J, Marcus ME, et al. The state of hypertension care in 44 low-income and middle-income countries: a cross-sectional study of nationally representative individual-level data from 1.1 million adults. Lancet 2019;394:652-62.
13. Chu L, Bhogal SK, Lin P, et al. AWAREness of diagnosis and treatment of chronic kidney disease in adults with type 2 diabetes (AWARE-CKD in T2D). Can J Diabetes 2022;46:464-72.
14. Levin A, Tonelli M, Bonventre J, et al. Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy. Lancet 2017;390:1888-917.
15. Stengel B, Muenz D, Tu C, et al. Adherence to the Kidney Disease: Improving Global Outcomes CKD guideline in nephrology practice across countries. Kidney Int Rep 2020;6:437-48.
16. Chu CD, Chen MH, McCulloch CE, et al. Patient awareness of CKD: a systematic review and meta-analysis of patient-oriented questions and study setting. Kidney Med 2021;3:576-85.e1.
17. Ene-Iordache B, Perico N, Bikbov B, et al. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. Lancet Glob Health 2016;4:e307-19.
18. Gummidi B, John O, Ghosh A, et al. A systematic study of the prevalence and risk factors of CKD in Uddanam, India. Kidney Int Rep 2020;5:2246-55.
19. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int 2022;102(5S):S1-127.
20. Nicholas SB, Daratha KB, Alicic RZ, et al. Prescription of guideline-directed medical therapies in patients with diabetes and chronic kidney disease from the CURE-CKD Registry, 2019-2020. Diabetes Obes Metab 2023;25:2970-9.
21. Grams ME, Yang W, Rebholz CM, et al. Risks of adverse events in advanced CKD: the Chronic Renal Insufficiency Cohort (CRIC) study. Am J Kidney Dis 2017;70:337-46.
22. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int 2024;105(4S):S117-314.
23. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney Int 2021;99(3S):S1-87.
24. Tuttle KR, Alicic RZ, Duru OK, et al. Clinical characteristics of and risk factors for chronic kidney disease among adults and children: an analysis of the CURE-CKD Registry. JAMA Netw Open 2019;2:e1918169.
25. Ismail WW, Witry MJ, Urmie JM. The association between cost sharing, prior authorization, and specialty drug utilization: a systematic review. J Manag Care Spec Pharm 2023;29:449-63.
26. Heerspink HJ, Vart P, Jongs N, et al. Estimated lifetime benefit of novel pharmacological therapies in patients with type 2 diabetes and chronic kidney disease: a joint analysis of randomized controlled clinical trials. Diabetes Obes Metab 2023;25:3327-36.
27. Nuffield Department of Population Health Renal Studies Group; SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium. Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials. Lancet 2022;400:1788-801.
28. Fernández-Fernandez B, Sarafidis P, Soler MJ, Ortiz A. EMPA-KIDNEY: expanding the range of kidney protection by SGLT2 inhibitors. Clin Kidney J 2023;16:1187-98.
29. McEwan P, Boyce R, Sanchez JJ, et al. Extrapolated longer-term effects of the DAPA-CKD trial: a modelling analysis. Nephrol Dial Transplant 2023;38:1260-70.
30. Vanholder R, Annemans L, Braks M, et al. Inequities in kidney health and kidney care. Nat Rev Nephrol 2023;19:694-708.
31. Agarwal R, Filippatos G, Pitt B, et al. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. Eur Heart J 2022;43:474-84.
32. Tuttle KR, Bosch-Traberg H, Cherney DZ, et al. Post hoc analysis of SUSTAIN 6 and PIONEER 6 trials suggests that people with type 2 diabetes at high cardiovascular risk treated with semaglutide experience more stable kidney function compared with placebo. Kidney Int 2023;103:772-81.
33. Rubin R. It takes an average of 17 years for evidence to change practice—the burgeoning field of implementation science seeks to speed things up. JAMA 2023;329:1333-6.
34. World Health Organization. Mid-point evaluation of the implementation of the WHO global action plan for the prevention and control of noncommunicable diseases 2013-2020 (NCD-GAP). Volume 1: Report. 2020. Available from: https://cdn.who.int/media/docs/default-source/documents/about-us/evaluation/ncd-gap-final-report.pdf?sfvrsn=55b22b89_5&download=true. Accessed 18 Nov 2023.
35. Kruk ME, Gage AD, Joseph NT, Danaei G, García-Saisó S, Salomon JA. Mortality due to low-quality health systems in the universal health coverage era: a systematic analysis of amenable deaths in 137 countries. Lancet 2018;392:2203-12.
36. Kingori P, Peeters Grietens K, Abimbola S, Ravinetto R. Uncertainties about the quality of medical products globally: lessons from multidisciplinary research. BMJ Glob Health 2023;6(Suppl 3):e012902.
37. Pan American Health Organization. Quality control of medicines. Available from: https://www.paho.org/en/topics/quality-control-medicines. Accessed 18 Nov 2023.
38. Tuttle KR, Wong L, St Peter W, et al. Moving from evidence to implementation of breakthrough therapies for diabetic kidney disease. Clin J Am Soc Nephrol 2022;17:1092-103.
39. Kalyesubula R, Conroy AL, Calice-Silva V, et al. Screening for kidney disease in low- and middle-income countries. Semin Nephrol 2022;42:151315.
40. Francis A, Abdul Hafidz MI, Ekrikpo UE, et al. Barriers to accessing essential medicines for kidney disease in low- and lower middle-income countries. Kidney Int 2022;102:969-73.
41. Rangaswami J, Tuttle K, Vaduganathan M. Cardio-renal-metabolic care models: toward achieving effective interdisciplinary care. Circ Cardiovasc Qual Outcomes 2020;13:e007264.
42. Neumiller JJ, Alicic RZ, Tuttle KR. Overcoming barriers to

implementing new therapies for diabetic kidney disease: lessons learned. Adv Chronic Kidney Dis 2021;28:318-27.
43. Mishra SR, Neupane D, Preen D, Kallestrup P, Perry HB. Mitigation of non-communicable diseases in developing countries with community health workers. Global Health 2015;11:43.
44. Joshi R, John O, Jha V. The potential impact of public health interventions in preventing kidney disease. Semin Nephrol 2017;37:234-44.
45. Patel A, Praveen D, Maharani A, et al. Association of multifaceted mobile technology-enabled primary care intervention with cardiovascular disease risk management in rural Indonesia. JAMA Cardiol 2019;4:978-86.
46. Ardavani A, Curtis F, Khunti K, Wilkinson TJ. The effect of pharmacist-led interventions on the management and outcomes in chronic kidney disease (CKD): a systematic review and meta-analysis protocol. Health Sci Rep 2023;6:e1064.
47. Sherrod CF, Farr SL, Sauer AJ. Overcoming treatment inertia for patients with heart failure: how do we build systems that move us from rest to motion? Eur Heart J 2023;44:1970-2.
48. Ramakrishnan C, Tan NC, Yoon S, et al. Healthcare professionals' perspectives on facilitators of and barriers to CKD management in primary care: a qualitative study in Singapore clinics. BMC Health Serv Res 2022;22:560.
49. Porter J, Boyd C, Skandari MR, Laiteerapong N. Revisiting the time needed to provide adult primary care. J Gen Intern Med 2023;38:147-55.
50. Peralta CA, Livaudais-Toman J, Stebbins M, et al. Electronic decision support for management of CKD in primary care: a pragmatic randomized trial. Am J Kidney Dis 2020;76:636-44.
51. Rios P, Sola L, Ferreiro A, et al. Adherence to multidisciplinary care in a prospective chronic kidney disease cohort is associated with better outcomes. PLoS One 2022;17:e0266617.
52. Stevenson JK, Campbell ZC, Webster AC, et al. eHealth interventions for people with chronic kidney disease. Cochrane Database Syst Rev 2019;8:CD012379.
53. Tuot DS, Crowley ST, Katz LA, et al. Usability testing of the kidney score platform to enhance communication about kidney disease in primary care settings: qualitative think-aloud study. JMIR Form Res 2022;6:e40001.
54. Verberne WR, Stiggelbout AM, Bos WJ, van Delden JJ. Asking the right questions: towards a person-centered conception of shared decision-making regarding treatment of advanced chronic kidney disease in older patients. BMC Med Ethics 2022;23:47.
55. Taha A, Iman Y, Hingwala J, et al. Patient navigators for CKD and kidney failure: a systematic review. Kidney Med 2022;4:100540.
56. Essue BM, Laba TL, Knaul F, et al. Economic burden of chronic ill health and injuries for households in low- and middle-income countries. In: Jamison DT, Gelband H, Horton S, et al, editors. Disease Control Priorities: Improving Health and Reducing Poverty. 3rd ed. The International Bank for Reconstruction and Development/ The World Bank; 2017: 121-43.
57. Khatib R, McKee M, Shannon H, et al. Availability and affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: an analysis of the PURE study data. Lancet 2016;387:61-9.
58. Kamath N, Iyengar AA. Chronic kidney disease (CKD): an observational study of etiology, severity and burden of comorbidities. Indian J Pediatr 2017;84:822-5.
59. Cirillo L, Ravaglia F, Errichiello C, Anders HJ, Romagnani P, Becherucci F. Expectations in children with glomerular diseases from SGLT2 inhibitors. Pediatr Nephrol 2022;37:2997-3008.
60. Donohue JF, Elborn JS, Lansberg P, et al. Bridging the "know-do" gaps in five non-communicable diseases using a common framework driven by implementation science. J Healthc Leadersh 2023;15:103-19.
61. Population Health Research Institute. Polypills added to WHO essential medicines list. 2023. Available from: https://www.phri.ca/eml/. Accessed 18 Nov 2023.
62. Sepanlou SG, Mann JF, Joseph P, et al. Fixed-dose combination therapy for prevention of cardiovascular diseases in CKD: an individual participant data meta-analysis. Clin J Am Soc Nephrol 2023;18:1408-15.
63. Dev V, Mittal A, Joshi V, et al. Cost analysis of telemedicine use in paediatric nephrology—the LMIC perspective. Pediatr Nephrol 2024;39:193-201.
64. Musacchio N, Zilich R, Ponzani P, et al. Transparent machine learning suggests a key driver in the decision to start insulin therapy in individuals with type 2 diabetes. J Diabetes 2023;15:224-36.
65. Zuniga C, Riquelme C, Muller H, Vergara G, Astorga C, Espinoza M. Using telenephrology to improve access to nephrologist and global kidney management of CKD primary care patients. Kidney Int Rep 2020;5:920-3.
66. van der Horst DE, Hofstra N, van Uden-Kraan CF, et al. Shared decision making in health care visits for CKD: patients' decisional role preferences and experiences. Am J Kidney Dis 2023;82:677-86.
67. Hole B, Scanlon M, Tomson C. Shared decision making: a personal view from two kidney doctors and a patient. Clin Kidney J 2023;16(Suppl 1):i12-9.

