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Early Identification of CKD—A Scoping Review of the Global Populations

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Introduction: Decisions on whether to screen for chronic kidney disease (CKD) or not remain contentious in nephrology. This study provides a global overview of early CKD identification efforts.

Methods: Guidelines for scoping reviews were followed and studies were identified by searching MEDLINE, EMBASE, Cochrane Library, CINAHL, ISI Web of Science, and PsycINFO. Data extracted from included studies focused on the following 4 themes: study population, measurement methods, interventions used, and available policies.

Results: We identified 290 CKD screening and detection programs from 83 countries. Overall sample size was 3.72 million (North East Asia: 1.19 million), detection of CKD was the aim in 97.6%, 63.1% used population-based screening methods, and only 12.4% were in rural populations. Reported CKD prevalence (stages 3–5) was higher in targeted- (14.8%) than population-based studies (8.0%). Number of persons needed to screen (NNS) to identify 1 case was also lower in targeted studies (7 vs. 13). Single measurements (80%) and the combination of estimation of glomerular filtration rate with a urine test (albuminuria/proteinuria) (71.4%) were frequently used to detect CKD. Only 2.8% of studies included an intervention such as pharmacotherapy in identified cases. Policies on early identification were available in 30.1% of countries included.

Conclusion: Methods for early CKD identification vary worldwide, often leading to wide variations in the reported prevalence. Efforts to standardize measurement methods for early detection focusing on high-risk populations and ensuring appropriate interventions are available to those identified with CKD will improve the value of programs and improve patient outcomes.

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The burden of CKD continues to increase worldwide. Most of the increase is projected to occur in low- and lower-middle-income countries (LLMICs) and among disadvantaged and indigenous communities in high-income countries (HICs) where access to care is significantly limited.[1,2] Early identification of CKD and institution of appropriate corrective measures may be one way of curtailing the expansion of morbidity and mortality related to CKD—with cardiovascular disease and kidney failure being the most consequential end points.[3–7] However, early CKD identification remains a much-debated subject in nephrology,[8,9] so much so that controversies conference has been convened on it.[10]

Early disease identification encompasses the following 2 main strategies[11]: (i) early detection programs that aim at reducing the proportion of patients who are diagnosed at a late stage and (ii) screening, which refers to the use of simple tests across a healthy population to identify those individuals who have a disease, but do not yet have symptoms. The opinions on whether to screen or not to screen often relate to the dynamics of several important questions. These relate to priority setting in the context of prevalent health systems and political/social dynamics, availability of tools, and pathways to ensure optimal utilization of limited human and material resources and ensuring appropriate "return on investment."

Real-world differences in health systems,[12] reimbursement,[13] and availability, accessibility, and affordability of kidney care[2] also drive this debate. The discussions on early identification programs often converge on the following 2 key points[14–17]: (i) the usefulness of the exercise (Is screening useful in asymptomatic individuals? Does earlier treatment improve outcomes? Are screening programs cost effective? etc.) and (ii) the methodology used for CKD screening (Are single measurements sufficient for detecting CKD? What tests should be selected for CKD screening? etc.). These questions often lead researchers to different conclusions depending on health system context, usually determined by the income level of the country and organization of health care delivery systems, including availability of measures of kidney care. For instance, Boulware *et al.*[18] did not find screening for proteinuria to be cost effective in the United States unless directed toward a high-risk group (older persons with hypertension) or conducted at infrequent intervals of 10 years. However, Mani[19] and Sumaili *et al.*[20] advocated for population-based screening as the diagnostic methods are cheap and those with risk factors can be identified and treated with cheap generic medicines. Disagreements among professional organizations on who and how to screen also add to these controversies.[21] Finally, transposition of guidelines from high-resource regions to low-resource parts of the world without appropriate adaptation is unlikely to be successful.

Until high-quality evidence becomes available, these debates are likely to continue including efforts for early CKD identification, especially in LLMICs where there have been many calls for enhanced prevention strategies given low availability and affordability of kidney failure treatment options (dialysis and kidney transplantation).[22] Where early detection programs are introduced before high-quality evidence is available, it is critical that they are conducted in ways that maximize benefit and minimize harm for those screened and for the health systems with robust embedded evaluation of effectiveness. The ISN embarked on this project to provide a global overview of efforts at early CKD identification to provide a framework that nephrologists can use to effectively communicate with health systems leads and policymakers, design optimized early CKD detection programs and interventions, and formally evaluate the effectiveness and cost effectiveness of these approaches.

METHODS

We developed and conducted this review using the methodology of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews.[23,24] The study design and protocol of this study have been published.[25]

Information Sources and Search Strategy

We developed the search strategy to ensure that a comprehensive review of the existing evidence base was achieved and searched MEDLINE (Ovid), EMBASE (Ovid), Cochrane Library, CINAHL, ISI Web of Science, and PsycINFO to identify relevant studies. We also searched gray literature (including ProQuest Dissertations and Theses Global, and Conference Proceedings Citation Index [Clarivate Analytics]). Additional hand searches were carried out by tracking citations and reference chaining of identified studies. The MEDLINE search strategy (Supplementary Table S1) was adapted for other databases.

Eligibility Criteria

We included studies that reported the results of early CKD identification programs. Two reviewers (EKT and AG) independently screened all identified citations for potential inclusion, and a third reviewer (IGO) was consulted for resolution when agreement on a citation could not be reached. The review process first involved screening of the titles and abstracts and then a detailed review of all selected full texts to ascertain eligibility

for inclusion (Supplementary Figure S1). Articles selected had to meet the following criteria:

1. Population: Studies that provided results of CKD screening carried out in any adult (≥18 years) population. For programs with serial publications on the same population, the result of the most recent publication was used, whereas studies conducted across multiple countries were reported separately as individual studies for each participating country.
2. Intervention: CKD screening, or CKD detection programs, or CKD early identification program, or CKD awareness programs.
3. Comparator: Standard of care (if applicable, otherwise none).
4. Outcomes: Studies reporting CKD prevalence either using estimated glomerular filtration rate (eGFR) or albuminuria (dipsticks, urine albumin-to-creatinine ratio, or urine protein-to-creatinine ratio, with or without reporting of methods used, investigators involved, interventions initiated, or costs involved).
5. Study design: All study designs on early CKD identification were included.
6. Limits: All databases were searched from inception to June 30, 2021, with no language restrictions.

The following studies were excluded:

1. Early identification programs in children.
2. Early identification programs for acute kidney injury, urologic diseases (e.g., prostate cancer), or CKD risk factors (e.g., hypertension and diabetes).
3. Longitudinal studies of screened populations focused on other outcomes, for example, mortality, rates of glomerular filtration rate decline to kidney failure, and quality of life.
4. Organ donor screening or awareness programs.
5. Review articles, editorials, commentaries, letters to the editor, and guidelines and recommendations on CKD screening.

Data Items and Data Abstraction Process

All relevant information from selected studies were summarized and collated in a Microsoft Excel spreadsheet. The data items were built around the following 4 themes[10]: (i) population screened and screening methods used, (ii) measurements used for assessing CKD, (iii) interventions initiated in those identified with CKD, and (iv) cost measures and available policies on early identification programs (Supplementary Table S2). Population-based studies were those that did not select populations for screening, whereas targeted studies were defined as any study that assessed CKD in a subset of the population (e.g., in those with CKD risk factors, such as hypertension or diabetes mellitus, or in other subset of the population not representing the general population, e.g., in indigenous groups or specific occupation groups). Prevalence of CKD was taken as stages 3 to 5 CKD (i.e., eGFR <60 ml/min per 1.73 m^2) according to the Kidney Disease: Improving Global Outcomes guideline.[26] Prevalence of albuminuria and/or proteinuria was taken as reported from each study. Elderly people were taken as those aged 65 years and above or as documented in the study.

Collating, Summarizing, and Reporting of the Results

All extracted data were reviewed for accuracy and completeness. We followed recommendations to extend the scoping review process by adding thematic analysis,[27] and the data were analyzed qualitatively using both deductive (preidentified themes) and inductive (new identified themes) approaches. Countries of included studies were grouped by their most recent World Bank income grouping (https://www.worldbank.org/en/home) and by their ISN regional groups (https://www.theisn.org/about-isn/governance/regional-boards/). Except for data on sample size, prevalence, and sex, all other data were captured as "yes" or "no" with the proportions of "yes" responses descriptively reported as percentages. Median and interquartile ranges (IQRs) were used to report data on prevalence and gender proportions by groups. Overall sample size for each ISN region was estimated by summation of the sample sizes of studies included in that region. We estimated the number (of persons) NNS to identify 1 case of CKD (or albuminuria) as: 1/(percentage prevalence of CKD/100). The data were not pooled for meta-analysis, and comparative analysis of data between groups was not performed.

Risk of Bias Assessment or Quality Appraisal

Following guidance on scoping review conduct, we did not perform a risk of bias assessment or quality appraisal for the included studies.[23,24]

Consultation Exercise

We contacted ISN regional board members to provide us with information on availability of policies or guidelines on early identification in countries within their regions.

Patient and Public Involvement

The patients and the public were not involved in this scoping review.

RESULTS

Overall Features of Included Studies

Demographic Features

We identified 7191 studies from databases and an additional 109 from reference chaining. Of these, 270

Table 1. Overall features of included studies

Demographic characteristics of included studies	
Variables	***n*** **(%)**
Gender, males, median (IQR)	44.6 (35.9–52.3)
ISN regions	
• Africa	81 (27.9)
• East and Central Europe	21 (7.2)
• Latin America	28 (9.7)
• Middle East	13 (4.5)
• North America and Caribbean	25 (8.6)
• NIS and Russia	2 (0.7)
• North and East Asia	37 (12.8)
• Oceania and South-East Asia	16 (5.5)
• South Asia	39 (13.4)
• Western Europe	28 (9.7)
Income groups	
• Low-income countries	25 (8.6)
• Lower-middle-income countries	111 (38.3)
• Upper-middle-income countries	63 (21.7)
• High-income countries	91 (31.4)
Type of early detection program	
• Mass screening	183 (63.1)
• Targeted screening	107 (36.9)
Study setting:	
• Rural	36 (12.4)
• Urban	110 (37.9)
• Mixed	85 (29.3)
• Not reported	59 (20.3)
Duration of study:	
• <3 mo	36 (12.4)
• 3–12 mo	75 (25.9)
• >12 mo	84 (29.0)
• Not reported	95 (32.8)
Purpose of study	
• Awareness	55 (19.0)
• CKD screening	283 (97.6)
• Risk factors screening	169 (58.3)
• Screening + treatment	7 (2.4)
Study design	
• Cross-sectional	246 (84.8)
• Prospective	17 (5.9)
• Database review	34 (11.7)
Study investigators	
• Physicians	131 (45.2)
• Nurses	59 (20.3)
• Laboratory technicians	8 (2.8)
• Community health workers + others	34 (11.7)

Measurements used, interventions reported, cost, and availability of early detection policies in countries of included studies	
Variable	***n*** **(%)**
Number of measurements	
• Once	232 (80.0)
• Twice or more (>1 mo apart)	58 (20.0)
Types of measurements	
• Serum creatinine/eGFR + urine dipsticks/UACR	207 (71.4)
• Serum creatinine/eGFR only	43 (14.8)
• Dipsticks or UACR only	40 (13.8)
• Cystatin C	3 (1.0)
Method of Serum creatinine measurement	
• Jaffe	76 (30.4)
• Enzymatic	19 (7.6)
• Jaffe and enzymatic	1 (0.4)
• Not reported	99 (39.6)
IDMS traceable serum creatinine (yes)	36 (14.4)
CKD equations for reporting CKD	
• CKD-EPI	85 (29.3)
• Cockcroft-Gault	30 (10.3)
• MDRD	150 (51.7)
• Other (e.g., Japanese eGFR equation)	3 (1.0)
CKD staging used (yes)	162 (5.9)
Interventions	
• Medication use reported	45 (15.5)
• RAAS blockade use reported	30 (10.3)
• Lifestyle measures instituted	20 (6.9)
• Any pharmacotherapy instituted	8 (2.8)
• Referral to physicians	139 (47.9)
Cost measures reported (yes)	5 (1.7)
Policy on CKD early detection	
• Yes	25 (30.1)
• No	21 (25.3)
• Uncertain	37 (44.6)

CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease-Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; IQR, interquartile range; IDMS, isotope dilution mass spectrometry; MDRD, Modification of Diet in Renal Disease; NIS, newly independent state; RAAS, renin-angiotensin-aldosterone system; UACR, urine albumin-to-creatinine ratio.

articles representing 290 unique programs (screening, awareness, and prevalence programs) conducted in 83 countries were included (Supplementary Figure S1, Supplementary Table S3, and Supplementary Appendix S1). Summary of overall demographic, measurement parameters, interventions used, and countries with available policies on early CKD identification is shown in Table 1 (summaries for individual studies are

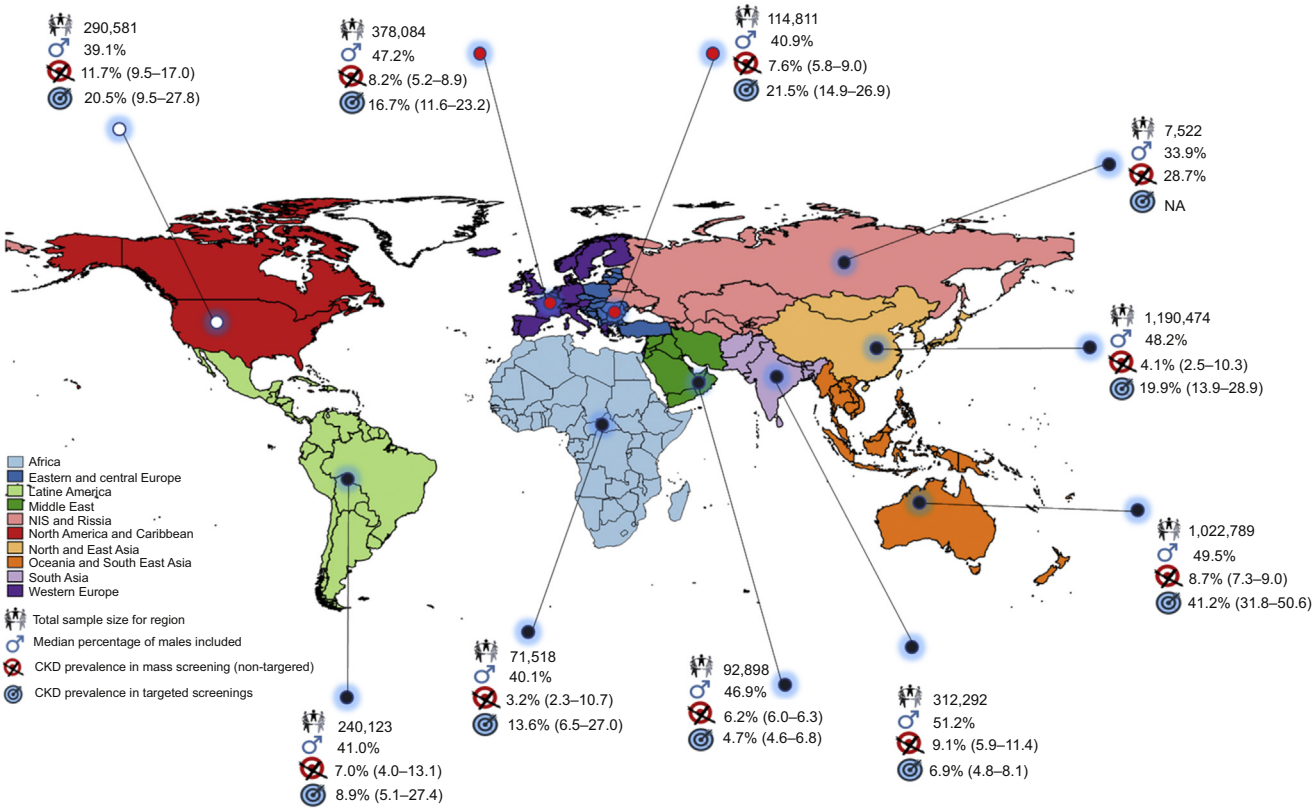

Figure 1. Demographic features of included studies by ISN regions. CKD, chronic kidney disease; NIS, newly independent states.

shown in Supplementary Tables S4 and S5). There were more population-based studies (63.1%) than targeted studies (36.9%), and only 38 (13.1%) programs were part of a national early detection program. The overall sample size of participants included from studies was highest in North and East Asia (1.19 million; $n = 37$), followed by Oceania and Southeast Asia (OSEA) (1.02 million; $n = 16$), Western Europe (0.38 million; $n = 28$), and South Asia (0.31 million; $n = 39$) (Figure 1). Overall, the median proportion of males participating in these programs was 44.6% (IQR: 35.9–52.3).

Most studies were performed in urban settings (37.9%), followed by mixed (29.3%), and rural (12.4%) settings (Table 1). In an overwhelming majority (97.6%), the aim was to screen for CKD (i.e., to identify CKD prevalence), followed by screening for CKD and risk factors (58.3%), raising CKD awareness (19.0%), and screen and treat (2.4%). The summaries of study designs used, duration of early identification programs, and investigators involved in the research are summarized in Table 1.

Measures Used to Identify CKD

In 80% of the programs, measurement at a single time point was used for identification of CKD. The combination of eGFR and a urine test was most frequently used (71.4%), and only 1% used cystatin measurements. Although some studies used multiple eGFR equations to report prevalence, the Modification of Diet in Renal Disease equation was the most frequently used (51.7%), followed by the CKD-Epidemiology Collaboration (29.3%), and the Cockcroft-Gault equation (10.3%). There were 3 studies (1.0%) from Japan that used the Japanese eGFR equation (Table 1).

Interventions Initiated

A small number of studies reported the proportion of patients receiving interventions (15.5% for medications used and 10.3% reported use of renin-angiotensin-aldosterone system inhibitors). Fewer studies reported initiation of therapies (lifestyle measures in 6.9% and any pharmacotherapy initiated in 2.8%). However, 47.9% reported referral of those with CKD to any health care practitioner for further assessments. Cost measures related to early identification were reported in 1.7% of the studies, and 25 countries (30.1%) reported the availability of policies/guidelines on early CKD identification, although we were uncertain in 44.6% who had given no response from countries contacted (Table 1 and Supplementary Table S6).

Prevalence of CKD

Overall, the prevalence of CKD ranged from as low as 0% to 76.5% (0%–30.3% in population-based studies and 0%–76.5% in targeted studies), whereas the prevalence of albuminuria ranged from as low as 0.2% to 57% (0.2%–46.3% in population-based

Table 2. CKD prevalence estimates and estimates of numbers needed to screen to identify 1 case of CKD (eGFR <60 ml/min per 1.73 m^2) from included studies

Variables	Prevalence (%) [median (IQR)]	Median numbers needed to screen (IQR)[a]
CKD prevalence [all studies] (n = 209)	8.8 (4.3–16.1)	11 (6–23)
CKD prevalence [population-based] (n = 131)	8.0 (3.0–11.4)	13 (9–33)
CKD prevalence [targeted screenings]		
• All targeted screenings	14.8 (6.4–25.5)	7 (4–16)
• Populations with hypertension (n = 6)	28.3 (24.9–44.5)	4 (2–4)
• Elderly population (n = 5)	26.9 (13.9–35.5)	4 (3–7)
• Population with diabetes mellitus (n = 22)	21.1 (15.5–25.5)	5 (4–7)
• Relatives of patients with CKD (n = 4)	10.8 (5.3–18.8)	9 (5–19)
• Populations with HIV (n = 9)	8.4 (2.4–11.5)	12 (9–42)
• Other targeted populations[b] (n = 46)	8.4 (5.1–19.9)	12 (5–20)
Albuminuria prevalence		
• Overall (n = 163)	12.5 (6.7–17.2)	8 (6–15)
• Population-based studies (n = 113)	11.2 (6.0–17.2)	9 (6–17)
• Studies with targeted screening (n = 50)	17.9 (10.9–33.4)	6 (3–9)
• Populations with hypertension (n = 3)	11.8 (9.3–13.4)	9 (8–11)
• Elderly population (n = 2)	23.0 (19.5–26.5)	4 (4– 5)
• Population with diabetes mellitus (n = 15)	32.7 (19.1–39.8)	3 (2–5)
• Relatives of patients with CKD (n = 4)	15.1 (6.7–26.6)	7 (4–15)
• Populations with HIV (n = 6)	9.8 (8.8–20.1)	10 (5–11)
• Other targeted populations[b] (n = 21)	17.1 (8.9–23.8)	6 (4–11)

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range.
[a]Number needed to screen was calculated as 1/(prevalence in %/100).
[b]Taxi drivers, school teachers, civil servants, military recruits, people experiencing homelessness, etc.

studies and 1.1%–57% in targeted studies) (Supplementary Table S5). The median prevalence of CKD (stages 3–5) from all studies was 8.8% (IQR: 4.3–16.1) which was higher than the rate for population-based studies (8.0% [IQR: 3.0–11.4]) (Table 2). However, prevalence rates were much higher in targeted studies: hypertension: 28.3% (IQR: 24.9–44.5); elderly: 26.9% (IQR: 13.9–35.5); diabetes mellitus: 21.1% (IQR: 15.5–25.5); and in relatives of patients with CKD: 10.8% (IQR: 5.3–18.8). The prevalence of CKD in other targeted groups (e.g., taxi drivers, market women, civil servants) with no clearly identified risk for CKD was also similar to the prevalence rates obtained for population-based studies (8.4% [IQR: 5.1–19.9]) (Table 2).

The overall prevalence of albuminuria was 12.5% (IQR: 6.7–17.2); it was 11.2% (IQR: 6.0–17.2) in population-based studies and was highest in diabetes studies (32.7% [IQR: 19.1–39.8]). Similarly, the NNS to identify 1 case of CKD was 7 (IQR: 4–16) for targeted studies compared with 13 (IQR: 9–33) for population-based studies. Lower NNS were identified in studies that focused on known risk factors for CKD, such as hypertension, diabetes mellitus, elderly, and relatives of patents with CKD. NNS trends for albuminuria were similar to those for CKD (Table 2).

Population-Based Versus Targeted Studies

Compared with population-based studies, targeted studies were more likely to carry out repeat testing for CKD within 1 month of first test (24.3% vs. 17.5%), more likely to use eGFR only as screening test (19.7 vs. 11.5%), and more likely to initiate an intervention: lifestyle (7.5% vs. 6.6%), pharmacotherapy (4.7% vs. 1.6%), and referral to health care (50.5% vs. 46.5%) (Figure 2).

Features of Included Studies by ISN Regions

Characteristics of included studies based on the ISN region are summarized in Table 3. Only South Asia had a greater proportion of males (51.2% [IQR: 42.8–61.8]) included in screening studies. The highest prevalence of CKD in population-based studies was in North America and the Caribbean (11.7% [IQR: 9.5–17.0]), whereas OSEA had the highest CKD prevalence in the targeted studies (41.2% [31.8–50.6]) (Figure 1 and Table 3). In most regions, the Modification of Diet in Renal Disease equation was frequently used for reporting CKD prevalence. More repeat testing for CKD was reported from OSEA (37.5%) than other regions. More than 50% of studies in Latin America, Middle East, North America and Caribbean, and OSEA reported that patients identified with CKD were referred, and the inclusion of intervention as part of the study aim was highest in OSEA (12.5%). The proportion of countries with available policies or guidelines on early CKD identification was lowest in Africa (13.0%), East and Central Europe (9.1%), Middle East (16.7%), and South Asia (16.7%) (Table 3).

Features of Included Studies by Country Income Group

The features of included studies from countries divided into different World Bank income groups are summarized in Supplementary Table S7. Most low-income countries (LICs) were from Africa (92.0%), whereas most HICs were from Western Europe (30.8%). CKD prevalence from population-based and targeted studies was lowest in LICs: 2.1% (IQR: 1.5–10.2) and 7.4% (IQR: 2.4–13.5), respectively. The proportion of studies that used repeat tests to confirm CKD was lowest in

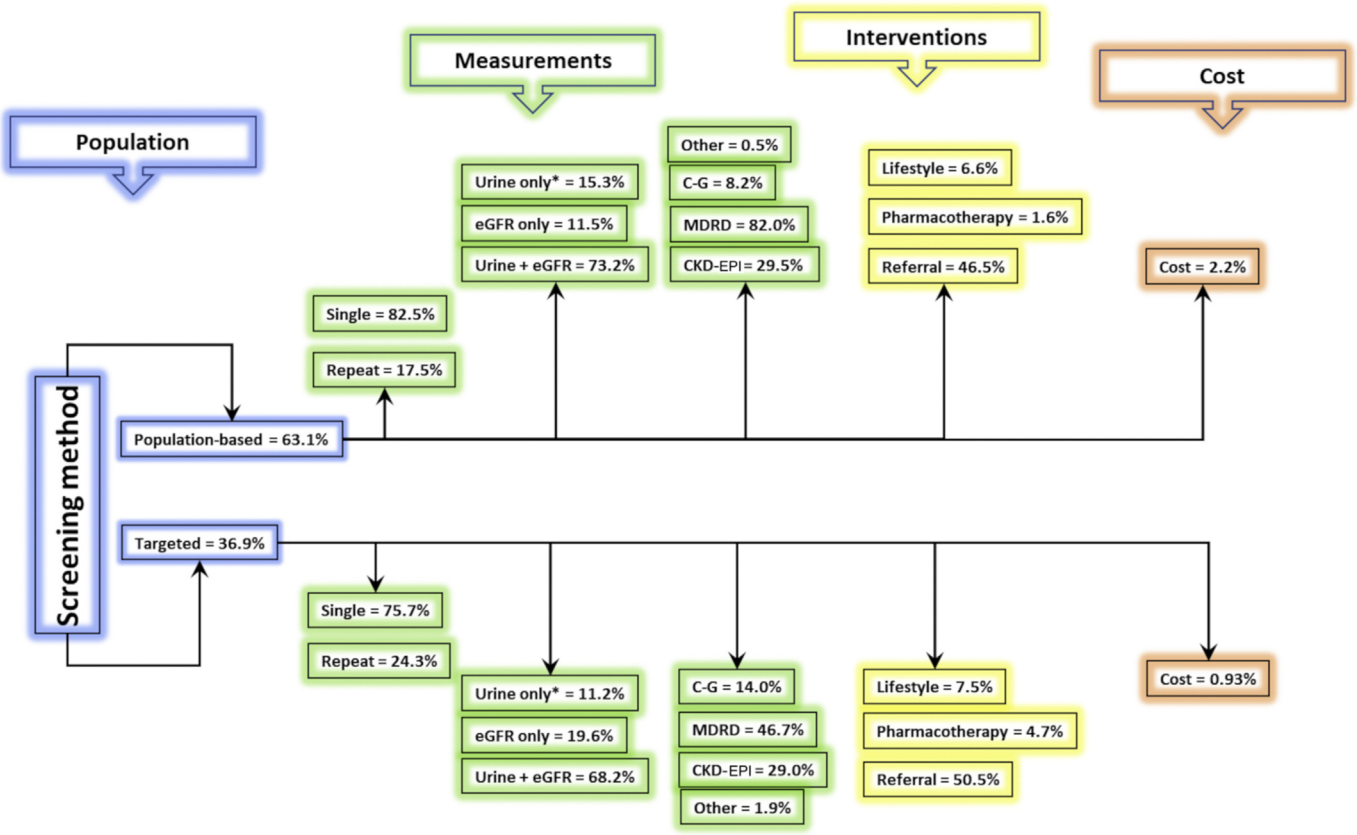

Figure 2. Features of early detection studies based on screening method. C-G, Cockcroft-Gault; CKD-EPI, Chronic Kidney Disease-Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; MDRD, Modification of Diet in Renal Disease. *Represents urine dipsticks only or urine albumin-to-creatinine ratio only.

LICs (12.0%) and highest in HICs (20.9%). The proportion of studies focused on screening and intervention was 3.3% (HICs), 3.2% (UMICs), 1.8% (LMICs), and 0% (LICs) (Supplementary Table S7). Similarly, the trend for initiating interventions and availability of screening policies reduced from HICs to LICs.

DISCUSSION

This study was designed to provide a global scan of identification programs for early CKD and was intended to provide nephrologists with relevant information to effectively communicate with health systems leads and policymakers the nuances of such programs for decision making. Some of the key findings of this study may be summarized as follows: (i) population-based screening methods were more commonly used for early CKD identification; (ii) most studies were set up for screening and to report CKD prevalence; (iii) studies that targeted a high-risk population reported greater CKD prevalence compared with population-based studies; (iv) single measurements of eGFR and/or albuminuria are mostly used to report CKD; (v) a vast majority of early detection programs do not include and/or report on interventions; and (vi) low availability of policies to guide early CKD identification—especially in LLMICs.

There have been many debates and controversies surrounding early CKD identification, including populations to be screened, cost effectiveness of measures used, frequency of screening, health system capacity to manage identified patient population, effective interventions to be used, to name a few.[8,9,28] The main question about who should be screened remains relevant given that issues on what test to use, cost effectiveness, and appropriateness of interventions can be traced back to this 1 question. Although most nephrology societies and professional organizations advocate for targeted screening in high-risk populations,[10,28,29] others have strongly recommended regular screening for kidney disease, regardless of risk factors given the potential to prevent and slow progression with simple, low-cost testing.[21] Gray *et al.*[30] have pointed out that "all screening programs do harm; some do good as well, and, of these, some do more good than harm at reasonable cost." This gives meaning to these debates, suggesting with early CKD identification, 1 size will not fit all.

Unlike certain medical conditions (e.g., breast or prostate cancer) where cure is the main goal of early

Table 3. Characteristics of CKD screening studies by ISN region

Variables	Africa	EC Europe	Latin America	Middle East	North America and Caribbean	NIS and Russia	North-East Asia	OSEA	South Asia	Western Europe
Male gender (%): median (IQR)	40.1 (30.7–49.1)	40.9 (27.4–46.0)	41.0 (29.3–47.9)	46.9 (36.8–54.9)	39.1 (35.4–47.9)	33.9 (24.0–43.7)	48.2 (39.2–54.7)	49.5 (42.1–53.8)	51.2 (42.9–61.8)	47.2 (45.6–55.4)
Study setting										
• Rural	10 (12.3)	1 (4.8)	5 (17.9)	2 (15.4)	3 (12.0)	0 (0.0)	4 (10.8)	2 (12.5)	9 (23.1)	0 (0.0)
• Urban	36 (44.4)	4 (19.0)	14 (50.0)	3 (23.1)	12 (48.0)	1 (50.0)	11 (29.7)	1 (6.3)	16 (41.0)	12 (42.9)
• Mixed urban + rural	26 (32.1)	8 (38.1)	6 (21.4)	2 (15.4)	5 (20.0)	1 (50.0)	10 (27.0)	9 (56.3)	9 (23.1)	9 (32.1)
• Not reported	9 (11.1)	8 (38.1)	3 (10.7)	6 (42.6)	5 (20.0)	0 (0.0)	12 (32.4)	4 (25.0)	5 (12.8)	7 (25.0)
Place of study:										
• Community	46 (56.8)	15 (71.4)	21 (75.0)	6 (46.2)	20 (80.0)	1 (50.0)	35 (94.6)	14 (87.5)	30 (76.9)	18 (64.3)
• Health-facility based	35 (43.2)	5 (23.8)	6 (21.4)	7 (53.8)	5 (20.0)	1 (50.0)	2 (5.4)	2 (12.5)	8 (20.5)	9 (32.1)
• Not reported	0 (0.0)	1 (4.8)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	1 (3.6)
Study design:										
• Cross-sectional	75 (92.6)	15 (71.4)	23 (82.1)	11 (84.6)	22 (88.0)	2 (100.0)	32 (86.5)	14 (87.5)	33 (84.6)	19 (67.9)
• Prospective	2 (2.5)	1 (4.8)	2 (7.1)	0 (0.0)	1 (4.0)	0 (0.0)	0 (0.0)	2 (12.5)	2 (5.1)	7 (25.0)
• Database review	5 (6.2)	4 (19.0)	3 (10.7)	2 (15.4)	4 (16.0)	0 (0.0)	5 (13.5)	2 (12.5)	4 (10.3)	5 (17.9)
CKD prevalence										
• Mass screening	3.2 (2.3–10.7)	7.6 (5.8–9.0)	7.0 (4.0–13.1)	6.2 (6.0–6.3)	11.7 (9.5–17.0)	28.7	4.1 (2.5–10.3)	8.7 (7.3–9.0)	9.1 (5.9–11.4)	8.2 (5.2–8.9)
• Targeted screening	13.6 (6.5–27.0)	21.5 (14.9–26.9)	8.9 (5.1–27.4)	4.7 (4.6–6.8)	20.5 (9.5–27.8)	NA	19.9 (13.9–28.9)	41.2 (31.8–50.6)	6.9 (4.8–8.1)	16.7 (11.6–23.2)
Study duration										
• <3 mo	20 (24.7)	0 (0.0)	3 (10.7)	0 (0.0)	2 (8.0)	0 (0.0)	2 (5.4)	0 (0.0)	8 (20.5)	1 (3.6)
• 3–12 mo	21 (25.9)	4 (19.0)	8 (28.6)	6 (46.2)	7 (28.0)	0 (0.0)	13 (35.1)	4 (25.0)	10 (25.6)	2 (7.1)
• >12 mo	15 (18.5)	1 (4.8)	11 (39.3)	1 (7.7)	11 (44.0)	1 (50.0)	12 (32.4)	6 (37.5)	10 (25.6)	16 (57.1)
• Not reported	25 (30.9)	16 (76.2)	6 (21.4)	6 (46.2)	5 (20.0)	1 (50.0)	10 (27.0)	6 (37.5)	11 (28.2)	9 (32.1)
Purpose of study:										
• Awareness	8 (9.9)	6 (28.6)	5 (17.9)	2 (15.4)	9 (36.0)	0 (0.0)	11 (29.7)	5 (31.1)	5 (12.8)	4 (14.3)
• CKD detection	81 (100.0)	21 (100.0)	27 (96.4)	13 (100.0)	24 (96.0)	1 (50.0)	36 (97.3)	15 (93.8)	39 (100.0)	26 (92.9)
• Risk factors detection	49 (60.5)	14 (66.7)	18 (64.3)	9 (69.2)	13 (52.0)	1 (50.0)	23 (62.2)	8 (50.0)	25 (64.1)	9 (32.1)
• Detection + intervention	1 (1.2)	1 (4.8)	0 (0.0)	0 (0.0)	1 (4.0)	0 (0.0)	0 (0.0)	2 (12.5)	1 (2.6)	1 (3.6)
Investigators										
• Physicians	27 (33.3)	9 (42.9)	15 (53.6)	5 (38.5)	16 (64.0)	0 (0.0)	18 (48.6)	8 (50.0)	14 (35.9)	19 (67.9)
• Nurses	21 (25.9)	0 (0.0)	10 (35.7)	3 (23.1)	6 (24.0)	0 (0.0)	6 (16.2)	3 (18.8)	8 (20.5)	2 (7.1)
• Laboratory technicians	1 (1.2)	0 (0.0)	5 (17.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.3)	1 (2.6)	0 (0.0)
• Community health workers	6 (7.4)	1 (4.8)	5 (17.9)	0 (0.0)	6 (24.0)	1 (50.0)	4 (10.8)	1 (6.3)	10 (25.6)	0 (0.0)
CKD equation used										
• CKD-EPI	30 (37.0)	8 (38.1)	8 (28.6)	4 (30.8)	9 (36.0)	1 (50.0)	8 (21.6)	3 (18.8)	8 (20.5)	6 (21.4)
• Cockcroft-Gault	12 (14.8)	2 (9.5)	0 (0.0)	3 (23.1)	0 (0.0)	0 (0.0)	3 (8.1)	1 (6.3)	7 (17.9)	2 (7.1)
• MDRD	40 (49.4)	14 (66.7)	13 (46.4)	6 (46.2)	9 (36.0)	0 (0.0)	21 (56.8)	7 (43.8)	26 (66.7)	14 (40.0)
• Japanese equation	-	-	-	-	-	-	3 (8.1)	-	-	-
Number of measurements performed										
• Once	71 (87.7)	16 (76.2)	21 (75.0)	8 (61.5)	19 (76.0)	2 (100.0)	30 (81.1)	10 (62.5)	33 (84.6)	22 (78.6)

(Continued on following page)

Table 3. (Continued) Characteristics of CKD screening studies by ISN region

Variables	Africa	EC Europe	Latin America	Middle East	North America and Caribbean	NIS and Russia	North-East Asia	OSEA	South Asia	Western Europe
• ≥2 (>1 mo apart)	10 (12.3)	5 (23.8)	7 (25.0)	5 (38.5)	6 (24.0)	0 (0.0)	7 (18.9)	6 (37.5)	6 (15.4)	6 (21.4)
Types of measurements used										
• eGFR + dipsticks/UACR	62 (76.5)	16 (76.2)	21 (75.0)	6 (46.2)	18 (72.0)	0 (0.0)	31 (83.8)	9 (56.3)	32 (82.1)	12 (42.9)
• eGFR only	9 (11.1)	5 (23.8)	2 (7.1)	4 (30.8)	3 (12.0)	1 (50.0)	4 (10.8)	3 (18.8)	3 (7.7)	8 (28.6)
• Dipsticks/UACR only	10 (12.3)	0 (0.0)	5 (17.9)	2 (15.4)	4 (16.0)	1 (50.0)	2 (5.4)	4 (25.0)	4 (10.3)	8 (28.6)
Interventions										
• Medication use reported	9 (11.1)	5 (23.8)	3 (10.7)	2 (15.4)	4 (16.0)	0 (0.0)	3 (8.1)	4 (25.0)	2 (5.1)	13 (46.4)
• RAAS blockade use reported	5 (6.2)	6 (28.6)	3 (10.7)	1 (7.7)	3 (12.0)	0 (0.0)	1 (2.7)	2 (12.5)	1 (2.6)	8 (28.6)
• Lifestyle measures instituted	2 (2.5)	1 (4.8)	2 (7.1)	0 (0.0)	6 (24.0)	0 (0.0)	3 (8.1)	3 (18.8)	1 (2.6)	2 (7.1)
• Any pharmacotherapy instituted	0 (0.0)	1 (4.8)	1 (3.6)	1 (7.7)	1 (4.0)	0 (0.0)	0 (0.0)	1 (6.3)	2 (5.1)	1 (3.6)
• Referral to physicians	34 (42.0)	8 (38.1)	18 (64.3)	8 (61.5)	18 (72.0)	0 (0.0)	13 (35.1)	9 (56.3)	19 (48.7)	12 (42.9)
Cost measures reported	0 (0.0)	1 (4.8)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (12.5)	1 (2.6)	0 (0.0)
Policies available for CKD early detection										
• Yes	3 (13.0)	1 (9.1)	4 (44.4)	1 (16.7)	2 (50.0)	1 (100.0)	2 (40.0)	5 (83.3)	1 (16.7)	5 (41.7)
• No	6 (26.1)	5 (45.5)	0 (0.0)	3 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (83.3)	2 (16.7)
• Uncertain	14 (60.9)	5 (45.5)	5 (55.6)	2 (33.3)	2 (50.0)	0 (0.0)	3 (60.0)	1 (16.7)	0 (0.0)	5 (41.7)

CKD, chronic kidney disease; CKD-EPI, chronic kidney disease-epidemiology collaboration; EC Europe, East and Central Europe; eGFR, estimated glomerular filtration rate; IQR, interquartile range; MDRD, Modification of Diet in Renal Disease; NIS, newly independent state; OSEA, Oceania and Southeast Asia; RAAS, renin-angiotensin-aldosterone system; UACR, urine albumin-to-creatinine ratio.

identification, CKD is incurable and therefore does not meet all the requirements of screening according to Wilson *et al*.[31] For example, CKD in its early stages (1–3) is almost always asymptomatic meaning that population-based screening is likely to increase the need for baseline testing for CKD to identify cases. Recent consolidated principles of screening recommend that a target population for screening should be clearly defined, identifiable, and able to be reached.[32]

If CKD early identification programs follow the principles of screening those at high risk for CKD, the yield from early detection programs is likely to be improved at lower costs. Various studies confirm this as they show that the NNS to identify 1 case of CKD is lower in targeted screening with a better yield of detecting CKD.[20,33–35] One study from the Democratic Republic of Congo reported that to identify 1 case of proteinuria, 4 people with diabetes, 5 people with hypertension, 5 elderly (≥72 years), or 9 persons without any of these conditions would need to be screened.[20] The HUNT II study (Nord-Trøndelag County, Norway)[35] also reported CKD prevalence of 4.7% in a homogeneous population of adults and showed that to identify 1 person, 20.6 people would need to be screened. However, limiting screening to hypertension, diabetes, or age >55 years would identify 93.2% (92.4%–94.0%) with NNS of 8.7 (8.5–9.0).

Available analyses from HICs do not show population-based screening to be cost effective.[18,36–38] Manns *et al*.[38] using data from the Alberta Kidney Disease Network reported cost per quality-adjusted life-years gained of USD$86,548 for population-based screening, showing that if a cohort of 100,000 people were screened for CKD, the number of people who develop kidney failure over their lifetime will only reduce from 675 to 657. They also found that the cost per quality-adjusted life-years gained was USD$18,645 (with diabetes) and USD$471,900 (without diabetes). A study from the United States also concluded that early detection of urine protein to slow progression of CKD and decrease mortality is not cost effective unless selectively directed toward high-risk groups or if conducted at infrequent intervals.[18] These studies show that, in HICs, if the program purpose is to identify, treat, slow progression to kidney failure or cardiovascular disease, and reduce mortality, then targeted methods are more effective and should be used. Any population-based programs for identifying CKD, especially in LLMICs, will be more impactful if used as advocacy strategy to promote CKD and noncommunicable disease diagnosis and treatment policies.

Given that the available cost-effectiveness studies suggest benefit only in target populations, identification of such groups is a key prerequisite to set up

efficient screening/early detection programs. Globally, diabetes and hypertension are the 2 biggest risk factors for CKD. However, significant geographic heterogeneity in the distribution of risk factors has been noted around the world. According to the Global Burden of Disease Study,[39] although diabetes and hypertension account for almost 80% of the CKD burden in the high and high-middle social development index countries, their contribution comes down to approximately 50% in low social development index countries. Furthermore, there have been increasing reports of clusters of CKD developing young agricultural communities in the absence of any known risk factor in different parts of the world.[40] In some communities, CKD prevalence in excess of 20% has been reported.[41] Therefore, it is important that such high-risk groups are identified through properly designed surveillance studies so that targeted CKD detection programs can be implemented appropriately. Moreover, population-level screenings also uncover an undetected burden of other noncommunicable diseases, such as diabetes and hypertension. Such findings make a case for integrated population-level screening programs that extend beyond CKD.

What tests to use for screening/early detection is also relevant.[42] Kidney function testing usually depends on serum creatinine measurement (with or without calculation of eGFR), whereas structural damage is assessed by determination of albuminuria and/or proteinuria, depending on setting and affordability.[10] Although quantitative estimation of albuminuria using measures such as urine albumin-to-creatinine ratio is preferred and recommended by guidelines, it may be unaffordable in many settings, and alternate tests, such as urine protein-to-creatinine ratio or dipstick test for proteinuria, are commonly used.[43,44] Furthermore, serum creatinine or urinalysis at 1 time point may have overestimated the reported prevalence.

Recent recommendations from a joint task force of the National Kidney Foundation and American Society of Nephrology are for cystatin C testing to be made more available and more widely used for assessment of kidney function given that when combined with serum creatinine, it produces a more accurate assessment of kidney function.[45] Others have previously noted that this may not be feasible in LLMICs owing to cost and availability and its benefits for early identification still needs to be studied.[10,14] Given that even reliable serum creatinine testing is not available in the primary and secondary care settings in many LLMICs,[46] actions that will bring the biggest gains include ensuring access to serum creatinine testing using standard methodology for those who need it. Finally, in geographies where glomerulonephritis is an important contributor to overall CKD burden, screening for hematuria might need to be considered.

A major reason for screening should be to implement appropriate approaches to prevent progression of CKD and/or its complications in the identified cases.[31] The consolidated principles of screening recommend treatment or intervention, and follow-up care that will modify the natural history and clinical pathway for the disease should be available, accessible, and acceptable to those affected.[32] Overall, <1 in 10 studies reported interventions, although it is possible that such interventions were instituted but not reported. One of the controversies surrounding early identification programs is that early detection will not always translate to change in treatment.[14] According to the current management paradigm, risk factor control is the cornerstone of CKD management, which means relatively little change in recommended management for people with key risk factors, such as diabetes and hypertension, whether CKD is detected or not.[14] Tonelli *et al*.[34] found that most additional individuals with CKD identified by population-based screening programs did not need a change in treatment compared with a strategy of assessing risk factors and concluded that case finding was more efficient than population-based screening for CKD. Also, although there are questions surrounding the benefits of initiating interventions such as renin-angiotensin-aldosterone system inhibitors in those with low levels of proteinuria,[47] there is evidence of benefit for the use of renin-angiotensin-aldosterone system inhibitors in diabetic and nondiabetic CKD.[48–50] Whether this strategy could be used in all identified patients will need to be further studied. Other implications of intervening in screened populations relate to use of newer therapies (e.g., sodium glucose co-transpoter-2 inhibitors[51] and mineralocorticoid receptor antagonists[52]) and should be evaluated from a cost, benefit, and harm perspective. This is relevant for LLMICs, which have a high burden of CKD from nontraditional causes that have lower levels of proteinuria. An important secondary analysis of the dapagliflozin-CKD study showed that the effect of dapagliflozin was evident in those with lower levels of albuminuria (urine albumin-to-creatinine ratio of 200–1000 mg/g).[53] This strategy needs to be tested formally in clinical trials.

Finally, any screening should at least include patient education on risk factors, complications, and factors that could worsen CKD and the need for referral should be at an individual level. Identified prevalence data should also be used for advocacy on policies that ensure availability of preventative measures and other options of treatment.

This study has some limitations, including inability to use World Bank income grouping at time of the study. This would have meant some countries with changed categories being classified into 2 (or more) income categories. We used current income classification for ease of representing studies and classifying representative countries. It was not possible to explore the effect of ethnicity because most studies were not performed in homogeneous populations or did not report the racial composition of participants (Supplementary Appendix S1). For instance, in the study by Wong *et al.*,[54] the ethnic/racial distribution was as follows: Asians (43%), Whites (23%), Pacific Islanders (13%), Mixed race/ethnicity (11%), Black (<1%), American Indian (<1%), and unknown race/ethnicity (10%). However, we think that by grouping studies by ISN regions, some perspective on the ethnicities of those screened is observed. A major strength of this study is the use of a scoping method because this allowed us to present a broad overview of early identification programs—focusing on the where, how, who, and what of early identification programs.

In conclusion, there have been many attempts to detect CKD early in different populations, using different methods, including targeting high-risk populations. This approach has been shown to be cost effective in HICs. This approach may be adapted in LLMIC economies, with emphasis on standardized methods of measurement and access to interventions (e.g., patient education, patient referral, initiation of therapies) for those identified with CKD. Such recommendations are likely to be sensitive to local differences in primary care infrastructure and the availability of drugs for secondary prevention. Further systematic evaluations of programs are still needed.

DISCLOSURE

JAD reports receiving personal fees from the ISN, outside of the submitted work. MMa reports receiving a grant from Fresenius Medical Care; receiving consultancy fees from Bayer, AstraZeneca, and Boehringer Lilly; and collaborating with the RRI Institute, outside of the submitted work. CM and MMo report receiving personal fees from the ISN, outside of the submitted work. RPF reports receiving grants from Baxter Healthcare and Fresenius Medical Care and honorariums from AstraZeneca, AKEBIA, Bayer, and Boehringer, all paid to his institution, outside of the submitted work. VT reports receiving consultancy fees from Calliditas, Omeros, Otsuka, Pfizer, and Travere, outside of the submitted work. VJ reports receiving grants from GlaxoSmithKline and Baxter Healthcare, providing scientific leadership to George Clinical, and receiving consultancy fees for Biocon, Zudis Cadilla, and NephroPlus, all paid to his institution, outside of the submitted work.

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AUTHOR CONTRIBUTIONS

VJ, AL, IGO, and FJC conceived the study design. The first version of the protocol was drafted by IGO and was revised by FJC, AG, EKT, JJN, EE, UEE, LNH, GA, JAD, AEF, RI, MMa, CM, MMo, RPF, VT, AL, and VJ. The search strategy was developed and performed by LNH. AG and EKT performed the screening, study selection, and collection of data from all included studies, and IGO adjudicated conflicts in study selection. All authors revised and critically reviewed this manuscript and approved the final version.

DATA SHARING STATEMENT

Data extracted from the included studies in this review are available on request from the corresponding author.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. PRISMA flowchart for study selection.

Appendix S1. Reference list of the included studies.

Table S1. MEDLINE search strategy.

Table S2. Data extraction items from empirical literature sources.

Table S3. Countries and number of articles identified included in the study.

Table S4. Demographic characteristics of included studies.

Table S5. Measurements and interventions used in included studies.

Table S6. Countries with available policies/guidelines on CKD early detection programs.

Table S7. Characteristics of CKD screening studies by country income group.

PRISMA Checklist.

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