Kidney health for everyone everywhere - from prevention to detection and equitable access to care

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ABSTRACT

Chronic kidney disease (CKD) is rapidly becoming the 5th most common cause of years of life lost globally by 2040. Crucially, the onset and progression of CKD is often preventable. The World Kidney Day 2020 campaign highlights the importance of preventive interventions on CKD. Primary prevention should focus on risks modification as well as reduced exposure to environmental risk factors and nephrotoxins. Blood pressure optimization and glycemic control should be one of the main interventions in persons with pre-existing kidney disease. Management of co-morbidities such as uremia and cardiovascular disease is highly recommended to avoid or delay dialysis or kidney transplantation. Globally, specific policies directed toward education and awareness about CKD screening, management and treatment are often lacking. Hence, there is an urgent need to increase the awareness of the importance of preventive measures throughout populations, professionals and policy makers around the world.

Key words: *chronic kidney diseases, risk factors, prevention, health policies, awareness.*

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INTRODUCTION

Around 850 million people currently are affected by different types of kidney disorders.[1] Up to one in ten adults worldwide has chronic kidney disease (CKD), which is invariably irreversible and mostly progressive. The global burden of CKD is increasing, and CKD is projected to become the 5th most common cause of years of life lost globally by 2040.[2] If CKD remains uncontrolled and if the affected person survives the ravages of cardiovascular and other complications of the disease, CKD progresses to end-stage renal disease (ESRD), where life cannot be sustained without dialysis therapy or kidney transplantation. Hence, CKD is a major cause of catastrophic health expenditure.[3] The costs of dialysis and transplantation consume 2–3 % of the annual health-care budget in high-income countries; spent on less than 0.03 % of the total population of these countries.[4]

Importantly, however, kidney disease can be prevented and progression to ESRD can be delayed with appropriate access to basic diagnostics and early treatment including life style modifications and nutritional interventions.[4-8]

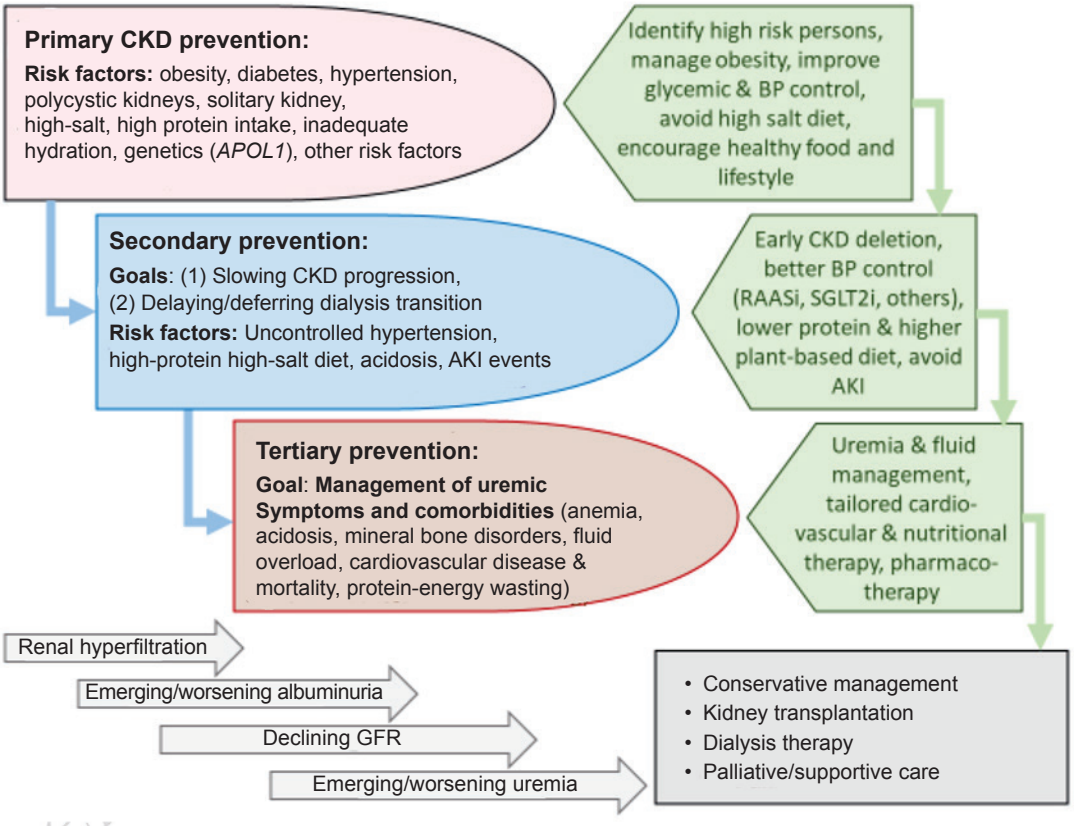
In adhesion to this international event, the World Kidney Day 2020 editorial was published in more than 50 journals worldwide. *Archivos Argentinos de Pediatría* adheres to this important international diffusion.

Despite this, access to effective and sustainable kidney care remains highly inequitable across the world, and kidney disease a low health priority in many countries. Kidney disease is crucially missing from the international agenda for global health. Notably absent from the impact indicators for the Sustainable Development Goal (SDG) Goal 3. Target 3.4: By 2030 (By 2030, reduce by one third premature mortality from non-communicable diseases (NCDs) through prevention and treatment and promote mental health and well-being) and the latest iteration of the United Nation (UN) Political Declaration on NCDs. Kidney diseases urgently need to be given political attention, priority and consideration.[9] CKD is a major risk factor for heart disease and cardiac death, as well as for infections such as tuberculosis, and is a major complication of other preventable and treatable conditions including diabetes, hypertension, HIV and hepatitis.[4-7] As the Sustainable Development Goals (SDG) and Universal Health Coverage (UHC) agendas progress and provide a platform for raising awareness of NCD health care and monitoring needs, targeted action on kidney disease prevention should become integral to the global policy response.[1]

DEFINITION AND CLASSIFICATION OF CKD PREVENTION

According to the expert definitions including the Center for Disease Control and Prevention,[10] the term "prevention" refers to activities that are typically categorized by the following three definitions: (1) Primary prevention, implies intervening before health effects occur in an effort to prevent the onset of illness or injury before the disease process begins; (2) Secondary prevention suggests preventive measures that lead to early diagnosis and prompt treatment of a disease to prevent more severe problems developing and includes screening to identify diseases in the earliest stages, and (3) Tertiary prevention indicates managing disease after it is well established in order to control disease progression and the emergence of more severe complications, which is often by means of targeted measures such as pharmacotherapy, rehabilitation, and

FIGURE 1. *Overview of the preventive measures in chronic kidney disease (CKD) to highlight the similarities and distinctions pertaining to primary, secondary, and tertiary preventive measures and their intended goals*



screening for and management of complications. These definitions have important bearing in the prevention and management of the chronic kidney disease (CKD), and accurate identification of risk factors that cause CKD or lead to faster progression to renal failure as shown in *Figure 1* are relevant in health policy decisions and health education and awareness related to CKD.[11]

Primary prevention of CKD

Measures to achieve effective primary prevention should focus on the two leading risk factors for CKD including diabetes mellitus and hypertension. Other CKD risk factors include polycystic kidneys or other congenital or acquired structural anomalies of the kidney and urinary tracts, primary glomerulonephritis, exposure to nephrotoxic substances or medications (such as nonsteroidal anti-inflammatory drugs), having one single kidney, e.g. solitary kidney after cancer nephrectomy, high dietary salt intake, inadequate hydration with recurrent volume depletion, heat stress, exposure to pesticides and heavy metals (as has been speculated as the main cause of Mesoamerican nephropathy), and possibly high protein intake in those at higher risk of CKD.[8] Among non-modifiable risk factors are advancing age and genetic factors such as apolipoprotein 1 (*APOL1*) gene that is mostly encountered in those with sub-Saharan African ethnicity, especially among African Americans. *Table 1* shows some of the risk factors of CKD.

Among measures to prevent emergence of de novo CKD are screening efforts to identify and manage persons at high risk of CKD, especially those with diabetes mellitus and hypertension. Hence, targeting primordial risk factors of these two conditions including metabolic syndrome and overnutrition is relevant to primary CKD prevention as is correcting obesity.[12] Promoting healthier lifestyle includes physical activity and healthier diet. The latter should be based on more plant-based foods with less meat, less sodium intake, more complex carbohydrates with higher fiber intake, and less saturated fat. In those with hypertension and diabetes, optimizing blood pressure and glycemic control has shown to be effective in preventing diabetic and hypertensive nephropathies. Persons with solitary kidney should avoid high protein intake above 1 gram per kilogram body weight per day.[13,14] Obesity should be avoided, and weight reduction strategies should be considered.[12]

Secondary prevention in CKD

Evidence suggests that among those with CKD, the vast majority have early-stage of the disease. i.e., CKD Stages 1 and 2 with microalbuminuria (30 to 300 mg/day) or CKD Stage 3B (eGFR between 45 to 60 ml/min/1.73 m^2).[14] For these earlier stages of CKD, the main goal of kidney health education and clinical interventions for "secondary prevention" is how to slow disease progression. Uncontrolled or poorly controlled hypertension is one of the most established risk factors for faster CKD progression.

The cornerstone of the pharmacotherapy in secondary prevention is the renin-angiotensin-aldosterone system inhibitors (RAASi). Low protein diet appears to have a synergistic effect on RAASi therapy.[15] Recent data suggest that a new class of anti-diabetic medications known as sodium-glucose cotransporter-2 Inhibitors (SGLT2i) can slow CKD progression, but this effect may not be related to glycemic modulation of the medication.[16] Whereas acute kidney injury (AKI) may or may not cause de novo CKD, AKI events that are superimposed on preexisting CKD may accelerate disease progression.[17] A relatively recent case of successful secondary prevention that highlights the significance of implementing preventive strategies in CKD is the use of a vasopressin V(2)-receptor antagonists in adult polycystic kidney disease (ADPKD).[18]

Tertiary prevention in CKD

In patients with advanced CKD, management of uremia and related comorbid conditions such as anemia, mineral and bone disorders, and cardiovascular disease is of high priority, so that these patients can continue to achieve highest longevity. Whereas many of these patients will eventually receive renal replacement therapy in form of dialysis therapy or kidney transplantation, a new trend is emerging to maintain them longer without dialysis by implementing conservative management of CKD.

Approaches to identification of chronic kidney diseases

the lack of awareness of CKD around the world is one of the reasons for late presentation of CKD in both developed and developing economies.[19-21] The overall CKD awareness among general population and even high cardiovascular risk groups across 12 low-income and middle-income countries was less than 10 %.[21]

Given its asymptomatic nature, screening of CKD plays an important role in early detection. Consensus and Positional Statements have been published by International Society of Nephrology,[22] National Kidney Foundation,[23] Kidney Disease Improving Global Outcomes,[24] NICE Guidelines[25] and Asian Forum for CKD Initiatives.[26] There was lack of trials to evaluate screening and monitoring of CKD.[27] Currently most will promote a targeted screening approach

TABLE 1. *Risk factors for de novo CKD and pre-existing CKD progression*

*Risk factor	Contribution to de novo CKD	Contribution to CKD progression
Diabetes mellitus	~50 % of all CKDs	
Hypertension	~25 % of all CKDs	
Obesity	10-20 %	
Age	Seen with advancing age, especially in the setting of comorbid conditions.	Some suggests that older CKD patients may have slower progression.
Race, genetics and other hereditary factors: *APOL1* gene Hereditary nephritis (Alport's)	Common among those with African American ancestors.	
Acute glomerulonephritis: • Post-infectious GN • Rapidly progressive GN	<10 %	Recurrent GN or exacerbation of proteinuria.
Polycystic kidney disorders	<10 %, family history of cystic kidney disorders.	
Acute kidney injury (AKI) • Acute tubular necrosis (ATN) • Acute interstitial nephritis (AIN)	Repeated AKI bouts can cause CKD.	Repeated AKI bouts can accelerate CKD progression.
Autoimmune disorders • Lupus erythematosus • Other connective tissue disorders		
Pharmacologic: • Medications causing interstitial nephritides (NSAIDS, CNI, chemotherapy, PPI, etc.) or ATN (aminoglycosides) • Herbs and herbal medication	Variable, e.g. in Taiwan, Chinese herb nephropathy may be an important contributor.	
Environmental: • Heavy metal exposure	Rare.	
Acquired or congenital solitary kidney • Cancer, donor or traumatic nephrectomy • Congenital solitary kidney, unilateral atrophic kidney		
Acquired urinary tract disorders & obstructive nephropathy	BPH in men. Gynecologoical cancers in women.	
Congenital anomalies of the kidney and urinary tract	Mostly in children and young adults.	
Inadequate fluid intake • Mesoamerican nephropathy • Others	Unknown risk, but high prevalence is suspected in Central America.	Whereas in earlier CKD stages adequate hydration is important to avoid pre-renal AKI bouts, higher fluid intake in more advanced CKD may increase the risk of hyponatremia.
High protein intake	Unknown risk, recent data suggest higher CKD risk or faster CKD progression with high protein diet, in particular from animal sources.	Higher protein intake can accelerate the rate of CKD progression.
Cardiovascular diseases (cardiorenal)	Ischemic nephropathy.	
Liver disease (hepatorenal)	NASH cirrhosis, viral hepatitis.	

* Many of these risk factors contribute to both de novo CKD and its faster progression and hence are relevant to both primary and secondary prevention.

to early detection of CKD. Some of the major groups at risk for targeted screening includes: Patients with diabetes, hypertension, those with family history of chronic kidney disease (CKD), individuals receiving potentially nephrotoxic drugs, herbs or substances or taking indigenous medicine, patients with past history of acute kidney injury and individuals older than 65 years.[26,28] CKD can be detected with 2 simple tests: a urine test for the detection of proteinuria and a blood test to estimate the glomerular filtration rate (GFR).[23,26]

Given that currently a population screening for CKD is not recommended and it was claimed that it might add unintended harm to the general population being screened,[27] there is no specialty society or preventive services group which recommends general screening.[29] Low-income to middle-income countries are ill-equipped to deal with the devastating consequences of CKD, particularly the late stages of the disease. There are suggestions that screening should primarily include high-risk individuals, but also extend to those with suboptimal levels of risk, e.g., prediabetes and prehypertension.[30]

Cost-effectiveness of early detection programs

Universal screening of the general population would be time-consuming, expensive and has been shown to be not cost-effective. Unless selectively directed towards high-risk groups, such as the case of CKD in disadvantaged populations.[31] According to a cost-effectiveness analysis using a Markov decision analytic model, population-based dipstick screening for proteinuria has an unfavorable cost effectiveness ratio.[32] From an economic perspective, screening CKD by detection of proteinuria was shown to be cost-effective in patients with hypertension or diabetes in a systematic review.[33] CKD screening may be more cost-effective in populations with higher incidences of CKD, rapid rates of progression, and more effective drug therapy.

A rational approach to CKD early detection

The approach towards CKD early detection will include the decision for frequency of screening, who should perform the screening and intervention after screening.[22] Screening frequency for targeted individuals should be yearly if no abnormality is detected on initial evaluation. This is in line with the Kidney Disease Improving Global Outcomes (KDIGO) resolution that the frequency of testing should be according to the target group to be tested and generally needs not be more frequent than once per year.[24] Who should perform the screening is always a question especially when the healthcare professional availability is a challenge in lower income economies. Physicians, nurses, paramedical staff and other trained healthcare professionals are eligible to do the screening tests. Intervention after screening is also important and patients detected to have CKD should be referred to primary care and general physicians with experience in management of kidney disease for follow up. A management protocol including referral to nephrologists should be provided to the primary care and general physicians.[21,24,26]

Integration of CKD prevention into national NCD programs

Given the close links between CKD and other NCDs, it is critical that CKD advocacy efforts be aligned with existing initiatives concerning diabetes, hypertension, and cardiovascular disease, particularly in LMIC. Some countries and regions have successfully introduced CKD prevention strategies as part of their NCD programs. As an example, in 2003, a kidney health promotion program was introduced in Taiwan, with its key components including a ban on herbs containing aristolochic acid, public-awareness campaigns, patient education, funding for CKD research, and the setting up of teams to provide integrated care.[34] In Cuba, the Ministry of Public Health has implemented a national program for the prevention of CKD. The integration of CKD prevention into NCDs program, has resulted in the reduction of renal and cardiovascular risks in the general population. There has been an increased rate of the diagnosis of diabetes and of glycemic control, as well as an increased diagnosis of patients with hypertension, higher prescription use of renoprotective treatment with ACEI and higher rates of blood pressure control.[35,36] Recently, the US Department of Health and Human Services has introduced an ambitious program to reduce the number of Americans developing end-stage renal disease by 25 percent by 2030. The program, known as the Advancing American Kidney Health Initiative, has set goals with metrics to measure its success; among them is to put more efforts to prevent, detect, and slow the progression of kidney disease, in part by addressing traditional risk factors like diabetes and hypertension.[37] Ongoing

programs, like the Special Diabetes Program for Indians (SDPI) represents an important part of this approach by providing team-based care and care management. Since its implementation, the incidence of diabetes-related kidney failure among American Native populations decreased by over 40 percent between 2000 and 2015.[38]

The interdisciplinary prevention approach

Since 1994, a National Institute of Health consensus advocated for early medical intervention in predialysis patients. Owing to the complexity of care of CKD, it was recommended that patients should be referred to a multidisciplinary team consisting of nephrologist, dietitian, nurse, social worker, and health psychologist, with the aim to reduce predialysis and dialysis morbidity and mortality.[39] In Mexico, a nurse-led, protocol driven, multidisciplinary program reported better preservation in eGFR and a trend in the improvement of quality of care of CKD patients similar to those reported by other Multidisciplinary Clinic (MDC) programs in the developed world.[40] Future models should address region-specific causes of CKD, increase the quality of diagnostic capabilities, establish referral pathways, and provide better assessments of clinical effectiveness and cost-effectiveness.[41]

Online educational programs for CKD prevention and treatment

The e-Learning has also become an increasingly popular approach to medical education. Online learning programs for NCD prevention and treatment, including CKD, have been successfully implemented in Mexico. By 2015, over 5000 health professionals (including non-nephrologists) had been trained using an electronic health education platform.[42] It is equally important to promote "Prevention" with education programs for those at risk of kidney disease and with the general population at large. Education is key to engaging patients with kidney disease. It is the path to self-management and patient-centered care. Narva found patient education is associated with better patient outcomes.[43] Obstacles include the complex nature of kidney disease information, low baseline awareness, limited health literacy, limited availability of CKD information, and lack of readiness to learn. Schatell found Web-based kidney education is helpful in supporting patient self-management.[44] Reputable healthcare organizations should facilitate users to have easier access to health information on their websites *(Appendix 1*). Engagements of professional society, patient groups, charitable and philanthropic organizations promote community partnership and patient empowerment on prevention.

RENEWED FOCUS ON PREVENTION AND AWARENESS RAISING AND EDUCATION

Given the pressing urgency pertaining to the need for increasing education and awareness on the importance of the preventive measures, we suggest the following goals to redirect the focus on plans and actions:

1. Empowerment through health literacy in order to develop and support national campaigns that bring public awareness to prevention of kidney disease.
2. Population-based approaches to manage key known risks for kidney disease, such as blood pressure control and effective management of obesity and diabetes.
3. Implementation of the World Health Organization (WHO) 'Best Buys' approach including screening of at-risk populations for CKD, universal access to essential diagnostics of early CKD, availability of affordable basic technologies and essential medicines and task shifting from doctors to front-line healthcare workers to more effectively target progression of CKD and other secondary preventative approaches.

"Kidney Health for Everyone, Everywhere" should be a policy imperative which can be successfully achieved if policy makers, nephrologists, healthcare professionals and the general public place prevention and primary care for kidney disease within the context of their Universal Health Coverage programs.

ABBREVIATION LIST

ACEI: Angiotensin converting enzyme inhibitor.
ADPKD: Autosomal dominant polycystic kidney disease.
AIN: Acute interstitial nephritis.
AKI: Acute kidney injury.
APOL1: Apolipoprotein 1.
ATN: Acute tubular necrosis.
BPH : Benign prostate hypertrophy.
CKD: Chronic kidney disease.
CKDu: Chronic kidney disease of unknown cause.
CNI: Calcineurin inhibitor.
CVD: Cardiovascular disease.
ESRD: End-stage renal disease.

GFR: Glomerular filtration rate.
GN: Glomerulonephritis.
ISN: International Society of Nephrology.
KDIGO: Kidney Disease Improving Global Outcomes.
LMIC: Low middle income countries.
MDC : Multidisciplinary Clinic.
NASH: Non-alcoholic steatohepatitis.
NCD: Non-communicable disease.
NHSP: National Health Screening Program.
NICE: National Institute of Clinical Excellence.
NSAID: Non-steroidal anti-inflammatory drugs.
PEW: Protein energy wasting.
PPI: Proton pump inhibitor.
RAASi: Renin-angiotensin-aldosterone system inhibitors.
SDG: Sustainable Development Goal.
SDPI: Special Diabetes Program for Indians.
SGLT2i: Sodium-glucose cotransporter-2 inhibitors.
UHC: Universal Health Coverage.
UN: United Nation.
WHO: World Health Organization.

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APPENDIX 1 :
Selected websites with information on CKD patient education

World Kidney Day
International Federation of Kidney Foundations
International Society of Nephrology

USA:	American Nephrology Nurse Association American Association of Kidney Patients America Renal Associates (Kidneyman: Patient Education Videos) Kidney School by Medical Education Institute, INC. National Kidney Disease Education Program National Kidney Disease Education Program of National Institute of Diabetes and Digestive and Kidney Diseases The National Kidney Disease Education Program National Kidney Foundation
Canada:	The Kidney Foundation of Canada
United Kingdom:	Kidney care UK National Kidney Foundation NHS England
Australia:	Kidney Health Australia The Australian Kidney Foundation
Others	National Kidney Foundation India National Kidney Foundation Malaysia National Kidney Foundation Singapore New Mexico Kidney Foundation