PREVALENCE OF CHRONIC KIDNEY DISEASE IN THE GENERAL POPULATION IN LATIN AMERICA AND THE CARIBBEAN: A SYSTEMATIC REVIEW AND META-ANALYSIS

PREVALENCIA DE ENFERMEDAD RENAL CRÓNICA EN LA POBLACIÓN GENERAL EN LATINOAMÉRICA Y EL CARIBE: UNA REVISIÓN SISTEMÁTICA Y META-ANÁLISIS

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ABSTRACT

Background: Global projects have informed about the epidemiology of chronic kidney disease (CKD) in Latin America and the Caribbean (LAC), yet there are no regional efforts to contrast or advance these global endeavours. We aimed to summarize the CKD prevalence in LAC. **Methods:** Systematic review, random-effects meta-analysis and meta-regression. We searched Embase, Medline, Global Health, Scopus and LILACS (January 11th, 2021). We included observational studies which enrolled a random sample of the general population in LAC. The outcome was CKD prevalence, which should have been defined by eGFR and/or with a biomarker. **Results:** The search identified 5,050 publications and 15 reports (16 studies) were included. The prevalence of CKD defined with eGFR only, ranged between 1.7%-20.0%; the pooled prevalence was 7.0% (95% CI: 5.0%-10.0%; I2: 99%). This pooled prevalence was similar between national and non-national studies: 8.0% (95% CI: 4.0%-12.0%; I2: 99%) and 7.0% (95% CI: 3.0%-10.0%; I2: 99%). This pooled prevalence was similar between men and women: 10.0% (95% CI: 5.0%-14.0%; I2: 98%) and 8.0% (95% CI: 4.0%-13.0%; I2: 99%). The CKD prevalence defined with eGFR and/or other biomarkers, ranged between 12.0%-16.8%; the pooled prevalence was 13.0% (95% CI: 9.0%-17.0%; I2: 98%). In meta-regressions, the CKD prevalence was weakly correlated with the year of data collection. **Conclusions:** In LAC, the CKD prevalence is non-negligible and similar to that of other non-communicable diseases which has received more attention (e.g., diabetes). Research is needed to generate more epidemiological data on CKD throughout LAC.

Key words: Non-communicable diseases; cardio-metabolic risk factors; low- and middle-income countries.

RESUMEN

Antecedentes: Los proyectos globales han informado sobre la epidemiología de la enfermedad renal crónica (ERC) en América Latina y el Caribe (LAC), pero no existen esfuerzos regionales para contrastar o avanzar estas iniciativas globales. Nuestro objetivo fue resumir la prevalencia de la ERC en LAC. **Métodos**: Revisión sistemática, metanálisis de efectos aleatorios y meta-regresión. Se realizaron búsquedas en Embase, Medline, Global Health, Scopus y LILACS (11 de enero de 2021). Incluimos estudios observacionales que contaron con una muestra aleatoria de la población general en LAC. El resultado fue la prevalencia de la ERC, que debería haberse definido con un biomarcador. **Resultados**: La búsqueda identificó 5050 publicaciones y se incluyeron 15 reportes (16 estudios). La prevalencia de ERC definida solo con TFGe osciló entre 1,7% y 20,0%; la prevalencia agrupada fue del 7,0 % (IC del 95 %: 5,0 %-10,0 %; I2: 99 %). Esta prevalencia agrupada fue similar entre estudios nacionales y no nacionales: 8,0 % (IC 95 %: 4,0 %-12,0 %; I2: 99 %) y 7,0 % (IC 95 %: 3,0 %-10,0 %; I2: 99%). Esta prevalencia agrupada fue similar entre hombres y mujeres: 10,0 % (IC del 95 %: 5,0 %-14,0 %; I2: 98 %) y 8,0 % (IC del 95 %: 4,0 %-13,0 %; I2: 99%). La prevalencia de ERC definida con TFGe y/o otros biomarcadores osciló entre 12,0%-16,8%; la prevalencia agrupada fue del 13,0 % (IC del 95 %: 9,0 %-17,0 %; I2: 98 %). En las meta-regresiones, la prevalencia de ERC se correlacionó débilmente con el año de recolección de datos. **Conclusiones**: En LAC, la prevalencia de la ERC no es despreciable y es similar a la de otras enfermedades no transmisibles que han recibido mayor atención (p. ej., Diabetes). Se necesita con urgencia investigación para fortalecer la epidemiología de la ERC en LAC.

Palabras clave: Enfermedades no transmisibles; factores de riesgo cardiometabólicos; países de bajos y medianos ingresos.

I. INTRODUCTION

Chronic kidney disease (CKD) is a global health problem which disproportionately affects low- and middle-income countries like those in Latin America and the Caribbean (LAC), (1–3) where the CKD prevalence in 2019 appears to be slightly higher than the global prevalence (10.1% vs 9.3%), according to the Global Burden of Disease study. (4) In addition, metrics of mortality and disability as a consequence of CKD are higher in LAC in comparison to global estimates. (4) Although these figures alert about the high burden of CKD in LAC, they are mostly informed by data from high-income countries where risk factors levels and access to health-care may be different than in LAC. (5–10) This overrepresentation of non-LAC data challenges the validity of these metrics to inform clinical guidelines and public health policies in LAC. Whether population-based (national) studies in LAC agree with these international metrics, is largely unknown. (11)

The epidemiology of CKD in LAC needs to be comprehensively characterized to inform research priorities (e.g., where data are needed), to inform clinical guidelines with local epidemiological metrics (e.g., prevalences), and to provide recommendations for policies and interventions (e.g., to focus efforts on specific groups or places). However, to begin an exhaustive characterization of the CKD epidemiology in LAC, the prevalence and basic determinants such as age, sex and geographic variations, need to be well estimated. There have not been any large multi-country studies in LAC to provide this information, and individual efforts, either at the national and community levels, have not been

systematically gathered, appraised and meta-analysed to provide evidence for LAC. Consequently, we aimed to quantify and appraise the prevalence of CKD in LAC, through a systematic review and meta-analysis of population-based studies conducted in LAC.

II. METHODS

Study design

This is a systematic review and meta-analysis of summary data. This work adheres to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Supplementary Table 1). (12) The study protocol was planned beforehand and published online. (13)

Literature search

We used five search engines: through OVID, we searched Embase, Medline and Global Health; in addition, we used Scopus and LILACS. The search was conducted on January 11th, 2021. No date or language restrictions were set. The search strategy can be found in Supplementary Table 2, 3 and 4. We included one more publication which became available after the search date and another publication suggested by colleagues. (14,15)

Eligibility criteria

We designed our eligibility criteria following the CoCoPop (condition, context and population) acronym. The condition was CKD defined as the presence of kidney damage indicated by urine albumin-creatinine ratio, urine protein-creatinine ratio, albumin excretion ratio, complete urine examination, kidney images, kidney biopsy or any combination of these, or alteration of the glomerular filtration rate (GFR) estimated by using serum creatinine and/or serum cystatin C regardless of the formula used to compute the estimated glomerular filtration rate (eGFR). (2) Concerning the context, we included prevalence studies of CKD from countries in LAC. Finally in population, we

included men and women aged 18 years or above of the general population from countries in LAC. We sought original studies in which participants were selected following any kind of random sampling technique. Overall, we aimed to include original reports in which the study population resembled -as much as possible- the general population.

Regarding publication type, we included population-based epidemiological cross-sectional observational studies. We included national studies defined as population-based nationally representative health surveys; that is, health surveys which estimates were meant to be representative of the whole country and which included a representative sampling frame. We also included non-national and community studies; non-national were those not powered to be nationally representative (e.g., including only a few states) and community studies were those conducted in a limited area such a community or neighborhood. Conversely, we excluded the following study designs: case-control, case reports, editorials, commentaries, narrative and scoping reviews, clinical trials, grey literature (e.g., dissertations/thesis), and systematic reviews/meta-analyses. We excluded studies with LAC populations outside the LAC region (e.g., Latin Americans immigrants). We excluded studies which only sampled people under 18 years of age, studies in which the outcome was ascertained based on self-reported history of CKD only, studies in which only patients (e.g., people with diabetes) were studied, and studied in which participants were selected based on a risk factor history (e.g., consumers of nephrotoxic drugs only).

Data collection

The search results were downloaded and duplicates were deleted. Titles and abstracts were screened by two reviewers independently (pairwise combinations between DAS-B, CSV-A, and MW-C). Full-text reports of the selected publications were studied in detail by two reviewers independently (pairwise combinations between DAS-B, CSV-A, and MW-C). Discrepancies at any stage were solved by consensus or by a third party (RMC-L).

Data extraction

We developed a data extraction form in an Excel spreadsheet. We piloted this form with a random sample of ten selected publications. After this pilot phase, we updated the extraction form as needed; the extraction form was not modified thereafter. Data extraction was conducted by two researchers independently (pairwise combinations between DAS-B, CSV-A, MW-C); discrepancies were solved by consensus or by a third party (RMC-L). We extracted information about the study design (e.g., year and country of data collection), about the study population (e.g., male proportion, mean age, selection criteria), and about the outcome of interest (e.g., prevalence of CKD). When possible, the CKD prevalence estimates were extracted by sex. When multiple reports analyzed the same population, we included one report only. We selected the report with the largest sample size or the one providing most information.

CKD of unknown origin (CKDu) is a condition of growing interest; (16) however, we focused on traditional CKD because of its much broader impact and close relationship with cardio-metabolic risk factors. (17) When a

publication reported prevalence estimates for both traditional CKD and CKDu, we only extracted the information of traditional CKD. Similarly, if a report included children and adults, we only extracted data from the latter.

Risk of bias assessment

We used the risk of bias assessment tool by Hoy and colleagues for studies reporting prevalence estimates. (18) The items of this tool were implemented in an Excel spreadsheet and two reviewers independently completed the information for each selected report (DAS-B and CSV-A). Discrepancies were solved by consensus or a third party (RMC-L).

Statistical analysis

We used the information we extracted from each original report to narratively describe their main characteristics. Due to the diverse populations and countries with different underlying risk factors for CKD, laboratories methods and procedures, as well as data collection protocols followed by the included studies, we suspected a high level of heterogeneity. Therefore, this was managed by conducting a random-effects meta-analysis (rather than fixed-effects) to summarize the prevalence of CKD in LAC. We presented this pooled estimate stratified by CKD ascertainment method; that is, a pooled prevalence estimate for studies in which CKD was defined with eGFR only, and a pooled prevalence estimate for studies in which CKD was defined with eGFR and/or other biomarker(s). The pooled prevalence estimate from studies based on eGFR alone was presented overall and by sex.. The random-effects meta-

analysis for prevalence estimates was conducted with the *metaprop* command in Stata 16.1 (College Station, Texas 77845 USA).

Exploratorily, we conducted meta-regressions to study potential explanatory variables of the studied outcomes (i.e., CKD prevalence). We also did the meta-regression to identify potential drivers of heterogeneity in the prevalence estimates. First, we developed a meta-regression model in which the outcome was the CKD prevalence ascertained with eGFR only, and the explanatory variables were the formula used to compute the eGFR, if it was a national study or not, region in which the study was conducted (South America vs. Central America), year of data collection and mean age of the study population. Second, we developed a meta-regression model in which the outcome was the CKD prevalence regardless of the ascertainment method, and the explanatory variables were CKD ascertainment method, formula used to compute the eGFR, whether it was a national study, region in which the study was conducted (South America vs. Central America), year of data collection and mean age of the study population. These meta-regression models were conducted with the *metareg* command in Stata 16.1 (College Station, Texas 77845 USA).

In our original protocol we planned to study publication bias by inspection of funnel plots and with the Egger's test if there were at least ten publications. However, we did not have ten publications in each analysis sub-group (e.g., CKD ascertained with eGFR only). Consequently, and line with our protocol, (13) we did not study publication bias.

Ethics

No human subjects were directly involved in this study. This was a literature review of scientific publications which can be accessed online through repositories or libraries. This study was approved by the ethics committee of Universidad Peruana Cayetano Heredia

III. RESULTS

Study selection

The literature search identified 5,050 publications. We screened 4,780 titles and abstracts and of these, 116 reports were studied in detail. After the search date we included two more reports. (14,15) (Supplementary figure 1). Three reports provided estimates for CKDu along with traditional CKD; (14,19,20) we only extracted and herein reported the results for traditional CKD.

Finally, for the systematic review we included 15 original reports which provided information of 16 studies (i.e., one report analyzed two studies). (14,15,19–31) For CKD prevalence defined with eGFR only, we meta-analysed 9 reports (10 studies); (14,15,23–28,31) the sex-stratified results were informed by 6 reports. (14,15,25–28) For CKD prevalence defined with eGFR along with other biomarker(s), we meta-analysed 5 reports. (19–21,29,30)

Study characteristics

Of the 15 selected reports, 3 studied people from Nicaragua, (24–26) 2 from Peru, (14,29) El Salvador, (19,20) and Brazil, (23,28) 1 from Costa Rica, (27) Panama, (21) Suriname, (30) Haiti, (22) Guatemala (15) and Chile (31). All reports included both men and women); the largest proportion of men was 50.2%, (29) while the largest proportion of women 69.7%. (21) The mean age of participants ranged between 38.5 and 54.9 years, except for one study in which the mean age was 76 years. (27)

In 9 out of 15 reports, CKD was only defined with eGFR <60 mL/min/1.73m2 (14,15,23–28,31). In 2 out of 15 reports, CKD was defined with eGFR and/or

proteinuria. (21,29) The remaining 4 reports used different diagnosis criteria (Table 1). (19,20,22,30) Among the reports that computed the eGFR, 10 of these used the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, (14,15,20,21,23,24,27,29–31) 4 the Modification of Diet in Renal Disease (MDRD) equation (19,25,26,28) and 1 the Cockrolf-Gault equation. (22)

CKD prevalence in LAC

Overall, the prevalence of CKD ranged from 1.7% to 20%.(14,27) Similarly, the CKD prevalence in studies in which CKD was defined with eGFR only ranged from 1.7% to 20%.(14,27) Conversely, the CKD prevalence in studies in which CKD was defined using eGFR and/or biomarker(s) went from 5.4% to 18%. (19,30)

The overall pooled prevalence of CKD defined with eGFR only was 7% (10 point estimates; 95% CI: 5%-10%; I2: 99%; Figure 1); in a sensitivity analysis we excluded studies which only included elderly people (23,27) yet the pooled CKD prevalence estimate did not change substantially: 5% (8 point estimates; 95% CI: 3%-7%; I2: 98%).

The overall pooled prevalence of CKD defined with eGFR only in national studies (27,28,31) was slightly higher than in non-national studies: (14,15,22–26) 8% (4 point estimates; 95% CI: 4%-12%; I2: 99%; Figure 2) versus 7% (6 point estimates; 95% CI: 3%-10%; I2: 99%).

The pooled prevalence of CKD defined with eGFR only in men was 10% (6 point estimates; 95% CI: 5%-14%; I2: 98%; Supplementary Figure 2) and in

women 8% (6 point estimates; 95% CI: 4%-13%; I2: 99%; Supplementary Figure 3).

The overall pooled prevalence of CKD defined with eGFR along with other biomarker(s) was higher: 13% (5 point estimates; 95% CI: 9%-17%; I2: 98%; Figure 3).

Meta-regression

When the outcome was CKD defined with eGFR only, there appeared to be a negative yet marginal association with year of data collection (Table 2); this suggest that the CKD prevalence based on eGFR only has slightly decreased over the years. When CKD was defined based on eGFR and/or other biomarker(s), we also observed a negative though small association with year of data collection. Furthermore, a positive but small association was observed with the mean age of the study population (Table 2); this suggests that the CKD prevalence would marginally increase in older age groups.

Risk of bias of independent studies

All reports showed low risk of bias (Supplementary Table 5), particularly in the criteria about study population and ascertainment of the outcome because we only studied random samples from the general population and CKD was defined with biomarkers.

IV. DISCUSSION

Summary of evidence

Depending on how CKD was defined, the overall CKD prevalence in LAC ranged from 7% (eGFR alone) to 13% (eGFR along with other biomarkers). Apparently, additional biomarkers could capture cases missed with eGFR only, hence the prevalence increase. While international modelling studies have started to characterize the epidemiology of CDK in LAC, this is the first systematic and comprehensive approach to appraise and quantify the CKD prevalence in LAC based on evidence from this region alone. We provided a list of reports that can serve as inputs in future modelling studies; furthermore, we provided estimates of CKD prevalence in LAC based on recent local evidence which could inform clinical guidelines and public health policies and priorities in LAC.

Strengths and limitations

We conducted a solid literature search. Furthermore, we focused on random samples of the general population, as opposed to selected or biased populations; therefore, our results provide strong evidence at the general population level. However, there are limitations we need to acknowledge to better understand our findings and to identify research needs in LAC.

There are limitations about our systematic review and meta-analysis. First, we did not include grey literature which could have increased the number of retrieved reports and eventually the number of selected reports. Nonetheless, we strongly believe that population-based random samples of the general

population are sophisticated enough to have been published in a peer-reviewed journal versus grey literature. Therefore, we do not expect results from grey literature to have substantially changed our findings or conclusions. In addition, focusing on peer-reviewed publications is a common practice in systematic reviews. Second, as per our protocol, we did not have enough original publications to assess publication bias (e.g., Egger's test). More than publication bias, probably the reason to not have found more reports about CKD prevalence in LAC is because of limited resources to conduct population-based studies with biomarkers. As CKD gains more attention because it is both a consequence of cardio-metabolic risk factors and a risk factor for cardiovascular diseases, we hope to see more researchers working on population-based studies to disentangle the complexities of CKD in LAC. Our work will also spark this interest. In this line, national and international health organizations should include kidney function biomarkers (e.g., serum creatinine) in health surveys. Chile is a wonderful example, where they have serum creatinine in the national health surveys; also, some WHO STEPS surveys included serum creatinine.

There are also limitations in the original reports we studied. First, although most of these used only eGFR to ascertain CKD, there were others that complemented the diagnosis with other biomarkers (e.g., albuminuria). While we acknowledge the latter approach would provide more robust clinical evidence, this would also introduce complexities to large population-based studies. We argue that, to study and monitor CKD in the general population, serum creatinine and eGFR estimates could be enough. Nevertheless, we would

suggest that professional bodies or international health organizations reach a conclusion and recommendations on this matter so that future research can follow these suggestions. Second, only a handful of publications studied a national sample. This limits the scope of our work to inform all (or most) countries in LAC, and yet also calls to conduct more national health surveys with kidney function biomarkers. Researchers could also use other statistical methods to model eGFR levels and CKD prevalence throughout LAC. In any case, more and larger research is needed to characterize CKD epidemiology in LAC.

Results in the international context

Our meta-analysis showed a 7% CKD prevalence when the diagnosis was based on eGFR only. This prevalence is higher in comparison to studies conducted with a similar methodology in the African continent (4.6%), (32) and also higher than in other selected countries like 1% in Australia (33) and 3.8% in Germany. (34) Conversely, similar studies outside LAC reported higher prevalence estimates than our findings. A global analysis reported a CKD prevalence of 10.6%; (35) studies in other countries also found higher prevalence estimates: England (7.3%); (36) India (10.2%); Nepal (10.6%), Bangladesh (17.3%) and Pakistan (21.2%). (37)

These discrepancies could be explained by the increase in the prevalence trend in recent decades of underlying risk factors, such as raised blood pressure in these areas of the world, representing an increase in both men and women population of approximately 10%, whereas 6% are in LAC. (10)

Likewise, another proposal could be the increase in life expectancy in 8 years in South Asia in recent decades compared to the 3 years that increased in LAC, thus showing a higher proportion than in other regions of the world, taking into account that the older the age, the greater the risk of developing CKD. (38,39)

Our meta-analysis also showed a 13% CKD prevalence when the diagnosis was based on eGFR and/or other biomarker(s). Studies outside LAC following a similar methodology reached similar results; for example a global analysis reported a CKD prevalence of 13.4%.(35) Likewise, in England and the USA, they reported 14.2% and 13.6%, respectively. (36,40) Similarly, in the African continent they reported a 15.8%, (32) and in northeast Germany a 17.3%. (41) Overall, it seems that eGFR along with other biomarkers could capture more cases, hence the larger prevalence estimates than with eGFR alone. At the national level, where more biomarkers could introduce complexities for population-based large surveys, further research is needed to understand the gains of more sophisticated biomarkers for the population-based surveillance of CKD. In other words, would serum creatinine and eGFR be enough for the monitoring of CKD in LAC? We need a consensus and strategies. For example, serum creatinine could be enough in yearly national surveys, but more sophisticated biomarkers could be added every five year for more comprehensive surveillance. Professional and regional health organizations should provide guidance.

Additionally, the inclusion of race as a coefficient for equations estimating the GFR has recently become controversial due to this term being a social construct

rather than a biological category. However, a recent study regarding race, genetic ancestry, and estimating kidney function in CKD found that when eliminating the race coefficient, the eGFR was underestimated by a median of 3.99ml/min/1.73m2. Likewise, regardless of age, sex, or eGFR, black population is associated with serum creatinine levels 10.7% higher than non-Black population. Therefore, the removal of this factor can lead to a misclassification of eGFR.(42) However, this limitation was not encountered in our study because reports included made use of the formulas without the exclusion of the race coefficient.

Potential correlates

Even though these were not far apart, the CKD prevalence (eGFR only) was slightly higher in men than in women. This could potentially be explained by the increase in the prevalence of the most important risk factors for kidney damage such as elevated blood pressure and hypertension. These risk factors are usually higher in men than women. (17,43,44) Another potential explanation is the predisposition of men to lose renal function faster than women. (45) This is because the protective and deleterious effects on renal function of estrogens and testosterone, respectively. (46)

Our meta-analysis and the meta-regression did not alert of substantial differences between national and non-national studies regarding the CKD prevalence (eGFR only). While non-national studies would be “easier” to conduct, we encourage local and regional health authorities to work alongside researchers to include kidney function biomarkers in national surveys, even if

it is only possible in a random sub-sample. Alternatively, countries could choose large sentinel sites (e.g., capital cities or places with high risk factor levels) to conduct sub-national surveys with kidney biomarkers.

Public health relevance and research needs

Our work has summarized the most recent population-based evidence about CKD prevalence in LAC published in peer-reviewed scientific journals. We provided a unique list of studies and researchers working to strengthen the evidence about CKD in LAC. This could be used by regional health organizations to organize a panel of experts and decide on the most suitable methodologies to study CKD in LAC at the population level, as well as to set the research agenda for the next years. Ideally, and as it occurs with other diseases (e.g., NCD Global Monitoring Framework 25x25), they could also set targets (e.g., to reduce the CKD prevalence in X percentage points by 2040) and use our results as a baseline point.

The findings herein depicted suggested that the prevalence of CKD could range between 7% (eGFR ony) and 13% (eGFR plus other biomarkers). This range is not far apart from the prevalence of diabetes in LAC (9.7%), (47) for which much more research and capacity is available. Overall, our findings suggest that CKD is not a "rare" disease with a low frequency; all the opposite, our results urgently call to strengthen the opportunities for primary prevention and early diagnosis of CKD in LAC. This should not happen in isolation or separated from other non-communicable diseases, but following a holistic

approach in which all cardio-metabolic risk factors are targeted following the best evidence and resources available.

Even though we found a non-negligible number of original reports studying a random sample of the general population, few of these were national surveys. National estimates are needed to have a solid understanding of the epidemiology of CKD in LAC. Furthermore, researchers need to provide population-based evidence of CKD prevalence and its determinants in countries for which we failed to find any scientific literature. The Caribbean appears to be a region in which much more evidence is warranted. Regional organizations, for example the Panamerican Health Organization (PAHO), could suggest the inclusion of serum creatinine measurements in the STEPS surveys, some of which already collect glucose and lipid biomarkers. Research is also needed in modelling strategies to maximize the available information to produce estimates for more countries in LAC.

V. CONCLUSIONS

Depending on how CKD was defined, the prevalence in population-based studies in LAC ranged between 7% (eGFR only) and 13% (eGFR and other biomarkers), with no large differences between men and women and whether it was a national or non-national study. These estimates suggest that CKD is not a rare disease in LAC, with a prevalence comparable to that of other conditions (e.g., diabetes) that receive more attention from researchers and public health organizations. It is necessary to strengthen primary prevention of CKD and to implement population-based research to quantify the CKD burden in LAC.

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VII. TABLES AND FIGURES

Table 1. Characteristics of selected reports.

Author	Country of study	Women (%)	Men (%)	Mean age	Method to ascertain CKD diagnosis	Formula used for GFR
Lebov, J.(26)	Nicaragua	1324 (58.20%)	951 (41.80%)		eGFR<60 ml/min/1.73 m2	MDRD equation
Harhay, M.(27)	Costa Rica	1461 (55%)	1196 (45%)	76	eGFR<60 ml/min/1.73 m2	CKD-EPI

Malta, D.(28)	Brazil	4343 (58.2%)	3114 (41.8%)		eGFR<60 ml/min/1.73 m2	MDRD equation
Francis, E.(29)	Peru	201 (49.80%)	203 (50.20%)	54.9	eGFR<60 ml/min/1.73 m2 and/or proteinuria (protein-creatinine ratio) ≥150 mg/g creatinine	CKD-EPI
Nannan Panday, R.(30)	Suriname	700 (62.7%)	417 (37.3%)	42.2	eGFR < 60 mL/min/1.73 m2 or proteinuria stage A2/A3 (strip).	CKD-EPI

Walbaum, M. (31)	Chile				eGFR <60 mL/min/1.73 m2	CKD-EPI
Moreno Velásquez, I. (21)	Panama	2469 (69.7%)	1074 (30.3%)		eGFR of <60 ml/min/1.73 m2 and/or albuminuria ≥30 mg/g creatinine	CKD-EPI
DeGennaro Jr, V.(22)	Haiti			40.8	eGFR<60 ml/min	Cockroft-Gault
Orantes Navarro,	El Salvador	1412 (59.1%)	976 (40.9%)		GFR < 60	MDRD equation

C(19).					mL/min/1.73 m2 or persistence of renal damage markers for > 3 months	
Orantes-Navarro, C.(20)	El Salvador	3111 (56.8%)	1706 (43.2%)	44.9	eGFR of <60 ml/min/1.73 m2 or eGFR ≥60 mL/min/1.73m2 and ACR (A2/A3)	CKD-EPI
Amaral, T.(23)	Brazil	577 (58.7%)	406 (41.3%)		eGFR of <60 ml/min/1.73 m2	CKD-EPI
Ferguson, R.(24)	Nicaragua			40.4	eGFR of <60	CKD-EPI

					ml/min/1.73 m2	
O'Donnell, J.(25)	Nicaragua	473 (61%)	298 (39%)	38.5	eGFR <60 mL/min/1.73 m2	MDRD equation
Ruiz Alejos, A.(14)	Peru	836 (55.2%)	678 (44.8%)	45.1	eGFR<60 ml/min/1.73 m2	CKD-EPI
Miller A.(15)	Guatemala	527 (65.3%)	280 (34.7%)	39.5	eGFR<60 ml/min/1.73 m2	CKD-EPI

Table 2. Meta-regression analyses of selected outcomes and meta-characteristics of the included reports.

	Outcome: CKD as eGFR only	Outcome CKD any definition
eGFR formula*	**N=10**	**N=15**
CKD-EPI	1	1
MDRD	0.025 (-0.081; 0.131)	0.029 (-0.053; 0.111)
National study	**N=10**	**N=16**

No	1	1
Yes	0.013 (-0.088; 0.113)	0.002 (-0.069; 0.074)
Region	**N=10**	**N=16**
South America	1	1
Central America/Caribbean	0.034 (-0.061; 0.129)	0.041 (-0.025; 0.106)
Mean age of the study population	**N=5**	**N=9**
Mean age	0.004 (-0.002; 0.010)	**0.004 (0.000; 0.008)**

Year of data collection	**N=10**	**N=16**
Year	**-0.011 (-0.019; -0.003)**	**-0.011 (-0.018; -0.003)**
CKD ascertainment method*		**N=15**
eGFR		1
eGFR and/or other biomarker(s)		0.056 (-0.014; 0.128)

(*) estimated Glomerular Filtration Rate

Figure 1. Forest plot summarizing the prevalence of CKD based on eGFR only.

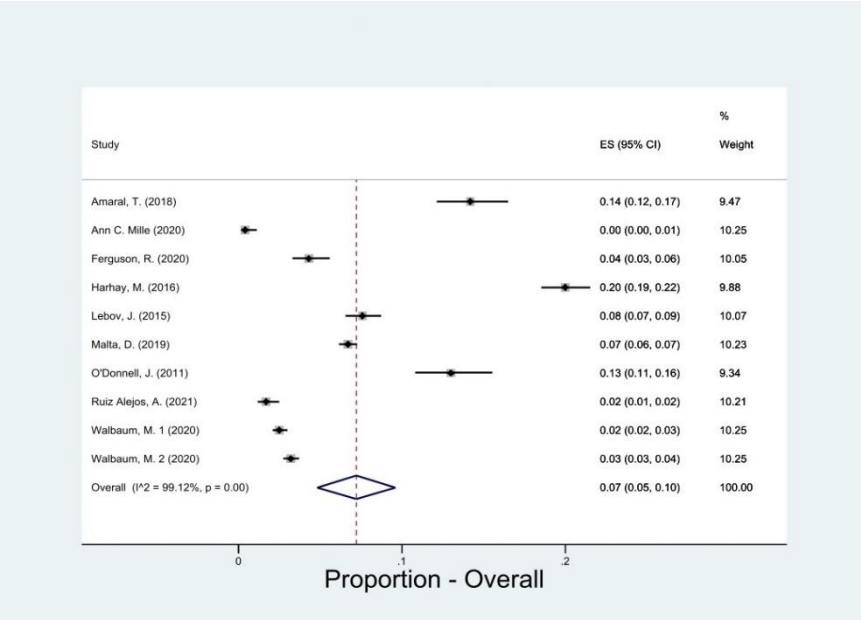
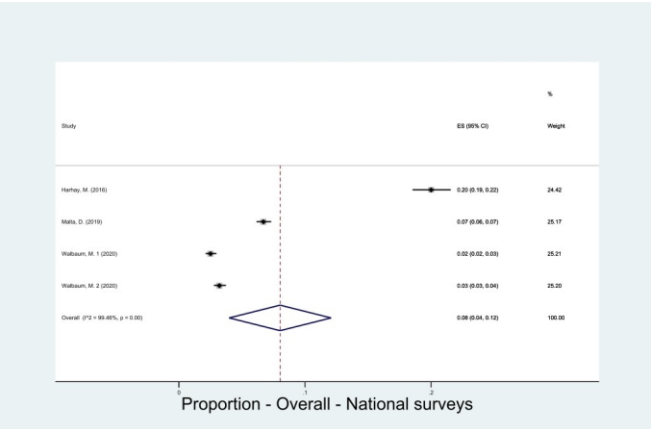


Figure 2. Forest plot summarizing the prevalence of CKD based on eGFR only in (A) national and (B) non-national studies.



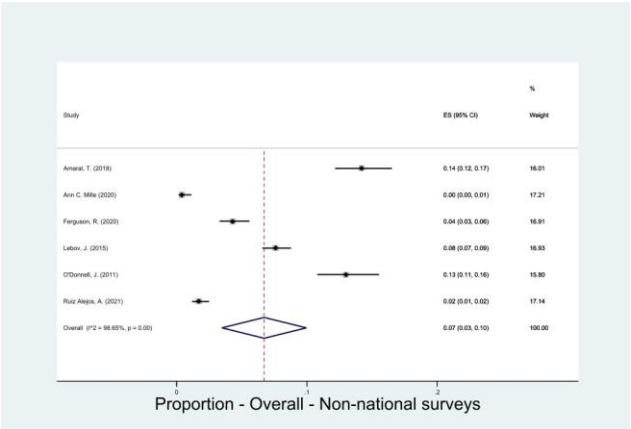
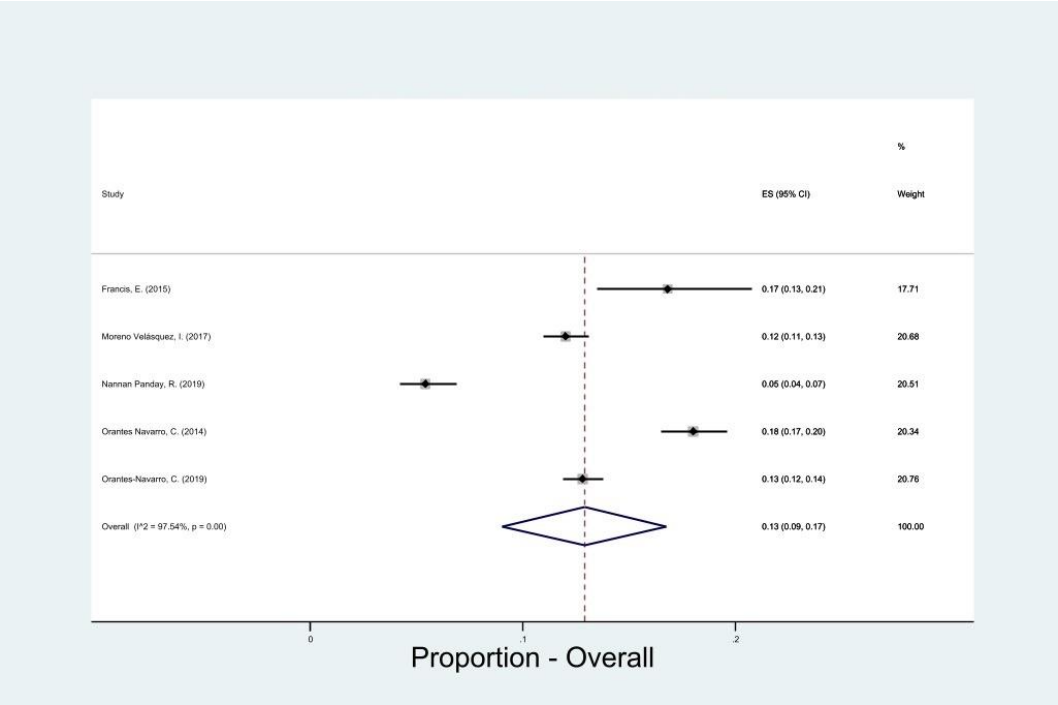


Figure 3. Forest plot summarizing the prevalence of CKD based on eGFR along with other biomarker(s).



VIII. SUPPLEMENTARY MATERIAL

Supplementary table 1. PRISMA 2009 checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	i
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	v, vi
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	1
METHODS			

Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	ST* 2,3,4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2, 3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3, 4

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	NA**
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5, ST* 5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5,6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5, 6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA**
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5, 6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons	7, SF[&] 1

		for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7, 8, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA*
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8, 9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8, 9; Figure 1, 2; SF[&] 2,3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9. 10; Table 2
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their	10

		relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	NA**

* Supplementary Table

** Not Applicable

$ Supplementary Figure

Supplementary Table 2. Search strategy through OVID

#	Searches
1	exp animals/ not humans.sh.
2	chronic renal insufficiency.mp.
3	chronic kidney disease.mp.
4	chronic kidney failure.mp.
5	CKD.mp.
6	exp Renal Insufficiency, Chronic/
7	(chronic adj2 kidney adj2 disease).mp.
8	(chronic adj2 kidney adj2 failure).mp.
9	chronic renal failure.mp
10	chronic renal disease.mp.
11	chronic kidney insufficiency.mp.
12	end stage renal disease.mp.
13	ESRD.mp.

14	kidney function.mp.
15	renal function.mp.
16	kidney dysfunction.mp.
17	renal dysfunction.mp.
18	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
19	("Antigua and Barbuda" or "Argentina" or "Bahamas" or "Barbados" or "Belize" or "Bolivia" or "Brazil" or "United States Virgin Islands" or "British Virgin Islands" or "Chile" or "Colombia" or "Costa Rica" or "Cuba" or "Dominica" or "Dominican Republic" or "Ecuador" or "El Salvador" or "Grenada" or "Guatemala" or "Guyana" or "Haiti" or "Honduras" or "Jamaica" or "Mexico" or "Nicaragua" or "Panama" or "Paraguay" or "Peru" or "Puerto Rico" or "Saint Kitts and Nevis" or "Saint Lucia" or "Saint Vincent and the Grenadines" or "Suriname" or "Trinidad and Tobago" or "West Indies" or "Uruguay" or "Venezuela" or "Latin America" or latin amer$ or "South America" or south amer$ or "Central America" or central amer$ or "Caribbean Region").mp.
20	18 and 19
21	20 not 1
22	remove duplicates from 21

Supplementary table 3: Search strategy through Scopus

(TITLE-ABS-KEY("Antigua and Barbuda") OR TITLE-ABS-KEY("Argentina") OR TITLE-ABS- KEY("Aruba") OR TITLE-ABS-KEY("Bahamas") OR TITLE-ABS-KEY("Barbados") OR TITLE- ABS-KEY("Belize") OR TITLE-ABS-KEY("Bolivia") OR TITLE-ABS-KEY("Brazil") OR TITLE-

ABS-KEY("United States Virgin Islands") OR TITLE-ABS-KEY("British Virgin Islands") OR TITLE- ABS-KEY("Cayman Islands") OR TITLE-ABS-KEY("Chile") OR TITLE-ABS-KEY("Colombia") OR TITLE-ABS-KEY("Costa Rica") OR TITLE-ABS-KEY("Cuba") OR TITLE-ABS-KEY("Curacao") OR TITLE-ABS-KEY("Dominica") OR TITLE-ABS-KEY("Dominican Republic") OR TITLE-ABS- KEY("Ecuador") OR TITLE-ABS-KEY("El Salvador") OR TITLE-ABS-KEY("Grenada") OR TITLE- ABS-KEY("Guatemala") OR TITLE-ABS-KEY("Guyana") OR TITLE-ABS-KEY("Haiti") OR TITLE- ABS-KEY("Honduras") OR TITLE-ABS-KEY("Jamaica") OR TITLE-ABS-KEY("Mexico") OR TITLE-ABS-KEY("Nicaragua") OR TITLE-ABS-KEY("Panama") OR TITLE-ABS- KEY("Paraguay") OR TITLE-ABS-KEY("Peru") OR TITLE-ABS-KEY("Puerto Rico") OR TITLE-

ABS-KEY("Saint Kitts and Nevis") OR TITLE-ABS-KEY("Saint Lucia") OR TITLE-ABS- KEY("Saint Vincent and the Grenadines") OR TITLE-ABS-KEY("Suriname") OR TITLE-ABS- KEY("Trinidad and Tobago") OR TITLE-ABS-KEY("Turks and Caicos Island") OR TITLE-ABS- KEY("Uruguay") OR TITLE-ABS-KEY("Venezuela") OR TITLE-ABS-KEY("Latin America") OR TITLE-ABS-KEY(latin amer*) OR TITLE-ABS-KEY("South America") OR TITLE-ABS-KEY(south amer*) OR TITLE-ABS-KEY("Central America") OR TITLE-ABS-KEY(central amer*) OR TITLE- ABS-KEY("Caribbean Region")) AND (TITLE-ABS-KEY(chronic renal insufficiency) OR

TITLE- ABS-KEY(chronic kidney disease) OR TITLE-ABS-KEY(chronic kidney failure) OR TITLE-ABS- KEY(CKD) OR TITLE-ABS-KEY(chronic renal failure) OR TITLE-ABS-KEY(chronic renal disease) OR TITLE-ABS-KEY(chronic kidney insufficiency) OR TITLE-ABS-KEY(end stage renal disease) OR TITLE-ABS-KEY(ESRD) OR TITLE-ABS-KEY(kidney function) OR TITLE-ABS-

KEY(renal function) OR TITLE-ABS-KEY(kidney dysfunction) OR TITLE-ABS-KEY(renal dysfunction) OR TITLE-ABS-KEY(chronic W/2 kidney W/2 disease) OR TITLE-ABS-KEY(chronic W/2 kidney W/2 failure)) AND NOT DBCOLL(medl)

Supplementary table 4. Search strategy through LILACS

((insuficiencia renal crónica) OR (enfermedad renal crónica) OR (falla renal crónica) OR (ERC) OR (enfermedad renal crónica en estadío terminal) OR (función renal) OR (disfunción renal)) AND(("Antigua y Barbuda") or ("Argentina") or ("Aruba") or ("Bahamas") or ("Barbados") or ("Belice") or ("Bolivia") or ("Brasil") or ("Islas Vírgenes de los Estados Unidos") or ("Islas Vírgenes Británicas") or ("Islas Caimán") or ("Chile") or ("Colombia") or ("Costa Rica") or ("Cuba") or ("Curazao") or ("Dominica") or ("Republica Dominicana") or ("Ecuador") or ("El Salvador") or ("Granada") or ("Guatemala") or ("Guyana") or ("Haití") or ("Honduras") or ("Jamaica") or

("México") or ("Nicaragua") or ("Panamá") or ("Paraguay") or ("Perú") or ("Puerto Rico") or ("San Cristóbal y Nieves") or ("Santa Lucía") or ("San Vicente y las Granadinas") or ("Surinam") or ("Trinidad y Tobago") or ("Turcas y Caicos") or ("Uruguay") or ("Venezuela") or ("América Latina") or ("Latinoamérica") or ("América del Sur") or ("Sudamérica") or ("Suramérica") or ("América Central") or ("Centroamérica") or ("América del Centro") or ("Caribe"))

Supplementary table 5. Risk of bias

		EXTERNAL VALIDITY				INTERNAL VALIDITY						
Title	**Author**	1. Was the study's target population a close representation of the national population in relation to relevant variables?	2. Was the sampling frame a true or close representation of thetarget population?	3. Was some form of random selection used to select the sample, OR was a census undertaken?	4. Was the likelihood of nonresponse bias minimal?	5. Were data collected directly from the subjects (as opposed to a proxy)?	6. Was an acceptable case definition used in the study?	7. Was the study instrument that measured the parameter of interest shown to have validity and reliability?	8. Was the same mode of data collection used for all subjects?	9. Was the length of the shortest prevalence period for the parameter of interest appropriate?	10. Were the numerator(s) and denominator(s) for the parameter of interest appropriate?	**11. Summary item on the overall risk of study bias**
A population-based study of prevalence and risk factors of chronic kidney disease in León, Nicaragua	Lebov, J.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

Altitude and regional gradients in chronic kidney disease prevalence in Costa Rica: Data from the Costa Rican Longevity and Healthy Aging Study	Harhay, M.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Evaluation of renal function in the Brazilian A8adult population, according to laboratory criteria from the National Health Survey	Malta, D.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Burden of chronic kidney disease in resource-limited settings from Peru: a population-based study	Francis, E.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

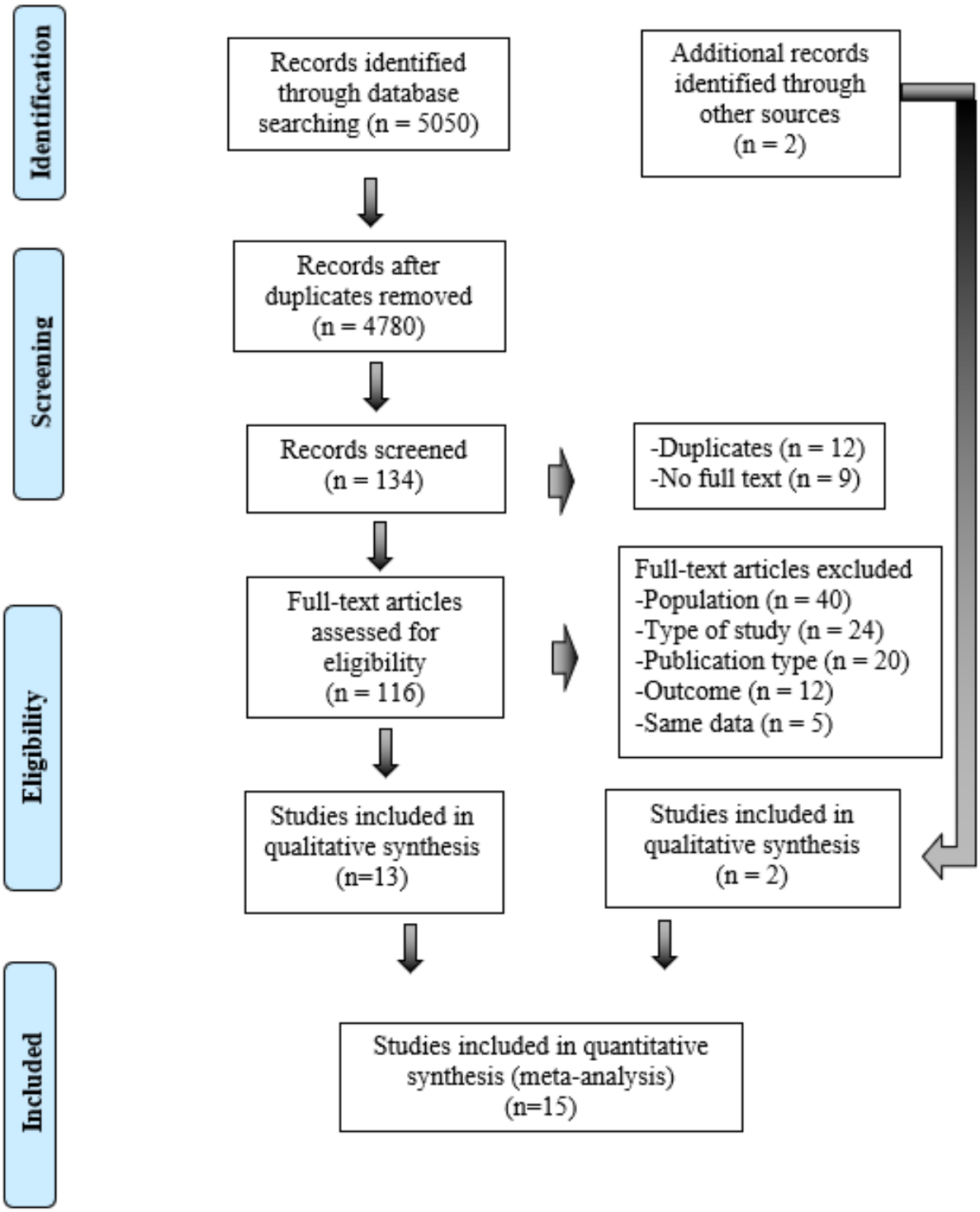
Chronic kidney disease and kidney health care status: the healthy life in Suriname (HeliSur) study	Nannan Panday, R.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Chronic kidney disease in adults aged 18 years and older in Chile: findings from the cross-sectional Chilean National Health Surveys 2009–2010 and 2016–2017	Walbaum, M.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Chronic Kidney Disease in Panama: Results From the PREFREC Study andNational Mortality Trends	Moreno Velásquez, I.	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

Community-based diagnosis of non-communicable diseases and their risk factors in rural and urban Haiti: a cross-sectional prevalence study	DeGennaro Jr, V.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Epidemiology of Chronic Kidney Disease in Adults ofSalvadoran Agricultural Communities	Orantes Navarro, C.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Factors associated with chronic kidney disease, according to laboratory criteria of the National Health Survey	Aguiar, L.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

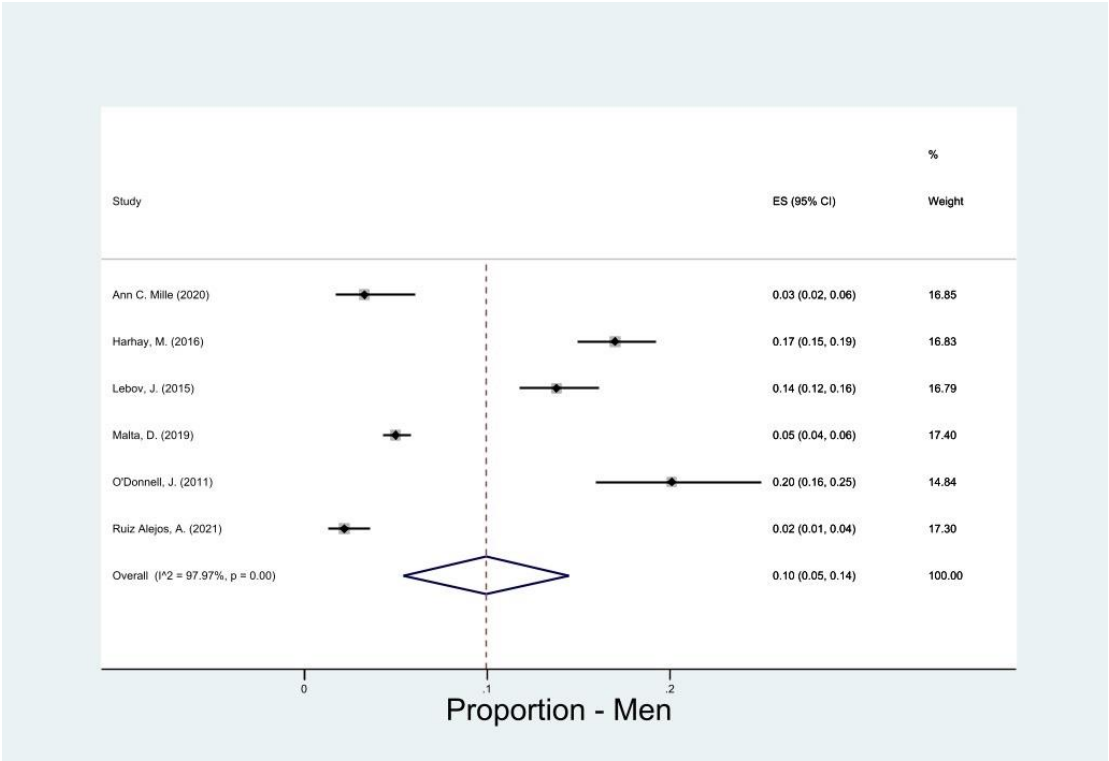
The Chronic Kidney Disease Epidemic in El Salvador: A Cross-Sectional Study	Orantes-Navarro, C.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Prevalence and factors associated to chronic kidney disease in older adults	Amaral, T.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Prevalence and Risk Factors for CKD in the General Population of Southwestern Nicaragua	Ferguson, R.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

Prevalence of and risk factors for chronic kidney disease in rural Nicaragua	O'Donnell, J.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
CKD and CKDu in northern Peru: a crosssectional analysis under the DEGREE protocol	Ruiz Alejos, A.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk
Population Estimates of GFR and Risk Factors for CKD in Guatemala	Ann C. Mille	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low risk

Supplementary figure 1. PRISMA Flowchart



Supplementary figure 2. Prevalence of CKD defined with eGFR only in men



Supplementary figure 3. Prevalence of CKD defined with eGFR only in wome