EXPERIENCES WITH SICKLE CELL DISEASE SCREENING AND DIAGNOSIS

USING PARENTAL EXPERIENCES WITH SICKLE CELL DISEASE SCREENING AND DIAGNOSIS TO GUIDE HEALTH SCIENCE EDUCATION: A SYSTEMATIC REVIEW AND INTEGRATIVE QUALITATIVE META-SYNTHESIS

BY

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A THESIS

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Abstract

Sickle cell disease (SCD) is a chronic, lifelong, often debilitating, inherited disorder that can affect every organ system. Affected individuals often experience repetitive pain crises, multiple hospitalizations and a diminished quality of life. Many people at risk for SCD are unaware of their sickle cell carrier status and surprisingly health care providers' knowledge of SCD is limited. Research literature focuses mainly on management of clinical manifestations of the disease. This systematic review and integrative qualitative meta-synthesis aims to capture parents' perspectives on the screening process and diagnosis of SCD or sickle cell trait (SCT). Information generated by this review will be helpful in contributing to the development or enhancement of guidelines and protocols in SCD and SCT management for health care providers and health care educators.

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I am grateful to Dr. Lawrence Grierson, whose support facilitated my ability to complete this program. The members of my Thesis Committee graciously gave of their time, too often on short notice, and provided critical and positive feedback, all while navigating scholastic challenges during the COVID pandemic. They offered kind words of encouragement and gently guided me.

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And my family, who I have most certainly neglected in the months preceding my Master's thesis defence. My mother, Cecile, has been invaluable, loving me and supporting me as always, and my son, Kyle, always the cheerleader. I am fortunate to have their support now and always.

Table of Contents

List of Tables

List of Figures

List of Diagrams

List of Abbreviations

CF	**Cystic Fibrosis**
GPs	**General Practitioners**
HbP	**Haemoglobinopathies**
HbA	**Normal Haemoglobin**
HbS	**Haemoglobin S (Sickle Haemoglobin)**
HSCT	**Haematopoietic Stem Cell Transplant**
MV	**Meredith Vanstone**
NBS	**Newborn screen**
NSAID	**Non Steroidal Anti-Inflammatory Drug**
PCP	**Primary Care Provider**
SC	**Sickle Cell**
SCD	**Sickle Cell Disease**
SCT	**Sickle Cell Trait**
SG	**Simone Griffith**
T	**Thalassemia**
UK	**United Kingdom**
USA	**United States of America**

Declaration of Academic Achievement

Simone Griffith completed this research work independently, with scholarly guidance from her supervisor (Dr. Meredith Vanstone) and committee members (Dr. Madeleine Verhovsek and Dr. Melissa Kimber). She received instrumental support from research assistants to sort the references for the systematic review and integrative qualitative meta-synthesis.

Introduction

Sickle cell disease (SCD) is an inherited blood disorder that affects millions of people worldwide (Diagram 1) (1-4). The disease is chronic, lifelong and can be debilitating. It has the potential to affect virtually every organ system in the body; potential consequences include - acute chest syndrome (chest pain, cough and fever), stroke, chronic anaemia, leg ulcers, dactylitis (inflammation of the hands), gallstones, kidney damage, bacterial infections and early death (1, 2). The disease not only impacts the quality of life of affected individuals, from frequent hospital admissions to higher rates of absence from school or work, but also the quality of life of the immediate family (5). Family caregivers of sickle cell patients often experience job loss, decreased earning potential and mental and physical fatigue (5).

SCD is the most commonly inherited group of blood disorders (6, 7). Mutations on the gene encoding the haemoglobin subunit β result in the change of the structure of the haemoglobin molecule (3, 6, 8). Sickle haemoglobin (HbS) carriers oxygen in the same way as normal haemoglobin (HbA) but there can be reduced oxygen delivery to tissues when there is sickle vaso-occlusion (blockage of post-capillary venules, causing reduced blood flow through the capillary beds) (1, 7, 8). SCD is an autosomal recessive disorder – affected individuals inherit two copies of the abnormal gene, one from each parent.

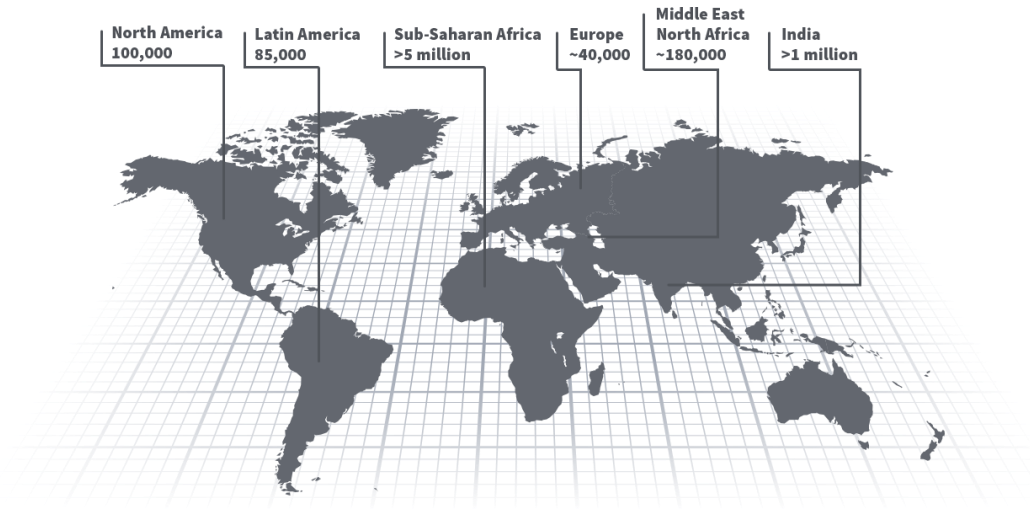
Drug therapy and blood transfusions are the treatment of choice to manage SCD. Haematopoietic stem cell transplantation (stem cells from bone marrow or blood) is the

only curative option for SCD, however, it carries a risk of complications such as infection, graft rejection and death (8, 9). The lack of available matched donors makes this therapy out of reach for the majority of patients with SCD (9). Gene therapy as a curative option for SCD is on the horizon – multiple gene therapy strategies are in clinical trials (9). Eighty to ninety percent of children born with SCD in high income countries will survive to adulthood, nonetheless, medical complications of SCD often lead to a shortened lifespan of 54-65 years (10, 11). Without early diagnosis of SCD and comprehensive medical care, children with SCD in low income countries and Africa may die before the age of five years (2, 11, 12). SCD is a global public health issue – 75% of the SCD population live in sub-Saharan Africa where inadequate health infrastructure, limited access to drug treatment, and poor nutrition leads to a high incidence of morbidity and mortality (2).

SCT is the carrier state for SCD. A normal haemoglobin gene is inherited from one parent and a sickle haemoglobin gene in inherited from the other parent (6-8, 11). Most people are unaware of their SCT carrier status (1, 2). SCT typically presents as a benign condition, however, venous thromboembolism (blood clots) and renal complications can occur at higher rates, and other complications can occur under periods of extreme exercise in affected individuals (13, 14).

It is believed that 3,000 to 5,000 people in Canada have SCD (4). SCD is most prevalent in people of Black African, South Asian, Mediterranean (Italian, Greek, Turkish), and Middle Eastern descent – regions endemic for malaria (11).

Diagram 1. Prevalence of Sickle Cell Disease Worldwide



Not Alone in Sickle Cell (15)

As the demographic of the population of Canada continues to become more ethnically and racially diverse, the incidence of SCD will continue to increase, as will the burden on the Canadian healthcare system (16). Aside from a set of national consensus recommendations for the care of patients with SCD in Canada (4), no nationally based strategies, policies or registries exist for guidance on the management of SCD in Canada (16). Health care providers, educational institutions and researchers are left to create policies and research at their discretion.

For many parents, the diagnosis of their child's SCD or sickle cell carrier status through newborn screen (NBS), will also act as the first diagnosis, albeit indirect, of their own sickle cell carrier status (17, 18). Research literature reveals that while many people at risk for SCD may be familiar with the disease, 25% – 50% of them will be unaware of

their own sickle cell carrier status (19-23). The psychological and physical demands of caring for a child with SCD can be devastating – from upheaval of the family dynamics, parental exhaustion of balancing multiple hospital admissions and medical appointments to financial challenges associated with absences from their job (5). There is value in understanding parents' lived experience with SCD and SCT given their important role in the identification, management and access to treatments for SCD and SCT for their children, respectively.

This systematic review and integrative qualitative meta-synthesis aims to consolidate what is known of SCD and SCT from the perspective of parents, it will also generate recommendations on aspects of the health care system that function well and those that do not function well and identify any gaps that exist. Information generated by this review will be helpful in contributing to the development or enhancement of guidelines and protocols in SCD and SCT management for health care providers and health care educators.

Clinical Background

Research has shown that while people may be familiar with term SCD they are not familiar with the details of the disease (19). Rudimentary information on SCD is provided to enhance the reader's ability to appreciate the complexity of the SCD and dispel misconceptions of the disease.

Etiology of Sickle Cell Disease

SCD is an inherited disease of the blood affecting the formation of haemoglobin. Haemoglobin is a protein in the blood that carries oxygen from the lungs to rest of the body (1, 6, 11). A single point mutation on the sixth codon of the beta-globin chain on chromosome 11, causes a permanent change of the haemoglobin structure, creating a new and abnormal haemoglobin gene (designated haemoglobin S - HbS). Mutations can also occur in different locations of the alpha globin and beta globin chain, which causes the creation of different or variant forms of haemoglobin genes (1, 6, 11).

Types of Sickle Cell Disease

Sickle cell disease: results from the inheritance of two abnormal haemoglobin genes (Diagram 2). Any combination of one abnormal haemoglobin S gene paired with another variant (abnormal) haemoglobin gene results in SCD. Sickle cell anaemia, the most prevalent and well known type of SCD, results from the inheritance of two abnormal haemoglobin S genes (3, 7, 12). Other SCD variants are described in Table 1.

Sickle cell trait: is characterized by the inheritance of one normal haemoglobin gene and one abnormal haemoglobin S gene (Table 1.) (1, 3, 6, 11). SCT is typically an asymptomatic and benign condition, however, in rare instances and under extreme conditions, such as excessive exercise, people affected with SCT can experience health concerns (13, 14). It is not uncommon for people affected with SCT to be unaware of

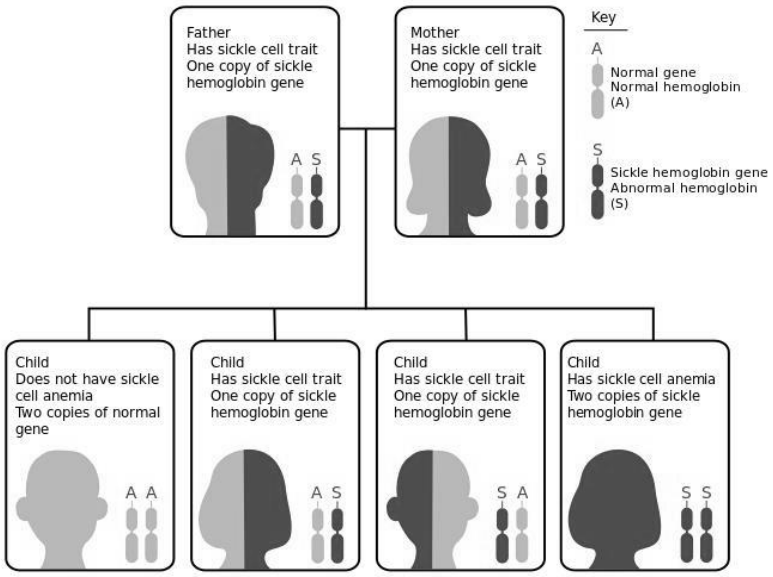
their carrier status. Furthermore, there remains confusion or misunderstanding of the genetic significance of SCD among people who know they are sickle cell carriers (13, 20). These potential parents may then be surprised to have a child affected with SCD (13, 20).

Table 1. Sickle Cell Disease Variations

Sickle Cell Disease	**Haemoglobin Variants**	**Prevalence**	**Disease Manifestation**
Sickle Cell Anaemia	HbSS	Most common form of sickle cell disease	Severe symptoms
Sickle Cell Beta Thalassemia $^{+}$	HbSβ^{+}	Less common	Less severe symptoms than sickle cell anaemia
Sickle Cell Beta-zero Thalassemia ^{0}	HbSβ^{0}	Less common	Severe symptoms
Sickle Cell C	HbSC	Less common	Less severe symptoms than sickle cell anaemia
Sickle Cell D	HbSD	Rare	Rare, almost no symptoms
Sickle Cell E	HbSE	Rare	Rare, almost no symptoms
Sickle Cell Arab	HbSO	Rare	Rare, almost no symptoms

Ware et al (2017) (8)

Diagram 2. Inheritance Pattern of Sickle Cell Anaemia and Sickle Cell Trait



Microsoft Library

Inheritance Pattern of Sickle Cell Disease

If both parents have SCD, all their children will also have SCD.

If both parents have SCT, in each conception there is a 25% chance that their child will have SCD.

If both parents have SCT, in each conception there is 50% chance that their child will have SCT.

If both parents have SCT, in each conception there is a 25% chance that their child will have normal haemoglobin.

If one parent has SCT and one parent has SCD, in each conception there is a 50% that their child will have SCD.

If one parent has SCT and one parent has SCD, in each conception there is a 50% that their child will have SCT (if the SCD consists of a haemoglobin S gene and a variant haemoglobin gene, in each conception there is a 25% chance their child will have SCT and a 25% chance their child will have a haemoglobin variant trait).

If one parent has SCT and one parent has normal haemoglobin, in each conception there is a 50% chance that their child will have normal haemoglobin.

If one parent has SCT and one parent has normal haemoglobin, in each conception there is a 50% chance that their child will have SCT (1, 6).

Sequelae of Sickle Cell Disease

Normal red blood cells are flexible, round in shape and travel easily through blood vessels (squeezing and changing shape) as they transport oxygen through the body (3, 6). Conditions of deoxygenation (oxygen molecules detach from the haemoglobin molecule) typically have no significant affect on normal haemoglobin molecules. However, deoxygenation of abnormal haemoglobin S molecules causes them to link together, leading to a change in the shape of the red blood cell (they assume a sickle shape, denoted by the notation of HbS) (1, 2, 7). The abnormal HbS red blood cells experience an episode of sickling. Sickled shaped red blood cells transport fewer oxygen molecules, are more fragile, rigid and less flexible and become jammed in the blood vessels because they cannot flow through blood vessels easily. Episodes of sickling deprive organs of vital oxygen which leads to periods of pain that are often termed pain crises. Repeated cycles of sickling, shorten the lifespan of the fragile sickle cell red blood cell to an average of 17 days versus 90 days for a normal red blood cell (1, 2, 7).

Chronic anaemia, fatigue, lethargy and frequent pain crises are the hallmark symptoms of SCD (6-8). Every organ system is subject to injury and permanent damage in SCD. The severity of symptoms and damage to organs in SCD is largely dependent upon the type of variant haemoglobin gene(s) inherited.

Lifespan, Treatment and Cure

Lifespan

The quality of life and life expectancy of people affected with SCD vary widely depending on country of birth, age of diagnosis, age at initiation of drug treatment, and access to care (1, 11, 24). In high income countries, more than 90% of infants born with SCD will survive to adulthood. Early diagnosis of SCD by NBS and greater access to drug therapy and comprehensive medical care, reduce the incidence of childhood morbidity and mortality (2, 11, 24). Clinical manifestations of SCD can vary from person to person and within the types SCD (6). Some patients will experience many symptoms while other patients will experience few symptoms over their lifetime (6). Adherence to prophylactic drug regimens and vaccination schedules, and general health routines affect the quality of life and life span of SCD patients. However, the lifespan of people affected with SCD is generally reduced by 15 to 24 years as compared to people not affected with SCD (25).

Infants born in low income or low resource countries, as in African countries, where NBS is not routine and there is limited access to drug treatment, or low resources of drug treatment early in life, may only have a 10%-50% survival rate to the age of five years (12, 24). Low rates of early detection in infancy and early childhood and limited access to prophylactic penicillin and hydroxyurea, limit the lifespan to 15-20 years for children who survive beyond the age of five years in low income countries (11, 12).

Treatment

- Prophylactic penicillin (preventative), initiated by three months of age, is used for management of SCD in children and reduces the frequency of infections.
- Hydroxyurea, is an oral medication that is used to prevent anaemia and reduce the incidence of pain crises and other acute and chronic complications.
- L-glutamine is an oral powder used to help reduce the frequency of pain crises
- Crizanlizumab is an intravenous drug that is used to help reduce the frequency of pain crises.
- Morphine is an opioid drug used to help relieve pain. Other opioid and/or nonsteroidal anti-inflammatory drug (NSAID) analgesics are also among the available options for pain treatment.
- Voxelotor is an oral drug that is used to improve anaemia.
- Blood transfusions are frequent and commonly used to manage severe and chronic anaemia associated with the SCD.

Cure

Haematopoietic stem cell transplantation (HSCT): is the only curative treatment for SCD. It is expensive, with a risk of toxicity, and health concerns post transplant, including early death. HSCT is often reserved for cases in which repeated blood transfusions are no longer feasible (4, 6). Periods of sickling can lead to progressive organ and tissue damage as SCD patients age. Organ dysfunction can increase risks of

organ toxicity, morbidity and transplant-related mortality exponentially and for this reason, HSCT is often reserved for children younger than 17 years (4, 6).

Gene therapy: is a relatively new curative option in the clinical trial phase (9).

Screening and Diagnosis of Sickle Cell Disease and Sickle Cell Trait

Screening for SCD can be offered to women and men pre-maritally, pre-conception, and antenatally. The United Kingdom (UK) offers universal antenatal screening for SCD for women at risk for SCD (26, 27). Antenatal screening for SCD in Canada, the USA, and the Netherlands is offered at the discretion of the health care provider (26). Infants can be screened via the NBS within a few days of birth. In other instances, infants may not be offered screening or diagnosis for SCD until symptoms manifest.

Haemoglobin electrophoresis: a blood test used to identify normal and abnormal haemoglobins. This test is able to diagnose all forms of SCD and SCT (8).

Sickle cell solubility test (commonly called SICKLEDEX®): a blood test used to identify the presence of haemoglobin S. The test is unable to detect other abnormal haemoglobins and can only be used as a screening tool (8). Further diagnostic tests need to be run when haemoglobin S is identified. The absence of haemoglobin S can be used to exclude SCD or SCT only. This test is not reliable in the neonatal period.

Newborn screen: a blood test used on newborn infants to assess the probable presence of disorders (genetic, metabolic, blood or hormone related) that may not be

apparent immediately after birth. The disorders that can be screened are not uniform and vary by jurisdiction. Canada does not have a national universal newborn screening program – each province and territory operates its own newborn screening program. Currently only eight provinces and one territory offer universal screening for SCD (Alberta, British Columbia, New Brunswick, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, Quebec and the Yukon) (28).

Genetic counseling for pre-marital or pre-conception: can be offered to couples if each parent carries one sickle cell gene. These couples have a one in four chance of baby with SCD (Diagram 2). A genetic counselor may enquire of the family history of each couple and offer pre-implantation screening of embryos, which can identify embryos that may carry SCD or SCT.

Genetic counseling during the antenatal period: can be offered to parents when each parent screens positive for the sickle cell gene during pregnancy. Prenatal diagnosis for the fetus (unborn baby) can be offered in early pregnancy to determine whether the fetus has SCD.

- *Chorionic villus sampling:* is performed between 10 and 12 weeks of pregnancy and involves obtaining a sample of the placental tissue (8).
    - The procedure can be performed transcervical – a catheter is inserted through the cervix into the placenta to obtain tissue.
    - The procedure can be performed transabdominal - a needle is inserted through the abdomen and the uterus into the placenta to obtain tissue

- *Amniocentesis:* is performed between 15 and 20 weeks of pregnancy and involves the insertion of a thin needle through the abdomen and the uterus into the amniotic fluid to obtain a small sample of amniotic fluid.

Chorionic villus sampling and amniocentesis carry a risk of infection, miscarriage, preterm labour and limb defects.

Author's Professional Experience with Sickle Cell Disease Screening

In my practice as a midwife, I have chosen to offer antenatal screening for haemoglobinopathies, which encompasses SCD, to all my clients irrespective of their ethnicity as anyone of any ethnicity can have SCT (6). I also have encouraged all my colleagues to offer haemoglobinopathy screening to all their clients. The midwifery profession is prefaced on the belief of empowering and supporting women during pregnancy and I believe I have an opportunity and obligation to educate all my clients about SCD. While I have not maintained accurate statics, during 17 years of midwifery practice, the vast majority of my clients and their partners have either never heard of SCD or they are familiar with SCD, but unaware of their sickle cell carrier status. Through this screening practice, many of my clients have learned of their sickle cell or thalassemia carrier status for the first time. It is important to be aware that the sickle solubility test is the only test that can be ordered within a midwife's scope of practice in Ontario. Only one diagnostic laboratory processes haemoglobin electrophoresis tests ordered by midwives.

Method

Methodology

This systematic review and integrative qualitative meta-synthesis uses Sandelowski and Barosso's methodology (29). Integrative qualitative meta-synthesis is also known as qualitative research integration. It aims to summarize the findings of multiple studies with two aims: first, this technique aggregates results to reflect the range of findings across studies while still retaining original meaning. Second, it produces a new integrative interpretation by comparing and contrasting findings across studies.

Integrative qualitative meta-synthesis is the appropriate synthesis methodology for the current project because it balances description and interpretation, focusing on understanding what has been said about a topic and offering new understanding by looking at the cumulative evidence. This approach is more consistent with systematic review methodology than many other qualitative synthesis approaches because it allows a priori definition of the research question and search strategy, as opposed to using a progressively iterating research question with a more flexible search strategy (29). This methodology focuses on the synthesis of qualitative findings, which is congruent with my exploratory research question about experiences.

Study Design

This systematic review and integrative qualitative meta-synthesis answers the research question - What are parents' experiences with sickle cell disease screening and diagnosis?

Table 2. Inclusion and Exclusion Criteria

Inclusion	**Exclusion**
English language, full text articles	Quantitative
Published, peer reviewed, research	Not empirical
Primary qualitative empirical research (using any descriptive or interpretive qualitative methodology, including the qualitative component of mixed-methodology)	Not English
	Not patient or parent perspective
Studies involving the experiences or perspectives of people who have sickle cell disease or trait and/or their parents	Not peer reviewed
	Not primary
Studies published after 2006	Not sickle cell
	Animal study
	No abstract
	Plant Study
	Relevant but not eligible
	Sickle cell is secondary focus
	Studies published before 2006

Search terms were developed based on truncations of the words sickle cell, sickle cell trait, anaemia, and combined with a validated search mega-filter developed and validated to identify qualitative research (30) (Appendix A). Wild card and Boolean Search Operators were used to capture the most relevant studies. A total of seven databases were searched, which included OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946 to Present, Embase (1974-2019), PsychINFO, AMED, OVID Emcare, and CINAHL. The

search process began 2019 June 18 and was complete 2019 June 28. No date limits were applied. Backward citation chaining of the included studies supplemented the database searches.

Article screening was completed in duplicate independently by SG and research assistants, who resolved disagreements through discussion. Eligible articles included English-language primary qualitative research studies addressing the experiences of parents or intended parents relevant to screening and diagnosis of SCD or SCT (Table 2).

Data Extraction

Each study was carefully reviewed and the country of origin, number of participants, and study design was recorded in an excel spreadsheet. Themes identified in the original study that represented the experiences of the participants were extracted and analyzed using the process detailed below.

Data Analysis

Following the analytic instructions of qualitative meta-synthesis (29), we aimed for findings which produced both a comprehensive summary of the original study articles, as well as an interpretation of the meaning of this information from the perspective of parents. This was achieved through multiple rounds of coding, following an adapted version of the staged coding process of Grounded Theory (31). First, descriptive codes were used to summarize key points in each article. Next, codes were gathered together

with similar ideas into categories. The third stage of coding involved the application of interpretative ideas, another pass through the data to recognize relevant data excerpts, and then a re-combination of the categories. Analysis was led by SG, who discussed emerging analytic ideas with MV.

Figure 1. Systematic Literature Search PRISMA Diagram

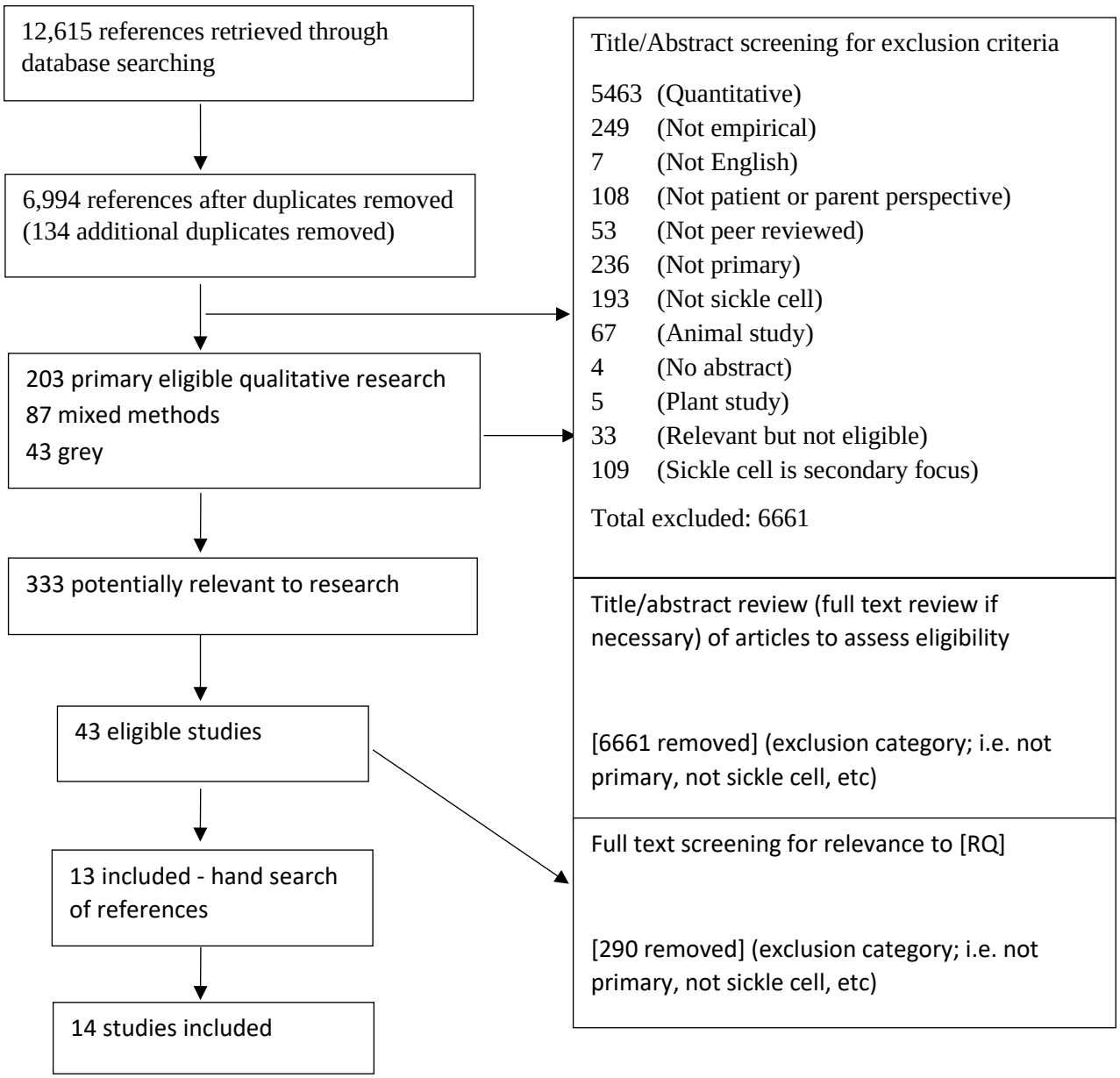


Table 3. Characteristics of Included Studies

Author(s)	Title	Country	Topic	Style	Participants
Biwott, P.J. et al (2017)	Disclosure of Sickle Cell Disease Results to Parents/Guardians Participating In a Research at a Hemato-Oncology Clinic in Eldoret Kenya	Kenya	Screening of children	Interviews and questionnaire	46 parents, guardians, health care providers
Bruce, A.A., et al. (2018)	A complex interface: Exploring sickle cell disease from a parent's perspective, after moving from Sub-Saharan Africa to North America.	Canada	Screening of children	Interviews	12 parents
Chudleigh, J., et al. (2016)	Parents' Experiences of Receiving the Initial Positive Newborn Screening (NBS) Result for Cystic Fibrosis and Sickle Cell Disease	UK	Newborn screening	Interviews	22 parents
Collins, J. L., et al. (2013)	Factors that influence parents' experiences with results disclosure after newborn screening identifies genetic carrier status for cystic fibrosis or sickle cell hemoglobinopathy	USA	Newborn screening	Interview and questionnaire	270 parents

Table 3. cont. Characteristics of Included Studies

Author(s)	Title	Country	Topic	Style	Participants
Holtkamp, K.C.A, et al. (2018)	Experiences of a High-Risk Population with Prenatal Hemoglobinopathy Carrier Screening in a Primary Care Setting: a Qualitative Study	Netherlands	Antenatal screening	Interviews	26 expectant women
La Pean, A., et al. (2012)	A qualitative secondary evaluation of statewide follow-up interviews for abnormal newborn screening results for cystic fibrosis and sickle cell hemoglobinopathy	USA	Newborn screening	Interviews	195 parents
Lebensburger, J.D., et al. (2015)	Understanding and improving health education among first-time parents of infants with sickle cell anemia in Alabama: A mixed methods approach	USA	Newborn screening	Interviews and questionnaire	8 parents
Locock, L. and Kai, J. (2008)	Parents' experiences of universal screening for haemoglobin disorders: implications for practice in a new genetics era	UK	Antenatal and newborn screening	Interviews	39 parents
Miller, F.A., et al. (2010)	Understanding sickle cell carrier status identified through newborn screening: a qualitative study	Canada	Newborn screening	Interviews	6 parents, 8 community based advocates, 42 health care providers

Table 3. cont. Characteristics of Included Studies

Author(s)	Title	Country	Topic	Style	Participants
Reed, K. (2009)	'It's them faulty genes again': women, men, and the gendered nature of genetic responsibility in prenatal blood screening	UK	Antenatal screening	Interviews	48 parents
Reed, K. (2011)	'He's the dad isn't he?' Gender, race and the politics of prenatal screening	UK	Antenatal screening	Interviews and focus groups	48 parents
Tsianakas, V., et al. (2012)	Offering antenatal sickle cell and thalassaemia screening to pregnant women in primary care: a qualitative study of women's experiences and expectations of participation	UK	Antenatal screening	Interviews	21 expectant women
Ulph, F., et al. (2011)	Familial influences on antenatal and newborn haemoglobinopathy screening	UK	Antenatal and newborn screening	Interviews	37 parents
Ulph, F., et al. (2015)	Parents' responses to receiving sickle cell or cystic fibrosis carrier results for their child following newborn screening	UK	Newborn screening	Interviews	67 parents

Table 4. Themes as identified by the Authors of the Studies Reviewed

Author	Title	Themes
Biwott, P.J. et al (2017)	Disclosure of Sickle Cell Disease Results to Parents / Guardians Participating In a Research at a Hemato-Oncology Clinic in Eldoret Kenya	• How the parent or guardian found out about the illness • Communication process • The person communicating sickle cell disease information • Expectations on the results • Perception of health care providers on the disclosure process • Adequacy of disclosure • Adequacy of time used during disclosure • Feelings after disclosure • Perception of health care providers on the adequacy of information disclosed and psychological impact • Tests used to screen sickle cell disease • Ethics of the disclosure
Bruce, A.A., et al. (2018)	A complex interface: Exploring sickle cell disease from a parent's perspective, after moving from Sub-Saharan Africa to North America.	• Parents recalling cases about SCD in their communities in Africa • Shock • Acceptance • Thinking about the future • Self-reliance • Guarded trust
Chudleigh, J., et al. (2016)	Parents' Experiences of Receiving the Initial Positive Newborn Screening (NBS) Result for Cystic Fibrosis and Sickle Cell Disease	• Prior knowledge of the condition (CF and SCD) and NBS • Receiving the initial positive NBS result • Reactions to the positive NBS result • Impact of the screening process on parental relationships • Future support strategies

Table 4 cont. Themes as identified by the Authors of the Studies Reviewed

Author(s)	Title	Themes
Collins, J. L., et al. (2013)	Factors that influence parents' experiences with results disclosure after newborn screening identifies genetic carrier status for cystic fibrosis or sickle cell hemoglobinopathy	• Specific content messages that influenced parents' experiences • PCP traits that influenced parents' experiences and reactions • Aspects of the setting that influenced parents • Positive and negative reactions reported by parents • Associations between factors and reactions
Holtkamp, K.C.A, et al. (2018)	Experiences of a High-Risk Population with Prenatal Hemoglobinopathy Carrier Screening in a Primary Care Setting: a Qualitative Study	• Familiarity with HbP's and carrier screening • HbP carrier screening: reasons to accept or decline testing • multistep process of decision making • perceived information overload during counseling
La Pean, A., et al. (2012)	A qualitative secondary evaluation of statewide follow-up interviews for abnormal newborn screening results for cystic fibrosis and sickle cell hemoglobinopathy	• Parents' opinions about the Project's follow-up interview • Reasons why parents found the Project's follow-up interview beneficial • Parents' emotional reactions to the Project's follow-up interview
Lebensburger, J.D., et al. (2015)	Understanding and Improving Health Education among First-Time Parents of Infants With Sickle Cell Anemia in Alabama: A Mixed Methods Approach	• Parental fear of sickle cell anemia and trust in sources of health information • Trust in sources of health information
Locock, L. and Kai, J. (2008)	Parents' experiences of universal screening for haemoglobin disorders: implications for practice in a new genetics era	• Being informed about screening • Timing of screening tests • Understanding carrier status and genetic risk • Communication of carrier results and advice about options • Religious influences on individual decision making

Table 4 cont. Themes as identified by the Authors of the Studies Reviewed

Author(s)	Title	Themes
Miller, FA., et al. (2010)	Understanding sickle cell carrier status identified through newborn screening: A qualitative study	• Uncertainty • Dissonant claims of clinical significance • Health-care providers' equivocation
Reed, K. (2009)	'It's them faulty genes again': women, men and the gendered nature of genetic responsibility in prenatal blood screening	• Women and 'embodied' responsibility • 'It's them faulty genes again': women and accountability
Reed, K. (2011)	'He's the dad isn't he?' Gender, race and the politics of prenatal screening	• 'He's the dad isn't he?' BME men and the positive result • Whiteness, and men's participation • Ethnicity, men and screening professionals
Tsianakas, V., et al. (2012)	Offering antenatal sickle cell and thalassaemia screening to pregnant women in primary care: a qualitative study of women's experiences and expectations of participation	• The perceived benefits of early screening • Satisfaction and expectations of being involved in decision making • The need for information
Ulph, F., et al. (2011)	Familial influences on antenatal and newborn haemoglobinopathy screening	• Family providing knowledge base • Family involvement in decisions • The control of information within families • Intergenerational control • Facilitating the messengers
Ulph, F., et al. (2015)	Parents' responses to receiving sickle cell or cystic fibrosis carrier results for their child following newborn screening	• Impact of knowing carrier results • Effect of process of communication • Considering 'cascade' testing within the family • Sharing carrier information with extended family

Results

Fourteen studies were reviewed for this paper, of which only three focused exclusively on SCD or SCT (32-34). Of the remaining 11 studies, it was not always possible to accurately discern whether the participants' comments related to experiences with screening for SCD, cystic fibrosis (CF) or thalassemia. By combining all these conditions, important nuances related to experiences of particular conditions (e.g., impact of race or stigma of an invisible chronic pain condition) may have been missed by the original researchers. Given that the current work was a secondary analysis, it was not possible to re-design the studies and so the current findings are limited by these existing design features.

From an initial body of 12, 615 references, the full text of 43 articles were reviewed. Thirteen eligible studies were identified (Figure 1). The reference section of each of the included studies (n=13) was hand searched. One additional study resulted from this process, for a total of 14 included studies.

Of the 14 studies analysed for this systematic review and integrative qualitative meta-synthesis, six focused on antenatal screening for SCT, four studies focused on SCT diagnosis from the NBS and four studies focused on SCD diagnosis from the NBS. There were no studies addressing the opportunity for screening before an individual reached reproductive age, married, or planning to conceive a pregnancy.

These 14 studies were conducted in Africa (n=1), Canada (n=2), the Netherlands (n=1), the UK (n=7) and the USA (n=3) and used a variety of methodologies including

grounded theory and focused ethnographies. A total of 876 participants were included across the studies - 766 women, 108 men and two participants of unspecified gender. Women constituted 87% of the study population. The participants in the study were described by the authors as: Black, Black-Caribbean, Black African, White, Asian, Latino, Middle Eastern, Chinese, and Mixed-race ethnicities. The terms SCD, SCT, haemoglobinopathy and haemoglobinopathies were used variably in the studies - a reflection of the topic addressed in different studies – and these terms are reflected in the results section of this paper.

The UK employs universal antenatal screening of women at risk for SCD or any haemoglobinopathy, whereas in Canada, the Netherlands and the USA, antenatal screening is performed at the discretion of the health care provider (26, 27). Conversely, the UK offers newborn screening as a choice, while eight Canadian provinces and one territory, the Netherlands and the USA employ universal NBS to detect SCD (26-28). No formal SCD screening systems exist in Africa, although pilot studies for SCD screening have been conducted in several African countries (35).

SCD screening of adults serves the purpose of detecting the sickle cell gene affording prospective parents the opportunity for pre-conception planning, prenatal diagnosis or termination of a pregnancy should the fetus have SCD or SCT. The primary purpose of the NBS is the identification of infants who have SCD. SCT detection from the NBS is an incidental finding (23, 34). The results have been divided into the themes - screening for SCT antenatally, and SCD and SCT screening post delivery (via the NBS) to capture the differences in parents' experiences with SCD screening.

Antenatal Screening for Sickle Cell Disease (Haemoglobinopathy)

Analysis of the studies revealed that experiences of screening for SCD (haemoglobinopathies) related to six themes: informed choice to screen and reasons to accept SCD (haemoglobinopathy) screening, awareness and education of SCD or SCT, timing of SCD (haemoglobinopathy) screening and planning of pregnancy and termination of pregnancy, responsibility for SCD (haemoglobinopathy) screening, family influence on SCD (haemoglobinopathy) screening and the role of religion in SCD (haemoglobinopathy) screening.

Informed Choice to Screen and Reasons to Accept Sickle Cell Disease (Haemoglobinopathy) Screening

Women's reasons for accepting screening varied. Most women in the studies accepted screening when it was offered to them and expressed satisfaction with their choice to be screened for SCT or a haemoglobinopathy (26, 27, 36). Some women felt their doctor provided a clear explanation of the purpose for screening and the significance of inheritance patterns of SCD and offered them time to accept or decline screening (27, 36); others reported feeling poorly informed of screening options and uncertain of the risks of SCD (36).

Women who expressed dissatisfaction with the information they received, reported receiving only a pamphlet or leaflet regarding haemoglobinopathies (36). Tsianakas et al reported that some women wanted more information from their doctor: "At the initial

consultations with their GPs, women were given a leaflet about SC and T [sickle cell and thalassemia] to take home and read. However, a number of women explained that in addition to that, GPs should have spent more time explaining the conditions face-to-face." (36, pg. 120).

Some women reported they were not offered a choice to screen or felt they were encouraged or led by their doctor or midwife to accept screening (26, 36). Other women, although given the choice to screen, felt incapable of making an educated decision, opting instead to defer to the doctor or midwife "who is the expert" (26, 27, 36). These women expressed complete trust in the health care provider and deemed them to be more knowledgeable about SCD.

The ease of the test - one extra blood test added to the standard tests done at the initial doctor or midwifery antenatal visit - was the impetus for a few women to accept screening (26). Holtkamp et al found that: "Women argued that screening is performed simultaneously with other blood tests, and thus entails only one extra sample of blood." (26 pg. 639). Along this same line of reasoning, some of the women who agreed to be screened never gave thought to the consequences of having a positive screen for SCT (26).

Women for whom English was a second language expressed dissatisfaction, confusion or misunderstanding with the screening process. One woman's request for an interpreter went unfulfilled while another woman complained of lack of educational literature in her native language (36).

Men constituted a small proportion of study participants. Reed reported that many of the men of colour in her study were familiar with SCD or haemoglobinopathies, all of whom accepted antenatal screening (38). Only half of the White men accepted screening. Some of the White men who declined to be screened were surprised they were offered screening, because they did not think they, as White men, were at risk for a haemoglobinopathy (38). Holtkamp et al also reported that some of the White men in their study did not expect the need to be screened (26).

Awareness and Education of Sickle Cell Disease or Sickle Cell Trait

Knowledge or lack thereof and understanding/misunderstanding of SCD risk factors, as well as related health concerns of the disease were inextricably linked to women's choices to accept or decline screening for SCD (haemoglobinopathies). Some women were aware of SCD or haemoglobinopathies, but they did not understand the hereditary nature of the disease when they accepted SCD (haemoglobinopathy) screening. Others, who were aware of SCD and its hereditary consequences, still declined antenatal screening on the premise the test results would only provide information of their own sickle cell carrier status and that "carrier screening would not provide certainty about the condition of their unborn child." (26, pg. 640). These women deferred to the NBS of the baby instead (26, 27).

With respect to risk factors, some women thought, mistakenly, that their advanced age was a risk factor for SCD (haemoglobinopathy) (36).

Several women reported they were unfamiliar with SCD or haemoglobinopathies. Other women suggested they were more aware of Zika disease than SCD suggesting the healthcare system did not provide enough information about haemoglobinopathies (26).

A few White women were surprised to be offered antenatal screening for SCD (haemoglobinopathy) (26).

Only a few women declined antenatal screening for SCD (haemoglobinopathy). Holtkamp et al found that women used lack of family history of a haemoglobinopathy as a reason to decline screening: "One woman argued that there was no need for haemoglobinopathy carrier screening as haemoglobinopathies did not run in her family and that she already has healthy children" (26, pg. 639). Other women chose to decline screening on the belief they were healthy (26, 27) and other women declined screening on the basis that their partners had been screened previously and were told that they did not have a haemoglobinopathy (36).

Timing of Sickle Cell Disease (Haemoglobinopathy) Screening, Planning of Pregnancy and Termination of Pregnancy

Women overall were happy with the opportunity to be screened, however many questioned the timing of screening.

Some women reported feeling overwhelmed when SCD (haemoglobinopathy) screening was offered during the initial antenatal visit for a pregnancy. They reported too

much information was provided at one time making it difficult to process screening options and make a decision at one visit (26). Many of these women were either unfamiliar with SCD or had not appreciated the hereditary risks or aspects of SCD (haemoglobinopathies) (26). Women offered suggestions of a separate appointment time to discuss SCD (haemoglobinopathy) screening as a solution to minimize excessive information at the first antenatal visit. Yet other women felt capable to process the information provided to them at the initial antenatal visit for that pregnancy (26, 27).

Tsianakas et al found that some women believed waiting to offer SCD (haemoglobinopathy) screening during the pregnancy was not ideal: "Some women said SC&T [sickle cell and thalassemia screening] should be done pre-conceptually in order for parents to be aware of their carrier status before conceiving." (36, pg. 119). Many women suggested that SCD (haemoglobinopathy) screening should be offered pre-maritally, preconception, prenatally or as early as possible in pregnancy to afford women or couples the time to make decisions about marriage partners, conception, prenatal diagnosis or termination of a pregnancy (26, 27, 36).

Responsibility for Sickle Cell Disease (Haemoglobinopathy) Screening

Women reported, in two studies, they felt they bore the majority of the burden of the choice to screen (36, 37) since "the screening was happening within their body" (37, pg. 350). They reported feeling a connection to the baby and responsibility for the baby's well being (36, 37).

Some of the women who were involved in relationships with men who were at risk for SCD (haemoglobinopathy), found it difficult to persuade their partner to be screened (27). Locock et al found that: "Some men felt sure they were not carriers because they were fit and healthy, and told their partners they did not need to be screened." (27, pg. 164). A complicating factor of partner screening was hesitancy related to fetal paternity (27); other women declined partner screening on the basis their partner had previous carrier screening (26).

The men who participated in screening for SCD articulated an increased sense of responsibility for the well being of their baby as the reason they chose to screen (38).

Family Influence on Sickle Cell Disease (Haemoglobinopathy) Screening

One study focused on the role of family members in the decision process of antenatal screening (39). One woman deferred decision making to her family stating that her partner, family and friends discouraged her from screening for SCD (39).

Other women opted to control or limit the influence their family had on screening by selectively choosing which aspects of the screening process to share with their family. Some women chose not to disclose they had learned they were at risk for SCD, while others chose not to disclose they had been screened (39). Many "participants felt that when information was conveyed to family so was a right to be involved." (39, pg. 367).

Role of Religion in Sickle Cell Disease (Haemoglobinopathy) Screening

Women of strong Christian and Muslim faiths framed reasons to decline or accept screening around their belief in God. Some women believed that their willingness or need to accept any child precluded their ability to accept screening. They "described a sense of resignation to God's plan." (27, pg. 165)

On the contrary, other women described the belief that early antenatal screening and detection could allow for prenatal diagnosis of the baby. Some women of both Christian and Muslim faiths stated that termination of an affected baby was a possibility provided it occurred early in the pregnancy (27).

Sickle Cell Trait Diagnosis

Some studies differentiated between screening and diagnosis of SCT. SCT is not a disease. It results from the inheritance of one normal haemoglobin gene and one sickle cell gene. Most people with SCT will have no symptoms and may be unaware of they carry the sickle cell gene (1-3).

Analysis of this group of studies revealed that experiences of disclosure of SCT results related to seven themes: awareness and education of SCT, disclosure of SCT results, communication of SCT results, emotional response to SCT diagnosis, sharing of SCT results and family support, paternity, and cascade testing. Two studies focused on

antenatal SCT (haemoglobinopathy) screening and four studies focused on newborn screening.

Awareness and Education of Sickle Cell Trait

Antenatal screening

Women who screened positive for SCT in pregnancy needed to make follow-up decisions. For one woman the decision was simple as her partner willingly chose to be screened (38). Women in another study were unprepared for a positive SCT results despite willingly accepting antenatal screening for SCD. They were unsure of the consequence of SCT for them or their unborn baby (36).

Newborn Screening

Several studies described the existence of SCT screening in population based newborn screening (17, 18, 34, 40). In these studies, it was common for parents to be unaware of their own sickle cell carrier status prior to the NBS.

The vast majority of families in the studies reviewed were unfamiliar with SCT and all wanted to learn more about sickle cell carrier status, in particular, information on the impact sickle cell carrier status would have on the health of their baby (17, 18, 27, 34). Some parents reported they were not aware their child had been screened for SCD or they reported they did not understand the purpose of the NBS.

Often parents wanted more information on the inheritance pattern of SCT, in particular, they wanted to know which parent carried the sickle cell gene (18). This was particularly relevant to parents who did not know they were at risk for SCT, such as a White couple who were confused by the SCT results of their baby (27).

Some parents misunderstood the role haemoglobin or blood played in SCT. Many reported hearing that their child had a problem associated with their blood. Parents interpreted this to mean their baby had bad blood (27).

Disclosure of Sickle Cell Trait Results

Disclosure of SCT detected by newborn screening differed by jurisdiction. SCT diagnosis is habitually disclosed to parents in the UK and the USA, but not every province or territory in Canada (17, 18, 27, 34).

All but one parent reported gratitude for knowledge of their child's sickle cell carrier status (18, 34, 39). Some parents found identification of sickle cell carrier status a helpful tool to plan for the child's future. Parents who did not receive disclosure of sickle cell carrier status, argued for continued disclosure of sickle cell carrier status (34).

Communication of Sickle Cell Trait Results

Parents received SCT (carrier) results by letter, phone call or in person. A few parents reported they had not received any results and others had no recollection of being informed that their baby was being screened for SCD (27).

Almost all parents preferred to receive positive SCT results in person, by a practitioner who had knowledge of SCD and SCT, and preferably known to them (18, 27, 34). They emphasized the importance of being able to speak directly with a health care provider about the meaning and implication of results and for this reason they preferred not to receive results via the telephone, or voicemail and on Fridays. They reported messages left on a Friday provided little opportunity to speak with a health care provider before the week ended. Some parents reported receiving a letter alerting them of the need to call their doctor for disclosure of the SCT test results. None of these parents reported liking this method of results disclosure (27).

Parents reported they had greater understanding of SCT when health care providers were patient, used non-medical terms and took time to explain in detail SCT and the implications of sickle cell carrier status. Several parents also reported additional written material enhanced their comprehension of SCT (18, 39).

Emotional Response to Sickle Cell Trait Diagnosis

Parents experienced a range of emotions when first learning of their child's SCT diagnosis. The detail provided to parents and the manner in which their health care provider delivered test results contributed to a parent's positive or negative emotional state (40). Even parents who reported good understanding of SCT or parents who had personal experience of SCT experienced negative emotional response upon learning their child had SCT (34); emotional responses included shock, surprise, sadness, and anxiety (17, 39). Many parents reported feeling scared and worried for their child's future and health; this was the case even if parents were made aware that SCT is considered benign (39). Other parents reported feeling reassured, calm, relieved, confident, and comfortable after their health care provider carefully explained the details of SCT, which emphasizes the important role health care providers have in providing information to contextualize test results (27).

Sharing of Sickle Cell Trait Results and Family Support

Parents' decision to share the SCT results for their baby seemed to be linked to their own experience with SCD or family history of SCD (39). Families for whom SCD or SCT had evoked negative experiences, criticism, or pity, seemed less willing to openly share their child's sickle cell carrier status (39). This pattern was more common in families of African descent or African immigrants. Parents reported a desire to avoid negative comments, pity, or shunning behaviour (39).

Some families found that SCT information was too difficult to explain to family members (39). Others preferred to remain secretive and one woman was very upset when she learned that her SCT results had been shared with her sister without her consent (39).

The need for secrecy was not expressed by all parents. Some parents believed it important to share the SCT results while others had no concern regarding informing family members of their child's results (27, 40). Families who had positive experiences with sharing the results of their baby's screen were also more likely to receive emotional family support (39). Sometimes the parents turned to their families for support when they first received the SCT results (39).

Paternity

It is not uncommon for many people to be unaware of their own sickle cell carrier status and issues of paternity were more common when the SCT diagnosis was unexpected. A White mother expressed gratitude that her White husband did not question the paternity of their child upon learning that her child had SCT. She stated she associated SCT as a disease that affects the Black race (27).

Cascade Testing

Upon learning of their child's sickle cell carrier status, some parents expressed a desire to know their own sickle cell carrier status and that of their other children (40).

This pattern of one diagnosis leading to many other tests is referred by Ulph et al as "cascade testing" (40). Some parents expressed frustration and worry when they were unable to have immediate family members tested. Yet other families reported that conflict arose between families when other relatives chose not to pursue their own sickle cell carrier status (40).

Sickle Cell Disease Diagnosis

Some studies focused on the diagnosis of SCD, rather than SCT (32, 33, 41, 42). Analysis of the studies revealed that experiences of disclosure of SCD results related to six themes: awareness and education of SCD, communication of SCD results, emotional response to SCD diagnosis, child's future, implication for future pregnancy planning and parental relationship, and sharing SCD diagnosis and support. In North America children who have SCD are most likely to be identified at birth. It is not uncommon, however, for many African children to be identified in early childhood. Two studies were based on NBS results, one study was based on SCD screening of children in Kenya, and one study was based on SCD screening of children who had immigrated to Canada from sub-Saharan African countries.

Awareness and Education of Sickle Cell Disease

Many of the parents who lived in African or had recently immigrated to Canada from Africa had witnessed children with symptoms characteristic of SCD. It is not

uncommon for children living in Africa to be misdiagnosed with malaria. Most of these parents did not anticipate a positive SCD diagnosis (32, 33). Some parents reported they were not aware their child had been screened or reported they did not understand the purpose of the NBS.

Many of the parents knew of family members or friends who had SCD. However, a few parents had no prior experience with SCD (41, 42). Most parents were unaware of their own sickle cell carrier status (32, 33).

All the parents expressed a desire to learn more information about SCD and the inheritance pattern of SCD. Some parents reported their health care provider was very informative of SCD and provided additional literature which they found helpful (42). Other parents reported relying on the internet, books or pamphlets to fill the gap left by health care providers (42).

Communication of Sickle Cell Disease Results

Many of the parents received results in person by a doctor or health care provider (32, 33), while some parents received a letter informing them a health care provider would deliver the newborn screen results in person at their home. Parents reported a preference for in person disclosure of SCD diagnosis.

Parents also reported that some doctors or health care providers appeared rushed, had too many patients or had busy clinics that did not afford the time required to discuss

the SCD results in detail (32). The parents in this group did not feel they had the opportunity to ask questions or learn enough about SCD. Some of these parents reported relying on family, friends or the internet to learn more about SCD when they perceived the doctors did not answer their questions (42).

Other parents also revealed lack of privacy or confidentiality during the disclosure process (32).

Emotional Response to Sickle Cell Disease Diagnosis

Almost all parents expressed profound reactions to the SCD diagnosis. Most parents expressed surprise and shock despite witnessing many unwell children in their hometown or village (32, 33). The results were at variance with their expectations (32).

Emotions expressed by many parents ranged from shock, disbelief, sadness, anger, and devastation to fear, guilt, blame and regret (32, 33, 41, 42). Many parents expressed difficulty reconciling their child's diagnosis and some expressed regret for having a child (41).

Child's Future

All parents reported feeling consumed with worry for their child's future. Many wanted to know how to recognize when their child was ill or in pain, other parents worried they would not know how to take care of their child and many were fearful their

child would die young (32, 33, 41, 42). Parents also expressed concern their child would not find a partner as an adult.

Parents who had family members with SCD reflected on their memories of relatives' experiences of being labeled a drug addict or drug seeker when they sought morphine treatment to manage painful sickle cell crises (32).

Implication for Future Pregnancy Planning and Parental Relationships

Parents expressed regret for not knowing their own sickle cell carrier status. They reflected that prior knowledge (pre-marital or preconception) of their sickle cell carrier status would likely have influenced their choice of partner or provided more options for pregnancy planning and prenatal diagnosis (32, 41, 42).

Other parents contemplated the option of not staying with their partner or choosing not to have more children (33).

S*haring Sickle Cell Disease Diagnosis and Support*

Parents often chose not to disclose their child's SCD diagnosis to family or friends. Many parents expressed fear their child would be treated differently than other children (33, 41). They also anticipated being shunned or pitied. Parents stated they did not want friends and family speaking poorly of them in their absence. Many parents desired for their children to be treated the same as children who did not have SCD (33, 41).

Parents' choice to remain secretive regarding their child's diagnosis ultimately created a feeling of isolation and lack of support (32). Some parents reported that they trusted only their health care provider and one or two close family members (32).

It is clear from the results that study participants would have benefited from prior knowledge of their own sickle cell carrier status.

Discussion

This systematic review and integrative qualitative meta-synthesis described the perspective of parents' experiences with SCD screening and diagnosis. The predominant themes from the 14 studies reviewed were; awareness and education of SCD or SCT, informed choice, communication between health care provider and parents, emotional impact of a positive diagnosis of SCD or SCT, and stigma and shame.

Across all of the studies reviewed, it was apparent that many of the parents were unfamiliar with SCD or SCT, and of the parents who knew of SCD or SCT, only a handful were aware of their own sickle cell carrier status. Futhermore, there was general misunderstanding of the health implications of SCD and SCT or that SCD and SCT are inherited, not communicable diseases (26, 27, 36, 40, 41, 42). While most parents accepted the offer to be screened for SCD or SCT, it was evident that not all parents perceived they had a choice to decline screening (27). Additionally, of the parents whose infants screened positive for SCD or SCT from the NBS, most failed to recall any discussion or offer of the NBS (26, 27, 36, 40, 41, 42).

Communication between health care providers and parents was a very important theme in all fourteen studies during the antenatal SCD screening process or disclosure of positive SCD or SCT results. Consistently in all of the studies, parents who perceived their health care provider as informative, thorough and clear, either during the screening process or disclosure of positive SCD or SCT results, overall reported more positive experiences (17, 18, 26, 27, 41, 42). Conversly parents who perceived their health care provider as uninformative, or unclear or not helpful during the SCD screening process and disclosure of results, reported more negative experiences, particularly when screening results were positive for SCD or SCT (17, 18, 26, 27, 41, 42).

Almost all of the parents of children who were diagnosed with SCD, reported experiencing a range of negative emotions ranging from disbelief to guilt to despair (32, 33, 41, 42). For many parents, the manner in which positive results were disclosed was imporant, with parents overwhelming preferring to be informed in person or by telephone rather than by letter (18, 26, 32, 42) .

Many of the parents of children diagnosed with SCD reported a need or desire to hide their child's positive SCD results from their family for fear of being shunned, or treated differently by their family.

Interpretation of Results

Lived Experience of People with Sickle Cell Disease

The studies reviewed in this paper captured parents' experiences with the screening process for SCD. An appreciation of the impact of SCD on affected individuals and their caregivers and family is important. SCD is a chronic, lifelong and often debilitating disease. Children living with SCD in high income countries have many appointments with family doctors, SCD clinics (where available) and often have high absenteeism from school. Parents or family caregivers often are required to be absent from work or need to change their career to facilitate the care of a child affected with SCD (5). The lived experience of a young man with SCD and a parent of young man with SCD are captured on the Centers for Disease Control and Prevention website:

One young man named Lance, reflected on his experience living with SCD:

> "The news altered my family dynamic in a major way. My mom, a nurse at the time, lost her job because she needed to stay home and take care of me. Her career goals were gone. My parents also had a separation period because of the hardships." (43)

Lance also shared his relationship with his siblings:

> "Every time I got sick and had to go to the hospital, they [my sister and brother] went to our grandmother's house. To them, I received special treatment because I needed it and they got less time and attention from my parents. To me, my parents' focus was always on keeping me healthy, not on my goals and dreams. My parents always saw me as the sick child. But my siblings, they let them spread their wings." (43)

A parent of a child affected with SCD shared her views on the manner in which SCD impacted her life and that of her child:

> "I finally met a man who was on track to be older than the age [doctors] gave me for how long my son would live. When he talked to us, he didn't talk to us from a sense of hopelessness. He talked to us about living a life, enjoying life, and the reality that we would have challenges, but how we view those challenges could not take away from the life that we were still meant to live. It was a level of hope that I had not allowed myself to have up to that point. Up until then, all I thought about was that sickle cell was a disease that was going to kill my child, and it was devastating. That encounter changed the course of my life and my son's life. I truly believe that my son is still alive today because of that conversation." (42)

These testaments highlight the psychological impact that SCD has on individuals affected with SCD and their families and the value and importance of SCD screening. In essence, SCD is a preventable disease as tools exist to detect carriers of SCT. The incidence of SCD could be reduced or eliminated by the intentional choice of a life partner or donor sperm that does not carry the sickle cell gene, or parents' choice not to procreate, or the option of prenatal diagnosis and/or pre-implantation testing (available in high income countries) (46).

Informed Choice

The screening process for SCD in most countries is optional, whether offered universally or at the discretion of a health care provider, prospective parents have the choice to opt in or opt out of the screening process. The health care provider is responsible for offering the opportunity to be screened. Informed choice is the

cornerstone of the screening process. The terms informed consent and informed choice are often used interchangeably, even in medical literature, but they are fundamentally two different processes. Informed consent is the choice to accept the test(s) that have been recommended by a clinician. Informed choice involves a deliberate decision based on relevant knowledge and values (44). The clinician does not seek to recommend or encourage any particular course of action, and counsels with the aim of providing information and facilitating an autonomous choice from the patient (45). Informed choice is the foundation of prenatal screening in Canada and many countries (45). Martineau et al describe informed choice as:

> "..an informed choice to undergo screening occurs when an individual has a positive attitude towards undergoing a test, and has relevant knowledge about the test and undergoes it. An informed choice to decline a test occurs when an individual holds a negative attitude towards undergoing the test, has relevant knowledge about the test and does not undergo it." (44)

Within the context of this review, the health care providers were responsible for not only offering SCD screening (either antenatally or post delivery through the newborn screening process) but were also responsible to ensure parents fully comprehended the purpose of the SCD screen, and the subsequent consequences and follow up options should they or their baby screen positive for SCD or SCT. Thus, in order for women or parents to make an informed decision to accept or decline SCD, do they need to fully understand SCD?

The challenge is that unlike other routine tests offered during pregnancy, for example, diabetes screening, blood tests or screening for Down Syndrome, that may be

familiar to women, either from experience with a previous pregnancy or through experiences of friends and family, SCD is not well known or understood (20, 21). This was true for many of the women in the studies reviewed, particularly for women who were not Black, who reported they were not familiar with SCD or haemoglobinopathy screening (26, 36). Many women accepted the offer of antenatal SCD screening but stated they did not fully understand the purpose of the SCD screen, while others reported that the antenatal SCD screen was not presented as a choice or they perceived their health care provider wanted them to screen for SCD, and consequently agreed to be screened (26, 27, 36). Essentially, these women exercised informed consent rather than informed choice (44).

Of the parents whose infant was diagnosed with SCD or SCT from the NBS, most could not recall being informed or offered the NBS. This was true whether the NBS was offered as a choice (opt-in program), as in the UK, or performed routinely (opt-out program) as in Canada and the USA (17, 26, 27, 41, 42).

Brown et al propose that women make informed choices to accept or decline antenatal SCT screening when they are offered screening at appropriate time during their pregnancy, understand the screen and the consequences of the screen (46). Conversely, women make an uninformed choice to accept or decline an antenatal SCD screen when the test is offered at an appropriate time during pregnancy, but they may not understand the screen or the consequences of not screening (46). Some of the participants in the studies reviewed, expressed regret for accepting the SCD screen once they learned they screened positive for SCT, as they had not contemplated the need for follow up

testing (26). While other women's choice to decline SCT could be interpreted as an uninformed choice, particularly when they stated that "sickle cell disease doesn't run in my family" or "I don't feel as though I have sickle cell disease" (26, pg. 639).

The question remains when screening tests are offered for health conditions for which most patients will be unfamiliar or are misunderstood, who bears the responsibility of educating patients so that they may make an informed decision rather than uninformed decision to accept or decline the screen?

Role of the Health Care Provider and the Responsibility of Education System

Role of the Health Care Provider

Family doctors, nurse practitioners and midwives are well positioned to offer antenatal SCD screening to pregnant women, as they will often see pregnant women within the first trimester of pregnancy. Conducting a SCD screen in the first trimester affords women who screen positive for SCT more reproductive options, including prenatal diagnosis, partner screening and early termination of their pregnancy should the fetus screen positive for SCD (26). However, in my experience as a midwife, the majority of my clients who are at risk for SCT, enter care unaware of their sickle cell carrier status and they often report they have little or no knowledge about SCD. Literature suggests that health care providers may have a basic knowledge of SCD but many of them do not believe they have sufficient knowledge to counsel patients effectively on SCD, SCT or the genetic inheritance pattern of the disease (47-50). In order to facilitate informed

choice for antenatal SCD screening, health care providers need to be equipped to explain SCD to their patients and answer relevant questions about SCD (49). In the studies reviewed, some parents expressed they felt that their health care providers offered good counsel on SCD, while others reported feeling confused and unsure of the value of SCD screening (26, 27, 36).

Role of the Health Care Education System

Given that SCD affects millions of people worldwide and causes recurrent morbidity, shortened life span and negatively impacts the quality of life of affected people, do health care education systems have an obligation to arm practitioners with the knowledgeable and capability to educate, inform and screen their patients? I argue that every health care provider who treats patients should be able to counsel their own patients. Most medical school, nursing and midwifery curricula fall short on teaching students about SCD (51). SCD modules may be offered in post graduate medical haematology residency programmes with focus on disease presentation and management, but a more generalist approach is required, to ensure that all health care providers understand the epidemiology, presentation, and treatment of SCD.

Vaso-occlusive crises (pain crises) are often characterized by periods of excruciating pain that may persist for several weeks (52-54). Morphine and/or fentanyl are the standard drugs used to manage the pain crisis. It is very well documented that physicians and nurses are more likely to doubt SCD patients' claims of pain, leading

many patients to be under medicated, labeled as drug addicts and stigmatized (52-54). There is evidence that the stigmatizing medical language such as “narcotic dependant”, “frequent flyer in the ER department” “insisting their pain is still a 10” is frequently written in SCD patients’ medical charts (53). Comments such as these, when read by and verbally relayed to health care providers, can lead to them to acquire implicit bias toward SCD patients (53, 54). It behooves the medical and nursing academia to make more effort to reduce and eliminate racist, harmful and stigmatizing language.

SCD may be addressed briefly and at a basic level in midwifery education programme, in large part because midwives do not care for sickle cell patients, however, midwives still have the capacity and responsibility, at the very least, to ensure clients understand SCD when offering SCD screening.

Individual Screening versus Population Based Screening for Sickle Cell Disease

Antenatal Screening for Sickle Cell Disease

In the UK SCD screening is offered universally to women who are a higher risk for SCD, that is, women of Black African, South Asian, Mediterranean or Middle Eastern descent. In Canada and the USA, antenatal SCD screening is offered as individual screening (26, 27). In Canada and the USA, each couple or woman is screened based on criteria commonly associated with SCD – ethnicity of the parents and values of routine blood work (mean corpuscular volume) (55, 56). Individual screening aims to offer autonomy to the patient and reduce the ethical dilemma that can occur with population

based screened (57). However, individual screening for SCD leads to the potential of not identifying people who may carry the SCT.

Population Based Screening for Sickle Cell Disease

Screening all people for SCD would aim to identify people who carry the sickle cell gene irrespective of ethnicity, thus affording more reproductive options, such as choosing not to conceive, choosing a partner who does not have SCT or engage in prenatal diagnosis (54, 57). In the context of the studies reviewed for this paper, all the women in the studies conducted in the UK and the Netherlands were offered antenatal screening, which functioned as a form of population based screening (26, 36, 37-39). Universal newborn screening in the USA functions as a population-based screening program as all infants in the USA are screened for SCD (unless a parent declines the NBS). All infants who carry the sickle cell gene are identified, however, there remained a challenge with communication of SCT results in the studies reviewed (17, 18, 40).

The universal newborn screening program in Canada falls short of functioning as population based screening for SCD on two fronts; 1) SCD is not included in the NBS in all provinces or territories and 2) only four of the provinces and one territory that include SCD in the NBS, disclose SCT results to parents. Parents in Ontario have the option to request their child's NBS results. It is unclear how many parents and primary care health care providers are aware of this option or how many parents request their child's results.

It is important to understand that a positive SCT result from a NBS indicates at least one parent must carry the sickle cell gene (Diagram 2) (1-3). Considering that most people are unaware of their sickle cell carrier status, and most health care providers are not screening their patients for SCD (18, 19, 21, 26), I find it difficult to reconcile how a government institution can justify wilfully with holding medical information that has the potential to upend a parent's future. One can argue that the SCT results can be released upon request, but most parents and health care providers are unaware of the option to request SCT results (56).

Racism in Health Care and Research

Comparing SCD education, research, treatment and screening to those for genetic conditions with comparable consequences and hereditary patterns reveals some stark inequities.

Many people affected with sickle cell anaemia report they feel they are treated differently, judged and stigmatized, in particular when seeking pain relief during a pain crisis (51).

The term racism is often difficult for many people to accept. It often conjures images of slavery, name calling, hatred or prejudice most commonly depicted as unjustified acts committed by the majority race toward a minority race (58). However, it is even more difficult to accept the term racism when paired with the term healthcare – health care providers are expected to take care of all people equally. Yet numerous

studies have confirmed that racism is not only alive a well in healthcare, but it is institutionalized (59-61). Jones defines institutional racism as "differential access to the goods, services and opportunities of society by race" (58). Racism in healthcare should not be seen as the blatantly obvious, segregating actions practiced in the 1950s and 1960s, but in the manner in which people are presented or not represented in medicine. Terms such as 'pink', and 'blue' are still used in medical textbooks today to describe skin tone.

In the context of the studies reviewed for this thesis, I acknowledge that it may be more difficult to align racism with the screening process for SCD since many of the acts attributed to racism against people with SCD are missing – no denial of anaelgeisc drugs, no reference to the study participants as drug addicts or drug seeking and the study participants ethnically diverse. However, it is problematic that although the World Health Organization (WHO) declared in 2006 that SCD is a significant global public health concern and recommended the implementation of counselling, screening and raising public awareness of SCD (62), parents and some health care providers in the studies reviewed still reported having little knowledge and understanding of SCD (26). Furthermore, although the American College of Gynecologists (55) and the Society of Obstetricians and Gynecologists of Canada (56) recommend offering SCD screening in early pregnancy to women and their partners who are at risk for SCD, many obstetricians fail to meet or follow these guidelines (63). The lack of parental and health care provider knowledge of SCD represent significant barriers to care (64), potentially leading to missed opportunities for parents or prospective parents to be screened prior to pregnancy, ultimately limiting parents' reproductive options (63). Little to no public awareness of

SCD and limited or brief education modules on SCD for health care providers contribute to the knowledge deficit of SCD (47-49, 65).

Dr. James Herrick first identified the peculiar, sickled shape red blood cells of his medical student in 1910 (1). A century later, much progress has been made from identifying the gene for many haemoglobin variants and development of medications to improved management of SCD. Yet in comparison to the progress made in the management and screening for Tay-Sachs disease and CF, SCD has a long way to go. In the USA disease-specific drug development has favoured CF (four versus one drug approval for CF and SCD respectively) (52).

Tay-Sachs disease is a rare, lethal, neurodegenerative, autosomal recessive disease that is prevalent in people of Ashkenazi Jewish descent (66). A voluntary population based screening program for Tay-Sachs disease began in the 1970's and to date more than 1.4 million people have been screened for Tay-Sachs disease worldwide (66). The incidence rate of Tay-Sachs was reduced by more than 90% by 2000 (66). Montreal implemented a high school based voluntary population screening program for Tay-Sachs disease from 1973 to 1993, resulting in a reduction rate of the disease by 90%-95% (67). Tay-Sachs disease is included in the newborn screening program nationally in Canada.

CF is a rare, autosomal recessive disease most prevalent in people of Northern European ancestry, affecting the respiratory and digestive system (68). Voluntary population based screening has been offered for CF since 1989 in many countries, including Canada. CF disease is included in the newborn screening program nationally in

Canada. Additionally, CF is offered as a pre-conception screening in all provinces in Canada (68).

There are no population based screening programs for SCD that can compare with population based screening programs for Tay-Sachs disease or CF. In fact, a search of most medical databases for the term 'population based screening and sickle cell disease' produces no specific articles. The research in SCD is still focused on disease management, treatment and screening. A study by Farooq et al, found that more federal funding was provided for CF as compared with SCD in the USA (52).

The SCD birth rate worldwide is estimated at more than 300,000 annually with numbers projected to be 400,000 annually by 2050 (69). Conversely, the incidence CF is declining worldwide and the survival rate of CF patients is increasing to a median lifespan of 50 years (70). Early diagnosis of CF by the newborn screen, genetic counselling for prospective parents, prenatal diagnosis and new advances in medications, and treatment of CF, account for significant improvements in the management of CF (70).

SCD is estimated to affect 3,000 – 5,000 people in Canada (4) in comparison to 4,000 people affected with CF (70). It is difficult not to compare the SCD statistics with CF statistics and question whether similar, nationally based strategies for SCD, such as population based screening, national universal newborn screening for SCD and national universal disclosure for SCT could positively impact the course of SCD in Canada.

At the writing of this thesis, a very well known and popular National Hockey League player donned custom hockey skates and a stick bearing the SickKids' logo, in an

effort to raise public awareness and money for CF and CF research. A description of CF disease was featured prominently on several social media platforms. I could find no similar public awareness campaigns for SCD current or past.

It is problematic that SCD receives far less focus and funding despite the burden of the disease on patients, their families and the health care system. It is worthy to note that SCD and SCT is the most common genetic condition identified in the newborn screening program (71).

Reflexivity

Personal Experience of a Midwife

I have practiced midwifery for 17 years, during which time I have routinely offered antenatal haemoglobinopathy screening, which encompasses screening for SCD and thalassemia, to all my clients. I have also encouraged all my colleagues to follow suit. I genuinely believed I was well informed on SCD – I understood the inheritance pattern of SCD, and I knew that SCD and SCT trait was prevalent amongst people of Black African descent (1). I prided myself in delving deeper and taking the time to elucidate the ethnic background of all my clients, even when they appeared White.

Through the process of conducting this thesis, reviewing the studies for this thesis, and being guided by a haematologist, one of my committee members, I realise that my knowledge of SCD was inadequate. I did not know that people of Italian, Greek, South

Asian, and Middle Eastern descent, are at risk for SCD (1-4). I believed they were only at risk for thalassemia. I also did not know that an incidental finding of SCT on the NBS is only routinely disclosed to health care providers in some provinces in Canada (Table 7), and therefore I was not aware that parents can request the SCT results from the NBS (71). I am very embarrassed.

As I read the studies for this thesis, I recognized that I may not have offered SCD and newborn screening as an informed choice discussion to my clients. I now recognize my own failure to participate in informed choice discussions about SCD screening (44-48). I should clarify that informed choice discussion is one of the three tenants of midwifery care – of all health care providers surely, I should excel at informed choice discussion? For all other tests that I offer in the antenatal period I do excel at conducting an informed choice discussion (44, 45).

The problem is that my own strongly held beliefs, as a Black midwife, that all people at risk should know their sickle cell carrier status, and my own personal experience of being screened for SCD as an adult, have clouded my perspective. I have been as guilty as some of the health care providers in the studies in this review. I did not always explain the consequences of a positive SCT result – further follow-up testing for the father of the baby, potential referral to a Prenatal Diagnostic Clinic in Hamilton. I also did not thoroughly review the NBS with my clients during the antenatal period.

I have since changed my habits – I endeavour to engage in an informed choice discussion for antenatal screening for SCD and NBS. I am still trying to reconcile my own knowledge deficit of SCD.

Experience of a Black Nurse

My adult son works is a registered nurse at a hospital. He relayed to me his experience with one of his patients - a young, Black man, age 20, who has SCD. He reported to me that his patient was in the hospital for pain crisis that required management by intravenous hydromorphone and fentanyl. It was not uncommon for his patient to be hospitalized for a period of four weeks, during which time he always receives opioid medication for pain relief. Two things stood out. My son reported that none of his White, nurse colleagues believed the severity of this Black patient's reports of pain. The nurses allegedly assumed that his ability to ambulate in his room or to the bathroom, was proof that his pain was not severe. They all believed he was drug seeking and used the hospital to access opioid drugs. Unfortunately, intravenous opioids, are the only drug of choice to manage sickle cell pain crisis. My son is unaware whether his patient has been offered palliative care as an option to manage SCD.

This young, Black patient reported he was thrilled to have a Black, male nurse, a first experience for him. The patient reportedly stated that none of the nurses nor physicians believed the severity of his pain, and he reportedly expressed no one

comprehends his experience with pain crisis or SCD. My son's patient's experience highlights the discrimination, labeling and stigma associated with SCD.

Recommendations

I believe that there is no simple solution to resolving the issues with SCD screening and diagnosis. A multistep, interdisciplinary approach is necessary. I will outline some options.

Implicit bias: it is important to acknowledge and embrace that the terms racism in conjunction with the term healthcare cannot be easily unpacked. It is easier to identify explicit bias, that is, overt expressions of prejudice and negative racial stereotypes (72), than implicit bias, unconscious negative ethnic and racial stereotypes and attitudes (72, 73). Studies have shown that it is not uncommon for health care providers to have unconscious negative attitudes toward Black people, while having positive attitudes to White people (73). The challenge is that implicit bias too often negatively affects the quality of care delivered to Black people – for example they are less likely to be referred to specialists, are offered fewer clinical tests, their pain is poorly managed, and they are more likely to be perceived as being less cooperative, less compliant and combative (72, 73).

Implicit racial and ethnic bias training courses have shown promise at improving health care providers' recognition of their own biases (74-76) and should be included in the curriculum of all health care programs as well as a requirement of ongoing

certification for health care providers in practice, much like the Accessibility for Ontarians with Disabilities Act (AODA) training that is required for all employers and employees in Ontario (77). It should be noted that some health care learners and health care providers may resist or deny their own implicit bias (78).

Increase funding for sickle cell disease research: in the era of evidence based medicine, medical research is often used to guide medical procedures, protocols and policies. Health care education in turn, is influenced by updated and newly developed procedures, protocols and policies (79, 80). SCD research continues to be underfunded compared to funding for other inherited disorders such as CF and Tay-Sachs disease (52). Farooq et al, found that despite SCD being three times as prevalent as CF in the USA, both diseases received a similar amount of federal government research funding between 2008 and 2018 (52). Unfortunately, there are no comparable Canadian based studies.

There is a dire need for more SCD specific research, specifically Canadian based SCD research. Additionally, 75% of people affected with SCD live in Africa where most African countries lack the infrastructure and resources to conduct scientific studies, let alone studies that would meet the rigour expected by Western world standards (69). However, I recognize a caveat - the people for whom SCD and SCT is more prevalent are of Black African descent. Black people are underrepresented in research and they also tend to have distrust in medical research (79). It would be beneficial to determine ways to engage Black sickle cell patients to participate in more research – research that could

potentially lead to better disease management. It is beyond the scope of this thesis to address this in detail - this may be a topic is appropriate for PhD.

I initially wanted to focus on parents' experiences with SCD diagnosis for my Master's thesis, but after a thorough and detailed search, only three studies specific to SCD met the criteria, of which only one was Canadian. I had to expand my topic to include the screening process for SCD and diagnosis for SCT. To compound this problem, of the 14 studies that met eligibility criteria for this review, only two were conducted in Canada (33, 34) and 11 studies focused on SCD or SCT and cystic fibrosis or SCD or SCT and thalassemia (17, 18, 26, 27, 36-41). This trend was also reflected in the references of the studies - only a small percentage of the references were dedicated to SCD or SCT only. There is need for more sickle cell specific research to guide health care practices, policies, protocols, pharmaceutical advancement and curative treatments.

Improve sickle cell disease health care education: many studies have identified that health care providers and health care learners, have poor knowledge and understanding of SCD, which in turn affects their management of sickle cell patients (19, 21, 80). SCD is still a relatively rare disease and it is likely that most health care providers will have limited experience treating SCD patients. Furthermore, SCD is rarely included in the core curriculum of health care programs, which could represent a missed opportunity to study the disease in depth (51).

The studies reviewed for this thesis showed that many of the study participants had little knowledge of SCD and they also expressed dissatisfaction with the SCD information

provided to them by their health care providers (26, 27, 36). Given that the majority of health care providers who offer sickle cell disease screening and disclose positive results are not hematologists, it would be beneficial for all non-specialty health care providers to improve their knowledge of SCD (as well as their communication skills) thus improving the care of their patients or clients (63).

It is also important to remember that not all sickle cell patients will have access to SCD specialty clinics, as SCD clinics in Hamilton, or Toronto. Their care may be managed by a health care provider who may have limited knowledge and understanding of SCD (47-49). SCD education modules and SCD conferences have been shown to help improve baseline knowledge of SCD, however it is unclear whether improved knowledge is sustained (47, 50, 51, 80, 81). More research is warranted.

One study has shown that a 90 hour, three month distance course on SCD, increased the knowledge of health care providers (81). An elective course designed by Bulgin et al shows promise to address the knowledge gaps for SCD in core curricula (51).

There is also value in incorporating the lived experience of SCD patients and their caregivers to guide health care providers and enhance SCD curricula (5, 82).

Hidden curriculum: there is a difference between health care pedagogy and the clinical teaching environment. Given that SCD education is limited in most health care programs, health care learners would likely need to learn about SCD management from observation during clinical rotations or clinical placements (83). Stigmatizing and labelling language is often used to describe sickle cell patients who seek medical care

when experiencing a pain crisis (53). The patient's pain is usually managed with intravenous opioid medication, and it is not uncommon for health care staff to discredit a patient's pain which can lead to poor management of their pain (53). Stigmatizing language such as "frequent flyer in the ER department" "insisting their pain is still a 10" is often used and documented in a patient's chart, which can lead to the transmission of bias in the medical records (53). The health care learner may acquire habits that have the potential to become incorporated in to their practice and the cycle of stigma and labeling could repeat once the health care learner becomes the teacher.

Health care programs should endeavour to remember that the clinical observation may serve as a stronger and more permanent teaching tool that traditional literature based pedagogy (84). Health care staff need to acknowledge the stigma and bias inherent in the health care setting and appreciate the emotional and physical impact on the patient, as some sickle cell patients develop and aversion and fear of the health care providers and have been known to delay seeking treatment (53, 79).

Informed choice discussion and communication: the parents in this systematic review and integrative qualitative meta-synthesis generally accepted the offer to be screened but expressed surprise if they or their children were diagnosed with SCD or SCT. It would appear that some the parents did not fully understand purpose for SCD screening, the impact of the disease or the hereditary pattern of SCD (26, 27). The parents' comments in this review are supported by literature that reveals that knowledge and understanding of SCD is limited (19, 20). A review by Asnani et al, revealed that

intervention strategies were successful at improving patient knowledge of SCD that were sustained for a period of time (62). This lends support that a public health education program could be beneficial for improving the knowledge of general public on SCD.

Some parents' failure to fully comprehend the consequences of SCD screening may also suggest that they provided inform consent for SCD screening rather than making an informed choice decision (26, 44, 46). It would be beneficial for health care providers to have a deeper understanding of the difference between informed consent and informed choice (44-46), a reminder of the power dynamic of the clinician-patient dyad and the challenges some patients may face making decisions for their health management (85).

Sickle cell disease patient directed health care provider education: the voices of the SCD patients and caregivers of SCD patients need to be included in the development of SCD curricula for health care learners and health care providers (5, 82). Policy statements made only from the perspective the health care provider risks distancing and alienating SCD patients. However, change can only occur if policy stakeholders, health care providers, health care educators and health care learners are willing to address their implicit biases and engage in reflexive behaviour (72-76).

It is evident from the parents' comments in the studies in this review that health care provider's method of communication, whether in offering SCD screening or the disclosure of results, is very important. Parents' expressed more positive experiences – feeling informed, better understanding of test results, decreased stress and anxiety – when

they perceived their health care provider as thorough, caring, patient and knowledgeable of SCD (17, 18, 26, 32, 36, 42).

The studies revealed that poor communication from health care providers often had a negative impact on experience with SCD screening and the diagnosis process of SCD and SCT (17, 18, 26, 32, 36, 42). It would be beneficial for health care providers to engage in education programs/courses that focus on the value of good communication, the disadvantages to using complex and technical medical terminology and an appreciation of patients' reliance on internet based medical information (80). Health care providers should also be reminded or taught the true value of reflexivity.

Limitations

Many of the parents in the studies reviewed, live in the USA. Unlike Canada, the Netherlands, the UK, the USA does not have a universal health care system. It is possible that some of the parents had to pay for their infant's NBS and subsequent follow-up appointments with doctors, potentially adding to a parent's emotional and financial burden. It is possible that not all the parents' comments may be applicable to the Canadian population. Parents of two of the studies were from Africa, where SCD is more prevalent and SCD screening and newborn screening is not offered routinely. Once again, these parents' experiences may not relate well to parents who were raised or lived in Canada, the UK or the USA.

Conclusions

This systematic review and integrative qualitative meta-synthesis explored parental experiences with screening for SCD as a tool to guide health science education. Parents overall accepted screening for SCD and appreciated learning of their own sickle cell carrier status and that of their child. However, it is clear that many parents did not fully understand the significance of SCD, or its inheritance pattern. Additionally, it is clear that health care providers need to ensure they practice an informed choice discussion rather than informed consent for SCD screening. Health care providers also need to be mindful of the manner in which diagnostic results are delivered to patients. In particular Canada requires a nationally based SCD strategy and network. Finally, a better follow-up system and future reproductive options should be in place for parents and infants who have SCT.

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Appendix A

Table 5. Sickle Cell June 2019 Search Strategy

Search date: June 18, 2019

Databases searched:

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946 to Present: 3054 hits
Embase (1974-2019): 5744 hits
PsychINFO: 787 hits
AMED: 14 hits
OVID Emcare: 1120 hits
CINAHL: 624 hits
Web of Science: 542 hits
6994 references after duplicates removed

Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946 to Present

Line #	Search	Notes
1	TS=interview*	Hybrid Filter: ISI Web of Science, Social Science Citation Index Would recommend citing in methods/report: DeJean D, Giacomini M, Simeonov D, Smith A. Finding Qualitative Research Evidence for Health Technology Assessment. Qual Health Res. 2016
2	TS=(theme*)	
3	TS=(thematic analysis)	
4	TS=qualitative	
5	TS=nursing research methodology	
6	TS=questionnaire	
7	TS=(ethnograph*)	
8	TS= (ethnonursing)	
9	TS=(ethnological research)	
10	TS=(phenomenol*)	
11	TS=(grounded theor*) OR TS=(grounded stud*) OR TS=(grounded research) OR TS=(grounded analys?s)	
12	TS=(life stor*) OR TS=(women's stor*)	
13	TS=(emic) OR TS=(etic) OR TS=(hermeneutic) OR TS=(heuristic) OR TS=(semiotic) OR TS=(data saturat*) OR TS=(participant observ*)	
14	TS=(social construct*) OR TS=(postmodern*) OR TS=(post structural*) OR TS=(feminis*) OR TS=(interpret*)	
15	TS=(action research) OR TS=(co-operative inquir*)	

16	TS=(humanistic) OR TS=(existential) OR TS=(experiential) OR TS=(paradigm*)	Aug;26(10):1307-17.
17	TS=(field stud*) OR TS=(field research)	
18	TS=(human science)	
19	TS=(biographical method*)	
20	TS=(theoretical sampl*)	
21	TS=(purposive sampl*)	
22	TS=(open-ended account*) OR TS=(unstructured account) OR TS=(narrative*) OR TS=(text*)	
23	TS=(life world) OR TS=(conversation analys?s) OR TS=(theoretical saturation)	
24	TS=(lived experience*) OR TS=(life experience*)	
25	TS=(cluster sampl*)	
26	TS=observational method*	
27	TS=(content analysis)	
28	TS=(constant comparative)	
29	TS=(discourse analys?s) or TS =(discurs* analys?s)	
30	TS=(narrative analys?s)	
31	TS=(heidegger*)	
32	TS=(colaizzi*)	
33	TS=(spiegelberg*)	
34	TS=(van manen*)	
35	TS=(van kaam*)	
36	TS=(merleau ponty*)	
37	TS=(husserl*)	
38	TS=(foucault*)	
39	TS=(corbin*)	
40	TS=(strauss*)	
41	TS=(glaser*)	
42	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	This line combines all the qualitative filter keywords
43	Limit 42 to (English language and humans)	
44	TS=exp Anemia, Sickle Cell	Intervention terms
45	TS=exp Since Cell Trait	
46	TS=sickle cell.mp.	Key word
47	#44 OR #45 OR #46	This line combines the intervention concepts and key word

48	#43 AND #47	Combine Intervention and filter

Database: PsychINFO (1987-2019)

Line #	Search	Notes
1	TS=interview*	Hybrid Filter: ISI Web of Science, Social Science Citation Index Would recommend citing in methods/report: DeJean D, Giacomini M, Simeonov D, Smith A. Finding Qualitative Research Evidence for Health Technology Assessment. Qual Health Res. 2016 Aug;26(10):1307-17.
2	TS=(theme*)	
3	TS=(thematic analysis)	
4	TS=qualitative	
5	TS=nursing research methodology	
6	TS=questionnaire	
7	TS=(ethnograph*)	
8	TS= (ethnonursing)	
9	TS=(ethnological research)	
10	TS=(phenomenol*)	
11	TS=(grounded theor*) OR TS=(grounded stud*) OR TS=(grounded research) OR TS=(grounded analys?s)	
12	TS=(life stor*) OR TS=(women's stor*)	
13	TS=(emic) OR TS=(etic) OR TS=(hermeneutic) OR TS=(heuristic) OR TS=(semiotic) OR TS=(data saturat*) OR TS=(participant observ*)	
14	TS=(social construct*) OR TS=(postmodern*) OR TS=(post structural*) OR TS=(feminis*) OR TS=(interpret*)	
15	TS=(action research) OR TS=(co-operative inquir*)	
16	TS=(humanistic) OR TS=(existential) OR TS=(experiential) OR TS=(paradigm*)	
17	TS=(field stud*) OR TS=(field research)	
18	TS=(human science)	
19	TS=(biographical method*)	
20	TS=(theoretical sampl*)	
21	TS=(purposive sampl*)	
22	TS=(open-ended account*) OR TS=(unstructured account) OR TS=(narrative*) OR TS=(text*)	
23	TS=(life world) OR TS=(conversation analys?s) OR TS=(theoretical saturation)	
24	TS=(lived experience*) OR TS=(life experience*)	
25	TS=(cluster sampl*)	
26	TS=observational method*	
27	TS=(content analysis)	

28	TS=(constant comparative)	
29	TS=(discourse analys?s) or TS =(discurs* analys?s)	
30	TS=(narrative analys?s)	
31	TS=(heidegger*)	
32	TS=(colaizzi*)	
33	TS=(spiegelberg*)	
34	TS=(van manen*)	
35	TS=(van kaam*)	
36	TS=(merleau ponty*)	
37	TS=(husserl*)	
38	TS=(foucault*)	
39	TS=(corbin*)	
40	TS=(strauss*)	
41	TS=(glaser*)	
42	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	This line combines all the qualitative filter keywords
43	TS=sickle cell disease	Intervention term
44	TS=sickle cell.mp.	Key word
45	#43 OR #44	This line combines the intervention concepts and key word
46	#42 AND #45	Combine Intervention and filter

Database: Embase (1974-2019)

Line #	Search	Notes
1	TS=interview*	Hybrid Filter: ISI Web of Science, Social Science Citation Index Would recommend citing in methods/report: DeJean D, Giacomini M, Simeonov D, Smith A. Finding Qualitative Research Evidence for Health Technology Assessment. Qual Health Res. 2016 Aug;26(10):1307-17.
2	TS=(theme*)	
3	TS=(thematic analysis)	
4	TS=qualitative	
5	TS=nursing research methodology	
6	TS=questionnaire	
7	TS=(ethnograph*)	
8	TS= (ethnonursing)	
9	TS=(ethnological research)	
10	TS=(phenomenol*)	
11	TS=(grounded theor*) OR TS=(grounded stud*) OR TS=(grounded research) OR TS=(grounded analys?s)	
12	TS=(life stor*) OR TS=(women's stor*)	
13	TS=(emic) OR TS=(etic) OR TS=(hermeneutic) OR TS=(heuristic) OR TS=(semiotic) OR TS=(data saturat*) OR TS=(participant observ*)	
14	TS=(social construct*) OR TS=(postmodern*) OR TS=(post structural*) OR TS=(feminis*) OR TS=(interpret*)	
15	TS=(action research) OR TS=(co-operative inquir*)	
16	TS=(humanistic) OR TS=(existential) OR TS=(experiential) OR TS=(paradigm*)	
17	TS=(field stud*) OR TS=(field research)	
18	TS=(human science)	
19	TS=(biographical method*)	
20	TS=(theoretical sampl*)	
21	TS=(purposive sampl*)	
22	TS=(open-ended account*) OR TS=(unstructured account) OR TS=(narrative*) OR TS=(text*)	
23	TS=(life world) OR TS=(conversation analys?s) OR TS=(theoretical saturation)	
24	TS=(lived experience*) OR TS=(life experience*)	
25	TS=(cluster sampl*)	
26	TS=observational method*	
27	TS=(content analysis)	
28	TS=(constant comparative)	
29	TS=(discourse analys?s) or TS =(discurs* analys?s)	
30	TS=(narrative analys?s)	
31	TS=(heidegger*)	

32	TS=(colaizzi*)	
33	TS=(spiegelberg*)	
34	TS=(van manen*)	
35	TS=(van kaam*)	
36	TS=(merleau ponty*)	
37	TS=(husserl*)	
38	TS=(foucault*)	
39	TS=(corbin*)	
40	TS=(strauss*)	
41	TS=(glaser*)	
42	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	This line combines all the qualitative filter keywords
43	Limit 42 to (English language and humans)	
44	TS=sickle cell	Intervention terms
45	TS=((sickle cell anemia) OR (hemoglobin sc disease) OR (hemoglobin sd disease) OR (sickle cell beta thalassemia) or (sickle cell crisis) OR (sickle cell trait)	
46	TS=sickle cell.mp.	Key word
47	#44 OR #45 OR #46	This line combines the intervention concepts and key word
48	#43 AND #47	Combine Intervention and filter

Database: AMED (1985-2019)

Line #	Search	Notes
1	TS=interview*	Hybrid Filter: ISI Web of Science, Social Science Citation Index Would recommend citing in methods/report: DeJean D, Giacomini M, Simeonov D, Smith A. Finding Qualitative Research Evidence for Health Technology Assessment. Qual Health Res. 2016 Aug;26(10):1307-17.
2	TS=(theme*)	
3	TS=(thematic analysis)	
4	TS=qualitative	
5	TS=nursing research methodology	
6	TS=questionnaire	
7	TS=(ethnograph*)	
8	TS= (ethnonursing)	
9	TS=(ethnological research)	
10	TS=(phenomenol*)	
11	TS=(grounded theor*) OR TS=(grounded stud*) OR TS=(grounded research) OR TS=(grounded analys?s)	
12	TS=(life stor*) OR TS=(women's stor*)	
13	TS=(emic) OR TS=(etic) OR TS=(hermeneutic) OR TS=(heuristic) OR TS=(semiotic) OR TS=(data saturat*) OR TS=(participant observ*)	
14	TS=(social construct*) OR TS=(postmodern*) OR TS=(post structural*) OR TS=(feminis*) OR TS=(interpret*)	
15	TS=(action research) OR TS=(co-operative inquir*)	
16	TS=(humanistic) OR TS=(existential) OR TS=(experiential) OR TS=(paradigm*)	
17	TS=(field stud*) OR TS=(field research)	
18	TS=(human science)	
19	TS=(biographical method*)	
20	TS=(theoretical sampl*)	
21	TS=(purposive sampl*)	
22	TS=(open-ended account*) OR TS=(unstructured account) OR TS=(narrative*) OR TS=(text*)	
23	TS=(life world) OR TS=(conversation analys?s) OR TS=(theoretical saturation)	
24	TS=(lived experience*) OR TS=(life experience*)	
25	TS=(cluster sampl*)	
26	TS=observational method*	
27	TS=(content analysis)	
28	TS=(constant comparative)	
29	TS=(discourse analys?s) or TS =(discurs* analys?s)	
30	TS=(narrative analys?s)	
31	TS=(heidegger*)	

32	TS=(colaizzi*)	
33	TS=(spiegelberg*)	
34	TS=(van manen*)	
35	TS=(van kaam*)	
36	TS=(merleau ponty*)	
37	TS=(husserl*)	
38	TS=(foucault*)	
39	TS=(corbin*)	
40	TS=(strauss*)	
41	TS=(glaser*)	
42	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	This line combines all the qualitative filter keywords
43	TS=anemia, sickle cell	Intervention term Key word
44	TS=sickle cell.mp.	
45	#43 OR #44	This line combines the intervention concepts and key word
46	#42 AND #45	Combine Intervention and filter

Database: OVID Emcare

Line #	Search	Notes
1	TS=interview*	Hybrid Filter: ISI Web of Science, Social Science Citation Index Would recommend citing in methods/report: DeJean D, Giacomini M, Simeonov D, Smith A. Finding Qualitative Research Evidence for Health Technology Assessment. Qual Health Res. 2016 Aug;26(10):1307-17.
2	TS=(theme*)	
3	TS=(thematic analysis)	
4	TS=qualitative	
5	TS=nursing research methodology	
6	TS=questionnaire	
7	TS=(ethnograph*)	
8	TS= (ethnonursing)	
9	TS=(ethnological research)	
10	TS=(phenomenol*)	
11	TS=(grounded theor*) OR TS=(grounded stud*) OR TS=(grounded research) OR TS=(grounded analys?s)	
12	TS=(life stor*) OR TS=(women's stor*)	
13	TS=(emic) OR TS=(etic) OR TS=(hermeneutic) OR TS=(heuristic) OR TS=(semiotic) OR TS=(data saturat*) OR TS=(participant observ*)	
14	TS=(social construct*) OR TS=(postmodern*) OR TS=(post structural*) OR TS=(feminis*) OR TS=(interpret*)	
15	TS=(action research) OR TS=(co-operative inquir*)	
16	TS=(humanistic) OR TS=(existential) OR TS=(experiential) OR TS=(paradigm*)	
17	TS=(field stud*) OR TS=(field research)	
18	TS=(human science)	
19	TS=(biographical method*)	
20	TS=(theoretical sampl*)	
21	TS=(purposive sampl*)	
22	TS=(open-ended account*) OR TS=(unstructured account) OR TS=(narrative*) OR TS=(text*)	
23	TS=(life world) OR TS=(conversation analys?s) OR TS=(theoretical saturation)	
24	TS=(lived experience*) OR TS=(life experience*)	
25	TS=(cluster sampl*)	
26	TS=observational method*	
27	TS=(content analysis)	
28	TS=(constant comparative)	
29	TS=(discourse analys?s) or TS =(discurs* analys?s)	
30	TS=(narrative analys?s)	
31	TS=(heidegger*)	

32	TS=(colaizzi*)	
33	TS=(spiegelberg*)	
34	TS=(van manen*)	
35	TS=(van kaam*)	
36	TS=(merleau ponty*)	
37	TS=(husserl*)	
38	TS=(foucault*)	
39	TS=(corbin*)	
40	TS=(strauss*)	
41	TS=(glaser*)	
42	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	This line combines all the qualitative filter keywords
43	Limit 42 to (English language and humans)	
44	TS=(sickle cell) or (sickle cell anemia) or (sickle cell beta thalassemia) or (sickle cell crisis)	Intervention terms
45	TS=sickle cell.mp.	Key word
46	#44 OR #45	This line combines the intervention concepts and key word
47	#43 AND #46	Combine Intervention and filter

Database: CINAHL

Line #	Search	Notes
1	TS=interview*	Hybrid Filter: ISI Web of Science, Social Science Citation Index Would recommend citing in methods/report: DeJean D, Giacomini M, Simeonov D, Smith A. Finding Qualitative Research Evidence for Health Technology Assessment. Qual Health Res. 2016 Aug;26(10):1307-17.
2	TS=(theme*)	
3	TS=(thematic analysis)	
4	TS=qualitative	
5	TS=nursing research methodology	
6	TS=questionnaire	
7	TS=(ethnograph*)	
8	TS= (ethnonursing)	
9	TS=(ethnological research)	
10	TS=(phenomenol*)	
11	TS=(grounded theor*) OR TS=(grounded stud*) OR TS=(grounded research) OR TS=(grounded analys?s)	
12	TS=(life stor*) OR TS=(women's stor*)	
13	TS=(emic) OR TS=(etic) OR TS=(hermeneutic) OR TS=(heuristic) OR TS=(semiotic) OR TS=(data saturat*) OR TS=(participant observ*)	
14	TS=(social construct*) OR TS=(postmodern*) OR TS=(post structural*) OR TS=(feminis*) OR TS=(interpret*)	
15	TS=(action research) OR TS=(co-operative inquir*)	
16	TS=(humanistic) OR TS=(existential) OR TS=(experiential) OR TS=(paradigm*)	
17	TS=(field stud*) OR TS=(field research)	
18	TS=(human science)	
19	TS=(biographical method*)	
20	TS=(theoretical sampl*)	
21	TS=(purposive sampl*)	
22	TS=(open-ended account*) OR TS=(unstructured account) OR TS=(narrative*) OR TS=(text*)	
23	TS=(life world) OR TS=(conversation analys?s) OR TS=(theoretical saturation)	
24	TS=(lived experience*) OR TS=(life experience*)	
25	TS=(cluster sampl*)	
26	TS=observational method*	
27	TS=(content analysis)	
28	TS=(constant comparative)	
29	TS=(discourse analys?s) or TS =(discurs* analys?s)	
30	TS=(narrative analys?s)	
31	TS=(heidegger*)	

32	TS=(colaizzi*)	
33	TS=(spiegelberg*)	
34	TS=(van manen*)	
35	TS=(van kaam*)	
36	TS=(merleau ponty*)	
37	TS=(husserl*)	
38	TS=(foucault*)	
39	TS=(corbin*)	
40	TS=(strauss*)	
41	TS=(glaser*)	
42	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	This line combines all the qualitative filter keywords
43	TS=anemia, sickle cell	Intervention terms
44	TS=sickle cell trait	
45	TS=sickle cell.mp.	Key word
46	#43 OR #44 OR #45	This line combines the intervention concepts and key word
47	#42 AND #46	Combine Intervention and filter

Database: Web of Science (Social Science Citation Index)

Line #	Search	Notes
1	TS=interview*	Hybrid Filter: ISI Web of Science, Social Science Citation Index Would recommend citing in methods/report: DeJean D, Giacomini M, Simeonov D, Smith A. Finding Qualitative Research Evidence for Health Technology Assessment. Qual Health Res. 2016 Aug;26(10):1307-17.
2	TS=(theme*)	
3	TS=(thematic analysis)	
4	TS=qualitative	
5	TS=nursing research methodology	
6	TS=questionnaire	
7	TS=(ethnograph*)	
8	TS= (ethnonursing)	
9	TS=(ethnological research)	
10	TS=(phenomenol*)	
11	TS=(grounded theor*) OR TS=(grounded stud*) OR TS=(grounded research) OR TS=(grounded analys?s)	
12	TS=(life stor*) OR TS=(women's stor*)	
13	TS=(emic) OR TS=(etic) OR TS=(hermeneutic) OR TS=(heuristic) OR TS=(semiotic) OR TS=(data saturat*) OR TS=(participant observ*)	
14	TS=(social construct*) OR TS=(postmodern*) OR TS=(post structural*) OR TS=(feminis*) OR TS=(interpret*)	
15	TS=(action research) OR TS=(co-operative inquir*)	
16	TS=(humanistic) OR TS=(existential) OR TS=(experiential) OR TS=(paradigm*)	
17	TS=(field stud*) OR TS=(field research)	
18	TS=(human science)	
19	TS=(biographical method*)	
20	TS=(theoretical sampl*)	
21	TS=(purposive sampl*)	
22	TS=(open-ended account*) OR TS=(unstructured account) OR TS=(narrative*) OR TS=(text*)	
23	TS=(life world) OR TS=(conversation analys?s) OR TS=(theoretical saturation)	
24	TS=(lived experience*) OR TS=(life experience*)	
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27	TS=(content analysis)	
28	TS=(constant comparative)	
29	TS=(discourse analys?s) or TS =(discurs* analys?s)	
30	TS=(narrative analys?s)	
31	TS=(heidegger*)	

32	TS=(colaizzi*)	
33	TS=(spiegelberg*)	
34	TS=(van manen*)	
35	TS=(van kaam*)	
36	TS=(merleau ponty*)	
37	TS=(husserl*)	
38	TS=(foucault*)	
39	TS=(corbin*)	
40	TS=(strauss*)	
41	TS=(glaser*)	
42	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41	This line combines all the qualitative filter keywords
43	TS=sickle cell.mp.	Key word
44	#42 AND #43	Combine Intervention and filter

Appendix B

Table 6. Characteristics of Excluded Studies

Author(s)	Title	Country	Topic	Style	Exclusion Criteria
Acharya, K., et al. (2009)	A Pilot Study to Explore Knowledge, Attitudes, and Beliefs about-Sickle Cell Trait and Disease	USA	Opinions about sickle cell trait	Interviews and surveys	Not about parental experience with screening
Ahmad, N.Y., Farrell, MH (2014)	Linguistic markers of emotion in mothers of sickle cell carrier infants: What are they and what do they mean?	USA	Diagnosis of carrier status from newborn screening	Interviews and surveys	Results presented quantitatively
Alexander, S., et al. (2017)	Knowledge of and attitudes toward heel prick screening for sickle cell disease in Saint Lucia	Jamaica	Knowledge of newborn screening	Interviews and survey	Not about parental experience with screening
Atkin, K., et al. (1998)	Screening and counseling for sickle cell disorders and thalassaemia: the experience of parents and health professionals	UK	Screening	Interviews	Prior to 2006
Dennis-Antwi, J. A., et al. (2011)	I can die today, I can die tomorrow': Lay perceptions of sickle cell disease in Kumasi, Ghana at a point of transition	Africa	Fathers perspective of their child's sickle cell disease	Interviews	Not about experience with the screening process

Table 6. cont. Characteristics of Excluded Studies

Author(s)	Title	Country	Topic	Style	Exclusion Criteria
Dormandy, E., et al. (2007)	Development of a measure of informed choice suitable for use in low literacy populations	UK	Informed choice	Interviews and surveys	Quantitative
Dyson, S. M., et al. (2007)	Ethnicity questions and antenatal screening for sickle cell/thalassaemia (EQUANS) in England: observation and interview study	UK	Antenatal barriers to screening	Interviews	Not about parental experience of screening for sickle cell disease
Guedes, C. (2012)	Reproductive decisions and newborn screening: The perspective of female caregivers of children with sickle cell disease	Brazil	Mothers of children with sickle cell disease perception of screening	Interviews	Not English
Hill, M., et al. (2014)	Client views and attitudes to non-invasive prenatal diagnosis for sickle cell disease, thalassaemia and cystic fibrosis.	USA	Opinion of genetic testing	Interviews	Not about parental experience of screening for sickle cell disease
Hill, S. A. (1994)	Motherhood and the obfuscation of Medical Knowledge: The Case of Sickle Cell Disease	USA	Screening of know sickle cell disease mothers	Interviews	Prior to 2006

Table 6. cont. Characteristics of Excluded Studies

Author(s)	Title	Country	Topic	Style	Exclusion Criteria
Kai, J., et al. (2009)	Communication of carrier status information following universal newborn screening for sickle cell disorders and cystic fibrosis: qualitative study of experience and practice	UK	Disclosure of carrier status	Interviews	Not primary
Lang, C. W., et al. (2009)	Maternal knowledge and attitudes about newborn screening for sickle cell disease and cystic fibrosis	USA	Knowledge of Newborn screen	Interview and surveys	Quantitative
Lawrence, R.H., Bediako, M.S. (2012)	Social and behavioral implications of the NCAA-mandated sickle cell trait testing policy	USA	Screening of athletes	Interview and surveys	Abstract
Lebensburger, J.D., et al. (2012)	The process of acquiring health education for first time parents of an infant with sickle cell disease	USA	Health education for parents with sickle cell child	Interviews and surveys	Poster

Table 6. cont. Characteristics of Excluded Studies

Author(s)	Title	Country	Topic	Style	Exclusion Criteria
Leppert, K., et al. (2018)	Genetic Counselors' Experience with and Opinions on the Management of Newborn Screening Incidental Carrier Findings	USA	Disclosure of incidental sickle cell trait finding	Interviews and surveys	Not Parent
Long, K. A., et al. (2011)	Attitudes and beliefs of African-Americans toward genetics, genetic testing, and sickle cell disease education and awareness	USA	Perception of genetic testing	Interviews	Not about parental experience of screening for sickle cell disease
Mayo-Gamble, T.L. et al (2018)	'It means everyone should know their status': exploring lay conceptions of sickle cell trait and sickle cell trait screening among African Americans within middle reproductive age	USA	Screening antenatally	Interviews and surveys	Not about parental experience of screening for sickle cell disease
Middleton, J., et al. (2018)	Communication with children about sickle cell disease: A qualitative study of parent experience	UK	How parents interact with children with sickle cell disease	Interviews	Not about parental experience of screening for sickle cell disease

Table 6. cont. Characteristics of Excluded Studies

Author(s)	Title	Country	Topic	Style	Exclusion Criteria
Moody, L., et al. (2017)	Healthcare professionals' and parents' experiences of the confirmatory testing period: a qualitative study of the UK expanded newborn screening pilot.	UK	Experience with positive newborn screen -	Interviews	Not sickle cell
Noke, M. and Ulph, F. (2014)	Young adults' pre-existing knowledge of cystic fibrosis and sickle cell diseases: implications for newborn screening	UK	Knowledge of newborn screening	Interviews	Not about the experience of screening for sickle cell disease
Noke, M., et al. (2016)	A qualitative study to explore how professionals in the United Kingdom make decisions to test children for a sickle cell carrier status	UK	Health care professionals opinion on screening	Interviews	Not parent
O'Connor, S., et al. (2014)	Attitudes among healthcare providers and patients diagnosed with sickle cell disease.	USA	Diagnosis - Experience of diagnosis of sickle cell disease – young adults	Interviews	Not parent

Table 6. cont. Characteristics of Excluded Studies

Author(s)	Title	Country	Topic	Style	Exclusion Criteria
Ross, P. T. (2015)	Motivations of women with sickle cell disease for asking their partners to undergo genetic testing	USA	Partner testing for sickle cell disease	Interviews	Not about the experience of screening for sickle cell disease
Shook, L. M., et al. (2011)	Preferences for genetic counseling and educational materials for African immigrant families with a child diagnosed with sickle cell disease	UK	Diagnosis – African Immigrants experience	Interviews	Not parent
Skirton, H., et al. (2015)	An easy test but a hard decision: Ethical issues concerning non-invasive prenatal testing for autosomal recessive disorders	UK	Antenatal screening	Interviews	Not sickle cell
Stewart, K. A. (2008)	An examination of African American college students' knowledge and attitudes regarding sickle cell disease and sickle cell disease carrier testing: A mixed methods study	USA	Screening – knowledge about screening	Interviews	Not peer reviewed

Table 6. cont. Characteristics of Excluded Studies

Author(s)	Title	Country	Topic	Style	Exclusion Criteria
Treadwell, M. J., et al. (2006)	Using qualitative and quantitative strategies to evaluate knowledge and perceptions about sickle cell disease and sickle cell trait	USA	Knowledge of sickle disease – indirectly related to screening	Interviews	Not about the experience of screening for sickle cell disease
Ulph, F., et al. (2014)	Informing children of their newborn screening carrier result for sickle cell or cystic fibrosis: qualitative study of parents' intentions, views and support needs	UK	Disclosure of sickle cell status to children	Interviews	Not about the experience of screening for sickle cell disease
Warren, N. S., et al. (1982)	Newborn screening for hemoglobinopathies in New York State: Experience of physicians and parents of affected children	USA	Screening and diagnosis -	Interviews	Prior to 2006
Wright, S. W., et al. (1994)	Screening for sickle-cell trait in the emergency department."	USA	Screening - Antenatal/Pre-conceptual screening of me and women in an ER	Interviews	Prior to 2006

Appendix C

Table 7. Newborn Screen for Sickle Cell Disease in Canada

Province	Sickle Cell Disease included in the Newborn Screen	Routine Disclosure of Sickle Cell Trait Results
Alberta	Yes	Yes
British Columba	Yes	No (disclosed only upon request)
Manitoba	No	N/A
New Brunswick	Yes	Yes
Newfoundland	Yes	Yes
North West Territories	No	N/A
Nova Scotia	Yes	Yes
Nunavut	No	N/A
Ontario	Yes	No (disclosed only upon request)
Prince Edward Island	Yes	Yes
Quebec	Yes	No (disclosed only upon request)
Saskatchewan	No	N/A
Yukon	Yes	Yes

Sickle Cell Awareness Group of Ontario (86)

Appendix D

Table 8. Sickle Cell Trait Disclosure Practice (countries listed in the studies reviewed)

Country (in studies reviewed)	Antenatal Screening	Sickle Cell Disease included on Newborn Screen	Disclosure of SCT finding
Canada	Offered at health care provider's discretion	Universal screening offered in 8 provinces and one territory[2]. Opt-out system[3]	Alberta, New Brunswick, Newfoundland and Labrador, Nova Scotia, Prince Edward Island and the Yukon
Netherlands	Universal Screening (for study only)	National Universal screening	Not reported to parents
United Kingdom	Universal screening offered for women at risk[1]	Offered as a choice. Opt-in [4]	Reported to parents. No national reporting standard
United States of America	Offered at health care provider's discretion	National Universal screening (50 states). Opt-out system[3]	Reported to parents. No national reporting standard

1 Includes women of African, Black Caribbean, Mediterranean, Middle Eastern or South Asian descent (26)

2 Offered in Alberta, British Columbia, New Brunswick, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, Quebec and the Yukon (28)

3 Opt-out system – Infants will be tested automatically unless parent(s) decline(s). A refusal form required to be signed (28)

4 Opt-in system – Parent(s) is/are offered newborn screen. Consent required (27)