SICKLE CELL DISEASE AWARENESS, WILLINGNESS TO BE TESTED AND WILLINGNESS TO PARTICIPATE IN GENETIC COUNSELING AMONG AFRICAN IMMIGRANTS OF THE DEMOCRATIC REPUBLIC OF CONGO IN NORTH TEXAS

Ndolembai S. Njesada, MPH, BS

APPROVED

Dennis Thombs, Dean, UNTHSC
School of Public Health
David A. Sterling, Committee Co-Chair
Karabi Nandy, Committee Co-Chair
Amy Raines-Milenkov, Committee Member
Richard Young, Committee Member
Ubydul Haque, University Member

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Ndolembai S. Njesada, MPH, BS

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DEFINITIONS

For the purpose of this dissertation, the following definitions are provided as a reference:

- Sickle cell disease (SCD): An inherited disease in which the red blood cells have an abnormal crescent shape, block small blood vessels, and do not last as long as normal red blood cells. Sickle cell disease is caused by a mutation (change) in one of the genes for hemoglobin (the substance inside red blood cells that binds to oxygen and carries it from the lungs to the tissues) (NHI, 2019).
- Sickle cell trait: A person carrying the defective gene, HbS, who also has some normal hemoglobin HbA. Persons with the sickle cell trait are usually without symptoms of the disease, but mild anemia may occur under intense, stressful conditions, exhaustion, hypoxia (low oxygen), and/or severe infection. The sickling of the defective hemoglobin may occur and result in some complications associated with sickle cell disease (UMMC, 2010).
- Sickle cell awareness is the ability to understand that SCD is an inherited (genetic) blood disorder that is transmissible by both parents to their progenitures. This also includes understanding that SCD is predominantly found among Black (Africans).
- Willingness to be screened for SCD/T is to agree, if opportunity is given, to be screened for sickle cell trait or sickle cell disease.
- Genetic counseling is the process through which knowledge about the genetic aspects of illnesses is shared by trained professionals with those who are either at an

increased risk, have an inheritable disorder or may pass a disease on to their unborn offspring (WHO, 2019).

CHAPTER 1

BACKGROUND AND SIGNIFICANCE

Background

While considerable efforts are being dedicated to tropical and infectious diseases worldwide, multiple hemoglobinopathies are not being significantly considered. The establishment of the Global Fund to fight HIV-AIDS, Malaria and Tuberculosis are great examples of global investment in reducing the global impact of these preventable and curable diseases (Katz, Komatsu, Low-Beer, & Atun, 2011; Komatsu, Korenromp, Low-Beer, Watt, & Dye, 2010). However, the continued burden of birth defects has been considerably neglected (Christianson, Howson, & Modell, 2006; Howson, Christianson, & Modell, 2008; Weatherall, 2011). Among the most recurrent hemoglobinopathies, sickle cell disease (SCD) is the largest disorder of public health concern resulting in over 300,000 children born every year with the defective gene worldwide. Although the exact number of SCD patients in the USA is unknown, there are an estimated 72-100,000 diseased cases in the USA with 1 in every 13 Black or African American babies born with sickle cell trait (SCT) and more than 2 million African Americans who have the traits, with an incidence of 1 out of every 365 Black or African-American births (Christianson et al., 2006; Creary, Williamson & Kulkarni, 2007; Piel et al., 2013; United Nation General Assemby, 2008; World Health Organization [WHO], 2006b). It was only beginning in 2010 that hemoglobinopathies were included in Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) (Murray et al., 2012), a study to provide assessment of the burden of major diseases and injuries through a systematic and comprehensive evidence base.

Sickle cell anemia (SCA) is defined as a multisystem disease associated with acute episodic illnesses that leads to organ disfunction, recognized by the polymerization of hemoglobin. This leads to the rigidity of erythrocyte and vaso-occlusion that are central to the pathophysiology of SCD (Rees, Williams, & Gladwin, 2010). From SCA, chronic anemia, vasculopathy and hemolysis have also been established from the common cause that results from the hemoglobin S (HbS) variant. This abnormal hemoglobin (HbS) is produced by a point mutation in the β-globin chain of adult hemoglobin (HbA) (Ingram, 1958).

Hemoglobin S (HbS), compared to normal hemoglobin Hb, has a lower affinity to oxygen and is prone to polymerization upon deoxygenation. The polymerization leads to the distorted shape of the red blood cell (sickled) appearance. Vaso-occlusion results from the adherence of sickled red blood cells, and its fragility leads to hemolysis. The fragility and polymerization lead to multiple clinical consequences of vascular occlusion, including but not limited to acute chest pain, venous thrombosis, bone and joint pains and stroke (Rees et al., 2010). From multiple studies conducted by Pawloski, Hess, & Stamler, it was concluded that abnormal or sickled red blood cell vaso-activity contributes to the vaso-occlusive pathophysiology of SCA depending on the phenotype variation of the gene that leads to various expression of the disease in patients (2001, 2005).

The highest frequency of sickle cell disease is seen in the sub-Saharan regions of Africa (Piel et al., 2010). Nigeria and the Democratic Republic of Congo (DRC) are the two countries in the region with the highest prevalence and mortality related to SCD (Debaun & Galadanci, 2018; Piel, Hay, Gupta, Weatherall, & Williams, 2013). Many of the cases are seen in low and middle-income countries where, without early diagnosis

and treatment of the disorder, those who fully develop the disease die within the first few years of life with reported excess mortality exceeding 90% (Grosse et al., 2011; Piel et al., 2013). Undiagnosed and diagnosed patients may produce early series of painful swelling of the hands and feet known as dactalytis, jaundice in newborns, and icteris-whites of the eyes. Such symptoms and early signs arise at about 5 to 6 months of age in newborns (Piel et al., 2013). Furthermore, many of the carriers of the hemoglobin S, who are heterozygous (children and adults) are asymptomatic and are less likely to be tested, despite continued epidemiological transition and improvement of public health policies and infrastructures (Piel et al., 2013) in low and middle-income countries. Hence, there is a need for further studies.

The economic cost related to SCD is rising in low, middle and high-income countries. Even though the focus on early diagnosis (newborn) is proven to provide proper treatment and pain management, and therefore reducing mortality and increasing life expectancy in the high-income countries like United States of America (USA), the burden of the economic cost related to sickle cell continues to increase (Piel et al., 2013). The cost related to emergency department visits, hospital (re-)admissions and pain crises management continues to rise with a lifetime cost care averaging $460,151 per patient with sickle cell disease and higher mortality rates among adults in the USA (Kauf, Coates, Huazhi, Mody-Patel, & Hartzema, 2009; Lanzkron, Carroll, & Haywood, 2013; Quinn, Rogers, McCavit, & Buchanan, 2010). The economic cost is growing with an average of $13,237 per child per hospital stay (Mvundura, Amendah, Kavanagh, Sprinz, & Grosse, 2009) with a yearly hospitalization cost of $488 million (Singh, Jordan, & Hanlon, 2014).

Significance

Following the globalization pattern of the world linked to migration related to economic and educational opportunities and political stabilities, SCD is now being seen around the world, whereas it used to be rare. This global migration of sickle cell disease has led the United States, France and the United Kingdom (UK) to amend universal screening for newborns (Weatherall & Clegg, 2001). However, the noted universal screening is merely a partial solution to the migratory pattern of sickle cell disease. The complexity and continuity of migration will continue to challenge the cost, the treatment, healthcare utilization and the preventive measures of sickle cell anemia in high income countries like the United States of America. Sickle cell disease comprises not only sickle cell anemia, but also combined hemoglobinopathies, such as sickle hemoglobin C (Hgb SC) and sickle β-thalassemia (Hgb ST). On a worldwide basis, more than 300,000 children are born each year with SCD (Piel et al., 2013). However, inadequate screening and lack of diagnosis lead to underestimation of sickle cell disease and sickle cell traits. Immigration to the U.S. may have led to an increased number of SCD patients due to the lack of selective screening of immigrants originating from endemic countries (Weatherall & Clegg, 2001).

Since the United States is seen as a land of opportunities, many people come as students, visitors, businessmen, refugees or asylees. Regardless of their status of entry or their country of origin, immigrants seek education, economic stability and integration within the American system. According to the Migration Policy Institute (MPI), in 2016 there were 43.7 million immigrants living in the United States, which represented 13.5 percent of the total U.S. population (Zong, Batalova, & Hallock, 2018). Of the immigrant

population, African immigrants accounted for 2.1 million (Migration Policy Institute, 2018b). Nearly half of the immigrants reside in three states, of which Texas is ranked second after California with 11% of all immigrants (Lopez, Bialik, & Radford, 2018). In Texas alone, the number of immigrants in 2016 totaled over 4.7 million, with more than 235,000 coming from Africa (Migration Policy Institute, 2018a). More specifically, 41 percent of all refugees arriving in Texas in fiscal year 2017 were from Democratic Republic of Congo (Department of State Bureau of Population, Refugees, and Migration, 2018). Such movement, specifically from countries endemic to sickle cell disease, could have a role in the medical cost and the increased severity of SCD in the U.S. The above-mentioned severity lies in the following fact: Nigeria, the Democratic Republic of Congo and India alone represent 57% of the annual number of newborns with sickle cell disease globally. This number is projected to increase with Nigeria's relative contribution from 30% to 35% by 2050 (Piel et al., 2013). Nigeria alone is estimated to have over 150,000 newborns with sickle cell disease each year (Odunvbun, Okolo, & Rahimy, 2018; United Nations International Children's Emergency Fund [UNICEF], 2018). Therefore, a specific focus on immigrants arriving from endemic countries is paramount to understanding the medical and economical complexity of sickle cell disease in the U.S.

Despite the influx of immigrants from countries with high prevalence rates of sickle cell disease to the United States (Weatherall & Clegg, 2001), and the efficacy of selective screening of SCD of at-risk populations (Panepinto, Magid, Rewers, & Lane, 2000), there is a lack of established screening systems and a continued poor understanding of the selective screening - other than the newborn mandatory screenings - for entering at-risk immigrants in the United States. Reducing health costs and emergency department visits

related to sickle cell disease in adults may see an alleviation, if such targeted screening is initiated.

In review of the current mandatory sickle cell disease screening in newborns, more than 10 states made screening mandatory by 1972. However, by 1974, all 10 states repealed these laws as the revealing of the disease was depicted as discriminatory, and medical insurance coverage was denied to such patients (Rutkow & Upton, 1974). It was only starting in 1975 that states began to successfully sustain these mandates. Over the years, there has been an increase in the number of states that legally mandate sickle hemoglobinopathies screening, with South Dakota being the last state to mandate in 2005 (Benson & Therrell, 2010). Nevertheless, sickle cell disease mortality continues to increase among adult patients, raising questions about whether mandatory screening laws for newborn are overall effective. One may argue that early detection and treatment of SCD have been shown to have a positive impact on managing the disease and the traits later in life (Myundura et al., 2009). However, the effectiveness of such laws in reducing medical cost in adults remains unclear.

Although curative and management measures are known, sickle cell disease continues to ravage young people, vulnerable populations, and minority groups (WHO, 2006b). SCD causes high morbidity and mortality rates, predominately in children under the age of five and among adolescents and pregnant women in the United States (Dennis-Antwi, Dyson, & Ohene-Frempong, 2008). Sickle cell disease mortality continues to increase among adult patients (Quinn et al., 2010). Furthermore, women with SCD at childbearing age experience more gynecological complications than those who do not have the disorder and are more likely to pass on the disease to their offspring (Creary,

2007). Assessing the awareness – as understanding of SCD as a genetic disorder most frequent in Africans or Blacks–, the willingness of immigrants to be tested and their willingness to participate in genetic counseling will provide a greater understanding in the development of approaches to reduce pain crises, emergency department visits, and healthcare costs related to sickle cell disease in the U.S (Kauf et al., 2009).

Purpose Statement

The overall aim of this exploratory research was to assess the awareness of SCD defined as the ability to define SCD as genetic blood disorder most frequent in Africans, the willingness to be screened for sickle cell disease, and the willingness to participate in genetic counseling among African immigrants from the Democratic Republic of Congo in North Texas through in-person surveys. In this exploratory research we examined the following aims:

Specific Aims and Research Questions:

1. Specific Aim 1: Explore the awareness of sickle cell disease among African immigrants from Democratic Republic of Congo.

    Hypothesis 1.1: Gender is significantly associated with sickle cell awareness.

        Research Question 1.1.1: Is gender, a known factor for gender difference in SCD survival, significantly associated with sickle cell awareness in this population?

    Hypothesis 1.2: Demographic factors such as education, age, income level,

and marital status are significantly associated with sickle cell awareness.

Research Question 1.1.2: Are factors such as education, age, income level, and marital status significantly associated with sickle cell awareness, controlling for gender?

Hypothesis 1.3: Immigration factors such as immigrant status, interpreter needed during medical visit, and number of years lived in the USA are significantly associated with sickle cell awareness, controlling for gender.

Research Question 3: Are immigrants factors such as immigrant status, interpreter needed during medical visit, and number of years lived in the USA, controlling for gender?

Finally, all of the above factors under aim 1 are tested to determine which factors are significantly associated with sickle cell awareness among African immigrants from DRC.

2. Specific Aim 2: Explore willingness of African immigrants from Democratic Republic of Congo to undergo sickle cell testing.

Hypothesis 2.1: Gender is significantly associated with willingness to be tested for sickle cell disease.

Research Question 2.1.1: Is gender significantly associated with sickle cell testing in this population?

Hypothesis 2.2: Demographic factors such as education, age, income level, and marital status, are significantly associated with willingness to be tested for SCD.

Research Question 2.2.1: Are demographic factors such as

education, age, income level, and marital status, significantly associated with willingness to be tested for SCD?

Hypothesis 2.3: Immigration factors such immigrant status, language proficiency, and number of years lived in the USA are significantly associated with willingness to be tested for SCD.

Research Question 2.3.1: Are immigration factors such immigrant status, number of children, and number of years lived in the USA significantly associated with willingness to be tested for SCD?

Finally, all the above factors under aim 2 are tested to determine which factors are significantly associated with willingness to be tested for SCD among African immigrants from DRC.

3. Specific Aim 3: Explore willingness of African immigrants from Democratic Republic of Congo to participate in SCD genetic counseling.

Hypothesis 3.1: Gender is significantly associated with willingness to participate in SCD genetic counseling.

Research Question 3.1.1: Is gender associated with willingness to participate in SCD genetic counseling?

Hypothesis 3.2: Demographic factors such as education, age, income level and marital status are associated with willingness to participate in SCD genetic counseling.

Research Question 3.2.1: Are factors such as education, age, income level and marital status associated with willingness to

participate in SCD genetic counseling?

Hypothesis 3.3: Immigration factors such as immigrant status, language proficiency, and number of years lived in the USA are significantly associated with willingness to participate in SCD genetic counseling.

Research question 3.3.2: Are immigrations factors such as immigrant status, language proficiency, and number of years lived in the USA significantly associated with willingness to participate in SCD genetic counseling?

Finally, all the above factors under aim 3 are tested to determine which factors are significantly associated with willingness to participate in SCD genetic counseling among African immigrants from DRC.

Overview of Remaining Chapters

Chapter 2 will focus on a thorough literature review and critiques of established knowledge regarding sickle cell disease awareness and knowledge, and genetic counseling based on sociodemographic and socioeconomic of African immigrants in general but with specific attention to Congolese from the Democratic Republic of Congo. The findings and gaps from the review will elucidate on the gap related to the constantly increasing healthcare costs related to sickle cell patients in high income countries like the United States of America. Furthermore, this chapter will investigate the root causes of the continuous increase in healthcare expenditures of sickle cell disease, which is due mostly to the lack of information on the sickle cell status of immigrants in the USA from most endemic countries of the world. This chapter will draw on the gaps in literature to guide

the methodology used to fill these gaps through the exploratory cross-sectional study resulting from a survey.

Chapter 3 will focus on the methodology used to obtain the information and/or test the stated aims above. The study used a cross-sectional in-person survey design method. This survey was developed for the purpose of this study and was administered to immigrants from Democratic Republic of Congo who live in North Texas to investigate awareness of sickle cell disease and willingness of subjects to be tested for the disorder. The goal was to complete at least 186 convenient sample interviews from the defined African immigrant population of North Texas.

Chapter 4 presents the results of the survey and its findings specific to the research aims. Chapter 5 discusses the results of the survey and its findings. This chapter considers the implication of the findings in relationship with previously available knowledge. Furthermore, this chapter contrasts the results presented with existing knowledge. A conclusion is drawn in Chapter 6 with suggested alternatives to increase awareness and willingness to be screened, along with proposed solutions to reduce healthcare expenditure directly related to sickle cell disease. This section also suggests implementation of state legislative laws for selective screening for immigrants arriving from countries where sickle cell disease is endemic.

Assumptions and Limitations

The survey was designed to collect general information on sickle cell disease, but some sensitive information was requested as well. Given the sensitivity of such information, it is assumed that responses from participants were based on honesty. The consent form clearly stated the anonymity of the data collected for the protection of the

participants. It is also assumed that the participants accurately recalled information regarding previous screening for SCD. The limitations of this survey included limiting the interview to being only in English.

The geographical limitation of the study to only immigrants of DRC aleniates immigrants from other endemic countries like Nigeria and India. Additionally, the survey was conducted only in the Dallas, Denton, Fort Worth and Arlington Metroplex area of North Texas. This limits the generalizability of the study. Moreover, the study design being an exploratory cross-sectional study did not allow the inference of cause and effect relationship. Finally, the sampling design was a convenient sampling from selected known places that may introduce some form of biaises.

The research protocol and tools used to collect the information were approved by the North Texas Regional Institutional Review Board, approval # 2019-054 on August 12th 2019.

Significance of the Study

Although sickle cell disease is endemic in the study population's country of origin, little is known of individual awareness and understanding of this hemoglobinopathy in the United States. Additionally, despite the increasing number of sickle cell disease and traits cases in Black and African Americans in the United States, as indicated by the universal newborn screening, little is known about the status of immigrants arriving from the endemic country Democratic Republic of Congo. The findings from Aim One can guide in developing tailored programs to meet the potential gap in the targeted population's awareness of the disease. Being the largest public health blood disorder among the most

recurrent hemoglobinopathies, the costs of treating SCD continue to rise. Understanding the impact of health insurance in relation to this disorder is a significant factor to explore, more specifically among immigrants from endemic countries like DRC in the USA. The second aim elucidates on the accessibility to healthcare based on having (or not) health insurance among the targeted population. The third aim determines previous screening status of the targeted population. It also assesses the willingness of the subjects whose screening status is unscreened or unknown while determining the feasibility of preventive measures for the transmission of sickle cell disease through premarital genetic testing and counseling.

CHAPTER 2

LITERATURE REVIEW

History of Sickle Cell

It was 1904 when Dr. James B. Herrick consulted a 20-year-old, young, black immigrant from Grenada in Chicago to discover “Peculiar Elongated and Sickle-shaped Red Blood Capsules in a Case of Severe Anemia,” as his case report of 1910 was titled (Herrick, 2001). Based on the health status of the patient and the discovery of a newly “out-of-the-way disease”, such as chronic acetanilide intoxication and uncinariasis, focus was diverted away from SCA as a possible emerging disease. However, Herrick clearly stated that diagnosis of such cases must remain open. Within fifteen years of Herrick’s description, similar observations of peculiar elongated sickle-shaped red blood cells (RBC) were observed resulting in earlier pathological and clinical descriptions in multiple case notes (Sydenstricker, 1924). Multiple other clinicians and researchers hypothesized the origin of the sickling of red blood cells to likely be due to their exposure to carbon monoxide when saturated. This hypothesis was further demonstrated in vivo experiments (Frenette & Atweh, 2007; Scriver & Waugh, 1930; Sydenstricker, 1924). However, in this early era, linking this new disorder to be predominant among black origin patients was not explicitly stated. Despite its discovery over a century ago, sickle cell disease continues to be less of a priority disorder in comparison to HIV/AIDS, Tuberculosis and Malaria. From the multiple case notes and reviews, gap exists in research as to the migratory factor related to the expression of the disorder. This gap is exasperated by the

early lack of interest in the understanding of the patient level of awareness and understanding of the disease.

It was in 1945 that Linus Pauling first hypothesized that the sickling of the RBC may have originated from a hemoglobin abnormality that is likely to be genetic (Pauling, 1964). Four years after Pauling's hypothesis, in 1949, through gel electrophoresis, this hypothesis was validated showing the difference in migration in sickle versus normal hemoglobin (Pauling, Itano, Singer, & Wells, 1949). Many of the observations and clinical experiments were conducted simultaneously in the 1940s. That period of time was seen as the era of "out-of-the-way disease" (Frenette & Atweh, 2007). In 1949, the inheritance connotation of the disease was presented and showed the autosomal recessive inheritance of the sickle cells (Neel, 1949). During the same period, a hypothetical prediction of the importance of fetal hemoglobin (HbF) in newborns led to longer periods of sickling of red blood cells when compared to mothers who were recessive to sickle cell disease (SCD). Further clinical studies then demonstrated the difference between normal hemoglobin A and a mutant sickle hemoglobin (HbS) by a single amino acid (Frenette & Atweh, 2007). Based on these results, studies focused on the molecular level of the structure and physical properties of the mutant hemoglobin S, which, upon deoxygenation, formed intracellular polymers (Ferrone, 2004). The continuous investigations of SCD that led to our current understanding resulted from the openness of early investigators to diagnose cases of sickle-shaped red blood capsules and the multiple clinical diagnoses and experiments. These various interventions elucidated the basis of the current human molecular disease. However, little was known about the clinical course of the disease during the era of laboratory investigations between 1910

and the early 1970s, and almost no studies looked at the potential migratory nature of the disorder given the fact that the first case recorded was from a black immigrant. From the multiple case notes and reviews, knowledge gaps exist in research as to the migratory factors related to the expression of the disorder. Also, given the newness of the disease, almost no research focused on the patients' understanding of the disease. Given the primitive understanding of the disorder itself in the first few decades, no research focused on determining the willingness of at-risk population – black population—to be screened. This challenge was aggravated by the complexity of screening/testing for SCD/A and the ambiguity of the global aspect of the disorder. This is one of the gaps this thesis is focused on addressing.

Retrospective studies and case reports were not able to comprehensively narrate the natural history of SCD, despite their capacities to inform research communities on the wide-ranging manifestation of SCD. Up to this point in history, the clinical course of the disease from early childhood to death remained misunderstood and lacking statistical stature. In large, this was due to the variability in manifestation and severity, along with the complexity of possible interaction of the disease process with other health-related events. Consequently, to grasp the natural course of SCD as a complement to the scattered knowledge available through anecdotal case reports, in 1978, the National Heart, Lung and Blood Institute (NHLBI) initiated a multi-institution prospective cohort Cooperative Study of Sickle cell disease (CSSCD) of over 4,000 patients from 23 centers across the United States (Gaston & Rosse, 1982). Through the use of a database, this analytical and specific initiative-based process aimed to provide knowledge of the risk factors, the rates of progression, the incidence and natural complications, and ways to

improve medical management at that time but with little to no interest on the impact of migration on the cases under study and the level of awareness of the disease. The landmark accomplishments of CSSCD were: the understanding of a high mortality rate of severe pneumococcal infections among children with SCD despite the vulgarization of pneumococcal vaccination, the development of Prophylactic Penicillin Study (PROPS), the implementation of the mandatory neonatal screening for SCD, and the administration of prophylactic penicillin therapy for children (4-60 months) with SCD (Benson & Therrell, 2010; Gaston & Rosse, 1982; Gaston et al., 1986; Rutkow & Lipton, 1974). An additional discovery from the CSSCD studies was the shortening of life expectancy of SCD patients with over half dying before the age of 50 with no overt chronic organ failure but as a result of stroke, an episode of acute pain, or chest syndrome (Platt et al., 1994). Additionally, CSSCD expounded on the determination of the risk factors, incidence, and prognosis of the acute chest syndrome. Despite the holistic nature of the multi-institution prospective cohort Cooperative Study of Sickle cell disease initiated by NHLBI of over 4,000 patients, CSSCD had not taken into consideration the participants' understanding of the sickle cell blood disorder. Given the scale of the study, it would have been an ideal platform to assess the patients' awareness of the disease and how their awareness may have played a role. This gap is addressed in this dissertation even though the scale is limited to African immigrants from Democratic Republic of Congo.

The 1997 prospective study of over 3,700 SCD patients conducted by CSSCD shed more light on the previously conflicted report on the acute chest syndrome (ACS) as an important cause of morbidity and mortality. The resulting findings showed ACS was milder in children and more severe in SCD adults. The mortality was four times higher in

adults compared to children; however, cases of ACS were more common among children in the winter with less hospitalization days compared to adults (Vichinsky et al., 1997). These early CSSCD studies helped shape and determine therapeutic interventions, the risk factors, the incidence, the presentation and the prognosis of ACS (Castro et al., 1994; Vichinsky et al., 1997) but they also serve as signs of environmental risk factors. This benchmark prospective research contributed to pediatric studies that confirm ACS as being the secondary manifestation of SCD along with vaso-occlusive pain crisis (VOC) and increased risk factor of death during pediatric and young adult hospitalization (Bou-Maroum, Meta, Campbell, & Yanik, 2018; Castro et al., 1994). According to concurrent studies to CSSCD, the risk of developing clinically apparent stroke was 11% for patients with SCD under the age of 20 and 24% by the age of 45 (Ohene-Frempong et al., 1998). The results of these simultaneous studies confirmed the benefit of prophylactic intravenous transfusion in avoiding a first stroke in patients with SCD (Adams et al., 1998). Furthermore, they contributed to the understanding of the multifaceted manifestation and complication of sickle cell disease that resulted from a single missense mutation on the twentieth nucleotide of the hemoglobin gene for the most common SCD cases (Frenette & Atweh, 2007; Mine, Zeinab, Stefan, & Madelon, 2011).

From the history of the disease to the discovery of its various manifestations, attention to the impact of migration to the disease during that era did not catch much traction. This could be because much was to be discovered at the molecular level and the mechanism related to expression of signs and symptoms of the disorder. Despite the missing link of migration patterns, from the history to the clinical manifestation, knowledge of SCD in the scientific community is progressing. However, the status of the awareness

of patients and at-risk population remains unknown. Hence, this dissertation elucidates on the awareness and understanding of SCD/A within at-risk populations from the African endemic country of DRC by focusing on factors such as sociodemographics, educational levels, and years of life spent in the United States.

The Genetics of Sickle cell disease

SCD disease was known in early years of its discovery by Pauling et al., to be a result of a mutation in a hemoglobin molecule, and its inheritance is autosomal recessive (Neel, 1949; Pauling et al., 1949). A work completed almost 50 years after the first case report of sickled red blood cells by Ingram and team elucidated on the mutation of glutamine to valine substitution observed at the sixth residue of beta globin polypeptide (1959) to cause the sickling red blood cell. Many years after this discovery, genetic cloning of human globin helped establish DNA sequences that provided insight on the regulatory mechanisms of the DNA expression. At the biomolecular level, human hemoglobin molecule is a quaternary structure that is composed of two pairs of identical subunits of polypeptide wired with different genes. These two pairs are the human alpha-like globin genes and the beta-like globin that are respectively located on chromosomes 16 and 11 during development (Frenette & Atweh, 2007). At embryonic phase, hemoglobin F (HbF) is predominant while hemoglobin A (HbA) takes over HbF during postnatal period. It is only after completion of switching from HbF to HbA that the clinical expression of disorders related to beta globin genes will start to be expressed in carrier patients (Stamatoyannoploulos, 2005). The approval and use of hydroxyurea as treatment for SCD by the Food and Drug Administration (FDA) results from the expansion of research

pinpointing the molecular mechanism of switching of fetal hemoglobin to adult (Sankaran & Orkin, 2013).

The interaction of various mutations of the β-globin genes results in multiple variants of SCD; however, the most common and severe variant of SCD is caused by the homozygote mutation HbSS (Frenette & Atweh, 2007). The mild sickle cell disease results from the interaction of β^S gene with β^C gene, known as HbSC (Lopez et al., 2018). The β-thalassemia gene results from a mutation of β-globin that produces either a failed normal β-globin mRNA or a variant of decreased levels. Therefore, a severity of the sickling disorders results from the interaction of β^S with the inherited β-thalassemia. When β^S gene interacts with the failed or inactive β-thalassemia known as β^0-thalassemia, the resulting combination Sβ^0-thalassemia is closer in disease severity with the full homozygous HbSS disease (Serjeant, Sommereux, Stevenson, Mason, & Serjeant, 1979). However, when the partially active β^+-thalassemia gene interacts with β^S gene, the resulting variant Sβ^+-thalassemia expresses an array of clinical severity (Serjeant, Ashcroft, Serjeant, & Milner, 1973). Phenotypically, when β^+-thalassemia gene mutation is mild, as commonly noticed in people with African descent, the resulting interaction (Sβ^+-thalassemia) tends to have mild clinical implication, but when β^+-thalassemia gene mutation is severe, as in the case in the Mediterranean populations, the severity of the sickling disorder tends to be moderate in nature (Serjeant et al., 1973). The difference in severity classified geographically (mild in African descent and severe in Mediterranean populations) provides insight of possible impact of human migration on the expression of sickle cell disease. There was no study, to my knowledge, that focused on these differences in severities, which is out of the scope of this dissertation but warrants an investigation.

Understanding the relationship between severity differences of sickling cells and marital and family history, migration, and awareness of the disease may elucidate on the various impacts of the disease.

This dissertation will partially address the relationship between awareness of the disease and the impact of the disease on the more homogenic subgroup of African immigrants of DRC in North Texas. Table 1 displays an abridged version of the Freenet et al. study that shows the genotypes and phenotypes of different sickling disorders.

Table 2.1

Genotypes and Phenotypes of Different Sickling Disorders

Genotypes	Interacting Genes	Clinical Severity
HbAA (normal)	β and β	None
HbSS	β^S and β^S	Severe
HbSC	β^S and β^C	Mild
HbSβ^0	βS and β^0-thalassemia	Severe
HbSβ^+	βS and β^+ -thalassemia (severe thalassemia mutation)	Moderate

Note: Adapted from Sickle cell disease: Old discoveries, new concepts, and future promises by Frennet, S.P., and Atweh, F.G. (2007).

Diagnostics and treatment of Sickle cell disease

From the history of its discovery to unprecedented research focused on multiple aspects of its manifestation, sickle cell disease diagnosis is relatively simple, and usually diagnosed by gel electrophoresis and other molecular diagnoses that are widely available. For better response and care management, it is crucial to diagnose sickle cell disease in the early age of prenatal period even though it can be challenging (Frenette &

Atweh, 2007). The difficulty of prenatal diagnosis is due to the fact that fetal blood sampling must be drawn after the 20th week of pregnancy for analysis; but at that time, if the couple decides to terminate the pregnancy, it is much harder as the pregnancy is too advanced and probably unsafe to terminate. Given the advances in the biomedical field, through chorionic villous biopsy, definitive diagnoses are made possible for different sickling disorders through fetal DNA analysis during the first trimester or even earlier in harvested fetal cells from maternal circulation (Cheung, Goldburg, & Kan, 1996; Orkin, Little, Kazazian, & Boehm, 1982).

There are multiple therapeutic ways to alleviate the impact of sickle cell disease. They include: bone marrow transplant, the administration of hemoglobin F (HbF), hydroxyurea, 5-Azacytidine and decitabine drugs, and butyrate. Some are more practical and relatively less risky than others. However, proper medication can only be prescribed when the disease is diagnosed. In the case of immigrants in the USA from endemic countries, the lack of selective screening upon arrival may complicate the applicability of proper medication and increased healthcare costs and utilization. Hence, this dissertation proposes to provide preliminary information regarding the awareness and assess the subscription to health insurance related to the impact of immigration from the SCD endemic country of the Democratic Republic of Congo.

Awareness of SCD and SCT and Genetic counseling

In general, information on awareness about SCD and SCT are sporadically available with limited information on public knowledge (Boyd et al., 2005). In mutlitple studies, individual groups at high risk are unaware of SCD or SCT. A cross-sectional

study conducted among pregnant women in Ghana has revealed deficiency in the awareness of the disease or trait. Even though 87% of the participants in the above mentioned study were aware of their status, only 29% of the awareness questions were answered correctly (Obed, S.A., et al. 2017). Other community studies revealed the gap in the understanding of SCD/SCT. A study conducted by Boyd et al (2005), showed 91% of African American women aged 18-30 believed that SCD is an inherited disease, but only 9.3% understood the inheritance pattern, and 11% were unaware of their SCT status. Even though one may argue that from Boyd et al. the awareness seems elevated, participants did not understand treatment strategies for SCD. In addition, a study conducted in California shows that less than 18% of families who have birthed a child with SCT participated in free counseling related to SCT, SCD and risk for future pregnancy; this lack of follow up is noted to be very common in the United States (Treadwell, M.J; McClough, L. and Vichinsky, E., 2006), and limited to no studies are available for African immigrants and those who live on the African continent. These above studies suggest strong evidence that individuals at risk and at reproductive age were lacking adequate information regarding SCD and its inheritance pattern.

In the Democratic Republic of Congo, there are almost no studies that focus on the knowledge of patients or family members of the carrier of the diseased. A study conducted by Mukinayi et al. (2018) that specifically focused on families affected by sickle cell even showed that the awareness level among such group is low and directly impacts the diseased and their families, in addition to the lack of health insurance. In the U.S., studies conducted among college students demonstrated a lack of knowledge of sickle cell disease. For example, a study conducted in Texas by Ogamdi (1994) evaluated the

general knowledge of SCD among 334 students. The study concluded that about 81% of the students were unaware of the genotypes describing SCD, but most surprising was that over 60% were unaware that SCD is a preventable disease through genetic premarital counseling. Another study by Prabhakar (2009) focused on 191 African American college students of reproductive age (19-30 years old). The finding of this study noted lack of knowledge of participants regarding family history, carrier status, and genetic testing.

In a comparative study conducted by Dyson (1997), 104 carriers and non carriers of SCD were recruited to assess and compare their level of knowledge and awareness of sickle cell disease. The question related to the patern of inheritance of the disease was poorly answered by both groups. Only 25% and 29% of the patterns of inheritance questions were answered correctly respectively by non carriers and carriers of the disease, and no significant difference was noted in the knowledge of the SCD between the two groups.

Multiple studies expose cultural practices and views, health beliefs, guilt and socioeconomic barriers majorly contribute to the lack of interest and support for genetic counseling and sickle cell testing (Gustafson, Gettig, Morse, Krishnamurti, & Lakshmanan 2007; Yang, Andrews, Peterson, Arvind, & Cepeda, 2000). Several articles suggest that multiple factors negatively affect the follow up counseling and screening for prenatal sickle cell screening education. A study by Yang et. al (2000) suggests that anticipated anxiety and fears from parents in knowing that their child will have a heminoglobinopathy disease like SCD, and fear from being the author of such disease to their innocent child keep them from participating in counseling. From Hill (2000) study, fathers were most

likely the one to refuse learning their status and more likely to deny their genetic contribution to passing on the disease to their offspring.

Health Insurance and SCD

In most of sub-Sahara Africa where SCD and SCT are predominant, evidence has shown that the lower class has the highest burden of disease and causes an exponential increase in healthcare expenditure (WHO, 2010). In order to better understand the level of healthcare coverage for Africans in their countries of origin, a few studies have shown that most African countries do not have social health insurance. This means most healthcare costs are paid out of pocket. Some countries like Ghana, Ethiopia, Rwanda, Kenya and Tanzania who have established social health insurance schemes seem to have difficulties executing their program (Fenny, A.P., Yates, R., and Thompson R., 2018). Social health Insurance Schemes in Africa leave out the poor.) For example, 12 years after introducing social health insurance in Ghana, only 40% of its population are covered by the scheme (Fenny, A.P., Yates, R., and Thompson R., 2018). Socioeconomic and educational levels are seen as factors that play a key role in enrolling in social health insurance schemes among Africans in sub-Sahara (Preker A.S., et al. 2002). Not until poverty is seen as a risk factor for not participating in social health insurance in sub-Saharan Africa, a successful social insurance program in this region will continue to be a challenge. In light of the difficulties of enrolling Africans in social health insurance schemes in their countries of origin, discussions should focus on the following questions for the African immigrants in the USA: What percentage of this population have a higher education and/or have insurance? Does having health insurance and/or higher

education predispose one to the likelihood of being screened for SCD/T? These are are some the questions this thesis will try to answer.

Socioeconomic Impacts of Sickle cell disease

Healthcare costs in general are on the rise, but the associated costs of sickle cell disease in particular have been ambiguous to quantify despite SCD's constantly increasing costs. In a study conducted in England based on Episodic Statistic Data for all hospital episodes between 2010 and 2011, only 6011 patients admitted for SCD or anemia as primary diagnostics incurred costs over USD $24.4 million during the study period with the cost of admission increasing with age (Pizzo et al., 2015). These findings are concordant with similar studies conducted in the USA. For example, a study conducted on black African American children ages 0-17 with SCD, based on data derived from the 1997-2005 National Health Interview Survey Children Sample core, showed that SCD children have higher odds of using drug prescriptions with fair or poor health status compared with black African American children without SCD from the same age group (Boulet, Yanni, Creary, & Olney, 2010). Such frequent drug prescriptions and hospital usage results in driving up the cost of health care utilization. The study of Kauf et. al. in the state of Florida found that the healthcare costs for SCD children aged 0-9 years is $892 per patient-month and $2,562 per patient-month for SCD patients aged 50-64 years, with an average monthly patient-month of $1,389 (Kauf et al., 2009). Furthermore, 51.8% of overall healthcare cost is related to SCD with inpatient hospitalization accounting for over 80% and a lifetime healthcare cost averaging $460,151 per patient with SCD. The economic cost for sickle cell treatment is growing

with an average of $13,237 per child per hospital stay (Myundura et al., 2009) a yearly hospitalization cost of 488 million (Singh et al., 2014).

In sub-Sahara Africa where more than 75% of sickle cell diseased children are born and over 6% of deaths for children under the age of 5 are attributed to SCD (Modell & Darlison, 2008; WHO, 2006a), reliable data on cost related to the disorder is sporadically available. Small scale studies conducted in the Republic of Congo and Kenya have shown variability in estimated cost. In Kenya, an estimated annual economic cost for SCD patients attending sickle cell clinics ranges between USD $94-$229 (Amendah, Mukamah, Komba, Ndila, & Williams, 2013), whereas in the Republic of Congo, the average annual cost is about USD $111.67 per episode in children (Ngolet et al., 2016) and about USD $155.52 in adult patients with the family minimum monthly income of USD $158.40 (Ngolet, Ntsiba, & Dokekias, 2013). In Nigeria, a similar study estimates the average cost of hospitalization to be USD $132.67 with a range of USD $69.48-$320.83 (Bou-Maroum et al., 2018).

In the developing nations, the paucity of SCD data is a paramount obstacle to properly estimating the economic burden of the disorder. Having a proper data source will guide policy and regulation, such as universal newborn SCD screening programs. Even though inpatient pediatric SCD has been associated with significant healthcare expenditure in developed nations (Pizzo et al., 2015), the children's lives saved through such programs is worth the cost as the lack of newborn screening contributes to the high mortality rate among children in developing nations (Modell & Darlison, 2008; WHO, 2006a). The increased cost of healthcare related to sickle cell is more prominent in adults in high income countries. This is probably the same in low income countries, but due to

limited data and lack of studies focused on adult patients, it is difficult to assert. The mechanism leading to such increased mortality and cost in adults is the purpose of this exploratory research that the next two chapters try to reveal as immigrants from endemic countries are not screened upon arrival.

Conclusion

From its first discovery in 1904 to the multiple research and discoveries of its cure, sickle cell disease, a genetic disorder that is considered a public health threat, remains a topic of multiple studies and discussions. The advances done in the field of molecular biology in regard to sickle cell must be continuously supported to lead to more advanced discoveries in blocking the sickling process of RBC to relieve SCD patients of constant pain crises. Given the number of lives it claims yearly and the economic burdens it causes, developing nations must converge their efforts in establishing a universal newborn screening system to detect early cases for proper care. The aims of this dissertation will identify fundamental factors associated with willingness to be screened and willingness to attend genetic counseling that could guide discussion toward establishing SCD/A selective screenings for incoming migrants from endemic countries. Studies have proven that early diagnosis leads to better care and management of crises related to SCD and longer life expectancy (Platt et al., 1994). Attention must be drawn to migratory patterns of humans from endemic developing countries to developed nations. Considering the high prevalence of SCD in many African countries, selective screening of immigrants from endemic countries like Nigeria and Democratic Republic of Congo upon arrival in developed nations and providing an accurate diagnosis will not only lead

to proper management and treatment of the disease, but it will also inevitably lead to reduction of healthcare expenditures related to SCD in the United States. This exploratory study will focus on the adult immigrants from endemic countries of DRC to try to determine their willingness to be screened and willingness to attend genetic counseling as preventive measures to address the root causes of the increased cost and mortality in adult patients with sickle cell disease in the United States of America.

CHAPTER 3

METHODOLOGY

Target population

The targeted population for the survey for this dissertation was African immigrants from the Democratic Republic of Congo in the Dallas-Fort Worth-Arlington metropolitan area in North Texas. For the purpose of this study, North Texas is defined as the Dallas-Fort Worth-Arlington metropolitan area (DFWA). According to Census Bureau projections, by 2060, one in every five people in the USA will be an immigrant (foreign born) with the majority of them living in metropolitan cities (White et al., 2017a). The Dallas–Fort Worth–Arlington metropolitan area was selected because immigration in the state of Texas favors urban over rural (White et al., 2017b), and DFWA is one of the "Big Four" metropolitan areas in Texas, areas having a population of at least one million. In DFWA, the number of immigrants arriving from other countries exceeded the number of both internal (those moving within Texas) and domestic (those moving to Texas from another U.S. state) migrants combined. In addition, of all metropolitan areas in Texas, DFWA has the highest proportion of African immigrants at 8.5% of the total immigrant population (White et al., 2017a).

While the total number of incoming immigrants to the US is known and made available by the United States Citizenship and Immigration Services (USCIS), the exact number of African immigrants specifically from DRC in North Texas is not known. However, in Texas alone, the number of immigrants in 2016 totaled over 4.7 million, with more than 235,000 coming from Africa (Migration Policy Institute, 2018a). Between 2008-

2013 a total number of 10,960 Congolese refugees arrived in the USA, and 18.3% reside in Texas. Furthermore, in fiscal year 2016, 41% of the total number of refugees arriving in Texas were from Democratic Republic of Congo (Department of State Bureau of Population, Refugees, and Migration, 2018). While these numbers are substantial, they only account for refugee arrivals and do not encapsulate interstate migration, students or visitors from DRC.

Sampling Design

For the purpose of this dissertation, a convenience sample design is used. This is based on the proximity and ease of access to the Congolese community in North Texas and their relatively dense community. The Congolese community represents 41% of all refugees arrival in Texas, which makes it a readily accessible sample. The recruitment process was through referral, walk up, and outreach to Congolese community leaders using flyers. Such communities have a tendency to aggregate in close proximity and participate in the same worship and cultural centers. Through the Building Bridge Initiatives, a UNTHSC program that works with refugee communities, leaders of Congolese community were contacted as a port of entry for recruitment. Also, through google search, Congolese churches in DFW metroplex were contacted as source of recruitment in addition to the flyers that were posted at the university campus and in pinpointed apartment complexes that host such communities.

Sample Size Estimation

For the calculation of sample size of each research question below, Gpower 3.1 was used (Erdfelder, E., Faul, F., Buchner, A.1996). Gpower inputs parameters to compute required sample size, given alpha, power and effect size. This required using

the z-tests under logistic regression and following are the input parameters that were used under that framework based on each research question:

Research questions 1.1.1 and 2.1.1: (1) Two sided test; (2) In calculation of odds ratio: Pr(Y=1|X=1) under H1 = 0.32; Pr(Y=1|X=1) under H0 = 0.1. This resulted in OR = 4.325; (3) R squared with other X = 0.14 (R-squared represents the amount of variability between the main categorical predictor that is accounted for by other covariates in the model;) (4) Power = 0.8; alpha = 0.05; X parm π = 0.3 (proportion of cases who have sickle cell awareness). The sample size increases to detect the same effect size in a multivariable model, assuming that the target predictor was modestly correlated (about 0.14) with other covariates, then the sample size would be 141.

Research questions 1.1.2, 2.2.1 and 3.2.1: (1) Two sided test; (2) In calculation of odds ratio: Pr(Y=1|X=1) under H1 = 0.30; Pr(Y=1|X=1) under H0 = 0.1. This resulted in OR = 3.857; (3) R squared with other X = .14; (4) Power = 0.8; alpha = 0.05; X parm π = 0.3; The sample size increases to detect the same effect size in a multivariable model, assuming that the target predictor was modestly correlated (about 0.14) with other covariates, then the sample size would be 164.

Research questions 1.3.1; 2.3.1 and 3.3.2: (1) Two sided test; (2) In calculation of odds ratio: Pr(Y=1|X=1) under H1 = 0.31; Pr(Y=1|X=1) under H0 = 0.1. This resulted in OR = 4.043; (3) R squared with other X = 0.13; (4) Power = 0.8; alpha = 0.05; X parm π = 0.3; The sample size increases to detect the same effect size in a multivariable model, assuming that the target predictor was modestly correlated (about 0.13) with other covariates, then the sample size would be 150.

Table 3.1 Sample Size Calculations for All Research Questions

Research Questions	Statistical framework	Sample size using GPower
1.1 Research Question 1.1.1: Is gender, a known factor for gender difference in SCD survival, significantly associated with sickle cell awareness in this population?	Logistic regression for SCD awareness with 1 predictor	141
1.2 Research Question 1.1.2: Are factors such as education, age, income level, and marital status significantly associated with sickle cell awareness, controlling for gender?	Logistic regression for SCD awareness with 4 predictors	164
1.3 Research Question 1.3.1: Are immigrants factors such as immigrant status, interpreter needed during medical visit, and number of years lived in the USA, controlling for gender?	Logistic regression for having health insurance with 3 predictors	150
1.4 Research Question 2.1.1: Is gender significantly associated with sickle cell testing in this population?	Logistic regression for willingness to be screened for SCD with 1 predictors	141
1.5 Research Question 2.2.1: Are demographic factors such as education, age, income level, and marital status, significantly associated with willingness to be tested for SCD?	Logistic regression for willingness to be undergo genetic	164

	counseling for SCD with 4 predictors	
1.6 Research Question 2.3.1: Are immigration factors such immigrant status, number of children, and number of years lived in the USA significantly associated with willingness to be tested for SCD?	Logisitc regression for willingness to be screened with 3 predictors	150
1.7 Research Question 3.2.1: Are factors such as education, age, income level and marital status associated with willingness to participate in SCD genetic counseling?	Logistic regression for willingness to be screened for SCD with 4 predictors	164
1.8 Research Question 3.3.2: Are immigrations factors such as immigrant status, language proficiency, and number of years lived in the USA significantly associated with willingness to participate in SCD genetic counseling?	Logistic regression for willingness to participate in genetic counseling with 3 predictors	150
Overall Research Question: Which factors are associated with willingness to participate in SCD awareness/willingness to be tested/genetic counseling?	Logistic regression for willingness to participate in genetic counseling with 5 predictors	186

A sample size of 136 should allow detection of an odds ratio for a single predictor of approximately 4.2 with power of 0.80, assuming an outcome of awareness of sickle cell at 32%, and with alpha = 0.05. The sample size increases to detect the same effect size in a multivariable model, assuming that the target predictor was modestly correlated (about 0.10) with other covariates, then the sample size would be *186*. Considering the estimated sample sizes for all our hypotheses, we choose to go with the maximum among them, which is *186, as our final sample size.*

Inclusion and Exclusion Criteria

The inclusion criteria included: any African immigrant of the Democratic Republic of Congo: men and women of age 18 years or older living in the Dallas–Fort Worth–Arlington metroplex during the research period. The exclusion criteria included: any African immigrants men from DRC under the age of 18 and women under the age of 18 and not currently living in the Dallas–Fort Worth–Arlington metroplex.

Variables

The independent variables were:

1. Sociodemographic information
    a. Gender - coded as categorical data with male as reference.
    b. Income level - coded as categorical data with less than $20,000 as reference. The other income levels were: $20,000 to $25,000 and greater than $25,000.
    c. Age - coded as continuous variable.
    d. Educational level - coded as categorical data with less than high school as reference. The other levels for educational were: High school graduate or GED

completed; Some college/vocational graduate, college graduate or more than college.

e. Marital status: coded as categorical data with ‘married’ as reference. The other levels for widowed, separated or divorced; never married.

2. Immigration Information

a. Interpreter needed – coded as binary with ‘no’ as reference.

b. Year in Texas – continuous variable.

c. English language proficiency: binary with ‘not well spoken and written’ as reference.

d. Native language proficiency: binary with ‘not well spoken and written’ as reference.

e. Status when entered USA: categorical variable with ‘permanent resident’ as refernence. Other levels were: student, refugee, and asylum.

The dependent variables were:

1. Awareness of Sickle Cell Anemia – coded as dichotomous variable;
2. Willingness to be screened for SCA - coded as dichotomous variable;
3. Willingness to attend genetic counseling - coded as dichotomous variable.

Awareness of Sickle Cell Anemia

Questions focused on the participants’ awareness of sickle cell disease and assessed if they had ever been tested in the past. The screening question regarding testing for SCA included two options of results: negative test result or positive test result. When positive, it was asked whether the result was a trait, a disease or unknown. For

positive result patients, assessing their level and frequency of pain were also measured. This variable focused on the participant's awareness of the test result.

Willingness to be Screened for SCA and Genetic Counseling

The willingness of participants to be tested for sickle cell was assessed. Regardless of their answer (yes, no, or I don't know), participants' willingness to participate in genetic counseling was also evaluated. If married, the participants awareness of their spouse's and/or children's status was also asked. This section of the questionnaire was central to the study as it related the participants' awareness of SCD to various parameters, such as disease status and genetic counseling, associated pain, consanguineous or interfamily marriage, and children's status, when applicable. This section consisted of nine questions.

Research Design

This was an exploratory cross-sectional study that used a survey design method. One hundred and eighty six in-person surveys of immigrants from Democratic Republic of Congo age 18 and older for men and women who reside in North Texas were performed using a convenience sampling method.

Since the intent was to identify preliminary contextual factors that may be associated or influenced by sickle cell proliferation and its related rising costs in a specific target group in North Texas, a mixed methods approach seemed appropriate (Creswell, 2014). The data for this research was collected using in-person surveys. The independent variables were sociodemographic information, educational level, income level and immigration status. The sociodemographic variables included gender, age, marital status, number of siblings and children who may or may not reside in the USA,

country of origin, number of years in the USA, number of years in Texas, and immigration status upon arrival in the USA. Educational level encompassed the ability to read/write both a native language and English, as well as the level of formal education. Refer to Table 3.2 below for more details.

Data Collection Procedures

Currently, there is no database or list of immigrants from sickle cell endemic country like Democratic Republic of Congo. Therefore, constructing a sampling frame could be challenging, and probability sampling could be difficult to achieve. Since this research was formative in nature, convenient sampling procedures were appropriate, so a non-probabilistic sampling method was used (Enticott et al., 2017).

To begin recruiting, organizations such as refugee resettlement agencies and ethnic churches were contacted to determine their willingness to inform their respective members and clients. Culturally, African immigrants tend to live together in close communities and neighborhoods, attending the same cultural churches and mosques and participating in community events within their community. For example, in Fort Worth, the congregations of The Redeemed Christian Church of God and Abundant Life Church consist of huge numbers of West Africans; Ladera Palms Apartment Complex houses a large population of African refugees; and The Fountains Clubhouse hosts cultural orientation weekly for recently arrived African refugees.

The recruitment period included a total of three months of posted flyers from August 12 - November 5, 2019 and the spread of information by word of mouth. The recruitment flyers were posted in approved areas: schools, apartment complexes,

churches, and refugee resettlement and placement organizations. Flyers were also posted at university campuses, like UNTHSC, that host a large number of African students. Interested participants, upon reading the flyer (Appendix B), contacted the researchers to conduct the in-person survey. When researchers were contacted, they organized a meeting time with participants based on their convenience. When a survey was completed, the raw data was stored in a locked cabinet in the investigator's office. Data was manually transcribed in Microsoft Excel, then exported into SAS by the researcher. All identifiable data was password-protected for confidentiality.

Before continuing with the survey, three screening questions were first asked to ensure inclusion criteria was met:

1. What is your current age?
2. What is your country of origin?
3. Do you live in the Dallas – Fort Worth – Arlington area?

If participants responded as being 18 years of age or older, originally from the Democratic Republic of Congo and living in DFWA area, then the investigator proceeded with the survey. However, if their responses to the above questions regarding age (less than 18 years old) and/or country of origin (not from DRC) did not correspond to the inclusion criteria, the researcher thanked them for their interest in participating in the survey and ended the survey.

When participants passed the pre-assessment for the inclusion criteria, a time and place for the survey were agreed upon. The researchers met with participants in public

places like churches, coffee shops, apartment clubhouses, school libraries and classrooms, or in private homes and apartments to conduct the survey.

No incentives were offered as part of the recruitment. When participants were met to take the survey, a consent form (Appendix C) was read by participants or read to participants either in English or French, depending on their level or understanding and/or education. Participants were informed of their right to request information anytime regarding the survey and could stop the survey if they did not feel comfortable. However, any information already gathered was used in the analysis of the data. Whenever the participants completed the survey, the investigator thanked them for their participation. The participants were informed that the survey results were anonymous with no self-identifying information collected.

The survey questionnaire is located in Appendix A, and it took approximatively 10-15 minutes to complete. The survey consisted of only 36 items with appropriate skip patterns subdivided into four sections:

1. Demographic Information
2. Health Insurance Information
3. Social Determinants of Health
4. Sickle Cell Information

Questionnaire Design

The questionnaire used to collect information regarding these variables was validated on previous survey research in immigrant populations in the USA (Kroenke, K., Spitzer, R.L., & Williams J.B., 2003; BBI, 2018) The questionnaire was adapted from a

standard questionnaire under the guidance of Dr. Raines-Milenkov, an assistant professor in the pediatrics department at UNTHSC, who has extensive experience in surveying immigrants in North Texas as the Director of Building Bridge Initiative (BBI). The topic of this study was presented to Dr. Raines-Milenkov, and multiple meetings were set to discuss the questionnaire involving an expert in genetic questionnaires, Dr. Deanna Cross, an assistant professor from the Microbiology, Immunology and Gene department of UNTHSC. The experts guided the design of the questionnaire with the assistance of other experts to ensure the reliability of the questionnaire. The initial survey was designed to assess colorectal cancer awareness and screening habits of refugees. The version used in this survey adapted the original questionnaire with focus on SCD awareness and screening among immigrants from DRC. Multiple versions of the questionnaire were produced as a result of exchange and discussion between the expert and the researcher. Feedback was collected via email and in-person meetings, and changes were made to reflect the expert's point of view prior to submitting the questionnaire to IRBnet for review.

Data Analysis

Data analysis was conducted using descriptive statistics, frequency distributions, and regression analysis. Data analysis was conducted using SAS 9.4 software. A *p* value of <0.05 was used for statistical significance.

Aim 1: Explore the awareness of sickle cell anemia among African immigrants from Democratic Republic of Congo.

Research Question 1: Is gender, a known factor for gender difference in SCD

survival, significantly associated with sickle cell awareness in this population?

Research Question 2: Are sociodemographic factors such as education, age, income level, number of years lived in the USA and country of origin significantly associated with sickle cell awareness, controlling for gender?

The outcome variable for this aim is sickle cell awareness. This was assessed based on the question: 'Have you ever heard of sickle cell disease?' Sickle cell awareness coded as binary data with "Yes" having some awareness of SCD and "No" as having no awareness of SCD. A logistic regression was used to assess if social and demographic factors such gender, age, education, income level, and number of years lived in Texas were predictors of sickle cell awareness.

Aim 2: Explore willingness of African immigrants from Democratic Republic of Congo to undergo sickle cell testing.

Research Question 2.1: Is gender significantly associated with sickle cell testing in this population?

Research Question 2.2.1: Are demographic factors such as education, age, income level, and marital status, significantly associated with willingness to be tested for SCD?

Research Question 2.3.1: Are immigration factors such immigrant status, number of children, and number of years lived in the USA significantly associated with willingness to be tested for SCD?

The outcome variable for this aim was being willing to undergo sickle cell testing. This was assessed based on the question: “Are you willing to be screened for sickle cell disease?” Willing to be screened for sickle cell disease was coded as binary data with “Yes” being willing to screened for SCD and “No” as not being willing to screened for SCD. A logistic regression was utilized to assess predictors of being willing to screened for SCD. A multiple logistic regression was used to identify predictors associated with being willing to screened for SCD.

Aim 3: Explore willingness of African immigrants from Democratic Republic of Congo to undergo genetic counseling.

Research Question 3.1.1: Is gender associated with willingness to participate in SCD genetic counseling?

Research Question 3.2.1: Are factors such as education, age, income level and marital status associated with willingness to participate in SCD genetic counseling?

Research question 3.3.2: Are immigrations factors such as immigrant status, language proficiency, and number of years lived in the USA significantly associated with willingness to participate in SCD genetic counseling?

This was assessed based on the question: “Are you willing to participate in genetic counseling?” A logistic regression was utilized to identify predictors of willingness to attend genetic counseling. Predictors that were assessed in the regression models included: demographic factors and immigration factors.

Finally, the overarching question combining all the above factors provided the fellowing questions:

1. What are the factors associated with SCD awareness?
2. What are the combined factor associated with willingness to participate in SCD screening?
3. What are the combined factor associated with willingness to undergo genetic testing?

The analysis was based on logistic regression modeling for each individual research question.

Table 3.2

Types of Variables and Analysis in accordance with Specific Aims

Research Questions	Independent Variables	Dependent Variables	Type of Data	Type of Analysis
Specific Aim #1 **Research Question # 1.1.1:** Is gender, a known factor for gender difference in SCD survival, significantly associated with sickle cell awareness in this population	Gender	Sickle cell awareness	Dichotomous	Logistic regression
Research Question # 1.1.2: Are sociodemographic factors such as education, age, income level, and number of years lived in the USA significantly associated with sickle cell awareness, controlling for gender?	Education and Income level, Age, number of years lived in the USA	Sickle cell awareness	Dichotomous	Logistic regression
Research Question # 1.3.1: Are immigrants	immigrant status,	Sickle cell awareness	Dichotomous	Logistic regression

factors such as immigrant status, interpreter needed during medical visit, and number of years lived in the USA, controlling for gender?	interpreter needed during medical visit, and number of years lived in the USA			
Overall: Combining all of the above factors, which ones are associated with SCD awareness?	Education and Income level, Age, number of years lived in the USA, immigrant status, interpreter needed during medical visit, and number of years lived in the USA	Sickle cell awareness	Dichotomous	Logistic regression
Specific Aim # 2				

Research Questions	Independent Variables	Dependent Variables	Type of Data	Type of Analysis
Research Question # 2.1.1: Is gender significantly associated with sickle cell testing in this population?	Gender	willingness to be tested for SCD	Dichotomous	Logistic regression
Research Question # 2.2.1: Are demographic factors such as education, age, income level, and marital status, significantly associated with willingness to be tested for SCD?	education, age, income level, and marital status	willingness to be tested for SCD	Dichotomous	Logistic regression
Research Question # 2.3.1: Are immigration factors such immigrant status, number of children, and number of years lived in the USA significantly associated with willingness to be tested for SCD?	immigrant status, interpreter needed during medical visit, and number of years lived in the USA	willingness to be tested for SCD	Dichotomous	Logistic regression

Research Questions	Independent Variables	Dependent Variables	Type of Data	Type of Analysis
Overall: Combining all of the above factors, which ones are associated with willingness to be tested for SCD?	Education and Income level, Age, number of years lived in the USA, immigrant status, interpreter needed during medical visit, and number of years lived in the USA	willingness to be tested for SCD	Dichotomous	Logistic regression

Research Question # 3.1.1: Is gender associated with willingness to participate in SCD genetic counseling?	Gender	Willingness to participate in genetic counseling	Dichotomous	Logistic regression
Research Question # 3.2.1: Are factors such as education, age, income level and marital status associated with willingness to participate in SCD genetic counseling?	Marital status, Age, Education, income levels	Willingness to participate in genetic counseling	Dichotomous	Logistic regression
Research Question # 3.3.2: Are immigration factors such immigrant status, number of children, and number of years lived in the USA significantly associated with willingness to participate in SCD genetic counseling?	immigrant status, interpreter needed during medical visit, and number of years lived in the USA	Willingness to participate in genetic counseling	Dichotomous	Logistic regression

Overall: Combining all of the above factors, which ones are associated with willingness to participate in SCD genetic counseling?	Education and Income level, Age, number of years lived in the USA, immigrant status, interpreter needed during medical visit, and number of years lived in the USA	Willingness to participate in genetic counseling	Dichotomous	Logistic regression

CHAPTER 4

RESULTS

General Demographics (Table 4.1)

The survey conducted in North Texas successfully interviewed 186 participants from the Democratic Republic of Congo who have been living in Texas an average of three years. The mean age was 32.1 (SD:9.7), with a minimum age of 18 and a maximum age of 62. The participants included 81 (43.5%) males and 105 (56.5%) females. The participants' had an average of 2.0 (SD:1.7) siblings in the USA.

Most participants were either married (46%) or never married (44.3%). Only 9.6% were either widowed, divorced or separated. 29% of the participants had less than a high school education, 31% were high school graduates, and 39.35% either had some college education, were college graduates or had gone beyond college. 24.5% of participants earned less than $20,000, 34.4% earned between $20,000 and less than $25,000, and 41% earned more than $25,000 yearly.

Overall, 140 (75%) participants were employed for wages, 8.6% were students who were not employed, and 4.8% were unable to work for unknown reasons. None of them were self-employed or retired. About 85% of participants had a car. 46.8% used public transportation (buses) while 52.2% did not. As for their status at the port of entry to the United States, none of the participants entered as visitors. A combined total of 92.4% entered the USA as permanent residents, which included both refugees and permanent residents combined, and only 6.2% entered as students. At the time of survey, 13 (7%) participants did not speak English at all, 90 (48.4%) did not speak it well, 70 (37.6%) spoke it well and 13 (7%) said they spoke it very well. When asked about their

ability to write English, 28% said they do not write it at all, 42.5% said they do not write well, about 24% said they write well and about 5% said they write very well.

Health Insurance

About 66% of all participants had health insurance and 44% did not. From the 66% who had health insurance, 66.4% of them had private insurance through their employer. About 19% depended on government insurance, and less than 2% used military insurance. None of the participants purchased their own insurance. 25 (13.5%) of the participants were enrolled in a health assistance program.

When asked about their children and their health insurance, over 52% had children, and 91 (93.8%) of them had health insurance for their children. 90% of the insurance for children was Medicaid, and 9% was private healthcare or Affordable Care Act.

The demographics of the population is summarized below in table 4.1.

Table 4.1: Participants' Characteristics (N=186)

A

Characteristics	N (%)
Age (years)	
Mean (SD)	32.1 (9.7)
(Min, Max)	(18.0, 62.0)
Gender	
Male	81 (43.5)
Female	105 (56.5)
Marital Status	
Married	85 (46.0)
Widowed/Separated/Divorced	18 (9.7)
Never Married	82 (44.3)
Annual Income	
<$20,000	40 (24.5)
$20,000-<$25,000	56 (34.4)
>$25,000	67 (41.1)
Education	
Less than HS	54 (29.0)
HS Graduate	59 (31.7)
Some College/College/More than College Graduate	73 (39.3)
Employment Status	
Employed for Wages	140 (75.3)
Self-employed	0 (0.0)
Out of Work (< 1 year)	7 (3.8)
Out of Work (> 1 year)	1 (0.5)
Student	16 (8.6)
Retired	0 (0.0)
Unable to Work	9 (4.8)

B

Characteristics	N (%)
Adult Health Insurance	
Yes	121 (66.12)
No	62 (33.9)
Insurance Type	
Private/Employer	81 (66.4)
Purchased	0 (0.0)
Government	23 (18.9)
Military	2 (1.6)
Obamacare	0 (0.0)
Other	15 (12.4)
Car Ownership	
Yes	158 (84.9)
No	28 (15.1)
Speak English	
Not at All	13 (7.0)
Not Well	90 (48.4)
Well	70 (37.6)
Very Well	13 (7.0)
Write in English	

Not at All	53 (28.5)
Not Well	79 (42.5)
Well	45 (24.2)
Very Well	9 (4.8)
Interpreter Needed for Medical	
Yes	120 (64.5)
No	66 (35.5)

C

Characteristics	**N (%)**
Year in Texas	
Mean (SD)	3.1 (2.5)
US Entry Status	
Visitor	0 (0.0)
Permanent Resident	70 (37.6)
Student	12 (6.5)
Refugee	102 (54.8)
Asylum	2 (1.1)
Have Children	
Yes	97 (52.2)
No	89 (47.8)
Children Insured	
Yes	91 (93.8)
No	6 (6.2)
Children Insurance Type	
Private/ACA	8 (8.7)
Medicaid	83 (90.2)
CHIP	0 (0.0)
Medicare	0 (0.0)
Other	0 (0.0)
Siblings in US	
Mean (SD)	1.7 (1.7)
Use Bus	
Yes	87 (46.8)
No	97 (52.2)
Health Assistance Program	
Yes	25 (13.5)
No	160 (86.5)

SCD characteristics among participants (Table 4.2).

173 (93%) had heard of SCD, and none of the total participants had the SCD symptoms. Over 65% were willing to be tested for SCD; however, only 32 (32.7%) had had prior screening. From the previously screened participants, only one confirmed positive (3.1%) with a trait status and no related pain frequency, medication, or medical visits.

About half of the total participants (52%) were willing to attend SCD education programs, while 48% declined such offer. None of them had previously been referred to genetic counseling. Only 18 (9%) had heard of genetic counseling and six (3%) had participated in genetic counseling. However, 135 (72.6%) were willing to participate in genetic counseling, if offered.

52.2% of participants had children or were pregnant, with 51.5% of them having had their children in the USA. A total of 95 children were related to the participants with 56 males and 39 females. Only two (2.2%) of the children had ever been screened for SCD, 14 (15%) had never been screened and 77 (82%) did not know if their children had ever been screened. Both screened children had sickle cell disease with pain and doctor visits at a frequency of once every three months while on medication.

Table 4.2: Sickle Cell Characteristics (N=186)

A

Characteristics	N (%)
Heard of SCA	
Yes	173 (93.0)
No	13 (7.0)
SCA Symptoms	
Yes	0 (0.0)
No	186 (100.0)
Willing to Screen for SCA	
Yes	122 (65.6)
No	64 (34.4)
Prior Screen for SCA	
Yes	32 (32.7)
No	66 (67.3)
Screen Result Positive	
Yes	1 (3.1)
No	31 (96.9)

B

Child/Children born in the US	
Yes	50 (51.5)
No	46 (47.4)
Screened while Pregnant in the US	
Yes	0 (0.0)
No	0 (0.0)
Child/Children Gender	
Male	56 (58.9)
Female	39 (41.1)
Child/Children Screened for SCD/T	
No	14 (15.1)
Yes	2 (2.2)
Don't Know	77 (82.8)
Willing to Attend SCD Education	
Yes	96 (51.6)
No	90 (48.4)
Heard of Genetic Counseling	
Yes	18 (9.7)
No	168 (90.3)
Participated in Genetic Counseling	
Yes	6 (3.2)
No	180 (96.8)
Willing to Participate in Genetic Counseling	

Yes	135 (72.6)
No	51 (27.4)
Have Child/Children or Pregnant	
Yes	97 (52.2)
No	89 (47.8)

Aim 1:

Association of gender with SCD awareness

Testing the association of gender to SCA awareness showed that females have lower odds of being aware of SCA compared to males, although this finding was not statisticly significant (O.R.:0.55, p=0.34). (Table 4.3)

Association of Demographic factors (Gender, Age, Education, Income and Marital Status) with SCD awareness (Table 4.4.A)

When exploring the association of gender to SCD awareness, the result showed that there was no association of awareness and age (p=0.341), even though survival differs between male and female for sickle cell disease. Looking at association of each demographic factors with sickle cell disease, only those who have some college education or more had a lower odds of being aware of sickle cell disease compared to the comparison group of less than high school educated (O.R:0.13; p=0.0350). All the remaining factors such as annual income, marital status age and gender were not statistically associated with SCD awareness. This lack of association was also observed between SCD awareness and all immigration factors.

Association of Immigration factors (Interpreter needed, Years in Texas, and English Languages Profeciency) with SCD awareness (Table 4.4.B)

Participants who needed interpreter during medical visit had 1.536 times higher odds of of being aware of sickle cell disease compared to those who did not, though, not statistically significant. Year lived in Texas and being proficient in speaking and writing

English were both negatively associated with SCD awareness (O.R.s 0.929, 0.789 respectively) but not statistically significants for both of them (p = 0.5708, p = 0.7928 respectively).

Table 4.3 Gender associated with SCD Awareness

Variable	Odds Ratio (95% CI)	P-value
Gender		
Male	Reference	
Female	0.55 (0.16-1.87)	0.3410

Combining all factors to test the association of SCD awareness and Immigration and demographic factors (Table 4.4.C)

Only two factors had significantly associated with SCD awareness among DRC immingrants from North Texas when combing all the demographic and immgration factors. Females had a significantly lower odds of being aware of SCD compared to male (O.R: .0398, C.I:0.068-0.939, p = 0.0242). Following the same negative association, those who had some college education or more had lower odds of being aware of sickle cell compared to those who had less than high school education (O.Rs.:0.12; C.I:0.015-0.994; p = 0.0493). The remaining factors showed no statistically significant association with SCD awareness.

Table 4.4.A: Demographic factors associated with SCD Awareness

Variable	Odds Ratio (95% CI)	P-value
Gender		

Male	Reference	
Female	0.252 (0.068-0.938)	0.0398
Age	0.998 (0.904-1.102)	0.9747
Education		
Less than HS	Reference	
HS Graduate	0.579 (0.053-6.297)	0. 6539
Some College/College/More than College Graduate	0.122 (0.015-0.994)	0.0493
Marital Status		
Married	Reference	
Widowed/Separated/Divorced	0.227 (0.031-1.660)	0.1440
Never Married	0.632 (0.119-3.362)	0.5903

Table 4.4.B: Immigration factors associated with SCD Awareness

Variable	**Odds Ratio (95% CI)**	**P-value**
Interpreter needed		
No	Reference	
Yes	1.536 (0.214-11.05)	0.6697
Year in Texas	0.929 (0.722-1.197)	0.5708
English language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	0.780 (0.122-0.4989)	0.7928

Table 4.4.C: All factors associated with SCD Awareness

Variable	Odds Ratio (95% CI)	P-value
Gender		
Male	Reference	
Female	0.252 (0.068-0.938)	0.0398
Age	0.998 (0.904-1.102)	0.9747
Education		
Less than HS	Reference	
HS Graduate	0.579 (0.053-6.297)	0. 6539
Some College/College/More than College Graduate	0.122 (0.015-0.994)	0.0493
Marital Status		
Married	Reference	
Widowed/Separated/Divorced	0.227 (0.031-1.660)	0.1440
Never Married	0.632 (0.119-3.362)	0.5903
Interpreter needed		
No	Reference	
Yes	1.536 (0.214-11.05)	0.6697
Year in Texas	0.929 (0.722-1.197)	0.5708
English language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	0.780 (0.122-0.4989)	0.7928

Aim 2

Association of Demographic factors (Gender, Age, Education, Income and Marital Status) with Willingness to be Screened for SCD (Table 4.6.A)

Testing of gender association showed that female participants had 2.4 times higher odds of being screened for sickle cell disease compared to male (O.R.:2.406; p=0.0053). When combining gender with other demographic factors, females maintained their higher odds of willingness to be screened compared to males (O.R:2.98; p=0.0094). However, when looking at association of willingness to be screened and education, high school graduates, those with some college education, as well as college graduate participants had lower odds of being willing to screen for SCD compared to those who had less than high school education (O.Rs.: 0.33; 0.09; p=0.0057; p=<0.0001 respectively). On a positive side of association, never married participants had a 2.8 times higher odds of being willing to screen compared to those who were married (p=0.0450).

Association of Immigration factors (Interpreter needed, Years in Texas, Immigration Status, Native and English Languages Profeciency) with willingness to be screened for SCD (Table 4.6.B)

When looking at immgration factors to determine their association with willingness to be screened for SCD, only one factor had a statistitically significant association. Refugees had 7.238 times higher odds of being willing to be screened compared to participants with permanent resident status (C.I: 3.253-16.105; p=<0.0001) (Table 4.6.B). All the remaining factors under immgration factors groups did not produce a statistically significant association with willingness to be screened for SCD.

Table 4.5: Gender associated with willingness to be screened for SCD

Variable	Odds Ratio (95% CI)	P-value
Gender		
Male	Reference	
Female	2.406 (1.297-4.461)	0.0053

Table 4.6.A: Demographic factors associated with willingness to be screened for SCD

Variable	Odds Ratio (95% CI)	P-value
Gender		
Male	Reference	
Female	2.98 (1.31-6.81)	0.0094
Age	1.00 (0.95-1.06)	0.9773
Education		
Less than HS	Reference	
HS Graduate	0.33 (0.11-0.99)	0.047
Some College/College/More than College Graduate	0.09 (0.03-0.29)	<0.001
Annual Income		
<$20,000	Reference	
$20,000-<$25,000	1.05 (0.37-3.01)	0.9252
>$25,000	1.98 (0.71-5.50)	0.1900
Marital Status		
Married	Reference	
Widowed/Separated/Divorced	0.4550 (0.818-25.31)	0.0835
Never Married	2.8 (1.02 – 7.69)	0.0450

Table 4.6.B: Immigration factors associated with willingness to be screened for SCD

Variable	Odds Ratio (95% CI)	P-value
Interpreter needed		
No	Reference	
Yes	1.864 (0.630-5.517)	0.2606
Year in Texas	0.898 (0.780-1.034)	0.1357
Status when Entered USA		
Permanent Resident	Reference	
Students	1.099 (0.266-4.545)	0.8965
Refugees	7.238 (3.253-16.105)	<0.0001
Asylum	0.389 (0.009-17.694)	0.6276
Native language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	2.647 (0.651-10.765)	0.1739
English language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	0.663 (0.208-2.113)	0.2606

Immigrant Factors Associated with Willingness to be Screened for SCD

Combining all factors to test the association with willingness to be screend and Immigration and demographic factors (Table 4.6.C)

Within this construct of combining all demogaphic and immigration factors, females had higher odds of being willing to screened for SCD compared to males. This is statistically significant (O.R: 4.095 C.I: 1.532-10.943 p=0.0049). Never married also had 3.60 times higher odds of being willing to screening for SCD compared to male (C.I:1.118-11.592; p=0.0318). This trend of positive association continued among refugees compared to permanent resident participants (O.R:7.158; C.I:2.360-21.717; p=0.0005).

Table 4.6.C: All combined factors associated with willingness to be screened for SCD

Variable	**Odds Ratio (95% CI)**	**P-value**
Gender		
Male	Reference	
Female	4.095 (1.532-10.943)	0.0049
Age	1.004 (0.942-1.069)	0.9047
Education		
Less than HS	Reference	
HS Graduate	0.430 (0.092-2.020)	0.2852
Some College/College/More than College Graduate	0.0313 (0.053-1.829)	0.1971
Annual Income		
<$20,000	Reference	
$20,000-<$25,000	0.919 (0.253-3.337)	0.8978
>$25,000	2.915 (0.731-11.628)	0.1295
Marital Status		
Married	Reference	
Widowed/Separated/Divorced	0.227 (0.031-1.660)	0.1440

Never Married	0.632 (0.119-3.362)	0.5903
Interpreter needed		
No	Reference	
Yes	3.001 (0.756-11.912)	0.1183
Year in Texas	0.849 (0.695-1.036)	0.1067
Status when Entered USA		
Permanent Resident	Reference	
Students	3.994 (0.497-32.134)	0.1930
Refugees	7.158 (2.360-21.717)	0.0005
Asylum		
Native language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	6.048 (0.891-41.070)	0.0656
English language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	0.574 (0.149-2.206)	0.4186

Aim 3

Association of Demographic factors (Gender, Age, Education, Income and Marital Status) with willingness to participate in genetic counseling (Table 4.9.A)

Gender association with willingness to participate in genetic counseling was shown to be positive. Females were more predisposed to participate in genetic counseling than

males (O.R:3.841; p = 0.0287; C.I.1.150-12.83). When combining gender and demographic factors to test for association with willingness to participate in genetic counseling, female maintained higher odds of 5.551 times compared to male (p=0.0496). However, participants who had some college education or more had lower odds compared to participants with less than high school education O.R: 0.153; p=0.0435; C.I: 0.025-0.947). The remaining factors had no statistically significant association with willingness to screened for SCD.

Association of Immigration factors (Interpreter needed, Years in Texas, Immigration Status, Native and English Languages Profeciency) with willingness to participate in genetic counseling (Table 4.9.B)

When analyzing the association of immigration factors associated with willingness to participate in genetic counseling, it was only number of years spent in Texas that was associated with one's willingness to participate in genetic counseling (O.R: 1.065, p=0.0093; C.I: 0.893-12.72). No other immigration factors were statistically associated with willingeness to participate in genetic counseling. This trend of no association was also observered when combing all demographic and immigration factors together (Table 4.9.C).

Table 4.8: Gender associated with willingness to participate in genetic counseling

Variable	**Odds Ratio (95% CI)**	**P-value**
Gender		
Male	Reference	
Female	3.841(1.150-12.83)	0.0287

Table 4.9.A: Demographic Factors Associated with willingness to participate in genetic counseling

Variable	Odds Ratio (95% CI)	P-value
Gender		
Male	Reference	
Female	5.551 (1.001-30.73)	0.0496
Age	1.000 (0.919-1.088)	0.9925
Education		
Less than HS	Reference	
HS Graduate	0.405 (0.091-1.802)	0.2350
Some College/College/More than College Graduate	0.153 (0.025-0.947)	0.0435
Marital Status		
Married	Reference	
Widowed/Separated/Divorced	0.4550 (0.818-25.31)	0.0835
Never Married	2.256 (0.508-10.013)	0.2845

Table 4.9.B: Immigration factors associated with willingness to participate in genetic counseling

Variable	Odds Ratio (95% CI)	P-value
Interpreter needed		
No	Reference	
Yes	2.032(0.401-10.21)	0.3917

Year in Texas	1.065 (0.893-12.72)	0.0093
Status when Entered USA		
Permanent Resident	Reference	
Students	0.810 (0.033-19.683)	0.8972
Refugees	2.054 (0662-6.373)	0.2126
Asylum	4.131 (0.78-219.01)	0.4838
Native language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	1.001 (0.203-4.942)	0.9987
English language Proficiency		
Not Well spoken and written	Reference	
Well spoken and written	1.216 (0.235-6.289)	0.8158

Table 4.9.C: All combined factors associated with willingness to participate in genetic counseling

Variable	**Odds Ratio (95% CI)**	**P-value**
Gender		
Male	Reference	
Female	2 (0.580-6.903)	0.2726
Age	0.950 (0.875-1.031)	0.2223

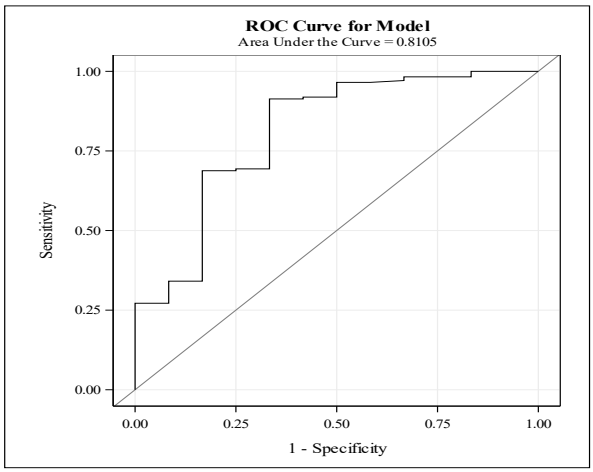
Education		
Less than HS	Reference	
HS Graduate	0.329 (0.086-1.260)	0.1046
Some College/College/More than College Graduate	0.332 (0.093-1.189)	0.0903
Year in Texas	1.078 (0.891-1.303)	0.4397
Marital status		
Married	Reference	
Widowed/Separated/Divorced	3.086 (0.709-13.426)	0.1331
Never Married	0.763 (0.212-0.2747)	0.6790

Model Goodness-of-Fit

A study conducted by Metz (1978) on the basic principal of Receiving Characteristic Curves (ROC) suggested the following grading of accuracy based on the surface under the curve: an area under the curve is deemed excellent with it is between 90%-100%, good between 80%-90%, fair between 70%-80%, poor between 60%-70% and fail between 50%-60%. This suggestion by Metz was used for all the goodness-of-fit in this research. Also, we looked at the Hosmer Lemeshow (HL) statistic for goodness of fit of our models where a p-value greater than alpha of 0.05 indicated that the null hypothesis was not rejected and therefore the model was an adequate fit to the data.

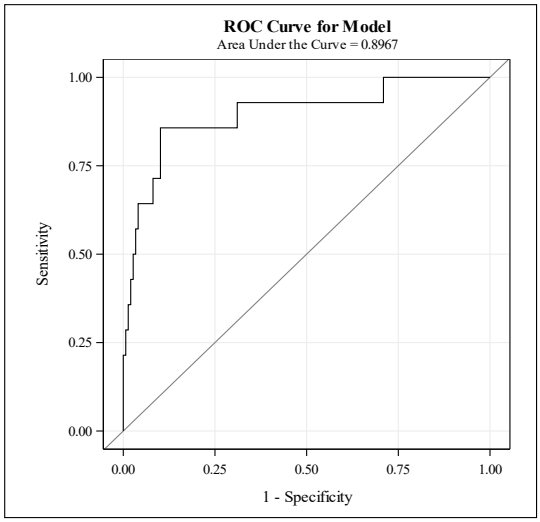
For Aim 1, the model provided a p-value of 0.553, indicating adequate fit based on the HL statistic. Area under the ROC curve was .81, indicating good fit of the model.

Figure 4.1: Model Receiver Operating Characteristic Curve (ROC) for the model with all factors associated with SCD awareness



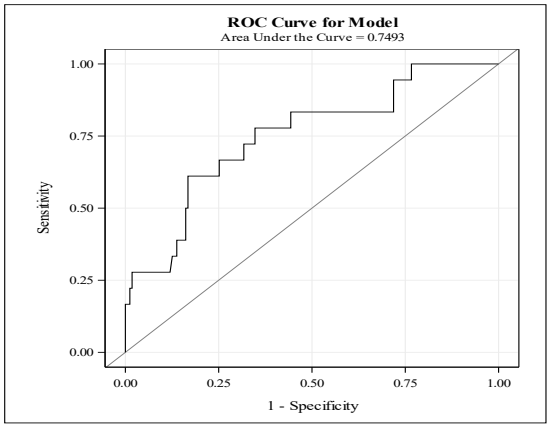
The overall model for aim 2 had a p-value of 0.42 corresponding to the HL statistic; therefore, signifying adequate fit of the model. Area under the ROC curve was .90, indicating an excellent fit.

Figure 4.2: Model Receiver Operating Characteristic Curve (ROC) for the model with all factors associated with willingness to be screened for SCD



The overall model for aim 3 produced for all factors a p-value of 0.21 for the HL statistic indicating adequate fit of the mode. Area under the ROC curve was .75.

Figure 4.3: Model Receiver Operating Characteristic Curve (ROC) for all factors associated with willingness to be participate in genetic counseling



CHAPTER 5

DISCUSSION

Investigating sickle cell disease among citizens of Democratic Republic of Congo, one of the countries with the highest prevalence and incidence, who resided in North Texas may provide useful information for preventive measures among immigrants, and it may indirectly reduce hospital related costs. According to previous studies, many cases of SCD are recorded in low- and middle-income countries, like DRC, with high mortality and shortened lifespan when early diagnosis is lacking (Grosse et al., 2011; Piel et al., 2013). Therefore, assessing the awareness, willingness to be screened, and willingness to participate in genetic counseling may elucidate on the proper medical and educational measures to support migrants from DRC, as well as others living in the USA.

As with other research completed using primary data, the results presented here rely on the accuracy of the responses provided by the participants and the accuracy of translating the paper form of the interview results into electronic data, an important caveat that is further discussed in limitations. This study encompassed an adequate number of participants from DRC and enables sufficient power analysis of the understudied category of populations. The study revealed that 93% of participants had heard of SCD/A; however, less than 66% of them were willing to be screened for it, and only 32% had had prior screening.

Given that practically no research has been conducted on the awareness and willingness to be screened in the targeted population (DRC) living in the USA, the difference in hearing about a given disease and being predisposed to screening or having prior screening varied in the current study. This variation was consistent with health

literature (Shalini, Varghese D, Nayak M 2011). Participants of this research were split on their willingness to attend a SCD educational program (51.6% agree to attend if offered). However, this disagreement deepens when asked about hearing of genetic counseling. Only about 9.7% had heard of genetic counseling. Though only 9.7% had heard of genetic counseling, more than 72% of them were willing to participate in genetic counseling. Furthermore, more than 65% of participants in this research showed their willingness to be screened. Despite that 64.5% of participants would require interpretation for medical visits, since over half spoke little to no English (54.4%), and 71% had little or no ability to write English, the higher rate of willingness to participate in genetic counseling and screening was major progress. This was especially significant given that African immigrants are, in general, very reticent when it comes to participating in genetic screening for fear of discrimination (health insurance and employment) and racial profiling (Buseh et. Al., 2012).

One may argue that higher rates of willingness to participate in genetic counseling and screening (72% and 65% respectively) could be related to having health insurance. Although more than 65% of participants had health insurance, having insurance was only significantly associated with willingness to be screened, but it was not associated with genetic counseling. Those who had insurance had 2.23 higher odds of participating in SCD screening compared to those who did not ($p = 0.0134$). Furthermore, only 6 (3.2%) had participated in previous genetic counseling, though insurance ownership was high (65%). The small number of participants to consider genetic screening was concordant with previous studies. For instance, studies conducted among students in Ghana showed high awareness level (98.6%), but less than half of them had been screened for SCD

(Boadu, I., Addoah, T., 2018). This finding was also concordant with studies conducted by Ameade E.P.K, Mohammed, B.S., Helegbe, G.K., and Yakubu, S. (2015); Moronkola, O.A., and Fadairo, R.A. (2006); and Bazuaye, G.N., and Olayemi, E.E. (2006).

In this research, almost all participants (93%) were aware of SCD. This finding was not different from earlier reports from other authors (Ameade E.P.K. et al. 2015; Alao, O.O., Araoye, M., Ojabo, C., 2009), even though those previous studies were conducted only on students in educational institutions. From previous studies, schools were seen as an effective institution and platform for people to acquire sickle cell education follow by media (Ameade E.P.K, Mohammed B.S., Heledbe G.K., Yakubu, S. 2015; Alao, O.O., Araoye, M., Ojabo, C., 2009). However, in contrast with previous studies, in this research, the educated population (those who have some college education and above), had lower odds (O.R 0.13; C.I: 0.02-0.87; p = 0.035) of being aware of sickle cell disease compared to those who had less than high school education, even though those who had some college education and above represented almost 40% of the total study population. This trend was also observed when asked for their willingness to be screened. High school graduates had lower odds (O.R. 0.33, C.I: 0.11-0.99; p = 0.047) of being screened compared to those who did not graduate from high school. Also, those who had some college education (O.R 0.09; 0.03-0.2; p = <0.001) were less likely to participate in sickle cell screening compared to less than high school graduates. When looking at immigrations factors, only refugees had 7.238 higher odds of being willing to screened for SCD compared to permanent resident status holders. This called for more investigation on this status.

The negative association of education and SCD awareness, education and willingness to be screened, and education and willingness to be participate in genetic counseling in this study warrants further studies. However, it is known from previous studies among at risk populations that SCD awareness, testing and counseling were lacking (Boyd et al., 2005; Prabhakar, H., 2009). In this study, the majority of participants agreed to participate in genetic counseling (72.6%), and over half (51.6%) agreed to participate in SCD educational programs. This signals the potential importance and benefits of SCD education and genetic counseling as sources of preventive measure to control SCD and its associated medical costs. This is supported by previous studies by Boadu I. and Addoah T. (2018), and Laskey et al. (2003) where most participants who were interviewed agreed to genetic counseling. But, in this particular African community of DRC, where over half are refugees and asylum seekers (55.9%), internal barriers such as mistrust, fear, perceived discrimination and confidentiality concerns may not readily predispose them to engage in genetic counseling, even though they agreed to it. This was supported by a study conducted by Asgry, R., & Segar, N. (2011) that pointed to the internal individual barriers to healthcare access among refugees and asylum seekers.

The participants who disagreed to genetic counseling (27.4%) and SCD education programs, if offered (48.4%), may have done so because of fear— fear of discrimination or fear of losing a prospective life partner if screened positive for SCD. This is also supported in research conducted by Boadu I. and Addoah T. (2018). Moreover, beliefs, attitudes, and past experiences were known to influence the way individuals approach decision making, new knowledge, and learning (Catz, D.S., 2005). It is important to target at risk populations with tailored messages that empower them to consider screening for

SCD. Such action could have a beneficial impact on the target population, while indirectly having a positive repercussion on related healthcare costs.

The majority of participants (58.9%) had an income between $20,000 and less than $25,000/year. None of the participants earned more than $50,000/year, and over half of the participants (54.8%) were refugees with a mean average year of 3.1 years lived in Texas. This means that they were more likely to be blue collar workers given their low income, which could play a role in their ability to access adequate information in general, but health information in particular. Additionally, 132 (71%) participants did not write English well or at all. These factors may have negatively impacted their informational and educational capabilities. Furthermore, those who earned between $20,000 and less than $25,000/year had 4.72 times higher odds to be aware of SCD than those who earned less than $20,000/year, but this is not statistically significant. Income is not significantly associated with SCD awareness across the income level groups. However, participants who earned more than $25,000/year had lower odds (O.R.: 0.31; p = 0.023) of owning health insurance compared to those who earned less than $20,000/year. The majority of participants had insurance through their employers (66.4%), while 18% of them received insurance through the government. This high insurance ownership was significantly associated with willingness to be screened for SCD (O.R 2.23, p =0.0134. Table not shown). Participants in this study who had insurance were less likely to participate in genetic counseling and less likely to participate in both genetic counseling and to be screened for SCD. This may be related to insurance not covering counseling or fear and mistrust as described in previous studies (Asgry, R., & Segar, N. 2011; Catz, D.S., 2005).

In this study, 44.3% of participants had never been married, but they are 2.8 times more likely to be willing to be screened for SCD compared to married couples. This positive association might be seen as progress, especially in non-married participants, particularly in light of a previous study in Ghana which reported that 78% of public servants agreed to call off marriage if they become aware of the genetic incompatibility (Ameade E.P.K, Mohammed B.S., Heledbe G.K., Yakubu, S. 2015). This result between married and never been married participants was similar to the comparison of women to men in this study group (O.R.:2.98, p = 0.0094) since almost 2.4 times as many women were willing to receive genetic testing on hereditary diseases than men, which also confirmed the results of a previous study conducted by Childers, K.K. et al. (2018).

Limitations

The results from this study may serve as a basis for further studies of immigrant populations, even though the focus was solely on the population from DRC residing in Dallas-Denton-Fort Worth-Arlington metropolitan area of North Texas. The specific delimitation of the geographical and origin of the participants may limit the generalizability of the study to other populations. The nature of the study design – exploratory cross sectional study – and the convenience sample limit the findings of this study to the targeted group and cannot infer cause and effect relationship. Additionally, the responses collected were solely based on the trust of the participants; therefore, it is difficult to ascertain whether the participants were truthful in their responses to the survey questionnaire. The survey questionnaire was also filled in by hand, then translated and entered into Microsoft Excel for data analysis. This translation process of hand-written

response to the electronic data could lead to some human error affecting the accuracy of the data. However, the multiple verifications of the paper format to match the electronic form corrected possible errors.

Another limitation of this study was the cultural beliefs of many potential participants who believed that by signing a consent the survey team would profit monetarily, even though the purpose of the study was clearly stated to participants. The approval of the oral consent by IRB resolved this limitation.

A further limitation of this study was the limited interview in English only, and it was also limited to only female and male adults. Even though the study collected more than the minimum significant number of participants of 164, the time limit for the research, the lack of resources to interview more participants, and the inability to extend the reach to all African immigrants from endemic countries like Nigeria and India were some other limitations. Nonetheless, the data collected consistently supported studies conducted in the past on similar topics although some contradiction was noted.

CHAPTER 6

CONCLUSION

In a quest for economic, social, and educational opportunities, as well as political stabilities, people from around the world migrate, which has resulted in SCD showing up in places where it did not used to be. This migration was at the origin of the first case of sickle cell disease discovered in the USA over a century ago. Given that more than 13% of the US population are immigrants, and with Texas being one of the hubs for African immigrants from the Democratic Republic of Congo, one of the countries with the highest incidence of SCD, this study has rightfully focused its aims at the awareness of SCD, willingness to be screened for SCD and participate in genetic counseling for SCD among the immigrants from DRC. Understanding the above-mentioned aims confirmed the need of specifically designed approaches to reduce emergency department visits – therefore reducing healthcare costs – but most importantly, to prevent the disease and manage it properly as suggested by Kauf et al., 2009.

This study drew attention to migratory patterns of humans from endemic, developing countries to developed nations. Considering the high prevalence of SCD in many African countries, selective screening of immigrants from endemic countries like Nigeria and Democratic Republic of Congo upon arrival in developed nations would not only lead to proper diagnosis, management and treatment of the disease, but it could also inevitably lead to reduction of healthcare expenditures related to SCD in the United States.

Further studies are needed to focus on the root cause for the lack of interest in genetic counseling, even though there are pieces of evidence pointing to beliefs. In order

to properly dissipate any fear of discrimination or lack of interest in the vulnerable population regarding their participation in SCD screening and testing, proper educational programs are needed. Programs will need to consider prior experience, life changing events of immigrants (particularly refugees, as this was the majority of cases in this study), and traditional beliefs of participants. The use of the health belief model in an educational program will provide the most benefit to immigrants in the USA from SCD endemic countries. A greater scale study involving all the immigrants of high risk countries in the USA will provider a bigger and better understanding of the global need and how to properly tailor programs to inform, educate, and train beneficiaries in order to alleviate the majority of the nefaste effects associated with SCD. However, focusing on a smaller scale like the one in this current studies with a mixed methods could potentially provide more information on multiple aspects on the potential explanations of the negative association of SCD awareness, screening and testing and higher education among DRC immigrants in North Texas.

Since early diagnosis leads to better care and management of crises related to SCD and longer life expectancy (Platt et al., 1994), as immigrants continue arriving from SCD endemic countries, the establishment of selective screenings for such immigrants may provide a basis to capturing, for the first time, immigrated cases of SCD as an addition to the existing universal newborn screening system in place in the USA. Other successful programs like the Dor Yeshorim program – a premarital screening program for Tay-Sachs disease among the Jewish community – and the Cyprus premarital screening for Thalassemia that prevented the births of 90% of possible affected children and resulted in an 80% reduction of thalassemia births (Verma, I.C, & Puri, R.D., 2015) could

be also implemented as an additional step. As previously suggested by Atolagbe, T., (2018), an adaptation of similar studies of public health importance might play a key role as the basis for a sustainable reduction in sickle cell incidence and mortality in the United States.

APPENDIX A

APPENDIX A: SURVEY QUESTIONNAIRE

DEMOGRAPHIC INFORMATION

1. What is your current age? _____
2. What is your country of birth or origin? _____ (*if not from DRC, end survey)*
3. What is your gender? ❑ Male ❑ Female
4. What year did you leave your home country of origin? _____ (YYYY)
5. What year did you arrive in the United States? _____ (YYYY)
6. How many years, or months, have you lived in Texas? _____ months _____ years
7. Did you enter the United States as a:
   ❑ Visitor ❑ Permanent Resident ❑ F-1/F-2 Student
   ❑ Refugee ❑ Asylum seeker ❑ Don't know ❑ Other _____❑ Declined to answer
8. What is your native language? _____
9. Do you speak other languages? ❑ Yes ❑ No
   ➔ *If YES*: What other languages do you speak?
   _____ _____
   _____ _____
10. How well do you READ your own language?
    ❑ Very Well ❑ Well ❑ Not Well
    ❑ Not at all ❑ Don't know ❑ Declined to answer
11. How well do you WRITE in your own language?
    ❑ Very Well ❑ Well ❑ Not Well ❑ Not at all
12. How well do you SPEAK English? ❑ Very Well ❑ Well ❑ Not Well ❑ Not at all
13. How well do you WRITE English? ❑ Very Well ❑ Well ❑ Not Well ❑ Not at all
14. Do you usually need an interpreter for medical appointments? ❑ Yes ❑ No
15. What is the highest grade of school you have completed?
    ❑ Less than High school ❑ High School graduate or GED completed
    ❑ Some College/Vocational school ❑ College graduate
    ❑ More than college ❑ Don't know ❑ Declined to answer
16. Do you have living siblings? ❑ Yes ❑ No
    ➔ *If YES*: How many live in the US? _____

17. Do you or a family member have a car? ❑ Yes ❑ No

18. Do you use the bus system in the area? ❑ Yes ❑ No

HEALTH INSURANCE INFORMATION

Next, I will ask you a few questions about where you get care when you are sick and about health insurance.

When you are sick or need a doctor, where do you go to get healthcare? *Select one answer.*

❑ Doctor's Office
❑ Hospital Emergency Room
❑ Clinic or Health Center
❑ Retail Store Clinic or "Minute Clinic"
❑ Some other place (specify:_____)

19. Do you have health insurance or health coverage? ❑ Yes ❑ No

➔ *If YES*: What type of health insurance do you have? *Select all that apply*

❑ Private health insurance through my job, or the job of my spouse, partner or parents
❑ Insurance purchased directly from an insurance company
❑ Medicaid, Medical Assistance, or any kind of government assistance plan for those with low income or a disability
❑ TRICARE or other military health care
❑ Affordable Healthcare "Obama Care"
❑ Other, specify: _____
❑ No insurance

20. Are you enrolled in healthcare assistance programs? (JPS Connection, Parkland Community Health Plan etc.) ❑ Yes ❑ No

21. Do you have children? ❑ Yes ❑ No

22. Do they have health insurance? ❑ Yes ❑ No

➔ *If YES*: What type of health insurance do they have?

❑ Private/ACA ❑ Medicaid ❑ CHIP ❑ Medicare ❑ Other _____

SOCIAL DETERMINANTS OF HEALTH

23. Are you currently married or living with a partner, separated, divorced, widowed, or have you never been married?

❑ Married or living with partner (if yes go to Q# 24) ❑ Widowed (Go to Q# 25)

❑ Separated (Go to Q# 25) ❑ Never married (Go to Q# 25)

❑ Divorced (Go to Q# 25)

24. Since you are married or living with a partner:

a. Is your spouse/partner from the same country? ❑ Yes ❑ No

➔ From what country?_____

b. Is your spouse related to you? (arranged/family marriage) ❑ Yes ❑ No

➔ *If YES*: ❑ 1st Cousin ❑ 2nd Cousin ❑ 3rd Cousin ❑ Don't know ❑

Other_____

Has your spouse/partner ever been screened for Sickle Cell Disease? ❑ Yes ❑ No ❑ Don't know

25. Are you currently….

(*Please read responses to participant:)*

❑ Employed for wages ❑ A student

❑ Self-employed ❑ Retired

❑ Out of work for 1 year or more ❑ Unable to work

❑ Out of work for less than 1 year

26. What is your yearly total household income before taxes? Include your income, your spouse's or partner's income, and any other income you may have received.

❑ Less than $10,000 ❑ $20,000 to less than $25,000

❑ $10,000 to less than $15,000 ❑ $25,000 to less than $35,000

❑ $15,000 to less than $20,000 ❑$35,000 to less than $50,000

❑ $50,000 or more DO NOT READ OUT LOUD

❑ Declined to answer

SICKLE CELL INFORMATION

{Next I will ask you a few questions and talk to you about sickle cell anemia,}

27. Have you ever heard of Sickle Cell Anemia? ❑ Yes ❑ No

{Sickle cell anemia is an inherited blood disorder from both parents. Inherited means transmitted from parents to children through genes. SCA is very common in African descendants but also is seen in Caucasians, Asians, Middle Easterners, Indians, and Hispanics. Basic symptoms are recurrent pain events, and paleness/yellowing of skin and gums, and shortness of breath. These symptoms come and go throughout the patient's life.}

28. Have you had or do you currently have any of the above described symptoms?
    ❑ Yes ❑ No
29. Are you willing to be screened for Sickle Cell Disease/Trait?
    ❑ Yes ❑ No
30. Have you ever been screened for Sickle Cell Disease/Trait?

    ❑ Yes ❑ No (*Go to question # 31.)* ❑ I don't know (*Go to question # 31.)*

    ➔ *If YES*:

    a. Was the result positive? ❑ Yes ❑ No

        ➔ *If YES*: What is your status? ❑ Trait ❑ Disease

        1. How often are you in pain?
           ❑ Every day ❑ 2-3 times a week ❑ 1x every 3 months ❑ Never
        2. Do you take pain medication for this condition regularly? ❑ Yes ❑ No
        3. How often do you see the doctor for this condition?
           ❑ 1 time/week ❑ 2-3 times/month ❑ 1 every 3 months ❑ 1/ year

31. Would you be willing to attend a sickle cell educational program?
    ❑ Yes ❑ No
32. **Genetic counseling** is a process to evaluate and understand a family's risk of an inherited medical condition such as sickle cell Disease/Trait. Have you heard of genetic counseling?
    ❑ Yes ❑ No
33. Have you ever been referred to genetic counseling?
    ❑ Yes ❑ No
34. Have you ever participated in genetic counseling?
    ❑ Yes ❑ No
35. Are you willing to participate in genetic counseling? ❑ Yes ❑ No
36. Do you have any children or currently pregnant? ❑ Yes ❑ No *(If checked, end the survey.)*

➔ *If YES*:

a. How many biological children do you have? _____

b. Were any of your children born in the United States?

❑ Yes (if male, go to Q# 36.d) ❑ No*(If male, go to Q# 36.d)*

{Carrier screening is a term use to provide genetic testing on an individual who does not have any overt phenotype for a genetic disorder but may have one variant allele within a gene(s) associated with a diagnosis. }

c. During your pregnancy in the USA, have you received carrier screening?

❑ Yes ❑ No

d. What are your children's genders, ages and countries of birth?

Child#1: Age ____ M/F Country _____Child#5: Age ____ M/F Country _____

Child#2: Age ____ M/F Country _____Child#6: Age ____ M/F Country _____

Child#3: Age ____ M/F Country _____Child#7: Age ____ M/F Country _____

Child#4: Age ____ M/F Country _____Child#8: Age ____ M/F Country _____

e. Have any of your children been screened for Sickle Cell Disease/Trait?

❑ Yes ❑ No ❑ I don't know

➔ *If YES*:

❑ Trait ❑ Disease ❑ Negative ❑ Don't Know

➔ *If Disease:* How often is s/he in pain?

❑ Every day ❑ 2-3 times a week ❑ 1x every 3 months ❑ Never

➔ How often does he/she see the doctor for this condition?

❑ 1 time/week ❑ 2-3 times/month ❑ 1 every 3 months

❑ 1/ year

➔ Does he/she take pain medication for this condition regularly?

❑ Yes ❑ No

Thank you for participating in this study.

APPENDIX B

Participate in Research!!

A Survey to Study Sickle Cell Anemia (SCA) among African Immigrants

Are you from Democratic Republic of Congo (DRC)?

- **Are you a man 18 years or older?**
- **Are you a female between the age of 18 and 48?**

What is this Study about?

- We want to learn more about your experiences and awareness of Sickle Cell Disease among African immigrants from DRC living in the North Texas area.

Who can participate?

- African immigrants from DRC
- Men 18 years of age and over
- Women aged between 18 and 48 years old
- Live in North Texas (Dallas-Denton – Fort Worth – Arlington area.)

What's involved?

- This study involves answering questions about your health, health care and screenings, sickle cell disease awareness and related questions. A researcher will ask you the questions and record your answers.

What are the benefits of participating?

- We know very little about sickle cell screening, awareness and genetic counseling of African immigrants in the United States. The information you share in this study will increase our knowledge. This information may also help guide outreach, education, screening and access to health care efforts.

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Investigators:
Amy Raines-Milenkov, DrPH
Ndolembai S. Njesada, MPH
Karabi Nandy, PhD

CONTACT INFORMATION:
Ndolembai Njesada, MPH
214 282 0770
nsn0012@live.unthsc.edu

NORTH TEXAS REGIONAL IRB

Approval Date: August 12, 2019

APPENDIX C

APPENDIX C: CONSENT FORM

Study Title: Sickle Cell Disease Knowledge, Use of Medical Care and Willingness to be tested among Congolese of the Democratic Republic of Congo (DRC) African Immigrants in the North Texas Community.

Name of Principal Investigator: Amy Raines-Milenkov, DrPH

Department of Pediatrics and Women's Health, University of North Texas Health Science Center

Name of Co-Investigators: Ndolembai S. Njesada, MPH

Karabi Nandy, PhD

Department of Biostatistics and Epidemiology, School of Public Health, UNTHSC.

It contains important information about this study and what to expect if you choose to participate.

What you should know about this study:

- You are being asked to join a research study.
- You must be from the Democratic Republic of Congo
- You must be 18 years of or older
    - If you are female, must 18 to 48 years of age
- Participation in this study should take about
- This form explains the study and your part in the study.
- Please read it carefully and take as much time as you need.
- You are a volunteer. You can choose not to take part and if you join, you may quit at any time. There will be no penalty if you decide to quit the study. Your decision will not affect any relationship you may have with the University of North Texas Health Science Center.

Why is This Study is Being Done?

This research study of Sickle Cell Disease Knowledge, use of Medical Care and Willingness to be tested among African Immigrants in the North Texas Community will help us understand and advocate for the improvement of immigrant health. We want to understand more about sickle cell knowledge and experiences among African immigrants. This information can be used to guide education and health care programs.

Why Are You Being Asked to Participate?

You are being asked to participate in the study because you are from Africa, and

specifically from Democratic Republic of Congo. Sickle cell is known to be endemic in many countries in Africa. Because of the limited studies done in the endemic countries like Democratic Republic of Congo, we are asking you to help improve the understanding of sickle cell anemia and participation in genetic counseling among African immigrants in the U.S.A. Your participation could help guide interventions for African immigrants in the United States.

What Will Happen in This Study?

If you agree to participate in the study, you will be asked a series of questions, such as your knowledge, awareness of Sickle Cell Anemia, your willingness to be tested for the disorder, and your willingness to participate in genetic counseling. No identifying information will be collected, shared or stored as part of this study. The survey also includes questions about you and your family's history of sickle cell diagnosis, screening tests and healthcare utilization and your income. While talking with you, I will write down your answers on a paper survey. The interview will not be audio recorded. The researchers will be allowed to see and to use your health information for this research study. We may share your de-identified health information only with people from the Health Science Center who help with the research, or work with us on the research, or with the Office for Human Research Protection to make sure we do the research properly and protect your privacy. Some of these people may share your health information with someone else. If they do, the same laws that the Health Science Center must obey may not protect your health information. The researchers will obtain the following information during the survey:

- Demographic information such age, income, country of origin, marital status etc.
- Questions about members of your family such as number of siblings and/or children
- Immigration status, years of U.S. residency
- Health care system: access and use of medical care, including question about health insurance status, medical diagnosis and health insurance status of members of the household.
- Questions regarding education such as literacy, language, higher education etc.

How Long Will You Be in the Study?

This authorization will expire at the end of the study. We will keep all the information as long as necessary in case we need to look at it again. This information will be protected and kept confidential. When the survey is completed, all the data collected will be stored in a locked cabinet in the office of the Principal Investigator.

Study Costs, Compensation and Time:

Your participation in this study is completely voluntary. A series of questions will be asked and it will last about 25 minutes to one hour to complete.

What are the Possible Risks and Benefits of Participating?

The risks with this study are minimal. You might experience some stress, discomfort, or embarrassment associated with answering questions on the topic of sickle cell anemia. You may decline to answer a question or stop the study at any time, but the information you already provided may still be used.

Withdrawing From (or Leaving) the Research Study:

Participation in the research is completely voluntary. You can decide not to participate in the study. You can stop taking part in the study (withdraw) at any time before or during the survey. Deciding to participate, not participate, or withdrawing at any time will not affect your relationship with the study investigator or the University of North Texas Health Science Center. Since we are not collecting information that could identify you, such as your name, it will be impossible to withdraw your survey responses once you completed the survey and we have returned the survey to the UNTHSC. Signed consent forms will be stored separately from the survey.

Questions/Concerns

You may have questions about participating in the evaluation research study. The researcher conducting this study is Dr. Amy Raines-Milenkov. She can be contacted at 817-735-0109, or by email amy.raines-milenkov@unthsc.edu to answer questions.

If you have any question regarding your rights as research participant, please contact the North Texas Regional Institutional Review Board at 817-735-0409.

Do you voluntarily agree to participate in this study?
□ **Yes** □ **No**

Signature: _____ **Date:**_____

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

_____
Printed name of the Person Obtaining Informed Consent

_____ _____
Signature of Person Obtaining Informed Consent **Date**

APPENDIX D

Appendix D: Verbal Script/Consent

"Hello, my name is _____ and I am a part of the Building Bridges program. As a participant of the Building Bridges Initiative, you agreed to be notified for future/additional research during your consent. I am inviting you to participate in another research study. Your participation in this study is completely voluntary, and will in no way affect your current participation in the Building Bridges program. Can I tell you more about this research study?

The purpose of this study, called Sickle Cell Disease awareness, willingness to be tested and willingness to participate in genetic counseling among African immigrants from the Democratic Republic of Congo (DRC) in North Texas, is to to assess the awareness, willingness to participate in genetic counseling and willingness to be screened for Sickle Cell Disease (SCD) among African immigrants from DRC in North Texas. This study is being conducted by Dr. Amy Raines-Milenkov as a Principal Investigator and her co-investigators. A series of questions will be asked, and it will last about 25 minutes, but no longer than 1 hour.

There will be no compensation to participate in this study. In order to participate, you must be between 18 and 48 years of age female or male age 18 and older from DRC and be willing to participate in a phone interview or in person interview.

If you agree to participate in the study, you will be asked a series of questions, such as your awareness of sickle cell disease, your willingness to be tested, and to participate in genetic counseling. The survey also includes questions regarding your immigration status, your age, income level, your marital status, your families, educational level, and healthcare access. While talking to you, I will write down your answers on a paper survey. The interview will **not** be audio recorded. The investigators and their assistants will be allowed to use your health information for this research study. To do this research we need information that will be de-identified from you such as demographic information like your age and race, health insurance status, level of incomes and matrimonial status. This authorization will expire at the end of the study. We will keep the information as long as necessary in case we need to look at it again. This information will be protected and kept confidential.

There is minimal risk with this study. You may experience discomfort answering question regarding health insurance status, income level or immigration status. You may decline to answer a question or stop the study at any time, but the information you already provided may still be used. If you choose to end your participation, there will be no penalty and it will in no way affect the services or relationship you have with UNTHSC or the Building Bridges programs.

Do you voluntarily agree to participate in this study? **□ Yes** **□ No**

If you have any questions, concerns or complaints regarding this study, you can ask me at any time during our conversation, you can contact the Principal Investigator, Dr. Amy Raines-Milenkov at 817-735-0109, or you may contact UNTHSC's Institutional Review Board at 817-735-0409.

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