BMJ Open

Assessing the impact of screening, early identification, and intervention programs for CKD: Protocol for a scoping review.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-053857
Article Type:	Protocol
Date Submitted by the Author:	26-May-2021
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Keywords:	Chronic renal failure < NEPHROLOGY, End stage renal failure < NEPHROLOGY, Adult nephrology < NEPHROLOGY, EPIDEMIOLOGY

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Title: Assessing the impact of screening, early identification, and intervention programs for CKD: Protocol for a scoping review.

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Abstract word count: (251)

Manuscript word count: (2,841)

Running Title: CKD screening and early identification programs

Keywords: chronic kidney disease, early identification, implementation, interventions, screening,

Abstract:

Introduction

Chronic kidney disease (CKD) is a major threat to public health, especially in low-income and lower-middle-income countries where resources for treating patients with advanced CKD are scarce. Although early CKD identification and intervention holds promise for reducing the burden of CKD and risk factors, it remains unclear if a uniform strategy can be applicable across all income groups. The aim of this scoping review is to provide an overview of all screening attempts and identify components of such programs to advance screening toolkits for CKD based on income group.

Methods and analysis

This review will be guided by the methodological framework for conducting scoping studies developed by Arksey and O'Malley. Empirical (Medline, Embase, Cochrane Library, CINAHL, ISI Web of Science and PsycINFO) and grey literature references will be searched to identify studies on CKD screening, early identification, and interventions across all populations. Two reviewers will independently screen references in consecutive stages of title/abstract screening and then full-text screening. We will utilize a general descriptive overview, tabular summaries, and content analysis on extracted data.

Ethics and dissemination

The findings from our planned scoping review will enable us to identify items in early identification programs that can be used in advancing screening toolkits for CKD. We will disseminate our findings using traditional approaches that includes open-access peer-reviewed publication, scientific presentations, and a white paper (call to action) report. Ethical approval will not be required for this scoping review as the data will be extracted from already published studies.

Strengths and limitations of this protocol:

- This study will provide a comprehensive overview (where, when, why, how, and who) of all attempts to screen people for CKD.

- This study will be able to identify proportion of studies that utilized interventions following CKD identification, the types of interventions that were used, and the types of programs more likely to use interventions.

- Our study findings will provide information on screening efforts that have been successfully evidenced by utilization of various interventions as well as programs that have become implemented / integrated as health policies.

- This study will also identify international variations and components of successful screening / early identification programs to be used for advancing a CKD screening toolkit for countries in different income groups.

- A potential limitation of this study could include our inability to access policy documents related to implementation of screening and early detection programs, particularly in low-income and lower-middle income countries.

Introduction

Worldwide, the burden of chronic kidney disease (CKD) continues to rise. This is evidenced by its climb in ranking of global causes of death from 17th in 1990 to 12th in 2017 when the global prevalence of CKD was 697.5 million with an estimated 1.2 million deaths.[1] More recently, the World Health Organization (WHO) ranked CKD as the 10th commonest cause of death.[2] It is currently the 3rd fastest growing cause of death and, according to projections, will become the 5th commonest cause of years of life lost (YLL), rising from 16th in 2016.[3] Even more alarmingly, most of this growth is projected to be in low-income and lower-middle-income countries (LLMICs) where access to care is significantly limited.[1,4]

Although cost,[4-6] workforce,[7] leadership,[8,9] and organization of care[10] represent major barriers to accessing kidney care in LLMICs, the impact of cost of care and excessive out-of-pocket payment systems affect the people directly and are more devastating. While governments pay for dialysis in high-income countries (HICs), patients in LLMICs often have to partly or fully cover the cost of treatment out-of-pocket. One study has estimated that the annual cost of providing hemodialysis (HD) in Kenya, Nigeria and Senegal to be (International dollar) Int$1·7 billion, Int$3·5 billion, and Int$450 million respectively, equivalent to 15.2%, 55.8% and 35.8% of the total domestic government health expenditure of those countries.[6] The annual cost of HD in Nepal is about $2,500, far higher than the minimum wage.[11] Moreover, CKD, even in early stages, massively increases the risk of development of cardiovascular disease (CVD).[12,13] In addition, other modalities of kidney replacement therapies (KRT – i.e. peritoneal dialysis [PD] and kidney transplantation [KT]) are unavailable in many LLMICs. Compared to HICs, PD and KT availability was very low in low-income countries: 0.9 per million population [pmp] versus 53.0 pmp[14] and 23% countries versus 89% countries, respectively.[4]

The massive cost of KRT suggests the need to prioritize preventive strategies to delay kidney failure, rather than expand dialysis services.[6] This requires implementation of efficient and cost-effective screening and early detection and treatment programs to delay progression of kidney disease.[15-17] A few studies have shown that this is indeed possible. Out of 20,811 individuals screened for CKD in Nepal[18], 4471 were found to have hypertension, diabetes, proteinuria, or impaired kidney function. After 3 years of treatment with low-cost anti-hypertensive medications, anti-diabetic medications or ACE-inhibitors, 63 % of dipstick positive proteinuria had decreased to normal and 48 % of those with mildly to moderately impaired kidney function at baseline had stabilized or improved, highlighting the impact of early disease detection for reducing or halting CKD progression and cardiovascular morbidity and mortality in such settings.[18]

Screening and early identification programs are also used in HICs to assess disease burden and institute measures to improve kidney health, prevent dialysis and improve cardiovascular outcomes.[19-22] However, these measures have sometimes been criticized as ineffective as they show no overall benefits[23] or are not cost-effective.[24,25]

The concept of prevention being better than cure is not new – but preventive measures are more effective if directed at those identified to be in danger of harm. Intuitively, screening, and early CKD detection, should lead to better outcomes as patients and their care givers are able to apply measures to retard progression and improve outcomes; however, this has not always been the case, and has prompted the age-old nephrology debate "To Screen or not to Screen?".[25-27] In many instances, attempts to determine CKD prevalence, increase awareness, and determine cardiovascular risk through screening or early detection programs,

have not been coupled with follow-up actions.[28] The futility and possible harms of screening for CKD without availability of treatment have been pointed out.[29] Other programs have included interventions, e.g. referral to nephrology[30-32] or commencing specific therapies[33,34] when CKD or risk factors were detected. Despite these, various questions persist regarding the usefulness and methodology of CKD screening programs (Table 1).[15,26,29,35,36] As these questions linger, there remains limited evidence to guide choices and decisions about screening which continues to be based on available local and regional resources as well as the cultural acceptability of modality of screening. An initial approach with risk scores and questionnaires to identify high-risk individuals appears to be potentially useful for large-scale screening. However, available models for risk prediction and CKD progression are largely based on European or North American populations and often require measuring biomarkers. This is a major inconvenience in many LLMICs where laboratory testing is not readily available.[15]

These persistent questions led to a controversies conference on "early identification and interventions in CKD" organized by Kidney Disease Improving Global Outcomes (KDIGO) after which a consensus emerged that CKD screening coupled with risk stratification and treatment should be implemented in primary or community care settings for high-risk persons.[37] Major nephrology groups and regional bodies of nephrology have also developed guidelines for CKD screening tailored to their population with differences arising around who to test (general public *versus* those at risk), recommended tests to use (urine protein *versus* serum creatinine *versus* cystatin C assays) and frequency of testing (once annually *versus* more than once annually).[38-40] As most of the recommendations are largely based on evidence from observational studies (there are no randomized controlled studies assessing the benefits or harms of screening), selective approaches have been used in making

recommendations for screening in different income groups and populations, including CKD hotspots.[29]

Due to the weak and observational nature of the evidence base, guidelines that have made recommendations have tended not to be readily accepted, based on the degree of uncertainty and the magnitude of impact of kidney disease on public health. In 2012, the report of a systematic review on CKD screening and monitoring conducted for the United States Preventive Services Task Force (USPSTF) and the American College of Physicians (ACP) did not recommend CKD screening in asymptomatic adults without risk factors as no direct evidence was found that such screening improved outcomes.[23] The American Society of Nephrology (ASN) countered this with a strong recommendation to continue regular screening for kidney disease, regardless of an individual's risk factors.[41]

Lack of awareness of CKD is still perceived as a significant challenge to tackling the public health problems of CKD, particularly in LLMIC where most individuals with CKD remain undetected until they have progressed to kidney failure.[42] Population-wide studies in high-risk individuals have reported high prevalence and low awareness of CKD.[43-45] In Mexico, of 1,519 participants of a CKD screening program, only 1% of those with CKD were aware, despite 71% having visited a physician in the preceding year.[44] However, recent data from participants with CKD in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a national, longitudinal, population-based cohort did not show an association between awareness of CKD with odds of subsequent changes in health behaviors, CKD management indicators, or changes in eGFR and urine albumin-creatinine ratio (UACR).[46] The study concluded that clinician education needs to be coupled with

interventions to increase popular awareness of CKD for optimal impact on health behaviors and chronic disease management indicators.

As these controversies continue and given the large body of literature on screening, early identification programs, and interventions in CKD, we have designed a scoping review to identify, describe and assess all attempts that have been made to establish CKD early identification / screening / awareness programs worldwide. Our aim is to provide an overview of approaches to screen and detect CKD at an early stage and to advance strengths and weaknesses of such programs into a toolkit that can be used for early identification and intervention programs in CKD, based on country income groups.

Methods and Analysis

Approach

We will be guided by the methodological framework for conducting scoping studies developed by Arksey and O'Malley in 2005.[47] This framework provided an excellent foundation for scoping study methodology but has been further enhanced by work done by others.[48-50] This framework will include five steps (with an optional sixth step): (1) identifying the research question; (2) identifying the relevant studies; (3) study selection; (4) charting the data and (5) reporting the results; (6) consultation (optional). We will also utilize best practices for conducting and reporting systematic reviews (i.e., Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for Protocols and Scoping Reviews (PRISMA-ScR) for reporting our findings.[51,52]

Stage 1. Identifying the research question

We utilized a comprehensive approach that included screening methods, target population, and interventions utilized in framing our research question: "*What attempts have been made to establish CKD early detection / screening / awareness programs?"*. Using key themes in the conclusions from KDIGO[37] and to be able to fully answer the main study question, other questions will need to be addressed, including:

1. *What populations have been screened for CKD and what risk stratification has been included in screening?*
2. *What measurements methods have been used to screen for CKD?*
3. *What secondary preventive interventions have been utilized in those identified with CKD?*
4. *What efforts have been made to implement or integrate CKD screening programs into health system?*

We believe that answering these questions will enable us to identify all potential components required to launch and sustain a CKD screening or early detection program.

Stage 2. Identifying the relevant studies

Development of the search strategy will aim at getting a comprehensive review of the existing evidence base. We will identify studies through a detailed search (from inception) of the following bibliographic databases: Medline (Ovid), Embase (Ovid), Cochrane Library, CINAHL, ISI Web of Science and PsycINFO. We will also search grey literature (including ProQuest Dissertations & Theses Global, and Conference Proceedings Citation Index [Clarivate Analytics]) using recommended resources in consultation with our medical librarian (LH). We have developed the search strategy to be used in Medline (Table 2) and will adapt this strategy for other databases. The search strategy includes subject headings, related terms and key words necessary for the research question. We will use Boolean logic

and operators (ie, 'AND', 'OR', 'NOT') to combine and refine search terms. Given the complexities associated with implementing CKD early identification programs, and that post-program implementation policies may not have been included in primary publications, we will search for secondary publications and documents and where necessary contact authors of selected studies to ascertain if such programs became health policy.

Stage 3. Study selection

We will include studies that report the results of CKD screening. We will group the studies based on the World Bank country income groups and type of screening. Two reviewers (EKT and AG) will independently screen all identified citations for potential inclusion. When agreement on a citation cannot be reached between the two reviewers, a third reviewer (MM) will be consulted for reconciliation. The review process will first involve screening of the titles and abstracts and then a detailed review of all selected full texts to ascertain eligibility for inclusion (Figure 1). An article will be included if it meets the following criteria:

- **Population**: Studies that provided results of CKD screening (with or without an intervention) carried out in any adult (≥18 years) population. For studies in the same population with multiple years of publications, the result of the latest study will be used, and studies conducted across multiple countries will be reported as "multinational" with the list of participating countries provided.
- **Intervention**: CKD screening, or CKD early detection programs, or CKD awareness programs.
- **Comparator**: Standard of care (if applicable)

- **Outcomes**: CKD early identification programs / studies reporting at least one of the following: CKD detection rate (with or without risk factor detection rate), methods utilized for screening, people who carried out the screening, interventions utilized (e.g. proportion referred to nephrology clinics, proportion that started treatment, etc), cost-effectiveness of the program, and CKD screening policies implemented.
- **Study design**: all screening study designs that reported at least one of the outcomes.

– **Limits:** All databases will be searched from inception with no language restrictions.

The following studies will be excluded:

– Screening studies in children

– Screening studies for acute kidney injury (AKI), urological diseases (e.g. prostate cancer awareness programs), or CKD risk factors (e.g. hypertension and diabetes), if no attempt was made to specifically screen for CKD.

– Organ donor screening or awareness programs

– Review articles, editorials, commentaries, letters to the editor, and guidelines and recommendations on CKD screening.

Stage 4. Data Extraction

Results of the search will be collated in a Microsoft Excel spreadsheet. We will follow recommended data charting methods [47] to capture relevant details for included studies (Table 3). The data items collected will follow 4 themes: (i) population screened and screening methods used (e.g., duration of screening, country of study, type of program: "national" or "other", screening type: mass (community-based) / targeted (within a known CKD risk factor cohort), workforce involved in screening, repeat evaluation, motivation for the program (e.g., World Kidney Day program, public health concerns for rising kidney

disease, etc.), (ii) measurements utilized for assessing CKD (e.g. urine dipsticks, serum creatinine, eGFR, etc.), (iii) interventions utilized in those identified with CKD (e.g. referral to nephrology or specialist care, initiation of specific treatment (lifestyle measures, ACE-inhibitors, attempts to follow up patients offered interventions, etc.), and (iv) health systems and economic factors associated with screening (e.g. implementation programs, cost-effectiveness, etc.). All extracted data will be reviewed for accuracy and completeness.

Stage 5. Collating, summarizing, and reporting of the results

We will follow recommendations to extend the scoping review process by adding thematic analysis.[48] Hence, extracted data will be analysed qualitatively using both deductive (pre-identified themes) and inductive (new identified themes) approaches. These approaches will enable us to answer the broad research question and allow us to expand our response with new findings that were not previously included. Although specific data (e.g. CKD detection rate) will be collected, such data will not be pooled for further analysis. Textual data from included papers will be coded individually using simple "yes" or "no" responses and other broad-based coding scheme by (EKT) and (AG) to look for common themes across papers. We will present overall results using percentages of "yes" responses.

Stage 6. Consultation exercise

Consultation is an optional part of conducting a scoping review, however, where necessary, we will contact primary authors, regional nephrology leaders or Departments / Ministries of Health for policy documents on implementation of CKD screening programs.

Patient and public involvement

Patients and the public will not be involved in any stage of the project.

Discussion, Ethics, and dissemination

The findings from our planned scoping review will enable us to identify items in screening and early identification programs that can be used in advancing screening toolkits for CKD. The results will also enable us to understand what is feasible and the capacity of countries in different income groups for conducting and sustaining screening programs. Various reviews and recommendations have suggested using different screening approaches in LLMICs given the lack of capacity to integrate identified CKD cases into the broader health system and the general lack of capacity to measure the quality of care in existing CKD cases.[29,37] Thus, based on our results, this scoping review will be able to suggest components for consideration for inclusion in screening toolkits for countries in different income groups, though these are likely to need testing for effectiveness. Furthermore, we anticipate that this scoping review will likely lead to more specific questions (e.g. how sensitive and specific are urine dipsticks findings for screening?) that require detailed interrogation through systematic reviews or randomized controlled study designs. A potential limitation of this scoping review could be our inability to access policy documents backing the implementation / integration strategies of early identification programs to health systems, particularly in LLMICs. We hope that by contacting nephrology leaders and experts in those regions, we will be able to obtain information on the availability of such policy documents. Finally, ethical approval will not be needed for this study as data used will be extracted from already published studies. Our dissemination strategy will use traditional approaches, including open-access peer-reviewed publication(s), scientific presentations, and a report.

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, LNH, GA, AF, RI, MM, CM, MM, RP-F, VT, AL, and VJ. The search strategy was developed and performed by LNH. AG and EKT will perform the screening, study selection and collect data from all included studies and MM will adjudicate any conflicts in study selection. All authors revised and critically reviewed this manuscript and approved the final version.

Funding:

International Society of Nephrology (ISN)

Competing interests:

RP-F reports grants from Fresenius Medical Care, provides scientific leadership to George Clinical, and consultancy fees for Astra Zeneca, B-I, Bayer, Akebia, Novo Nordisk, all paid to his institution, outside the submitted work. VT reports consultancy fee from Boehringer-Ingelheim, Calliditas, Fresenius Medical Care, Novartis and Travere. VJ reports grants from GlaxoSmithKline and Baxter Healthcare, provides scientific leadership to George Clinical, and consultancy fees for Biocon, Zudis Cadilla, and NephroPlus, all paid to his institution, outside the submitted work.

Patient consent:

Not required.

Data sharing statement:

We will make data available on request

References

1. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet (London, England).* 2020;395(10225):709-733.
2. World Health Organization. The top 10 causes of death. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death. Published 2020. Accessed 19 March 2021.
3. Foreman KJ, Marquez N, Dolgert A, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. *Lancet (London, England).* 2018;392(10159):2052-2090.
4. Bello AK, Levin A, Lunney M, et al. Status of care for end stage kidney disease in countries and regions worldwide: international cross sectional survey. *Bmj.* 2019;367:l5873.
5. Tang SCW, Yu X, Chen HC, et al. Dialysis Care and Dialysis Funding in Asia. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2020;75(5):772-781.
6. Crosby L, Baker P, Hangoma P, Barasa E, Hamidi V, Chalkidou K. Dialysis in Africa: the need for evidence-informed decision making. *The Lancet Global health.* 2020;8(4):e476-e477.
7. Riaz P, Caskey F, McIsaac M, et al. Workforce capacity for the care of patients with kidney failure across world countries and regions. *BMJ Glob Health.* 2021;6(1).
8. Bello AK, Alrukhaimi M, Ashuntantang GE, et al. Global overview of health systems oversight and financing for kidney care. *Kidney Int Suppl (2011).* 2018;8(2):41-51.
9. Lunney M, Alrukhaimi M, Ashuntantang GE, et al. Guidelines, policies, and barriers to kidney care: findings from a global survey. *Kidney Int Suppl (2011).* 2018;8(2):30-40.
10. Htay H, Alrukhaimi M, Ashuntantang GE, et al. Global access of patients with kidney disease to health technologies and medications: findings from the Global Kidney Health Atlas project. *Kidney International Supplements.* 2018;8(2):64-73.
11. Divyaveer SS, Ramachandran R, Sahay M, et al. International Society of Nephrology Global Kidney Health Atlas: structures, organization, and services for the management of kidney failure in South Asia. *Kidney International Supplements.* 2021;11(2):e97-e105.
12. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular Disease in Chronic Kidney Disease: Pathophysiological Insights and Therapeutic Options. *Circulation.* 2021;143(11):1157-1172.
13. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet (London, England).* 2013;382(9889):339-352.
14. Cho Y, Bello AK, Levin A, et al. Peritoneal Dialysis Use and Practice Patterns: An International Survey Study. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2021;77(3):315-325.
15. George C, Mogueo A, Okpechi I, Echouffo-Tcheugui JB, Kengne AP. Chronic kidney disease in low-income to middle-income countries: the case for increased screening. *BMJ Glob Health.* 2017;2(2):e000256.
16. Perico N, Plata R, Anabaya A, et al. Strategies for national health care systems in emerging countries: the case of screening and prevention of renal disease progression in Bolivia. *Kidney international Supplement.* 2005(97):S87-94.

17. Perico N, Remuzzi G. Prevention programs for chronic kidney disease in low-income countries. *Intern Emerg Med.* 2016;11(3):385-389.
18. Sharma SK, Ghimire A, Carminati S, Remuzzi G, Perico N. Management of chronic kidney disease and its risk factors in eastern Nepal. *The Lancet Global health.* 2014;2(9):e506-e507.
19. Gansevoort RT, Verhave JC, Hillege HL, et al. The validity of screening based on spot morning urine samples to detect subjects with microalbuminuria in the general population. *Kidney international Supplement.* 2005(94):S28-35.
20. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2003;41(1):1-12.
21. Komenda P, Lavallee B, Ferguson TW, et al. The prevalence of CKD in rural Canadian indigenous peoples: results from the First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis (FINISHED) screen, triage, and treat program. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2016;68(4):582-590.
22. Takahashi S, Okada K, Yanai M. The Kidney Early Evaluation Program (KEEP) of Japan: results from the initial screening period. *Kidney international Supplement.* 2010(116):S17-23.
23. Fink HA, Ishani A, Taylor BC, et al. Screening for, monitoring, and treatment of chronic kidney disease stages 1 to 3: a systematic review for the U.S. Preventive Services Task Force and for an American College of Physicians Clinical Practice Guideline. *Annals of internal medicine.* 2012;156(8):570-581.
24. Manns B, Hemmelgarn B, Tonelli M, et al. Population based screening for chronic kidney disease: cost effectiveness study. *Bmj.* 2010;341:c5869.
25. Qaseem A, Wilt TJ, Cooke M, Denberg TD. The paucity of evidence supporting screening for stages 1-3 CKD in asymptomatic patients with or without risk factors. *Clinical journal of the American Society of Nephrology : CJASN.* 2014;9(11):1993-1995.
26. Kliger AS. Screening for CKD: a pro and con debate. *Clinical journal of the American Society of Nephrology : CJASN.* 2014;9(11):1987.
27. Berns JS. Routine screening for CKD should be done in asymptomatic adults... selectively. *Clinical journal of the American Society of Nephrology : CJASN.* 2014;9(11):1988-1992.
28. Cepoi V, Onofriescu M, Segall L, Covic A. The prevalence of chronic kidney disease in the general population in Romania: a study on 60,000 persons. *Int Urol Nephrol.* 2012;44(1):213-220.
29. Tonelli M, Dickinson JA. Early Detection of CKD: Implications for Low-Income, Middle-Income, and High-Income Countries. *Journal of the American Society of Nephrology : JASN.* 2020;31(9):1931-1940.
30. Garcia-Garcia G, Marquez-Magaña I, Renoirte-Lopez K, et al. Screening for kidney disease on World Kidney Day in Jalisco, Mexico. *J Nephrol.* 2010;23(2):224-230.
31. Galbraith LE, Ronksley PE, Barnieh LJ, et al. The See Kidney Disease Targeted Screening Program for CKD. *Clinical journal of the American Society of Nephrology : CJASN.* 2016;11(6):964-972.
32. Gayoso-Diz P, Otero-González A, Rodríguez-Álvarez MX, García F, González-Quintela A, Martin de Francisco AL. Strategy to estimate risk progression of chronic kidney disease, cardiovascular risk, and referral to nephrology: the EPIRCE Study.

Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia. 2013;33(2):223-230.

33. Sharma SK, Zou H, Togtokh A, et al. Burden of CKD, proteinuria, and cardiovascular risk among Chinese, Mongolian, and Nepalese participants in the International Society of Nephrology screening programs. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2010;56(5):915-927.
34. Diercks GF, Janssen WM, van Boven AJ, et al. Rationale, design, and baseline characteristics of a trial of prevention of cardiovascular and renal disease with fosinopril and pravastatin in nonhypertensive, nonhypercholesterolemic subjects with microalbuminuria (the Prevention of REnal and Vascular ENdstage Disease Intervention Trial [PREVEND IT]). *Am J Cardiol.* 2000;86(6):635-638.
35. Jaar BG, Khatib R, Plantinga L, Boulware LE, Powe NR. Principles of screening for chronic kidney disease. *Clinical journal of the American Society of Nephrology : CJASN.* 2008;3(2):601-609.
36. de Jong PE, van der Velde M, Gansevoort RT, Zoccali C. Screening for chronic kidney disease: where does Europe go? *Clinical journal of the American Society of Nephrology : CJASN.* 2008;3(2):616-623.
37. Shlipak MG, Tummalapalli SL, Boulware LE, et al. The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int.* 2021;99(1):34-47.
38. Johnson DW, Atai E, Chan M, et al. KHA-CARI guideline: Early chronic kidney disease: detection, prevention and management. *Nephrology (Carlton, Vic).* 2013;18(5):340-350.
39. National Institute for Health and Care Excellence (NICE). Assessment and monitoring of chronic kidney disease. http://pathways.nice.org.uk/pathways/chronic-kidney-disease. Published 2020. Updated 03 December 2020. Accessed 22 April 2021.
40. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *American journal of kidney diseases : the official journal of the National Kidney Foundation.* 2002;39(2 Suppl 1):S1-266.
41. ASN emphasizes need for early detection of kidney disease, a silent killer [press release]. American Society of Nephrology2013.
42. Garcia-Garcia G, Jha V, Li PKT, et al. Chronic kidney disease (CKD) in disadvantaged populations. *Clinical kidney journal.* 2015;8(1):3-6.
43. Vassalotti JA, Li S, McCullough PA, Bakris GL. Kidney early evaluation program: a community-based screening approach to address disparities in chronic kidney disease. *Seminars in nephrology.* 2010;30(1):66-73.
44. Obrador GT, García-García G, Villa AR, et al. Prevalence of chronic kidney disease in the Kidney Early Evaluation Program (KEEP) México and comparison with KEEP US. *Kidney Int.* 2010;77:S2-S8.
45. Liu Q, Li Z, Wang H, et al. High prevalence and associated risk factors for impaired renal function and urinary abnormalities in a rural adult population from southern China. *PLoS One.* 2012;7(10):e47100.
46. Tummalapalli SL, Vittinghoff E, Crews DC, et al. Chronic Kidney Disease Awareness and Longitudinal Health Outcomes: Results from the REasons for Geographic And Racial Differences in Stroke Study. *Am J Nephrol.* 2020;51(6):463-472.

47. Arksey H, O'Malley L. Scoping Studies: Towards a Methodological Framework. *International Journal of Social Research Methodology: Theory & Practice.* 2005;8(1):19-32.
48. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implementation science : IS.* 2010;5:69.
49. Colquhoun HL, Levac D, O'Brien KK, et al. Scoping reviews: time for clarity in definition, methods, and reporting. *Journal of clinical epidemiology.* 2014;67(12):1291-1294.
50. Daudt HM, van Mossel C, Scott SJ. Enhancing the scoping study methodology: a large, inter-professional team's experience with Arksey and O'Malley's framework. *BMC medical research methodology.* 2013;13:48.
51. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals of internal medicine.* 2018;169(7):467-473.
52. Peters MDJ GC, McInerney P, Munn Z, Tricco AC, Khalil, H. Chapter 11: Scoping Reviews (2020 version) In: In: Aromataris E MZE, ed. *Joanna Briggs Institute Reviewer's Manual, JBI, 2020.*2020.

FIGURE AND TABLE LEGENDS:

Figure 1: PRISMA-Flow chart for study selection

Table 1: Persisting questions on usefulness and methodology of CKD screening programs

Table 2: Medline search strategy

Table 3: Data extraction items from empirical literature sources

Table 1: Persisting questions on usefulness and methodology of CKD screening programs [15,26,29,35,36]

Questions related to the usefulness of CKD screening	Questions related to the methodology of CKD screening
- Should CKD screening be used in an asymptomatic population with or without CKD risk factors such as hypertension or diabetes?	- Are single measurements sufficient for detecting CKD?
- Are there unique risk factors in some populations we do not know about?	- Does population screening with serum creatinine and urine protein testing lead to improved outcomes without undue harm?
- Should therapies be initiated in those with mildly impaired eGFR or microalbuminuria?	- Should screening be conducted in younger age groups without CKD risk factors?
- Does earlier treatment improve the prognosis?	- What threshold of dipsticks positive proteinuria should be considered relevant for screening?
- Are CKD screening programs cost-effective?	- Who should manage screening and subsequent treatment?
- Do the potential harms of CKD screening outweigh the benefits?	- What tests should be selected for CKD screening?
- What is the yield of the screening service?	- How valid and repeatable is the screening test?
- What are the implications of CKD screening for public health policy?	

Abbreviations: CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate

Table 2: Medline search strategy

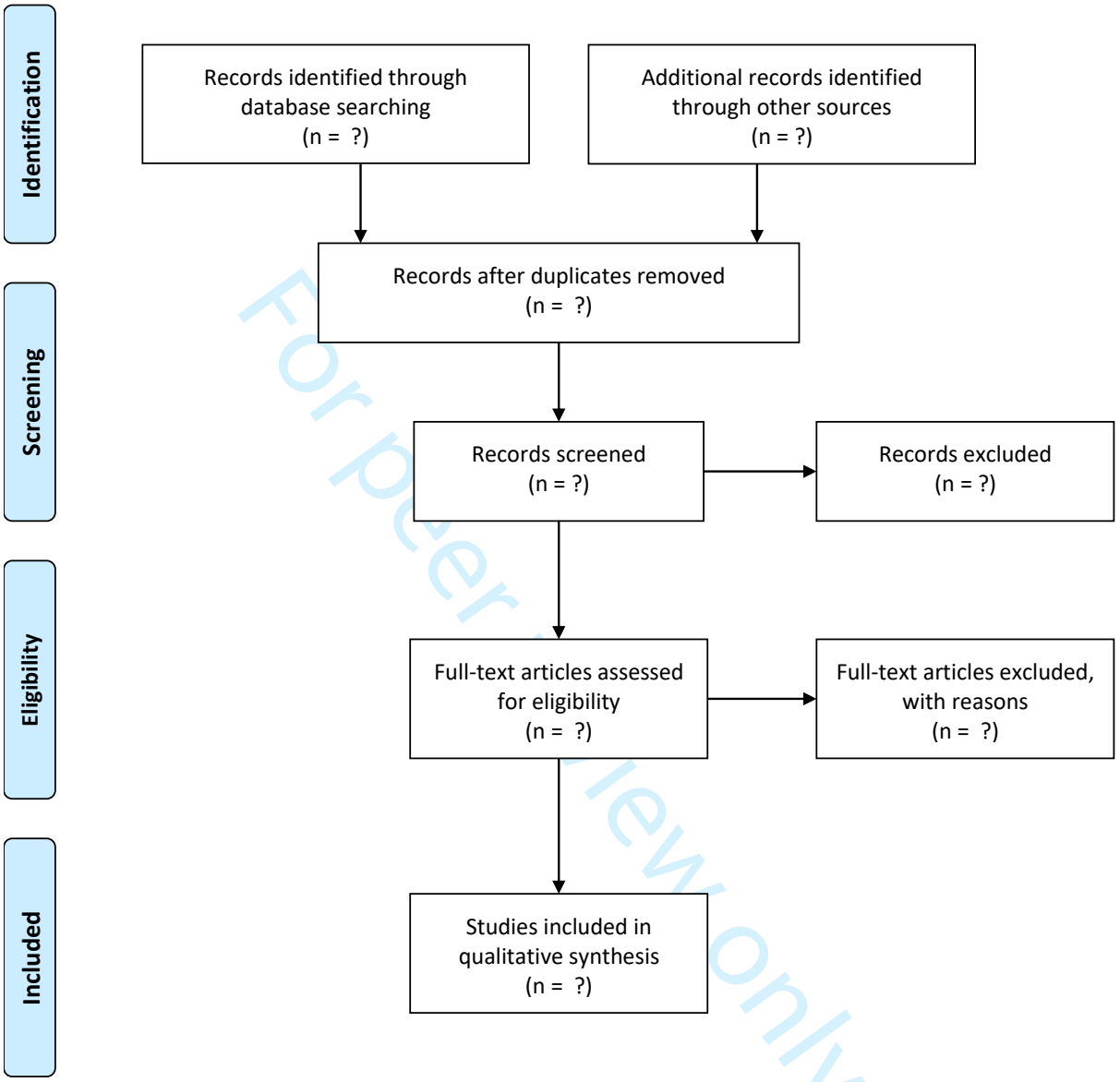
1. exp Renal Insufficiency, Chronic/
2. Chronic Kidney disease*.mp.
3. chronic kidney insufficienc*.mp.
4. chronic renal disease*.mp.
5. chronic renal insufficienc*.mp.
6. CKD.mp.
7. Renal fail*.mp.
8. Kidney fail*.mp.
9. or/1-8
10. Multiphasic Screening/ and (program* or campaign* or strateg* or initiative*).mp.
11. Mass Screening/
12. (screen* adj2 (program* or strateg* or campaign* or initiative*)).mp.
13. (awareness adj3 (program* or campaign* or strateg* or initiative*)).mp.
14. (detect* adj3 (program* or campaign* or strateg* or initiative*)).mp.
15. (National Health and Nutrition Examination Survey).mp.
16. Kidney Early Evaluation Program.mp.
17. (Prevention of Renal and Vascular End-Stage Disease).mp.
18. World Kidney Day.mp.
19. national kidney foundation.mp.
20. (Screening and Early Evaluation of Kidney disease).mp.
21. or/15-20
22. 21 and (screen* or detect* or awareness).mp.
23. or/10-14,22
24. 9 and 23
25. ((detect* or screen* or awareness) adj2 ("chronic kidney" or "chronic renal")).mp.
26. 24 or 25
27. exp animals/ not humans.sh.
28. 26 not 27

Table 3: Data extraction items from empirical literature sources

Population screened	Measurements	Interventions	Implementation
Country, income group	Number of measurements (1x / 2x)	Lifestyle measures*	Cost measures reported
Type of program (national / others)	Urine dipsticks (protein ± blood)	RAAS blockade	Reported to be cost-effective
Demographic features (Age, gender, ethnicity, rural / urban setting)	Urine ACR / PCR only	Antidiabetic medications (any)	Screening strategy adopted or not implemented due to lack of efficacy (e.g. policy document)
Workforce involved in screening	SCR / eGFR only	Anti-hypertensive medications (separate from RAAS)	
Screening type:	Urine + SCR / eGFR	Lipid treatment	
Mass screening (yes / no)	POCT	Avoidance of nephrotoxins	
Targeted screening (yes / no)	Other tests (e.g. cystatin C)	Referral to nephrology service	
• Hypertensives	Reported CKD prevalence (yes / no)	Referral for KRT	
• Diabetics			
• Elderly			
• Family history of CKD			
• HIV			
• Minority group (e.g., Indigenous populations)			
• Others			
Risk factors assessed and reported:			
• BP			
• Blood glucose			
• Body weight / BMI			
• Lipids			
• Others			
Risk stratification (yes / no)			

CKD – Chronic kidney disease, HIC – high-income country, UMIC – upper middle-income country, LMIC – lower middle-income country, LIC – low-income country, HIV – human immunodeficiency virus, ACR – albumin-creatinine ratio, PCR – protein creatinine ratio, SCR – serum creatinine, eGFR- estimated glomerular filtration rate, BP – blood pressure, BMI – body mass index, RAAS – renin-angiotensin aldosterone system, KRT – kidney replacement therapy (any of hemodialysis, peritoneal dialysis, kidney transplantation), POCT – point of care test (e.g. saliva), *(smoking cessation, weight reduction measures, dietary measures, etc.)

Figure 1: PRISMA-Flow chart for study selection



Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	#1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	#3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	#5 to #8
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	#9
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	NA
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	#11 to #12
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	#10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Table 2
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	#11
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	#12 to #13
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Table 3
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	#13

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	NA
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	NA
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	NA
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	NA
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	#14
Limitations	20	Discuss the limitations of the scoping review process.	#14
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	NA
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	#15

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

BMJ Open

Assessing the impact of screening, early identification, and intervention programs for Chronic Kidney Disease: Protocol for a scoping review.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-053857.R1
Article Type:	Protocol
Date Submitted by the Author:	18-Oct-2021
Complete List of Authors:	Okpechi, Ikechi G ; University of Cape Town Faculty of Health Sciences, Division of Nephrology and Hypertension; University of Alberta Faculty of Medicine & Dentistry Caskey, Fergus; North Bristol NHS Trust, Richard Bright Renal Unit; UK Renal Registry Gaipov, Abduzhappar; Nazarbaev universitet, Medicine Tannor, Elliot; Komfo Anokye Teaching Hospital, Department of Medicine Hamonic, Laura; University of Alberta, John W. Scott Health Sciences Library Ashuntantang, Gloria; University of Yaounde I, Department of Internal Medicine and Subspecialties Donner, Jo-Ann; International Society of Nephrology, Global Operations Centre Figueiredo, Ana; Pontifícia Universidade Católica do Rio Grande do Sul Inagi, Reiko; The University of Tokyo Graduate School of Medicine Faculty of Medicine Madero, Magdalena; Instituto Nacional de Cardiología Ignacio Chávez Malik, Charu; International Society of Nephrology, Global Operations Centre Moorthy, Monica; International Society of Nephrology, Global Operations Centre Pecoits-Filho, Roberto ; Arbor Research Collaborative for Health, Tesar, Vladimir; Charles University, Department of Medicine Levin, Adeera; The University of British Columbia Faculty of Medicine, Medicine Jha, Vivekanand; The George Institute for Global Health India
Primary Subject Heading:	Renal medicine
Secondary Subject Heading:	Epidemiology, Public health, Renal medicine
Keywords:	Chronic renal failure < NEPHROLOGY, End stage renal failure < NEPHROLOGY, Adult nephrology < NEPHROLOGY, EPIDEMIOLOGY

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Title: Assessing the impact of screening, early identification, and intervention programs for Chronic Kidney Disease: Protocol for a scoping review.

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Abstract word count: (265)

Manuscript word count: (2,890)

Running Title: CKD screening and early identification programs

Keywords: chronic kidney disease, early identification, implementation, interventions, screening,

Abstract:

Introduction

Chronic kidney disease (CKD) is a major threat to public health, especially in low-income and lower-middle-income countries where resources for treating patients with advanced CKD are scarce. Although early CKD identification and intervention holds promise for reducing the burden of CKD and risk factors, it remains unclear if a uniform strategy can be applicable across all income groups. The aim of this scoping review is to synthesize available evidence on early CKD identification programs in all world regions and income groups. The study will also identify efforts that have been made to utilize interventions and implementation of early identification programs for CKD across countries and income groups.

Methods and analysis

This review will be guided by the methodological framework for conducting scoping studies developed by Arksey and O'Malley. Empirical (Medline, Embase, Cochrane Library, CINAHL, ISI Web of Science and PsycINFO) and grey literature references will be searched to identify studies on CKD screening, early identification, and interventions across all populations. Two reviewers will independently screen references in consecutive stages of title/abstract screening and then full-text screening. We will utilize a general descriptive overview, tabular summaries, and content analysis on extracted data.

Ethics and dissemination

The findings from our planned scoping review will enable us to identify items in early identification programs that can be used in developing screening toolkits for CKD. We will disseminate our findings using traditional approaches that includes open-access peer-reviewed publication, scientific presentations, and a white paper (call to action) report. Ethical approval will not be required for this scoping review as the data will be extracted from already published studies.

Strengths and limitations of this protocol:

- This study will provide a comprehensive overview (where, when, why, how, and who) of studies on early detection of chronic kidney disease (CKD).

- This study will identify proportion of studies that utilized interventions following CKD early identification as well as the types of interventions commonly used.

- This study will also provide information on where early identification programs have become integrated or implemented in health policies and practices.

- This study will also identify international variations and components of early identification programs to be used for developing CKD screening toolkits for countries in different income groups.

- We foresee that a potential limitation of this study could include our inability to access policy documents related to implementation of screening and early detection programs, particularly in low-income and lower-middle income countries.

Introduction

Worldwide, the burden of chronic kidney disease (CKD) continues to rise. This is evidenced by its climb in ranking of global causes of death from 17th in 1990 to 12th in 2017 when the global prevalence of CKD was 697.5 million with an estimated 1.2 million deaths.[1] More recently, the World Health Organization (WHO) ranked CKD as the 10th commonest cause of death.[2] It is currently the 3rd fastest growing cause of death and, according to projections, will become the 5th commonest cause of years of life lost (YLL), rising from 16th in 2016.[3] Even more alarmingly, although increase in CKD is occurring globally, most of this growth is projected to be in low-income and lower-middle-income countries (LLMICs) and amongst disadvantaged and indigenous communities in high income countries (HICs) where access to care is significantly limited.[1, 4]

Although cost,[4-6] workforce,[7] leadership,[8, 9] and organization of care[10] represent major barriers to accessing kidney care in LLMICs, the impact of cost of care and excessive out-of-pocket payment systems affect the people directly and are more devastating. While governments pay for dialysis in HICs, patients in LLMICs often have to partly or fully cover the cost of treatment out-of-pocket. One study has estimated that the annual cost of providing hemodialysis (HD) in Kenya, Nigeria and Senegal to be (International dollar) Int$1·7 billion, Int$3·5 billion, and Int$450 million respectively, equivalent to 15.2%, 55.8% and 35.8% of the total domestic government health expenditure of those countries.[6] The annual cost of HD in Nepal is about USD$2,500, far higher than the minimum wage.[11] Moreover, CKD, even in early stages, massively increases the risk of development of cardiovascular disease (CVD).[12, 13] In addition, other modalities of kidney replacement therapies (KRT – i.e. peritoneal dialysis [PD] and kidney transplantation [KT]) are unavailable in many LLMICs. Compared

to HICs, PD and KT availability was very low in low-income countries: 0.9 per million population [pmp] versus 53.0 pmp[14] and 23% countries versus 89% countries, respectively.[4]

The massive cost of KRT suggests the need to prioritize preventive strategies to delay kidney failure, rather than expand dialysis services.[6] This requires implementation of efficient and cost-effective screening and early detection and treatment programs to delay progression of kidney disease.[15-17] A few studies have shown that this is indeed possible. Out of 20,811 individuals screened for CKD in Nepal[18], 4471 were found to have hypertension, diabetes, proteinuria, or impaired kidney function. After 3 years of treatment with low-cost anti-hypertensive medications, anti-diabetic medications or ACE-inhibitors, 63 % of dipstick positive proteinuria had decreased to normal and 48 % of those with mildly to moderately impaired kidney function at baseline had stabilized or improved, highlighting the impact of early disease detection for reducing or halting CKD progression and cardiovascular morbidity and mortality in such settings.[18]

Screening and early identification programs are also used in HICs to assess disease burden and institute measures to improve kidney health, prevent dialysis and improve cardiovascular outcomes.[19-22] However, these measures have sometimes been criticized as ineffective as they show no overall benefits[23] or are not cost-effective.[24, 25]

The concept of prevention being better than cure is not new – but preventive measures are more effective if directed at those identified to be in danger of harm. Intuitively, screening, and early CKD detection, should lead to better outcomes as patients and their care givers are able to apply measures to retard progression and improve outcomes; however, this has not always been the case, and has prompted the age-old nephrology debate "To Screen or

not to Screen?".[25-27] In many instances, attempts to determine CKD prevalence, increase awareness, and determine cardiovascular risk through screening or early detection programs, have not been coupled with follow-up actions.[28] The futility and possible harms of screening for CKD without availability of treatment have been pointed out.[29] Other programs have included interventions, e.g. referral to nephrology[30-32] or commencing specific therapies[33, 34] when CKD or risk factors were detected. Despite these, various questions persist regarding the usefulness and methodology of CKD screening programs (Table 1).[15, 26, 29, 35, 36] As these questions linger, there remains limited evidence to guide choices and decisions about screening which continues to be based on available local and regional resources as well as the cultural acceptability of modality of screening. An initial approach with risk scores and questionnaires to identify high-risk individuals appears to be potentially useful for large-scale screening. However, available models for risk prediction and CKD progression are largely based on European or North American populations and often require measuring biomarkers. This is a major inconvenience in many LLMICs where laboratory testing is not readily available.[15]

These persistent questions led to a controversies conference on "early identification and interventions in CKD" organized by Kidney Disease Improving Global Outcomes (KDIGO) after which a consensus emerged that CKD screening coupled with risk stratification and treatment should be implemented in primary or community care settings for high-risk persons.[37] Major nephrology groups and regional bodies of nephrology have also developed guidelines for CKD screening tailored to their population with differences arising around who to test (general public *versus* those at risk), recommended tests to use (urine protein *versus* serum creatinine *versus* cystatin C assays) and frequency of testing (once annually *versus* more than once annually).[38-40] As most of the recommendations are largely

based on evidence from observational studies (there are no randomized controlled studies assessing the benefits or harms of screening), selective approaches have been used in making recommendations for screening in different income groups and populations, including CKD hotspots.[29]

Due to the weak and observational nature of the evidence base, guidelines that have made recommendations have tended not to be readily accepted, based on the degree of uncertainty and the magnitude of impact of kidney disease on public health. In 2012, the report of a systematic review on CKD screening and monitoring conducted for the United States Preventive Services Task Force (USPSTF) and the American College of Physicians (ACP) did not recommend CKD screening in asymptomatic adults without risk factors as no direct evidence was found that such screening improved outcomes.[23] The American Society of Nephrology (ASN) countered this with a strong recommendation to continue regular screening for kidney disease, regardless of an individual's risk factors.[41]

Lack of awareness of CKD is still perceived as a significant challenge to tackling the public health problems of CKD, particularly in LLMIC where most individuals with CKD remain undetected until they have progressed to kidney failure.[42] Population-wide studies in high-risk individuals have reported high prevalence and low awareness of CKD.[43-45] In Mexico, of 1,519 participants of a CKD screening program, only 1% of those with CKD were aware, despite 71% having visited a physician in the preceding year.[44] However, recent data from participants with CKD in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a national, longitudinal, population-based cohort did not show an association between awareness of CKD with odds of subsequent changes in health behaviors, CKD management indicators, or changes in eGFR and urine albumin-creatinine ratio

(UACR).[46] The study concluded that clinician education needs to be coupled with interventions to increase popular awareness of CKD for optimal impact on health behaviors and chronic disease management indicators.

As these controversies continue and given the large body of literature on screening, early identification programs, and interventions in CKD, we have designed a scoping review to identify, describe and assess CKD early identification / screening / awareness programs worldwide. Our aim is to synthesize available evidence on early CKD identification programs in all world regions and income groups and to use the strengths and weaknesses of such programs into developing a toolkit that can be used by nephrologists across all income groups for early identification and intervention programs in CKD.

Methods and Analysis

Approach

We will be guided by the methodological framework for conducting scoping studies developed by Arksey and O'Malley in 2005.[47] This framework has been further enhanced by work done by others including the JBI International Committee.[48-51] The framework includes five steps (with an optional sixth step): (1) identifying the research question; (2) identifying the relevant studies; (3) study selection; (4) charting the data and (5) reporting the results; (6) consultation (optional). We will also utilize best practices for conducting and reporting systematic reviews (i.e., Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for Protocols and Scoping Reviews (PRISMA-ScR) for reporting our findings.[52, 53]

Stage 1. Identifying the research question

We utilized a comprehensive approach that included screening methods, target population, and interventions utilized in framing our research question: "*What attempts have been made to establish CKD early detection / screening / awareness programs?"*. Using key themes in the conclusions from KDIGO[37] and to be able to fully answer the main study question, other questions will need to be addressed, including:

1. *What populations have been screened for CKD and what risk stratification has been included in screening?*
2. *What measurements methods have been used to screen for CKD?*
3. *What secondary preventive interventions have been utilized in those identified with CKD?*
4. *What efforts have been made to implement or integrate CKD screening programs into health system?*

We believe that answering these questions will enable us to identify all potential components required to launch and sustain a CKD screening or early detection program.

Stage 2. Identifying the relevant studies

Development of the search strategy will aim at getting a comprehensive review of the existing evidence base. We will identify studies through a detailed search (from inception) of the following bibliographic databases: Medline (Ovid), Embase (Ovid), Cochrane Library, CINAHL, ISI Web of Science and PsycINFO. We will also search grey literature (including ProQuest Dissertations & Theses Global, and Conference Proceedings Citation Index [Clarivate Analytics]) using recommended resources in consultation with our medical librarian (LH). However, we will specifically hand-search for information (e.g., policy documents or position papers) on guidelines for CKD early identification / screening for countries and regions that will be represented in our study. We have developed the search

strategy to be used in Medline (Table 2) and will adapt this strategy for other databases. The search strategy includes subject headings, related terms and key words necessary for the research question. We will use Boolean logic and operators (ie, 'AND', 'OR', 'NOT') to combine and refine search terms. Given the complexities associated with implementing CKD early identification programs, and that post-program implementation policies may not have been included in primary publications, we will search for secondary publications and documents and where necessary contact authors of selected studies to ascertain if such programs became health policy.

Stage 3. Study selection

We will include studies that report the results of CKD screening. We will group the studies based on the World Bank country income groups and type of screening. Two reviewers (EKT and AG) will independently screen all identified citations for potential inclusion. When agreement on a citation cannot be reached between the two reviewers, a third reviewer (MM) will be consulted for reconciliation. The review process will first involve screening of the titles and abstracts and then a detailed review of all selected full texts to ascertain eligibility for inclusion (Figure 1). An article will be included if it meets the following criteria:

- **Population**: Studies that provided results of CKD screening (with or without an intervention) carried out in any adult (≥18 years) population. For studies in the same population with multiple years of publications, the result of the latest study will be used, and studies conducted across multiple countries will be reported as "multinational" with the list of participating countries provided.

- **Intervention**: CKD screening, or CKD early detection programs, or CKD awareness programs.
- **Comparator**: Standard of care (if applicable)
- **Outcomes**: CKD early identification programs / studies reporting at least one of the following: CKD detection rate (with or without risk factor detection rate), methods utilized for screening, people who carried out the screening, interventions utilized (e.g., proportion referred to nephrology clinics, proportion that started treatment, etc), cost-effectiveness of the program, and CKD screening policies implemented.
- **Study design**: all screening study designs that reported at least one of the outcomes.

– **Limits:** All databases will be searched from inception with no language restrictions.

The following studies will be excluded:

– Screening studies in children

– Screening studies for acute kidney injury (AKI), urological diseases (e.g., prostate cancer awareness programs), or CKD risk factors (e.g., hypertension and diabetes), if no attempt was made to specifically screen for CKD.

– Organ donor screening or awareness programs

– Review articles, editorials, commentaries, letters to the editor, and guidelines and recommendations on CKD screening.

Stage 4. Data Extraction

Results of the search will be collated in a Microsoft Excel spreadsheet. We will follow recommended data charting methods [47] to capture relevant details for included studies (Table 3). The data items collected will follow 4 themes: (i) population screened and screening methods used (e.g., duration of screening, country of study, type of program:

"national" or "other", screening type: mass (community-based) / targeted (within a known CKD risk factor cohort), workforce involved in screening, repeat evaluation, motivation for the program (e.g., World Kidney Day program, public health concerns for rising kidney disease, etc.). We will also extract data on race / ethnicity of the population screened. Although, race is not often well defined in numerous studies, we will capture data using the following races (if reported): Arabs / Middle Easterners, Asians, Black Africans / African Americans, Caucasians, Hispanics, Indigenous groups, Latin Americans, others, (ii) measurements utilized for assessing CKD (e.g. urine dipsticks, serum creatinine, eGFR, etc.), (iii) interventions utilized in those identified with CKD (e.g. referral to nephrology or specialist care, initiation of specific treatment (lifestyle measures, ACE-inhibitors, attempts to follow up patients offered interventions, etc.), and (iv) health systems and economic factors associated with screening (e.g. implementation programs, cost-effectiveness, etc.). All extracted data will be reviewed for accuracy and completeness.

Stage 5. Collating, summarizing, and reporting of the results

We will follow recommendations to extend the scoping review process by adding thematic analysis.[48] Hence, extracted data will be analysed qualitatively using both deductive (pre-identified themes) and inductive (new identified themes) approaches. Primary analysis of data will be based on four themes identified by KDIGO:[37] (i) population screened, (ii) diagnostic characteristics of tests for kidney disease utilized, (iii) treatments (interventions) utilized to reduce the risk of CKD progression and cardiovascular disease, and (iv) implementation strategies for early CKD identification programs. These approaches will enable us to answer the broad research question and allow us to expand our response with new findings that were not previously included. Although specific data (e.g., CKD detection rate) will be collected, such data will not be pooled for further analysis. Textual data from

included papers will be coded individually using simple "yes" or "no" responses and other broad-based coding scheme by (EKT) and (AG) to look for common themes across papers. We will present overall results using percentages of "yes" responses.

Stage 6. Consultation exercise

Consultation is an optional part of conducting a scoping review, however, where necessary, we will contact primary authors, regional nephrology leaders or Departments / Ministries of Health for policy documents on implementation of CKD screening programs. Consultation will be necessary after selecting studies to be included and only if we are unable to identify online policy documents on early CKD identification for countries represented in selected studies. This process will be facilitated by members of the ISN Regional Board (https://www.theisn.org/about-isn/governance/regional-boards/) for countries represented in selected studies.

Patient and public involvement

Patients and the public will not be involved in this scoping review; however, the ISN is seeking to establish a globally representative patient advisory group. It would be appropriate for such a group to make input into subsequent, more specific research questions that are generated from studies identified in this scoping review.

Discussion, Ethics, and dissemination

The findings from our planned scoping review will enable us to identify items in screening and early identification programs that can be used in developing screening toolkits for CKD. The results will also enable us to understand what is feasible and the capacity of countries in different income groups for conducting and sustaining screening programs.

Various reviews and recommendations have suggested using different screening approaches in LLMICs given the lack of capacity to integrate identified CKD cases into the broader health system and the general lack of capacity to measure the quality of care in existing CKD cases.[29, 37] Thus, based on our results, this scoping review will be able to suggest components for consideration for inclusion in screening toolkits for countries in different income groups, though these are likely to need testing for effectiveness. Furthermore, we anticipate that this scoping review will likely lead to more specific questions (e.g., how sensitive and specific are urine dipsticks findings for screening?) that require detailed interrogation through systematic reviews or randomized controlled study designs. A potential limitation of this scoping review could be our inability to access policy documents backing the implementation / integration strategies of early identification programs to health systems, particularly in LLMICs. We hope that by contacting nephrology leaders and experts in those regions, we will be able to obtain information on the availability of such policy documents. Finally, ethical approval will not be needed for this study as data used will be extracted from already published studies. Our dissemination strategy will use traditional approaches, including open-access peer-reviewed publication(s), scientific presentations, and a report.

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, LNH, GA, JD, AF, RI, MM, CM, MM, RP-F, VT, AL, and VJ. The search strategy was developed and performed by LNH. AG and EKT will perform the screening, study selection and collect data from all included studies and MM will adjudicate any conflicts in study selection. All authors revised and critically reviewed this manuscript and approved the final version.

Funding:

This is an International Society of Nephrology (ISN) initiative supported by an unrestricted educational grant from AstraZeneca (No grant number).

Competing interests:

RP-F reports grants from Fresenius Medical Care, provides scientific leadership to George Clinical, and consultancy fees for Astra Zeneca, B-I, Bayer, Akebia, Novo Nordisk, all paid to his institution, outside the submitted work. VT reports consultancy fee from Boehringer-Ingelheim, Calliditas, Fresenius Medical Care, Novartis and Travere. VJ reports grants from GlaxoSmithKline and Baxter Healthcare, provides scientific leadership to George Clinical, and consultancy fees for Biocon, Zudis Cadilla, and NephroPlus, all paid to his institution, outside the submitted work.

Patient consent:

Not required.

Data sharing statement:

We will make data available on request

References

1. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet (London, England)*. Feb 29 2020;395(10225):709-733. doi:10.1016/s0140-6736(20)30045-3
2. World Health Organization. The top 10 causes of death. Accessed 19 March 2021, https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death
3. Foreman KJ, Marquez N, Dolgert A, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. *Lancet (London, England)*. Nov 10 2018;392(10159):2052-2090. doi:10.1016/s0140-6736(18)31694-5
4. Bello AK, Levin A, Lunney M, et al. Status of care for end stage kidney disease in countries and regions worldwide: international cross sectional survey. *Bmj*. Oct 31 2019;367:l5873. doi:10.1136/bmj.l5873
5. Tang SCW, Yu X, Chen HC, et al. Dialysis Care and Dialysis Funding in Asia. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. May 2020;75(5):772-781. doi:10.1053/j.ajkd.2019.08.005
6. Crosby L, Baker P, Hangoma P, Barasa E, Hamidi V, Chalkidou K. Dialysis in Africa: the need for evidence-informed decision making. *The Lancet Global health*. Apr 2020;8(4):e476-e477. doi:10.1016/s2214-109x(20)30058-9
7. Riaz P, Caskey F, McIsaac M, et al. Workforce capacity for the care of patients with kidney failure across world countries and regions. *BMJ Glob Health*. Jan 2021;6(1)doi:10.1136/bmjgh-2020-004014
8. Bello AK, Alrukhaimi M, Ashuntantang GE, et al. Global overview of health systems oversight and financing for kidney care. *Kidney Int Suppl (2011)*. Feb 2018;8(2):41-51. doi:10.1016/j.kisu.2017.10.008
9. Lunney M, Alrukhaimi M, Ashuntantang GE, et al. Guidelines, policies, and barriers to kidney care: findings from a global survey. *Kidney Int Suppl (2011)*. Feb 2018;8(2):30-40. doi:10.1016/j.kisu.2017.10.007
10. Htay H, Alrukhaimi M, Ashuntantang GE, et al. Global access of patients with kidney disease to health technologies and medications: findings from the Global Kidney Health Atlas project. *Kidney International Supplements*. 2018;8(2):64-73. doi:10.1016/j.kisu.2017.10.010
11. Divyaveer SS, Ramachandran R, Sahay M, et al. International Society of Nephrology Global Kidney Health Atlas: structures, organization, and services for the management of kidney failure in South Asia. *Kidney International Supplements*. 2021;11(2):e97-e105.
12. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular Disease in Chronic Kidney Disease: Pathophysiological Insights and Therapeutic Options. *Circulation*. Mar 16 2021;143(11):1157-1172. doi:10.1161/circulationaha.120.050686
13. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet (London, England)*. Jul 27 2013;382(9889):339-52. doi:10.1016/s0140-6736(13)60595-4
14. Cho Y, Bello AK, Levin A, et al. Peritoneal Dialysis Use and Practice Patterns: An International Survey Study. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. Mar 2021;77(3):315-325. doi:10.1053/j.ajkd.2020.05.032
15. George C, Mogueo A, Okpechi I, Echouffo-Tcheugui JB, Kengne AP. Chronic kidney disease in low-income to middle-income countries: the case for increased screening. *BMJ Glob Health*. 2017;2(2):e000256. doi:10.1136/bmjgh-2016-000256
16. Perico N, Plata R, Anabaya A, et al. Strategies for national health care systems in emerging countries: the case of screening and prevention of renal disease progression in

Bolivia. *Kidney international Supplement*. Aug 2005;(97):S87-94. doi:10.1111/j.1523-1755.2005.09715.x
17. Perico N, Remuzzi G. Prevention programs for chronic kidney disease in low-income countries. *Intern Emerg Med*. Apr 2016;11(3):385-9. doi:10.1007/s11739-016-1425-7
18. Sharma SK, Ghimire A, Carminati S, Remuzzi G, Perico N. Management of chronic kidney disease and its risk factors in eastern Nepal. *The Lancet Global health*. Sep 2014;2(9):e506-e507. doi:10.1016/s2214-109x(14)70281-5
19. Gansevoort RT, Verhave JC, Hillege HL, et al. The validity of screening based on spot morning urine samples to detect subjects with microalbuminuria in the general population. *Kidney international Supplement*. Apr 2005;(94):S28-35. doi:10.1111/j.1523-1755.2005.09408.x
20. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. Jan 2003;41(1):1-12. doi:10.1053/ajkd.2003.50007
21. Komenda P, Lavallee B, Ferguson TW, et al. The prevalence of CKD in rural Canadian indigenous peoples: results from the First Nations Community Based Screening to Improve Kidney Health and Prevent Dialysis (FINISHED) screen, triage, and treat program. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. 2016;68(4):582-590.
22. Takahashi S, Okada K, Yanai M. The Kidney Early Evaluation Program (KEEP) of Japan: results from the initial screening period. *Kidney international Supplement*. Mar 2010;(116):S17-23. doi:10.1038/ki.2009.539
23. Fink HA, Ishani A, Taylor BC, et al. Screening for, monitoring, and treatment of chronic kidney disease stages 1 to 3: a systematic review for the U.S. Preventive Services Task Force and for an American College of Physicians Clinical Practice Guideline. *Annals of internal medicine*. Apr 17 2012;156(8):570-81. doi:10.7326/0003-4819-156-8-201204170-00004
24. Manns B, Hemmelgarn B, Tonelli M, et al. Population based screening for chronic kidney disease: cost effectiveness study. *Bmj*. Nov 8 2010;341:c5869. doi:10.1136/bmj.c5869
25. Qaseem A, Wilt TJ, Cooke M, Denberg TD. The paucity of evidence supporting screening for stages 1-3 CKD in asymptomatic patients with or without risk factors. *Clinical journal of the American Society of Nephrology : CJASN*. Nov 7 2014;9(11):1993-5. doi:10.2215/cjn.02940314
26. Kliger AS. Screening for CKD: a pro and con debate. *Clinical journal of the American Society of Nephrology : CJASN*. Nov 7 2014;9(11):1987. doi:10.2215/cjn.08990914
27. Berns JS. Routine screening for CKD should be done in asymptomatic adults... selectively. *Clinical journal of the American Society of Nephrology : CJASN*. Nov 7 2014;9(11):1988-92. doi:10.2215/cjn.02250314
28. Cepoi V, Onofriescu M, Segall L, Covic A. The prevalence of chronic kidney disease in the general population in Romania: a study on 60,000 persons. *Int Urol Nephrol*. Feb 2012;44(1):213-20. doi:10.1007/s11255-011-9923-z
29. Tonelli M, Dickinson JA. Early Detection of CKD: Implications for Low-Income, Middle-Income, and High-Income Countries. *Journal of the American Society of Nephrology : JASN*. Sep 2020;31(9):1931-1940. doi:10.1681/asn.2020030277
30. Garcia-Garcia G, Marquez-Magaña I, Renoirte-Lopez K, et al. Screening for kidney disease on World Kidney Day in Jalisco, Mexico. *J Nephrol*. Mar-Apr 2010;23(2):224-30.

31. Galbraith LE, Ronksley PE, Barnieh LJ, et al. The See Kidney Disease Targeted Screening Program for CKD. *Clinical journal of the American Society of Nephrology : CJASN*. Jun 6 2016;11(6):964-72. doi:10.2215/cjn.11961115
32. Gayoso-Diz P, Otero-González A, Rodríguez-Álvarez MX, García F, González-Quintela A, Martin de Francisco AL. Strategy to estimate risk progression of chronic kidney disease, cardiovascular risk, and referral to nephrology: the EPIRCE Study. *Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia*. 2013;33(2):223-30. doi:10.3265/Nefrologia.pre2013.Jan.11792
33. Sharma SK, Zou H, Togtokh A, et al. Burden of CKD, proteinuria, and cardiovascular risk among Chinese, Mongolian, and Nepalese participants in the International Society of Nephrology screening programs. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. Nov 2010;56(5):915-27. doi:10.1053/j.ajkd.2010.06.022
34. Diercks GF, Janssen WM, van Boven AJ, et al. Rationale, design, and baseline characteristics of a trial of prevention of cardiovascular and renal disease with fosinopril and pravastatin in nonhypertensive, nonhypercholesterolemic subjects with microalbuminuria (the Prevention of REnal and Vascular ENdstage Disease Intervention Trial [PREVEND IT]). *Am J Cardiol*. Sep 15 2000;86(6):635-8. doi:10.1016/s0002-9149(00)01042-0
35. Jaar BG, Khatib R, Plantinga L, Boulware LE, Powe NR. Principles of screening for chronic kidney disease. *Clinical journal of the American Society of Nephrology : CJASN*. Mar 2008;3(2):601-9. doi:10.2215/cjn.02540607
36. de Jong PE, van der Velde M, Gansevoort RT, Zoccali C. Screening for chronic kidney disease: where does Europe go? *Clinical journal of the American Society of Nephrology : CJASN*. Mar 2008;3(2):616-23. doi:10.2215/cjn.04381007
37. Shlipak MG, Tummalapalli SL, Boulware LE, et al. The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int*. Jan 2021;99(1):34-47. doi:10.1016/j.kint.2020.10.012
38. Johnson DW, Atai E, Chan M, et al. KHA-CARI guideline: Early chronic kidney disease: detection, prevention and management. *Nephrology (Carlton, Vic)*. May 2013;18(5):340-50. doi:10.1111/nep.12052
39. National Institute for Health and Care Excellence (NICE). Assessment and monitoring of chronic kidney disease. Updated 03 December 2020. Accessed 22 April 2021, http://pathways.nice.org.uk/pathways/chronic-kidney-disease
40. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. Feb 2002;39(2 Suppl 1):S1-266.
41. ASN emphasizes need for early detection of kidney disease, a silent killer. American Society of Nephrology; 2013. https://www.asn-online.org/news/2013/ASN_COMM_ACP_Screening_Response_102213_R12.pdf.
42. Garcia-Garcia G, Jha V, Li PKT, et al. Chronic kidney disease (CKD) in disadvantaged populations. Review. *Clinical kidney journal*. 2015;8(1):3-6. doi:10.1093/ckj/sfu124
43. Vassalotti JA, Li S, McCullough PA, Bakris GL. Kidney early evaluation program: a community-based screening approach to address disparities in chronic kidney disease. *Seminars in nephrology*. Jan 2010;30(1):66-73. doi:10.1016/j.semnephrol.2009.10.004
44. Obrador GT, García-García G, Villa AR, et al. Prevalence of chronic kidney disease in the Kidney Early Evaluation Program (KEEP) México and comparison with KEEP US. *Kidney Int*. 2010/03 2010;77:S2-S8. doi:10.1038/ki.2009.540

45. Liu Q, Li Z, Wang H, et al. High prevalence and associated risk factors for impaired renal function and urinary abnormalities in a rural adult population from southern China. *PLoS One*. 2012;7(10):e47100. doi:10.1371/journal.pone.0047100
46. Tummalapalli SL, Vittinghoff E, Crews DC, et al. Chronic Kidney Disease Awareness and Longitudinal Health Outcomes: Results from the REasons for Geographic And Racial Differences in Stroke Study. *Am J Nephrol*. 2020;51(6):463-472. doi:10.1159/000507774
47. Arksey H, O'Malley L. Scoping Studies: Towards a Methodological Framework. *International Journal of Social Research Methodology: Theory & Practice*. 2005;8(1):19-32. doi:10.1080/1364557032000119616
48. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implementation science : IS*. Sep 20 2010;5:69. doi:10.1186/1748-5908-5-69
49. Colquhoun HL, Levac D, O'Brien KK, et al. Scoping reviews: time for clarity in definition, methods, and reporting. *Journal of clinical epidemiology*. Dec 2014;67(12):1291-4. doi:10.1016/j.jclinepi.2014.03.013
50. Daudt HM, van Mossel C, Scott SJ. Enhancing the scoping study methodology: a large, inter-professional team's experience with Arksey and O'Malley's framework. *BMC medical research methodology*. Mar 23 2013;13:48. doi:10.1186/1471-2288-13-48
51. Peters MDJ, Marnie C, Tricco AC, et al. Updated methodological guidance for the conduct of scoping reviews. *JBI Evid Implement*. Mar 2021;19(1):3-10. doi:10.1097/xeb.0000000000000277
52. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals of internal medicine*. Oct 2 2018;169(7):467-473. doi:10.7326/m18-0850
53. Peters MDJ GC, McInerney P, Munn Z, Tricco AC, Khalil, H. Chapter 11: Scoping Reviews (2020 version) In: In: Aromataris E MZE, ed. *Joanna Briggs Institute Reviewer's Manual, JBI, 2020*. 2020.

FIGURE AND TABLE LEGENDS:

Figure 1: PRISMA-Flow chart for study selection

Table 1: Persisting questions on usefulness and methodology of CKD screening programs

Table 2: Medline search strategy

Table 3: Data extraction items from empirical literature sources

Table 1: Persisting questions on usefulness and methodology of CKD screening programs

Questions related to the usefulness of CKD screening	Questions related to the methodology of CKD screening
- Should CKD screening be used in an asymptomatic population with or without CKD risk factors such as hypertension or diabetes?	- Are single measurements sufficient for detecting CKD?
- Are there unique risk factors in some populations we do not know about?	- Does population screening with serum creatinine and urine protein testing lead to improved outcomes without undue harm?
- Should therapies be initiated in those with mildly impaired eGFR or microalbuminuria?	- Should screening be conducted in younger age groups without CKD risk factors?
- Does earlier treatment improve the prognosis?	- What threshold of dipsticks positive proteinuria should be considered relevant for screening?
- Are CKD screening programs cost-effective?	- Who should manage screening and subsequent treatment?
- Do the potential harms of CKD screening outweigh the benefits?	- What tests should be selected for CKD screening?
- What is the yield of the screening service?	- How valid and repeatable is the screening test?
- What are the implications of CKD screening for public health policy?	

Abbreviations: CKD – chronic kidney disease; eGFR – estimated glomerular filtration rate

Table 2: Medline search strategy

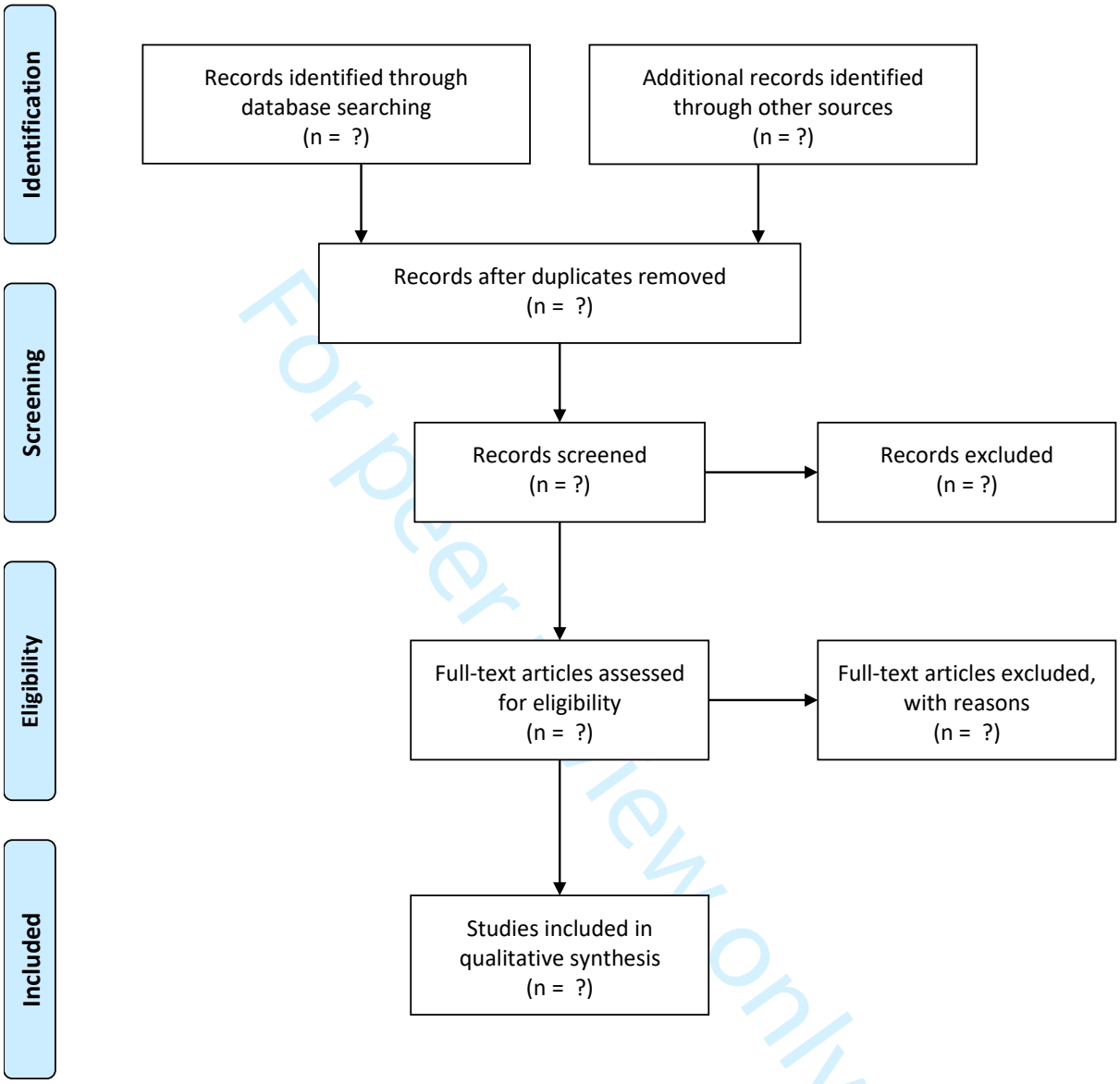
1. exp Renal Insufficiency, Chronic/
2. Chronic Kidney disease*.mp.
3. chronic kidney insufficienc*.mp.
4. chronic renal disease*.mp.
5. chronic renal insufficienc*.mp.
6. CKD.mp.
7. Renal fail*.mp.
8. Kidney fail*.mp.
9. or/1-8
10. Multiphasic Screening/ and (program* or campaign* or strateg* or initiative*).mp.
11. Mass Screening/
12. (screen* adj2 (program* or strateg* or campaign* or initiative*)).mp.
13. (awareness adj3 (program* or campaign* or strateg* or initiative*)).mp.
14. (detect* adj3 (program* or campaign* or strateg* or initiative*)).mp.
15. (National Health and Nutrition Examination Survey).mp.
16. Kidney Early Evaluation Program.mp.
17. (Prevention of Renal and Vascular End-Stage Disease).mp.
18. World Kidney Day.mp.
19. national kidney foundation.mp.
20. (Screening and Early Evaluation of Kidney disease).mp.
21. or/15-20
22. 21 and (screen* or detect* or awareness).mp.
23. or/10-14,22
24. 9 and 23
25. ((detect* or screen* or awareness) adj2 ("chronic kidney" or "chronic renal")).mp.
26. 24 or 25
27. exp animals/ not humans.sh.
28. 26 not 27

Table 3: Data extraction items from empirical literature sources

Population screened	Measurements	Interventions	Implementation
Country, income group	Number of measurements (1x / 2x)	Lifestyle measures*	Cost measures reported
Type of program (national / others)	Urine dipsticks (protein ± blood)	RAAS blockade	Reported to be cost-effective
Demographic features (Age, gender, ethnicity, rural / urban setting)	Urine ACR / PCR only	Antidiabetic medications (any)	Screening strategy adopted or not implemented due to lack of efficacy (e.g., policy document)
Workforce involved in screening	SCR / eGFR only	Anti-hypertensive medications (separate from RAAS)	
Screening type:	Urine + SCR / eGFR	Lipid treatment	
Mass screening (yes / no)	POCT	Avoidance of nephrotoxins	
Targeted screening (yes / no)	Other tests (e.g., cystatin C)	Referral to nephrology service	
• Hypertensives	Reported CKD prevalence (yes / no)	Referral for KRT	
• Diabetics			
• Elderly			
• Family history of CKD			
• HIV			
• Minority group (e.g., Indigenous populations)			
• Others			
Risk factors assessed and reported:			
• BP			
• Blood glucose			
• Body weight / BMI			
• Lipids			
• Others			
Risk stratification (yes / no)			

CKD – Chronic kidney disease, HIC – high-income country, UMIC – upper middle-income country, LMIC – lower middle-income country, LIC – low-income country, HIV – human immunodeficiency virus, ACR – albumin-creatinine ratio, PCR – protein creatinine ratio, SCR – serum creatinine, eGFR- estimated glomerular filtration rate, BP – blood pressure, BMI – body mass index, RAAS – renin-angiotensin aldosterone system, KRT – kidney replacement therapy (any of hemodialysis, peritoneal dialysis, kidney transplantation), POCT – point of care test (e.g. saliva), *(smoking cessation, weight reduction measures, dietary measures, etc.)

Figure 1: PRISMA-Flow chart for study selection



Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	#1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	#3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	#5 to #8
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	#9
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	NA
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	#11 to #12
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	#10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Table 2
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	#11
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	#12 to #13
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Table 3
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	#13

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	NA
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	NA
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	NA
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	NA
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	#14
Limitations	20	Discuss the limitations of the scoping review process.	#14
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	NA
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	#15

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.