Stakeholder Perspectives on Public Health Genomics Applications for Sickle Cell Disease: A Methodology for a Human Heredity and Health in Africa (H3Africa) Qualitative Research Study

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Abstract

Advances in omics technologies alone are not a guarantee that science will translate to robust responsible innovation that is firmly grounded in societal values. This study aimed to identify best practices for Ethical, Legal, and Social Implications (ELSI) research in Africa that allows for optimal integration of community perspectives into the design and implementation of genomics research. In a large sample of 346 stakeholders in Cameroon, Ghana, and Tanzania (59% women), we used a qualitative study design with a phenomenological approach and conducted 32 group and 74 individual interviews (25% rural). We imported interview recordings into NVivo software for analysis. We created a “concept map” to organize the coded information, with Perspectives on Genomics and Sickle Cell Disease (SCD) Public Health Interventions as the central themes. We found that (1) analyses of major subthemes across and within countries revealed differential knowledge and experiences of SCD, and perspectives on various aspects of research and genomics; (2) we were able to gather empirical data efficiently from urban and rural stakeholders, to study the issues related to sample sharing, consent processes, and return of clinical and genomic study results; (3) the concept of nondirectiveness in modern genetic medicine practice can be challenged by the views of stakeholders in the context of a high-burden disease such as SCD; and (4) linking community views to current and proposed public health interventions could be understood within the context of each specific country. Our work informs future qualitative social science and technology policy research designs on genomics applications in Africa.

Keywords: Africa, epistemology and ethics, genomics, global health, qualitative research, sickle cell disease, technology assessment

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Introduction

SICKLE CELL DISEASE (SCD) refers to a group of inherited red blood cell conditions, highly prevalent in sub-Saharan Africa (SSA), with 79% of more than 300,000 global births of Hb SS (homozygous genotype SS, sickle cell disease) occurring annually there (Piel et al., 2013). Inheritance of one sickle gene (heterozygous genotype AS, sickle cell trait [Hb AS]) affords protection against *Plasmodium falciparum* malaria (Elguero et al., 2015). However, inheritance of two sickle genes (Hb SS), or the sickle gene and another gene for a structurally abnormal hemoglobin (e.g., hemoglobin C, structural hemoglobin variant [Hb C]), leads to hemoglobin polymerization, loss of cell deformability, and changes in cell morphology during deoxygenation or dehydration (Makani et al., 2013). Clinical consequences include anemia, pain episodes, vulnerability to infection, and multiorgan failure (Makani et al., 2013).

Under-five mortality in SSA may be as high as 90% for children born with SCD (Grosse et al., 2011) with 70% of deaths estimated as preventable (Makani et al., 2011a). Despite the public health significance of SCD (World Health Organization, 2006), few countries in Africa have developed newborn screening programs for SCD; strategies for prevention and treatment of complications or family education and counseling (Wonkam et al., 2015). Understanding the genetics underlying the heritable subphenotypes of SCD would be invaluable in predicting vulnerability to stroke, kidney disease, and pulmonary hypertension, among other devastating sickle cell-related complications (Wonkam et al., 2015).

While SCD is caused by a single-gene mutation on the β -globin gene on chromosome 11, there is considerable phenotypic diversity, with a few known genetic modifiers—fetal hemoglobin (HbF) expression (Bae et al., 2012; Makani et al., 2011b; Mtatiro et al., 2014) and the coinheritance of alpha-thalassemia (Wonkam et al., 2014)—and many yet unknown. Advancements in genomics research could inform personalized therapeutics (Goodman et al., 2016) and contribute to discoveries of novel physiological targets for intervention (Steinberg and Sebastiani, 2012).

Innovations in genomics and multiomics research (proteomics, metabolomics, glycomics, and others) can lay the foundation for integrated approaches to addressing SCD health challenges in Africa, a veritable global health challenge (Tekola-Ayele and Rotimi, 2015; Wonkam et al., 2015). In particular, understanding the genomic basis of heritable SCD subphenotypes could inform personalized therapeutics and novel intervention targets. Advances in omics technologies alone are not a guarantee, however, that science will translate to robust responsible innovation that is firmly grounded in societal values, needs, and priorities. Hence, qualitative or social science research on genomics is critical to ensure translation of biotechnology to public health interventions. Despite the high prevalence of SCD in SSA and recurrent morbidity as well as the high risk of early death, there is limited research (particularly genomic research) on SCD in SSA and a paucity of data on attitudes toward genomic research.

There is also a paucity of data on the psychosocial impact and health-related quality of life of SCD on families. Obtaining information from families affected by SCD, professionals, and the lay public about attitudes toward genomic

research and the prevention of SCD-related complications would allow the identification of specific practical, psychosocial, and ethical challenges that need to be addressed to appropriately plan genomic research as well as SCD-related health resources and services and to guide provision of necessary support.

The Human Heredity and Health in Africa (H3Africa) initiative affords the opportunity to advance the study of genomics and environmental determinants of common diseases in Africa, including SCD (Rotimi et al., 2014). The H3Africa initiative as a whole draws increased attention to a number of long-standing and emerging issues in genetic and genomic research, such as informed consent, community engagement, privacy and confidentiality, (mis)use of genetic information, governance of biorepositories, reciprocity/benefit sharing, and ownership (http://h3africa.org/images/PDF/h3africa_whitepaper.pdf).

SCD research encounters most, if not all, of these issues, as well as others (e.g., genomic data sharing, return of research results and incidental findings, and obligation to family members) highlighted by genome-wide association studies (GWAS) and whole-exome/whole-genome sequencing that have been carried out in some settings, for example, Tanzania. Research on SCD also grapples with issues related to the inclusion of children in genomic research. There is a dearth of published research on the views of Africans and African communities concerning participation in genomic research, and virtually no information on their perspectives regarding several of these issues.

This range of issues suggests that ELSI research with the SCD population in Africa can inform broader discourse in relation to understanding how advances in genomics may impact the lives of people in developing countries (de Vries et al., 2011). It is not only critical to consider appropriate methodologies to gather perspectives from communities that simultaneously may benefit from emerging technologies and that may be at risk for exploitation in relation to these technologies but also to consider the social sciences and ethics context within which methodologies are designed and executed. It has been argued that current ELSI initiatives may constrain the structure and content of research agendas and in turn have limited influence on science and technology policies and practice (Williams, 2006).

Where ELSI research is by nature interdisciplinary and it is expected that the research will generate information about how to address potential pitfalls of technological development for societies and cultures, some scholars have cautioned that strategies for knowledge production, research questions, and individuals and organizations included in the ELSI field may have coalesced prematurely (López and Lunau, 2012; Williams, 2006). Juxtaposed with the assertion that the African voice and perspective remains marginalized in medicine and medical research generally (Tangwa, 2017) and genetic research specifically (Van Rinsum and Tangwa, 2004), it becomes imperative to ensure that appropriate methods are used for ELSI research conducted in Africa.

While there is a moderate amount of speculation and some theoretical/conceptual literature about the perceptions, utility, and impact of genomic research and SCD-related public health strategies in Africa, little empirical data are available. Empirical data from a broad spectrum of stakeholders are essential to the development of effective policies and

programs. It is therefore critical to understand implications of genomics research for individuals, families, and communities, and the most effective strategies to implement public health policies and regulations informed by research (Green and Guyer, 2011). Empirical data on perceptions about genomic research and about the utility and impact of SCD-related public health strategies in Africa are emerging for patients, families, and healthcare providers (Adeola Animasahun et al., 2012; de Vries et al., 2012; Dennis-Antwi et al., 2011; Marsh et al., 2011; Treadwell et al., 2015; Wonkam et al., 2011) but are lacking from other important stakeholders such as community and traditional leaders.

SCD research within the context of H3Africa provides an unprecedented opportunity to study genetic and genomic technologies in research, diagnosis, intervention, and treatment for SCD in Africa. This includes empirical social science research, critical for robust innovation. In particular, qualitative methods are well suited for the study of problems about which little is known and for health disparities research (Flaskerud et al., 2002).

In the current research, we included African centers already at the forefront of SCD research in Africa with moderate expertise on psychosocial research (Cameroon), newborn screening (Ghana), or genomics studies (Tanzania). We believe that this collaborative effort could serve as a reservoir for rigorous examination of a wide range of ethical, psychosocial, cultural, and policy SCD-related issues, and provides a model for the conduct of similar research with other conditions affecting African populations, and lays the groundwork for more extensive societal, ethics, and policy implications research in relation to emerging technologies.

While there is a growing literature describing ethical considerations for genomics research, the majority of that literature is not empirical in nature. This is true for issues relating, for instance, to broad consent (Tindana and de Vries, 2016), community engagement (Tindana et al., 2015), and

cell line creation (de Vries et al., 2014). Yet, a solid empirical understanding of individual and community views on genomic research and public health interventions is critical to informing the potential future development and application of such methods and interventions, as they may signal potential pitfalls as well as opportunities.

This report aims to identify best practices for ELSI research in Africa that allows for optimal community engagement and integration of community perspectives into the design and implementation of genomics research. Perspectives on the topics of interest were gathered from research scientists, health professionals, individuals with SCD and their families, traditional leaders, traditional healers, and other community stakeholders (e.g., lawyers, public servants, and educators). We also examined barriers to and facilitators of genomic research and public health interventions for communities in Africa, using SCD as an exemplar. In this article, we seek to contribute to an optimization of research methods for ELSI research in Africa.

Methods

Institutional review board (ethics) approval was obtained from all participating institutions. Informed consent was obtained from all study participants.

Sampling method

This cross-sectional study used a qualitative phenomenological approach to gather in-depth understanding of cultural influences on perspectives and attitudes about genomic research and on perceptions about public health interventions for SCD-related complications in Cameroon, Ghana, and Tanzania. We used purposive sampling of individuals and families affected by SCD, health professionals, and community leaders (Fig. 1). Our goals were to ensure participants would be knowledgeable informants within the domains of interest

FIG. 1. Schematic of the methodological approaches: training, pilot, and data collection. SCD, sickle cell disease; SCT, sickle cell trait.

(Matthie et al., 2015; Matua and Wal, 2015) and to capture the heterogeneity of the population potentially impacted by genomic research and SCD public health interventions (Tuckett, 2004).

Site principal investigators reached out in writing to potential key informants and to country and regional directors of health and heads of hospitals where patients with SCD were treated. Each country principal investigator obtained formal permission from local authorities and community elders to conduct the research. Key informants included SCD healthcare providers; traditional, governmental, and religious leaders; and patient advocates and SCD community support group leaders. Snowball sampling was used for later stages of data collection.

Participants

Participants were men and women, 18 years and older, representing both urban and rural areas of Cameroon, Ghana, and Tanzania. Inclusion criteria included the following: individuals affected with SCD and family members; health professionals (physicians, nurses, counselors, and health educators); members of the general public (students, teachers, and administrators); policy and religious leaders; and traditional leaders and traditional healers. Exclusion criteria included the following: patient populations and their families affected by conditions other than SCD; individuals younger than 18 years. Inclusion criteria were broad, as we anticipated that individuals we recruited would have some familiarity with SCD, given the high prevalence in the participating countries. However, familiarity with SCD was not required for participation nor was familiarity with issues in genomics research.

Instrumentation

Individual and group interview instrumentation was established in pilot focus groups conducted with healthcare providers in Ghana (Treadwell et al., 2015). Questions addressing perspectives on genomic research were added to the interview guides and pretested during the preparatory and training phase of the present study. To make the genomics research topics that were unfamiliar to study participants accessible, the final interview guide (available from M.J.T.) used vignettes depicting a couple (with a recognizable Cameroonian, Ghanaian, or Tanzanian family names) facing decision-making about genomics research and SCD public health interventions.

The vignettes, and standardized probes, guided discussion of the broad topics:

- (1) Perspectives on genomics research and its implementation and implications: informed consent; return of results; data sharing; data and sample storage; research with children; potential concerns with sample collection, that is, collection of blood versus saliva or skin samples; and strategies for community engagement to support participation in genomics research.
- (2) Perceptions of and experience with SCD and sickle cell trait: perceptions of and experience with newborn screening, genetic counseling, premarital screening, prenatal diagnosis, and stigmatization; and strategies for community engagement supporting uptake of sickle cell-related public health interventions and addressing stigmatization.

The interview guides included follow-up questions for answers that were vague or ambiguous to insure interpretability of results. Interview guides were translated and back translated for interviews conducted in French (Cameroon), Twi (Ghana), and Swahili (Tanzania). Interview participants completed a demographic information form indicating age, sex, marital status, ethnic group and region of origin, primary language, education, profession, and previous experience with SCD.

Procedure

Site principal investigators recruited research staff in each country to assist with study implementation. Research staff included geneticists, physicians, and nurses with previous experience with qualitative research and/or SCD research; medical residents; social scientists; and genetics or public health graduate students. Ghana research staff also included individuals who had obtained undergraduate degrees and who were completing National Service projects.

Research staff operated in teams, so that focus groups always included a discussion facilitator and a process facilitator who observed the group process and took detailed notes (Ruff et al., 2005). The process facilitator was also responsible for logistics and technical aspects of the sessions, for example, ensuring that the tape recorder was functioning and all needed supplies were available, including refreshments.

Before the onset of data collection, the primary investigative team (A.W., J.M., K.O.F., M.J.T., S.M.C., S.O.A.) conducted a week-long short course at the University of Cape Town for research team members, providing overviews of SCD, qualitative methods, and genomics research, with particular focus on principles and methods of ELSI research. We conducted in-country trainings to refine methodology as data collection commenced. In-country trainings focused on building team spirit for the field work; providing understanding of the H3Africa consortium; providing updates on SCD diagnostic, medical, and psychosocial issues, and issues in genomics research; and supervised practice in the conduct of the interviews.

To minimize variability in procedures, principal investigators provided active support in each country, assisting with trainings and data collection and also providing advice and guidance by e-mail, telephone, and Skype discussions. Sites were provided with a site coordinator's manual that contained information about strategies for participant recruitment and screening; enrollment logs; documentation forms for any unusual occurrences during data collection; site requirements; reference materials; and a template for recording field notes.

A feature of the individual and group interviews was the assurance of confidentiality, as much as possible, for study participants. Participants were assigned identification numbers and not identified by name, once consent forms were signed. Participants in the group interviews were assigned numbers that they wore as name tags, so that during group discussion, they were referred to only by number, for example, Ms. 4 and Mr. 7.

Data analyses

Digital recordings from individual and group interviews were cleaned of identifying information, translated as needed

into English and transcribed. Each transcription was reviewed for accuracy before being imported into NVivo qualitative data management program, version 11 (www.qsrinternational.com). We used thematic content analysis and deductive and inductive approaches, as we made successive coding passes through the verbatim transcripts generated from the interviews (Patton, 2002). We developed a pilot coding system for the thematic domains through a process of review and discussion. We started with initial themes generated from our formative research (Treadwell et al., 2015) and worked together on one transcript to update the coding scheme. Next, the lead investigator from each country coded two transcripts each and submitted these to the lead coder (J.D.V.), who created an NVivo “project” on a central, secure website at the University of Cape Town.

Two investigators (J.D.V. and D.B.) met in person over the course of a week to review the six coded transcripts in detail and further refined the coding structure and framework. This coding scheme was distributed to the research teams, who commenced coding transcripts. The coding scheme remained dynamic, with new codes developed by consensus as needed, given that we sought to split rather than lump content, not forcing text that did not quite fit into existing codes.

Data analysis is ongoing, as we are examining how different stakeholder groups and participants, based on country and setting (rural or urban), discuss and respond to topics raised in the interviews using the constant comparative method (Hsieh and Shannon, 2005). We make use of visual displays to examine relationships between different categories (Patton, 2002). Data from the different sets of interviews are triangulated so that data from each component are used to enhance understanding of results generated from the other sets of data. We are examining convergence of findings, different facets of the same phenomena and new perspectives.

We did examine participant characteristics (e.g., gender, education level, occupation) as self-reported on a brief questionnaire. However, because our research utilized qualitative methodology, thereby focusing on cases rather than samples, tests of statistical significance and the effect size statistic were not applicable to evaluating any differences between samples based on these characteristics.

Lessons Learned

In each country, the success of the project was based on first, engaging national SCD support groups (Sickle Cell Foundation of Ghana, Sickle Cell Foundation of Tanzania, and Globule Rouge Association in Cameroon) to build trust with the community of patients and their families, and second, by engaging leadership of the local investigators who had long-term research and clinical activities in SCD. The local investigators were able to facilitate various local administrative processes (e.g., ethics review boards), as well as the selection of local stakeholders for in-depth interviews. Third, we carefully selected field workers for the data collection and coding, and these included some medical or research professionals who were already working closely with individuals with SCD and their families. Fourth, we organized various strategies for ongoing communication across the sites, including in-country meetings, and convening at the biannual H3Africa consortium meetings.

Community engagement activities were embedded in the project from initiation, with the selection of in-country team members who had long-standing experience with individuals with SCD, their families, and healthcare systems. For example, in Ghana, we conducted the urban interviews in Kumasi, where the newborn screening program was started in 1995 and where 80–100 patients are seen in each specialist sickle cell clinic at Komfo Anokye Teaching Hospital. The Ghana research team was able to complete most of the individual and group interviews within a 2-week period, given their utilization of a full-time study recruiter, a nurse with a long-standing relationship with potential interviewees—individuals with SCD, and their families, and healthcare providers. The recruiter actively engaged the community, creating awareness about the research among affected individuals/families and with healthcare system leadership, and managed the interview schedule.

One important lesson learnt relates to the practicalities of analyzing data from multiple sites with a team of people residing at different locations. While the software we used for data analysis, NVivo, has a functionality that allows multiple people in different locations to work on the same data set (called NVivo Server), all participating institutions did not subscribe to this service and so it was not available to us. That meant that different teams worked on their own copy of NVivo and that we had to look for ways to e-mail the deidentified project files across countries and then merge databases while keeping track of each coder’s contributions. This complicated the work considerably, not in the least because we also worked on different operating systems (Apple and Windows). A second challenge relating to working with multiple country teams relates to ensuring that the development of coding schemes is transparent and inclusive of all individuals.

Because we were not able to work off the same file in disparate locations, we had to get people to travel to a central location to work on merging files and generating a coding scheme. This was not only costly it also delayed the work considerably because we were not always able to meet. Similarly, it also meant that only few individuals took a lead in developing the coding scheme, but they may not have had full knowledge of the particulars of each data set to ensure that the coding scheme represented the data set from each country. While we held regular Skype calls to try to ensure the development of the coding scheme was appropriate for each data set, with hindsight we think that this aspect of the multicountry project required some more careful thought and more significant resources.

Participant Demographics

Our aim was to conduct 18 group interviews with individuals with SCD and their families and 18 groups with healthcare providers and other community members, for a total of 36 groups, with equal representation of affected individuals/families and healthcare providers/other community members. We ended up conducting 32 groups, 12 in Ghana, 11 in Tanzania, and 9 in Cameroon—15 (47%) of these with individuals with SCD and their families. We also had the goal to collect data from approximately 360 participants across the three countries—we obtained data from 349 participants. Figure 1 depicts the study flow and number of participants.

TABLE 1. DEMOGRAPHICS AND CHARACTERISTICS OF HEALTHCARE PROVIDERS AND COMMUNITY MEMBERS IN CAMEROON AND GHANA (N=160)

	Cameroon (n=71)	Ghana (n=89)
Gender (female), n (%)	41 (58)	57 (64)
Location (rural), n (%)	21 (30)	26 (29)
Education, n (%)	39 (55) Tertiary 32 (45) Secondary	62 (70) Tertiary 12 (13) University 9 (10) Secondary 3 (3) Primary
Occupation, n (%)	26 (37) Nursing or midwifery 11 (15) Physicians 10 (14) Other medical 8 (11) Business and government 4 (6) Students 2 (3) Educators 1 (1) Religious leader 1 (1) Traditional leader 1 (1) Trader	39 (44) Nursing or midwifery 8 (9) Physicians 12 (13) Other medical 9 (10) Business and government 7 (8) Educators 5 (6) Religious leaders 3 (3) Traditional leaders

All participants did not provide a response in every category, so numbers in each category and percents in each category do not always add up to 100% for Cameroon and Ghana. Demographic information was not consistently collected from the Tanzanian sites and is not presented.

Tables 1 and 2 provide demographic details about study participants in Cameroon and Ghana. Overall, there were more females than males who participated (61% of providers and community members and 58% of individuals with SCD/families). Participants were predominantly interviewed in

TABLE 2. DEMOGRAPHICS AND CHARACTERISTICS OF INDIVIDUALS WITH SICKLE CELL DISEASE AND THEIR FAMILY MEMBERS IN CAMEROON AND GHANA (N=85)

	Cameroon (n=25)	Ghana (n=60)
Gender (female), n (%)	12 (48)	37 (62)
Location (rural), n (%)	3 (12)	11 (18)
Education, n (%)	8 (32) University 10 (40) Secondary 2 (8) Primary	3 (5) University 10 (17) Tertiary 40 (67) Secondary 4 (7) Primary
Occupation, n (%)	1 (4) Nurse 3 (12) Business and government 1 (4) Educator 8 (32) Students 3 (12) Housewives 1 (4) Trader 1 (4) Painter	4 (7) Business and government 2 (3) Educators 6 (10) Students 1 (2) Builder 1 (2) Farmer 21 (35) Traders 13 (22) Unemployed

All participants did not provide a response in every category, so percents in each category do not always add up to 100% for Cameroon and Ghana. Demographic data were not consistently collected from the Tanzanian sites and are not presented.

urban settings (71% of providers and community members and 84% of individuals with SCD/families). Healthcare providers/community members were more similar to individuals with SCD and their family members with regard to educational levels in Cameroon (45% secondary education compared with 40% secondary education), while healthcare providers/community members had obtained significantly higher education in Ghana (86% tertiary/university) compared with 22% of individuals with SCD and family members. Similarly, individuals with SCD and their family members evidenced greater representation in lower income professions (e.g., students, traders, housewives—49%) compared with community members who were predominantly in the healthcare professions (66%) in both Cameroon and Ghana. We were able to recruit six religious leaders, four traditional leaders, and three traditional healers into the study. English was used in the conduct of interviews in all countries, as well as Swahili in Tanzania, Twi in Ghana, and French in Cameroon.

Preliminary Coding Scheme and Planned Analyses

Figure 2 depicts an adaptation of the coding scheme developed by the project team as a “concept map,” a diagram that visually organizes information (L Allen et al., 2015; Novak, 2003; Wilson et al., 2015). Each concept or theme connects to another, and links back to the central concept Perspectives on Genomics and SCD Public Health Interventions. Our concept map reveals connections among individual ideas that form the larger whole. Subthemes that branch from the central concept include knowledge and experiences of SCD, and perspectives on various aspects of research, on screening and genetic tests, and on ethical issues. Education about SCD and genomics and issues of stigma comprises additional aspects of the coding scheme.

We are in the process of completing data analyses for research questions across the three-country collaborative and within each country based on our review of the coding. We are preparing reports on stakeholder perspectives on the sharing of genomic and health-related data and samples, linking our analysis to evolving international views on what constitutes good governance for global sharing of data and samples; on stakeholder perspectives on the consent process, including reasons for giving or refusing consent, who should be approached for consent, and the role of trust in consent. We are exploring stakeholder perspectives on the return of clinical and genomic study results to individual participants in SCD genomics research as well as the concept of non-directiveness in genetic counseling in the context of high-burden disease, here, SCD.

We are reviewing beliefs and understandings about causations and manifestations of SCD within our three collaborating countries separately, and linking community views to current and proposed public health interventions within each country. Because we were able to interview more religious leaders in Ghana, compared with the other countries, we have been able to explore perspectives on the importance of collaborating with religious institutions in establishing policy and practice related to sickle cell public health interventions in that country. Our data set offers one of the first empirical examinations of the influence of the worldview of Ubuntu (a person is a person through other people) on the research

FIG. 2. Concept map of preliminary coding framework. This concept map is adapted, for ease of viewing, from an image generated within NVivo Qualitative Software for Research. The original concept map is available in Supplementary Figure S1.

consenting process among a range of stakeholders in the three African countries.

Discussion

In this report, we have provided some clues to identify best research practices for ELSI research in Africa that allow for optimal community engagement and integration of community perspectives into the design and implementation of genomics research and intervention strategies. This research is important for H3Africa and for other geographies and technologies, as it provides an example of an efficient approach for best methodological practices in the conduct of rigorous research on ethical, legal, social, and/or policy implications of genetics and genomics in low- and middle-income countries not only in Africa and possibly globally.

Specifically, our approach emphasized the following: (1) the importance of engaging local motivated research leadership to optimize efficiency; (2) the importance of engagement of community stakeholders at all stages of data recruitment (here, including SCD patient support groups); (3) the inclusion of a carefully selected range of stakeholders, from urban and rural communities; (4) the need to combine approaches (in-depth interviews and focus group discussions) to allow a range of stakeholders to participate; and (5) the need to assemble an interdisciplinary team of African-based researchers and international experts in SCD, global health, and ethnography from various fields (genetics, psychology, social science, bioethics, philosophy, clinical) in a collaborative way, in designing and performing the research.

Our approach of sharing experiences across multiple disciplines has not only allowed for the generation of exceptional and much needed data on genomics and ELSI in Africa but has also enhanced experiences for our team members. We have also established a foundation for well-organized and effective training of future African scholars with expertise in bioethics and social sciences. The ultimate goals of H3Africa include investing in improving the general knowledge of genomics among African communities by identifying traditional knowledge and cultural practices around which new concepts in genomics can be built, for integration into the understanding of African populations. The present ELSI research will provide evidence-based support for the development of guidelines for regulatory aspects of genomics research and its use.

We hope that our research will inform the development of culturally appropriate means of engaging with research participants and communities about issues related to research—sample collection and the creation and governance of databases and biobanks and public health interventions, here in relation to SCD. Our goal is also to inform the broader scientific community with regard to emerging technologies, social science, ethics, and policy. Mapping the values associated with embedding new technologies into societies and cultures is of critical importance, for practical reasons, to ensure optimal uptake and also from a normative ethical stance (de Vries et al., 2011, 2012).

The past three decades have seen solid scholarship on the sociology of scientific knowledge that is often underappreciated in ethics research and yet highly relevant for robust

technology ethics and policy research (de Vries et al., 2011; López and Lunau, 2012; Williams, 2006). There are very limited data on this topic from Africa. Results from our full analyses and outcomes of this research will enhance a deeper discussion needed on innovation theory and epistemology of technology assessment, on how best to assess risk, uncertainty, and unknowns associated with emerging technologies or scientific applications in Africa.

The present research is innovative in three key ways. First, its focus on populations in SSA responds to the need for increased inclusion of diverse populations in research on the ethical, psychosocial, and societal implications of genomic research. The data have provided a unique opportunity to gather information, from populations in different countries and regions in SSA, on some topics that have not yet been explored in Africa.

Second, SCD, the first to be described as a molecular disease, continues to be a major cause of mortality, morbidity, and health disparities in SSA and globally. In addition, many of the newer tools and techniques in genetics and genomics are yet to be applied to SCD on a large scale, particularly in SSA. Research has explored novel societal implications research in a largely untapped patient and stakeholder population with regard to genomic technologies.

Third, although other studies have utilized qualitative approaches to gather perspectives that allowed identification of unanticipated phenomena and influences and lay the foundation for future hypothesis testing, we brought together a unique interdisciplinary, international, and collaborative team that has generated information to enrich the best practices for ELSI research in Africa and beyond. Overall, this research has generated a wealth of rigorous new knowledge on a broad range of complex, unresolved, and timely ethical, psychosocial, and public health issues related to genomic research and SCD in SSA.

We were able to recruit a large, diverse sample of stakeholders, who provided us with vital information about perspectives and attitudes about genomic research, and its implementation and implications in SSA. We effectively engaged the broadest range to date of community members in SSA as we gathered perceptions about public health interventions to increase awareness, early detection, and prevention of SCD-related complications. We have devised a coding scheme and have begun within- and across-country analyses that already show promise to elucidate key concepts in community perspectives on genomics and SCD public health interventions in SSA.

One of the biggest challenges that we faced in executing this complex study was limited face-to-face contact among the research team members in the participating countries. Despite our efforts to maintain e-mail and Skype communication (which was not always reliable), we believe that data collection would have been expedited if it had been possible to schedule more than one annual face-to-face meeting of the teams. This is particularly important because a goal of H3Africa is to build capacity (Dandara et al., 2014; Tekola-Ayele and Rotimi, 2015), here in the conduct of qualitative research.

When the principal investigators (PIs) were on the ground with the research teams, we found that we were able to problem solve issues as they arose. We believe that some of the logistics of organizing the research activities might have

moved along more quickly if the investigators were not dispersed within three U.S. states and four African countries. Momentum of the teams was sometimes slowed by lengthy timelines for completing and submitting ethical applications, as well as for training and the field testing instruments. Even within each country, members of the research team sometimes had competing activities from their usual employer so that interviews were postponed or canceled.

Limitations

Language differences posed some barriers, despite having multilingual research team members within each setting. Additional staffs were recruited to transcribe interviews that had been completed in Twi or Swahili back into English, to allow data analysis. Research team members were not always facile in the dialects of people in the rural areas and found that some scientific concepts were difficult to translate. Examples of challenging terms/concepts included prenatal diagnosis, use of saliva and hair in genetic testing, and data sharing across countries. We cannot know for certain that concepts that were discussed actually had equivalents in all languages that were represented.

Other issues included the length of the individual and group interviews, particularly for health professionals who needed to report back to work. In the future, we might ask that health professionals receive protected time to allow for their participation. Even individuals with SCD and their family members could appear fatigued with the length of the interviews and although we have not thus far observed deterioration in the quality of answers provided over the course of interviews and group discussions, we are alert to that possibility as our data analyses are finalized.

Organizing space for conducting the group interviews was sometimes a challenge. Individuals with SCD and their family members could become emotional, particularly when discussing feelings of stigmatization. It was critical that some research team members had experience with providing psychosocial support and were linked with the sickle cell support groups, so that they could provide support as needed immediately and could connect distressed individuals with the proper resources after the group session. Special circumstances arose for the teams, for example, one mother of two children with SCD ages 7 and 14 years who was contacted to participate in the research had in fact not been informed by the Newborn Screening Program of the children's diagnosis.

The differential health systems and levels of care across sites did not necessarily allow a reasonable comparison related to genetics and public health intervention. For example, in Ghana, newborn screening for SCD has been an integral part of clinical practice and well known to health professionals and families, while newborn screening has not yet been consistently implemented in Cameroon and Tanzania. In Cameroon and Ghana, the distinction between rural and urban healthcare settings was quite clear but in Tanzania, there was only one center, at Muhimbili Hospital in Dar es Salaam where individuals from throughout the country came to receive care.

Our community engagement efforts presented both strengths and weaknesses. Activities were not always well budgeted for, so were performed opportunistically, with the help of the long-term relationships of the local PIs with the support groups. A well-structured community engagement plan that

was consistent across counties would have allowed us to plan for measurable impact of the outcomes of the research and implementation of public health interventions and future policies in the three settings where the study was done. We may need to revisit our community engagement strategies as we develop programs and policies that are relevant to each community's needs.

Conclusion

There is a dearth of published research on the views/perspectives of Africans regarding genomic and ELSI issues. The values and practices of health professionals and community members must be considered, to ensure culturally appropriate strategies to fully realize the potential of genomic research to improve health and to here, improve awareness, early detection, and prevention of SCD complications. Our results will allow the identification of practical, psychosocial, and ethical challenges that are associated with genomics research in general and genomics and SCD prevention and care in SSA.

Our results will help to guide recommendations for ELSI research approach in African in general, and as various OMICs are implemented, for preventive and care policies that are optimally designed to engage potentially affected communities so as not to conflict with community perceptions, behaviors, and culture. Finally, our didactic and field training contributes to the development of the research infrastructure in SSA for the conduct of qualitative research. Our work informs future qualitative social science and technology policy research designs on genomics applications in Africa and resource-limited settings, and how best to engage with communities affected by SCD in the course of translational research from laboratory to society.

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Availability of Data and Materials

The data set supporting the conclusions of this article, including raw transcript data, is available from authors on request.

Authors' Contributions

M.J.T., J.M., K.O.F., S.O.A., S.M.C., J.D.V., G.T., C.D.R., and A.W. conceived the study, participated in its design, interacted with the participants, and drafted the manuscript. D.B., J.D.A., K.K.K., C.M., and E.T.W. performed interviews,

transcriptions, and translations and helped to draft the manuscript. All authors read and approved the final manuscript.

Author Disclosure Statement

The authors declare that no conflicting financial interests exist.

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Abbreviations Used

ELSI = Ethical, Legal, and Social Implications
 H3Africa = Human Heredity and Health in Africa
 HbF = hemoglobin F, fetal hemoglobin
 Hb SS = homozygous genotype SS, sickle cell disease
 SCD = sickle cell disease
 SSA = sub-Saharan African