The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis

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Summary

Background Amid rapid urbanisation, the HIV epidemic, and increasing rates of non-communicable diseases, people in sub-Saharan Africa are especially vulnerable to kidney disease. Little is known about the epidemiology of chronic kidney disease (CKD) in sub-Saharan Africa, so we did a systematic review and meta-analysis examining the epidemiology of the disease.

Methods We searched Medline, Embase, and WHO Global Health Library databases for all articles published through March 29, 2012, and searched the reference lists of retrieved articles. We independently reviewed each study for quality. We used the inverse-variance random-effects method for meta-analyses of the medium-quality and high-quality data and explored heterogeneity by comparing CKD burdens across countries, settings (urban or rural), comorbid disorders (hypertension, diabetes, HIV), CKD definitions, and time.

Findings Overall, we included 90 studies from 96 sites in the review. Study quality was low, with only 18 (20%) medium-quality studies and three (3%) high-quality studies. We noted moderate heterogeneity between the medium-quality and high-quality studies (n=21; I²=47·11%, p<0·0009). Measurement of urine protein was the most common method of determining the presence of kidney disease (62 [69%] studies), but the Cockcroft-Gault formula (22 [24%] studies) and Modification of Diet in Renal Disease formula (17 [19%] studies) were also used. Most of the studies were done in urban settings (83 [93%] studies) and after the year 2000 (57 [63%] studies), and we detected no significant difference in the prevalence of CKD between urban (12·4%, 95% CI 11–14) and rural (16·5%, 13·8–19·6) settings (p=0·474). The overall prevalence of CKD from the 21 medium-quality and high-quality studies was 13·9% (95% CI 12·2–15·7).

Interpretation In sub-Saharan Africa, CKD is a substantial health burden with risk factors that include communicable and non-communicable diseases. However, poor data quality limits inferences and draws attention to the need for more information and validated measures of kidney function especially in the context of the growing burden of non-communicable diseases.

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Introduction

Amid population ageing, lifestyle changes, and rapid urbanisation, the importance of non-communicable diseases in low-income and middle-income countries is becoming increasingly recognised, and in 2011 the United Nations General Assembly adopted a resolution acknowledging the impending global burden and threat of non-communicable diseases. However, few epidemiological studies of the incidence, prevalence, and cause of these diseases have been done. Chronic kidney disease (CKD), which nearly doubled as a cause of death worldwide between 1990 and 2010 and was the 18th highest cause of death worldwide in 2010, falls into this category of diseases.

Sub-Saharan Africa is a vast and heterogeneous region of roughly 24 million km² composed of 47 countries and more than 900 million people. By 2030, more than 70% of patients with end-stage renal disease are estimated to be living in low-income countries, such as those in sub-Saharan Africa, where the gross domestic product per person is on average less than US$1500 per year. This estimation is alarming in view of the fact that the global prevalence of maintenance dialysis has doubled since 1990, and that renal replacement therapy was accessed by 1·8 million people worldwide in 2004 with less than 5% of that population coming from sub-Saharan Africa. There are many potential causes of CKD in sub-Saharan Africa, making kidney disease especially burdensome in the region. In addition to non-communicable diseases, communicable diseases such as infectious glomerulonephritis, schistosomiasis, leishmaniasis, and HIV infection are common and can cause CKD. And because more than 22 million people in sub-Saharan Africa have HIV, the potential for an overwhelming burden of CKD in the region is high. As has been noted elsewhere, the challenging first step to address the burden of kidney disease in Africa is to establish the epidemiology of CKD. We hypothesised that CKD is an important disease in sub-Saharan Africa with
many potential causes. To assess the extent to which it is a public health and economic burden, we did a systematic review and meta-analysis to find out the prevalence of CKD in adults in the region.

**Methods**

**Search strategy and selection criteria**

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.17 We searched PubMed, Embase, and the WHO Global Health Library databases (which include the African [AFRO] Index Medicus, WHO Library Information System [WHOLIS], and Scientific Electronic Library Online [SciELO]) for published reports of kidney disease in sub-Saharan Africa up to March 29, 2012. We used Boolean logic with search terms including “chronic kidney disease”, “nephropathy”, “renal insufficiency”, and “Africa south of Sahara”. We used controlled vocabularies (eg, Medical Subject Heading terms) to identify synonyms. We applied no language restrictions. The study protocol and detailed search parameters are available in the appendix.

Two authors (JWS and RM) independently reviewed each title and abstract for inclusion. Randomised controlled trials and non-randomised studies including cross-sectional studies, cohort studies (retrospective and prospective), case-control studies, and literature reviews that report a prevalence or a calculable prevalence for CKD in adults from a sub-Saharan African country were eligible for inclusion. We excluded studies that were only composed of pregnant women or people admitted to hospital, or ones that specifically recruited participants on the basis of the presence or absence of kidney disease. We regarded the following terms as equivalent to chronic kidney disease: “renal insufficiency”, “chronic kidney failure”, “renal impairment”, “end/target-organ damage” (if renal function was recorded in some capacity), “end-stage kidney/renal disease”, “nephropathy”, “proteinuria”, “diabetes-dependent”, “status-post renal transplant”, “sonographic-evidence”, and “biopsy-proven renal disease”.

Two investigators (JWS and ST) did a second review assessing entire papers and their reference lists. Any disagreement resulted in joint review of the article with reconciliation. Articles in French were translated by one author (NH) and then independently reviewed by two authors (JWS and ST or JWS and RM) for inclusion and extraction (only one article was not in French or English, and it was excluded on the basis of title and abstract alone). Detailed inclusion and exclusion criteria are available in the appendix.

**Quality assessment and data extraction**

Three authors (JWS, ST, and RM) independently appraised each article for quality using previously described assessment criteria (panel).8-13 On the basis of these criteria, each article received a quality grade of low, medium, or high, and any disagreement resulted in joint review of the article.

Data were extracted from all included studies by two authors independently (JWS and ST) and in duplicate into a preformatted table; errors of data extraction were resolved by joint review of the original articles. In addition to the overall prevalence reported by each study, we extracted or calculated, as necessary, the prevalence of CKD as defined by proteinuria, a creatinine clearance of less than 60 mL per min by the Cockcroft-Gault formula,
or an estimated glomerular filtration rate (GFR) of less than 60 mL per min per 1·73 m² by the Modification of Diet in Renal Disease (MDRD) and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulae. Although prevalence was the primary summary measure of interest, we also extracted the following information from each study: authors, location, setting, study population, dates, comorbidities, sample size, methods of measurement for kidney disease, mean age, and sex. If studies did not specify the exact years of study, we used the year of publication. We extracted or calculated these specific data only when we were able to confidently establish that patients were not overlapping or being counted twice. In cases of uncertainty or missing data, we contacted the corresponding authors for additional information.

**Statistical analysis**

We investigated heterogeneity using an $R$ statistic and completed meta-analyses with the inverse-variance random-effects method, as described by DerSimonian and Laird.24 Each study prevalence estimate received a weight that was equal to the reciprocal of within-study variance ($\nu$) summed with between-study variance ($\tau^2$). The calculated tau-squared ($\tau^2$) or between-study variance for our analysis was 0·010766. Only medium-quality and high-quality studies were included in the meta-analyses. We then calculated pooled prevalence as a weighted mean among all the study estimates. We examined prevalence by region, country, method of kidney disease measurement, setting (urban or rural), date, and disease-specific populations (HIV, hypertension, and diabetes type 1 and 2).

We assessed inter-rater agreement for inclusion using Cohen’s kappa (κ) coefficient, and assessed inter-rater agreement for quality assessment using Fleiss’s κ statistic. We calculated 95% CIs using Wilson’s score method. This method for determination of two-sided CIs was equal to the reciprocal of within-study variance ($\nu$) summed with between-study variance ($\tau^2$). The calculated $\tau^2$ statistic. We calculated 95% CIs using Wilson’s score method. This method for determination of two-sided CIs was equal to the reciprocal of within-study variance ($\nu$) summed with between-study variance ($\tau^2$). The calculated $\tau^2$ statistic. We calculated 95% CIs using Wilson’s score method. This method for determination of two-sided CIs was equal to the reciprocal of within-study variance ($\nu$) summed with between-study variance ($\tau^2$). The calculated $\tau^2$

The 90 articles, done between 1962 and 2011, reported data for 21 countries with a geographical distribution covering most of sub-Saharan Africa. However, more than half the studies (48 [53%] studies) were from South Africa, Nigeria, and Ethiopia. Data for 64 307 people (42% men) were included, with a mean age of 41·4 years (SD 9·9). 46 494 (72%) people had diabetes, 37 169 (58%) had HIV, 7845 (12%) had hypertension, and 2765 (4%) were obese (body-mass index [BMI]>30 kg/m²).

18 (20%) studies27–44 from 25 sites met criteria for the medium level of quality, and three (3%) studies45–47 met criteria for the high level of quality. Inter-rater agreement for quality assessment was excellent (κ=0·916). The common reasons for studies not meeting the criteria were the sampling methods used, most commonly convenience sampling, and unreliable measurements of kidney function. Most studies (72 [80%] studies) examined populations thought to be high risk—for example, people with HIV, diabetes, hypertension, or other risk factors for kidney disease. The studies assessed kidney function by urine protein (62 [69%] studies), estimation of creatinine clearance by Cockcroft-Gault formula (22 [24%] studies), and estimation of GFR by MDRD formula (17 [19%] studies). Less often, biopsy (two [2%] studies) and calculation of GFR by CKD-EPI formula (two [2%] studies) were also used. Other measurements of kidney function included simple chart review, absolute creatinine value, and estimation of GFR by MDRD formula (17 [19%] studies). Less often, biopsy (two [2%] studies) and calculation of GFR by CKD-EPI formula (two [2%] studies) were also used. Other measurements of kidney function included simple chart review, absolute creatinine value,

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

**Results**

We identified 905 articles, of which 90 were included in the systematic review (figure 1; appendix). Inter-rater agreement for inclusion was excellent (κ=0·974), and any disagreement resulted in inclusion for full text review.
The overall prevalence of CKD from the 21 medium-quality and high-quality studies was 13.9% (95% CI 12.2–15.7; figure 2). Estimates ranged from 2% in Côte d’Ivoire to 30% in Zimbabwe. Nearly half (n=6) of the countries represented had prevalence estimates ranging between 4% and 16%, and all countries but one (Zimbabwe) had prevalence estimates of less than 20% (figure 2). In the case of Zimbabwe, the estimate is derived from only one study that included many people with HIV who had not received antiretroviral treatment, which probably explains the unusually high prevalence.45,46 The only other study to have measured a prevalence of CKD in Zimbabwe was a convenience sample of people with HIV who had not received antiretroviral treatment, and it showed that the prevalence of CKD when defined as a GFR of less than 60 mL per min per 1.73 m² by the MDRD formula was 7.8% (95% CI 7.6–8.1%).47 The one high-quality study from Ghana was done in a rural population in 2010 and reports a CKD prevalence of 30% when defined as a GFR of less than 90 mL per min per 1.73 m² by the MDRD formula but only 1.6% when defined as a GFR of less than 60 mL per min per 1.73 m².48

The method of measuring kidney disease also affected the prevalence estimates across countries (table). Measurement of urine protein was the most common method of determining the presence of kidney disease (69%). Among medium-quality and high-quality studies, the prevalence of proteinuria ranged between 6% in Sudan to 24% in Zambia. The estimate from Cameroon is derived by pooling two arms (one urban and one rural) from one case-control study that was designed to compare the prevalence of nephropathy in an onchocerciasis-endemic area, and the estimate from Ghana is derived from only one medium-quality study done in an urban population that was specifically designed to measure end-organ damage such as proteinuria in people with hypertension.49,50 The one high-quality study from Ghana did not measure proteinuria.47

Among the studies reporting both Cockcroft-Gault and MDRD formulae (n=10), estimates derived from the Cockcroft-Gault formula were higher in every study, although not significantly so (p=0.080), with the difference less apparent for people with a creatinine clearance and GFR between 60 and 90 (p=0.170). Only two studies, one medium-quality study from Rwanda and one high-quality study from Ghana, reported estimated GFR by the CKD-EPI formula, and they reported estimates that were similar to those reported by the MDRD formula (p=0.900 for difference) at a GFR of less than 60 mL per min per 1.73 m² and GFR 60–90 mL per min per 1.73 m².51,52 We could not further characterise the extent to which people with an estimated GFR of less than 60 mL per min per 1.73 m² had concurrent proteinuria.

The table shows the results for each country stratified by comorbidity. Among people with HIV, the prevalence of CKD was highest in Nigeria, Zimbabwe, and Uganda (table 1). The remaining countries of Cameroon, Côte d’Ivoire, Kenya, Mozambique, Rwanda, South Africa, and Zambia had prevalence estimates of 1–10%. The difference between these two sets of countries might be related to the treatment status of the HIV participants. Only 16% of the participants in the studies from Nigeria, Zimbabwe, and Uganda were receiving care for their HIV, whereas all participants from the remaining countries were receiving some form of care for HIV.

In people with diabetes or hypertension in DRC, Ghana, Nigeria, Rwanda, South Africa, Sudan, and Zimbabwe, the method of determining kidney disease also affected the prevalence estimates across countries (table). Measurement of urine protein was the most common method of determining the presence of kidney disease (69%). Among medium-quality and high-quality studies, the prevalence of proteinuria ranged between 6% in Sudan to 24% in Zambia. The estimate from Cameroon is derived by pooling two arms (one urban and one rural) from one case-control study that was designed to compare the prevalence of nephropathy in an onchocerciasis-endemic area, and the estimate from Ghana is derived from only one medium-quality study done in an urban population that was specifically designed to measure end-organ damage such as proteinuria in people with hypertension.49,50 The one high-quality study from Ghana did not measure proteinuria.47

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and presence of azotaemia as indicated by absolute blood urea nitrogen value. A third of studies (30 [33%] studies) measured kidney function by more than one method.

The overall prevalence of CKD in the 21 medium-quality and high-quality studies was 13.9% (95% CI 12.2–15.7; figure 2). Estimates ranged from 2% in Côte d’Ivoire to 30% in Zimbabwe. Nearly half (n=6) of the countries represented had prevalence estimates ranging between 4% and 16%, and all countries but one (Zimbabwe) had prevalence estimates of less than 20% (figure 2). In the case of Zimbabwe, the estimate is derived from only one study that included many people with HIV who had not received antiretroviral treatment, which probably explains the unusually high prevalence.45,46 The only other study to have measured a prevalence of CKD in Zimbabwe was a convenience sample of people with diabetes and was not included in the meta-analysis due to its low quality. We formally noted heterogeneity across the medium-quality and high-quality studies (n=21; I²=47.11%; p=0.0051). Heterogeneity across all studies was much higher (I²=67.64%, p=0.0051).

For many countries (Malawi, Burundi, Ethiopia, Tanzania, Benin, Burkina-Faso, Guinea, and Senegal) we detected no medium-quality or high-quality estimates for the prevalence of CKD. For instance, although nine studies were done in Ethiopia, including more than 4000 people, all were convenience samples in people with diabetes or HIV (table). Additionally, even though we report estimates for Sudan, Nigeria, and South Africa, most studies from these countries were not included in the combined analysis due to issues with convenience sampling of high-risk populations and inconsistent measurements of kidney function.

Of the three studies that met criteria for the highest quality grade, one was from Ghana and two were from the Democratic Republic of Congo (DRC). Both studies from DRC were done in an urban setting between 2006 and 2007 and reported proteinuria prevalence to be 5% and 17%, respectively.46 Only one of the studies estimated GFR, and it showed that the prevalence of CKD when defined as a GFR of less than 60 mL per min per 1.73 m² by the MDRD formula was 7.8% (95% CI 7.6–8.1%).47 The one high-quality study from Ghana was done in a rural population in 2010 and reports a CKD prevalence of 30% when defined as a GFR of less than 90 mL per min per 1.73 m² by the MDRD formula but only 1.6% when defined as a GFR of less than 60 mL per min per 1.73 m².48

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Zambia, the prevalence of CKD ranged from 4% to 24% (table), with proteinuria almost exclusively used (96%) as the marker.

The vast majority of studies were done in an urban setting (83 [93%] studies). Of the seven studies done in rural settings, most were of medium quality (n=6) and one was high quality. We detected no difference in the prevalence of CKD between urban (12·4%, 95% CI 11–14) and rural (16·5%, 13·8–19·6) settings (p=0·474).

Examination of the prevalence by decade suggested that CKD prevalence increased in each of the four previous decades. However, definitive conclusions are limited by low study quality, detection bias, and publication bias that prevent meaningful analysis. Only eight studies were done before 1980 and only 31 studies were done between 1980 and 1999; 57 studies were done in the 2000s. Before the year 2000, only five medium-quality studies and no high-quality studies were done.28,35,39,40,43

**Discussion**

Our systematic analysis of available studies showed that CKD is a prevalent and potentially escalating disease across sub-Saharan Africa with risk factors that include both communicable and non-communicable diseases. Although use of different measurement and sampling methods limit direct comparison between studies,
Prevalence studies and remain unvalidated. Additionally, it also implies that CKD might not be a burden exclusive to high-income regions. Poor quality data for the prevalence of CKD in sub-Saharan Africa was pervasive, and our review identified that the major reasons were related to poor sampling methods, unreliable kidney function measurements, and variable data availability in each country. Together, our findings draw attention to an important limitation to systematically addressing an increasing health problem throughout sub-Saharan Africa.

Non-communicable diseases are thought to be a rising global epidemic that disproportionately affect the economic, social, and health outcomes of resource-poor countries and low-income populations. For sub-Saharan Africa, conservative projections for the year 2030 predict that 18·65 million people will have diabetes, and predictions for hypertension, obesity, and tobacco use are similarly alarming. In the context of CKD, these are portentous forecasts in view of the high burden of CKD in people with diabetes or hypertension shown in our analysis.

Communicable diseases such as HIV might also be contributing to the large burden of CKD in sub-Saharan Africa. Management of chronic diseases in people living with and receiving treatment for HIV is becoming a challenge because fewer people die from HIV-related complications and more develop chronic diseases. This recognition has led to a strong international commitment to integrate HIV with the care of non-communicable diseases. Our findings suggest that CKD is among the important potential chronic complications of HIV in sub-Saharan Africa. HIV treatment for the 22 million people with the infection in sub-Saharan Africa has become an urgent issue within the global community. However, our findings suggest that the prevalence of CKD is substantial even in people receiving care for HIV, which further substantiates the call to integrate HIV treatment with the care of non-communicable diseases.

An important difficulty in the detection and management of CKD in sub-Saharan Africa is the absence of reliable and validated measures of kidney function. Our findings show that, depending on the method of measurement or definition of kidney impairment, prevalence estimates can vary substantially even within similar populations, and although the CKD-EPI and modified CKD-EPI formulae have been suggested to most closely approximate GFR in many African populations, they have been applied in only two prevalence studies and remain unvalidated. Proteinuria is another important and easily obtained clinical indicator of glomerular disease and might portend increased cardiovascular risk in people with HIV, diabetes, or hypertension. However, the best method of urinary protein detection remains unknown, and our findings showed that the variability and dearth of available data are major limitations. Nonetheless, our results still suggest that, when measured, the prevalence of proteinuria in people with diabetes, hypertension, or HIV is substantial, which again stresses a need for the integration of HIV and non-communicable diseases.

The major strength of our study was the comprehensive inclusion of many studies with a transparent assessment of CKD prevalence in sub-Saharan Africa. Because of the shortage of high-quality data, we chose not to limit our systematic review to any particular population, time period, or measurement of kidney disease. We saw much heterogeneity between studies, which is a common finding in many meta-analyses. Wherever possible, we presented the prevalence estimates descriptively in many different contexts to account for this heterogeneity, and we believe that exclusion of the low-quality studies from the review would have provided a restricted and false representation of the full state of renal epidemiology in sub-Saharan Africa. However, because such heterogeneity presented a less than ideal setting for pooling of data, we limited the meta-analyses to only studies of medium or high quality, and we felt that the absence of continent-wide epidemiological data for kidney disease justified the method. The lack of reliable measures of kidney function was a major limitation of systematically reviewing the prevalence of kidney disease in sub-Saharan Africa, but this finding has drawn attention to the large gap in reliable and validated estimates of kidney function. Additionally, we did not review articles in non-indexed journals, which might have introduced a slight publication bias.

There are many other implicated causes of CKD in sub-Saharan Africa that we were not able to analyse, including chronic glomerulonephritis and the widespread use of herbal or traditional medicine. Up to 80% of the populations in sub-Saharan countries are estimated to use herbal or traditional medicines, which are thought to have been associated with 35% of all new cases of acute kidney injury. Some of the most commonly used toxic herbs used as drugs are Securidaca longepedunculata (African violet tree), Cape aloes, and Euphorbia mabbalensis, but few follow-up studies have been done on kidney disease caused by these agents.

On a continent where chronic diseases and cardiovascular deaths are now drawing increasing attention, CKD should not be overlooked. Approaches to addressing the rising epidemic of non-communicable diseases might initially include screening for CKD in specific high-risk populations, especially in view of the fact that cardiovascular disease and chronic kidney disease share many common risk factors. Such might be especially important when considering that the incidence of end-stage renal disease, an almost uniformly...
fatal disease in sub-Saharan Africa, mirrors the prevalence of non-communicable diseases in high-income countries.18 Although poor data quality limit definive inferences, our findings suggest that CKD is a substantial health burden in sub-Saharan Africa with many risk factors, including many communicable and non-communicable diseases. These findings are of global interest and should signal a call to action.

Contributors
JWS contributed to protocol design, study design, the literature review, quality assessment, data extraction, statistical analysis, data interpretation, article preparation, article review, and correspondence. BJ contributed to statistical analysis, article preparation, and article review. ST contributed to the literature search, quality assessment, data extraction, data interpretation, article preparation, and article review. NH contributed to the literature search, quality translation, quality assessment, data extraction, and article review. RM contributed to the literature AS, GH and data extraction. SN contributed to article preparation and review. UP contributed to protocol design, study design, data interpretation, and article preparation and review.

Conflicts of interest
We declare that we have no conflicts of interest.

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References
22 Shamliyan T, Kane R, Dickinson S. A systematic review of tools used to assess the quality of observational studies that examine incidence or prevalence and risk factors for disease. J Clin Epidemiology 2010; 63: 1061–70.