

Establishing the Global Kidney Disease Prevention Network (KDPN): A Position Statement From the National Kidney Foundation

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The Global Kidney Disease Prevention Network is an international public health organization devoted to encouraging and enhancing efforts to increase awareness and recognition of kidney disease, detect it early, and provide treatment to prevent disease progression, improve patient outcomes, and decrease costs. Twenty-six participants from 12 low-, middle-, and high-income countries attended the first meeting, held in Geneva, Switzerland, on September 12-13, 2009. Work groups discussed target populations for chronic kidney disease (CKD) screening, optimal parameters for screening on a public health level, evaluating the impact of early screening programs, and use of screening data to inform health care policy. Of the screening programs discussed, most have targeted populations at high risk of CKD and have included medical history; weight, height, and blood pressure measurements; and blood and urine tests. In screenees, CKD prevalence ranged from 11%-33%. In screenees with CKD, few were aware of the disease, although substantial proportions had been seen by a physician in the previous 6-12 months. At the policy level, prevention of CKD implies prevention and control of risk-factor conditions, including diabetes, hypertension, and others. Given the high prevalence and under-recognition of CKD in different countries, a concerted effort to globally improve primary and secondary CKD prevention appears to be warranted.

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INDEX WORDS: Glomerular filtration rate; albuminuria; chronic kidney disease (CKD); screening; Global Kidney Disease Prevention Network.

The National Kidney Foundation (NKF) convened the first meeting of the Global Kidney Disease Prevention Network (KDPN) in Geneva, Switzerland, on September 12 and 13, 2009. Twenty-six participants from 12 low-, middle-, and high-income countries discussed their experiences with chronic kidney disease (CKD) detection and strategies to improve CKD prevention worldwide. The following issues were addressed by working groups: (1) target populations for screening, (2) optimal parameters for screening on a public health level, (3) evaluating the impact of early screening programs, and (4) use of screening data to inform health care policy. Representatives from the World Health Organization (WHO), Pan American Health Organization (PAHO), US Centers for Disease Control and Prevention (CDC), and The Transplantation Society (TTS) were in attendance. This article summarizes issues addressed.

CKD IN THE CONTEXT OF NONCOMMUNICABLE DISEASES

According to WHO, noncommunicable diseases (NCDs) account for 60% of all global deaths (35 million of 58.8 million); 80% (27.5 million) of NCD deaths occur in low- and middle-income countries, and this number is predicted to increase rapidly.¹ Approximately half these deaths (13.7 million) occur prematurely and are caused by preventable heart disease, stroke, diabetes mellitus, cancers, and asthma. These conditions result from

increased exposure to tobacco use, unhealthy diets, physical inactivity, harmful use of alcohol, and ineffective and inequitable health care services for NCDs.

NCDs impose a heavy burden on socioeconomic development and are associated closely with poverty. Evidence is emerging that these diseases could have serious implications for macroeconomic development due to lost or diminished labor supply related to premature death and disability in people of working age with heart disease, stroke, and diabetes. WHO estimates that these conditions alone decrease gross domestic product from 1%-5% a year in developing countries experiencing rapid economic growth.

WHO focuses on prevention of chronic diseases, such as heart disease, cerebrovascular disease, cancer,

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chronic respiratory diseases, and diabetes, but does not mention CKD. Data from US Renal Data System international comparisons indicate a strong relationship between major chronic diseases and CKD; people live longer and survive cardiovascular disease (CVDs) and cancer, but develop other diseases, including CKD.² Early CKD detection and intervention are necessary to prevent treatment of kidney failure from consuming huge and disproportionate amounts of global health care budgets. Fortunately, WHO has begun to consider CKD a major threat as an NCD. Furthermore, based on survey results showing a high prevalence of chronic diseases and associated risk factors in the Americas, PAHO, a WHO regional office, launched a collaborative initiative called the Central America Diabetes Initiative (CAMDI). This initiative includes a regional strategy and action plan for an integrated approach to the prevention and control of chronic diseases.³

CKD SCREENING AND SURVEILLANCE

Screening refers to detecting individuals with unrecognized or early stages of disease in a population. CKD screening is justified for several reasons: (1) CKD is an important public health problem, with prevalence rates of about 13% for stages 1-4 worldwide; (2) its natural history involves progressive loss of kidney function, increased risk of the development of CVD, and premature mortality; and (3) it has a recognizable latent or early symptomatic stage, can be diagnosed using simple and readily available tests, and treatment can delay or prevent progression to poor outcomes. Other criteria for screening proposed during the past 40 years can be applied to CKD.⁴

Distinguishing between screening and surveillance is important.⁵ CKD screening is an ongoing activity, not a one-time detection event, in which people in a defined population who are unaware of CKD are tested and, if CKD is present, subsequently are treated to decrease the risk of progression and complications. Screening is a classic public health approach to informing the public, medical caregivers, and governments of prevalence of a disease in the community and the effect on health and welfare of the population. Screening programs are intended to identify the greatest number of possible cases for referral to the health care system for comprehensive assessments, education, and treatment. Surveillance involves data collection at the population level to provide key information about CKD, such as timing, location, magnitude, and severity, to guide implementation of public health measures to control progression and complications.

The Kidney Early Evaluation Program (KEEP), which operates in the United States, Japan, and Mexico, is an example of a targeted CKD screening program.⁶ CKD Health Examination Risk Information Sharing (CHERISH), a state-level pilot detection program funded by the CDC in the United States, is an example of a CKD surveillance program.⁷

CKD SCREENING PROGRAMS AROUND THE WORLD

Table 1 summarizes the main characteristics of the CKD screening programs presented at the KDPN meeting. Some are ongoing programs (KEEP), and others combine screening and surveillance (Egypt Information, Prevention, and Treatment of CKD [EGIPT-CKD] in Egypt). Some are epidemiologic studies (China's population studies), and others are educational programs about kidney disease (Schools Initiative in Italy). Most programs target the general population, and a few target selected populations (taxi drivers in Iran, minority populations in the United Kingdom). Program settings are highly variable, including urban and rural areas, schools, public places, churches, hospitals, medical clinics, factories, and health fairs. Most programs use on-site stations, and a few use mobile screening vans. Most programs target populations at high risk of CKD, including people older than 50 years and those with diabetes, arterial hypertension, or a family history of diabetes, hypertension, or CKD. Most programs include medical history; weight, height, and blood pressure measurements; and body mass index calculation. Blood and urine tests are performed, including standardized and nonstandardized serum creatinine and estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) Study equation, blood glucose, total cholesterol, and proteinuria by means of albumin-creatinine ratio (ACR), microalbumin reagent strips, or standard proteinuria dipsticks. Some programs perform urinalysis and measure waist and hip circumference, triglycerides, low- and high-density lipoprotein cholesterol, hemoglobin A_{1c}, complete blood count, serum calcium, phosphorus, and parathyroid hormone.

CKD prevalence ranges from 11%-33%; microalbuminuria, 12%-19%; dipstick proteinuria, 6%-31%; and eGFR of 60 mL/min/1.73 m², 2.5%-18%. Few patients are aware of CKD, although substantial proportions had been seen by a physician in the previous 6-12 months. Most programs provide medical referral and follow-up.

Table 1. Characteristics of CKD Early Detection Programs Around the World

<p>Australia</p> <p>Type: Free kidney and CV health check; KEY</p> <p>Setting: General population, workplace based</p> <p>Target population: Adults aged >50 y (>35 y if aboriginal or Torres St Islander origin), DM, HTN, first-degree relative with CKD</p> <p>Screening components: Lifestyle questionnaire; weight; height; BMI; BP; waist-to-hip ratio; on-site lab point-of-care testing with immediate results to participants (ACR, urinalysis, standardized SCr, MDRD eGFR, random glucose, HbA_{1c}, total cholesterol)</p> <p>Methodology: Community site advertising; on-site stations, point-of-care lab equipment; follow-up questionnaire at 3 mo</p> <p>Main results: N = 402; mean age, 58 y; 47% women, 44% obese, HTN in 43%; overall CKD, 20%; CKD stage ≥3, 10%; 85% had regular GP; 77% had seen GP in previous 6 mo</p> <p>Other results: 58% referred to GP for advice on abnormal test results; 53% of those with CKD stage ≥3 were already using an ACEi/ARB; follow-up contact made with 82%; self-reported change to management made in 67% of participants who visited GP as response to KEY findings</p> <p>Comments: Community program aimed at identifying people with CKD and managing them in primary care; another CKD detection strategy involves opportunistic detection in high-risk people in primary care, workplaces, community pharmacy, and through mobile testing units</p>	<p>cities, 1.2%-3.5%; CKD in those with DM, 21%; CKD in those with HTN, 16%; eGFR <60 in 2.5% in mainland China</p> <p>Other results: Risk factors associated with microalbuminuria: older age, DM, HTN, dyslipidemia; risk factors associated with eGFR <60: older age, HTN, dyslipidemia, nephrotoxic medications</p> <p>Comments: 1,563 low-income people aged ≥40 y served by a community hospital in a district of Beijing were screened for CKD in 2004 and 2008; over the 4-y period, 10% of participants developed CKD</p>
<p>Brazil</p> <p>Type: Health fairs and mobile screening units; Pro-Renal Foundation</p> <p>Setting: General population; Curitiba, other cities in Parana province</p> <p>Target population: Adults aged >18 y</p> <p>Screening components: Weight; height; BMI; BP; waist-to-hip ratio; on-site lab tests (urinalysis, microalbuminuria for high risk [elderly, obese, DM, HTN, family history of CVD or kidney disease])</p> <p>Methodology: Community site advertising; on-site stations; multidisciplinary team of nurses, social workers, dietitians, pharmacists</p> <p>Main results: N = 8,883; mean age, 48 y; 56% women; mean BMI, 24.8; HTN in 16%; DM in 3%; proteinuria in 6%; hematuria in 30%; glucosuria in 4%; hematuria and proteinuria in 3%</p> <p>Other results: Comparison of participants aged >60 vs <60 y: DM in 7% vs 2%; proteinuria in 9% vs 5%; hematuria in 31% vs 29% (<i>P</i> < 0.05 for all)</p> <p>Comments: Campo Largo Study: random sample of 6,000 from a population of 120,000; screening will include medical history, weight, BP, urinalysis, microalbuminuria, SCr in high-risk patients to ascertain real prevalence of CKD in an urban Caucasian-Brazilian cohort</p>	<p>Egypt</p> <p>Type: Screening project; EGIPT-CKD (2007)</p> <p>Setting: General population; community based; Damanhour Institute, GOTH</p> <p>Target population: Adults aged >18 y with DM, HTN, first-degree relatives with ESKD</p> <p>Screening components: Questionnaire; weight; height; BMI; waist-to-hip ratio; on-site lab tests (ACR, urinalysis, nonstandardized SCr, urine Cr, MDRD eGFR, fasting glucose, HbA_{1c}, Hb, total cholesterol, triglycerides, kidney ultrasound [if indicated])</p> <p>Methodology: Advertising in dialysis units, community sites; on-site stations; screening program may be preceded by Kidney Health Risk Assessment (questionnaire, BP, BMI, glucose, albuminuria, eGFR, CKD awareness and education)</p> <p>Main results: N = 1,533; DM in 36%; HTN in 41%; DM & HTN in 24.6%; first-degree relative with ESKD in 54%; overall CKD (eGFR <60), 8.7%; CKD in those with DM, 14%; CKD in those with HTN, 20%; CKD (eGFR <60) in those with first-degree relatives who have ESKD, 5% (increased to 11.6% by adding ACR and to 18.6% by adding ultrasound to definition of CKD); 19% aware of CKD</p> <p>Other results: DM: 8% unaware of diagnosis, 4% no treatment, 50% no glycemia follow-up, 37% unaware of complications; HTN: 22% unaware of diagnosis, 25% no treatment, 32% no BP follow-up, 40% unaware of complications; microalbuminuria in those with relatives with ESKD, 10.6% (associated with older age, DM, HTN, CVD, dyslipidemia duration, BMI, low education)</p> <p>Comments: Uses computerized program for health risk assessment, database, and statistical analysis, which reduces bias in data entry, allows for accurate data analysis, decreases number of personnel required, and links different points of screening in 1 database online with 1 investigator at a low cost</p>
<p>China</p> <p>Type: Population screening studies</p> <p>Setting: General population, 4 cities</p> <p>Target population: Adults aged >18 y (Beijing, Shanghai); >20 y (Guangdong)</p> <p>Screening components: CKD prevalence; risk-factor assessment; hospital lab tests (ACR, hematuria, SCr, eGFR [using MDRD Study equation in Shanghai and Chinese-modified MDRD Study equation in Beijing and Guangdong])</p> <p>Methodology: 3 multistage randomized samplings performed at major medical centers were derived from 7 population studies</p> <p>Main results: N = 38,399; overall CKD in the 3 cities, 11.3%-12.1% (CKD in general population, 10%); hematuria in the 3</p>	<p>Iran⁸</p> <p>Type: Medical screening of taxi drivers (2007)</p> <p>Setting: Urban selected population, Tehran</p> <p>Target population: Taxi drivers</p> <p>Screening components: Age; smoking; BP; BMI; on-site lab tests (glucose, SCr, MDRD eGFR, Hb, total cholesterol, HDL and LDL, triglycerides)</p> <p>Methodology: Selective screening</p> <p>Main results: N = 31,999; overall CKD (eGFR <60), 6.4% in men</p> <p>Other results: Risk factors for eGFR <60: age, HTN, BMI, glycemia, LDL</p> <p>Italy</p> <p>Type: Camper Initiative; NKF Italy</p> <p>Setting: General population, community based</p> <p>Target population: General adult population</p> <p>Screening components: BP; on-site lab test (dipstick proteinuria)</p>

(Continued)

Table 1 (Cont'd). Characteristics of CKD Early Detection Programs Around the World

<p>Methodology: Mobile screening vans at public squares; participants with BP or urine abnormality called later for medical follow-up</p> <p>Main results: N = 11,053; newly diagnosed HTN in 22% (2004), 20% (2005), and 23% (2007); proteinuria in 4%</p> <p>Comments: Schools Initiative: CKD educational program in 48 high schools in 34 cities; Open Renal Unit Initiative: free full nephrology evaluation in many Italian hospitals during World Kidney Day</p>	<p>Screening components: Questionnaire; weight; height; BMI; BP; on-site lab tests (ACR, fasting glucose, Hb); central lab tests (nonstandardized SCr, MDRD eGFR, calcium, phosphorus, PTH if CKD stage \geq3)</p> <p>Methodology: Community site advertising, appointments given; 6 on-site stations (registry, informed consent, questionnaire, physical examination, lab tests, physician consult); follow-up questionnaire at 3 mo</p> <p>Main results: N = 1,519; DM in 28%; HTN in 34%; DM & HTN in 14%; family history of DM, HTN, or CKD in 52%; overall CKD, 22%; CKD in those with DM, 38%; CKD in those with HTN, 31%; CKD in those with DM & HTN, 42%; CKD in those with positive family history, 12%; ACR $>$30 in 19%; eGFR $<$60 in 7%; $<$1% aware of CKD; 71% had seen an MD in previous y</p>
Japan	
<p>Type: Free CKD screening program; KEEP Japan</p> <p>Setting: General population, community based</p> <p>Target population: Adults aged $>$ 18 y with DM, HTN, or family history of DM, HTN, or CKD</p> <p>Screening components: Questionnaire; weight; height; BMI; BP; waist circumference; central lab tests (ACR, standardized SCr, MDRD eGFR, fasting glucose, HbA_{1c}, Hb, total cholesterol, HDL and LDL, triglycerides)</p> <p>Methodology: Community site advertising; 6 on-site stations (registry, informed consent, questionnaire, physical examination, lab tests, physician consult); follow-up questionnaire at 3 mo</p> <p>Main results: N = 1,833; DM in 24%, HTN in 54%, DM & HTN in 15%, family history of DM, HTN, or CKD in 28%; overall CKD, 25%; CKD in those with DM, 35%; CKD in those with HTN, 36%; CKD in those with DM & HTN, 41%; CKD in those with positive family history, 23%; ACR $>$30 in 21%, eGFR $<$60 in 6%; 21% aware of CKD, 86% had seen an MD in the previous y</p> <p>Other results: \uparrow glucose, 36%; \uparrow BP, 35%; glycemic control in 27%; BP control in 10%; anemia in 7%</p>	<p style="text-align: center;">United Kingdom</p> <p>Type: Free CKD screening program; UK KEEP</p> <p>Setting: Targeted at-risk groups (minority populations, 3 localities, NHS care units)</p> <p>Target population: BAC, S Asians, relatives of existing kidney patients of any ethnic background</p> <p>Screening components: Questionnaire; weight; height; BMI; BP; central lab tests (ACR, urinalysis, standardized SCr, MDRD eGFR, glucose, Hb)</p> <p>Methodology: On-site recruitment by outreach clinics and nursing staff; walk ins allowed; 6 steps (registry, informed consent, physical examination, lab tests, health care check, postevent follow-up)</p> <p>Main results: N = 1,305; overall CKD, 17% (BAC) and 18% (S Asians)</p> <p>Comments: Pilot study to determine the feasibility of population screening for CKD in the UK; full results under embargo until research publication</p>
Mexico	
<p>Type: Free CKD, CVD risk-factor screening program; KEEP Jalisco</p> <p>Setting: General population, community based</p> <p>Target population: Adults aged $>$ 18 y with DM, HTN, or family history of DM, HTN, or CKD</p> <p>Screening components: Questionnaire; weight; height; BMI; BP; on-site lab tests (urine dipstick, nonstandardized SCr, MDRD eGFR, fasting glucose, CBC, total cholesterol, triglycerides)</p> <p>Methodology: Community site advertising; mobile screening vans with physical examination rooms and on-site lab</p> <p>Main results: N = 2,020; DM in 44%; HTN in 46%; DM & HTN in 17%; family history of DM, HTN, or CKD in 23%; overall CKD, 33%; CKD in those with DM, 35%; CKD in those with HTN, 38%; CKD in those with DM & HTN, 35%; CKD in those with positive family history, 31%; proteinuria in 31%; eGFR $<$60 in 10%; 0% aware of CKD, 91% had seen MD in previous y</p> <p>Other results: \uparrow glucose in 7%; \uparrow BP in 35%; glycemic control in 90%; BP control in 30%; anemia in 11%</p> <p>Type: Free CKD screening program; KEEP Mexico City</p> <p>Setting: General population, community based</p> <p>Target population: Adults aged $>$ 18 y with DM, HTN, or family history of DM, HTN, or CKD</p>	<p style="text-align: center;">United States</p> <p>Type: Free CKD screening program; KEEP US</p> <p>Setting: General population, community based</p> <p>Target population: Adults aged $>$ 18 y with DM, HTN, or family history of DM, HTN, or CKD</p> <p>Screening components: Questionnaire; weight; height; BMI; BP; central lab tests (ACR, standardized SCr, MDRD eGFR, fasting glucose, HbA_{1c}, Hb, total cholesterol, HDL and LDL, triglycerides)</p> <p>Methodology: Community site advertising; 6 on-site stations (registry, informed consent, questionnaire, physical examination, lab tests, physician consult); follow-up questionnaire at 3 mo</p> <p>Main results: N = 112,254; DM in 28%; HTN in 55%, DM & HTN in 20%; family history of DM, HTN, or CKD in 91%; overall CKD, 26%; CKD in those with DM, 35%; CKD in those with HTN, 32%; CKD in those with DM & HTN, 37%; CKD in those with positive family history, 25%; ACR $>$30 in 12%; eGFR $<$60 in 18%; $<$4% aware of CKD; 80% had seen an MD in previous y</p> <p>Other results: \uparrow glucose, 10%; \uparrow BP, 52%; glycemic control in 90%; BP control in 52%; anemia in 14%</p>

Note: eGFR given in mL/min/1.73 m², factor for conversion to mL/s/1.73 m², \times 0.01667; ACR given in mg/g; BMI given in kg/m².

Abbreviations and definitions: \uparrow , elevated; ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; ARB, angiotensin receptor blocker; BAC, black African Caribbean; BMI, body mass index; BP, blood pressure; CBC, complete blood cell count; CKD, chronic kidney disease; Cr, creatinine; CV, cardiovascular; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; EGIPT-CKD, Egypt Information, Prevention, and Treatment of Chronic Kidney Disease; ESKD, end-stage kidney disease; GOTH, General Organization for Teaching Hospital and Institutes; GP, general practitioner; Hb, hemoglobin; HbA_{1c}, hemoglobin A_{1c}; HDL, high-density lipoprotein cholesterol; HTN, hypertension; KEEP, Kidney Early Evaluation Program; KEY, Kidney Evaluation for You; lab, laboratory; LDL, low-density lipoprotein cholesterol; MDRD, Modification of Diet in Renal Disease Study equation; NHS, National Health Service; NKF, National Kidney Foundation; PTH, parathyroid hormone; SCr, serum creatinine.

OPTIMAL CKD SCREENING PARAMETERS

Target Population

CKD screening can be performed in the general population or target high-risk populations.⁹ The latter strategy has the advantage of decreasing the number of people needed to detect 1 case. Limited data are available regarding the cost-effectiveness of these approaches. In the United States, early detection of urinary protein to slow the progression of CKD and decrease mortality was found to be cost-effective for only high-risk groups of older people, people with hypertension, or when conducted at an infrequent interval of 10 years.¹⁰ People with diabetes were not included in the analysis because routine screening for urine protein already had been shown to be cost-effective for them. In a cost-effectiveness analysis performed by the CDC, CKD screening was cost-effective for only individuals with diabetes or hypertension or those older than 50 years.¹¹

Recent studies have reported a high CKD prevalence in detection programs targeted to high-risk groups. In the Kidney Evaluation and Awareness Program in Sheffield (KEAPS), microalbuminuria prevalence was 9.5% in individuals with a family history of CKD and 1.4% in the (age- and sex-matched) general population without a family history of CKD.¹² In KEEP US, CKD prevalence was 27.1% in individuals with diabetes, hypertension, or a family history of diabetes, hypertension, or CKD and 15.3% in the general population.¹³ In the Nord-Trøndelag County, Norway, health study (HUNT), eGFR <60 mL/min/1.73 m² was detected in 4.7% of the population; further analysis indicated that optimal CKD screening was restricted to people with diabetes or hypertension or those older than 55 years.¹⁴ This strategy would identify 93% of cases, and 9 people would be screened to identify 1 case.

To increase the yield of CKD screening programs, some investigators have developed CKD risk scores. Based on data from the US National Health and Nutrition Examination Survey (NHANES) 1999-2000 and 2001-2002, Bang et al¹⁵ suggest screening individuals who score ≥ 4 using the risk factors age, hypertension, diabetes, CVD, proteinuria, and anemia. Sensitivity was 92% and negative predictive value was 99% for the score. Unfortunately, only 18% of patients who score ≥ 4 have CKD (positive predictive value). Using data from the Atherosclerosis Risk in Communities (ARIC) Study and Cardiovascular Health Study (CHS), Kshirsagar et al¹⁶ suggest screening individuals who score ≥ 3 based on age, female sex, diabetes, hypertension, anemia, peripheral vascular disease, history of congestive heart failure, or CVD. With this score, 70% of incident cases (sensitiv-

ity) would have been identified during 4-9 years of follow-up. Although promising, CKD risk scoring methods need further validation before they can be recommended for use in CKD screening programs.

In a recent KDIGO (Kidney Disease: Improving Global Outcomes) Controversies Conference, participants concluded that diabetes, hypertension, and CVD were the highest priority risk factors for CKD.⁵ Other risk factors to be considered included older age, family history of kidney disease, other risk factors for CVD (hyperlipidemia, smoking, obesity, and metabolic syndrome), exposure to toxic drugs, certain infections (hepatitis C and human immunodeficiency virus), and cancers.

KDPN participants indicated that although diabetes and hypertension are the highest priority risk factors for CKD in most developed countries, they may not be in some developing countries. For example, only 38% of CKD in adult farmers living in the coastlands of El Salvador is caused by diabetes or hypertension; the remaining 62% is suspected to be related to agricultural pesticide and insecticide exposure.^{17,18} Frequent risk factors or causes of CKD include exposure to nephrotoxic medications in China,^{19,20} obstructive uropathy in Egypt,²¹⁻²³ and immunoglobulin A nephropathy²⁴ in Japan. Consequently, KDPN consensus was that each country should define its own high-risk groups to target for screening programs depending on the prevalence of CKD risk factors at a local level.

Thirty-four organizations from 28 countries responded to a survey of CKD screening programs by the International Federation of Kidney Foundations (IFKF).²⁵ Most respondents designated high-risk groups as priorities for screening and included as risk factors diabetes, hypertension, CVD, older age (>40 years in Singapore, older elsewhere), lipid disorders, smoking, obesity, personal or family history of kidney stones, high-risk ethnic or minority groups, and school age or youth (in Turkey, children with urinary incontinence or abnormal urine color). Screening settings varied and included hospital outpatient and diabetes clinics, primary care or family practice/general practitioner settings, community health centers in townships and villages, health fairs, community pharmacies, corporate offices, churches, factories, shopping malls, mobile clinics, village-wide or house-to-house screenings; screening camps for high-risk groups, and schools.

Recommended Tests

Clinical practice guidelines from the NKF's Kidney Disease Outcomes Quality Initiative (KDOQI) recommend testing for CKD with a first-morning or

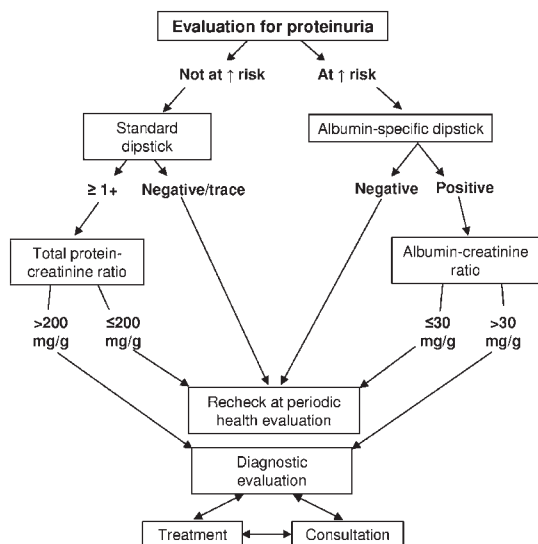


Figure 1. Evaluation of proteinuria according to National Kidney Foundation's (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines. Adapted and reproduced with permission of the NKF from reference.²⁵

random urine sample for albumin or protein and a blood test for serum creatinine to estimate GFR.^{26,27}

Albuminuria testing is preferred because increased urinary excretion of albumin is the earliest manifestation of CKD due to diabetes, other glomerular diseases, and hypertensive nephrosclerosis. Albuminuria also may accompany tubulointerstitial diseases, polycystic kidney disease, and kidney disease in kidney transplant patients. Random untimed spot urine samples are suitable for initial albuminuria testing. A first-morning urine sample is preferable but not required if obtaining it poses substantial inconvenience. Albuminuria results should be expressed as ACR because expression as a ratio corrects for variation caused by hydration, diuretics, osmotic diuresis, or concentration defects.²⁷ ACR has sensitivity and specificity of ~87% to detect microalbuminuria in 24-hour urine collections at a cutoff value of 9.9 mg/g.²⁸

Causes of false-positive (dehydration, hematuria, exercise, urinary infection, and extremely alkaline urine) and false-negative (excessive hydration and urine proteins other than albumin) results should be ruled out.²⁶ Verification of albuminuria requires 2 of 3 positive test results.²⁷ Reference values for ACR are <30 mg/g. Figure 1 shows the proteinuria evaluation algorithm recommended by the NKF-KDOQI clinical practice guidelines.²⁶ In selected populations, urine testing for hematuria and pyuria should be performed based on the local prevalence of glomerular and tubulointerstitial disease, respectively.

GFR estimated from serum creatinine level currently is the optimal widely available test of kidney function. Calibration of serum creatinine should be

traceable to the international reference creatinine method, isotope-dilution mass spectrometry.^{27,29,30}

Equations for estimating GFR should be appropriate for standardization of the serum creatinine assay and application to most racial and ethnic groups. The 4-variable MDRD Study equation commonly is used for estimating GFR in adults.³¹ A new equation, the CKD Epidemiology Collaboration (CKD-EPI) equation, appears to perform better than the MDRD Study equation, especially at higher GFRs, with less bias, improved precision, and greater accuracy.³² Although it requires further validation in elderly people and racial and ethnic minorities, it could replace the MDRD Study equation for routine clinical use.

Controversy is considerable regarding use of eGFR for CKD screening and a single eGFR threshold of <60 mL/min/1.73 m² to define CKD, especially in elderly people.³³⁻⁴⁰ Regarding use of eGFR, differentiating between screening and diagnosis of CKD is important. A single increased serum creatinine level, decreased eGFR, or abnormal urinalysis result initially should be viewed as a screening test, with diagnosis and prognosis determined by additional workup and follow-up of those affected by this heterogeneous condition with a variable course in individual cases. The CKD staging system proposed by KDOQI was developed as a public health model; early detection of individuals at increased risk and those affected by kidney injury or loss of function, irrespective of diagnosis or whether the disease is stable or progressive, is essential.⁴⁰ Likewise, a single eGFR threshold in a screening program may indicate suspicion, but not definition, of CKD.

Hallan et al⁴¹ recently reported that combining eGFR and albuminuria improves prediction of kidney failure. In the HUNT-2 Study, of 65,589 adults from Norway, 124 developed end-stage kidney disease after 10.3 years of follow-up. Multivariable survival analysis indicated that for most screening populations, high-risk or general population, combining ACR and eGFR substantially improves discrimination, whereas the effect of adding the best clinical variables to the model was only marginal.

The authors of the Prevention of Renal and Vascular End-Stage Disease (PREVEND) Study suggest screening the general population for microalbuminuria.⁴² In this cohort study of the population of Groningen, the Netherlands, the main findings were: (1) urine albumin concentration >20 mg/L was associated with increased risk of initiating kidney replacement therapy (KRT) over 10 years, but the risk was modest for levels of 20-100 mg/L (hazard ratio, 3.0 vs 47 for levels 100-200 mg/L); (2) approximately half the individuals who ultimately required KRT had microalbuminuria; (3) screening high-risk individuals

identified 55% with microalbuminuria, but 87% who progressed to KRT; and (4) because one of the listed risk factors was not present for 40%-50% of individuals with microalbuminuria, the investigators advocate screening the general population, not targeting people at increased risk, and suggest a cutoff of 20 mg/L. Arguments against screening the general population for albuminuria⁴³ include the following.

1. Many individuals would need to be tested to identify and prevent 1 case of KRT. In PREVEND, 25,587 participants had no risk factors for CKD; of these, 5.8% had microalbuminuria; of these, only 6 cases progressed to KRT, and of these, only 2 patients had microalbuminuria (0.08% of the population without risk factors).
2. Although the relatively low cost of the test favors massive screening, total costs of the screening program include time and effort to collect specimens, confirmatory tests for treatment of positive test results, and monitoring and treatment of complications of interventions. Given the small number of cases, screening the general population is unlikely to be cost-effective.
3. No data support that use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) decreases the risk of KRT or clinically significant loss of GFR in individuals with microalbuminuria but without other risk factors. Thus, advocating for screening the general population for microalbuminuria is premature.

In the IFKF survey of CKD screening programs,²⁵ 74% of programs tested glycemia and urine dipstick; 63% included serum creatinine measurement, some tested ACR or protein-creatinine ratio and lipids routinely, and others included those tests and serum creatinine only if other conditions were met. At least 7 organizations performed liver function tests, at least "if required."

Frequency of Testing

Frequency of testing for CKD in high-risk groups has not been studied rigorously. Many recommendations suggest yearly testing. KDIGO recommends yearly testing for people with risk conditions, such as diabetes, hypertension, or family history of CKD or CVD.⁵ For individuals with other risk factors, testing can be less frequent as long as test results remain normal.⁴⁴ These recommendations are opinion based and discretion is recommended. Clearly, this is an important area for future research.

EVALUATING THE IMPACT OF CKD EARLY DETECTION PROGRAMS

The impact of CKD early detection programs can be evaluated at the levels of participants, public health care systems and providers, and governments. For participants, clinical and economic parameters can be monitored, including degree of risk-factor control (blood pressure, glucose, lipids, smoking, and obesity) and appropriateness and effectiveness of management (access to health care and medications, quality of life, kidney and patient survival, and development of comorbid conditions). Factors affecting the general public include degree of awareness and lifestyle modifications. For the health care system, clinicians, and government, access to health care, changes in practice and policies, and cost-effectiveness are important factors.

Methods used to assess the impact of CKD early detection programs on participants include quantitative surveys of kidney disease awareness, longitudinal follow-up of clinical and laboratory parameters, and surveys of quality of life and satisfaction. In the health care system, indicators to be evaluated include awareness among policy makers shown by published health policy analysis mentioning kidney disease, initiatives such as government-run education programs on kidney disease, participation in events such as CKD summits, and organization of World Kidney Day. For clinicians, assessment of appropriate use and interpretation of CKD tests, appropriate use of ACE inhibitors/ARBs, continuing medical education programs, and telephone follow-up would be appropriate.

Regarding the impact of early detection programs on CKD cost and chronic kidney failure, CKD screening programs theoretically would allow for implementation of interventions in earlier stages, eventually decreasing costs because of less progression to end-stage kidney disease and improved health status at KRT initiation. Few studies published to date examine the effect of slowing CKD progression and cost savings. Health economics experts can provide frameworks to measure cost-effectiveness. Although this is time consuming and expensive, it is essential for the success of CKD early detection programs.

LEVERAGE OF CKD DETECTION DATA TO INFLUENCE HEALTH CARE POLICY

The kidney disease community must become familiar with NCDs and how kidney disease fits in. Detection programs must assess NCD activity within the country based on data for disease burden and action plans consistent with Ministry of Health policy and WHO initiatives. Specifically, determining changes in prevalence and death rates is necessary for the major

NCDs, as is determining the growth of the CKD and chronic kidney failure populations within the country and the burden on the health care system, the major rationales for prevention. When available, the extent of kidney transplant and patient wait listing provides another rationale for early detection and intervention. Additionally, it is necessary to determine the state of the health care delivery system that will provide care to most patients with CKD. Surveillance data should be collected from available sources to inform policy makers of the burden of kidney disease, its impact on health care costs, and estimates of prevention benefits. It is crucial for policy makers to understand that prevention and control of CKD and chronic kidney failure implies prevention and control of the risk-factor conditions, namely diabetes, hypertension, CVD, and possibly glomerulopathies in some parts of the world. Each country should collect data and target the main causes of CKD, particularly in the developing world. An example of a successful screening program is Japan's mandatory nationwide urinalysis screening in adults 40 years and older,⁴⁵ which has resulted in decreased age-adjusted rates of chronic kidney failure attributable to glomerulonephritis.^{24,46} Detection programs can provide information about the use of simple methods to define CKD and quality of care delivered.

To influence health care policy with CKD detection data at a country level, it is important to understand health care system operations and capacity and to engage health authorities. Specifically, it is essential to understand how public health policies are implemented, present reliable data to authorities, identify the right people to talk to, and define the best strategy. Some governments have implemented public health policies for early detection and management of all stages of CKD. The United Kingdom, for example, has appointed a National Clinical Director for Kidney Care and issued the National Service Framework for Renal Services, which includes dialysis and transplant, CKD, acute renal failure, and end-of-life care. More recently, the National Institute for Health and Clinical Excellence issued guidelines for the early identification of CKD in adults in primary and secondary care. Steps are being taken to implement these policies among general practitioners and nephrologists.

To influence health care policy with CKD detection data at a global or regional level, it is important to work with institutions such as WHO and PAHO. WHO started a global NCD network to decrease NCD burden, particularly in low- and middle-income countries. TTS is working with WHO to globally implement the Declaration of Istanbul on Organ Trafficking and Transplant Tourism. One principle of the declaration states that "national governments, working in

Box 1. Specific Aims of the Kidney Disease Prevention Network

1. To develop a global coordinated approach to detecting kidney disease and preventing progression, improving outcomes, and prolonging survival.
2. To work with WHO to bring kidney disease higher visibility on the global public health agenda.
3. To stimulate new kidney disease detection and prevention programs around the world and improve existing ones.
4. To facilitate sharing of data.
5. To focus governments on the challenge and opportunity of identifying kidney disease as a multiplier of risk, cost, and poor outcomes.
6. To foster collaboration with the International Society of Nephrology, The Transplantation Society, KDIGO, and other organizations.
7. To promote implementation of global, clinical practice guidelines from KDIGO and other sources.

Abbreviations: KDIGO, Kidney Disease: Improving Global Outcomes; WHO, World Health Organization.

collaboration with international and non-governmental organizations, should develop and implement comprehensive programs for the screening, prevention and treatment of organ failure." The Third Global Consultation on Organ Transplantation, which took place in Madrid in early 2010, included a section on identifying methods of successful CKD and end-stage kidney disease prevention. PAHO has achieved the commitment of several political organizations of various subregions of the Americas to fight chronic diseases, adding momentum to addressing prevention of kidney diseases in this region. PAHO also is enhancing collaboration with public and private entities through the Partner Forum, which is expected to further enhance prevention and control of chronic diseases.

KDPN MISSION AND ACTION PLAN

KDPN is a global public health organization devoted to encouraging and enhancing efforts to increase awareness and recognition of kidney disease, detect it early, and encourage proper treatment to prevent disease progression, improve patient outcomes, and reduce costs.

KDPN comprises members, organizations, companies, and research institutions from around the world. Managed by the NKF, KDPN intends to be collaborative and self-sustaining and not duplicate other efforts. It intends to leverage the NKF experience and resources in pursuit of this mission and vigorously respond to needs and opportunities. Specific aims of KDPN are listed in Box 1.

Activities planned to achieve these objectives include consensus meetings, coordinated publishing of data, country or regional CKD summits, liaison with WHO and regional entities, best practices publications, consultation with local programs, and establishment of kidney disease prevention centers.

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SUPPLEMENTARY MATERIAL

Figure S1: Global KDPN Roster.

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