

# Human Heredity and Health (H3) in Africa Kidney Disease Research Network: A Focus on Methods in Sub-Saharan Africa

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## Abstract

CKD affects an estimated 14% of adults in sub-Saharan Africa, but very little research has been done on the cause, progression, and prevention of CKD there. As part of the Human Heredity and Health in Africa (H3Africa) Consortium, the H3Africa Kidney Disease Research Network was established to study prevalent forms of kidney disease in sub-Saharan Africa and increase the capacity for genetics and genomics research. The study is performing comprehensive phenotypic characterization and analyzing environmental and genetic factors from nine clinical centers in four African countries (Ghana, Nigeria, Ethiopia, and Kenya) over a 5-year period. Approximately 4000 participants with specified kidney disease diagnoses and 4000 control participants will be enrolled in the four African countries. In addition, approximately 50 families with hereditary glomerular disease will be enrolled. The study includes both pediatric and adult participants age <1 to 74 years across a broad spectrum of kidney diseases secondary to hypertension-attributed nephropathy, diabetes, HIV infection, sickle cell disease, biopsy-proven glomerular disease, and CKD of unknown origin. Clinical and demographic data with biospecimens are collected to assess clinical, biochemical, and genetic markers of kidney disease. As of March 2015, a total of 3499 patients and controls have been recruited and 1897 had complete entry data for analysis. Slightly more than half (50.2%) of the cohort is female. Initial quality control of clinical data collection and of biosample and DNA analysis is satisfactory, demonstrating that a clinical research infrastructure can be successfully established in Africa. This study will provide clinical, biochemical, and genotypic data that will greatly increase the understanding of CKD in sub-Saharan Africa.

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## Introduction

Disparities in health care represent a worldwide challenge. Noncommunicable diseases are extremely common in developing nations, and rates of progressive kidney disease are rising. On the African continent, CKD is underestimated because studies are primarily from urban settings, are not population based, and lack rigorous assessments of kidney function. The overall prevalence of CKD is estimated at 14% throughout sub-Saharan Africa and is even higher in rural settings (1). Additional risk factors for CKD, such as diabetes, hypertension, GN, and HIV infection, are common among those with CKD (1). Despite this enormous burden, very little is known in Africa about the epidemiology, cause, progression, and prevention of CKD.

Until recently, the increased risk of CKD among those of African origin was attributed to social and environmental factors. In 2008, the discovery of the chromosome 22 locus associated with progressive ESRD among black Americans, and the subsequent identification of the implicated gene, *APOL1*, highlighted a genetic contribution to ESRD (2–4). *APOL1* consistently predicts progression among black

Americans with CKD from hypertension-attributed nephropathy, sickle cell disease, lupus, and FSGS. Carriers with two copies of the *APOL1* risk variants account for approximately 10%–15% of the black American population. The recessive trait, high prevalence of carriers with no apparent disease phenotype, and variable penetration raise questions that highlight the need for further study. Although *APOL1* renal risk variants are most frequent in West African populations, they are common in most sub-Saharan African populations, with lower frequency in East Africa (5,6).

To understand the association of *APOL1* and other genetic variants across multiple types of kidney disease and to explore potential gene-by-environment interaction, it is imperative to study populations in Africa in which the burden of kidney disease is on the rise and additional environmental risk factors, such as infection, are common. The Human Hereditary and Health in Africa (H3Africa) consortium was established by the Wellcome Trust (United Kingdom) and the National Institutes of Health in June 2012 to facilitate a contemporary research approach to the study of genomics and environmental determinants of common diseases, with the goal of improving the

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health of Africans. The initiative was formed as a community effort among African clinicians, scientists, and collaborators from outside Africa, and as of August 2014, the consortium comprises 23 individual projects (7).

The National Institutes of Health supports the H3Africa Kidney Disease Research Network through a U54 grant mechanism. The main aim is to increase the capacity to conduct genomic studies of kidney disease in sub-Saharan Africa. Ten institutions in five African countries contribute to this collaborative research network. Countries were included in the study on the basis of the burden of CKD, their geographic location and the availability of nephrologists committed to the collaborative study efforts. Clinical sites are located in Ethiopia, Ghana, Nigeria, and Kenya (combined population >362 million individuals) with supporting data and investigator sites in South Africa and four North American institutions.

The overall H3Africa Kidney Disease Research Network objective is to enroll approximately 4000 patients with kidney disease and 4000 controls, carry out comprehensive phenotyping of this cohort, and conduct genetic and translational research projects on CKD across the spectrum of kidney disease. In addition, scientist and clinician training and mentoring are key components of the study goals.

## Study Details

### Scientific Aims and Objectives

The four main objectives of the network are to: (1) perform comprehensive phenotyping of 8000 patients and controls and 50 families from four African countries (Ethiopia, Ghana, Kenya, and Nigeria); (2) train clinical research personnel and genomic investigators for Africa-based genomic research; (3) establish genomic research laboratories in West Africa using sustainable, low-capital-intensity laboratory technologies; and (4) conduct international-level quality genetic and translational research projects in CKD.

### Organizational Structure

The network consists of two coordinating centers at the University of Ghana and University of Michigan. These centers lead the management of the project with the nine clinical sites (locations and site investigators are listed in Supplemental Table 1). In addition, there are centers for data repositories in the United States, South Africa, and Ghana and sample processing laboratories in Ghana and Nigeria. The central repository for biologic and genetic materials is located at an H3Africa designated biorepository. Data management, specimen collection, shipping, and archiving of samples were performed with the web-based research data management system RedCap.

### Study Design

The H3Africa Kidney Disease Research Network involves a multinational, case-control approach wherein participants are characterized using standardized evaluation of risk factors and clinical outcomes. Approximately 4000 participants with specified kidney disease diagnoses and 4000 with no evidence of CKD who meet the inclusion criteria are to be enrolled over 48 months (Table 1). Approximately 50 families with hereditary glomerular

disease, specifically FSGS, will also be recruited. Eligible sub-Saharan African participants age <1–74 years will be screened and enrolled in the study after provision of informed consent. The eventual goal is longitudinal follow-up over 5 years. The lower age limit was chosen to include children under age 18 years who may have genetic kidney disease with early onset. The upper age limit of 74 addresses kidney disease in older patients, who have the highest prevalence of CKD (8). We did not study polycystic kidney disease because it has unique genetic determinants. However, a study of this disease may be important in future investigations from Africa.

### Ethics Approval

Participation in the study requires written informed consent across all four countries with language accessible to those of low literacy. In addition, videos were developed in two languages to facilitate recruitment and understanding of the consent form. Approvals obtained to date are from Ghana, Nigeria, and Kenya (Supplemental Table 2), and applications are under review at Addis Ababa University. At most sites, participants who have to travel to the hospital are given \$5 USD each, but this depends on the opinion of the local ethics review board about providing reimbursement, which may be considered an inducement.

### General Inclusion and Exclusion Criteria

The following are the inclusion criteria for patients with kidney disease: (1) CKD with two estimates of age-stratified eGFR <60 ml/min per 1.73 m<sup>2</sup> (Modification of Diet in Renal Disease or pediatric modified Schwartz formula) taken at least 3 months apart (9,10) and/or (2) one kidney ultrasonography report demonstrating two small echogenic kidneys; and/or (3) presentation of nephrotic syndrome or biopsy-proven glomerular disease. The inclusion and exclusion criteria are listed in Supplemental Table 3 and Table 2, respectively.

### Clinical Definitions

Standard definitions similar to those applied in other observational studies in kidney disease are used, with common definitions for diabetes and hypertension (Supplemental Table 3) (11–13). Target recruitment goals are given by disease subtype and specific definitions for types of kidney disease (Supplemental Tables 2 and 3, Table 1).

### Study Visits

**Screening Visit.** This first encounter with the participants after the provided informed consent includes use of a standardized screening data collection instrument with basic demographic information, data on inclusion criteria, and type of CKD. During the same or subsequent visits, a detailed questionnaire and medical abstraction form are completed by the study coordinator and, if necessary, translated.

Specific methods for each measurement use standard techniques and training similar to those used in the Chronic Renal Insufficiency Cohort (CRIC) (14) and are age appropriate. Additional clinical phenotyping includes anthropometrics, cardiovascular measures (Table 3), and collection of biologic specimens (whole blood, saliva, and urine).

**Table 1. Proposed study subcohorts for the H3Africa Kidney Disease Research Network**

Diagnosis-Specific Eligibility	Age (yr)	Patients (n)	Controls (n) <sup>c</sup>
Steroid-resistant nephrotic syndrome <sup>a</sup>	<18	200	200
Biopsy-proven glomerular disease <sup>b</sup>	≤74	200	200
HIV-related CKD	≤74	500	500
Sickle cell CKD	≤74	500	500
Hypertensive nondiabetic CKD	≤74	800	800
Diabetic CKD	≤74	800	800
CKD of unknown cause	≤74	1000	1000
Total		4000	4000

H3Africa, Human Heredity and Health in Africa.  
<sup>a</sup>Included 50 families with index cases and affected family members.  
<sup>b</sup>FSGS, minimal-change disease, or membranous nephropathy.  
<sup>c</sup>Controls with no evidence of CKD by eGFR>60 ml/min per 1.73 m<sup>2</sup> or no proteinuria.

**Table 2. Exclusion criteria in the H3Africa Kidney Disease Research Network**

Person unable or unwilling to provide informed consent Institutionalized individual (e.g., prisoner, nursing home resident, or skilled nursing facility resident) Person who appears unlikely or unable to participate in the required study procedures as assessed by the investigator Person with advanced heart failure at baseline Person with known cirrhosis based on patient self-report Pregnant or breast-feeding woman Patient receiving treatment with chemotherapy or alkylating agents for systemic cancer (other than nonmelanoma skin cancer) within 2 years before enrollment on the basis of patient self-report Patient with prior solid organ (including kidney) or bone marrow transplant based on patient self-report Patient with chronic obstructive uropathy Patient with known congenital kidney disease Patient with adult-onset monogenic forms of kidney disease, including autosomal dominant polycystic kidney disease and Alport syndrome Patient with maturity-onset diabetes of the young Person currently participating in an interventional clinical trial or in another research study that would overburden the participant
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H3Africa, Human Heredity and Health in Africa.

Blood, urine, and saliva samples are the source for determination of serum creatinine and eGFR, albumin-to-creatinine ratio, and complete blood count, as well as for genetic studies. Samples are stored in central H3Africa biorepositories for future studies.

**Follow-up Visits.** Yearly follow-up for 5 consecutive years will be conducted on all participants, with similar data collection of kidney disease progression, intervening clinical events, and biologic specimens. In an attempt to improve follow-up, contact details are obtained from participants as well as two of their contacts.

To standardize and increase the accuracy of data acquisition and clinical measurements, two training sessions were held for investigators, study nurses, laboratory technicians, and data entry staff and will be repeated annually.

### Recruitment Strategies

All clinical sites are located at university-affiliated teaching hospitals and recruit from nephrology clinics, dialysis units, and ward services, as well as specialized clinics, such as hypertension, diabetes, sickle cell, and HIV

clinics. Two strategies are used to approach eligible participants from both specialized clinics and the community. In the clinic setting, recruitment is facilitated by education of the clinic staff and physicians by the local kidney team. In the community, site investigators formed relationships with churches and businesses to discuss the research project. In addition, some sites worked with World Kidney Day events to increase awareness of kidney disease and provide free screening to attendees. The dedicated and highly motivated field staff, who speak the local languages, also help facilitate communication with potential participants, promote the awareness of kidney disease, and encourage participation in the study.

### Biologic Samples

Samples for DNA (including whole blood, isolated white blood cells [buffy coat], and saliva) from clinical sites are shipped by courier to MDS-Lancet Laboratories in Accra, Ghana. Samples are then transported to the kidney genomics laboratory at the Noguchi Memorial Institute for Medical Research, University of Ghana.

Variable	Schedule of Visits		
	V1 Screening	V2 Baseline Enrollment	V3 Annual
Eligibility confirmation	X		
Informed consent	X		
Demographic information (ethnicity, language)	X		
Contact information update	X		
Medical history (comorbidities, reproductive history, health behaviors and infectious history)		X	X
Standardized evaluations (MDRD, patient-reported symptoms list, SF-12 Health Survey, Environmental Exposures, Kansas City Questionnaire)		X	
Concomitant medications		X	X
Updated medical history and events			X
RRT		X	X
Genetic blood sample/mouth-rinse DNA <sup>a</sup>		X	
Laboratory tests: complete blood count, serum creatinine, metabolic panel, lipid panel <sup>b</sup>		X	X
HCV, HBsAg, HIV, hemoglobin electrophoresis, and hemoglobin A1c <sup>b</sup>		X	X
Spot urine assay collection: creatinine, albumin <sup>b</sup>		X	X
BP measurement <sup>c</sup>		X	X
Anthropometric measures <sup>d</sup>		X	X
Bioelectric impedance assessment <sup>e</sup>		X	X
Ankle brachial index <sup>f</sup>		X	X
Electrocardiography <sup>g</sup>		X	X

H3Africa, Human Heredity and Health in Africa; MDRD, Modification of Diet in Renal Disease; SF-12, Short-Form 12-item; HCV, hepatitis C virus; HBsAg, hepatitis B surface antigen.

<sup>a</sup>Samples will be processed for DNA extraction, centralized measurement, and aliquoting of specimens. DNA is extracted from the buffy coat using the Qiagen blood and body fluid spin protocol adapted from the QIAamp DNA Blood Mini Kit (QIAamp DNA Mini Kit and QIAamp DNA Blood Mini Kit 02/2003). DNA from whole blood is stored in three aliquots of 200  $\mu$ l in a  $-80^{\circ}\text{C}$  freezer. DNA is isolated from the mouth-rinse samples (saliva) by a simplified salting-out procedure. The pellet of DNA after processing is air dried for 5 minutes and ultimately suspended in 500  $\mu$ l of TE buffer. The DNA from each mouth-rinse samples is separated into aliquots and stored at  $-80^{\circ}\text{C}$ .

<sup>b</sup>Laboratory tests conducted at MDS-Lancet for all participants includes the following: urine albumin-to-creatinine ratio, measured by Beckman Coulter AU 480 Chemistry Analyzer (Beckman Coulter, Fullerton, CA) and Integra 400 plus; serum creatinine by Beckman Coulter AU 480 Chemistry analyzer; complete blood count by Coulter AcT Diff AL.

<sup>c</sup>BP is measured using the appropriate Omron HEM-907XL, and three measures are obtained in the seated position in 30-second intervals.

<sup>d</sup>Height measured by 213 Portable Stadiometer; weight by Seca 813 Robusta High Capacity Digital Scale; waist circumference by Gulick II Tape measure.

<sup>e</sup>Bioimpedance measured by Summit Doppler L250.

<sup>f</sup>Ankle-brachial index measured by Quantum 11 Body Composition Analyzer.

<sup>g</sup>Electrocardiography performed with GE MAC 1200.

Central biorepositories are under development as part of the H3Africa consortium. Specimens are currently stored at  $-80^{\circ}\text{C}$  at Noguchi Memorial Institute for Medical Research and will be subsequently shipped to the central biorepository.

### Bioinformatics

We have combined the bioinformatics capacity of the South African National Bioinformatics Institute (SANBI, University of the Western Cape), the University of Michigan, and Noguchi Memorial Institute for Medical Research to host and support a RedCap database for storage of participant information. Collaboration among the three sites allows for mirroring the database at three independent, geographically distinct sites, thereby permitting a secure backup system and

disaster recovery plan. The bioinformatics component of the Kidney Disease Research Network is closely integrated with the H3Africa Bioinformatics Network (H3ABioNet; [www.h3abionet.org](http://www.h3abionet.org)) for the entire consortium.

### Analyses

We plan to conduct comprehensive evaluation of the clinical characteristics, risk factors, treatment, and outcomes of the kidney disease cohorts (hypertension-attributed nephropathy, diabetes, HIV infection, sickle cell-associated CKD, and biopsy-proven glomerular diseases).

To conduct genetic analyses, we will use several approaches depending on the study question, such as case-control designs, family studies (whole exome), within-case, or candidate gene analyses of, for example, *APOL1* (15). A new

array to perform genome-wide genotyping across cohorts is being developed as part of the H3Africa consortium. Development of a new array will address the multiple African ancestry populations and maximize coverage of common and rare variants across Africa. This will be an important step to address the genetic architecture of Africans (16).

### Current Status of the Study

After a pilot study of 50 participants, we made changes to the case report forms and refined our recruitment methods and protocols for sample acquisition and sample integrity during shipment from international recruiting sites.

### Baseline Demographic, Clinical, and Biochemical Data

As of March 2015, a total of 3499 patients and controls have been recruited. Data entry at the clinical sites in Nigeria and Ghana is ongoing because intermittent Internet access has prevented complete data entry and corresponding data cleaning. Complete entry data for analysis are available for 1897 patients and controls, and the baseline data are shown in Table 4. There are 600 patients and 1297 controls.

About half (50.2%) of the cohort are female and 35 are children. Most patients with CKD are male (68.4%). The mean age of the CKD patients is  $48.5 \pm 14$  years. Diabetes mellitus was found in 14.0% and hypertension in 19.5% of patients.

Data quality was ensured by the use of a standard data entry interface (RedCap) with annual training and certification of data entry clerks. In addition, there is ongoing audit of entries. Duplicate testing on 90 randomly selected samples for serum creatinine, urine creatinine, and urine albumin showed close correlation between the assays.

Isolated DNA was of high molecular weight with only minor degradation and was usable for PCR and ligase detection reactions.

### Discussion and Unique Challenges for the Study

We have provided the rationale and methods to support the H3Africa Kidney Disease Research Network on the African continent with regional representation from West and East Africa. We have an ambitious goal to recruit approximately 4000 patients and 4000 controls with follow-up assessment of the cases to determine kidney disease progression. We are recruiting across the spectrum of CKDs that are common in Africa, including diseases related to sickle cell disease, HIV infection, diabetes, and hypertension-attributed nephropathy. Our study should shed light on the role of variants in the *APOL1* gene and hypertension-attributed nephropathy in individuals of African origin and new CKD genes (17–20). We have also included children in the overall cohort and specifically families with steroid-resistant nephrotic syndrome. We are making considerable strides in our recruitment and anticipate reaching our target goals in the next 2 years once all sites are recruiting.

The study aims to determine the health outcomes among patients with CKD of various causes in sub-Saharan Africa with detailed clinical phenotyping of both kidney disease and associated complications. This well characterized cohort will improve understanding of how environmental and genetic factors influence kidney disease. The study can also provide novel insight into the pathogenesis of kidney disease and its complications and therapies. Capacity building is also a cardinal objective of the study. This will be achieved through training of African clinicians and

**Table 4. Baseline demographic, clinical and biochemical data of participants in the H3Africa Kidney Disease Study (n=1897)**

Variable	Patients (n=600)	Controls (n=1297) <sup>b</sup>
Women, % (n)	35.2 (211)	57.2 (742)
Age (yr)	$48.5 \pm 14.0$	$43.1 \pm 14.7$
Weight (kg)	$70.0 \pm 15.7$	$70.1 \pm 17.9$
Body mass index (kg/m <sup>2</sup> )	$25.1 \pm 5.6$	$26.3 \pm 6.3$
<b>Study country</b>		
Ethiopia	0	0
Ghana	254	853
Kenya	0	0
Nigeria	346	444
Diabetes mellitus, % (n)	14.0 (84)	10.3 (133)
Hypertension, % (n)	19.5 (117)	9.1 (118)
<b>BP (mmHg)</b>		
Systolic	$141.4 \pm 25.8$	$124.7 \pm 21.7$
Diastolic	$83.1 \pm 16.8$	$74.9 \pm 13.8$
eGFR (ml/min per 1.73 m <sup>2</sup> ) <sup>a</sup>	$25.8 \pm 22.1$	$92.3 \pm 12.3$
eGFR $\leq 15$ ml/min per 1.73 m <sup>2</sup> , % (n)	46.5 (279)	0
Serum creatinine (mg/dl)	$5.9 \pm 5.5$	$0.9 \pm 0.2$
Urine albumin-to-creatinine ratio (mg/mmol)	$189.5 \pm 1471.8$	$10.2 \pm 61.7$
Hemoglobin (g/dl)	$10.5 \pm 6.2$	$13.4 \pm 8.7$

Values expressed with a plus/minus sign are the mean  $\pm$  SD. H3Africa, Human Heredity and Health in Africa.

<sup>a</sup>Measured with CKD-Epidemiology Collaboration equation (32) but without the race factor (33).

<sup>b</sup>Includes disease controls.

scientists in various aspects of genomic kidney disease research and providing infrastructure, including genomic laboratories and biorepositories, to be used for the current study and future projects.

### Ethical Issues

Rapid advances and decreasing costs of sequencing technology have resulted in growing engagement with human health genetics and genomics research on the African continent. This comes with many ethical challenges and responsibilities specific to Africa (21–23), which fall broadly into three categories. The first is the enormous cultural, linguistic, and ethnic diversity across the continent. This diversity means that each community may have very different needs from an ethics perspective and that limited data are available on local community-specific participant views of genomic data-sharing and related concepts, such as privacy and stigmatization. Our study will address this by employing trained local research nurses for the informed consent process.

Second, in many communities the population may be largely vulnerable because levels of education, literacy, and access to primary health care are poor. Specific efforts are therefore required to ensure that participants truly understand the aims of the study and any implications related to participation. Furthermore, where access to primary health care is limited, the informed consent process must be designed to ensure that participants do not consent to participation only because of perceived benefits of better access to health care. Insufficient funding and support for genetic counselors and ethicists can result in under-resourcing of these vital roles.

Third, at an administrative level, a lack of specific legislation or policy and differences in legislation across the many African countries can complicate studies involving multiple African partners. It is essential to harmonize the expectations and restrictions of multiple ethics review boards without compromising local legislature, and this can be a complicated process. It is becoming increasingly important to develop guidelines about how samples and data are shared going forward, and the H3Africa Data Sharing, Access and Release working group has addressed these issues with a consortium-wide policy (<http://h3africa.org/consortium/documents>). Availability of informed consent templates and documentation from prior or existing studies in Africa to inform approaches are limited, and the process must be developed anew for each study (23). The data and samples from all participants are de-identified and coded before being tested. Only the clinical centers hold identifying information, which allows return of biochemical and hematologic results to subjects. Other researchers have access only to coded data and samples. We obtained informed consent in a manner that permitted future DNA testing and data and sample sharing. Patient information and consent were designed to conform to H3Africa guidelines (24). In one center, patient information and consent documents were translated into local languages and videos of this were prepared to help comprehension.

### Challenges in Protocols and Institutional Ethics Review

This study has faced numerous challenges. A major delay is the process for institutional review board

approval. One of the nine clinical centers does not yet have approval from their national institutional review board. Approval in each country requires hospital, university, and often government approval. Because there are few studies spanning African countries with the goals of specimen collection and a central repository, each ethics board has also had concerns about study objectives and shipping specimens to other countries. This has affected the review process and also delayed material transfer agreements to allow shipment of biosamples between the sites. On the basis of the institutional ethics reviews across all sites, the total biosample collection also had to be reduced substantially. Moreover, collection of hair or nail samples was also removed because of various beliefs across the African continent concerning taking parts from a person.

An additional issue is the clinical phenotyping of CKD because detailed clinical tests or biopsies are not readily available in all countries and all participants. Hence, we have standardized definitions across all the centers in terms of clinical definitions of disease and will determine eGFR and proteinuria at time of enrollment.

### Recruitment Challenges

Initially, it was thought that piloting the study protocol in a dialysis population would provide a group that is highly motivated to participate. Recruitment of participants receiving dialysis, however, has been challenging. Most patients with ESRD are significantly anemic and cannot afford erythropoietin or thrice-weekly dialysis. Dialysis patients who consent to take part in the study often informed other patients about the amount of blood needed for the research study, which discouraged participation. Consented dialysis patients also started inquiring about having at least one free dialysis session or erythropoietin as a form of compensation for the amount of blood drawn. With some patient education, there is now a better understanding of a clinical research study and that there is no financial reward for participation. The participants' discussion of compensation is justified because almost all dialysis patients in sub-Saharan Africa either pay out of pocket or are sponsored by individuals or companies. The cost of dialysis in Africa does not differ significantly from that in developed countries; thus, most patients who are able to pay transition quickly to transplantation or pay for dialysis but infrequently (*e.g.*, <3 times per week). In fact, many children and adults cannot pay for RRT, and palliation is often offered. Advocacy for dialysis care and potential transplant is beyond the scope of the study goals, but investigators from all countries continue to work with clinical centers, governments, and the African Association of Nephrology to promote and advise about treatment options.

Surprisingly, recruitment of controls has been straightforward because they are recruited from churches, communities, and business offices, usually as part of screening or outreach programs. The eagerness on the part of most participants is driven by the fact that they wish to know their state of kidney health. Typically, an initial talk about the project is given to the community in the local language, with an open discussion to answer questions. Those who want to participate are given consent forms to read at home. Those who decide to participate are then recruited

after a week or two, when they have had ample time to read through the consent forms and understand the project. At the time of recruitment, additional questions are answered; after consent, they undergo a full study visit.

### Community Engagement

Our community engagement activities have focused on three different communities from which participants have been drawn: faith-based groups, professional organizations, and teaching hospitals. A fourth community engagement strategy is underway, involving setting up a community advisory board in each locale. For example, members of the National Kidney Foundation of Ghana, who are dialysis patients and are also opinion leaders in their communities, have been identified and are serving as liaisons between the research team and the stakeholders of the community, including chiefs, district chief executives, parliamentarians, and elders. Once this is fully established, we will facilitate training across all clinical sites to foster similar community engagement, in keeping with the policy of the H3Africa community engagement working group.

### Comparisons to CKD Epidemiology Studies Conducted in Other Settings

The protocols of the H3Africa Kidney Disease Research Network study and the CRIC study in the United States are similar; this allows comparisons because data were collected in a standard manner (25). Additional comparisons to European, Canadian, and Asian cohorts will also be important to understand the burden of CKD and the prevalence of comorbidities, such as cardiovascular disease across different ethnicities. The German CKD cohort study (26), the CKD Japan Cohort (27), the Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events (CanPREDDICT) (28), and the Spanish Morbimortalidad en Enfermedad Renal en pacieNtes diAbéticos y no diabéticos (MERENA) study (29) will also allow comparison for progression. We will also have the advantage of comparison with the CKD in Children study to understand differences in children (30). In Africa, the Moroccan population-based screening program entitled *Maladie Rénale chronique au Maroc (MAREMAR)* has identified CKD (eGFR < 60 ml/min per 1.73 m<sup>2</sup> or macroalbuminuria) in 2.9% of 10,524 patients with planned follow-up of 5 years. The study has been reported only in abstract form (31). The patients in the H3Africa Kidney Disease Research Network study were younger (mean ± SD, 48.5 ± 14.0 years) than those in CKD cohort studies in Europe and Japan, who were a decade or more older (26–29), but similar to those in CRIC (25). Of note, diabetes is less common, at 14.0%, than in the CRIC, CanPREDDICT, and CKD Japan studies, in which diabetes occurred in 29%–47% of cases (25,27,28). The H3Africa Kidney Disease Research Network study also differs from other studies in that it includes population and disease controls with no apparent kidney disease and also patients with a nephrotic syndrome. The use of young controls who may develop nephropathy in later life is justified because we are recruiting young participants. We will, however, test for an interaction effect between age and the gene variants studied.

### Building Capacity in Africa

An essential component of the Kidney Disease Network is to develop capacity within the continent to undertake further independent, large-scale research in genetic and environmental factors underlying the substantial disease burden of noncommunicable chronic diseases and specifically CKD. Key areas for capacity building include research skills development and data sharing among clinicians, molecular geneticists, clinical research field workers, trained bioinformatics specialists, ethicists, and genetic counselors; development of laboratory facilities and support to enable genetic analyses to be undertaken within Africa; and development of bioinformatics capacity and skills to enable storage and analysis of clinical, genetic, and genomic data within the continent. Developing the capacity for future kidney disease research projects that can be conducted locally in Africa or through pan-African collaborations will help retain skilled researchers and clinicians in their home countries. It will also ensure that samples and data collected from African participants can be fully used within Africa, by African researchers, to the benefit of African patients, according to the principles underpinning the H3 Africa initiative (7).

### Conclusion

The H3Africa Kidney Disease Research Network is making great strides to date, with >3000 participants recruited in just under 24 months. As additional centers obtain final ethics approval, recruitment targets will be met in the next few years. Despite the hurdles of conducting a sub-Saharan study among nine clinical centers from four countries, study investigators have been extremely successful in implementing and recruiting into the study. The results from this study will inform us on the environmental and genetic risk factors leading to CKD and its progression in Africa.

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### Disclosures

None.

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