


# The Chronic Kidney Disease in Africa (CKD-Africa) collaboration: lessons from a new pan-African network

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## ABSTRACT

Chronic kidney disease (CKD) is a global public health problem, seemingly affecting individuals from low-income and middle-income countries (LMICs) disproportionately, especially in sub-Saharan Africa. Despite the growing evidence pointing to an increasing prevalence of CKD across Africa, there has not been an Africa-wide concerted effort to provide reliable estimates that could adequately inform health services planning and policy development to address the consequences of CKD. Therefore, we established the CKD in Africa (CKD-Africa) Collaboration. To date, the network has curated data from 39 studies conducted in 12 African countries, totalling 35 747 participants, of which most are from sub-Saharan Africa. We are, however, continuously seeking further collaborations with other groups who have suitable data to grow the network. Although many successful research consortia exist, few papers have been published (with none from Africa) detailing the challenges faced and lessons learnt in setting up and managing a research consortium. Drawing on our experience, we describe the steps taken and the key factors required to establish a functional collaborative consortium among researchers in Africa. In addition, we present the challenges we encountered in building our network, how we managed those challenges and the benefit of such a collaboration for Africa. Although the CKD-Africa Collaboration is focused primarily on CKD research, many of the lessons learnt can be applied more widely in public health research in LMICs.

## INTRODUCTION

Chronic kidney disease (CKD) is one of the leading causes of morbidity and mortality, affecting 10%–16% of the general adult populations of Asia, Australia, Europe and North America,<sup>1 2</sup> with heterogeneous prevalence in African populations.<sup>3 4</sup> The rising burden of CKD is evidenced by its climb in ranking of global causes of disability-adjusted life-years, from 29th in 1990 to 18th in 2019.<sup>5</sup> Currently, more than 850 million people have kidney disease,<sup>6</sup> with a disproportionate burden of this number affecting people in low-income and middle-income countries

## Summary box

- The Chronic Kidney Disease in Africa Collaboration (CKD-Africa Collaboration) is an African network of CKD studies that pools individual participant data to: (1) determine the burden of CKD in Africa more accurately, (2) create resources that would allow the burden of CKD to be easily tracked and (3) enable CKD projections to be made in the context of Africa.
- To date, the network has curated data from 39 studies conducted in 12 African countries, totalling 35 747 participants, of which most are from sub-Saharan Africa.
- The estimates generated through this network will allow for the development of policy related to screening and prevention to address the consequences of CKD in Africa, inform health services planning, and aid understanding of the mechanisms driving CKD across the continent.
- This network has far-reaching potential for Africa, as it is in an ideal position to validate findings across geographical and national boundaries, to test hypotheses and to generate a new understanding of CKD progression and its complications.

(LMICs) where access to care is significantly limited.<sup>1 7</sup> In recent years, studies have shown that Africans are seemingly at a high risk for developing CKD,<sup>8</sup> are affected at a younger age<sup>9</sup> and have a more rapid progression to kidney failure.<sup>9 10</sup> This disproportionate risk is partly attributed to the rapid epidemiological transition, culminating in a high and rising prevalence of hypertension and type 2 diabetes mellitus,<sup>11 12</sup> combined with a high burden of infectious diseases<sup>13</sup> and a genetic predisposition to CKD.<sup>14</sup> Moreover, there are different methods used to detect kidney damage, which can influence the diagnosis and staging of CKD, and consequently the reported population prevalence.<sup>15</sup> Due to the lack of data in many African countries, and the limitations in the available data,<sup>3 4</sup> the true burden of CKD in Africa (epidemiological, including age-standardised rates, as



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well as cost of care and health impact on patients, their family and society) is probably underestimated and thus remains largely unknown.

Recognising the shortfall, in 2018/2019, the Non-Communicable Disease Research Unit of the South African Medical Research Council (SAMRC) established the CKD in Africa (CKD-Africa) Collaboration. The major goal of this network is to pool data at the individual participant data (IPD) level from all relevant existing African studies. This will enable the burden of CKD in Africa to be determined more accurately, create resources for the burden of CKD to be easily tracked in future and for projections of CKD to be made in Africa. This would provide reliable estimates to develop policy solutions to address the consequences of CKD in Africa, inform health services planning, and aid the understanding of the mechanisms driving CKD across the continent.

Globally, several successful research consortia focus on communicable and non-communicable diseases,<sup>16–18</sup> and various studies across Africa successfully employ the use of IPD.<sup>19–21</sup> One example of a successful consortium using IPD is the CKD-Prognosis Consortium (CKD-PC),<sup>17</sup> established to compile and analyse the best available data on kidney disease and clinical outcomes. This consortium has made a significant contribution to the definition, staging and management of CKD. However, despite the large number of participating cohorts globally, the CKD-PC has no data from Africa and thus there are uncertainties around using its findings to inform CKD management and prevention strategies in Africa.

This *Practice* contribution will introduce the CKD-Africa Collaboration, through describing the steps taken to establish the collaborative research consortium, as well as briefly summarising the current participating studies. Since few published papers currently exist detailing the challenges faced and lessons learnt in setting up and running a research consortium, we will present the challenges we have encountered and how they were managed. Also, we will report on the novelty and effectiveness of this kidney disease network in Africa.

## CONCEPTION OF THE NETWORK

Establishing the CKD-Africa Collaboration, by moving the idea of an African network of studies on kidney function and CKD to a functional continental resource, required several steps. These included forming the central structure responsible for initiating and managing the network, identifying research partners, inviting these partners to join the network, and establishing the database platform, by acquiring and processing the participant-level data.

### Forming the consortium central structure

We found it best to balance the central structure with a mixture of highly motivated emerging researchers to drive the initiative, with more senior members to act as advisors (online supplemental addendum A highlights the roles and responsibilities of the core team). In our

case, the members of the central structure have had a long-standing working relationship, and we learnt that these shared research interests and mutual trust and support proved beneficial to building a robust and sustainable network. In addition, we found it advantageous to involve a multidisciplinary group of specialists, including nephrologists, epidemiologists, statisticians and public health specialists, given that the catalyst for building this network arose from the recognised need to provide reliable estimates to guide policy. This diverse central structure, along with the other collaborators, are instrumental in shaping the consortium.

### Identifying collaborators and setting up a functional database platform

Building a robust and sustainable collaborative research consortium requires identifying research partners. We found that a good way to identify potential partners was by first tapping into our existing research partnerships. Indeed, as the result of our cumulative existing networks as the central structure, we had access to IPD from cross-sectional studies for about 7000 individuals even before the first formal call for participation in the consortium was sent. Also, we found that forging new networks with researchers in the broader field of non-communicable diseases was beneficial. These new networks were mainly established at international conferences and events organised by specialty organisations, such as the European Society of Hypertension, the International Society of Hypertension, the European Renal Association-European Dialysis and Transplant Association and the International Diabetes Federation. We found that these in-person conversations, at conferences, were often useful when explaining the purpose of the network and discussing complicated issues (eg, security of data storage servers). These conversations also led to the development of personal relationships with our collaborators which we felt eased correspondence throughout the data sharing process. Further research partners were sought through the systematic search of published literature.

### Search strategy

The reference list of the two most recently published systematic reviews of CKD prevalence in Africa<sup>34</sup> was used as the basis to identify relevant studies, further supplemented by searches of Medline via PubMed, EMBASE, relevant African journals and WHO Global Health Library databases (which included the African Index Medicus, WHO Library Information System, and Scientific Electronic Library Online) to identify more recent publications. This comprehensive search strategy was developed using the African search filter<sup>22</sup> and appropriate keywords, including “prevalence”, “incidence”, “screening”, “diagnosis”, “risk prediction”, “chronic kidney (or renal) disease”, “kidney (or renal) dysfunction”, “decreased kidney (renal) function”, “end-stage renal disease”, “glomerular filtration rate”, “albuminuria”, “proteinuria” “Cockcroft-Gault equation”, “Modification

of Diet in Renal Disease equation”, “CKD Epidemiology Collaboration equation”, strung together by MeSH terms. Additional citations were also searched by scanning the reference lists of review papers and conference proceedings. Thus, to date, the searches covers the time frame from 1 January 1995 to 31 January 2021. The search results were uploaded into the citation management database EndNote (Clarivate Analytics, Philadelphia, USA), and the duplicate check function used to identify citations retrieved from multiple sources. Unique citations were uploaded into the systematic review software, Covidence (Covidence, Melbourne, Australia), used to store and track search results in the review process.

### Process for selection of eligible studies

Using the Covidence software, two team members of the core working group (CG and SS) independently reviewed the articles referenced in the published systematic reviews<sup>3,4</sup> and those obtained through the systematic search processes. In instances where either team member determined that a study may be eligible based on the title or abstract review, a full-text article review was conducted. Disagreements between reviewers, after full-text review, was resolved by discussion and consensus. There was no restriction on language since translators were available, if needed, to evaluate titles/abstracts and full-text articles for languages other than those for which the team members were fluent. In instances where multiple surveys were conducted in different countries or in different calendar years and reported within the same article, each survey was accounted for separately.

Determining the membership criteria for the CKD-Africa Collaboration required careful consideration. With the aim of combining the IPD curated across the network to enhance the ability to examine multiple health outcomes related to CKD, in addition to the ability to report more accurate estimates on the burden of CKD across Africa, a set of common attributes were defined as prerequisites for membership into the network at inception:

1. Studies of observational research design with a priori hypotheses and defined study objectives, participant-level information, and primary data collection.
2. Studies reporting, or allowing computation of, the prevalence of CKD. CKD could be defined based on estimated glomerular filtration rate (eGFR) and/or the presence of proteinuria/albuminuria, according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines.<sup>23</sup> In the instance where eGFR is used to define CKD, investigators are required to report on the methods used to determine creatinine levels.
3. Studies with ethical approval from their respective ethics organisations, with deidentified data.
4. Studies with a minimum sample size of 300 participants for adult cohorts, aged 18 years and older. The justification for the selected sample size is that studies with small sample sizes are likely to include only few

people with CKD, and consequently contribute little or nothing to the estimates in the meta-analyses, while remaining a major contributor to the heterogeneity across studies. Furthermore, we opted for participants aged above 18 years as the main aim of the consortium is to determine the burden of CKD and preventable risk factors driving the disease in Africa. The aetiology of CKD in children differs significantly from CKD in adults, with CKD in children generally caused by birth defects and hereditary diseases, whereas in adults the main drivers being diabetes and hypertension.

5. Studies with participants of African descent residing in Africa.

Our first formal call for participation was organised in 2018 (online supplemental addendum B), where corresponding authors of studies containing datasets that met the inclusion criteria were contacted via email, inviting them to contribute primary data for inclusion into the network. From our experience, obtaining data sets through personal contact took as little as 4 months, however, not all contacted authors responded initially. In instances of non-response, we attempted to make contact several times, with at least 6 months between calls. Since many collaborators may lack time or organisational resources to support essential data sharing tasks (eg, converting data to prespecified digital formats, drafting data sharing agreement), we found a useful technique to obtain the IPD was to minimise the additional responsibilities on the collaborator, like allowing datasets in any digital format. In addition to the non-responding investigators, we also experienced an unwillingness to participate in the network in a very limited number of cases. The main reason for the unwillingness was due to the studies not being completed at the time of our request.

After agreement to participate in the network, a memorandum of understanding (online supplemental addendum C), and in some cases, a material transfer agreement (online supplemental addendum D), was signed by both parties as a declaration of mutual understanding. These documents highlighted the role of the parties, the area of focus, ethical and data sharing information, intellectual property rights, commercialisation and publications. This agreement was followed by the electronic version of the data requested. In our case, we used the expanded version of the WHO STEPwise Approach to non-communicable disease risk factor Surveillance (STEPS) Instrument<sup>24</sup> as the basis for the scope of variables required (online supplemental addendum B). In instances where investigators are unwilling or unable to transfer data, owing to legal or other logistical reasons, but are prepared to reanalyse their data according to a standard protocol, the CKD-Africa Collaboration secretariat data centre produce a computer code that can be used to generate the required summary statistics. All deidentified data are held centrally at the SAMRC. To maintain the data integrity, protective measures are employed, which include the data being kept on a virus-protected and access-restricted server at the SAMRC,

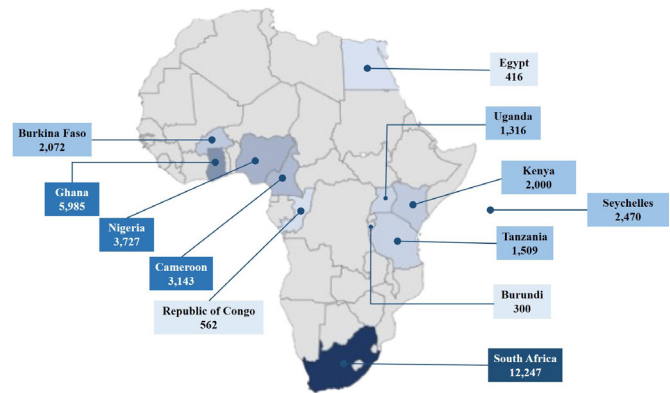
which is backed-up daily. This storing procedure is as per the ‘Ethics in health research: principles, processes and structures’, second edition (2015) requirements for electronic data storage, which is the SAMRC’s Ethics Committee’s terms of reference.

The process of searching for collaborators, getting everyone on board, finalising the legal aspects of the arrangement and data acquisition is a lengthy and sometimes challenging process. However, it is laudable how generally able and willing investigators conducting CKD research in Africa have been to participate in this network. This shows the level of awareness of the devastating consequences of the disease among the African CKD research community and the desire to work collectively to address the problem. The process of data management is also a labour-intensive process. The data coding and transfer from original studies into the IPD database is done by a senior staff member, or by a student under supervision of a senior staff member of the central structure. During this process, participant characteristics and screening accuracy results for each study, using the cleaned datasets, are compared with those from the original datasets to identify any potential discrepancies. In addition to obtaining the original IPD, aggregate data are extracted from the published articles of included studies. At this point, cross-checks between the published data with the original IPD obtained from each dataset are conducted and any inconsistencies discussed with the original authors. It is crucial to record and update contact information as this will ease subsequent communication, which often occurred years after the first data request was sent.

**PROGRESS TO DATE**

As of 1 April 2021, through our scoping efforts, we had identified 108 researchers who were the principal investigators (PIs) of 120 potential studies. Of these, 92 PIs were contacted to gauge their interest in collaborating in the consortium, as 16 PIs had either no author contact information or incorrect contact details. Of the 92 PIs contacted, 36 consented to participate in the network, with the remaining 56 PIs being either non-responsive to our call or, in two cases, unwilling to participate in the network. The consenting studies span across 12 African countries with a total of 46 276 participant-level data. To date, the network has successfully curated data from 39 studies conducted in 12 African countries, totalling 35 747 participants. Most enrolled studies are from sub-Saharan Africa, with one study representing north Africa<sup>25</sup> (figure 1). Of the included studies, the number of participants range between 300 and 2543 per study. Some studies are still undergoing enrolment, and therefore, the number of study participants continues to grow.

Of the participating studies (table 1), data collection of 14 studies (36%) took place before 2010,<sup>25–38</sup> with the remaining 64% sampled between 2010 and 2017. Four of the participating studies have not been published yet.



**Figure 1** Distribution of African countries enrolled in the CKD-Africa Collaboration. The individual participant data (IPD) ranges from 300 participants to 12 247 participants per country. The nine shaded countries represent those for which IPD are currently available. The shading from light blue to dark blue represents the increasing number of IPD available per country, thus, the darkest shading represents the countries with the most available IPD. CKD, chronic kidney disease.

Overall, 79% of the IPD are from studies in the general population,<sup>28 30–34 36 37 39–50</sup> 7% are from studies of people with HIV-infection,<sup>27 29 51–54</sup> 6% from studies of populations with hypertension<sup>35 55 56</sup> and 4% consists of people with diabetes mellitus<sup>57</sup> (figure 2). The final 4% of the IPD constitutes two studies in patients with kidney failure<sup>26 58</sup> and one study conducted in first-degree relatives of people with CKD.<sup>25</sup> Of the 25 studies conducted in general populations, 88% (n=22) are geographically defined cohorts, with two of the remaining studies conducted among teachers recruited from primary, secondary and intermediate public schools<sup>30 39</sup> and one study (not yet published) conducted in undergraduate students. The participants in the high-risk subpopulations were recruited from outpatient diabetes, hypertension and HIV clinics.

Most studies included adults in a broad age range, with the included cohorts comprising adults between the ages of 18–100 years. One unpublished study from Nigeria included only undergraduate students and therefore selected individuals in the age range 18–30 years. All studies recruited both male and female participants, with most having greater female participation. All, except one study used serum creatinine to estimate GFR and characterise CKD, with 76% additionally determining the presence of albuminuria or proteinuria. Only one study satisfied the 3-month chronicity criterion for diagnosing CKD.<sup>56</sup> All the studies include participants with normal kidney function and mild-to-severe stages of CKD (CKD stages 1–4), with 32% not having participants in the most severe stage of kidney failure (stage 5 CKD). All included studies used standardised creatinine assays, with the Jaffe method<sup>59</sup> being the most commonly used method for determining serum creatinine concentration. Three of the 38 studies<sup>44 48 50</sup> used enzymatic methods to determine serum creatinine concentrations. All studies have data on

**Table 1** Characteristics of participating studies in CKD-Africa Collaboration

Country	Study reference	Population	Cohort participants	Sample size (n)	Age range (years)	% Male	Creatinine measurement method	eGFR range	Proteinuria/albuminuria
Burkina Faso†	Ali <i>et al</i> <sup>62</sup>	GP	Geographical cohort	2072	38–69	50.4	Jaffe	11.8 to >90	Albuminuria
Burundi	Cailhol <i>et al</i> <sup>27</sup>	HIV	HIV clinic cohort	300	19–66	29.7	Jaffe	6.0 to >90	Proteinuria
Cameroon	Choukem* <sup>67</sup>	DM	Diabetes clinic cohort	790	19–82	65.0	Jaffe	1.7 to >90	NA
Cameroon	Feteh <i>et al</i> <sup>67</sup>	DM	Diabetes clinic cohort	645	20–86	53.0	Jaffe	4.0 to >90	NA
Cameroon	Kaze*	GP	Geographical cohort	433	21–90	49.0	Modified Jaffe	6.9 to >90	Albuminuria
Cameroon	Kaze <i>et al</i> <sup>45</sup>	GP	Geographical cohort	500	19–83	53.4	Modified Jaffe	23.0 to >90	Albuminuria
Cameroon	Kaze <i>et al</i> <sup>46</sup>	GP	Geographical cohort	439	19–90	42.1	Modified Jaffe	12.0 to >90	Albuminuria
Cameroon	Kaze <i>et al</i> <sup>66</sup>	HPT	HPT clinic cohort	336	33–90	36.6	Modified Jaffe	5.0 to >90	Albuminuria
Egypt	Gouda <i>et al</i> <sup>65</sup>	Other	FDR of CKD cohort	416	18–75	43.2	Jaffe	32.0 to >90	Albuminuria
Ghana†	Adjei <i>et al</i> <sup>40</sup>	GP	Geographical cohort	2543	25–96	33.0	Jaffe	15.5 to >90	Albuminuria
Ghana	Chadwick <i>et al</i> <sup>33</sup>	HIV	HIV clinic cohort	677	20–77	26.1	Jaffe	9.8 to >90	Proteinuria
Ghana	Osato <i>et al</i> <sup>65</sup>	HPT	HPT clinic cohort	754	19–90	21.3	Jaffe	1.4 to >90	Proteinuria
Ghana†	Ali <i>et al</i> <sup>62</sup>	GP	Geographical cohort	2011	40–61	45.8	Jaffe	12.3 to >90	Albuminuria
Kenya†	Ali <i>et al</i> <sup>62</sup>	GP	Geographical cohort	2000	35–67	46.0	Jaffe	13.9 to >90	Albuminuria
Nigeria	Adedeji <i>et al</i> <sup>61</sup>	HIV	HIV clinic cohort	304	18–80	54.7	Modified Jaffe	5.9 to >90	Albuminuria
Nigeria	Alasia <i>et al</i> <sup>26</sup>	Other	Renal clinic cohort	605	18–86	49.3	Jaffe	1.3 to >90	Proteinuria
Nigeria	Ayodele*	GP	Cohort of students	307	18–30	35.8	Modified Jaffe	39.9 to >90	NA
Nigeria	Ayodele*	GP	Geographical cohort	419	19–80	40.3	Modified Jaffe	37.1 to >90	NA
Nigeria	Ayokunle <i>et al</i> <sup>62</sup>	HIV	HIV clinic cohort	335	20–75	43.9	Jaffe	4.7 to >90	Albuminuria
Nigeria	Okoye <i>et al</i> <sup>32</sup>	GP	Geographical cohort	476	18–90	33.8	Modified Jaffe	22.4 to >90	Proteinuria
Nigeria	Oluombo <i>et al</i> <sup>33</sup>	GP	Geographical cohort	972	18–100	30.4	Modified Jaffe	23.9 to >90	Albuminuria
Nigeria	Raji <i>et al</i> <sup>68</sup>	Other	Renal clinic cohort	309	18–73	45.3	Modified Jaffe	1.2 to >90	NA
RoC	Ekat <i>et al</i> <sup>29</sup>	HIV	HIV clinic cohort	562	18–64	33.8	Jaffe	4.0 to >90	NA
SA	Adeniyi <i>et al</i> <sup>39</sup>	GP	Cohort of teachers	455	22–71	29.7	Modified Jaffe	32.4 to >90	Proteinuria
SA	Malan <i>et al</i>	GP	Cohort of teachers	409	20–65	49.4	Jaffe	1.3 to >90	Albuminuria
SA	Matsha <i>et al</i> <sup>31</sup>	GP	Geographical cohort	1620	18–91	24.8	Jaffe	8.2 to >90	Albuminuria
SA	Peer <i>et al</i> <sup>64</sup>	GP	Geographical cohort	1086	22–81	35.9	Jaffe	9.0 to >90	NA
SA	Rayner and Becker <sup>35</sup>	HPT	HPT clinic cohort	1107	18–94	48.8	NA	NA	Albuminuria
SA	Schutte <i>et al</i> <sup>67</sup>	GP	Geographical cohort	750	20–70	46.1	Jaffe	47.8 to >90	NA
SA	Schutte <i>et al</i> <sup>19</sup>	GP	Geographical cohort	1202	20–30	48.1	Jaffe	48.1 to >90	Albuminuria
SAT	Ali <i>et al</i> <sup>62</sup>	GP	Geographical cohort	2312	40–81	42.2	Jaffe	3.1 to >90	Albuminuria
SAT	Ali <i>et al</i> <sup>62</sup>	GP	Geographical cohort	1388	29–82	30.6	Jaffe	4.8 to >90	Albuminuria
SAT	Ali <i>et al</i> <sup>62</sup>	GP	Geographical cohort	1918	39–61	50.6	Jaffe	9.4 to >90	Albuminuria
Seychelles	Prujm <i>et al</i> <sup>38</sup>	GP	Geographical cohort	1230	25–64	46.2	Jaffe	3.2 to >90	Albuminuria

Continued

**Table 1** Continued

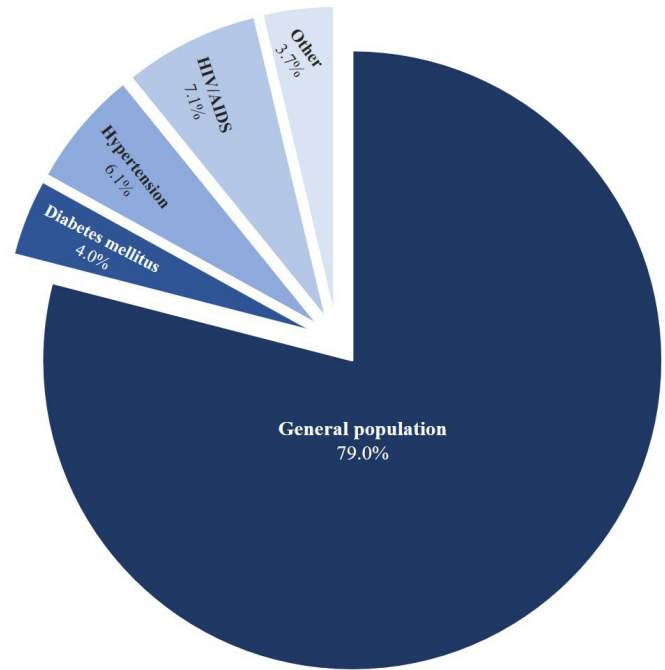
Country	Study reference	Population	Cohort participants	Sample size (n)	Age range (years)	% Male	Creatinine measurement method	eGFR range	Proteinuria/albuminuria
Seychelles	Heiniger <i>et al</i> <sup>63</sup>	GP	Geographical cohort	1240	26–64	42.8	Jaffe	4.5 to >90	Albuminuria
Tanzania	Peck <i>et al</i> <sup>48</sup>	GP	Geographical cohort	1041	18–92	46.2	Enzymatic	25.1 to >90	NA
Tanzania	Stanifer <i>et al</i> <sup>50</sup>	GP	Geographical cohort	468	18–88	25.6	Enzymatic	9.2 to >90	Albuminuria
Uganda	Kalyesubula <i>et al</i> <sup>44</sup>	GP	Geographical cohort	955	18–87	33.0	Enzymatic	44.7 to >90	Proteinuria
Uganda	Odongo <i>et al</i> <sup>54</sup>	HIV	HIV clinic cohort	361	18–66	36.3	Jaffe	4.6 to >90	Proteinuria

\*Unpublished data

†Part of the multisite study, Africa Wits-INDEPTH partnership for Genomics studies.<sup>62</sup>

‡Part of the multisite study, Research on Obesity and Diabetes among African Migrants.<sup>40</sup> GFR is estimated by the the CKD Epidemiology Collaboration equations,<sup>64</sup> with the ethnicity correction factor omitted.

CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FDR, first-degree relatives; GP, general population; HPT, hypertension; NA, not applicable; RoC, Republic of Congo; SA, South Africa.



**Figure 2** Average contribution of each subpopulation to the overall number of studies enrolled in the CKD-Africa Collaboration. CKD, chronic kidney disease.

potential confounders of the associations between kidney function and outcomes including, but not limited to, age, ethnicity, smoking, medical history and treatment, and comorbidities like diabetes mellitus, hypertension, and obesity.

Given the timeframe, we have made considerable progress in establishing the consortium, with included studies covering a fair proportion of Africa.

### EXPANDING THE CONSORTIUM

As a means of strengthening the network we plan to engage with the African Renal Association and the International Society of Nephrology’s Africa Regional Board, to form a broader platform which would assist in calls for funding for this project as well as funding of needed prevalence studies in the rest of Africa not yet represented in the consortium. Also, we have scheduled a process of updating our systematic search process to identify new studies every 6 months, as a means of expanding our database. Expansion of the consortium is indeed important to obtain a representative group of study participants and sufficient statistical power for the results to be meaningful, but we are cautious to not stretch resources too thin and risk failure of the project. We also recognised early on that a balance needed to be struck between awaiting adequate IPD to generate sufficiently powered evidence and getting this evidence out to policymakers and other researchers; bearing in mind that potential collaborators and funders are more likely to join and fund a successful consortium.

Interested research groups working in the field of CKD are welcome to join the network, by contacting the

CKD-Africa Collaboration manager at cindy.george@mrc.ac.za.

### Funding

There are more financial constraints in LMICs than in affluent high-income countries (HICs). Foreign funding for conducting research in Africa is sparse,<sup>60</sup> so having partners from HICs could help acquire important resources for the consortium. Besides funding from the South African National Research Foundation, our research efforts have yet to receive major funding. However, there are concerted efforts being made to attract funding from various sources, with the purpose of the funding geared at (1) capacity development, by attracting and supporting junior African researchers to undertake their postgraduate and postdoctoral projects using the consortium as basis; (2) popularising the work of the consortium, through a website, and workshops and (3) database maintenance.

### NOVELTY AND EFFECTIVENESS OF THE CKD-AFRICA COLLABORATION

There is a significant demand for research to direct and strengthen policies related to non-communicable diseases, in particular CKD research in Africa. This network is thus in the ideal position as we aim to provide evidence that could inform health services planning and shape policy and guidelines in Africa and drive the agenda for expanding CKD research. This would inevitably result in improved care for the vulnerable and most affected populations on the continent. The consortium is an ideal platform that will serve as background for future studies in which it is expected to play a major role. Indeed, this platform will allow for discussions centred on standardisation of approaches, related to study design, kidney function measurements and estimating prevalence, enhancing the interpretability of analyses, and integrating data from multiple cohort studies. Our work will create a forum for sharing analytical methods and enhance funding opportunities allowing for the development of ancillary studies using standardised methodology. Further, the potential to combine study data across the network will enhance the ability to examine multiple health outcomes related to CKD, in addition to the ability to report more accurate estimates on the burden of CKD across Africa. This will be used to inform prevention, detection and control strategies at a regional level. Through the evidence generated by the consortium we aim to actively engage policymakers to prioritise CKD reduction. Another major advantage of the large data capacity expected through this collaborative endeavour, is that this consortium could support the training of Masters students and Doctoral fellows across Africa. The consortium will also provide an opportunity for further research capacity training and networking for investigators across Africa.

IPD meta-analysis, which is the primary methodology used by the CKD-Africa Collaboration, has major

advantages above those of a conventional meta-analysis. Therefore, given the controversies surrounding the use of the various equations for estimating GFR to diagnose CKD, an IPD meta-analysis will provide standardised estimates across studies. Given the larger sample size through combined studies, IPD meta-analysis will also allow the performance of subgroup analyses (eg, by region, by country, epidemiological transition and over time), which would otherwise not have been possible by any primary study. Further, while there is little opportunity to check for biases from published aggregate data, IPD can be checked for missing, invalid, out-of-range and inconsistent datapoints in the datasets, before incorporating these into the larger merged dataset. Therefore, rather than implementing conventional meta-analyses, we seek opportunities to combine primary data from different groups to implement joint analyses, given the many commonalities between participating studies that will facilitate comparative research. By providing more detailed and reliable results, IPD meta-analyses offer greater potential than aggregate-data meta-analyses to impact on study design, conduct and analysis.

Naturally, this collaborative endeavour has both strengths and limitations. The variation in populations is one of the strengths of this network. Given the distribution of studies across Africa, the populations are genetically distinct, which will provide insights on possible genetic determinants of CKD. Furthermore, these populations also differ greatly with respect to health behaviours, healthcare delivery and environments. Conversely, while commonalities in study design will facilitate joint analysis, inconsistencies in the definition and capture of variables, as well as adjudication of outcomes, can complicate analyses. For example, the Jaffe method is less expensive and more readily used in the included studies compared with enzymatic assay but is more susceptible to interference from various biomolecules, like glucose.<sup>61</sup> However, despite the lack of standardisation of measurements of common laboratory parameters, calibration may be achieved by statistical means, given detailed descriptions of the collection processes. Also, this network can provide a unique opportunity to improve the quality of creatinine measurements by examining External Quality Assurance data of participating laboratories and encouraging those laboratories that are not participating in such programmes to do so. This allows for peer comparison and to ensure that methods being used are traceable to an internationally recognised standard. This will allow for greater precision and accuracy of eGFR measurements and permit comparisons. We do acknowledge that a single time point for serum creatinine determination for CKD diagnosis by eGFR, rather than over 3 months as recommended,<sup>23</sup> is not ideal. However, given the resource-poor settings in most of Africa, the probability of receiving data on repeated measures is low. Another limitation is the potential risk of participant duplication, where the same individual participates in different studies. Since we receive deidentified data, the various collaborators will

be required to inform the secretariat of such potential for duplication. A major limitation currently is that nearly 61% of the identified PIs have not yet responded to our call or are unwilling to participate in the network. Due to the potential large data contribution by these studies, the risk of significant bias could be introduced into our analysis. However, enrolment into the consortium continues and, to minimise the risk of bias, as far as possible, analyses will include both IPD and aggregated data from the published studies for which IPD is unavailable. In its current form, the network is only represented by 12 countries (22%) of the 54 countries in Africa, with most IPD coming from South Africa. However, with that said, this network covers all five subregions of Africa and as this is a growing network, the number of enrolled studies is expected to increase substantially over the coming years.

## CONCLUSION

This network will aid research in the field of CKD on the African continent. With this platform to facilitate interactions among active investigators, the commitment of all teams currently involved and the broadly defined research agenda, we are confident that there will be new studies across Africa, particular in the currently under-represented countries, that will join the network. In addition, we foresee the development of new studies originating from this collaboration. In that regard, this network has far-reaching potential for Africa, as it is in an ideal position to validate findings across geographical and national boundaries, to test hypotheses and to generate a new understanding of CKD progression and its complications. Although the CKD-Africa Collaboration is focused primarily on CKD, many of our lessons learnt can be applied more widely in public health research in LMICs.

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