Attitudes, decision-making processes, and preferences regarding preconception carrier screening among Hutterites in Manitoba

by

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ABSTRACT

In response to the increased prevalence of certain autosomal recessive conditions in the Hutterite population, a targeted carrier screening panel is under development at the Health Sciences Centre in Winnipeg, MB. Research on the implementation of other population-based carrier screening tests has shown that to be viewed as acceptable and valuable by the community offered screening, the test itself as well as related education and genetic counselling should be tailored. Tailoring requires an understanding of the perspectives of the target population regarding the benefits, risks, and utility of screening as well as their cultural practices and beliefs that might influence those perspectives. Little is known about the attitudes of Hutterites toward comprehensive carrier screening, how they would use the results, or what their preferences would be regarding provision of such a test. This cross-sectional exploratory study used a convergent mixed methods design to answer these questions, consisting of a chart review, survey, and semi-structured interviews. Surveys were completed by 95 Hutterites and 13 of these also participated in an interview.

Results showed that there is considerable support for carrier screening among Manitoban Hutterites but the sentiment is not universal. Many feel that carrier screening has the potential to be helpful to families and communities, but that it may also lead to an unintended loss of social cohesion through an increase in stigma or changes to cultural practices. Individuals need to consider both individual and community factors when making decisions related to carrier screening. Most respondents who expressed interest in carrier screening would alter their family planning after receiving a high-risk result, but an individual's life stage and life experiences modified this pattern. The results of this study illustrate that the provision of carrier screening can be tailored to the Hutterite community in many ways including at an organizational, educational, and counselling level. Successful implementation of the recommendations provided will help to ensure Hutterites in Manitoba have access to tailored and culturally sensitive care.

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LIST OF ABBREVIATIONS

A: Agree
ACMG: American College of Medical Genetics
ACOG: American College of Obstetricians and Gynecologists
AD: Autosomal dominant
AR: Autosomal recessive
CF: Cystic fibrosis
CS: Carrier screening
D: Disagree
DNA: Deoxyribonucleic acid
EJHG: European Journal of Human Genetics
ESHG: European Society of Human Genetics
H: Kruskal-Wallis test statistic
HBM: Health belief model
IBD: Identical/identity by descent
IQR: Interquartile range
IUD: Intrauterine device
MD: Muscular dystrophy
Mdn: Median
N: Neutral
OMIM: Online Mendelian Inheritance in Man
PGD: Preimplantation genetic diagnosis
PCP: Primary care provider
ROH: Region(s) of homozygosity
SA: Strongly agree
SCA: Sickle cell anemia
SD: Strongly disagree
SE: Standard error
SNP: Single nucleotide polymorphism
TSD: Tay-Sachs disease
WRHA: Winnipeg Regional Health Authority

CHAPTER 1. INTRODUCTION & LITERATURE REVIEW

1.1 Overview

Hutterites are a genetically isolated communal people composed of about 45,000 individuals living in colonies across the prairies of Canada and the US, with a relatively high incidence of autosomal recessive conditions due to founder effect. A founder mutation-specific DNA testing panel was recently developed and piloted at the Health Sciences Centre to offer comprehensive carrier screening for 32 conditions to people of Hutterite descent. Population-based carrier screening programs around the world have taken many approaches to offering carrier screening, including some which focus on premarital carrier screening, and others which focus on preconception or prenatal screening of couples, for example. Studies that have explored uptake of these programs have found that carrier screening programs which are viewed as helpful by the target population are tailored, based on the lifestyle and values of the community. There is currently a gap in knowledge regarding how people in the Hutterite community view carrier screening, how much information they would want to know about their carrier status, and how information about carrier status would influence their reproductive decision-making. The aim of this project is to understand the perspectives of Hutterites toward panel-based carrier screening to identify ways that provision of CS can be tailored from an educational, counselling, and laboratory perspective.

This introduction will begin with an exploration of the epidemiology of autosomal recessive conditions and the mechanisms by which populations can have an overrepresentation of these conditions. The purpose of carrier screening will be introduced as well as consensus guidelines on which conditions should be included on carrier screening panels. A critical analysis of historical approaches to population-based carrier screening will follow, accompanied by the specific ways that carrier screening programs can be tailored to each population. Finally, the characteristics of the Hutterite population will be reviewed, including their history, lifestyle, health practices, genetics, and attitudes toward genetic testing.

1.2 Introduction to carrier screening

1.2.1 Autosomal recessive conditions

Of the 20,000-25,000 genes in the human genome, nearly 6,000 have been associated with monogenic conditions (*Online Mendelian Inheritance in Man, OMIM®.*, 2020). Autosomal recessive disorders make up a significant proportion of the global burden of these conditions with ~1,875 of the 6,000 genes following this pattern of inheritance (Antonarakis, 2019). Recessive disorders arise through a distinct mechanism, in which both alleles of a gene have decreased or absent function. Typically, individuals who carry one copy with decreased or absent function are healthy and defined as carriers. However, when two people who are both carriers reproduce, each offspring has a 25% chance of inheriting 2 non-functional copies and presenting with the disease (Figure 1).

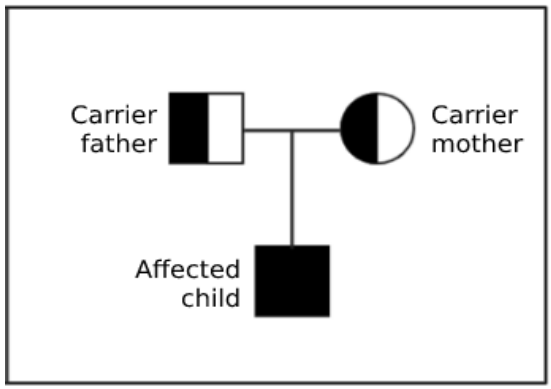

Figure 1. Autosomal recessive inheritance

Studies have shown that everyone is a carrier of at least a few recessive disorders. Mutational load is difficult to quantify for several reasons, including that many mutations are considered to be deleterious even when the effect on phenotype is mild or moderate, and that the science of predicting the pathogenicity of variants in both coding and non-coding regions is still developing (Henn et al., 2015). Estimates of the number of recessive disease-causing mutations carried by individuals ranges from 4 to 10 or more across different studies (Henn et al., 2015; McConkey, 1993), although some of these are also expected to have mild or moderate effects. As a result, several studies have focused on estimating the number of *lethal* recessive alleles

carried by individuals, which is easier to quantify due to their unambiguous effect on reproductive fitness. Estimates range from 0.5 to 2 lethal mutations per human genome (Gao et al., 2015; Narasimhan et al., 2016). However, there is reason to believe that these estimates may be off the mark. Some recessive alleles are likely to cause early embryonic death, and in these cases a genetic cause for the loss is unlikely to be found. Further complicating these estimates is the expectation that there are many disease-associated genes that have yet to be discovered. Some studies suggest that only about 20% of genes associated with autosomal recessive disorders have been identified (Antonarakis, 2019). Taken together, it seems that these estimates likely represent the lower limit of the true range.

Additionally, while the mutational burden per individual is thought to be fairly consistent across populations (Gao et al., 2015), the actual prevalence of recessive disorders (i.e. individuals who have biallelic mutations in a disease gene) is highly variable among groups. In isolated or endogamous populations with shared ancestry, offspring are more likely to harbor homozygous deleterious mutations resulting in disease due to founder effect (discussed below). Therefore, populations with increased ancestral and/or modern consanguinity tend to have a higher burden of recessive disorders, ranging from 1.4 in 1000 in the outbred and multiethnic population of British Columbia, to 7 in 1000 in Saudi Arabia where consanguineous marriages are common (Antonarakis, 2019).

1.2.2 Founder effect

As discussed above, humans on average carry from 4-10 mutations associated with recessive disorders. In a large, genetically heterogeneous population, these mutations may involve many genes, with the mutations present at low frequencies. However, when a small number of these individuals are separated from the original population and start a new population (i.e. undergo a population bottleneck), this genetic diversity decreases in a random fashion (Figure 2). The population then only contains the alleles that were present in the founders, and these are subject to genetic drift, so some recessive mutations will disappear from the new population altogether, while other mutations that were carried by the founders may propagate and

become more common. This phenomenon is known as founder effect and is essentially a consequence of random chance.

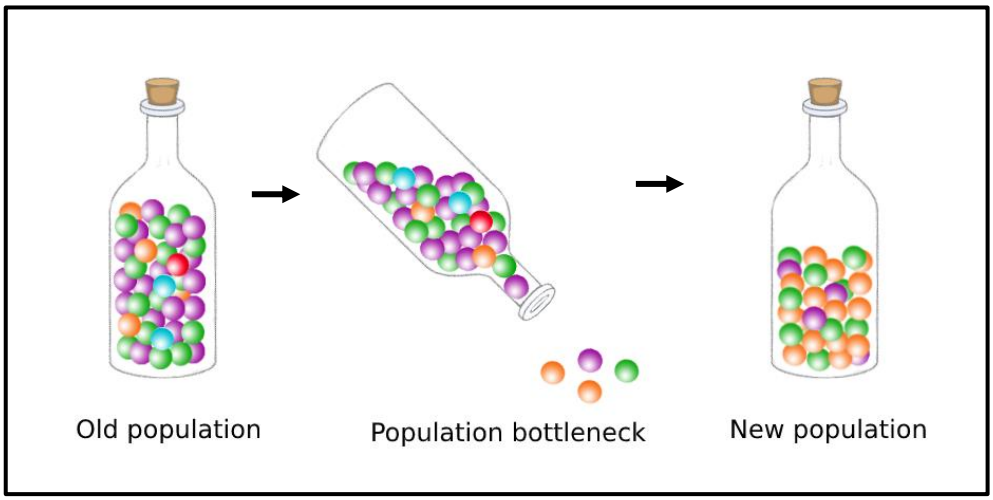

Figure 2. Demonstration of founder effect caused by a population bottleneck

Founder effect is intensified when the population remains reproductively isolated from others, which may occur due to geographical (e.g. population is on an island, a remote fly-in community) or cultural factors (i.e. linguistic, religious). As small, isolated populations are subject to stronger genetic drift (Whitlock, 2000), the number of initial founders, the rate of population growth in the new group, and the degree of endogamy all influence how drastically allele frequencies change in a founder population.

The strength of founder effect is reflected in the degree of relatedness between individuals in the population, which can be roughly quantified on a population level. Single nucleotide polymorphism (SNP) arrays are a commonly used genomic analysis technology which genotype individuals at a large number of SNPs throughout the genome. When two individuals share a segment of DNA because they have a common ancestor, all the SNPs in that region will be identical – the segments are identical by descent (Figure 3). If these individuals reproduce, their offspring are likely to have some regions of homozygosity that are identical by descent. If a given region of homozygosity contains a harmful genetic variant in a gene associated with a recessive condition, the individual will be affected.

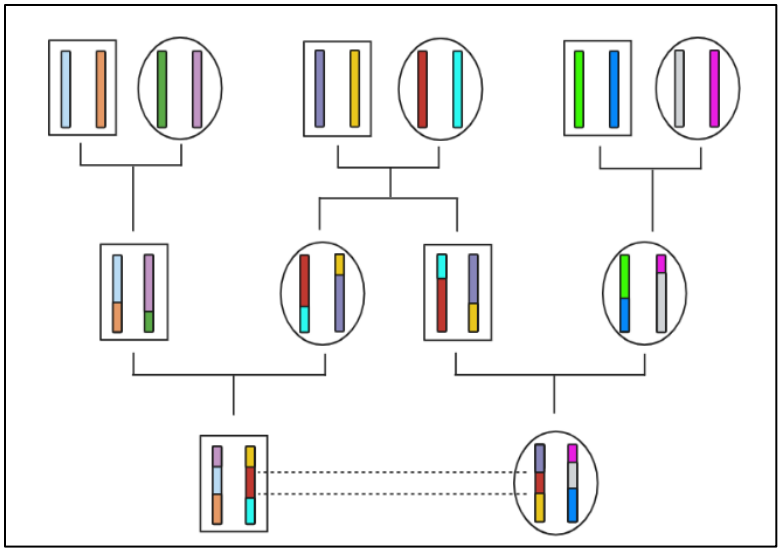

Figure 3. Genomic segments between the dotted lines are identical by descent because they were inherited from a common ancestor in the first generation

Populations that practice consanguineous marriage tend to have multiple long stretches of homozygosity (greater than ~1-2Mb), because individuals have recent common ancestors so there is less chance of the shared segments undergoing recombination. In contrast, shorter segments of homozygosity (less than ~1-2Mb) throughout the genome are reflective of ancestral relatedness and founder effect (Ceballos et al., 2018).

1.2.3 Purpose of carrier screening

When a family has a known history of a particular recessive disorder, carrier *testing* enables the identification of carriers, who may be at risk of having offspring with the condition. Carrier testing is specific to mutations or conditions that are known within a family. In contrast, CS is a test that identifies carriers of recessive disorders in the absence of a family history. It may be offered for a single disorder, such as cystic fibrosis, or for up to hundreds of different disorders at once in the case of expanded CS.

The main objective of CS differs between cultures and populations. In Western countries, the general consensus is that the goal of CS lies in enhancing reproductive autonomy (De Wert et al., 2012; Henneman et al., 2016). In this sense, the identification of carriers who are at risk of having a child affected with a recessive disorder allows for genetic risk counselling and

informed reproductive decision making. When faced with the knowledge that they are at risk, some carrier couples may choose to use the information to prepare for the birth of a medically complex child. Others may choose to avoid the birth of an affected child, which can be achieved by choosing not to have children, adopting, prenatal testing and termination of affected pregnancies, or utilizing assisted reproductive technologies such as preimplantation genetic testing or gamete donation. The key to the "autonomy" perspective on CS is maximizing individual choice rather than prevention of disease.

Another perspective on the goal of CS, taken in some regions with a high prevalence of severe recessive disorders, is to reduce the birth incidence of these disorders (De Wert et al., 2012). Examples of such CS programs include screening for Tay-Sachs disease in the Ashkenazi Jewish community and β-thalassemia in Cyprus, which both began in the 1970s (Laberge et al., 2010). The so called "prevention" perspective may be taken to reduce individual suffering, when the disorder results in severe morbidity or mortality, and/or due to the economic burden caused by the high prevalence of the disorder.

The perspective taken regarding the goal of CS influences how success of the programs is measured. The prevention perspective implies that unless there is a decrease in the birth incidence of the genetic disorder being screened for, the CS program would not be considered successful. If the autonomy perspective underlies the goal of CS, success may be measured by the effectiveness of the counselling aspect of screening - patient satisfaction, uptake of CS, or participants' knowledge of their carrier status or the condition after a defined follow-up period (Laberge et al., 2010). These outcomes may be onerous to quantify which could make it difficult to assess whether a given CS program is successful.

If the factors used to deem a "disease prevention" CS program as successful are used to assess the potential usefulness of CS for other disorders or populations, there is a risk that the potential benefits (i.e. reproductive autonomy) of screening will be overlooked. To illustrate, Laberge et al conducted a study which assessed the usefulness of offering CS for cystic fibrosis (CF) by comparing it to Tay-Sachs and β-thalassemia screening (Laberge et al., 2010). Both of the latter programs have had high uptake among the affected populations and have resulted in

a decrease in the birth incidence of the disorders of greater than 90% (Laberge et al., 2010). Common factors between the programs include that they are screening for a severely debilitating, often fatal childhood onset disease, with a predictable disease course, and consensus that decreasing the incidence of affected births is favourable (Laberge et al., 2010). The authors argued that since CF has treatments available that have significantly improved the life expectancy of affected individuals, avoiding the birth of affected children may be less important of a goal. Therefore, they argued that genetic screening for CF is less likely to be "successful" in their sense of the term and is a less favourable target for screening (Laberge et al., 2010).

Indeed, if success is measured by the reduction of affected births, perhaps CS for CF would not meet these criteria. Nonetheless, surveyed individuals in the general population of the US as well as those with a family history of CF are of the opinion that CS for this condition should be made available for the purpose of reproductive planning (Janssens et al., 2016; Lakeman et al., 2009). Therefore, a different framework for assessing the success of autonomy-driven CS programs is necessary.

1.2.4 Wilson & Jungner applied to genetic screening

European physicians and policymakers J.M.G. Wilson & J.G. Jungner were commissioned by the World Health Organization in 1968 to develop a set of principles guiding policy related to the early detection of disease in the general population (Wilson & Jungner, 1968). These principles, which are outlined in Table 1, provided a framework with which to assess which disorders would make good candidates for screening, as well as which factors to consider when designing screening programs. Presymptomatic screening was a new concept at the time, as medicine up to that point had focused primarily on treating the symptoms of disease when they presented.

Table 1. Principles of screening for disease (Wilson & Jungner, 1968)

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a "once and for all" project.

While these principles were certainly ahead of their time, in the subsequent generations Western medicine has shifted in multiple ways necessitating revisions of the original principles and addition of others (Andermann et al., 2011) . Changes that have been proposed to the original criteria reflect the need to be inclusive to screening for rare genetic conditions (including recognizing the familial implications of genetic testing), to shift away from paternalism toward informed choice, as well as to more explicitly describe the need for clinical and analytical validity in screening tests. There have been more than 50 publications making suggestions for revisions to the original Wilson & Jungner criteria, reviewed in Andermann et al., (2011). A synthesis of the proposed revisions has resulted in a new set of principles which are outlined in Table 2.

The original criteria specified that the condition being screened for should be an "important health problem" which meant that it should have high prevalence or represent a significant economic burden to the health care system (Wilson & Jungner, 1968). In contrast, the revised criteria reflect that many genetic conditions have low prevalence yet may still represent an important need. Other changes in the revised criteria specify the need for education in the screening process and promoting informed choice and autonomy, which were not part of the

original principles. These changes reflect the shift away from paternalistic medicine, as well as the need to ensure that counselling is an integrated part of the process of screening.

Table 2. Revised screening criteria (Andermann et al., 2011)

1. The screening program should respond to a recognized need.
2. The objectives of screening should be defined at the outset.
3. There should be a defined target population.
4. There should be scientific evidence of screening program effectiveness.
5. The program should integrate education, testing, clinical services and program management.
6. There should be quality assurance, with mechanisms to minimize potential risks of screening.
7. The program should ensure informed choice, confidentiality, and respect for autonomy.
8. The program should promote equity and access to screening for the entire target population.
9. Program evaluation should be planned from the outset.
10. The overall benefits of screening should outweigh the harms.

1.2.5 Disorders included in carrier screening panels – is more always better?

It is now possible to screen for thousands of disorders in one test, largely due to significant reductions in the cost of next-generation sequencing. Commercial laboratories now offer expanded CS panels that screen for hundreds of conditions (Kraft et al., 2019). While several professional organizations have released guidelines regarding which types of conditions to include on CS panels, there is no regulatory oversight to ensure they are following said guidelines. The panels offered by many companies include conditions which do not meet the minimum criteria, and concerns have been raised about whether this is appropriate (Andermann et al., 2011; Sparks, 2020).

A full discussion about the arguments for and against expanded CS is beyond the scope of this review but concerns with “bigger is better” expanded CS mainly concern the uncertainty of interpreting positive results from expanded CS when the condition in question is extremely rare, variable, poorly understood, or has weak genotype-phenotype correlations. These concerns especially pertain to prenatal expanded CS, where a woman or family would be asked to make decisions about continuing or terminating a pregnancy based on ambiguous results.

Several organizations have published guidelines on the types of disorders that should be included on expanded CS panels, and these guidelines are not necessarily consistent, leaving the decision in the hands of the clinician (Sparks, 2020). The American College of Obstetricians and Gynecologists' (ACOG) position is that disorders should be included in expanded CS panels only if they meet several of the following criteria: 1) carrier frequency of 1/100 or greater, 2) a well-defined phenotype (including genotype-phenotype correlation) with significant impact on quality of life, 3) childhood onset, 4) association with physical or cognitive impairment, and 5) require early medical or surgical intervention ("Committee Opinion No. 690: CS in the Age of Genomic Medicine" 2017).

The European Society for Human Genetics (ESHG) statement is in agreement that conditions screened for should be severe, with onset in childhood (Henneman et al., 2016). In contrast, the American College of Medical Geneticists (ACMG) guidelines do not make such restrictions and state that conditions with variable penetrance, variable expressivity, or those with adult-onset can be included. However, they do recommend that testing for these types of conditions should be optional and that the implications and limitations should be thoroughly discussed prior to screening (Grody et al., 2013).

Screening principles and practices have shifted over time and space. Global consensus on the "best" approach to CS is unlikely to be reached because each culture and society has unique characteristics, needs, and challenges. The following chapter illustrates several ways that CS has been adapted to specific populations, both successfully and unsuccessfully.

1.3 History of population-based carrier screening

Carrier screening is frequently offered on the basis of ethnicity, as certain genetic disorders are more prevalent in individuals of particular ancestral backgrounds. For instance, the Ashkenazi Jewish community is known to have high carrier frequencies for the recessive disorders Tay-Sachs disease and Gaucher disease, among others, due to founder effect (Bray et al., 2010). Hemoglobinopathies such as α- and β-thalassemia and sickle cell anemia are found at increased frequencies in regions where malaria has been historically endemic due to the protective effect instilled in carriers of these conditions against the blood-borne illness (Roberts & Williams, 2003). Since the 60s and 70s many regions have started CS programs aimed at the detection of carriers among those populations considered to be at elevated risk. The following case studies describe several historical approaches to population-based CS and illustrate the importance of program tailoring and community buy-in.

1.3.1 β-thalassemia screening

Some of the first CS programs were in response to the high prevalence of the hemoglobinopathies in Mediterranean and Middle Eastern countries and had the aim of preventing disease. Many governments have made screening for these conditions mandatory, as the goal of the CS programs are to decrease the prevalence of the disorder (Saffi & Howard, 2015). In these regions, proof of screening is required prior to being granted a marriage license, however there are no legal restrictions on carriers marrying. Carrier couples are presented with options, including dissolving the relationship, and can decide for themselves whether to get married, although in some cases the counselling is more directive (i.e. couples are advised not to marry) (Cowan, 2008a). In the 1970s, Cyprus was the first country to mandate premarital CS for β-thalassemia, where 15% of the population carries the mutation (Saffi & Howard, 2015). Other countries that have since implemented mandatory CS for β-thalassemia include Turkey, Iran, Palestine/Gaza strip, and Saudi Arabia.

These programs are acceptable to the population in part due to the widespread practice of arranged marriages (Cowan, 2009). Further, the consensus among both doctors and the general

population was that a decrease in the prevalence of affected births was beneficial. The public recognized the burden that caring for a child with thalassemia places on a family (e.g. regular transfusions for life and complications that can arise from both the condition and the treatment). Also, from a public health and economic standpoint, officials understood that access to medical treatment is limited for many in these countries, and supplies of blood for transfusions would not sustain an increase in the prevalence (Saffi & Howard, 2015).

In countries with mandatory screening that allow prenatal diagnosis and termination of pregnancy such as Cyprus, the incidence of this condition has been decreased by nearly 100% (Saffi & Howard, 2015). Iran implemented mandatory CS decades prior to prenatal diagnosis being accepted, and during that initial period, 50% of carrier couples decided to cancel the marriage resulting in a decrease in the incidence of affected births (Samavat & Modell, 2004). In contrast, the incidence of affected births in Saudi Arabia, a country in which abortion is not widely available (or not considered for cultural/religious reasons) has not changed significantly, as 90% of carrier couples decide to continue with the marriage (Alhamdan et al., 2007).

Many other countries in the region have had voluntary screening programs for the hemoglobinopathies with varying approaches. In Greece, there has been a voluntary screening program for β-thalassemia and sickle cell anemia in place since 1974. CS is offered both in the preconception period as well as during pregnancy. with education being provided in high school, military programs, maternity clinics, and through the mass media (Saffi & Howard, 2015). A 2011 assessment of their CS program indicated that over the 35 years the program had been active, 12,000 carrier couples were enabled to have healthy children and 4,000 affected fetuses were terminated. The authors predicted that as the use of PGD becomes more widely available in Greece that the number of terminated pregnancies will decrease (Loukopoulos, 2011).

While mandated screening programs in some countries have been accepted by their populations, the next section illustrates that mandatory screening has the potential to do harm. Therefore, in many countries voluntary screening programs are the norm.

1.3.2 Sickle cell anemia screening

In 1971, a mandatory CS program for sickle cell anemia (SCA) was implemented in 12 US states, targeting mainly people of African American descent, although they were not the only population affected by the condition (Markel, 1998; Siddiqi et al., 2013). A group of public health agencies, governments, African American activists, and physicians supported the creation of a mandated program because of the high carrier frequency for SCA (1/12) in the African American community and because of the burden it placed on Black families, especially as there was a lack of effective treatments or prenatal diagnosis methods (Markel, 1998). In some states, proof of CS was required before the state would grant a marriage license, and in others, CS was done in elementary or high schools. The intentions of the program may have been beneficent, but there were many reasons the mandatory program was controversial and ultimately a failure.

Part of the reason the program failed was the political climate at the time. For context, this program started in the height of the civil rights movement, when tensions and distrust between the Black community and the largely White rest of the country were high (Cowan, 2008b). The Tuskegee experiments (1932-1972) had recently come to light (Paul & Brookes, 2015). Furthermore, sickle cell anemia had a history of being highly stigmatized in the US after WWI as a “communicable” Black disease (which was misinformation) and targeted by White eugenicists as a threat to America. Understandably, many Black communities objected to mandated screening due to the stigma associated with SCA, especially since only one state implemented confidentiality measures (Cowan, 2008b). Other Black communities objected to mandated screening because it was another example of governments telling them what to do, as segregation had only recently been lifted in many states (Cowan, 2008b). Overall, there was not widespread support among the community for CS despite the programs having many African American proponents.

There were also technical and analytical issues with the testing kits used for widespread screening. The Sickledex screening test was a simple to use, cheap biochemical test that could detect the presence of sickled hemoglobin but could not distinguish carriers from affected

individuals (Cowan, 2008b). The only accurate way to tell the difference between carriers with a single HbS allele and affected individuals who have 2 HbS alleles at the time was electrophoresis, a more expensive and technically difficult assay. Electrophoresis was meant to used as a follow up test when someone tested positive with the Sickledex, but some public and private laboratories either misinterpreted this instruction or opted to save money and did not conduct the follow up test, resulting in many carriers being told they were affected with SCA (Cowan, 2008b). Further, education about the test in the screened population was lacking which further contributed to the misinterpretation of the test; many parents who were told their children were carriers incorrectly thought their children were affected (Cowan, 2008b).

A third major problem arose from the lack of confidentiality of the test result. Stigma in the general population against carriers was prevalent. The military discriminated against carriers by forcing them to resign or refusing them entry, carriers experienced discrimination by employers, and insurance companies increased rates for carriers (Cowan, 2008b). These confidentiality issues further added to the distrust within the Black community toward the government and medical community and eventually resulted in some American African activist groups labelling the screening programs as genocidal and attempts to control reproduction (Cowan, 2008b).

The mandatory CS programs were discontinued by 1980 and replaced by voluntary screening. Most CS for SCA in the US today takes place in the prenatal period and follow up testing including partner screening and prenatal testing have limited uptake. The lack of attention to potential harms associated with the sickle cell screening program has had a lasting impact on the African American population, with distrust and avoidance of medical genetics persisting in many individuals today (Cowan, 2008b). The history of SCA screening in the US illustrates how despite good intentions, a lack of attention to how CS was understood and perceived by the target community resulted in lasting harm. In contrast, the following example shows how flexibility and tailoring of CS to the specific characteristics of the target population can significantly improve the acceptability of CS.

1.3.3 Tay-Sachs disease screening

Tay-Sachs disease (TSD) is a rare, fatal childhood-onset condition that is 10 times more prevalent in people of Eastern European (Ashkenazi) Jewish descent than the general population (Edelson, 1997). TSD is one of several genetic conditions which are found at a higher prevalence in this community. CS was initiated for TSD and other conditions in the US in the 1970s, shortly after an enzyme assay for TSD had been developed that could distinguish between affected individuals and heterozygote carriers.

These CS programs were largely organized and promoted by the Jewish community itself, with many Jewish doctors, women's groups, and synagogues involved in providing education about the disorders prior to offering screening (Thomsen et al., 2020). Religious leaders and the public were involved in the development of the CS programs from the outset. As a result, the four predominant sects that make up the Ashkenazi Jewish population in North America (Conservative, Reformed, Orthodox, Hasidic) have had different approaches to offering CS within their communities partly as a result of differing views about the acceptability of pregnancy termination.

The majority of Ashkenazi Jewish CS in North America takes place in the prenatal period. As prenatal testing for TSD and other Jewish genetic disorders has been available since CS was initiated, and non-Orthodox communities typically allow abortion during the early stages of pregnancy, uptake of CS and prenatal testing is high in this community (Scott et al., 2010). Since the 1970s, the incidence of TSD and other severe genetic conditions in the community has decreased by 95% (Scott et al., 2010).

In Montreal in the 1980s, a CS program was initiated for high school students of Ashkenazi Jewish descent. After an educational session, students were asked to consider whether they were interested in CS, and after a period were invited to have the test and informed of the result. While this program was viewed as a convenient way of reaching potential screening participants before they had selected a partner, questions have been raised about the ethics of screening in high school when peer pressure might influence the decision to undergo screening

(Frumkin & Zlotogora, 2008). Further, 50% of carriers identified in the program later stated that they were depressed and/or worried about their result, indicating that the goal of empowering carriers to make informed reproductive decisions may have been overshadowed by the psychosocial burden of learning their carrier status at that age (Scott et al., 2010).

The ultra-Orthodox groups which include the Hasidic community do not permit abortion and have had a premarital carrier matching program since the 1983 known as Dor Yeshorim, which has a nearly 95% uptake among this group (Raz & Vizner, 2008). Blood samples are drawn during adolescence and each participant is given a number. When a marriage is being considered (which are arranged between families), Dor Yeshorim provides information about whether the match is genetically compatible without actually providing details about individual carrier status. If a carrier couple is identified, they are told the pairing is “unadvisable” and in most cases the union is dissolved (Raz & Vizner, 2008). Qualitative exploration into the experiences of participants in Dor Yeshorim suggests that many participants do not know (nor want to know) the basis of the test or what it means to be a carrier, as many participants stated that carriers are affected with the disease in a “dormant” state (Raz & Vizner, 2008). It has been suggested that the approach of not revealing individual carrier status, while intended to decrease the stigma of being a carrier, may have resulted in increased stigma against carriers (Raz & Vizner, 2008) due to a lack of widespread education and understanding about what the test results mean.

Regional approaches to population-based CS have taken many forms. The successes and failures described above demonstrate that understanding the target community and their perspectives regarding the CS test is critical to maximizing benefits and reducing harm. Specific areas of exploration and attention required when developing a population-based CS program are described in the next section.

1.4 Developing a population-based carrier screening test

1.4.1 Defining the goal, benefits, and risks of carrier screening

The updated Wilson & Jungner criteria outlined in chapter 1.2.4 and the lessons learned from past and present CS initiatives provide important organizational and ethical points to consider when planning to offer a population-based screening test. Similarly, Achterbergh et al (2007) proposed that tailoring of a successful health screening program to a specific population requires a sociotechnical co-evolution, or process of mutual learning between the technology (and providers) and the society being screened. An important part of the co-evolution is alignment between stakeholders (e.g. members of the target community, policy decision makers, providers) on important topics such as (1) the goal of screening, (2) prospective users/demand/process, and (3) political and cultural acceptability.

The objectives of the CS program or test should be defined from the outset. Most published guidelines as well as the outcomes of an EJHG workshop on the topic agree that the goal of population-based CS programs should be to enhance reproductive autonomy (Molster et al., 2017; Wilson et al., 2016). Doing so means maximizing individual choice which also includes the choice to not be tested, so CS should be strictly voluntary. The process of CS should be integrated with appropriate pre- and post-test counselling and have a well-defined plan for follow up when carriers are identified (Andermann et al., 2011; Molster et al., 2017). Also, the reproductive options available when couples are identified to be at risk should be acceptable and meaningful to the target population (Holtkamp et al., 2017).

The benefits of CS need to outweigh the risks and costs. Also, when assessing the benefits and costs of CS, the goal of enhancing reproductive autonomy needs to be foremost – for example, an affected child born to well-informed carrier parents who decided they were prepared to have a child with the condition should be counted as a benefit, not a cost (Campbell & Boyd, 1996). Potential harms associated with CS need to be understood and mitigated as much as possible. These might include discrimination within or from outside the community – against carriers, those that choose not to undergo CS, or those that are born with a genetic condition.

For example, among communities that practice arranged marriages, a woman who discloses she is a carrier of a genetic condition may be seen by the other family as someone to avoid (Frumkin & Zlotogora, 2008). Some of these risks might be mitigated by an increase in public awareness of genetics and screening. This could be achieved by integrating accurate education into the CS program that includes what it means to be a carrier, and the idea that everyone is a carrier for something. Another potential harm lies in the chance of insurance or employment discrimination, which necessitates having effective policies protecting participants' confidentiality.

1.4.2 When to offer carrier screening

If the goal of CS is to enhance reproductive autonomy, it makes the most sense to offer CS prior to conception, when the number of reproductive options is highest. In practice, CS is often done in the prenatal period, partially because this is when reproductive options and risks are most salient to a couple or individual, and also for convenience because screening can be integrated into prenatal care (Andermann & Blancquaert, 2010). However, prenatal CS limits the possible reproductive options to prenatal diagnosis with or without termination of pregnancy.

The characteristics of the population being screened should be taken into consideration when deciding on the timing of CS. If the population being offered screening would not consider termination of pregnancy, for example, offering CS to couples during pregnancy followed by prenatal diagnosis has less utility than preconception or premarital screening. But there is also the risk of offering CS too early – some argue that the offer of CS for TSD during high school in Montreal (chapter 1.3.3) was inappropriate due to the potential influence of peer pressure on the informed consent process (Frumkin & Zlotogora, 2008). Also, there is a question of whether results would be remembered accurately, due to the potentially long time period between receiving results and when those results would be relevant to the participants (Frumkin & Zlotogora, 2008).

1.4.3 Education about carrier screening

Education about the conditions being screened for, the implications of being a carrier, and the reproductive options available to high-risk couples is an essential aspect of offering a CS test. Effective education of the population in question about the existence of the CS test has also been shown to have a strong influence on uptake of CS (Loukopoulos, 2011). However, there have been different approaches to informing at-risk populations about the availability and process of CS.

Overall, providing education about CS in high school during the regular genetics curriculum seems to be an effective method of increasing awareness of screening and decreasing stigma against carriers (Barlow-Stewart et al., 2003; Frumkin & Zlotogora, 2008). Having several annual, grade-appropriate education sessions resulted in better retention and more accurate understanding about CS in long term follow up (Barlow-Stewart et al., 2003) than a single education session (Frumkin & Zlotogora, 2008). If a specific population is being targeted for screening, research shows that an emphasis on the fact that everyone is a carrier for something results in decreased stigma and negative feelings toward CS (Barlow-Stewart et al., 2003; Frumkin & Zlotogora, 2008).

As the number of disorders being screened for in a single test increases, the education component of counselling becomes more complicated. One study found that increasing the number of disorders screened from 1 to 2 (TSD and CF among Ashkenazi Jewish high school students) did not negatively impact retention of information about the conditions (Barlow-Stewart et al., 2003), but what about when the number of disorders increases to 20, or 200? It becomes cumbersome to counsel about all the individual conditions, and the risks and benefits of screening for each one. In addition, given the sheer volume of information, retention would likely be low (Sparks, 2020). Therefore the ACOG and ACMG recommend that counselling in these cases should be more general and include a discussion of the types and breath of conditions being screened (Sparks, 2020).

1.4.4 Community involvement

The extreme case of the failed US-based screening program for sickle cell anemia in the 1970s illustrated how support from the community at large is an essential factor in implementing population-based screening tests (chapter 1.3.2). Although there was top-down support for the program, prior engagement with the population being screened may have served to illuminate the issues that later became known surrounding distrust and stigma. On the other hand, widespread support for TSD screening among Ashkenazi Jewish populations and the involvement of the community in raising awareness and providing education and support (not to mention funding) is often cited as the most important factor in the success of these programs (Holtkamp et al., 2017).

The Ashkenazi Jewish experience is unique in the sense that there was broad grassroots community support for CS in the dozens of local community groups that were involved in the screening programs, but there were also Jewish doctors, religious leaders, and policymakers that approached the program from the top down. In the case of smaller founder populations, however, despite the lack of representation among policy makers and physicians, bottom-up community support for CS may still be substantial (Holtkamp et al., 2017).

Factors identified to correlate with community support and positive attitudes toward population-based CS include a high level of familiarity with the condition(s), high perceived benefits of screening, and low perceived risks (Holtkamp et al., 2017). These factors can be assessed effectively through survey research which allows the opinions of the community at large to be heard, rather than just the “loudest” voices (Gollust et al., 2005). These studies are important when developing new population-based screening tests because the data can be used to predict how the CS results will be used and whether the test will be perceived as useful or valuable by the community (Gollust et al., 2005). Further, these studies can be used to assess the counselling and educational needs of the community that is being offered CS (Gollust et al., 2005).

A significant amount of literature exists in regard to the ethics of working with specific communities in genetic research (Foster & Sharp, 2000; Juengst, 2000; Weijer, 1999), and many of the same principles apply when developing a population-specific genetic test. Some issues raised include the chance of discrimination against the population as a whole, disruption of internal social relationships, and risks to cultural or moral authority (Foster & Sharp, 2000). For example, if a population highly values collective decision-making before individual choice, informed consent for testing on an individual level (while certainly in line with dominant Western views on informed consent) has a risk of disrupting the collective norm in the population (Foster & Sharp, 2000). For these reasons, community engagement and express support of a new genetic test is necessary before such a test can be ethically implemented (Foster et al., 1997). The population should be engaged in the process in such a way that "empower[s] them to create local communities capable of making decentralized decisions about their own futures" (Juengst, 2000).

Tailoring the provision of a population-based CS test requires attention to many critical elements, including what the community perceives as the goals, benefits, and risks of screening, what they may do with the results, the life stage they want to be screened, and – perhaps most importantly – whether they want the screening test in the first place. The Hutterite population, the subject of this study, is highly unique suggesting that any of the aforementioned approaches to CS would be unlikely to fit with their beliefs and practices. The following section provides a glimpse into the specific features of the community that might affect their perspectives of CS.

1.5 The Hutterian Brethren

1.5.1 History

The Hutterian Brethren arose out of the Radical Reformation of the 16th century, in response to what they perceived as corruption in both the dominant Catholic Church and the early Protestant movement as led by Martin Luther and others. Early Anabaptists, which included both the Hutterites (est. 1528) and Mennonites (est. 1536), were radical primarily because of their practice of believer's baptism. Anabaptists reject infant baptism because they believe that faith is not something a person is born into. Rather, they view the choice to follow and commit to Christianity as a serious and personal decision that should only be made once a person reaches maturity. Adult baptism and the other central tenets of Anabaptism including non-violence and living separately were grounded in the desire to live as Jesus Christ had lived according to the New Testament, which they felt the Catholic Church and other Protestant groups had departed from. As these beliefs were highly nonconformist during a time when the Church held great sway over governing bodies, the beliefs and practices of Anabaptists were made punishable by death in 1526.

Jacob Hutter (1500-1536) was one of the early followers of Anabaptism in Tyrol (modern-day southern Austria/northern Italy) and became the leader of a group that later called themselves Hutterites. Tyrolean leaders were particularly opposed to this new and fast-growing group that threatened the power of the dominant churches of the time. After enduring years of increasing persecution and violence in Tyrol, Hutter and other early Anabaptist leaders began the first of a series of migrations that eventually resulted in a small number of followers settling in Russia. These migrations were interspersed with periods of prosperous settlement across Europe but in each case the community was driven from their established home with war and violence.

The first community of goods was established in Moravia (modern-day Czech Republic), with members pooling their resources and sharing everything according to need. While the practice of communal living was consistent with their framework of living according to the life of Christ, Hutterite records indicate that the first community of goods was established in response to dire

need as they had been forced to flee only with what they could carry (Hutterian Brethren, 1987).

Reaching Russia in 1819, approximately 400 Hutterites learned efficient farming techniques that the Mennonites had developed and eventually became self-sufficient. In 1859 several leaders within the Hutterites decided to re-establish their own colonies resulting in the three specific groups of Hutterites (*Schmiedeleut, Lehrerleut, Dariusleut*). Eventually some freedoms that had been allowed by the Russian government began to be revoked. In response, the entire population of Hutterites (1265 individuals) made the decision to emigrate to the United States, which they did in groups over a 5-year period from 1874-1879. While 400 Hutterites established colonies in South Dakota, the remaining ~800 settled on individual farms, calling themselves Präirieleut, and slowly assimilated into Mennonite groups.

When the US government began conscripting young men into military service at the start of WWI, Hutterites requested exemption on religious grounds and were denied. At the time, the Canadian government needed more people to settle in the prairie provinces and promised Hutterites religious freedom and military service exemption. Therefore, the majority of communal Hutterites emigrated to Canada in 1918. After WWII, some Hutterites returned to their abandoned colonies in the US.

Today, the Hutterite population in Canada exceeds 35,000 individuals according to the 2016 Census Report (Statistics Canada, 2017), and there are an additional 10,000 to 15,000 Hutterites living in the US. Schmiedeleut Hutterites are mostly located in Manitoba (107 colonies) and South Dakota (54), with a few others in North Dakota (6) and Minnesota (9). Lehrerleut Hutterite colonies are found in Alberta (69), Saskatchewan (31), and Montana (35). Dariusleut Hutterite colonies have been established in Alberta (98), Saskatchewan (29), British Columbia (2), Montana (15), Washington (5), and North Dakota (1).

1.5.2 Hutterite society today

Daily life for Hutterites is grounded strongly in a set of principles that has changed little during their 500-year history. One of their main tenets, gelassenheit, or “self-surrender”, reflects their

belief that the needs of the group should come before the needs of the individual, and that all goods should be held in common and shared for the benefit of the community (Schwartz, 1976). While families live in private homes and have personal items, these are provided by the community. No one receives a salary for working on the colony; rather, everyone in the community is provided for from birth to death. Clothing is conservative and home made, and has changed little in the past 150 years (Kerkhoven, 1996). Colony members gather daily to attend church services. Meals are shared in a communal dining area with a central kitchen, with men and women sitting at different tables, and children in a separate area.

There are few differences between the three *leute* in terms of daily life or religious practices; regardless, since 1910, they have remained virtually separate with little intermarriage occurring between them (Peter, 1987). There are subtle differences in dress and levels of conservatism among the *leute*. The Lehrerleut are considered to be the most conservative and private of the three groups, while the Schmeideleut tend to be the most liberal and open to interacting with outsiders. A common misconception about Hutterites is that they are a homogeneous group, to the contrary, every colony is different in regard to how strictly they adhere to Hutterian principles, their social behaviour, and interaction with outsiders (Katz & Lehr, 2013).

Colonies are made up of an average of 80-120 members, and all members over the age of 15 are considered to be adults and contribute to the work on the colony (Schwartz, 1976). Education has always been an important aspect of Hutterite society, although in the first half of the 20th century it was less emphasized and most did not study past the 8th grade. Today, the majority of colonies have a requirement for completing grade 12 and a number of Hutterites continue into higher education, especially in the fields of education, nursing, and agriculture.

The social order within Hutterite communities has also remained stable throughout their history. Hutterite society is patriarchal with clearly defined gender roles. Each colony has a spiritual leader or minister who is the ultimate authority at the colony, and other men have roles of managing the economic aspects of the colony and various enterprises which may include farming or manufacturing. Men are the only voting members of the community and in

addition to the management roles are responsible for the manual labour that takes place (Katz & Lehr, 2013).

Women are responsible for raising the children, making clothes, taking shifts working in the kitchen, cleaning, and helping in the colony garden (Katz & Lehr, 2013). While women do not vote and have few opportunities for leadership roles (aside from the role of Head Cook), they have influence on the colony with respect to the family and domestic operations (Katz & Lehr, 2013). Many Hutterite women report that they are not bothered by their inability to officially vote as they feel they have great sway over who their husbands vote for, although this sentiment is not universal (Katz & Lehr, 2013).

The survival of the Hutterite way of life throughout their long and difficult history is evidence of the strength of their beliefs and has resulted in Hutterites being widely recognized as the most successful communal society in modern history (Hostetler & Huntington, 1968). Historians have suggested that the key to their longevity is their adoption of "controlled acculturation" (Eaton, 1952), a term coined to describe the way that Hutterites, unlike their Anabaptist counterparts the Amish, use discretion in which aspects of the outside world to remain isolated from, and which to adopt for the benefit of the community. The way that the Hutterites adapt to the world changing around them allows them to "bend with the wind without breaking" (Peter, 1987). Indeed, Hutterites have embraced modern technologies in ways that allow them to be competitive in modern markets including farming and manufacturing. For example, one Hutterite colony in southern Manitoba is currently in the process of building what will be the "largest modern hog facility in all of Western Canada" (personal communication).

At the same time, other aspects of modern culture are not adopted or accepted. While each leut and individual colony differs in the level of conservatism expected of its members, for the most part, modern entertainment, the internet, and other luxuries are limited. Socialization of children into the belief system and way of life of the Hutterites begins early and is nearly complete (Hostetler & Huntington, 1968), such that resistance to their way of life is rare and only 3% of people leave the colony permanently (Shenker, 2011).

1.5.3 Marriage and family life

During their early history, marriages between Hutterites were typically arranged by the minister of the colony, however this was abandoned in the 1800s and today marriage is a matter of individual choice and based on love (Ingoldsby, 2001; Peter, 1987). However, marriage can only take place between baptized men and women who are members of the Hutterite church, so the community is strictly endogamous. First cousin marriages are taboo among Hutterites, and second cousin marriages are relatively common, however due to their patterns of endogamy, most Hutterites are related in multiple ways resulting in a high degree of relatedness between individuals regardless of whether they have a recent common ancestor (Boycott et al., 2005; Ingoldsby, 2001).

The average age at marriage is around 25 or 26 (Ingoldsby, 2001). As relationships are usually between individuals who live at different colonies, opportunities to meet potential partners are limited to events that bring people from different colonies together, including weddings, funerals, or during harvest season. It is common for couples to date for several years before committing to marriage. Once a couple is married, the woman will move to her husband's colony, leaving her home and family. It is expected that children will be produced within the first year or two of marriage (Hostetler & Huntington, 1968). Up until the 1950s, the fertility rate was one of the highest in the world, approaching the natural limit of human fertility, with each family having 10-13 children (White, 2002). Today, this has deceased to an average of 5-6 children per family (White, 2002).

1.5.4 Health beliefs and practices

Like all aspects of life, beliefs about health and illness in the Hutterite community revolve around their faith. They believe that good health is a gift from God and rather than viewing illness as a punishment, they view it is a test of faith and opportunity for spiritual growth (Brunt et al., 1997). Hutterites do not fear death, and instead it marks one of the most important and revered moments of life, transitioning to eternal life in heaven (Brunt et al., 1997). Therefore,

fear of death is not necessarily a motivating factor in how Hutterites make decisions about health behaviours.

Similar to how they have adopted modern technology to benefit their economic ventures, Hutterites make use of modern medicine when needed, primarily for emergencies and serious or chronic medical conditions (Kulig et al., 2002). Otherwise, for common or minor ailments the use of alternative medicine is common, including herbal medicine and homeopathy (Baumberger & Yutrzenka, 2018; Kulig et al., 2002). A study of D-leut and L-leut Hutterites in Alberta showed that Hutterites have mixed opinions about vaccinating their children, with about 30% accepting all vaccinations and 30% refusing all of them (the rest in between) (Kulig et al., 2002). Common responses among those that did not vaccinate include believing that it is God's will that will determine the health of their children, and others citing concerns about adverse reactions (Kulig et al., 2002).

Uptake of new health practices happens slowly as do other changes to Hutterite society, and for health professionals, respect for the principle of *gelassenheit* (i.e. community before the individual) necessitates obtaining the support of elders and leaders as well as the larger community when promoting a new health practice among Hutterites (Brunt et al., 1997). The concept of individual empowerment in the promotion of health behaviours (e.g. to reduce dependency/helplessness, take your health into your own hands), while a common motivator for secular individuals, may not be as appropriate of an approach with Hutterites who are less likely to value individual empowerment over their relationship with God or commitment to communal life (Brunt et al., 1997).

However, there is evidence that when making certain decisions about health behaviours, some Hutterites do consider their own preferences over the benefit to the community. The birth rate among Hutterites declined sharply after the 1950s, leading researchers to wonder why and how this occurred. Interviews with D-leut women showed that the practice of using various forms of birth control was prevalent among the community, despite its use being discouraged unless medically necessary (White, 2002). Most of the women interviewed knew of at least one other who had undergone a hysterectomy or tubal ligation for the purposes of stopping reproduction.

Other methods used included the rhythm method, IUDs, and the pill. In some cases, there were medical concerns associated with continuing to have children, however for many others, the choice to pursue contraceptive measures was a personal preference for a smaller family or to take back some control over their lives in the patriarchal community (White, 2002).

1.5.5 Genetics and carrier screening

Studies of genetics in the Hutterite population over the past few decades have been fruitful due to several historical and cultural elements that are unique to this population, as well as their willingness to participate in research that can benefit their community (Boycott et al., 2008). Since at least the 18th century Hutterites have kept detailed genealogical records, allowing for detailed pedigree analysis and study of inheritance patterns. This is further aided by their practice of having large families. Genealogical records indicate that the majority of Hutterites living today are descended from 89 founders (Martin, 1970).

Second, due to their near total endogamy, Hutterites have regions of homozygosity in their genomes that allow for IBD mapping to be used in the search for novel recessive loci. Analysis of SNP microarray data collected from Manitoba Hutterites that were seen in clinical genetics showed that every Hutterite patient tested had multiple regions of homozygosity (ROH) >5Mb throughout the genome (Frosk, 2019). On average, each individual had 92 Mb (~3% of the 2875Mb autosome) of homozygosity with some variability (Frosk, 2019). As discussed in section 1.4, these long segments of homozygosity demonstrate the effects of recent consanguinity. Since this data is based on clinical arrays that only report ROH > 5Mb in length, it is highly likely that the actual amount of homozygosity is much higher, with many shorter ROH segments reflective of their ancestral relatedness. There have been many loci for recessive disorders identified using IBD mapping and linkage analysis in the Hutterite population including those for limb girdle muscular dystrophy types 2H and 2I, Usher syndrome, disequilibrium syndrome, and dilated cardiomyopathy with ataxia (Boycott et al., 2008).

There have been around 40 genetic conditions identified to be over-represented in the Hutterite population to date (Boycott et al., 2008; Triggs-Raine et al., 2016, personal

observation). The majority are autosomal recessive, although there are also some autosomal dominant and X-linked conditions present in this population including hereditary breast and ovarian cancer (*BRCA1/2* genes, AD), a specific type of hereditary diabetes (MODY3, *HNF1A* gene, AD), androgen insensitivity (*AR* gene, X-linked), and hypohidrotic ectodermal dysplasia (*EDA1* gene, X-linked). It has been proposed there are likely more recessive disease-causing mutations present in the community that have not been identified yet due to lower carrier frequencies and absence of affected homozygotes (Boycott et al., 2008). Due to founder effect, many of these mutations are found at high carrier frequencies, and some are highly specific to the Hutterite population with no recorded cases in other populations.

After the majority of mutations related to known recessive diseases in the Hutterite population were identified, a CS panel was developed in Manitoba to offer CS to people of Hutterite descent (Triggs-Raine et al., 2016). There were 32 founder mutations comprising 30 autosomal recessive conditions included on this panel which used primer extension array technology. Prior to the development of the carrier testing panel, community consultation was pursued through town hall meetings, and overall there seemed to be support for the panel. However, anecdotally the uptake of carrier testing among the community was low, and the reasons for low uptake remain unclear.

One plausible reason identified by informal discussion with community members is that knowledge about the logistics of CS was limited among some individuals. The CS test was widely referred to as the “Hutterite Chip” in pamphlets and town hall meetings because of the array technology used; chip is a common term used to describe technologies that consist of a series of microscopic fragments of DNA attached to a solid surface. However, it appears that at least for some individuals, the term “chip” invoked images of a computer chip being implanted under the skin which made these individuals feel uneasy about having the test done (personal communication). Likely, in the future, referring to the test as a “CS blood test” or something similar will decrease the chance of this misconception.

Another possible reason for low uptake of CS is that support for the test is not as widespread as initially thought. Town hall meetings are a common approach to disseminating information in

the Hutterite community (Anderson et al., 2014; Bowen et al., 1985; Triggs-Raine et al., 2016). However, they are not necessarily the best way to obtain diverse opinions because people will generally attend the town hall meeting if they are interested in the topic. If there are a large number of people who do not believe CS is a good idea (or a smaller number of highly influential individuals), due to the collectivistic nature of Hutterite society, these individuals may influence others' choice to have the CS test done even if they personally want it. Another possible limitation of disseminating information about CS mainly through town halls is that the information may not reach the wider community. If some cannot attend due to distance, or if they do not hear about the meeting, they may not be aware that the CS test is available.

Regardless, after the CS panel was available for 1-2 years, it became clear that some of the results reported by the company commissioned to perform the test were incorrect (P. Frosk, personal communication). The decision was made to discontinue use of this panel and develop a new one based on next generation sequencing technology which would have fewer errors and allow for expansion of the panel as new mutations are identified. This new panel is currently under development and should be available for clinical use in late 2021. The conditions and specific mutations that will be included on the panel are listed in Table 3. For a full review of the features of each condition, see Appendix A.

Table 3. Disorders and associated mutations on the Hutterite-specific carrier screening panel under development. All are autosomal recessive except when noted. Further details and references can be found in Appendix A.

Disorder	Gene	Mutation	Protein	Carrier freq. (leut)
Alpha-mannosidase deficiency	*MAN2B1*	c.2248C>T	p.R750W	-
Androgen insensitivity (XL)	*AR*	c.2033T>C	p.L678P	
AR intellectual disability	*TECR*	c.545C>T	p.P182L	1/14.5 (S)
Arrythmogenic right ventricular cardiomyopathy 11	*DSC2*	c.1660C>T	p.Q554X	1/11 (S)
Bardet-Biedl syndrome	*BBS2*	c.472-2A>G	-	1/36 (S)
Beaulieu-Boycott-Innes	*THOC6*	c.136G>A	p.G46R	-
Bowen Conradi syndrome	*EMG1*	c.257A>G	p.D86G	1/10 (S,D,L)
Combined pituitary hormone deficiency 2	*PROP1*	c.301_302delAG	p.L102Cfs*8	-

Disorder	Gene	Mutation	Protein	Carrier freq. (leut)
Congenital disorder of glycosylation 2N	*SLC39A8*	c.112G>C	p.G38R	1/20-50 (D,L)
CPT1A deficiency	*CPT1A*	c.2129G>A	p.G710E	1/16 (S)
Cystic fibrosis	*CFTR*	c.3302T>A	p.M1101K	1/13.5 (S)
Cystic fibrosis	*CFTR*	c.1521_1523delCTT	p.F508del	1/45.5 (S)
Developmental delay, short stature, dysmorphic features, & sparse hair	*DPH1*	c.17T>A	p.M6K	-
Dilated cardiomyopathy with ataxia	*DNAJC19*	c.130-1G>C	-	1/36 (S)
Emery-Dreifuss MD type 3	*LMNA*	c.1445G>A	p.R482Q	1/65 (D,L)
Familial hyperinsulinemic hypoglycemia	*ABCC8*	c.823-7T>A	-	-
Hypohidrotic ectodermal dysplasia (XL)	*EDA*	c.607C>T	p.P203S	-
Hypophosphatasia	*ALPL*	c.1001G>A	p.G334D	-
Joubert syndrome type 14	*TMEM237*	c.52C>T	p.R18X	1/12.5 (S)
Joubert syndrome type 21	*CSPP1*	c.363delTA	p.H121Qfs*22	-
Joubert syndrome type 33	*PIBF1*	c.1910A>C	p.D637A	-
Joubert syndrome type 33	*PIBF1*	c.1997A>C	p.D666A	-
Juvenile onset cataract with arrhythmic cardiomyopathy	*LEMD2*	c.38T>G	p.L13R	1/8 (S)
Leigh syndrome	*NDUFS4*	c.393dupA	p.E132Rfs*15	1/27 (S)
Limb girdle MD type 2H	*TRIM32*	c.1459G>A	p.D487N	1/6.5 (S)
Limb girdle MD type 2I	*FKRP*	c.826C>A	p.L276I	1/9.5 (S)
Limb girdle MD type 2S	*TRAPPC11*	c.1287+5G>A		1/14 (S,D)
Maple syrup urine disease	*BCKDHB*	c.595delAG	p.P200X	-
Methylmalonic aciduria	*MMUT*	c.1420C>T	p.R474X	1/63 (S)
Morquio syndrome	*GALNS*	c.1139+1G>A	-	-
Nephronophthisis	*NPHP1*	c.1918delA	p.R640Dfs*10	-
Oculocutaneous albinism	*TYR*	c.272G>A	p.C91Y	1/7 (S)
Odontoonychodermal dysplasia	*WNT10A*	c.321C>A	p.C107X	-
Restrictive dermopathy	*ZMPSTE24*	c.1085dupT	p.L362Ffs*19	1/15.5 (S)
Segawa syndrome	*TH*	c.1481C>T	p.T494M	-
Sensorineural hearing loss	*GJB2*	c.35delG	p.G12Vfs*2	1/28 (S)
Sitosterolemia	*ABCG8*	c.320C>G	p.S107X	1/12 (S)
Thyroid dyshormonogenesis	*SLC5A5*	c.1183G>A	p.G395R	-
Usher syndrome type 1B	*MYO7A*	c.52C>T	p.Q18X	-
Usher syndrome type 1F	*PCDH15*	c.1471delT		1/40 (S)

1.5.6 Attitudes toward genetic testing and counselling

Several studies have explored the attitudes of people in the Hutterite community toward carrier testing and genetic counselling. All of these studies have been conducted with Schmiedeleut Hutterites in either South Dakota or Manitoba, so little is known about the opinions of the other leute and how they might differ.

Two studies have surveyed Hutterite individuals to assess their attitudes toward carrier testing for CF (Anderson et al., 2014; Miller & Schwartz, 1992). Among individuals who had children or siblings affected with CF, 82% stated that they would want to know their carrier status (Miller & Schwartz, 1992), while individuals without a family history of CF were less certain, with 41% stating they would want this information (Anderson et al., 2014). When reasons were given, many people stated that they wanted to know "just to know" or so they could avoid having a child with CF. In contrast, the people who said they did not want to know often felt like they were not at risk, or stated that they had already completed their family (Anderson et al., 2014).

None of the Hutterites surveyed approved of termination of pregnancies affected with CF (although a significant proportion were unsure), and only a minority approved of prenatal testing (31%) (Miller & Schwartz, 1992). However, participants were generally of the opinion that carriers should not marry carriers, and the majority of parents who had children affected with CF had decided to stop having children after the diagnosis (Miller & Schwartz, 1992), presumably due to the 25% recurrence risk. These studies indicate that while prenatal diagnosis and termination of pregnancy are likely not acceptable options for most Hutterites, some would consider using their carrier status for family planning.

One of these studies was part of a larger research program investigating carrier frequencies for several disorders that are prevalent in the Hutterite community (Anderson et al., 2014; Chong et al., 2012). After surveying participants on their opinions toward carrier testing for CF, participants were given the option of actually learning their carrier status for this condition. When given the opportunity, only 59% of participants who had stated they would want to know actually took up the offer, and about 30% of people who said they would not want to know or

were uncertain ended up asking for their results. Most of the individuals who had said they were interested but then did not ask for their results were older and beyond their reproductive years, suggesting they may have had less use for the results. Consistent with this, most of the individuals who ended up learning their carrier status did not have children or had not completed their families (Anderson et al., 2014). However, whether this difference is actually related to reproductive potential is unknown.

Another survey was conducted which explored Hutterites' understanding of, and willingness to use genetic counselling services (Gemmell et al., 2017). Overall, participants in this study had positive attitudes toward genetic counselling and most had an accurate understanding of the scope and practice of genetic counsellors. Based on open-ended responses, it was found that most participants had pragmatic attitudes toward the use of genetic counselling services, summarized with the title of the publication, "If it helps, it's worth a try". This study also found that younger participants were more likely to be willing to use genetic counselling services, and the reasons given were related to wanting more information about the conditions and associated risks, concern about the prevalence of genetic conditions in the population, and for family planning (Gemmell et al., 2017).

Overall, these studies have found that many people in the Hutterite community are concerned about their risk of being carriers of genetic conditions, have positive attitudes toward carrier testing for CF, and many take up the opportunity to learn their carrier status when given the opportunity. However, these studies have been limited in scope due to their primarily quantitative nature. Although they have provided some hypotheses as to the reasons behind individuals' willingness to use genetic counselling services and stated interest in carrier testing, none have provided an in-depth exploration of attitudes and decision-making processes about carrier testing. Furthermore, no studies have investigated how people in the Hutterite community feel about a more comprehensive CS test.

1.6 Rationale for this study

Previous consultation with the local Hutterite community as well as a few prior studies have indicated that Hutterites are interested in knowing their carrier status for recessive conditions. Beyond this, not much is known about how people in this community would make decisions about testing, how they would consider using this information, or how much information they would like to have. Now that a comprehensive CS panel is under development and designed specifically for this population, it is necessary to again engage with the community so that they have some control over the details of how and when the CS panel is offered to them. Previous studies in other populations offered ethnicity-specific CS have shown how important it is to have support from the community and to design the program in a way that fits with the values and practices of the population being screened.

Therefore, in this study we used a combination of quantitative and qualitative methods to explore these issues in depth. As previous studies have found that attitudes toward CS are influenced by the perceived risks and benefits of screening, we explored these two factors along with general attitudes toward CS through both surveys and individual interviews. We also wanted to know how individual experiences with genetic conditions influenced interest in CS. Our goal for this study was to gain a broad perspective on the variability of opinions within this community, to not only hear from people who were clearly interested in CS but also from those who are concerned about it, and especially, the reasons why. These data will be essential for providing tailored and sensitive counselling and education to this community moving forward.

A second important goal of our study was to ensure that the CS test is offered in a way that the community finds helpful and valuable. Therefore, many of the questions we asked in our survey and interviews surround the logistical aspects of the test. For example, we wanted to know whether the Hutterite community would be interested in learning their carrier status for all the disorders on the panel, or just specific categories (i.e. fatal in childhood/benefit from early detection and treatment/adult-onset). Professional organizations have raised concerns about CS for mild or adult-onset conditions, due to the ethical issues regarding termination of pregnancies for conditions that are manageable. But for a population that is unlikely to consider

termination as an option, as we suspect of Hutterites, we wanted to know whether they would find this information useful for reproductive planning purposes.

Ultimately, the results of this study can be used to design the CS panel and make recommendations for counselling and education, based on the feedback that we receive from participants. We hope that this will help to ensure Hutterites across Manitoba, as well as throughout North America, have access to tailored and culturally sensitive care.

CHAPTER 2. METHODOLOGY

2.1. Overview of research design

A mixed methods research design was selected for this study. Mixed methods research combines at least one qualitative and one quantitative component in a single research project, for a variety of purposes that centre around the idea that certain research questions can be better answered using a combined methodological approach (Bergman, 2008). This study utilized a chart review and survey for the quantitative component and interviews for the qualitative component to understand the attitudes, perspectives, and preferences of Manitoban Hutterites regarding a population-based genetic CS test. The rationale for choosing a mixed methods design was threefold. First, the purpose of the quantitative component was to provide a general overview of the diversity of perspectives in the community, while the qualitative component would provide contextual information, illustration, and explanation of those results (Bryman, 2008). Second, with both types of data, triangulation of results would be possible, allowing for mutual corroboration and comparison (Bryman, 2008). A mixed methods approach was also selected for pragmatic sampling purposes in that survey participants were invited for interviews and could indicate their interest by leaving their contact information on the survey or contacting the student researcher (Bryman, 2008).

The study followed a convergent design whereby the survey and interviews were conducted in parallel and analyzed separately (Creswell & Plano Clark, 2018). A detailed explanation of qualitative and quantitative sampling, methods, and analysis can be found in later sections. The two datasets were integrated through comparing and contrasting results, and using the context provided in the qualitative dataset to provide potential explanations for patterns observed in the quantitative datasets (Fetters et al., 2013).

This study was reviewed and approved by the University of Manitoba's Bannatyne Campus Research Ethics Board under approval number HS23758 (H2020:152) and the Health Sciences Centre Research Impact Committee (RI2020:075).

2.2 Retrospective chart review

A retrospective chart review was conducted to roughly estimate the uptake of the Hutterite-specific CS panel over the period it was previously available. First, records from the Winnipeg Regional Health Authority (WRHA) Molecular Diagnostic Laboratory were obtained to determine approximate dates of the first and last screening tests sent out as well as the total number of tests that were ordered. Historical charts from the WRHA Program of Genetics & Metabolism were obtained from an internal database and cross referenced by date and patient surname. Hutterites in Manitoba are represented by 11 surnames which are mostly specific to this population (Sommerfeld Hutterite Colony, 2014).

Consult letters were reviewed if they met the following criteria: (a) appointment took place between 2 months prior to the first panel sent out and 2 months after the last panel sent out according to laboratory records; (b) pertained to an initial consult or follow-up appointment, excluding results-only and other communication; (c) patient surname was one of the 11 known Manitoba Hutterite surnames; and (d) contained the words “carrier” or “chip” or “panel”. Data extracted from reviewed letters included (a) the month/year of appointment; (b) clinic type; (c) reason for appointment; (d) whether CS panel was discussed; (e) whether CS panel was ordered; and (f) if it was ordered whether it was for preconception or diagnostic purposes.

2.3 Community engagement & recruitment

For several decades, researchers and clinicians in Winnipeg have worked with members of the Manitoba Hutterite community on various research initiatives related to genetics. Most recently, the development of the first Hutterite founder mutation-specific CS panel (2013-2014) was a joint effort between members of the Hutterite community in Southern Manitoba and clinicians/researchers at the University of Manitoba. For this study, several of the same Hutterite individuals who were involved in earlier initiatives were contacted to gauge interest and acceptability of the research plan. Over the period of December 2019 to March 2020, several meetings were organized to propose the study, introduce drafts of the survey and

interview guide, obtain feedback, and discuss approaches to recruitment and other logistical aspects of the study.

Specific colonies were selected to be contacted on a referral basis. Community members who were involved in the initial planning phases were asked to suggest colonies who might be interested in participating. Ministers and/or managers of these colonies were contacted by phone, the study was introduced, and permission to recruit at the colony was requested. Leadership was asked to refer the study team to other colonies that may be willing to participate in the study and other ministers and/or managers were similarly contacted by phone. Additional colonies were recruited by snowball sampling through this referral process and later, by random/convenience sampling by contacting other colony ministers outside of the referral network.

2.4 Survey

2.4.1 Participants & sampling

Sampling for the survey component of the study followed two different methods, as changes were required once the COVID-19 virus necessitated restrictions in conducting fieldwork. Initially, participants were invited to fill out a survey when the student researcher (CM) visited the colony during a mealtime when all adults on the colony were gathered. The goal of this approach was to obtain a random sample that was unbiased regarding attitudes or experience with CS, however it ultimately was a convenience sample since not all in attendance filled out a survey (Collins et al., 2007).

Shortly after recruitment began, COVID-19 restrictions on fieldwork were implemented, and the sampling method for the survey was adjusted. To adapt to the public health recommendations and preventative measures with respect to COVID-19, study materials were sent to the colony via email or mail depending on their stated preference. Materials provided included a poster introducing the study and inviting members to participate, a recorded video of the student researcher introducing the study, and copies of the survey and/or link to the

online survey hosted by REDCap. Colony leadership and/or members distributed the study materials to members of the colony and those who were interested could fill out a survey.

Colonies differed in the way that the study was introduced to community members. In some, the video introduction on a tablet was passed between households, whereas in others, the video introduction was shared on chat groups including WhatsApp. Some communities had a single individual that circulated the study poster and did not use the video. As a result, the majority of surveys were collected through a combination of convenience and snowball sampling (Collins et al., 2007), although an effort was made to encourage maximal variation by emphasizing the importance of hearing from people with varied opinions on the topic. Inclusion criteria for the survey were that participants were members of a Hutterite colony, could read and write in English, and were at least 16 years of age.

2.4.2 Instrumentation

Surveys collected demographic information including age range, gender, marital status, number of children, and intent to have children (or more children). Participants were asked if they had heard of CS prior to the study, and if so, from where. The survey also assessed prior experience with genetic conditions with one question that asked participants to indicate whether they had a family member, were themselves affected, or knew someone else with a genetic condition. All survey questions were analyzed using the QUAID tool (Graesser et al., 2000), which assesses wording, grade level, syntax, and semantics of survey questions and provides suggestions for improvement. Where it was necessary survey questions were simplified to reach a grade 5-6 level of complexity.

Overall attitudes toward CS were assessed using a composite score from six items on the survey. Each item was a 5-point Likert scale (good-bad, important-unimportant, reassuring-alarming, wise-unwise, desirable-undesirable, beneficial-harmful). For analysis, these items were recoded, with a score of 1 representing negative views (bad, unimportant, alarming, unwise, undesirable, harmful), 3 indicating neutral, and 5 indicating positive views (good,

important, reassuring, wise, desirable, beneficial). The scores for each item were aggregated into a composite score for attitude toward CS by taking the mean of the six items.

Parts of the survey were adapted from previously published theory-guided surveys administered to assess attitudes toward CS/testing in other populations (Lakeman et al., 2009; Mathijssen et al., 2018; Plantinga et al., 2016). Other Likert-style items on the survey assessed factors influencing attitudes toward CS and were guided by the Health Belief Model (HBM). The HBM is a theory in health psychology that assumes that predictors of an individual engaging in a health-related behaviour include perceived benefits, risks/barriers, susceptibility (to the potential outcome of not performing the behaviour), and severity (of that outcome) (Janz & Becker, 1984; Rosenstock, 1974). The factors of perceived benefits, risks, and susceptibility were each assessed with 3-item Likert scales by indicating how strongly they agree or disagree with statements (e.g. “I think there is a high chance I’m a carrier” for susceptibility) on a 5-point scale. A composite score from each 5-point scale was assigned to each factor.

Participants were asked to indicate if they would like to have the CS test done. If so, they were asked to indicate which health care providers they would like to access CS through (PCP or genetics specialists) as well as the preferred modality of appointment (in person or video conferencing). Additionally, participants were asked to indicate whether they would like to know their carrier status for all 32 conditions on the carrier screening panel, or whether they would prefer to choose a subset of conditions (those that benefit from early detection/treatment, severe untreatable childhood onset, treatable or untreatable adult onset).

The ways in which participants would consider using information from the CS panel was assessed using 6 Likert-style questions. Participants were asked to rate, using a 5-point scale (strongly agree to strongly disagree), how much they agree with statements that began with “I would consider using…” followed by different potential uses of CS. These included using the results from the panel in selecting a partner or for family planning purposes, or whether they would consider options like prenatal testing, termination of pregnancy, or assisted reproductive technologies.

2.4.3 Analysis

Statistical analysis was conducted using SPSS for Windows V27.0 (*IBM SPSS Statistics for Windows, Version 27.0.*, 2020). Survey items that were combined into a composite score (those corresponding to attitudes, perceived risks, perceived susceptibility) were tested for internal reliability using *omega,* which is recognized as a superior and less constrained measure for reliability of nominal scales than Cronbach's *alpha* (Gadermann et al., 2019; Hayes & Coutts, 2020). Split-half reliability was used for the 2-item scale for perceived benefits. Reliability scores of greater than 0.7 for each subscale were considered reliable. Comparisons between demographic characteristics, HBM factor scores, attitude toward CS, and reproductive intention were conducted. Kruskal-Wallis one-way ANOVA and Fisher-Freeman-Halton exact tests for comparisons between groups were performed appropriately with demographic and HBM factors as independent variables.

2.5 Interviews

2.5.1 Participants & sampling

Semi-structured telephone interviews ranging from 30 to 60 minutes were conducted with 13 participants. Participants were self-selected due to the nature of the recruitment process, as individuals who completed the survey volunteered for interviews by filling out their name on the survey or contacting the student researcher directly.

2.5.2 Instrumentation

The interview guide was developed to explore many of the same concepts as the survey but with more depth, richness, and context, so questions were open ended and prompts were used to encourage clarification, expansion, and explanation. The interview guide was reviewed by a member of the Hutterite community for feedback on clarity and language and modified appropriately. The interviewer (CM) practiced interviewing with a classmate and piloted the interview guide with a member of the Hutterite community to further assess for clarity and comprehension prior to data collection.

Interviews were all conducted, audio recorded, and manually transcribed by CM. Interviews began with an explanation of the purpose of the study and an overview of autosomal recessive inheritance and the CS panel. Informed consent using the approved consent form was obtained verbally and participants were asked if they consented to direct quotation. The interview guide was refined over the course of the study with some questions removed due to clarity issues and others added as common themes were identified from the data.

2.5.3 Qualitative analysis

Qualitative analysis was performed concurrently with data collection, with the student researcher making note of common patterns and perspectives brought up by participants and iteratively modifying the interview guide to explore these patterns in depth. Memos regarding initial interpretations, connections between aspects of the data, and potential themes were documented throughout the data collection and analysis process.

Analysis began with the student researcher becoming familiar with the data through transcribing, reading, and rereading the transcripts prior to coding. Coding of transcripts was conducted using Dedoose, a qualitative analysis software program (*Dedoose, Web Application for Managing, Analyzing, and Presenting Qualitative and Mixed Method Research Data.*, 2018). First cycle coding of the transcripts was conducted using a qualitative description framework. Qualitative description is a common framework for working with qualitative data and yields a descriptive summary of the data rather than being overly interpretive in nature (Neergaard et al., 2009). This framework was selected because results generated from qualitative description tend to stay close to the surface of the data, while attempting to capture all elements of the experience in language that remains true to the participants' points of view (Milne & Oberle, 2005). Qualitative description is also amenable to integration within a mixed methods study as it provides a straight-forward description of participant's views and experiences that can be complementary to quantitative data on the same phenomenon (Turale, 2020).

The first cycle of coding resulted in ~150 unique codes which were then categorized into a smaller number of categories based on the features of the codes (i.e. "concerned about gossip

about CS results" and "will this affect my relationship prospects" were collapsed into "concerns about stigma"). Fifteen categories were identified, after which thematic analysis was applied to identify overarching themes. After the themes were defined, a final cycle of coding was completed of all transcripts to ensure the final codes and themes were consistently applied and adequately captured the data.

2.5.4 Reflexivity & rigor

Qualitative research is an inherently subjective and contextual process which requires the researcher to maintain awareness of their positionality, biases, and influence on the data collection and analysis process (Dodgson, 2019), a concept known as reflexivity. Reflexivity was integrated in multiple ways throughout the qualitative data collection and analysis process. After each interview, the student researcher maintained a reflexivity journal to aid in reflection regarding how interviewer bias and influence over the research process may have impacted the direction of the interview or participant responses. The student researcher had regular discussions with members of the advisory committee about interview style and the role of the researcher within the qualitative data collection process.

Rigor in qualitative research methods is essential for producing trustworthy data and conclusions that reflect the views of participants and fully capture the contextual factors that influence those views (Maher et al., 2018; Milne & Oberle, 2005). Several methods of improving rigor were integrated throughout the design, data collection, and data analysis phases of the study. The research questions were clearly defined prior to design of the interview guide, and the guide was iteratively modified throughout the data collection period to ensure the data collected mapped on to the initial research questions. The coding process as well as the evolution from initial codes to themes was clearly described to provide an audit trail of decision making by the researcher during analysis.

Peer review was used throughout the analysis process due to the subjective nature of qualitative methods. Two transcripts were independently coded by another member of the research team (KR), and any discrepancies were resolved through discussion. A third member of

the research team (PF) reviewed and evaluated the codes assigned to each passage to ensure consistency in code application across all 13 transcripts.

2.6 Integration of qualitative and quantitative data

The qualitative and quantitative data obtained from each phase of this study were integrated after each was analyzed in isolation. The five themes that were identified from interview data were used as a framework for integration, whereby the survey results were systematically compared to the main interview findings. Similarities as well as discrepancies were highlighted between the two datasets, and where possible, qualitative results were used to contextualize patterns identified within the quantitative dataset.

CHAPTER 3. QUANTITATIVE RESULTS

3.1 Chart review results

Over the period of April 2015-March 2017, the Program of Genetics and Metabolism saw 163 unique individuals or families with Hutterite surnames, including both initial consultations and follow-up appointments. If there were multiple appointments with the same patient/family over the period (e.g. initial consultation and follow up appointment), the patient/family was only counted once toward analysis. Table 4 shows that there were 21 appointments in which the CS panel was discussed with the patient or family. Of these, 11 appointments took place in the Adult Genetics clinic, 7 took place in the Pediatric Genetics clinic, and 3 took place in the Prenatal Genetics clinic.

Table 4. Summary of appointments that included a discussion or offer of carrier screening

Clinic Type	Panel Offered (# of appointments)	Panel Ordered (# of appointments)	Panel Ordered (# of individuals)
Adult Genetics	11	9 (5 couples)	14
Pediatric Genetics	7	2 (2 couples)	4
Prenatal Genetics	3	0	0
Total	21	11	18

Of the 21 times the CS panel was brought up with the patient or family, there were 11 instances where the offer was accepted and the panel was ordered. Among the 11 appointments where the offer was accepted, 9 were in the Adult Genetics clinic and 2 were in the Pediatric Genetics clinic. Therefore, the offer was declined in 2/11 (18%) of adult appointments, 5/7 (71%) of pediatric appointments, and 3/3 (100%) of prenatal appointments. Most appointments where the offer was accepted were for couples (already parents or planning their family), however there were 4 individuals who accepted the offer for CS in the Adult Genetics clinic who did not attend with a partner. In total, the consultation letters reviewed account for 18 out of 25 of the total number of times the panel was ordered according to laboratory records. The other 7

orders not accounted for in the current dataset may reflect the CS panel being ordered by non-genetics providers outside of the reviewed database.

Other data extracted from the consultation letters that indicated the CS panel was discussed included the reasons for referral, which are shown in Table 5. The majority of appointments that included a discussion about the CS panel were scheduled because the individual or couple had a personal or family history of one or more of the conditions that would be included on the panel. Other than one patient seen in the Adult Genetics clinic who was being evaluated for a potential genetic condition, every couple and individual who requested CS had a known personal or family history of recessive conditions included on the panel. In other words, there were no individuals or couples who sought out CS in the absence of a known history of genetic conditions in their families (or themselves).

The chart review also included assessment of the purpose of CS in the instances when it was requested. Among the instances where the discussion led to the individual or couple requesting CS, the majority requested it for the purpose of preconception screening – to learn about their own reproductive risks, whether or not they already had children. There was one instance within the consultation letters reviewed where the CS panel was used as an indirect way to diagnose a child.

In summary, out of the 163 possible appointments where the CS panel could have been discussed with Hutterite patients, it was discussed as an option in 21 appointments (13%). It is likely that many of these appointments were with patients who were older and beyond their reproductive years, so discussion of CS for reproductive purposes may not have been of relevance. It is also likely that a proportion of appointments would have been with families undergoing stressful events, such as illness in themselves or a child, so discussion of future reproductive planning may have been inappropriate. Unfortunately, the chart review was not able to discern whether the discussion of the CS panel was initiated by the patient, or the provider, so it is unclear whether any individuals or couples requested an appointment specifically because of the availability of the CS panel.

Table 5. Characteristics of appointments where the Hutterite carrier screening panel was discussed. Superscript 'a' specifies a condition that would not be tested for using the panel, superscript 'b' specifies a condition that would be included on the panel

Clinic Type	Reason for Referral	Panel Ordered	Individual/Couple	Reason
Adult	Family history of genetic condition[b]	Yes	Couple	Preconception
	Personal history of genetic condition[b]	Yes	Couple	Preconception
	Family history of genetic condition[b]	Yes	Individual	Preconception
	Family history of genetic condition[b]	Yes	Individual	Preconception
	Patient evaluated for genetic condition	Yes	Couple	Preconception
	Family history of genetic condition[b]	Yes	Couple	Preconception
	Family history of genetic condition[b]	Yes	Couple	Preconception
	Family history of genetic condition[b]	Yes	Individual	Preconception
	Personal history of genetic condition[b]	Yes	Individual	Preconception
	Family history of genetic condition[a]	-	-	-
	Previous child with genetic condition[a]	-	-	-
Pediatric	Previous child with genetic condition[b]	Yes	Couple	Preconception
	Child evaluated for genetic condition	Yes	Couple	Diagnostic
	Previous child with genetic condition[b]	-	-	-
	Previous child with genetic condition[b]	-	-	-
	Previous child with genetic condition[b]	-	-	-
	Previous child with genetic condition[b]	-	-	-
	Previous child with genetic condition[b]	-	-	-
Prenatal	Family history of genetic condition[b]	-	-	-
	Ultrasound abnormalities	-	-	-
	Ultrasound abnormalities	-	-	-

3.2 Survey results

3.2.1 Participants

A total of 95 Hutterite participants from 12 colonies in Manitoba filled out at least 80% of the survey items and were included in the following analyses. Of the total, 22 surveys were completed on the web-based survey platform REDCap and 73 were completed on paper. A copy of the survey instrument can be found in Appendix B. Participant demographics including sex, age range, and marital status are shown in Table 6. Of the 95 survey respondents, 71 were female and 24 were male (74% and 26% respectively). Most respondents were in the 18-25 and 26-35 age categories (28% and 33%, respectively), 16% of respondents were in each of the 36-45 and >45 age categories, and 6% were younger than 18 years old. Most respondents were either single (32%) or married (54%), 2% reported that they were dating someone, and 12% indicated they were in a long-term relationship or engaged.

Table 6. Survey participant demographics

		Male		Female		Total
		n	%	n	%	n
Total Participants		24	*26*	71	*76*	95
Age Range	<18	2	*2*	5	*5*	7
	18-25	3	*3*	24	*25*	27
	26-35	10	*11*	21	*22*	31
	36-45	5	*5*	10	*11*	15
	>45	4	*4*	11	*12*	15
Marital Status	Single	3	*3*	27	*28*	30
	Dating	1	*1*	1	*1*	2
	Long-term relationship/engaged	4	*4*	7	*7*	11
	Married	16	*17*	35	*37*	51
Have you heard of carrier screening before, if so, where did you first hear of it?	Yes: primary care provider	5	*5*	12	*13*	17
	Yes: town hall meeting	2	*2*	6	*6*	8
	Yes: school	3	*3*	12	*13*	15
	Yes: from someone else	7	*7*	17	*18*	24
	No	7	*7*	24	*25*	31
Do you know someone with a genetic condition, if so, who?	Yes: myself	0	*0*	2	*2*	2
	Yes: my child/sibling/parent	5	*5*	10	*11*	15
	Yes: another family member	12	*13*	26	*27*	38
	Yes: someone not in my family	6	*6*	25	*26*	31
	No	1	*1*	6	*6*	7

Participants were asked whether they had heard of CS prior to participating in the study, and if so, where they had first heard of it. Most participants indicated that they had heard of CS prior to the study (n=64, 71%) and the remaining 31 participants (33%) indicated they had never heard of it prior to the study. Of those who were familiar with it, 17 learned about it through their PCP (27%), 8 learned about it at a town hall meeting (13%), 15 learned about it in school (23%), and 24 indicated they heard about it through someone else (38%).

Participants were also asked to indicate whether they knew anyone with a genetic condition or were themselves affected with one. Responses were categorized by the degree of relationship to the person affected (myself, first-degree relative, other family member, unrelated individual). Most participants responded that they knew someone with a genetic condition (n=86, 92%). Of these, 2 participants reported they had a genetic condition (2%), 15 had a first degree relative who was affected (17%), 38 had another relative (44%), and 31 knew someone who was unrelated to them (36%) who was affected.

3.2.2 Attitudes toward carrier screening

Overall attitudes toward CS were evaluated using 6 items on the survey (questions 7a-7f) in which participants could indicate their attitudes on a 5-point Likert scale. Results from all participants are shown in Figure 4. Most participants had positive attitudes toward CS, as shown by the majority selecting the extreme or moderate positive value on all six 5-point scales (e.g. good and somewhat good).

While most participants indicated positive attitudes toward CS, there were a subset of participants who had neutral or negative attitudes. To further characterize attitudes toward CS among the different demographic groups as well as among individuals with prior knowledge/experience of genetic conditions and CS, each participant was given a composite score derived from the 6 items from question 7.

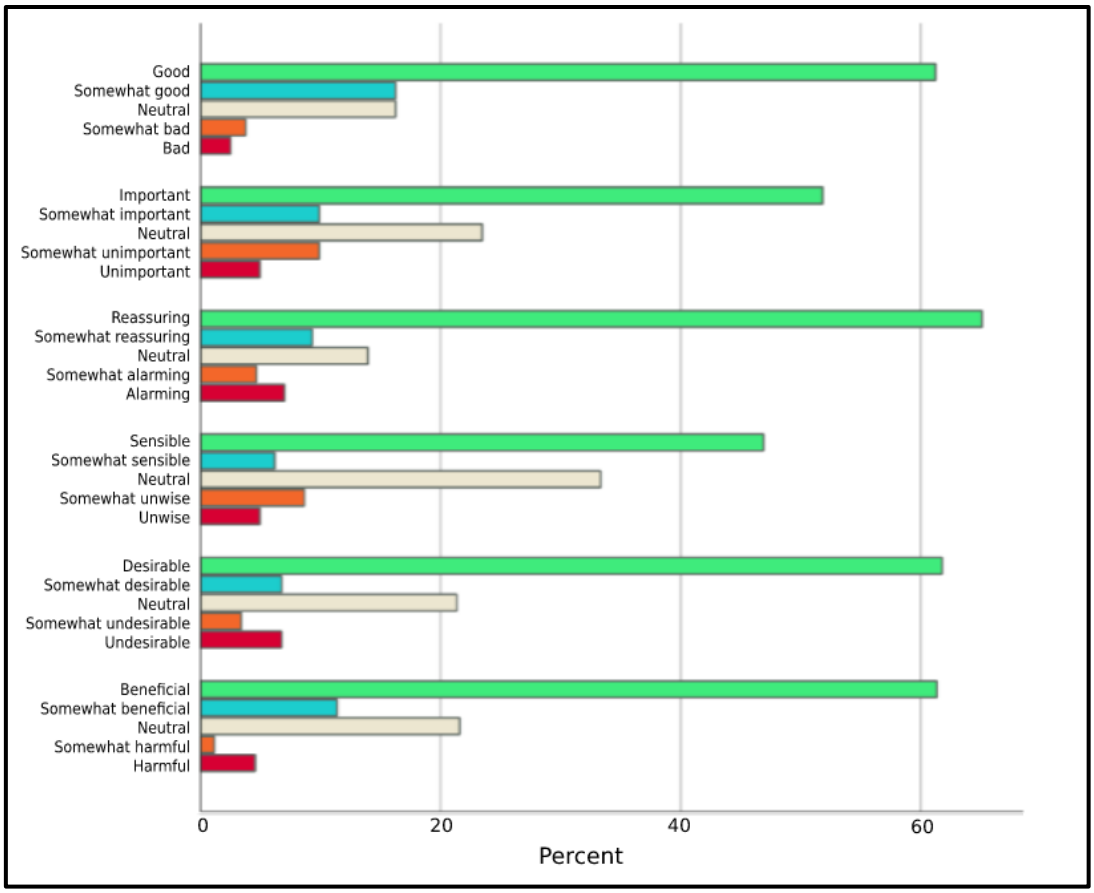

Figure 4. Results from 6-item Likert scale assessing participant attitudes toward carrier screening (derived from Lakeman et al 2009)

To ensure the 6 items were consistent in measuring the same construct (i.e. attitudes toward CS), reliability analysis was conducted using McDonald's *omega*. Results indicated that *omega* for the total scale was 0.932 (SE=0.017, 95% CI=0.893-0.957) indicating a high degree of internal consistency among the items (ω>0.7 is generally accepted as sufficiently consistent). Each of the 6 items was assigned an integer from 1 (extreme negative value) to 5 (extreme positive value), with 3 assigned for neutral responses. Each participant's composite score for attitudes toward CS was calculated by taking the mean of the 6 items with a range of 1 (negative attitude) to 5 (positive attitude). The median score for attitude toward CS among all 95 participants was 4.67 (IQR=4.33-5.00) indicating generally positive attitudes. A substantial proportion of participants (n=41, 43%) selected the extreme positive values for all 6 items and had a composite score of 5 as shown in Figure 5. Overall, 70 participants had attitude scores

greater than 3 (74%, positive attitudes) and 13 participants had scores less than 3 (14%, negative attitudes).

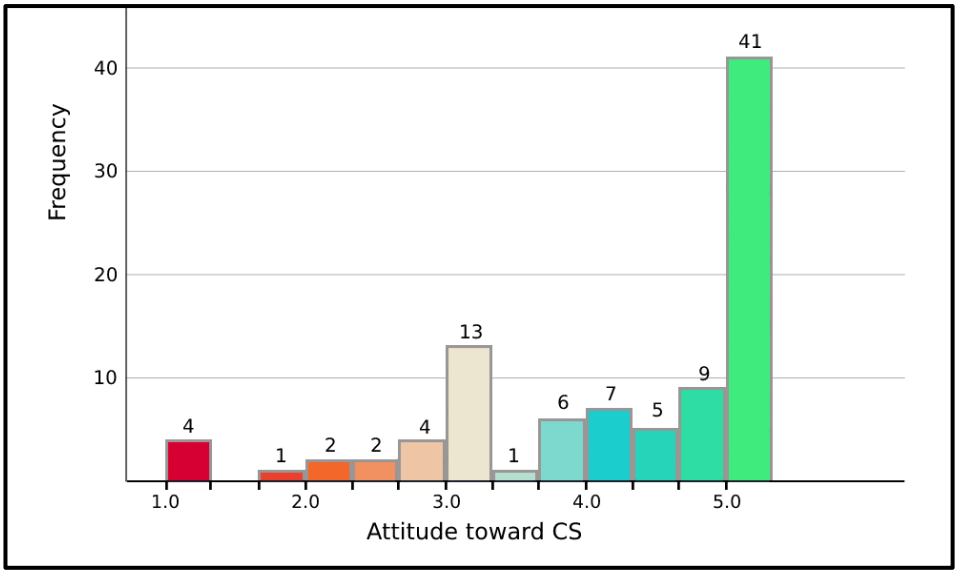

Figure 5. Histogram showing frequencies of composite attitude scores among participants. X-axis intervals are 0.33

Attitude scores were then compared across demographic groups including participant age, sex, childbearing status, and marital status (Figure 6a-d). The two smaller age categories (<18 years and 18-25 years) were collapsed due to a small sample size in the <18 group. No significant differences were detected between participants of different age groups (Figure 6a), sex (Figure 6b) or groups based on childbearing status (Figure 6c). There was a significant difference in attitude scores among marital status categories (Figure 6d, $H(3)=9.05$, $P=0.029$). Post-hoc Dunn pairwise comparison with Bonferroni correction indicated that participants who were single reported more positive attitudes toward CS (Mdn=5.00, IQR=4.67-5.00) than those who were married (Mdn=4.00, IQR=3.00-5.00), and this difference was statistically significant (P=0.022).

As was shown in Table 6 (p. 48), most participants knew someone with a genetic condition, and most were familiar with CS prior to the study. Attitude scores were compared between groups based on how closely related they were to the person with the genetic condition (Figure 7a) as well as where they had learned about CS (Figure 7b). Due to a small sample size in the group of

participants who were affected with a condition, this group was collapsed with participants who had an affected first-degree relative.

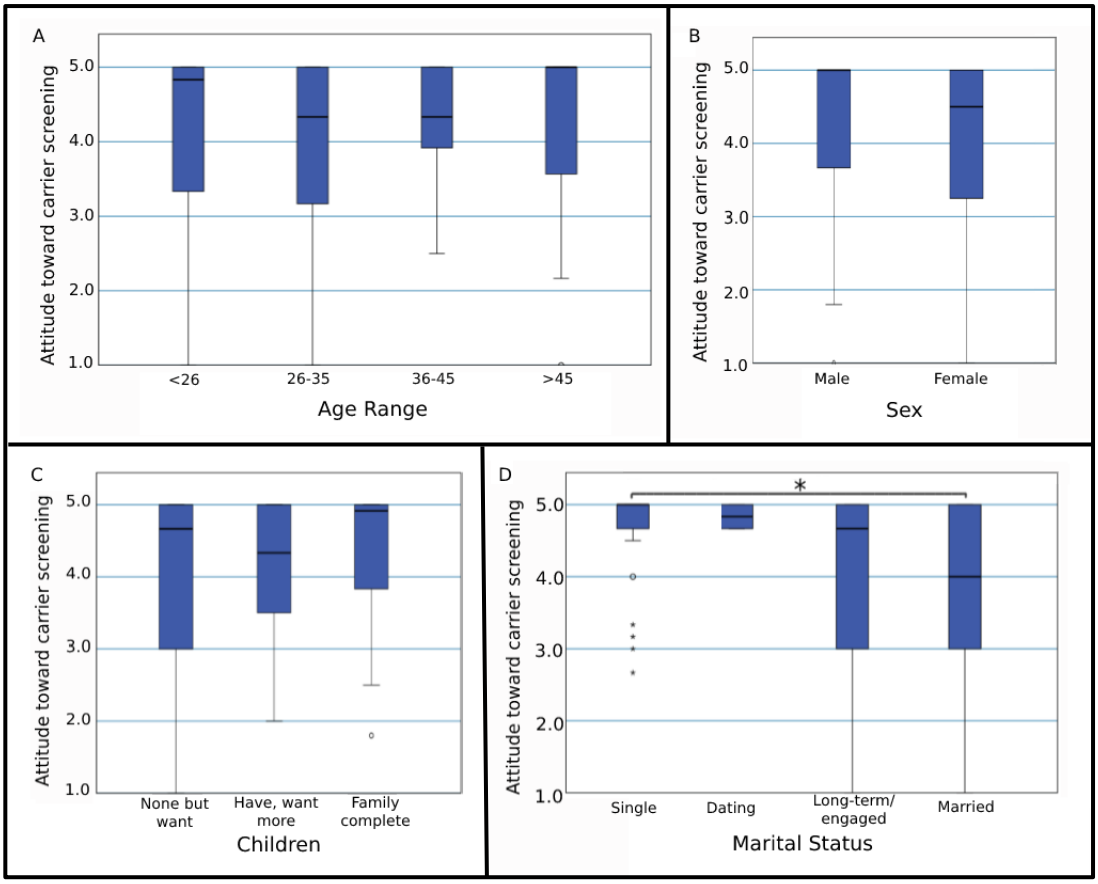

Figure 6. Comparison of participant attitudes toward carrier screening among demographic groups. Black line indicates median, box indicates interquartile range, whiskers indicate range, asterisk indicates significant differences between groups

Participants who reported that they did not know anyone with a genetic condition showed a trend toward more negative attitudes about CS compared with those who knew someone, but the difference was not significant (Figure 7a, H(3)=3.82, P=0.281). Additionally, there were significant differences between groups based on where they had learned about CS (Figure 7b, U(4)=17.07, P=0.002). Post-hoc Dunn pairwise comparison with Bonferroni correction was applied and showed that participants who had not heard of CS prior to the study had more negative attitudes (Mdn=3.80, IQR=2.83-4.67) than those who had learned about it either at school (Mdn=5.00, IQR=4.67-5.00, P=0.039) or at a town hall meeting (Mdn=5.00, IQR=4.92=5.00, P=0.01).

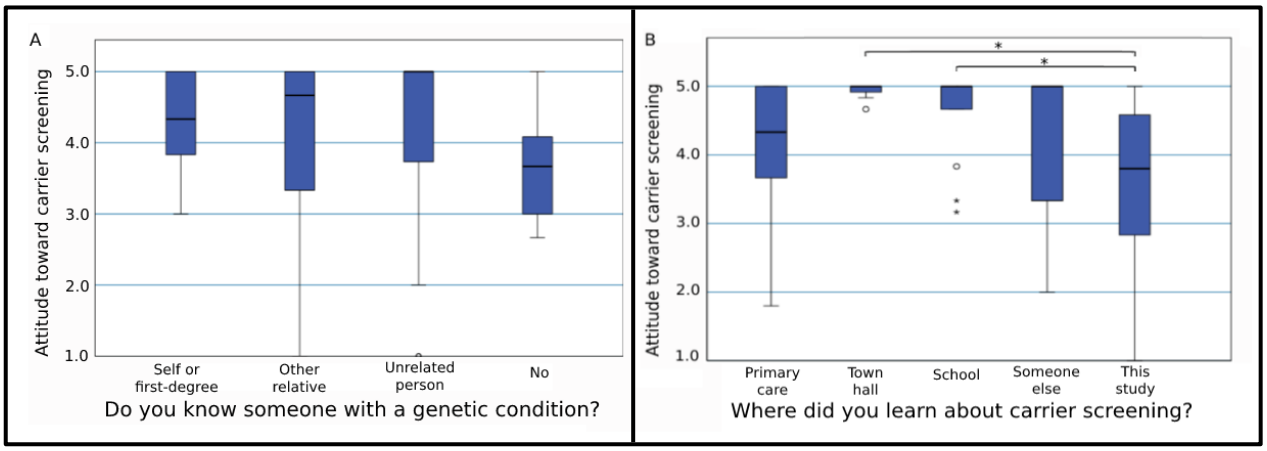

Figure 7. Participant attitudes toward carrier screening among varying levels of familiarity with genetic conditions and carrier screening. Black line=median, box=IQR, whiskers=range, asterisk=p<0.05

Participants could indicate their interest in accessing CS by selecting "interested" in any of the options presented in survey questions Q22-Q23. If participants indicated interest in any of the options (which specifically pertained to interest in the full CS panel versus specific categories of conditions, as well as interest in accessing the test from different providers), their response was coded as "interested in CS. Overall, 76 participants (80%) selected at least one option, indicating they were interested in CS, and 19 (20%) indicated they were not interested in CS (Figure 8).

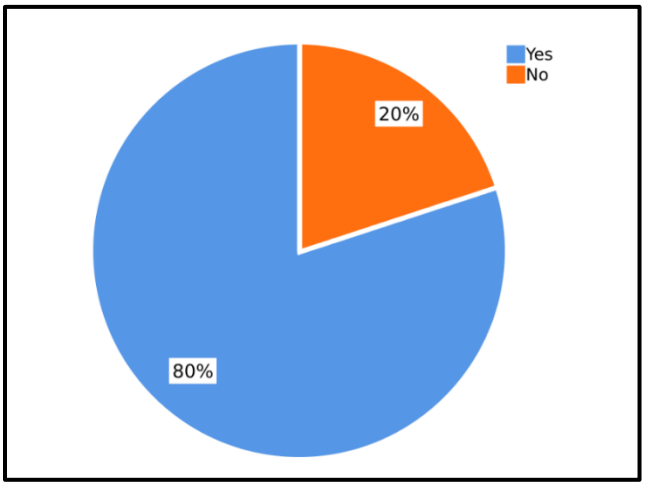

Figure 8. Percent of participants who indicated they were interested in accessing carrier screening

3.2.3 Risks and benefits of carrier screening

Survey questions 8-16 assessed specific benefits, risks, and psychological implications associated with CS (Figure 9), and participants could select their response on a 5-point Likert scale (strongly disagree: SD, disagree: D, neutral, agree: A, strongly agree: SA). Participant perceptions of the benefits of CS were evaluated with two questions which pertained to benefits to individuals (risk information providing reassurance, Q8) as well as to the community (Q9). Results indicated that most participants perceived benefits associated with CS; the majority felt that they would want to be reassured about whether they were at risk of having a child with a genetic condition (65.6% A/SA), and most felt that CS could help the community (70.2% A/SA).

Three questions on the survey evaluated how susceptible participants felt to being a carrier or having a child with a genetic condition (Q10-Q13). Results showed that only a minority of participants were concerned. Most participants did not feel particularly worried about being a carrier with an equal proportion either disagreeing (37.2% D/SD) with the statement or indicating neutral feelings (39.2%). When asked whether they were worried about having a child with a genetic condition, an approximately equal proportion of participants agreed (30.9% A/SA), disagreed (38.3% D/SD), and indicated neutrality (30.9%) with the statement. Interestingly, only 16.1% of participants indicated (A/SA) that they felt there was a high chance they were carriers, despite 58% having a family history of genetic conditions (Table 6).

Taken together, these results show that most participants did not feel a significant amount of susceptibility to being a carrier. Participant views about the psychological risks associated with CS were evaluated with three survey questions (Q14-Q16). Results showed that while most participants were not overly concerned about the risks presented in the survey questions, there was a substantial proportion who indicated they agreed there were risks. A larger proportion of participants disagreed (43.2% D/SD) than agreed (34.7% A/SA) with the statement that CS would cause anxiety. Similarly, about half of participants did not feel that CS would burden individuals with unwanted information (46.3% D/SD), compared with 33.7% who agreed (A/SA). In contrast, only 14.7% of participants agreed (A/SA) that they would feel unhealthy if they

were a carrier, and most disagreed with the statement (61.1% D/SD), possibly indicating a general understanding of what it means to be a carrier (since carriers are generally expected to be healthy).

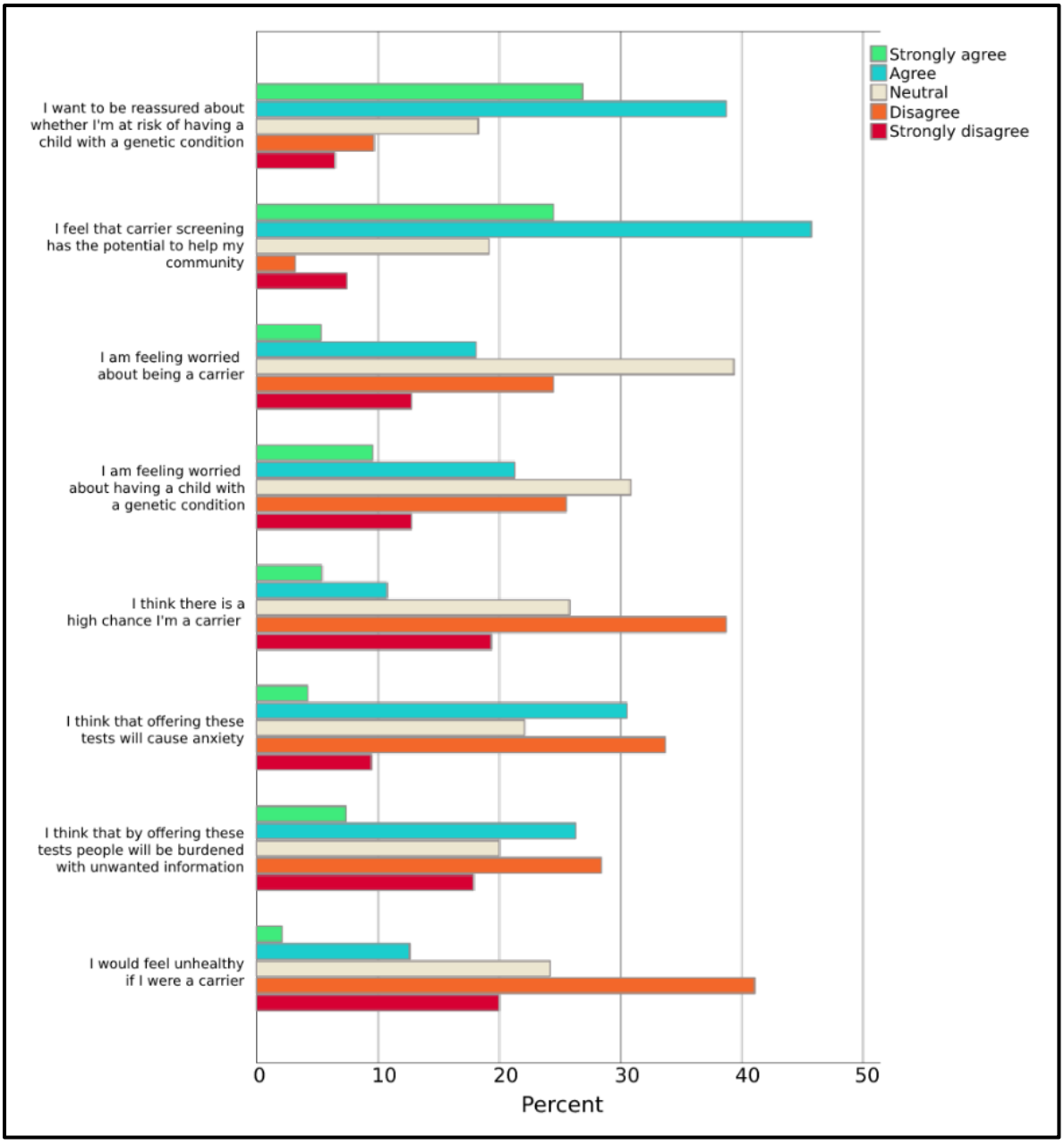

Figure 9. Participant responses regarding perceived benefits and risks associated with carrier screening as well as perceived susceptibility to being a carrier (survey questions 8-16, derived from Lakeman et al 2009)

Overall, these results showed that survey participants felt that CS was associated with more benefits than risks. Additionally, most participants indicated that they were not particularly worried about being a carrier or having a child with a genetic condition. To further evaluate differences in participant perceptions of the benefits and risks of CS, as well as perceived individual susceptibility to being a carrier, composite scores for these 3 categories were generated for each participant.

First, internal consistency of the items within each subscale (benefits, risks, susceptibility) was assessed to ensure reliability of each measure. The two questions (Q8-Q9) pertaining to perceived benefits of CS were tested for reliability using split-half reliability (valid for 2-item measures). Results indicated that the two items were consistent in measuring the same construct with a Spearman-Brown coefficient of 0.877 (greater than 0.7 is generally accepted as reliable). The three questions pertaining to perceived risks of CS were evaluated for reliability using McDonald's *omega*. Results showed that the three items were only moderately consistent with each other as *omega* for the scale was 0.672 (SE=0.087, 95% CI=0.539-0.906). To determine whether a single item was discordant with the other two, follow-up split-half reliability testing for 2 of 3 items with sequential exclusion of each of the three items was completed. As this did not improve the reliability of the scale, the decision was made to continue analysis with all 3 items to form a composite score. Therefore, results pertaining to composite "perceived risks" scores should be interpreted with caution. The three survey items pertaining to perceived susceptibility were evaluated for reliability using McDonald's omega. Results showed that the three questions consistently measured the same construct with omega equal to 0.827 (SE=0.036, 95% CI=0.753-0.893).

Composite scores for perceived benefits, perceived risks, and perceived susceptibility were compared between demographic groups including sex, age range, marital status, and childbearing status (Table 7). Results from these comparisons showed few differences in scores among groups. Specifically, no significant differences in score distribution were identified among any demographic groups for perceived risks or perceived susceptibility. Comparison of scores for perceived benefits across age groups, sex, and childbearing status also failed to

identify any differences. However, there was a significant difference in perceived benefit scores among participants of differing marital status (H(3)=9.623, P=0.022). Post-hoc Dunn pairwise comparison indicated that participants who were single perceived more benefits associated with CS (Mdn=4.00, IQR=4.00-5.00) than participants who were married (Mdn=3.5, IQR=3.00-4.00).

Table 7. Median scores for perceived benefits, perceived risks, and perceived susceptibility among demographic groups. 'a' indicates a significant difference between groups

		Perceived benefits			Perceived risks			Perceived susceptibility		
		Median	Q1	Q2	Median	Q1	Q2	Median	Q1	Q2
Sex	Male	**4.00**	*3.50*	*4.50*	**2.67**	*2.17*	*3.50*	**2.83**	*2.00*	*3.67*
	Female	**4.00**	*3.00*	*4.50*	**2.67**	*2.00*	*3.33*	**2.67**	*2.00*	*3.67*
Age Range	Under 25	**4.00**	*3.50*	*4.50*	**2.33**	*2.00*	*3.00*	**2.67**	*2.00*	*3.33*
	26-35	**3.50**	*3.00*	*4.00*	**2.67**	*2.00*	*3.67*	**2.67**	*2.00*	*3.33*
	36-45	**4.00**	*3.50*	*4.00*	**2.67**	*2.00*	*3.00*	**3.00**	*1.67*	*3.67*
	Over 45	**4.00**	*3.00*	*5.00*	**2.67**	*1.67*	*3.33*	**2.33**	*2.00*	*3.67*
Marital status	Single	**4.00**[a]	*4.00*	*5.00*	**2.33**	*2.00*	*2.67*	**3.00**	*2.67*	*3.67*
	Dating	**4.00**	*4.00*	*4.00*	**3.00**	*2.00*	*4.00*	**3.17**	*3.00*	*3.33*
	Long term/engaged	**4.00**	*3.00*	*5.00*	**2.33**	*2.00*	*3.00*	**2.00**	*2.00*	*2.67*
	Married	**3.50**[a]	*3.00*	*4.00*	**2.67**	*2.33*	*3.33*	**2.67**	*1.67*	*3.67*
Children	None, but want	**4.00**	*2.00*	*5.00*	**2.33**	*2.00*	*3.67*	**2.00**	*1.00*	*2.67*
	Have, want more	**4.00**	*3.00*	*4.00*	**2.67**	*2.33*	*3.33*	**2.67**	*2.00*	*3.67*
	Family complete	**4.00**	*3.50*	*4.25*	**2.67**	*1.50*	*3.17*	**2.83**	*2.00*	*3.67*

Perceptions of risks, benefits, and susceptibility were also compared between individuals who had a known family history of genetic conditions and those who did not (Figure 10). There was a small but highly significant difference between these groups with respect to their perceptions of how susceptible they are to being a carrier or having a child with a genetic condition. Individuals who had a family history of genetic conditions indicated that they felt more susceptible (Mdn=3.00, IQR= 2.33-3.67) than those who did not have any known genetic conditions in their family (Mdn=2.33, IQR=1.67-3.00, H(1)=12.130, P=4.96×10^{-4}). There were no differences between these groups with respect to their scores for the perceived risks or perceived benefits scales.

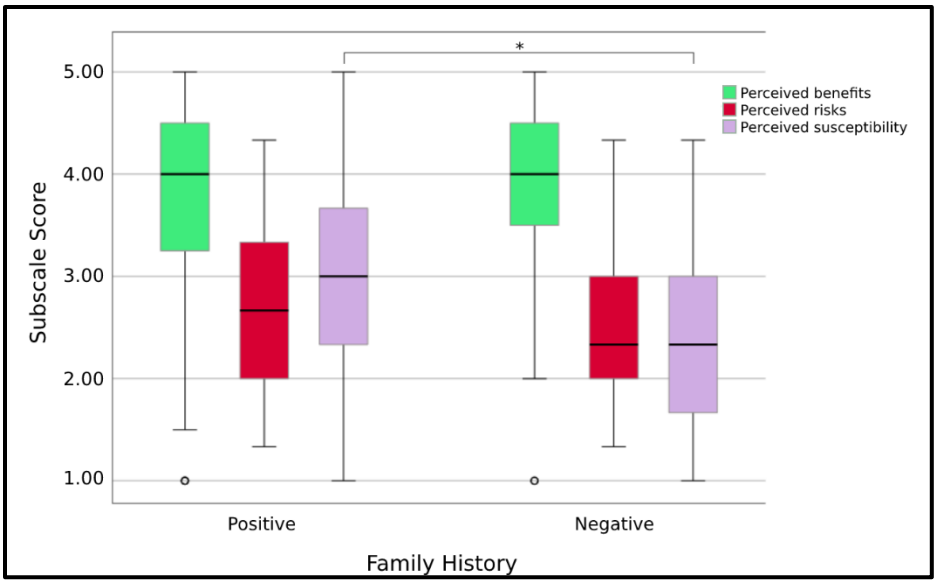

Figure 10. Comparison of composite scores for perceived benefits, perceived risks, and perceived susceptibility between individuals who have a family history of genetic conditions and those who do not. Asterisk indicates a significant difference between groups

Composite scores for perceived benefits, risks, and susceptibility were also compared between individuals who indicated they were interested in CS and those who were not (Figure 11). Results showed that participants who stated they were interested in having the test done had significantly higher scores for perceived benefits than those who were not interested (Mdn(interested)=4.00, Mdn(not interested)=3.00, H(1)=11.511, P=6.92×10^{-4}). Additionally, participants who were interested in CS perceived lower risks associated with it (Mdn(interested)=2.33, Mdn(not interested)=3.33, H(1)=14.390, P=1.49×10^{-4}) than those who were not interested. Lastly, participants who indicated their interest in CS perceived themselves to be more susceptible to being a carrier, or having an affected child, than those who indicated they were not interested (Mdn(interested)=3.00, Mdn(not interested)=2.00, H(1)=13.378, P=2.55×10^{-4}).

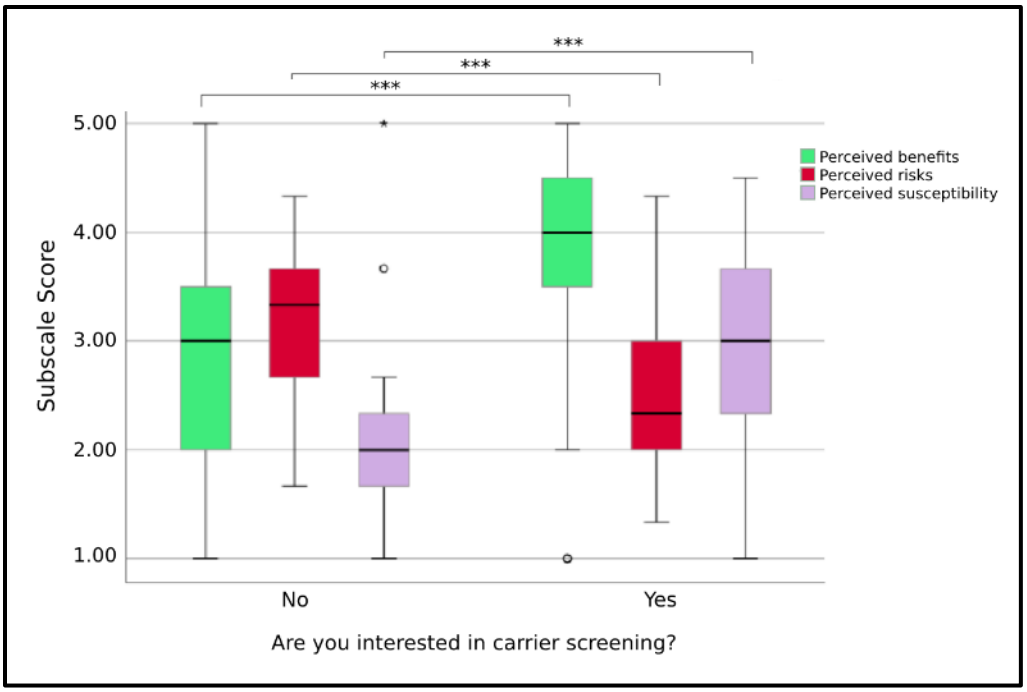

Figure 11. Comparison of composite scores for perceived benefits, perceived risks, and perceived susceptibility between individuals who indicated they were interested in accessing carrier screening and those who were not. Asterisk indicates a significant difference between groups

Taken together, these results demonstrate that demographic characteristics of participants in this study did not significantly influence their perceptions of the benefits or risks of CS, nor how susceptible they feel toward being a carrier or having an affected child. It is possible that the differences in perceived benefits among single and married individuals reflect differences in the personal relevance of receiving risk information, given that individuals not yet partnered may feel that they have an increased number of possible ways carrier information could be used, which is discussed in the following section. The difference in perceived susceptibility toward being a carrier between participants with and without a family history is possibly reflective of their awareness that they are at increased risk due to their family history.

Finally, although few significant differences were identified regarding participant perceptions of benefits, risks, and susceptibility among the demographic/experiential groups compared above, these factors were strong predictors of whether participants would consider accessing CS for themselves. Specifically, Hutterites who were interested in CS perceived significantly higher

benefits and lower risks associated with CS, as well as a stronger perception of individual susceptibility to being a carrier.

3.2.4 Intentions of how carrier information would be used

Participants were asked how they would consider using the results from CS in their reproductive decision making (Q16-Q21). Responses from individuals who indicated they were personally interested in CS are included in the following analyses, excluding those who indicated they were not interested. Among these individuals, there was considerable variability in responses to most of the options presented in the survey (Figure 12). Many participants felt that they would consider using the results of CS in decision making regarding partner selection (42.7% A/SA), and an even greater proportion felt that learning they were a carrier would influence their decisions about having children (55.3% A/SA). A similar majority of participants felt that if they and their partners were both carriers for the same condition, they would choose to not have children (or more children, if they already had them).

Most participants felt that they would want to undergo prenatal testing if they were aware that they and their partner were both carriers for the same condition (46.7% A/SA). However, the survey did not provide information about the risks of invasive prenatal diagnostic procedures (e.g. 1/200 risk of pregnancy loss with amniocentesis), so it is unclear whether participants would have answered this question differently if they were faced with the decision and learned about the potential risks. When asked whether they would consider termination of pregnancy if a fetus were affected with one of the genetic conditions, almost all participants indicated that they would not consider it (92% D/SD). Most participants also indicated that they would not consider assisted reproductive technologies if they and their partner were both carriers of the same condition (44% D/SD versus 22.7% A/SA).

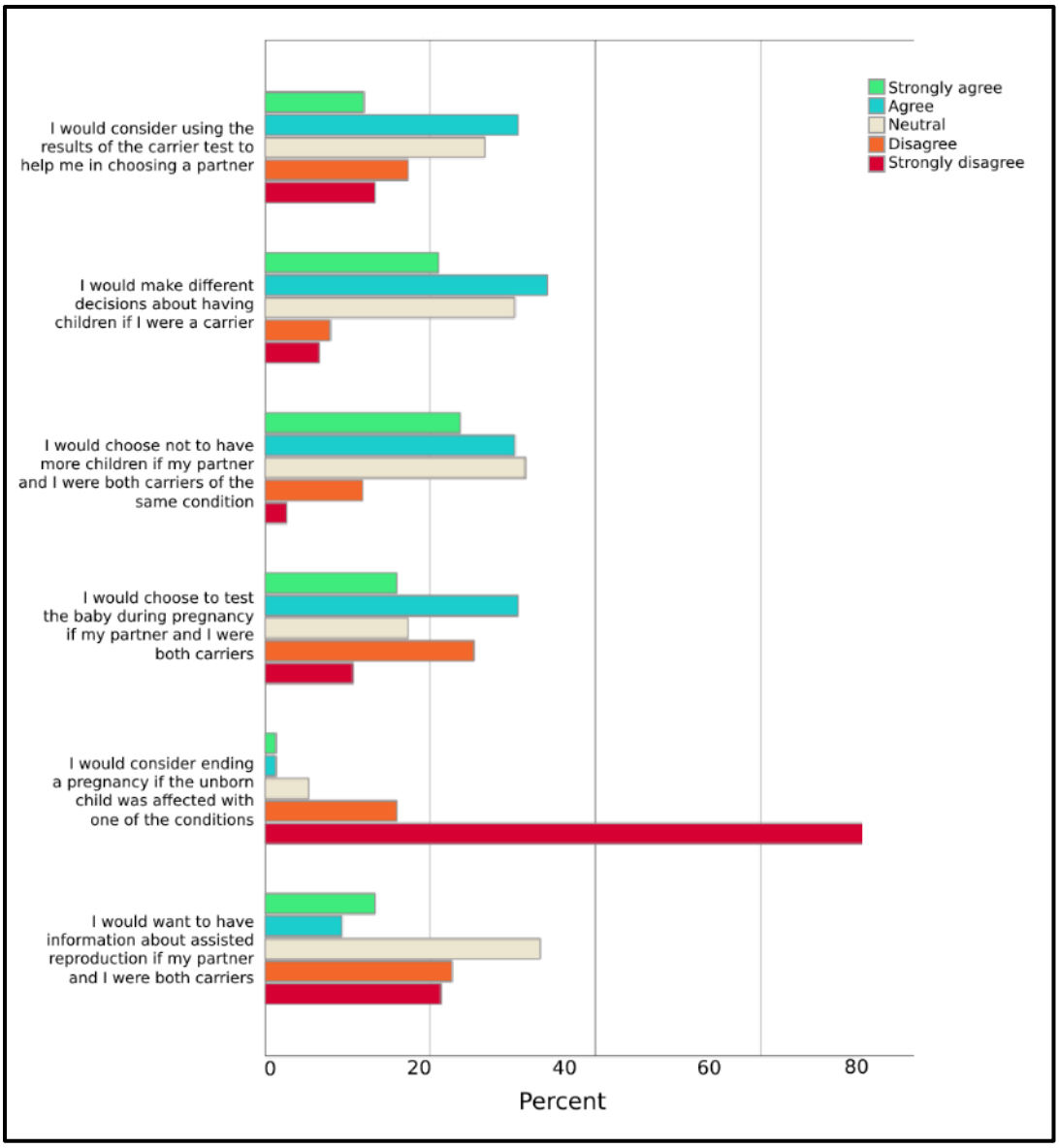

Figure 12. Participant responses regarding how they would use carrier status information in reproductive decision making. Participants who indicated they were not interested in carrier screening are excluded

Overall, these results demonstrate that many participants in this study who indicated they were interested in accessing CS feel that they would use information about their carrier status in family planning, and to a lesser extent, in selecting a partner. Interestingly, there was also a substantial proportion who indicated they were interested in CS but would not base any reproductive decisions on the information. This suggests that these participants may want to know the information just to be aware of the risk. To explore this distinction further, the group

who indicated interest in CS was divided into two based on whether they selected agree or strongly agree to any of the reproductive options presented in Q16-Q21 (displayed in Figure 12). Participants who did not agree with any of the statements but who were still interested in CS were considered to be interested in CS “just for information”, while participants who agreed with at least one statement were put in the category “CS would change decisions”.

Participant demographic and experiential factors were compared among those who were not interested in CS, those who wanted CS just for information, and those who would use carrier information in their decision making (Figure 13a-d). Among the study population on average, 20% indicated they were not interested in CS, 16% indicated they were wanted CS just for information, and 64% indicated they would make different decisions based on their CS results (Figure 13a). Observed frequencies of cases in each category were compared among participants of different age groups (Figure 13b), marital status (Figure 13c), and degree of relationship to someone affected with a genetic condition (Figure 13d).

Results showed that participants who were less than 25 years of age were significantly less likely than expected to state they were not interested in CS (13.1%), and significantly more likely (78.8%) to want to use screening to inform their reproductive decisions (Figure b, P=0.023, Fisher exact test). Similarly, participants who were single showed the same pattern (Figure 13c), with 90% indicating that they would use CS information in decision making and only 5.3% indicating they were not interested in CS (P=0.001, Fisher exact test). In contrast, participants who were married were more likely to state they were not interested in CS (33.3%) and less likely to want to base any decisions on carrier information (49.0%, P=0.001, Fisher exact test).

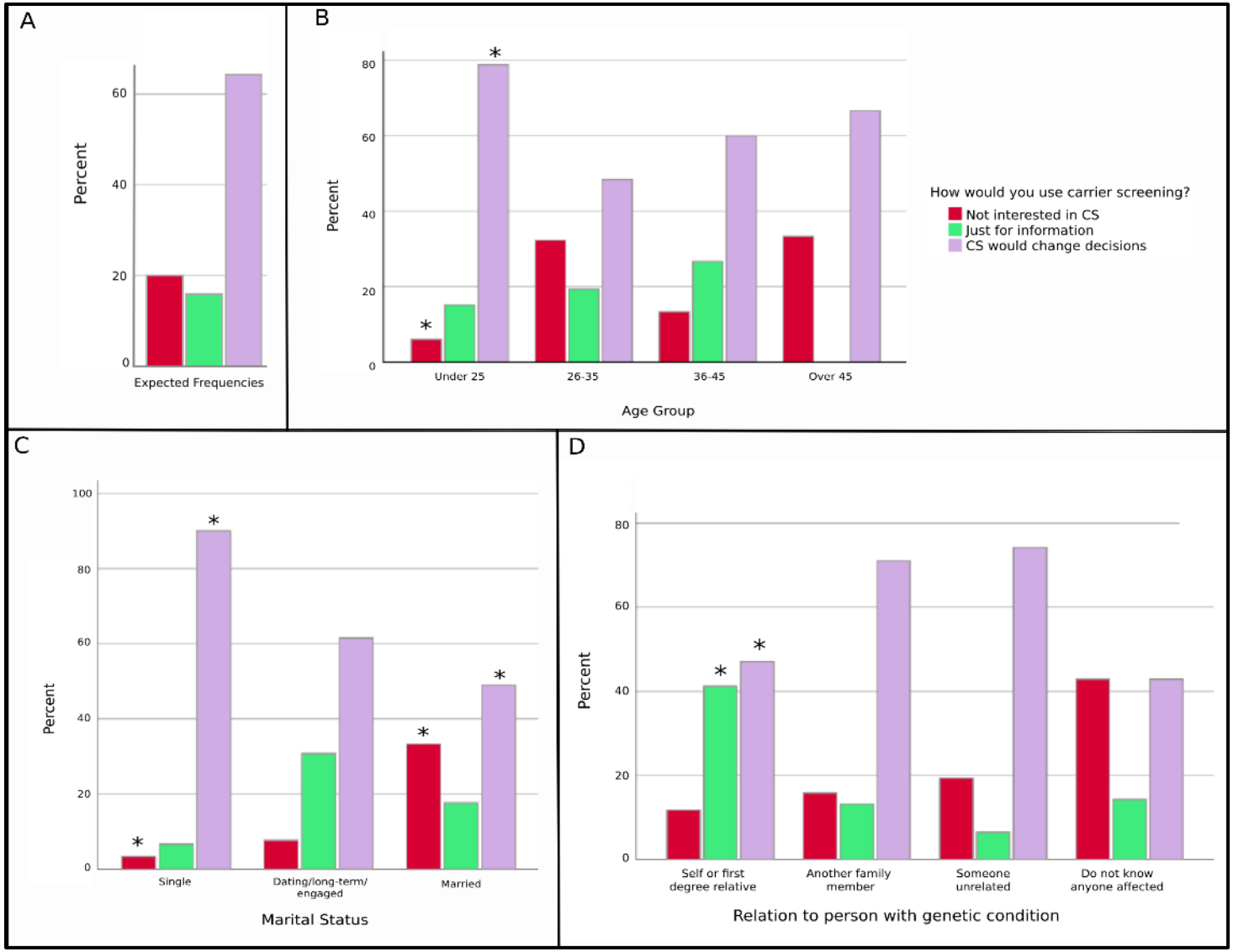

Figure 13. Participant interest and intention of how carrier information would be used. A: expected frequencies based on total study population. B: comparison between age groups, C: comparison of marital status groups, D: comparison of groups based on experience with genetic conditions. Asterisk indicates observed frequencies significantly different than expected frequencies

Additionally, participants' family history of genetic conditions influenced how they would use CS. If a participant stated that they had a first degree relative with a genetic condition, they were significantly more likely to want CS just for the information (41.2%), and less likely to want to base any decisions off of that information (47.1%, P=0.05, Fisher exact test). There was also a trend towards participants who did not know anyone affected with a genetic condition being more likely to state a lack of interest in CS, although this difference was not significant.

Taken together, these results show that age and marital status influence interest in CS, as well as whether individuals would use this information in their reproductive decision making. Participants who were younger and single were more likely to want to use carrier information in decision making. Participant experience with genetic conditions also impacted how CS would be used. More specifically, those with an affected close family member were more likely to be interested in CS just for the information, rather than wanting to make any decisions based on the information.

3.2.5 Preferences regarding providers of carrier screening and panel design

Survey participants were asked to indicate which provider(s) and/or appointment modality they would prefer to access CS through, by selecting one or more of primary care provider (PCP), geneticist/genetic counsellor in person, or geneticist/genetic counsellor via telehealth. As participants could submit multiple responses for this survey item, the total responses were summed and presented as proportions of the total number of selections among participants (Figure 14). Overall, a greater proportion of participants were interested in accessing CS through their PCP (44% of responses).

An open text field where participants could provide a reason for their selection was available on the paper version of the survey but not the online version hosted by REDCap. Thematic analysis on the open text responses revealed that the most common reasons stated for preferring to access CS through the PCP were "more accessible", "trust", and "knows me".

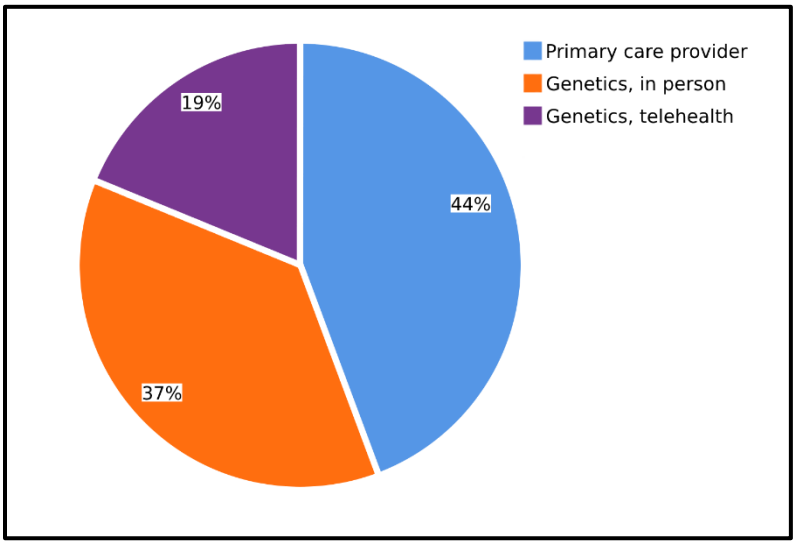

Figure 14. Participant preferences regarding which provider they would be interested in accessing carrier screening through

A slightly lower proportion of participants indicated that they would like to access CS through an in-person genetics consultation (37%), and a minority of participants indicated that they would be interested in accessing CS through a telehealth-based genetics consultation (19%). Thematic analysis of the open text fields indicated that the most stated reason for preferring a genetics consultation was because they wanted to speak with an expert about the CS test. Many participants wrote that they would prefer an in-person visit over telehealth, because they felt appointments through videoconferencing were too impersonal.

Participants were also asked to indicate whether they would like to know their carrier status for all 32 conditions on the CS panel, or if they would prefer the option to specify categories of conditions. The subcategories that participants could select from were a) childhood onset conditions that benefit from early detection and treatment, b) severe and untreatable childhood onset conditions, and c) conditions with onset later in life which may be treatable or not. If participants selected “all conditions”, their other selections were excluded from analysis, as many participants who were interested in the full panel selected all of the options.

Table 8. Participant interest in the full carrier screening panel versus having the choice of a subset of conditions. A: total participants who did not want full panel, B: number of times participants indicated interest in each category, C: percent of the 15 participants who did not want full panel.

		n	%
Interested in full panel	Total	61	*80*
Not interested in full panel[a]	Total	15	*20*
Not interested in full panel[b]	Benefit from early detection and treatment	14	*93*[c]
Not interested in full panel[b]	Severe untreatable with childhood onset	9	*60*[c]
Not interested in full panel[b]	Treatable or untreatable with adult onset	7	*47*[c]

The majority of participants (n=61, 80%) indicated they would want to know their carrier status for all 32 conditions on the panel (Table 8). Of those that did not want the full panel but to have the choice of certain categories (n=15, 20%), participants could select multiple responses. Of the 15 individuals who did not want the full panel, 14 (93%) indicated that they would want to know their carrier status for conditions that could benefit from early detection and treatment. Nine individuals (60%) indicated that they were interested in screening for severe and untreatable childhood diseases, and 7 (47%) were interested in screening for adult-onset conditions.

3.2.6 Summary of survey results

A total of 95 Hutterite individuals from 12 colonies completed the survey. Overall, attitudes toward CS among survey participants were positive, with the majority indicating they thought CS was good, important, sensible, reassuring, desirable, and beneficial. There were no differences in attitudes toward CS between participants of different age groups, childbearing status, or sex. However, on average, participants who were married had more negative attitudes toward CS than participants who were single.

Individuals who did not know anyone affected with a genetic condition tended to have more negative attitudes toward CS compared with those who did know someone. There were no differences in attitude between those who had an affected family member compared with those who knew someone who was not related to them. Participant familiarity with CS prior to

the study also seemed to influence attitudes; additionally, the setting in which participants had learned about CS also seemed to have an effect. Participants who had learned about CS either at a town hall meeting, or at school, tended to have more positive attitudes than those who first heard about it as a result of the study.

In general, most participants indicated that they were interested in CS, and most felt that the benefits outweighed the risks. Additionally, the majority were not overly concerned about their own risk of being a carrier, although participants who had a family history of genetic conditions scored higher in the domain of perceived susceptibility. Overall, participants who indicated they were interested in CS scored higher in the domains of perceived benefits and perceived susceptibility, and lower in the domain of perceived risks.

There was substantial variability in the ways that participants indicated they would use results from CS. Most participants indicated that they would consider altering their family plans if they knew they were at risk of having a child with a genetic condition. Slightly fewer participants would consider taking the results into account when choosing a partner. There was also a subset of participants who indicated they were interested in CS, but that the results would not change any of their reproductive decisions. Specifically, individuals who had a first-degree relative affected with a genetic condition were significantly more likely to be interested in CS solely for informational purposes. Younger individuals (<25) and those who were single were more likely to use the results in their decision making.

Lastly, participants shared their preferences with respect to the provider they would like to access CS from, as well as how much carrier information they would like to know. There was an approximately equal proportion of people who were interested in accessing CS through their PCP compared with a genetics specialist. However, there was more interest in in-person genetics consultations as compared with a telehealth appointment. Most participants with stated interest in CS wanted to have the full 32-condition panel, but there was a subset of participants who would prefer to be able to choose subsets of conditions, with most of these preferring early-onset conditions that have treatments available.

CHAPTER 4. QUALITATIVE RESULTS

4.1 Overview

In the previous section, our quantitative results showed the attitudes and intentions of a sample of Hutterites toward panel-based carrier screening, as well as some relationships between these attitudes and individual characteristics. To gain further insight into the perceptions of Hutterites toward carrier screening and to identify ways to tailor CS provision, 13 semi-structured interviews were conducted with Hutterite participants. An overview of participant demographics is provided in the following section. A copy of the interview guide and consent form can be found in Appendices C and E, respectively.

Five major themes were identified from thematic analysis of the interview data (Figure 15). These themes are closely related to the initial research questions that the interview guide was designed to answer. Theme 1, “Perceptions of CS,” explores the perceptions of Hutterites about the benefits of carrier screening as well as some common concerns. The individual factors that were found to have the greatest influence on perceptions of carrier screening are presented in Theme 2, “Factors influencing attitudes toward CS”. Subsequently, Theme 3 (“Impact of CS”) explores the psychological and behavioural impact that a high-risk carrier screening result might have on an individual. Theme 4 (“Decision making about CS”) describes the multifaceted decision-making process that Hutterites may engage in when considering whether to pursue carrier screening. Lastly, participant preferences and recommendations related to tailoring CS to the population are reported in Theme 5.

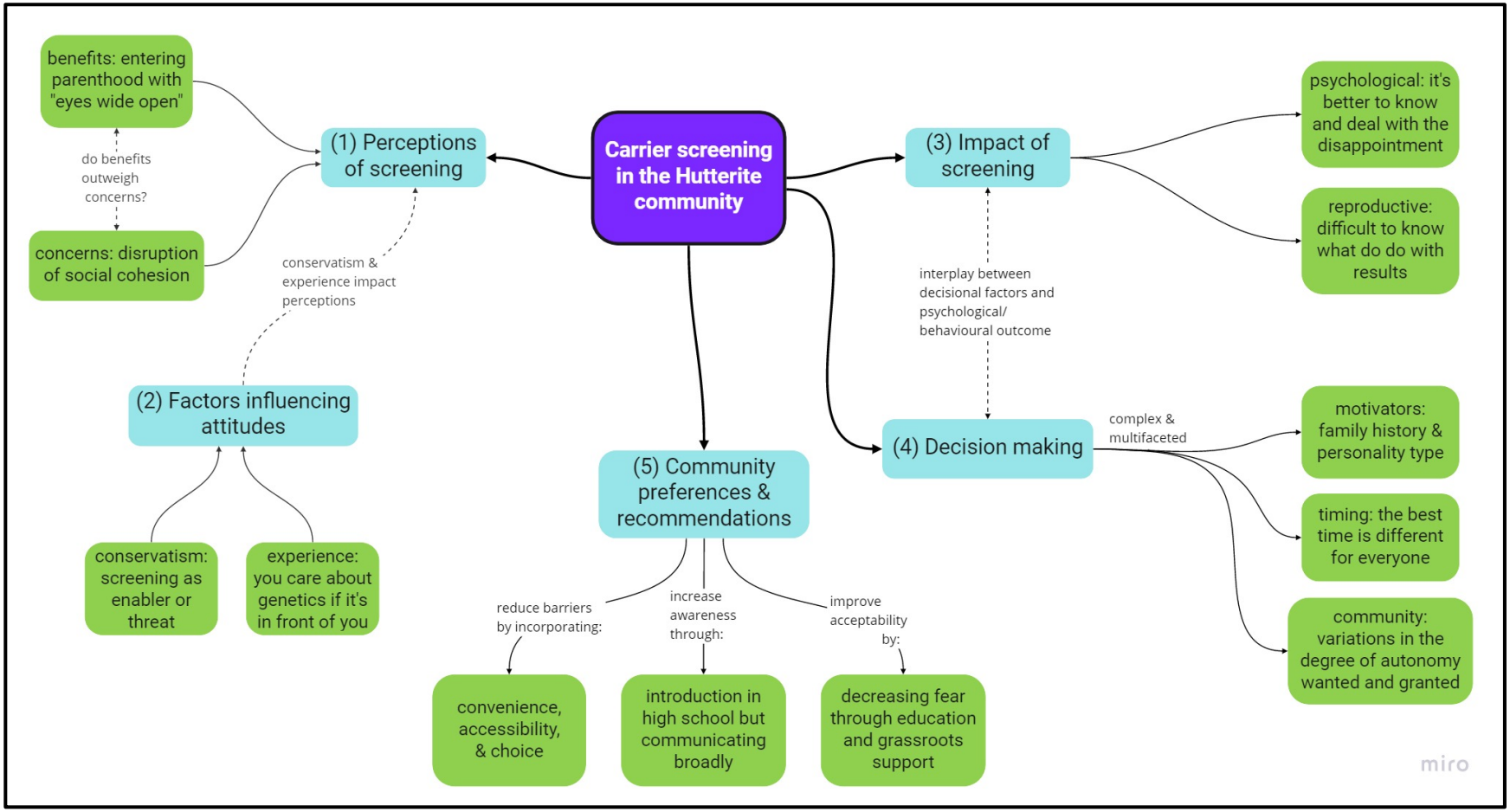

Figure 15. Results from thematic analysis of qualitative data.

4.2 Participants

Semi-structured interviews were conducted over the phone with 13 individuals including 8 females and 5 males. Interviews varied in length from 25-55 minutes. A summary of participant demographics is displayed in Table 9. To preserve participant anonymity, the specific demographic characteristics of each participant are not provided. Most participants were married (n=7, 54%), 4 (31%) were single and 1 (8%) were in each of the dating or long-term relationship/engaged categories. There were 5 participants (38%) who were older than 45 years, 4 (31%) who were in the range of 18-25, and 2 (8%) in each of the 26-35 and 36-45 categories.

Table 9. Interview participant characteristics

		Male		Female		Total
		n	%	n	%	n
Total Participants		5	*38*	8	62	13
Age Range	18-25	0	*0*	4	*31*	4
	26-35	1	*8*	1	*8*	2
	36-45	1	*8*	1	*8*	2
	>45	3	*23*	2	*15*	5
Marital Status	Single	0	*0*	4	*31*	4
	Dating	1	*8*	0	*0*	1
	Long-term relationship/engaged	0	*0*	1	*8*	1
	Married	4	*31*	3	*23*	7

4.3 Theme 1: Perceptions of carrier screening

4.3.1 Benefits of carrier screening: entering parenthood with "eyes wide open"

When asked how carrier screening could be helpful, participants responses seemed to come from two different lenses: one focused on how CS could help individuals or families, and another focused on how CS could help the larger community. With respect to the individual/family lens, many Hutterites in this study highlighted the value of knowledge for the sake of knowledge. They felt that learning about their own reproductive risk was beneficial because they could then make informed decisions based on the information. Regardless of whether they ultimately ended up acting on the results, they felt it was empowering to know.

> *I do understand that with the information, people can still choose. They can choose to either not have kids or to still go ahead and have kids. Even if they do decide to have children, knowing that both parents are carriers, they are going into this with information and with their eyes wide open (P10).*

> *Well, it can help you make better informed decisions, so even if it doesn't change the decisions that you make, at least you know what you're getting into (P08).*

Although some individuals may choose not to act on the results, many participants felt CS was still important because it would enable parents to be prepared for the birth of an affected child, rather than it being a surprise. One participant described how she owed it to her potential children to be prepared, and "…if not... then maybe don't have them" (P08). For some, that chance to prepare meant that they would seek out information about the condition, and the support of others with similar experiences. One participant reflected on how she had a friend who was aware she was at risk of having a child affected with Joubert syndrome, and how having the knowledge ahead of time was particularly helpful in preparing.

> *I am positive that if you talk to her, that it gave her time to prepare. She talked to people who had Joubert children… she knew what she was getting into. She was able to prepare mentally. So, having a baby arrive today and not being able to research what are the symptoms, what are the expectations, when can I expect my baby to do this, that, or the other thing? I think your brain needs time to wrap itself around those ideas (P10).*

Some felt strongly that the benefit of CS was to have the opportunity to avoid having children affected with a genetic condition. One participant who had a child affected with a severe condition reflected about how his parenting journey was different than what he'd anticipated, and said "you know, you don't sign up for this. And had I known beforehand... would I still have gone ahead with marrying my wife?" (P03).

The above participants focused on the impact of early onset, severely debilitating disorders. Others also discussed the benefits of knowing whether their child would have a later onset condition, due to the potential benefits of encouraging lifestyle changes that could change disease progression. One participant felt that another benefit of knowing about later onset conditions was that new treatments may become available before the onset of symptoms that could improve outcomes, and he would want to be aware of that for his child. This was based on an experience the participant had with someone in his community who was diagnosed with muscular dystrophy.

> *…Medicine and science is advancing so fast, having MD [muscular dystrophy] in any decade is different than in the previous decade, and I saw that in the person that had [it] here... so I think he would have straight up said, he tried an experimental drug, and it got him basically many years on his life. Well, I don't know if it was many years, but many years of mobility. Where he was, like, going downhill, and then medical advancements slowed down his deterioration (P11).*

Some looked at this benefit through an altruistic community lens – rather than not wanting to deal with the challenges of raising a child with disabilities themselves, they felt CS was an important strategy to decrease the amount of suffering in the community. Despite there being abundant support for parents raising medically complex children, some questioned whether it was fair to bring a child into the world who would be suffering for most of their life.

> *You are in a community and the community steps in so much, there's always other people helping with the baby at all hours of the night, but... Then you just kind of wonder how fair is that for the child? (P04).*

> *I wouldn't want to bring a child into the world knowing they're going to be sick their entire life and would suffer. Because it wouldn't be fair to them (P09).*

Another way that participants viewed the benefits of CS through a community lens was to reflect on the long-term impact of genetic conditions on the sustainability of the Hutterite way of life rather than the short-term impact of decreasing individual suffering. They felt CS could be used to decrease this burden by reducing the number of infants born with genetic conditions. One participant compared CS to vaccines, in the sense that she viewed it as another form of preventative medicine (perhaps also in the sense that CS and vaccines are both subject to strong opinions on both sides of the debate, see theme 2).

> *I just think it's in the line of preventative medicine basically is the way I see it. I don't have a problem with it, I do know people who would, I've had this conversation with other people, but I personally don't think this. The whole thing of genetic screening for Hutterites should be on the same line as the vaccines for other kind of, "do you or don't you" conversations (P04).*

In addition, several participants reflected on the factors that have contributed to the increased prevalence of recessive conditions in the community. One participant mentioned that he was concerned about the small founding population and endogamy practices which have resulted in limited genetic diversity among Hutterites; he felt that "it's not something that appears to be sustainable" (P07). Several individuals felt that consanguineous marriages were also a contributing factor. They shared that although first cousin marriages are prohibited and second cousin marriages are often discouraged, many people end up marrying second, third, and fourth cousins. They described how it can be challenging to meet people who have no common relatives within the past several generations, and others described how they did not find out they were related until they had already committed.

> *I have a huge family, and… I have lots of relatives. And we're very discouraged with marrying second cousins. We trying to go further than that, but even that... most are not more than third or third cousin once removed (P13).*

> *I never knew I was even related to my wife and I think I found out just before I was married that we are related. But I honestly didn't know that it was that close... But there are more and more people getting married who are even more closely related than we are and the potential of having more cases like this... I think I think it's going to get worse if I could use that term (P03).*

Aside from prohibiting marriages between first cousins, participants described other strategies that the community is considering to decrease risks associated with endogamy and consanguinity, including marrying Hutterites from different *leutes* (those from Alberta/Saskatchewan), or inviting more non-Hutterites to join their communities.

> *…it's always been that way… being too close related… and we need to maybe broaden our gene pool or whatever you would call it, maybe we need to go more to Alberta or Saskatchewan colonies. Like they may be a different group (P06).*

> *I think in our situation… we don't have other people join our communities. And we have to do something like that. It's either that or that, either letting other people join our society and join our communities. And I'm talking about just ordinary people from anywhere, it's either that or its carrier screening (P03).*

In summary, participants identified many ways that CS could be helpful or beneficial. Many responses pertained to the benefits to the individual or family, including allowing families to prepare for having a child affected with a genetic condition, allowing for informed decision-making regarding family planning, or reducing suffering by avoiding the birth of affected individuals. Other responses pertained to the benefit to the community, including reducing the risks associated with their small founding population, endogamy practices, and consanguineous partnerships.

4.3.2 Concerns about carrier screening: disruption of social cohesion

While most participants focused on the benefits of CS, there were several common concerns that arose during interviews that made some participants hesitant. A common thread between these concerns was that they related to disruptions in social or cultural cohesion between members of the community. Specifically, participants had concerns about stigma and CS leading to unwanted changes in Hutterite relationship/marriage practices.

Several participants were concerned about what would happen if they pursued the CS test and the community found out that they were carriers. Some were worried about this impacting their prospects for finding a partner, and several identified that this is already somewhat of an

issue – parents of young adults will often discourage them from marrying a person from a colony that has affected children.

> *Well, it could... um, there could of course be stigma where OK, I probably, you know, based on what I've heard about that… maybe I don't want to marry anyone from there, which, to be honest with you, testing aside, that does happen. I guess it's just human nature where, you know, let's say a community has had several Joubert babies or several people with muscular dystrophy. And there would be people who would discourage their children from marrying somebody from there. And I guess that testing could... do that, too. And I guess if you look at it that way, but then again, life is always a risk, isn't it? (P07).*

> *I guess I was talking before about if I don't get married, I was looking for a marriage partner, how would that be perceived and how would members of the opposite sex respond to their knowing that I [was a] carrier if I chose to reveal it to them (P01).*

Others were concerned about the impact of stigma from the community if their carrier status became common knowledge or material for gossip. Several highlighted the importance of confidentiality of CS results.

> *Well, if someone's carrier status was open knowledge, like if they were... um, dating, or looking for a potential marriage partner, if there was common knowledge that they were carrier of a certain disease... I don't know how much of a problem that would be, but that would just be kind of a general concern, so then, I would just think that secrecy, or confidentiality would be important. I just don't think it's the kind of information that you want everyone you run into to know. It's not something they need to know (P08).*

> *Well, I guess if... like, socially, I think if you're, you know, you're not married yet. And like we have groups, and we go to other colonies to visit. And what happens sometimes is, OK, you know, like you could be labeled as a carrier. And I just feel that that could be a potential reason for ostracizing people or... I mean I'm probably overthinking it, but I just I think that could potentially be an issue where all, this and this person is a carrier of this disease or whatever or. Yeah. So, it could be an issue, I think (P03).*

Another concern that was brought up several times by participants was stigma or judgement from community members, related to the choices that individuals make regarding CS. Some felt that if they were to pursue CS, there would be some members of the community who would not approve. Others were concerned about judgement from the community if they chose to have children despite knowing they were at risk of having an affected child.

> *I do know, if I were to talk to my parents about this, they would think it would be unnecessary. So, they would disapprove (P08).*
>
> *[Reflecting on what others may say] How can you bring a child that has, you know, how can you do that to a child, to an offspring, to bring them into the world when you know there's the possibility (P10).*

Some participants made comments that indicated concern about CS changing the way that Hutterites approach relationships, leading to a loss in the sanctity of marriage.

> *In a world where everybody was screened and everybody knew… it could, you could I guess end up overthinking it, making that the primary source of choosing partners, based on biological (P08).*

A different participant worried that if CS was widely implemented, it could lead to a decrease in the number of people choosing to get married or start families, which could impact the community in the long term.

> *But if one would do it on every colony and it pops up there, he tested, he tested, she tested, then they might sit back and say... what are we doing? I mean, pretty soon, nobody wants to get married... they're all scared (P06).*

Some participants worried that CS would lead to missed opportunities, such as the chance of having healthy children despite both partners being carriers or missing out on a relationship because a couple decided not to pursue marriage due to their carrier status.

> *I think it's... like, it limits your options as far as marriage partners go (P08).*
>
> *So, if it would affect your decision, for example if you really liked someone within that extended family, maybe it would shut down opportunities (P11).*
>
> *If my mom would have tested and known, and quit… before, or after my sister, she wouldn't have had 3 more babies that were healthy (P06).*

In summary, common concerns about CS shared by participants related to disruptions in the social or cultural cohesion of the Hutterite community. One of the most common risks brought up was regarding the potential for stigma against carriers. They identified several different ways that stigma could be an issue, from people wanting to avoid partnerships with carriers, to being a source of gossip in the community, or experiencing stigma from disapproving community

members as a result of having CS done. Other concerns brought up by participants included worrying about unintended consequences of CS on the relationship practices of Hutterites and wondering what sorts of opportunities would be missed if people base their reproductive decisions on carrier results.

Ultimately, the results from Theme 1 show that interview participants identified many potential benefits of CS, as well as several common concerns. Overall, the interviewer's impression was that most interview participants felt that the benefits outweighed the risks. As a result, most participants had a positive attitude toward the fact that the CS test would soon be available.

4.4 Theme 2: Factors influencing attitudes toward carrier screening

4.4.1 Is carrier screening an enabler or a "threat" to the Hutterite way of life?

While most interview participants viewed CS in a positive light, most also talked about how it is considered a controversial topic to others in the community. They described how there are many in the community who feel that CS departs too far from tradition, and others who feel that science (and thus also modern medicine/genetics) is at odds with religion.

Essentially every participant described how there is a great diversity of viewpoints within every community with respect to almost every topic, and how CS is no exception. Participants shared how conversations about CS and genetics in general can sometimes become heated, and they talked about discussions they had been having in the community which were prompted by the study. Among their communities, they described how they have individuals who align with science and public health, but others who are suspicious or distrustful of organizations outside of the Hutterite community. Several participants compared conversations about CS with conversations they had had about the COVID-19 pandemic.

> *It's often hard to talk about controversial things [like carrier screening] with other Hutterites because some Hutterites are so... like they're so... their mindset about some things is so strong, that they will get instantly offended if you have a different mindset. They're so... closeminded and they grow up thinking that's the way it is, you're not supposed to question it because if you question it, it's wrong. And so, it's hard to get through to some people, sometimes (P09).*

> *Other aspects include just being suspicious of anything outside the colony, especially when it's coming from academia or it's coming from government. If you take a look at community responses during the COVID crisis, there's been a whole variety, a whole spectrum from some being very open, some inviting speakers into their communities or via Zoom, or others just saying it's a government conspiracy. They're just not being open to it at all (P01).*

Some of the conversations that the participants had with others in the community surround the idea that CS is too different from what Hutterites have always done. Some community members may feel that CS is a threat to the Hutterite way of life.

> *[Describing what others may say] Like if we're going to go this far with controlling things, are we really sure that that's a good idea? You know, we've done it, you know, Hutterites have existed since 1528, we've done it this way for so long. Are we really sure we want to do this? (P07).*
>
> *Um... for a lot of Hutterites, when it comes to things like genetics, I feel... they're a little close minded, thinking... that it's interfering with our culture (P09).*

However, many participants disagreed with this viewpoint; rather than being a threat to their way of life, they viewed CS as a way of moving forward and protecting the community. Many participants felt that this tension between CS and the traditional Hutterite way of life was rooted in a conflict between their religion and modern science. They have always been taught to "trust in God" and that he would provide what they were meant to have. Some participants reflected about how some community members feel that science and religion are mutually exclusive, and how choosing to influence what children one will have is like "playing God".

> *Science and religion don't mix for many people. And that's a personal, that's how people view it personally. Like science is ungodly, science is not something that... is not something that we should entertain. The Bible is the truth. What is said and written in the Bible is the truth. And scientists really don't know anything. And I'm just giving you the point of view of what others would say (P03).*
>
> *And the conversations I've had, there's mostly this idea that you don't talk about it. And if you have a child with disabilities, it is as God intended it to be…. I think that's mostly what the argument is, [the] you're playing God argument. And I don't see it that way (P04).*

Several described how they feel science and religion can exist together in harmony; they believed in both creation and evolution, and that they can have faith in God and his plan but still make use of modern medicine.

> *I totally believe that science and religion fit together perfectly. The more I understand the science, the more sense my religion makes. It's not an either or for me. They both work together. Creation and evolution, and everything makes sense like a puzzle…and we're also playing God when we put people on ventilators and do heart transplants… (P10).*
>
> *[Reflecting on someone's death] We knew that the chances weren't good... throughout that all, we tried cures. He was willing to do anything the doctors told him, and we tried... to put it clearly, we tried cures, but we were still perfectly OK with God's plan. We*

> *didn't look at it in any way as fighting or going against it. I don't think that way at all. Like, if it goes badly or if it goes well, my personal approach is, God is present (P11).*

Similarly, several participants described how they felt that it was true that God gave them the ability to have children and build families, but at the same time gave them the ability to think and decide for themselves whether they wanted to. As one participant put it, "God gave us brains for a reason" (P08). One participant felt like the tension between religion/tradition and science was starting to subside within Hutterite culture, and that this was one of the reasons that CS may be more acceptable to Hutterites now than it would have been in previous decades.

> *And we are becoming more of a culture where, that looks at science as enabling and maybe helping our religion along as well, being an integral part of figuring out the world. Figuring out how the world works and being good stewards of the world (P03).*

Many participants felt like there were differences between the older and younger generations with respect to their attitudes towards technology like CS. However, this difference was ultimately due to differences in how strongly the older and younger generations adhered to tradition. They felt that generally, the older generation were more conservative and cautious when it came to new ideas or technologies.

> *I think the older generation of... the older generation might not like if the younger generation did this, just because, like that person who I talked about earlier who thinks that every child is just a gift from God, and they should take whatever they get. They might think that it's meddling into something that they shouldn't be meddling in (P12).*

> *My parent's generation, or my grandparent's are a lot more conservative when it comes to the conversation about genetics, about, anything involving relationships or intercourse or anything like that… (P04).*

However, several participants felt strongly that age was not what created the differences between age groups, but rather, the difference lay in education level and interest in continued education. These participants commented on how completing high school was only common starting in the 1990s, and anyone who went to school prior to that period would not have had much (if any) teaching about reproduction, genetics, or genetic disorders/testing.

> *Well, the connection you're going to find is going to be 100% linked to not just the level of education, but the type of education that people have. People who are well read, people who understand science, you're going to find it much more likely to think the way that I do. Whereas if you meet people who have yes, they might have a grade 12 education, heck, they might have a university degree, but they don't read a lot. They don't read the news. They don't read different perspectives. They're going through life with blinders. You're going to find that there are going to be more likely to shy away from this kind of science (P10).*

> *And those are usually the older generation that would say that. I think more so, nowadays because of education and because of our education standards have improved over the last 20, 30 years (P03).*

Overall, while most participants felt that CS was compatible with the Hutterite way of life, and didn't feel that it went against their religion, there were others in the community who felt differently. The diversity of opinions toward CS seemed to be fundamentally rooted in differences in conservatism among community members, both within a single colony and between different colonies. Participants identified several factors that seemed to influence how others felt about CS including age and education levels, however the differences between these groups also came down to how conservative or open to innovation individuals were.

4.4.2 Individuals care about genetics if it's "right in front of them"

Another key factor that many participants identified as strongly influencing attitudes toward CS was whether individuals had experience knowing someone affected with one of the conditions. Many reflected on how hard it is to care for a person with complex needs, and how this had a considerable influence on why they feel CS is important.

> *We have friends who are dealing with genetic disorders every day and it does... it makes their life more complicated. It makes you see that people are dealing with it... it makes you think about what you can do to maybe avoid it (P08).*

> *My cousins passed away from [Joubert syndrome], and that impacted me a lot… it really impacted the way I look at genetics, how I view... Just how I look at prevention, because I remember always just thinking like this, could this have been prevented? Could situations like this be avoided? (P04).*

Several participants reflected on how the experience of having an affected family member or friend is almost a prerequisite to caring about CS, in the sense that they felt that people

wouldn't think about it at all if they hadn't had the experience. One participant who had children with a genetic condition felt that anyone who lives at their colony would likely see the utility of CS, because "it's right [there], it's evident, it's in front of them" (P03).

> *I think it for the most part because we don't really have any special needs children on the place [sic], and most of them aren't even... they don't even have it in their families. They, I don't think they'd be interested in it... unless they'd have somebody in their family (P13).*

> *Yeah, like more aware to the extent where you could almost call it changing my view on it, making it seem a lot more important, whereas otherwise, I wouldn't think about it at all (P11).*

Several common patterns emerged from participant's reflections on the impact of genetic conditions on their lives or the lives of their families and friends. There were unique challenges and benefits associated with having a diagnosis of a severe genetic condition within families and communities. One of the shared challenges brought up by participants was the impact on time – they described how when a child has a severe disability, care becomes a 24/7 job that takes a toll on the family.

> *Like for example my wife and I, this is a family thing, my wife and I have spent countless hours just being with [name] and like essentially since he was born, he's been just agitated with his tummy and stuff. And we've had to do all sorts of, you know, staying up all night and then trying to work the next day. That part has you know, impacted my family (P03).*

> *I think on some of the more severe cases, the people that I know have children like that, have ones that are pretty, pretty severe. So it's basically, they take up their entire time. It's just how, or where, life goes (P12).*

Additionally, many participants talked about how caring for a child with a severe disability impacts the family by taking away opportunities for leisure activities and normal life experiences within Hutterite communities. They described how difficult travel becomes, which substantially limits the experiences the family can have; someone always has to stay home and miss events, which are an important part of what Hutterites look forward to.

> *And so, I'll give you one example, a couple of times where I had to make a sacrifice was when both of my sisters got married and moved to different colonies, I had to stay home*

> *with my brother because that wedding was just not a situation where he would have been able to function. And so, like those are the things and it's just, it is what it is. It's tough, but that's just the way of it (P07).*

> *For my wife, for example, she has had to spend a lot more time at home than would have liked. She would have liked to go out and do more garden work in the summer and things like that. We've now come to a point where she we've decided that she is going to do some of that stuff no matter what. And we find ways to accommodate that because it's just healthy for her. It's healthy for our child (P01).*

While participants identified several challenges associated with caring for a child with complex needs, they also identified many ways that it has had a positive impact. For example, many participants talked about how intensely the affected child is loved and cherished, because "if you know that someone needs you that much, it's not hard to be there" (P12). They perceived them to be more special than their typical relatives, bringing a lot of joy. Every milestone that the child meets, although delayed, seems to mean more than it would for a child who was typical.

> *They're so sweet in their own ways, and they're smart, in what they want and like and stuff like that, it's amazing… And every little milestone is such a huge accomplishment and joy to hear and see. Whereas like a normal child, it is too, but since it's quicker.... I don't want, I don't know how to word this, but it's not as rewarding, now that it sounds wrong, the wording, but this accomplishment that this little guy makes it so much, it looks bigger than with a normal child, because of what he goes through (P13).*

Knowing someone with a severe condition or who had a disability made people more accepting of people who are different. It changed the outlook of caregivers towards others who have unique challenges.

> *And it's... it's made... like a child doesn't have to be perfect, what we call perfect, to be loved and cared about. I mean, everybody wants a perfect child. Sure. But it's... yeah, I like what it does to people. What I find is that it's made them a lot softer towards other people, other kids, kids who have children like that, all love their kids so, so much... they become almost more special, more special than a normal child (P05).*

Many participants also talked about how having to work together to care for an individual with complex needs brings the family closer together. They talked about how much the community

helps with care and material needs (such as taking turns caring for a baby at night, building a new house with ramps, purchasing a van) which brings them together.

> *And that can be heartbreaking to watch, but it's also very heartwarming to watch them. They do a very good job of taking care of them, and the colony is very, very helpful to them (P02).*

> *I know that it brings them closer in some ways, like, they need a lot of help. So, his mom... it's his sister's kid, so his mom at his sister's place a lot more than she would be at his other sister's place, who has a very healthy little boy. It brings them closer and that they know that... they know that they need the help, so one is there for them more (P12).*

In summary, while participants identified both challenges and benefits associated with having children with genetic conditions in their lives, all agreed that these experiences were highly influential with respect to their positive attitudes toward CS. The results from Theme 2 demonstrate that personal experience with genetic conditions, as well as an individual or community's level of conservativism and adherence to tradition, seem to be some of the most important factors impacting how people in the Hutterite community feel about CS.

4.5 Theme 3: Impact of carrier screening

4.5.1 It's better to know and deal with the disappointment

Despite most participants feeling optimistic about CS, they described how it might impact them emotionally if they did the test and found out that they were carriers, or that they were at risk of having a child affected with a genetic condition. These emotions ranged from reassurance to anxiety and disappointment. Many participants shared that they would be worried, scared, or anxious if they found out they were carriers. Aside from the concerns about stigma explored in the first theme, these feelings of anxiety often surrounded one's own ability to cope with the information, or to care for a child with a disability.

> *But it obviously also comes with... you'd be a little bit scared. Can you cope with this? Will I understand it enough... will I know what to do? How will the child look? (P05).*

Other participants reflected that the anxiety might be too much for some individuals, especially if they feel that there is nothing they can do with the information – they felt that "it would almost be viewed as an unnecessary fear…" (P04). Some participants also expressed concern about having to communicate the results to a prospective partner if they knew their carrier status prior to entering the relationship. They felt a sense of responsibility that they would have to, but worried about whether it would derail the relationship.

> *So, you have to, now that you know, you sort of have a responsibility to let others know, especially your partner. And that may cause some concerns. If you don't know, you can I guess play the ignorance card, but once you do know, I think there's a responsibility aspect that comes with it (P01).*

Many participants felt they would be extremely disappointed if they found out that they were carriers. Throughout the interviews, the importance of family to Hutterites was a central point of discussion, to the extent that the participants viewed family as part of their identity as a Hutterite. Therefore, receiving CS results that caused them to rethink or question their decision to start a family would have the potential to be disappointing, or even devastating.

> *I definitely want quite a few kids, and I know it would that would be a deterrent for me on that because it would prevent that to some extent. So, it would make me feel a bit sad... more disappointed (P12).*

However, despite the anxiety or disappointment that could follow a couple's positive screening result, most participants still felt that they would want to have the test done: "I think that it's better to know and deal with the potential disappointment that you're a carrier than to not know" (P08).

One participant who has children affected with a genetic condition reflected how finding out they were a carrier impacted their self-image for a time, in that they felt "this feeling of defectiveness, that [they were] defective" (P01). This impact on self-image was further explored in later interviews, but it was not a common feeling; on the contrary, most participants felt that finding out they were carriers would not change the way they looked at themselves, since they recognized that "[they've] been a carrier [their] whole life, what would change?" (P04).

> *I think of it like this is the way it is, and this is just the way it turned out, you know, I don't view myself as being different or worse off than anybody else (P03).*

> *I see as everything, we're all, all humans are on a continuum. There is no normal … So, if you look at it from that perspective... then, no, I was created differently and of course, there's going to be mutations and different stuff going on, and that's OK (P10).*

Other participants felt that finding out they were carriers would provide reassurance. They described how even if the test showed them that they were at risk of having a child with a severe condition, they would be glad to know.

> *Well for me, it would give me peace of mind. At least, then I would know, I wouldn't be wondering, like, is my child going to potentially… somehow the certainty of knowing would be more comforting, I guess. Because you're not living in this not knowing... maybe, maybe not (P08).*

There were a number of different emotions that participants anticipated if they were to find out that they were carriers, from negative emotions like anxiety or disappointment, to those that were potentially more positive such as reassurance. It is important to note that the participant who stated that there was a period of feeling defective upon learning their results, was the only participant that had confirmation that they were, in fact, a carrier. Therefore,

although the perspectives of most other participants were that they did not feel that this would be an issue for them, there is the potential that they may feel differently when faced with receiving similar results.

4.5.2 Difficult to know what to do with results

There was a wide variety of responses with respect to what participants felt they would do with CS results if they turned out to be positive. Some were certain that it would have an impact on their family planning, while others were less so. A common theme that arose from participant responses was that it was simply too difficult to say how they would respond without being in that situation.

> *It's really difficult to know what I'd do because it's really easy to be sitting here thinking I'd be doing this and doing that, but actually relationships are a lot messier... it's not that straightforward (P08).*

> *If you know your carrier of something, do you tell your partner to go test themselves too, and if they also are carriers, what do you do then? There's so many other follow up questions. Yeah, I'm not even sure (P04).*

Many felt that the decisions they would make would depend heavily on what the result was. For example, they felt like they would be more likely to act on a result that showed they were at risk of having a child with a severely disabling condition, whereas they may not alter their plans if the condition was milder or later-onset.

Some participants indicated that they would consider using the results from the CS test to make decisions about who they were going to marry. Several individuals were already married with children, and reflected how, if they found out that both partners were carriers prior to the marriage, they thought they might have reconsidered the union. However, they often followed up by recognizing that it would have been a difficult decision to make and that it was hard to know what they would have actually done.

> *I would hope that as a young person if I knew I was a carrier... I wish that I wouldn't start a relationship with a person like that, if I knew in time and would be able to, but I know life doesn't always work like that (P05).*

> *Had we known before we married that this would be the case, I would love to be able to believe that I wouldn't have married my wife (P03).*

Another perspective shared by several participants was that they were certain CS results would not affect their choice of a partner. They described how for them, marriage is based on love and God's will, and it is not something for them to decide.

> *Because we believe that you have a soul mate and God directs your path to the right person… if I would have found out about this before I got married, it would not have changed my opinion. But maybe for some it would, I can only speak for myself (P13).*

Many interview participants indicated that if a CS test showed them that they were at risk of having a child with a severe disorder, they would use that information to make different family planning decisions. For example, many participants discussed that they would choose to adopt instead of having biological children. Others felt that it probably would not affect whether they had biological children, but that they would consider having smaller families instead of large families as was their preference.

> *I definitely wouldn't have a large family. I wouldn't say I wouldn't want any because I wanted kids badly, and I would... I would look into adoption (P05).*

> *And I don't think it would even impact if I... who my partner is, it would simply impact which kind of prevention methods I would take to avoid pregnancy. How much more seriously I need to take that and what other... do I want to consider adoption or something like that (P04).*

There were several contrasting viewpoints on the utility of prenatal testing if a pregnancy was known to be at risk due to the parents' carrier status. Some participants felt like prenatal testing would not be helpful to them, since most shared that they would not consider termination of pregnancy under any circumstances. They felt like once a person is pregnant, it is too late to do testing.

> *I don't know that I [would find] it helpful to know, because I couldn't see myself aborting it, if that were the case, I would simply think along the lines of, I've done it this far, I tend to think I would see it through (P02).*

Others felt that despite termination of pregnancy not being an option they would consider, prenatal testing may still be helpful, as it would let them know ahead of time whether the child was affected and give them time to prepare.

> *Yeah, I would have no problem with that. I mean, if you are having to take care of a child, potentially with a genetic disease, you need to prepare yourself mentally, and probably maybe prepare some things in your home (P08).*

As stated above, the vast majority of participants had extremely strong feelings toward termination of pregnancy – most felt like the thought of it was "extremely abhorrent" (P10). However, one participant shared that they felt they were different than most Hutterites on the topic, in that they were more open to the idea in certain circumstances. At the same time, this participant recognized that it would be an extremely difficult decision to make, not only because it would be "something a lot heavier than [they would know] how to handle", but also due to the perception of Hutterites toward termination of pregnancy and the potential backlash from the community if they were to pursue that option.

With respect to assisted reproductive technologies such as in vitro fertilization and preimplantation genetic diagnosis, most participants appeared to be uncomfortable with the idea. Many were unfamiliar with the process prior to the interview, and when the researcher explained it to them, they did not feel like it was something they would consider. For those who were familiar with the process, several participants were of the mind that it was "beyond the pale" (P07), meaning outside the bounds of acceptable behaviour for Hutterites, and one participant felt that it was "playing with fire" (P06). They felt that the process of choosing embryos to implant and discarding the others was along the same lines as selective abortion, so most indicated that it wouldn't be an option for them.

Overall, participants identified many ways that the CS test would have an impact on them if they were to pursue it. These ranged from varied emotional responses, to being faced with a decision of what they would do with a positive result. Many participants felt it was hard to predict how they would use carrier information, and there were few consistent patterns among responses. Some would consider CS results when they were looking for a marriage partner,

while others would not. A proportion of individuals would consider prenatal testing, but very few among the participants would consider termination of pregnancy if a fetus were affected. In summary, results from Theme 3 again illustrate the diversity of viewpoints among Hutterites when it comes to CS, and particularly on the impact that CS would have on an individual, both emotionally and on the decision-making process.

4.6 Theme 4: Decision making about carrier screening

4.6.1 Family history and personality type play a role in wanting to know

Participants were asked to share the main reason that they would personally want to pursue CS. Aside from the benefits explored in Theme 1, participants identified several other individual factors that influenced their own interest in CS. These ranged from being an "information seeker" personality type, to feeling like they were highly susceptible due to their family history of genetic conditions or feeling like they wanted to show community members that it was not something to be afraid of.

Several individuals indicated that they would make the decision to pursue CS because they had a family history of genetic conditions. These participants seemed to be unaware that they would already be eligible for carrier testing for the condition(s) present in their family members. One participant shared that she would definitely not consider CS, nor even participate in the current study, if she didn't have a confirmed family history of one of the conditions on the panel.

> *I know for sure that if it wasn't in my family, I wouldn't really care. I might not even do this interview... and since it is, it definitely made an impact because I have a special needs nephew (P13).*

Several participants indicated that they would want to pursue CS because of their personality type – they felt like they were the type of person who wanted to as much information as possible when entering a new situation (such as parenthood). For one participant, they felt this set them apart from other Hutterites.

> *Umm, I think I myself am a very knowledge-based person, I like knowing all the facts before making the decision. Which, not many Hutterites are. I find it's difficult to, just kind of jump into something and see what the outcome is. I like to be prepared and just, know what I'm in for. Because if I didn't, I would just go insane. With worrying about whatever the result could be (P08).*

Several individuals discussed how even though they did not necessarily plan to use CS results for any specific purpose (because they had completed their families and/or planned to adopt),

they would pursue CS to raise awareness about it and to show others that it was not something to fear.

> *If someone were to be interested in this stuff, and were to further educate themselves, and kind of go through the test, would be able to influence more Hutterites and show them it's not... uhh... it's not a taboo topic, as it seems to be... that it's not something to be afraid of (P09).*

> *But I would probably also say that I'm interested even just for, like even if we were to never have a biological child, which we might not, we don't know for sure. I would still be interested, for promotional reasons. Like, OK, there is a person over there that got this done and it's not a big deal (P07).*

To summarize, there were several common factors that participants identified as influencing their personal interest in CS, which went beyond the general benefits explored in Theme 1. These included having a family history of genetic conditions, being an "information seeker", and wanting to raise awareness about CS in the community. These results demonstrate that there are many additional factors that individuals might consider when deciding whether or not to pursue CS.

4.6.2 The best time for carrier screening is different for everyone

Another of the potentially challenging decisions that individuals would have to make regarding CS is deciding when the right time is to have the test done. Similar to many of the other themes identified in this study, there was a wide variety of responses and opinions to this question. Responses were often related to participants' intentions of whether CS would be used for reproductive decision making, as was explored in the previous chapter. Many participants were uncertain about the best time for an individual to have CS and reflected on how there were pros and cons of having it at each life stage. Several discussed how while it might make sense to have CS done early in life, it might be challenging for a young person to bring it up in conversation with prospective partners.

> *Although, one could also say that before you're in a relationship is also a good idea. I mean, I don't see people talking about that much before they are actually in a relationship, because one generally doesn't talk about having kids until they have a*

> *boyfriend or girlfriend. "Oh hey, I'm a carrier for this disease..." I don't see that coming up in a social interaction (P12).*

Several participants said that the best time to have CS was before you were in a long-term relationship or married, because it would leave your options open, in the sense that individuals could then decide whether to take CS into account when considering a relationship with someone. Some people felt that it would make the most sense to have CS available in the late teens, “before you’re even in love with anybody” (P06).

> *I guess when you're in your teens, would probably be the best time, so that you have a chance to actually think about it. But especially the late teens, like 18, and up, early 20s... because that's when you're thinking about that, you're starting to be involved with people, you might want to take the screening results into consideration (P08).*

Others felt that since they would not want CS to influence their choice of partner, they would rather start thinking about pursuing it after they are committed to a relationship but prior to starting their families.

> *I just think that most would only do it once, once they, once the possibility of marriage would come up. I kind of think that's what I would have done. (P05)*

> *For the most part, as Hutterites, knowing that your partner and you are carriers will more than likely not change anything in the line of getting married or getting a new partner, like I said before. For some it might... but I'm thinking for most it wouldn't (P13).*

Overall, there was a wide range of opinions as to when the most appropriate time would be to have CS. This was reflective of the range of responses to the question of what participants would use CS for. While some felt that screening early in life, prior to committing to a relationship, would make the most sense because individuals could then decide whether to take results into account when entering a relationship, many felt that young people would not want to have that conversation with one another so early in the relationship. Since Hutterite marriages are based on love, several participants felt that they would not want to have their carrier results impacting that decision. These individuals felt that as a result, it would be most appropriate to have CS done after committing to a relationship but prior to starting a family. Ultimately, there was no consensus on the best time to have CS among participants in this

study – similar to decisions about how to use CS results, what is right for one person may not be for another.

4.6.3 Colonies differ in the amount of autonomy wanted and granted

Often, before new technologies or practices are integrated into Hutterite society and available to community members, many levels of community leadership deliberate about the benefits and risks that the new technology may bring to their culture. Participants were asked about who should be making the decisions about CS. Specifically, they were asked whether CS should be vetted by community leadership prior to its widespread availability, or whether individuals and families should be able to pursue it without the influence of leadership. Again, there was a wide range of responses to this question – while the majority felt that it should be left to the individual or family to decide, there was one participant who felt it was important to have trusted leadership exploring the ways it might impact their culture before it was made available.

> *I think it should be a communal decision… I don't think there's any decisions that are rushed into in Hutterite communities, because of the amount of discussion that happens. And once a decision is reached, the chances that it will change are very low and usually all the side questions and all the small nuances like the what ifs have been so much discussed, that by the time a decision is reached, it's usually... I've never seen such a situation come up where the decision is a bad one because you have all the people and all the voices involved in making these decisions (P04).*

In contrast, several participants felt that the decision should be left up to individuals, and that management and the larger community should not be involved in the decision as to whether CS is an option. At the same time, many of these participants recognized that it was unavoidable that a discussion with colony leadership would likely happen if an individual or family was considering CS, and that there may be some colony leaders who do not approve (perhaps due to differences in conservatism as discussed in Theme 2).

> *My best-case scenario is that it's left up to the individual to decide whether they want to take the carrier screening or not. But you can't avoid the fact that colonies will be making decisions about it. Because there are some colonies that I can imagine would have a negative feeling towards this (P08).*

There were some participants who felt that support on both levels was important. They discussed how while they would want the ultimate decision to be left to the individual or family, there was value in having overall community support for CS availability. Additionally, several participants described how many colonies are moving away from colony leadership being the ultimate decision makers, especially with respect to reproductive decisions. Some individuals described how members of their colonies used to have to ask for permission to start on birth control, but now this decision is left up to individuals to decide. They felt that CS would be similar, in that leadership at their colony would not be involved in this type of decision.

> *I think that quite a few colonies are moving a little bit away from the minister having the full authority. Where, like in my colony, for example... he leaves it sort of up to the individual to decide, you know what, if you want to do carrier screening, that's up to you. Or if you want to go into Planned Parenthood, this is this is something that you decide as a family… I think it should be the individual making the decision, but that... I know that that would be controversial even to my fellow members… it's just the way I see it (P03).*

Participants had a wide range of opinions about who should be able to make decisions about CS. The majority felt that while a discussion with community leadership would likely be a part of the process, they felt it was important that the decision be left up to the individual or family. Participants identified that there were differences in this process between different colonies, with some colonies allowing their members more autonomy in these decisions, and others where leadership would have more influence. Some felt that if the community decided against CS being available for their colony members, they would accept this decision, while others felt that they would still want to pursue it. Overall, these results reflect that within the Hutterite community, each colony is very different with respect to how decisions are made.

In summary, the results from Theme 4 demonstrate that decision making about CS is complicated – each person considering pursuing it has differing personal motivations, opinions about when it should be done, as well as community differences to consider. As with most other topics explored in this study, there is no "one size fits all" approach to the decision-making processes involved regarding CS among Hutterites.

4.7 Theme 5: Preferences and recommendations

4.7.1 Convenience, accessibility, and choice

An important goal of this study was to explore the preferences of participants regarding how they would like to access CS, as well as how much information they would like to know. Therefore, participants were first asked their opinion about which providers they would prefer to obtain CS from. Most interview participants preferred to have CS done through their primary care doctor, either because it was more convenient and accessible, or because they had a trusting relationship with their family doctor. Several participants described how they would need to ask permission from their colony leadership for a trip to Winnipeg or another health center (for a telehealth appointment) if the appointment were with the genetics team, which could introduce challenges, especially if they were concerned about the response of the community to their decision.

> *Well certainly having it available to each person's family doctor would make it more accessible, that's certainly true. Some people might find it very difficult to come to Winnipeg and specifically to that location. Probably more of a process, in terms of getting the permission to come there, if it's available at the family doctor that's usually quite accessible (P01).*

Others felt that they would prefer accessing CS through their family doctor because they already have a relationship with them. Some felt like the process of meeting a new provider to access CS was intimidating, so if they could access it the same way as a normal doctor's appointment, they would feel more comfortable.

> *I think family doctor will probably be the least...I mean, I don't want to use the word intrusive, but it seems it seems like it would probably be like many Hutterites have a really good relationship with a family doctor, whereas like going to a geneticist, would be scary so to speak. But I don't know. I guess that's just how I feel, I think from the doctor will probably be the best (P03).*

While most interview participants preferred their PCP, there were a few who indicated they would prefer accessing CS through the genetics clinic, because they wanted to make sure they

were getting accurate information. Others said that it made no difference but preferred that it would not be too inconvenient.

> *I don't really have a difference, so if I was getting the test from… whoever was doing the genetics… I wouldn't mind getting it directly from them just because they probably know more about it (P12).*

Participants were also asked how much information they would want to have about their carrier status. In particular, they were asked whether they would want to know if they were carriers for all the conditions on the panel, or whether they would prefer to have the choice of specific categories, such as conditions which are severe and untreatable in childhood, those with treatments available, or those with later onset that may be milder in nature.

Overwhelmingly, participants indicated that they would want to have their results for all 30 conditions. Most felt that it would be no different to them to receive their results for all the conditions as opposed to a subset. While some participants recognized that some categories would be more important for them to know, such as the conditions with an immediate impact in childhood, most participants preferred to have all the information. That being said, many participants recognized that there could be value in offering choice, for some people in the community. They felt that "offering choice would make it more widely acceptable" (P01), because for some people, getting too much information would have the potential to cause more anxiety. Additionally, some participants felt that some in the community would not feel that it was important to learn of their carrier status for all the conditions.

> *I could imagine people would... I can almost hear some people say, do I need to know these, they don't do anything. It's almost maybe making two categories, the ones that have an immediate and dangerous potential and the ones that are more mild. And say, OK, you have the option of either doing everything you're a carrier for or major ones (P04).*

Overall, participants in this study preferred to access CS through their PCP, not only because they have an existing relationship with them, but also because it would improve accessibility. An important perspective that was brought up by multiple participants was that by making CS accessible through PCPs, people who were interested in having the test could protect their

confidentiality. They could integrate the discussion into their regular care and would not need to provide an explanation to their colony leadership about the purpose of the appointment. Also, while most participants preferred to have information about their carrier status for all 32 conditions on the panel, many also recognized that allowing others to select categories of conditions may make the CS more widely acceptable to others in the community.

4.7.2 Teach the basics in high school then communicate broadly

To determine the best way to provide education about CS to Hutterites, in a way that is both effective and consistent with the processes and values of the community, participants were asked when they felt education about CS should be made available. Additionally, their opinions were elicited regarding the most effective means of communication about CS.

Many participants felt like there should be education about the availability of CS during the high school health curriculum. They felt like while some might find it controversial, it was also controversial in the not-too-distant past to discuss anything about reproduction in this setting. Many felt that this timing would give individuals time to think about it and decide whether it was something they wanted to pursue when they were older. Others felt that the best time to communicate about CS was during the family planning process and suggested that family doctors might be the best individuals to provide education about CS, at a time when it seemed most relevant.

Participants also had many different suggestions regarding how people could be informed about CS, including through presentations, online or paper reading materials, and word of mouth through key individuals or organizations. Several participants had attended the past town hall meetings that were organized when the CS panel was first developed and felt that this was still the best option. However, some felt that these were not accessible to everyone, and that using an online platform to reach a wider audience would be better. One participant suggested that this may be even more possible now than in previous years, due to adaptations to online learning and presentations that everyone has had to make due to the COVID-19 pandemic.

Several participants identified the organization called Hutterite Health, which has an online presence, and circulates information about many health topics relevant to Hutterites.

> *There is a group of Hutterites called the Hutterite Health society or something like that… they have ways of spreading it to their communities, access to the colony leaders Whatsapp groups, where they could put information like this, they have an Instagram page where they would probably post it as well, and send out emails, they have a website, as far as I know, too... so they might be able to post something on that if they have the information (P12).*

Other participants thought that word of mouth would be a sufficient means of communication, and they reflected that a lot of information is spread this way. They suggested contacting key influential people at different colonies and allowing them to spread the word about CS.

> *Perhaps if you could somehow get something started... for example, most colonies, their members are using Whatsapp or whatever, so if you could get an article forwarded, and then they would forward it to somebody else... if you got in contact with someone who had a lot of Hutterite contacts, they could probably do the sharing of the information for you. It wouldn't be hard, a single article, or a PDF or something, with all the information in one place, that would be really helpful (P08).*

One participant felt that it would be important for the information to come from people who are Hutterite, who recognize the benefits as well as potential tensions, and who could present the idea of CS in way that others could relate to.

> *I would guess they would be more motivated; they might be more equipped to... maybe handle... like there wouldn't be backlash, but... to present it well. I think they could approach it carefully and do a good job of presenting the information (P11).*

In summary, most participants in this study felt that it was important for information about CS to be included in the high school health curriculum, allowing for young people to learn about it and have time to think about whether it was something they wanted to pursue. There were many suggestions from participants about the best way to communicate about the availability of the CS. However, a common pattern among responses was that online communication between communities and community members is becoming much more common, so providing either online presentations, or online reading materials, may enable the information to reach a much wider audience.

4.7.3 Decreasing fear through education and grassroots support

Participants were asked what they thought was the most vital information that individuals would need to make an informed decision about whether to pursue CS. Many participants described how some people fear technologies like CS because they do not understand them. They felt that it was important to keep this in mind, and address some of the issues that make people hesitant in order to decrease this fear. Several participants also emphasized that the information needs to not be overly technical in nature, which would allow more people to understand it.

> *I think the solution is just education on it and just highlighting how this is actually beneficial, and it shouldn't create fear. I think the way to avoid fear is education… (P04).*

> *The more simplified it is, the easier that people will understand, even though we do live in a day and age when education in the Hutterite society is more accepted, a lot of people still don't want it, they see education as a threat, so the more simplified it is, the easier it would be for people to understand (P09).*

All participants felt like it was essential to include a description of the logistics of the CS test, including the basics of genetics and inheritance, the fact that it is a blood test, and a description of the conditions that are included. Many communicated that while a clear description of the logistics wouldn't necessarily change anyone's mind about the test, "it would make them more comfortable, knowing what to expect" (P08). One participant also suggested that it would be important to personalize the content – they felt that if a personal story were included within the information, it would allow more Hutterites to relate to it and see how they could also potentially benefit from CS.

> *I think that if you're speaking to Hutterites, it's important that some of the words that are said, are by people of their own culture. Like, even maybe a short story or snippet, because the more personal you make it, the more real you make it (P10).*

To summarize, most participants agreed that the most essential information for people to know about CS includes a description of how the test is carried out, as well as the possible results and implications of those results. Many felt that there are individuals who would be hesitant to

pursue CS because they do not understand it and communicating about the test in simple terms would be the best way to decrease this fear or hesitation.

The results from Theme 5 highlight that there are many ways in which the CS panel itself, as well as educational efforts pertaining to it, can be tailored to fit with the unique population it aims to serve. While most participants felt that they would personally be interested in receiving their results for all 30 conditions, allowing for choice may improve acceptance of the test among other community members. Enabling PCPs to deliver CS to this population may have the effect of increasing accessibility and protecting confidentiality for those who want to access it. Additionally, most participants felt that education about CS should be integrated within the high school curriculum, but that providing further education to community members through presentations and reading materials would also be of benefit.

4.8 Summary of interview results

Interview participants in this study were generally optimistic about CS. They identified many benefits that CS could provide, including allowing for informed choice in their reproductive decisions, reassurance, and a chance to prepare for having a child affected with a genetic condition. They also felt that CS could help reduce the risks associated with endogamy and consanguinity and allow for a decrease in the number of children born with genetic conditions. There were also some common concerns about CS that were brought up by participants, including the chance of stigma against carriers, changing the nature of romantic relationships, and leading to missed opportunities.

There were several factors identified by participants as being highly influential on attitudes toward CS among themselves and other community members. These included how strongly an individual or community feels about following the traditions of the Hutterite community, as well as whether one has any experience with genetic conditions. Participants felt like community members who were older or had attained a lower level of education may be more conservative and hesitant to adopt technologies such as CS. Also, they felt that having personal experience with individuals affected with genetic conditions was essential for community members to feel that CS could be valuable.

Participants identified many ways that CS results might impact them, both emotionally, and in terms of the decisions they make. Many participants felt that finding out they were carriers would provoke some level of anxiety or disappointment, either about what community members would think, or having to choose between raising a child with a disability or acting on the results in some way. There were a variety of ways that participants would use results from CS which ranged from preparing for the birth of an affected child, to using the results in their choice of a partner, to choosing to adopt or have a smaller family. In many cases participants were uncertain what they would do and felt that it would depend on the specific result. Most felt strongly that they would not consider termination of an affected pregnancy, although the sentiment was not universal.

The process of making decisions about CS involved many layers and factors to take into consideration. Many participants identified that they had specific motivations for being interested in CS, including personality characteristics and a family history which put them at higher risk of being carriers. When deciding about the best time to pursue CS, participants reflected on how they would want to use the results from the test. Since this was highly variable among study participants, their responses about the best time to have the test also varied. The characteristics of their individual home communities was also a factor that participants considered in the decision-making process. For some individuals, the decision to have CS would require a discussion with their community leaders, and for others, they felt they had more autonomy in the decision.

Finally, participants provided their preferences and recommendations with respect to how the test can be offered, and education delivered, in a way that aligns with their values and the unique characteristics of this community. Most participants preferred to access CS through their PCPs because they were familiar. Also, while the participants in this study felt they would want their results for all the conditions on the panel, they recognized it might be valuable to offer choice. They also felt that education about CS could be included in the regular curriculum in school, and that any educational materials provided to the community needed to be tailored and in simple language, to help decrease fear or hesitancy. Overall participants provided many suggestions for how counselling and education can be tailored to be more sensitive to the specific needs of the community.

The participants in this component of the study came from many different communities, age groups, life stages, and levels of experience with genetic conditions. One factor that they all had in common was their willingness to talk about CS, which many felt was a controversial topic within the larger Hutterite community. It is likely that the people who volunteered to participate in these interviews were inherently more open to this technology than many others in the community. This is evidenced by the majority of participants indicating that they wanted to have the test done. Several also talked about how it was important to them to show others in the community that CS is not something to fear. Therefore, the views and opinions presented

in this section should not be interpreted as representative of the Hutterite community as a whole.

Despite the interview participants all having this willingness to participate in common, the results from this section demonstrate that this community is far from homogenous. Participants had a wide range of responses to almost every question presented during the interviews, showing that while they all come from the same community and culture, each is an individual with differing values and thought processes when it comes to deciding whether to pursue CS.

CHAPTER 5. INTEGRATION OF QUANTITATIVE & QUALITATIVE FINDINGS

Results from the quantitative and qualitative components of this study shed light on the perspectives of the Manitoban Hutterite community towards population-based CS. In some cases, the qualitative findings provided context and corroboration of the survey and chart review findings, but in others the datasets were discrepant. In this section the similarities and differences observed among the study phases will be reviewed.

5.1 Perceptions of carrier screening

Survey data showed that the majority of participants felt CS would be helpful. Most agreed that they would want to be reassured about whether they were at risk of having a child with a genetic condition, and most also agreed that CS could help the community. Interview participants provided context for these responses. They frequently discussed how CS would enable individuals and families to be reassured if they were not at risk of having an affected child. Several also felt they would even be reassured if they found out they *were* at risk, because it would allow them to make informed decisions. They felt it was important to be prepared, and that CS would provide that opportunity. Several interview participants identified ways that CS could help the community, including that it could help reduce the number of infants born with genetic conditions which they felt resulted from practices of endogamy and consanguinity.

5.2 Factors influencing perceptions of (and interest in) carrier screening

Most survey and interview participants were interested in CS for themselves, with 80% and 12/13 participants from the survey and interview phases, respectively, expressing their desire to have the test done. However, interview participants frequently brought up that CS is considered a controversial topic in the community and shared that many older and more conservative community members feel that it should not be available because it goes against tradition or is at odds with their religion. Due to the qualitative nature of the interview process,

it is unclear whether the individuals who have these concerns about CS represent a large proportion of the population, but survey data showed that 13 respondents (14%) had negative attitudes toward CS (composite attitude scores less than 3).

There were few survey participants who stated that they did not know anyone affected with a genetic condition (n=7), but these individuals showed a non-significant trend toward having more negative attitudes toward CS than those who did know someone. This finding was consistent with interview data. Many participants stated that their experiences with affected family members or friends prompted their interest in CS, and the single participant that was unsure whether he knew anyone affected stated “it really only hits home when you have a real close relative” (P06). Several participants indicated that having a family history of a genetic condition was their primary motivation for wanting to pursue CS.

Results from the chart review component of this study also support the finding that people in the Hutterite community may not be interested in CS unless they have a known family history of a genetic condition. Fourteen out of 18 individuals who underwent CS over the period it was previously available had a known family or personal history of one or more of the conditions on the panel. The remaining 4 individuals were two couples whose child was being evaluated for one of the conditions. Overall, these results from all 3 components of the study suggest that individuals in the Hutterite community may only feel that CS would be useful for them if they know that they are at risk due to their family history. However, survey data showed that despite having a family history, many individuals did not think it was highly likely they were carriers.

5.3 Making decisions about carrier screening

Both the qualitative and quantitative components of the study showed that there was substantial variability in the way that CS would be incorporated into reproductive decision making. Out of the survey participants who indicated they would want CS, the majority felt that they would change their decisions in some way if they learned they were at risk of having a child with a genetic condition. A smaller proportion of participants indicated they wanted to

know their risk, but that it would not change their plans. These results were supported by responses from interview participants, several of whom felt that the opportunity to prepare for having an affected child would be valuable in itself.

Survey participants who had a close relative who was affected with a genetic condition were significantly more likely to pursue CS just for information or preparation, as evidenced by a larger proportion indicating they would not base any reproductive decisions on the information. A possible explanation provided by the qualitative results is that when participants were involved in the care of children with severe conditions, they often reflected on the value and joy that these individuals brought to their lives, in addition to the challenges. On the other hand, participants who were more removed from the lives of affected individuals, such as those who were less closely related or unrelated to them, were more likely to reflect on the challenges. Those survey participants who were intimately involved in raising children with complex medical needs may have felt the same, in the sense that they see the value that people who are different bring to their family's lives, rather than only the challenges.

Of the individuals who indicated they would use CS results in their decision making, both the qualitative and quantitative findings support that very few Hutterite individuals would consider termination of an affected pregnancy. Similarly, most participants felt that assisted reproductive technologies were not something they would consider. Some interview participants struggled to identify exactly why ART was problematic, but others described how it was too invasive, too far from tradition, or in practice, similar to termination of pregnancy. Some indicated that they would consider prenatal testing if they knew they were at risk, although neither the survey nor interview preamble provided detailed information about the risks associated with invasive prenatal diagnostic testing. One participant indicated that she would want to have prenatal testing "if she knew it wouldn't hurt the baby" (P05), suggesting that fewer individuals may pursue these testing options if they went through the consenting process and learned of the risks.

Many interview participants, both prospectively and retrospectively, felt that they would consider CS results/genetic compatibility when choosing a partner. Similarly, about 42% of

survey participants indicated they would consider using the results in this way. However, there were several individuals who recognized that this would be a challenge because marriages are based on love in Hutterite society, and it would be an extremely difficult decision to back out of a relationship based on a genetic test. When asked what she thought about using carrier results in this way, one participant (P13) said most would probably not consider it, since part of their belief system includes that God directs their path toward the right partner.

The most common action that both survey and interview participants would take if they determined they were at risk of having a child affected with a genetic condition was to change their family planning decisions. The majority of survey participants agreed that they would make different decisions regarding their family planning and most also agreed that they would choose to not have (more) children if they were at risk of having an affected child. Qualitative data provided additional explanation of these results in the sense that many participants said they would choose to adopt. Additionally, more than one participant shared that they were concerned about the response of the community if they were to knowingly have a child affected with a condition after CS showed they were at risk. This suggests that for some people, there may be an element of perceived or real community pressure to prevent the birth of an affected child for those whose carrier results indicate they are at risk.

5.4 Preferences & recommendations

Participants in both phases of the study preferred to be able to access CS through their PCPs. Thematic analysis of survey responses in the open text field where participants could indicate the reason for their preference suggested that participants felt they would be more comfortable with a provider that was familiar. Additionally, they felt that it would be more convenient and accessible. Several interview participants raised another important benefit of access through PCPs, which was that they would not need to get permission from community leadership to attend an appointment with their regular doctor. If accessing CS through the genetics department required travel to Winnipeg, they shared that they would need to arrange travel and if their community leader did not approve of CS, they may not be permitted to go.

Therefore, accessing CS through their PCP would not only be more comfortable and convenient, but it would also protect their confidentiality.

Across both phases of the study, participants showed a preference for receiving their carrier results for all the conditions on the panel rather than just a subset. Eighty percent of survey participants preferred the full panel, with the other 20% indicating they would prefer to know their results for a subset of the conditions. Interview results were consistent with this pattern, in the sense that most participants felt that they would want the full panel. Common responses from participants who felt this way were variations of "if I'm going to do [CS] for some conditions, I might as well do it for all of them, it makes no difference". However, some survey and interview participants indicated that they would want to be able to choose which categories were included in their screening test. Of the various categories presented, most survey participants were interested in the conditions which could benefit from early detection and treatment. A smaller proportion indicated they would want to know if they were carriers for severe and untreatable childhood-onset conditions, and fewer still were interested in adult-onset conditions. While most interview participants were interested in the full panel, several expressed the opinion that offering choice of disease categories to individuals and couples may increase acceptance among community members, since they felt that anxiety may increase along with the size of the panel.

To summarize, the quantitative and qualitative components of the study explored answers to related questions. In combination these datasets provided both an overview of viewpoints in the community as well as in-depth contextual understanding of where these viewpoints might be coming from. These results show that decision making surrounding CS is complex, with individuals taking individual-level, family-level, and community-level factors into account when making the decision about whether to pursue CS. Finally, the preferences and recommendations put forth by participants in this study provide many ways in which this population-based CS test can be tailored to the community.

CHAPTER 6. DISCUSSION

6.1 Overview of study

The overarching goal of this research was to ensure the provision of carrier screening for Hutterites is tailored to the community. Tailoring of such initiatives is essential because it allows the CS test to be presented in a way that the target population can relate to, while addressing common misconceptions or concerns, which allows individuals in the community to make a fully informed decision about whether to be screened (Achterbergh et al., 2007; Holtkamp et al., 2017). To identify ways to tailor the delivery of CS for the Hutterite community, we aimed to answer three questions. First, we wanted to get a sense of the attitudes of Hutterites toward this type of test and the factors that influence these attitudes, as well as what Hutterites feel are the goals and benefits/risks of CS. We also wanted to understand the decision-making process – both in terms of how individuals decide whether to pursue CS, and what kinds of decisions they would make based on the results. Finally, we wanted to hear from Hutterites about their own preferences and recommendations regarding how design of the panel, service delivery, and educational efforts can be adapted to best suit the community.

6.2 Tailoring delivery and education to community beliefs

Our results show that Hutterite society is unique in many ways, suggesting that direct application of the various described approaches to CS (chapter 1.2) might be problematic. However, our results provide a number of insights into ways CS in the Hutterite community can be approached to ensure harmony between the screening test and the needs and values of the community.

We found that the goals of CS brought up by Hutterites aligned with the “reproductive autonomy” perspective outlined in section 1.1, in the sense that CS allows parents to choose between preparing for the birth of a child affected with a condition or avoiding having one by choosing not to have children. They perceived CS as beneficial regardless of whether the results are acted upon, showing that “prevention” is not the main goal of CS from their perspective.

This is consistent with predominant views on the goals of CS in Western cultures (De Wert et al., 2012; Henneman et al., 2016) and is therefore also consistent with the genetic counselling approach that is already taken toward CS in Canada.

The risks of CS most commonly brought up by participants pertained to disruptions in the social cohesion and typical practices of the community. Stigma or ostracism of carriers, judgement by Hutterites who disagree with one's decision to be screened or decisions based on the results, as well as concerns about the sanctity of marriage being reduced to genetic compatibility, were all brought up as concerns. Our results also highlighted that there may be a segment of the population that is distrustful or suspicious of outside organizations and may feel that CS represents a threat to their way of life. These concerns highlight the importance of emphasizing confidentiality and choice in educational materials, presentations, and pre-test counselling.

Specifically, it should be emphasized that CS is available and is meant to be a helpful tool for those who would value information, but that it would never be forced on anyone. Another way that choice and autonomy can be emphasized is by allowing people to have choice in the conditions that they are screened for as was recommended by the ACMG position statement on preconception CS (Grody et al., 2013). While most participants were interested in the full panel, there were a subset that preferred to only learn their carrier status for certain categories of conditions. Allowing for some choice, rather than a one-size-fits-all approach to the panel, may have the effect of increasing the sense of autonomy in those interested in screening who have reservations.

An unexpected finding that bears attention is the way that the accessibility of the CS panel has a direct impact on confidentiality. In many colonies, travelling to Winnipeg for an in-person appointment in the genetics clinic, or even to the local health centre to access telehealth services, would require permission from colony leadership and an explanation of the reason for the appointment. Some participants described how they were not sure their colony leadership would approve of such a trip. Accessing CS through their primary care providers was preferred by many participants for this reason, in addition to an increased level of trust and comfort with primary care. Currently, the molecular diagnostics laboratory in Manitoba requires all CS and

testing to be ordered through genetics professionals and to be done through a blood draw. The feasibility of training and enabling primary care providers to offer CS is unclear and would require collaboration and significant resources.

However, there are other potential strategies to improve accessibility of CS for Hutterites. For example, the COVID-19 pandemic has necessitated widespread use of telephone counselling and studies have shown that this modality has similar outcomes and is acceptable to patients (Shannon et al., 2020). Providing pre-and post-test counselling over the phone may eliminate the need for travel in those cases where it is a barrier. Another strategy for improving accessibility is to transition from the requirement of a blood sample and obtain DNA through a buccal swab or saliva sample which can be sent in the mail. We feel that enabling Hutterites to access CS without having to travel from their colony is a critical adaptation that would improve accessibility and protect confidentiality.

With respect to the timing of CS, our study participants generally opposed termination of pregnancy. Many also felt that CS during the prenatal period would not be useful because of their beliefs about termination of pregnancy, because by that point, there would be no way to act on a high-risk result. These findings are consistent with prior studies conducted with Hutterites (Miller & Schwartz, 1992). Accordingly, offering CS to Hutterites prior to pregnancy may make the most sense for this population, in contrast with the typical practice of prenatal screening for Tay-Sachs disease in the non-Orthodox Jewish population (Scott et al., 2010). Beyond this distinction, there was variability in how our study participants would want to use CS results, suggesting there is no singular “best time” to offer CS to Hutterites. Therefore, trying to increase awareness of the CS test early in life would enable Hutterites to make the decision at a time that is right for them.

Education about human genetics is already a part of the high school curriculum, and many participants talked about how they learned of some of the specific recessive conditions that affect Hutterites during these lessons. Providing education about the CS test during this part of the curriculum would be one way to increase awareness of its availability, and the results of this study suggest this would be acceptable to the population. As discussed in chapter 1.3.3,

providing education about CS during high school not only increases awareness of the availability of the test, it has also been shown to decrease stigma against carriers (Barlow-Stewart et al., 2003; Frumkin & Zlotogora, 2008). As stigma was one of the main concerns that participants had about CS, engaging with the Hutterite community's educators to support incorporation of information about CS could benefit the community in multiple ways – both by increasing awareness and decreasing stigma against carriers.

6.3 Remembering that individuals live within communities

In the previous section we described ways that the CS test could be tailored to the community's needs and values as outlined by participants in this study. However, we do not mean to imply that the generalizations made in the previous section apply to all Hutterites. For example, we described how most Hutterites in our study as well as previous research are opposed to termination. Nonetheless there was one out of our 13 interview participants who was open to the idea of pregnancy termination in certain circumstances. While this participant may be the exception rather than the rule, we feel it is important to highlight that Hutterites are not necessarily of a singular mind on the issue of termination despite the cultural norm. This is one example of many which illustrated the range of beliefs within this community. In line with current perspectives on cultural humility in medicine, providers offering care to Hutterite patients should take care not to make assumptions based on the cultural background of their patients (Yeager & Bauer-Wu, 2013).

Our results show that many in the Hutterite community have positive attitudes toward CS and are interested in learning their carrier status, which is consistent with previous studies. Anderson et al (2014) found that when offered the option of learning their carrier status for 14 autosomal recessive conditions, 80% of Hutterites who had attended an educational town hall on the topic accepted the offer. Similarly, 80% of participants in our study indicated they would be interested in CS. However, our results also suggest that there are a wide range of strong opinions on the use of genetic technologies among Hutterites, which were only indirectly captured through our conversations with participants. Both our study and Anderson et al (2014) were limited by the self-selected participant pool resulting from convenience sampling. We feel

it is likely, based on our interview experiences as well as informal discussions with community members, that Hutterites who have strong feelings against the use of CS would be less likely to participate in this type of research or attend town halls on the topic.

We found that Hutterites who were married tended to have more negative attitudes toward CS than those who were single. At first glance, we thought that this may be explained by our married participants being older (thus possibly more conservative/traditional) or feeling like carrier information may be less relevant (if they had already completed their families). However, there were no differences in attitudes among participants based on age or childbearing intention – those who were married felt the same regardless of age or whether they were having more children or not, which makes these explanations less likely. This result was unexpected because previous studies have shown that people who are planning a pregnancy have more positive attitudes toward CS due to the increase in perceived relevance of the results to their current situation (Archibald & McClaren, 2012).

A possible explanation for our results in the context of community values is that single individuals perceive an open future; they have not yet committed to a partner and have not made concrete plans to build a family (even though they may wish to in the future). There are many options open to them with respect to how they could use the results from CS. In contrast, participants who are already married have a clear image in their mind about when and with whom they will have children. As previously discussed, the results of our study suggest that having a family is perceived by many in the community as integral to their identity as Hutterites. The commitment that married Hutterites have made to building their families, combined with the fundamental opposition to abortion shared by many, could result in married Hutterites viewing CS as unwanted interference in their life plans. Future research is needed to further evaluate this hypothesis.

Regardless, our results show that even those who are committed to having children, and those whose decision would not change based on a high-risk result, can still benefit from CS because it could give them the chance to prepare. Educational materials or counselling highlighting that some might find preparation in and of itself to be helpful, rather than simply focusing on the

benefits of avoiding the birth of an affected child, may help to improve acceptability of the CS test among Hutterites who are already married.

The factors influencing interest in CS among Hutterites are consistent with the health belief model (HBM). The HBM is a theory in health psychology which posits that the likelihood of someone performing a health behaviour is influenced by the perceived benefits and risks of performing the behaviour, their susceptibility to the outcome of not performing the behaviour, and the severity of that outcome (Rosenstock, 1974). Hutterites in our study who stated they would want the CS test scored higher in the domain of perceived benefits and perceived susceptibility, and lower in perceived risks, compared with those who were not interested. These results suggest that similar to other preventative health measures, the health belief model can be applied to not only predict use of CS among Hutterites, but also to develop targeted educational materials addressing the common perceived benefits and risks identified by participants which were reviewed in the last section.

There have been few studies investigating the applicability of the HBM in collectivist cultures, and it was unclear whether Hutterites would be as motivated by personal benefits and susceptibility as traditional Western societies are, given their practice of *gelassenheit* (self-sacrifice/community before the individual). Our results show that while HBM factors are predictive of interest in CS in the Hutterite community, the benefits and risks that are salient to Hutterites go beyond the personal impact of CS and extend to how CS can help or hinder the community as a whole. It follows that educational materials about CS can be tailored for Hutterites by highlighting the potential benefits and addressing the potential risks that apply to the greater community, rather than solely the individual.

Other aspects of the HBM were also reflected in our results. According to the HBM, in addition to the four factors identified above, the likelihood of performing a health behaviour is also dependent on individual sociopsychological characteristics (e.g. personality, culture) and cues to action (e.g. media campaigns, experiences with illness in self or others) (Janz & Becker, 1984). Our results show that Hutterites who are interested in CS may have more of an "information seeker" personality type and be those who are less conservative or less strictly

traditional in their beliefs. Additionally, a major predictor of interest in CS in our study was whether individuals had experience with genetic conditions, either in family members or people they were not related to. For individuals who were familiar with the challenges of having a genetic condition or caring for someone with one, these experiences provided a powerful cue to action, influencing their desire to pursue CS.

The connection between lived experience and interest in CS speaks to the way experiential knowledge impacts whether screening is perceived as personally relevant to Hutterites. Exploration of decision making about screening in other populations shows that experiential knowledge is a consistently important predictor of screening behaviour (Archibald & McClaren, 2012). However within the Hutterite community, one could argue that since the majority are going to be carriers for at least one of the conditions on the CS panel (Anderson et al., 2014; Chong et al., 2012), the sense of decreased personal relevance of CS is preventing individuals from making a truly informed decision about screening. This could be addressed through educational efforts that aim to provide a sense of experiential knowledge for those who do not already have it, by including stories or vignettes of Hutterites affected with genetic conditions, those who have had affected children, or someone who has gone through CS (Archibald & McClaren, 2012). Participants in this study also highlighted the importance of having stories that come from other Hutterites so that community members can better relate to the information.

Experiential knowledge of genetic conditions also changed the way that Hutterites in our study would use the results of CS. Those with a close family member affected with one of the conditions were less likely to want to avoid having an affected child and more likely to want to use the information to prepare. This effect of experiential knowledge on reproductive decision making has been consistently shown in the literature in many populations and across many types of disabilities (Boardman et al., 2018; Friedman & Owen, 2016). A study exploring attitudes toward CS for spinal muscular atrophy (SMA) showed that family members of affected individuals were unlikely to take action to avoid having a similarly affected child because of the personal value they placed on the lives of their SMA-affected relatives. In contrast, participants

from the general population were more likely to focus on the "worst-case scenario" and try to avoid that through screening and prenatal diagnosis (Boardman et al., 2018).

Similarly, participants in our study who had been involved in the care of a child with a disability described the benefits of their relationship with the affected individual, in that the relationships brought them joy, helped them to see beauty in the fragility of life, and made them more accepting of differences. The genetic counselling process often involves an exploration of how an individuals prior experiences influence how they might use the results of a genetic test (McCarthy Veach, 2018). These results highlight that this approach might be useful in facilitating the decision-making process among Hutterites who are considering CS.

6.4 Specific educational needs

Uncovering informational gaps or educational needs in the Hutterite community was not an initial aim of this study. However, through the process of conducting this research, we identified some commonly held misconceptions among Hutterites that should be addressed in future engagement or educational efforts in the community. These misunderstandings are certainly not unique to the Hutterite population; they are quite common among the general public and concern the details of autosomal recessive inheritance and risks.

Results from all three phases of our study showed that many people felt they were not susceptible to being a carrier if they did not have any family members affected with a recessive condition. However, the nature of recessive disorders is such that pathogenic variants can segregate within a family for many generations before a carrier partners with a carrier of the same disorder and has an affected child. Therefore, having a negative family history does not mean that one is not susceptible to being a carrier or having a child with a genetic condition. Prior research in the general population as well as our personal experiences working with the public in clinical genetics indicate that the conflation of family history and recessive disease risk is extremely common (Boardman et al., 2018; Nijmeijer et al., 2019).

Additionally, the genetic characteristics of the Hutterite population, namely the smaller number of deleterious variants circulating at high carrier frequencies due to founder effect, put them at

even higher risk of having children affected with recessive disorders than those in the general population. Previous studies that have screened Schmiedeleut Hutterites in South Dakota for 14 recessive disorders found that between 67-78% of Hutterites tested were carriers for at least one of the 14 conditions and many were carriers for more than one condition (Anderson et al., 2014; Chong et al., 2012). Given that the CS panel currently under development screens for twice the number of conditions, it is likely that an even greater proportion of individuals would be identified as carriers using this panel. Educational efforts should therefore include information that anyone could be a carrier. The message that "everyone is a carrier for something" may serve both to increase awareness of personal susceptibility, and to decrease stigma against carriers, as was shown in Barlow & Stewart (2003).

Another area of need identified in our study surrounds the idea that consanguineous unions are the primary cause of the increased prevalence of recessive disorders among Hutterites, and further, that a couple that are both carriers for the same condition must be consanguineous. Some comments made by participants in this study were concerning in the sense that they conveyed stigma or judgement toward people who marry their second, third, or fourth cousins. In reality, the small number of founders combined with endogamy practices of Hutterites blur the line between who is related and who is not, because any two individuals are likely to be related in multiple ways even when they do not have a *recent* common ancestor. Furthermore, with carrier frequencies in the community for some conditions reaching as high as 1 in 7 individuals (Chong et al., 2012), a couple being second or third cousins does not substantially increase their risk of having an affected child for one of these conditions over any two random Hutterites.

Our results also show that it can be a challenge for Hutterites to find prospective partners who lack any common ancestors in the past several generations. Additionally, some do not realize they are distantly related until after making a commitment. Therefore, educational materials for this community should attempt to clarify the reasons behind the increased prevalence of recessive disorders on the CS panel. Over time, accurate education about carrier frequencies

and the implications of founder effect may result in decreased stigma and blame toward those who knowingly or unknowingly engage in consanguineous unions.

6.5 Other findings

An incidental but nonetheless interesting insight provided by our study was a glimpse into how genetic conditions impact families within this highly collectivist society. Caring for a child with a disability or rare disorder is inherently stressful for families. A 2019 survey by the Canadian Organization for Rare Disorders (CORD) found that among caregivers of children with rare disorders in the Canadian general population, 87% experienced financial hardship (with 71% having to either quit their job or reduce working hours substantially and 63% taking on added debt) due to their caregiving responsibilities. Additionally, 75% reported experiencing social isolation from friends and family (Canadian Organization for Rare Disorders, 2019). In contrast, our results show that the challenges of caregiving in the Hutterite community pertained to disruptions and limitations in the expected or desired activities that individuals could pursue- participants described loss of time as the main challenge. Certainly, limitations in travel experienced by caregivers in the Hutterite community can decrease social connection with others outside of one's home community. However, the unique characteristics of Hutterite society, namely living closely with community members who are willing to help, and not having to worry about personal finances, make the experiences of caregivers in the Hutterite community quite different than others in the Canadian population. Financial worries and social isolation were notably absent from the challenges described by caregivers in our study.

6.6 Summary of recommendations

The previous sections have described many ways that CS can be tailored to the unique characteristics and needs of the Hutterite community. The following recommendations pertain to important organizational, educational, and counselling factors that will improve awareness, accessibility, and acceptability of CS among the members of this community.

Organizational

1. Offer choice in the categories of conditions being screened, rather than a one-size-fits-all CS approach. Some Hutterites prefer to only learn about their carrier status for conditions that have an immediate impact. Offering choice is aligned with the principle of autonomy and recommended by the ACMG (Grody et al., 2013).

2. Make carrier screening available to individuals or couples at any stage of life to allow for maximal opportunities for use of CS results in decision making.

3. Improve accessibility of CS by finding ways to offer screening that does not require travel, for example telephone counselling and saliva samples. Accessibility is directly linked to confidentiality in the Hutterite community as reasons for travel require disclosure to management.

Educational

4. Communication about CS should address the goals and benefits of CS as perceived by the community. The goal of CS is to enhance reproductive autonomy - providing information that people can choose to act on or not. The benefits include giving time for a couple to prepare or giving them a chance to make alternate family planning decisions.

5. Educational efforts should directly address the risks posed by the community. Stigma can be reduced by increasing awareness that everyone is a carrier for something, as well as by protecting confidentiality.

6. Education should also address common misconceptions, including that people who are carriers for recessive conditions will often have a negative family history, and consanguinity is not the primary driver for the increased prevalence of recessive conditions in the community.

7. Engage with the Hutterite community and particularly educators/leadership to ensure accurate information about CS is provided if they opt to include the topic during the high school curriculum.

8. Provide surrogate experiential knowledge of genetic conditions and CS to those who do not have personal experience, by including stories from Hutterites impacted by genetic conditions.

Counselling

9. Recognize that each person is an individual and despite the cultural norms and generalizations identified in this study, not every Hutterite will make decisions in the same way.

10. Facilitate exploration into the ways that experiential knowledge of genetic conditions impacts each person's decision-making process to empower patients.

6.7 Limitations of this study

This study has several limitations, mostly pertaining to the limited generalizability of our findings. Our participant population was largely self-selected, due to the necessity of the convenience sampling approach we used. Our results suggest that some participants who volunteered for interviews were active proponents of CS; for example, several shared that they would want to be screened to raise awareness and show others that screening should not be feared. Additionally, we found a discrepancy between interviewee's perceptions of attitudes toward CS among other community members, and the survey result that showed positive attitudes fairly consistently. Taken together these results show that our study population may have a more positive outlook toward CS than the community as a whole. Therefore, our findings should not be interpreted as being representative of the entire Manitoba Hutterite population.

There are also well-described differences in conservatism between Hutterites of different leute, and thus in different provinces of Canada (Katz & Lehr, 2013). Schmeideleut Hutterites tend to be more liberal than those of Lehrerleut and Dariusleut. A review of the literature also indicates that most studies pertaining to attitudes toward genetic testing with Hutterites have been conducted with Schmiedeleut populations (Anderson et al., 2014; Baumberger & Yutrzenka, 2018; Gemmell et al., 2017; Miller & Schwartz, 1992). The results and recommendations presented in this study may therefore not be applicable to Hutterites in different regions of Canada. Further research is required to understand the perspectives of different leute to the topics explored in this study.

The COVID-19 pandemic necessitated significant changes to our recruitment and data collection strategies which likely affected the diversity of respondents as well as the results of this study. For example, the initial recruitment plan included the student researcher visiting participating colonies to describe the study and invite participants. However, recruitment was ultimately conducted through a variety of different methods, which were likely not as effective at explaining the study as a face-to-face visit may have been. Further, the previous experiences of researchers who have worked with Hutterites in the past have suggested that trust is an extremely important prerequisite for engagement with the Hutterite population, and the lack of personal contact required during this time prevented the relationship- and trust-building visits that would have otherwise been possible. Finally, all interviews were conducted over the phone rather than providing an in-person option for participants. Phone interviews are inherently less rich in content and context than in-person interviews due to the diminished ability of the researcher to pick up on non-verbal communication. Therefore, it is likely that some participants' responses during the interviews were less rich and/or contextual than they may have been if an in-person interview had been possible.

6.7 Future research directions

Several avenues for further research were illuminated through this study. As described in the previous section, we did not capture the perspectives of Hutterites who have significant reservations about CS in our sample. Research in other groups has shown that the reasons for

non-participation in genetic screening are often different than simply the absence of reasons cited by those who do participate (Chen & Goodson, 2007). While we indirectly heard from participants that many who object do so for religious reasons, future research should attempt to directly engage with this segment of the community to more clearly understand the factors involved in non-participation.

In this study we explored the factors that influence interest in CS. However, there is strong evidence that suggests that interest or intent to participate in screening or testing is not highly correlated with actual screening behaviours (Anderson et al., 2014; Baig et al., 2016; Lakeman et al., 2009). As the CS panel is still under development, an exploration of factors that influence actual participation in CS was not possible for this project. We recommend a follow-up study exploring factors associated with CS participation within the first few years of implementation to further tailor the provision of CS for the Hutterite community.

There was a preference among participants in this study for accessing CS through primary care providers rather than genetics professionals. The feasibility of this approach is currently unclear because it would require collaboration and buy-in from multiple stakeholders including primary care providers, laboratory personnel, and genetics professionals. Future research should explore the feasibility of this approach by engaging with all stakeholders to determine educational and organizational needs and willingness of all involved.

CHAPTER 7. CONCLUSION

Cultural sensitivity in medicine, and genetics in particular, is a critical component of empowering patients of varied backgrounds to make fully informed decisions about their own health and that of their families. In this study we identified several ways that the provision of CS can be tailored for the Hutterite community in Manitoba to ensure the care they receive is attuned to their unique cultural characteristics. Through a combination of quantitative and qualitative methods we explored Hutterites' perceptions of the utility, benefits, and risks of CS, and elicited their input as to how the upcoming CS panel and related educational efforts should be designed to best suit their community.

These results from this study will enable providers offering CS to anticipate the needs of their Hutterite patients and tailor their approach appropriately. We showed that while there is substantial support in the community for a comprehensive CS panel, there are also individuals who have reservations about its use. Some Hutterites have concerns about CS interfering with social cohesion and cultural norms, as well as leading to anxiety and disappointment. However at least for the participants in this study, they felt the benefits to families and the greater community that screening could provide outweighed these risks. We showed that within this communal society, making decisions about CS is a complex process requiring consideration of multiple individual-level and community-level factors. The decision of what to do with results is equally complex and influenced by an individual's life stage and life experiences.

The recommendations provided herein supply a framework by which to develop informational resources and education sessions using the perspectives and language of the community. Engaging with interested educators or organizations like Hutterite Health to empower them to provide information to community members is also recommended. Evidence from past CS initiatives indicates that tailoring information and having grassroots support is beneficial because it makes the information relatable to the community and increases acceptability. The CS panel can also be tailored from an organizational perspective by providing some choice of what conditions are included, which will promote autonomy in individuals seeking out CS.

Additionally, accessibility can be improved and confidentiality protected by continuing to offer telephone-based genetic counselling into the future, as well as by offering alternative sample collection methods such as buccal swabs or saliva samples which can be mailed. The role of the primary care provider in overseeing CS should be further explored.

The information and recommendations provided in this study are a first step toward providing a CS test that aligns with the values and perspectives of individuals in the Hutterite community. However, the coevolution of a technology and the culture it was designed for, which is required for a new health practice or technology to be truly tailored, is a process which does not happen overnight. Continued engagement with the community as the CS panel begins to be offered will ensure this process is optimized to the fullest extent possible.

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APPENDIX A. Disorders on the carrier screening panel

Note: Most of the disorders described below follow autosomal recessive inheritance, except for 2 X-linked conditions which are noted. Sources are OMIM and GeneReviews unless otherwise cited.

Alpha-mannosidase deficiency [MIM:248500]

Alpha-mannosidase deficiency is a lysosomal storage disorder caused by mutations in the MAN2B1 gene, characterized by lysosomal accumulation of mannose-containing oligosaccharides. The clinical features are variable and resemble other lysosomal storage disorders, including immune deficiency, skeletal abnormalities known as dysostosis multiplex, dysmorphic features, and progressive neurological dysfunction with poor long-term prognosis. Age at onset and severity of presentation are also variable and form the basis for classification of subtypes of alpha-mannosidase deficiency. The carrier frequency of the MAN2B1 mutation c.2248C>T in the Hutterite population has not been determined.

Complete androgen insensitivity syndrome [MIM: 300068]

Androgen insensitivity is an X-linked disorder of sexual development caused by mutations in the androgen receptor gene (AR). When individuals with a 46XY karyotype have particular pathogenic mutations in AR, the body cannot respond to the androgens testosterone and DHT, which are essential for the development of male external genitalia and secondary sexual characteristics. Patients present as phenotypically female, although with a blind vagina and absent uterus, primary amenorrhea, absent pubic and axillary hair, and have abdominal or inguinal testes. The testicles are traditionally surgically removed to reduce the risk of cancer, although this is becoming controversial as the risk is quite low. The carrier frequency of the c.2033T>C mutation among Hutterites is unknown, although all published affected individuals have been part of a large Schmeideleut kindred (Belsham et al., 1995).

Autosomal recessive intellectual disability [MIM: 614020]

Biallelic mutations in the TECR gene are associated with nonsyndromic intellectual disability.

Patients with this condition have developmental delay from birth, minimal ability to read and write, and are generally able to work jobs requiring manual labour but have difficulty with fine motor function. The carrier frequency of the c.545C>T mutation in TECR is estimated to be 1/14.5 in S-leut Hutterites (Chong et al., 2012) and this condition has not been observed in any other population.

Arrhythmogenic right ventricular cardiomyopathy (ARVC) type 11 [MIM:610476]

Biallelic mutations in the DSC2 gene cause progressive fibrofatty infiltration of the right ventricle which impairs electrical conduction in the heart and can result in arrhythmias and sudden death. Management of patients with ARVC involves monitoring progression of the cardiomyopathy with echocardiogram and cardiac MRI, with implantation of an ICD if the cardiomyopathy is severe. While DSC2-associated ARVC is typically associated with autosomal dominant inheritance, the c.1660C>T mutation found at a carrier frequency of 1/11 in the Hutterite population follows autosomal recessive inheritance (Gerull Brenda et al., 2013).

Bardet-Biedl syndrome type 2 [MIM:615981]

Bardet-Biedl syndrome type 2 (BBS2) is a condition caused by biallelic mutations in the BBS2 gene, resulting in defects in protein trafficking in cilia which are essential for the function of a variety of cell types throughout development. BBS2 is clinically characterized by variable intellectual disability and occasionally variable congenital anomalies including postaxial polydactyly, retinitis pigmentosa, renal abnormalities, hypogonadism, short stature, and obesity. Management of Bardet-Biedl syndrome involves treating the manifestations and is largely supportive. The carrier frequency of the c.472-2A>G mutation in BBS2 is 1/36 in S-leut Hutterites (Chong et al., 2012).

Bowen-Conradi syndrome [MIM:211180]

Formerly known as “Hutterite syndrome”, Bowen-Conradi syndrome (BCS) is caused by homozygous mutations in the EMG1 gene which is essential for ribosomal function. Deficiency in the EMG1 protein is thought to impair cell growth and proliferation (Armistead et al., 2015). Clinical features of BCS include low birth weight, slow growth, microcephaly, multiple contractures, feeding difficulties, absence of developmental progress, and usually death in the

first few months of life. There is no treatment available for Bowen-Conradi syndrome. The carrier frequency of the c.257A>G mutation in Hutterites is approximately 1/10 in all three leuts (Flanagan et al., 2012) and has not been observed in any other population.

Beaulieu-Boycott-Innes syndrome (BBIS) [MIM:613680]

BBIS is a neurodevelopmental disorder caused by biallelic mutations in the THOC6 gene which encodes a protein involved in mRNA processing (Beaulieu et al., 2013). Patients present with moderate to severe intellectual disability, developmental delay, microcephaly, dysmorphic features, and variable congenital anomalies including cardiac, renal, and genital defects. The carrier frequency of the c.136G>A THOC6 mutation in Hutterites has not been determined.

Combined pituitary hormone deficiency type 2 (CPHD2) [MIM: 262600]

CPHD2 is caused by biallelic mutations in the PROP1 gene and is characterized by ADD GENE FUNCTION variable and progressive deficiency of several hormones released by the anterior pituitary, including growth hormone (GH), thyroid-stimulating hormone, prolactin, sex hormones, and others (Böttner et al., 2004). Patients with this condition have a normal birth weight and length but decreased height velocity and height 3-4 SD below the mean for age (average adult height 109-134 cm). Eventually most patients develop adrenal insufficiency. Management of CPHD2 involves hormone replacement therapy, with GH often administered in childhood, sex hormones at pubertal age, and hydrocortisone in the 2nd or 3rd decade of life if secondary adrenal insufficiency develops. The carrier frequency of the c.301_302delAG mutation in PROP1 among Hutterites has not been determined.

SLC39A8-congenital disorder of glycosylation (CDG2N) [MIM:618005]

SLC39A8 encodes the divalent cation transporter ZIP8 which functions to transport primarily Mn2+, but also Zn2+and Fe2+ into cells across a wide range of human tissues (Park et al., 2015, p. 8). Biallelic mutations in SLC39A8 are associated with variably decreased manganese levels in blood and tissues which impairs the function of a number of manganese-dependent enzymes, including α1,4-galactosyltransferase, resulting in a secondary congenital disorder of glycosylation (type II). Patients with SLC39A8-CDG can present with cerebral and cerebellar atrophy with associated neurodevelopmental deficits, skeletal abnormalities, immune

dysfunction, and restricted growth. No treatment currently exists for SLC39A8 deficiency, however supplementation of oral manganese has shown potential in a small case series to improve manganese levels and correct the glycosylation defect in these patients (Park et al., 2018). The carrier frequency of the c.112G>C SLC39A8 mutation has been estimated to be 1/50 and 1/20 in L-leut and D-leut Hutterites, respectively (Boycott et al., 2015). While this condition has been observed in S-leut Hutterites (personal communication, P. Frosk), the carrier frequency in this group is unknown.

CPT1A deficiency [MIM:255120]

CPT1A encodes a transporter essential for normal β-oxidation of fatty acids in the mitochondria, and homozygous loss of this gene results in impaired fatty acid metabolism. Patients with CPT1A deficiency are at risk of episodes of hypoketotic hypoglycemia, seizures, hepatosplenomegaly, and coma during periods of fasting or increased metabolic demand. Treatment of patients with CPT1A deficiency consists of a low-fat diet and avoidance of hypoglycemia, especially during intercurrent illness. Early identification and management of this disorder results in good outcomes, and Manitoba has included CPT1A deficiency as part of the provincial newborn screening program since 2000. Data from the DNA-based newborn screening program has determined the carrier frequency of the c.2129G>A mutation in CPT1A to be 1/16 in the Manitoba S-leut Hutterites (Prasad et al., 2001).

Developmental delay, short stature, dysmorphic features, and sparse hair [MIM: 616901]

Biallelic mutations in the DPH1 gene cause a cranioectodermal dysplasia-like phenotype. Patients with this condition typically have delayed psychomotor development, variable intellectual disability, dolichocephaly (long and narrow head shape) with dysmorphic features, sparse hair on the head and face, and toenail hypoplasia. Some patients present with malformations of the central nervous system including Dandy-Walker malformation. The carrier frequency of the DPH1 c.17T>A mutation in Hutterites has not been determined but the condition has been reported in three families (Loucks et al., 2015, p. 1).

Cystic fibrosis [MIM:219700]

Cystic fibrosis is a multisystem disorder caused by biallelic mutations in the CFTR gene which

encodes a chloride transporter expressed primarily in the gastrointestinal tract, pancreas, and lungs. Altered chloride homeostasis results in defects in nutrient absorption, pancreatic insufficiency, and abnormally thick mucus in the lungs resulting in impaired oxygen uptake and recurrent infections. Most males with CF are infertile. Management of CF involves oxygen supplementation, inhalers which act to decrease mucus viscosity, targeted molecular therapy with combination ivacaftor/lumacaftor, antibiotics, lung transplants, pancreatic enzyme replacement, management of diabetes mellitus, nutritional support, and more. CF benefits from early detection and is included in newborn screening programs across North America and globally. There are two CFTR mutations in the Hutterite population, c.1521_1523delCTT (p.F508del) and c.3302T>A at a combined carrier frequency of 1/11 (Chong et al., 2012).

Dilated cardiomyopathy with ataxia (3-methylglutaconic aciduria, type 5) [MIM:610198]

Biallelic mutations in the DNAJC19 gene are hypothesized to result in defects in mitochondrial transport because the DNAJC19 protein is part of a mitochondrial transport complex (Davey et al., 2006). This condition causes a severe, early onset (infancy or early childhood) dilated cardiomyopathy with or without long QT syndrome. In a cohort of 17 Hutterite children with this condition, 10 passed away of congestive heart failure or arrhythmias before the age of 5 years (Davey et al., 2006). Patients also present with postnatal growth failure, nonprogressive cerebellar ataxia, and male genital abnormalities. The frequency of the DNAJC19 c.130-1G>C mutation among S-leut Hutterites is 1/36 (Chong et al., 2012).

Emery-Dreifuss muscular dystrophy, type 3 [MIM: 616516]

Autosomal recessive Emery-Dreifuss muscular dystrophy (EDMD) is caused by specific homozygous mutations in the LMNA gene, while other mutations in the same gene can cause autosomal dominant EDMD, as well as several other conditions. EDMD is characterized by weakness in the pelvic and shoulder girdles, contractures in the elbows, neck, and Achilles tendon, and cardiac involvement, most commonly, arrhythmias. Additionally, some patients present with a partial lipodystrophy, with loss of subcutaneous fat. Heterozygous carriers of an LMNA mutation also present with partial lipodystrophy and metabolic abnormalities, with autosomal dominant inheritance [MIM:151660] (Wiltshire et al., 2013). Management of EDMD

involves monitoring and treatment of arrhythmias with medication, ICDs, and heart transplant for end-stage heart failure; as well as surgery, stretching, and physical therapy to treat and prevent contractures and scoliosis. The carrier frequency of the c.1445G>A LMNA mutation has been estimated at 1/65 in D-leut and L-leut Hutterites (Wiltshire et al., 2013).

Familial hyperinsulinemic hypoglycemia [MIM: 256450]

Biallelic mutations in the ABCC8 gene can result in familial hyperinsulinemic hypoglycemia (FHH), the main feature being hyperplasia of the islet cells of the pancreas causing hyperinsulinemia. Congenital hyperinsulinism in this condition causes recurrent episodes of hypoglycemia. Infants are born large for gestational age, and if the condition is not aggressively treated, seizures and significant intellectual disability result from hypoglycemic episodes. Management of FHH is highly demanding, including administration of multiple drugs and hormones to suppress insulin production and frequent glucose feedings to avoid hypoglycemia. Partial pancreatic resection may be indicated. The carrier frequency of the c.823-7T>A mutation in ABCC8 among Hutterites is unknown.

Hypohidrotic ectodermal dysplasia [MIM: 305100]

HED is an X-linked disorder caused by mutations in the EDA1 gene which causes abnormal development of tissues derived from ectoderm including the skin, hair, and teeth. Due to X-linked inheritance males are typically severely affected and females may be variably affected. Patients present with dysmorphic features, decreased or absent hair that is thin and brittle when present, hypodontia with abnormally shaped teeth, thin and dry skin, and decreased or absent sweat glands. Due to the lack of sweat glands individuals with HED are intolerant to heat. Mucous glands in the nasal and respiratory passages are underdeveloped or absent leading to respiratory difficulties. Management involves treatment of manifestations including dental implants, adequate supply of water and a cool environment, and a humidifier to help with dry respiratory passages. The carrier frequency of the c.607C>T EDA mutation in Hutterites is unknown.

Hypophosphatasia [MIM:241510]

Hypophosphatasia is caused by biallelic mutations in the ALPL gene which encodes alkaline

phosphatase. Autosomal recessive forms of HPP tend to be more severe than dominant, with onset in the perinatal period, infancy, or early childhood. Deficiency of this enzyme results in decreased mineralization in the bones, causing deformations, propensity to fracturing, early loss of teeth, and respiratory insufficiency in severe cases. Enzyme replacement therapy with asfotase alfa is available for patients with severe forms of HPP. The Dutch-German Mennonite population in Canada is known to have an increased carrier frequency (1/25) of the c.1001G>A ALPL mutation, and the same mutation has been observed in the Hutterite population, reflecting the two groups' common founding populations.

Joubert syndrome, types 14, 21, 33 [MIM: 614424, 615636, 617767]

Joubert syndrome (JS) is a genetically heterogeneous ciliopathy in which a key feature is the molar tooth sign, a malformation of the brainstem and cerebellum visible on MRI. Other key features of JS are hypotonia, developmental delay, and congenital anomalies. Patients with JS often have abnormal breathing patterns, nystagmus, and ataxia. Congenital anomalies are variable and can include retinal dystrophy, renal and hepatic disease, polydactyly, ocular colobomas, and occipital encephalocele. Cognitive impairment is variable but can be severe. Management of JS can include respiratory support, speech therapy, physical therapy, and surgery for some congenital anomalies. There are 3 genes which have been found to cause JS in the Hutterite population, TMEM237 (JS type 14), CSPP1 (JS type 22), and PIBF1 (JS type 33). The carrier frequency for the TMEM237 c.52C>T mutation in S-leut Hutterites has been estimated at 1/12.5 (Chong et al., 2012).

Juvenile onset cataract with arrhythmic cardiomyopathy [MIM:212500]

Homozygous mutations in the LEMD2 gene are associated with rapid onset of cataracts during childhood. Cataracts develop bilaterally. Most patients go on to develop a unique fibrotic cardiomyopathy phenotype in the second and third decade of life that can result in arrhythmia and sudden cardiac death as early as age 28 (Abdelfatah et al., 2019). Management of these patients involves surgery to replace the lenses and regular monitoring for cardiomyopathy with echocardiogram and cardiac MRI, with implantation of an implanted cardioverter defibrillator (ICD) or cardiac transplantation as options if the cardiomyopathy is severe. The carrier

frequency of the LEMD2 c.38T>G mutation in S-leut Hutterites is estimated to be 1/8 (Abdelfatah et al., 2019) and the disorder has not been observed in any population other than Hutterites.

Leigh syndrome (mitochondrial complex I deficiency) [MIM: 252010]

Leigh syndrome is a genetically heterogeneous fatal disorder of mitochondrial oxidative phosphorylation. Patients with LS present with feeding difficulties, failure to thrive, seizures, hypotonia, and respiratory complications. On MRI, hyperintensities in the brainstem and/or basal ganglia can be observed. Symptoms present in the first few months of life, often brought on by intercurrent illness, and death often occurs within a few weeks of initial presentation. There are no treatments available to alter the course of LS. The carrier frequency of the c.393dupA NDUFS4 mutation among S-leut Hutterites is 1/27 (Chong et al., 2012), although it is thought that D-leut Hutterites have a higher carrier frequency as the condition has been reported more frequently among this group (Lamont et al., 2017).

Limb girdle muscular dystrophy, types 2H, 2L, 2S [MIM: 254110, 611307, 615356]

Limb girdle muscular dystrophies (LGMDs) comprise a group of proximal myopathies characterized by elevated serum creatine kinase (CK) and weakness primarily in the shoulder and pelvic girdles resulting in an abnormal gait and difficulty with stairs. There have been three subtypes of autosomal recessive LGMD identified in the Hutterite population which differ slightly in their clinical characteristics. Biallelic mutations in TRIM32 cause LGMDR8 (LGMD2H using former nomenclature) which is a relatively mild, slowly progressive form of LGMD characterized by onset of weakness at approximately age 24 and requirement for a wheelchair around the age of 50. The carrier frequency of the TRIM32 c.1459G>A mutation among S-leut Hutterites is estimated to be 1/6.5 (Chong et al., 2012). Biallelic mutations in FKRP cause LGMDR9 (formerly LGMD2I) which is characterized by onset of weakness at age 12 (range 2-25) (Frosk et al., 2005). A subset of patients with LGMDR9 also present with cardiomyopathy and skeletal abnormalities including scoliosis. The carrier frequency of the c.826C>A mutation in FKRP has been estimated to be 1/9.5 in S-leut Hutterites (Chong et al., 2012). LGMDR18 (formerly LGMD2S) is caused by biallelic mutations in the TRAPPC11 gene and is associated with

onset of weakness in infancy or early childhood. Children with LGMDR18 often have developmental delay, poor feeding, and poor growth, and a subset of patients develop a movement disorder, seizures, and/or cataracts. The carrier frequency of the c.1287+5G>A mutation in TRAPPC11 among S- and D-leut Hutterites is estimated to be 1/14 (Bögershausen et al., 2013, p. 11).

Maple syrup urine disease, type 1B [MIM: 248600]

Maple syrup urine disease (MSUD) type 1B is an inborn error of metabolism caused by mutations in the BCKDHB gene, which results in impaired metabolism of the branched chain amino acids valine, leucine, and isoleucine. If untreated, classic infantile MSUD presents in the first days of life with poor feeding, vomiting, lethargy, and a maple syrup odor in the urine and cerumen. Intermediate MSUD has a variable age of onset and may present similarly, although some patients may present later with seemingly nonsyndromic intellectual disability. All MSUD patients are at risk for episodes of metabolic decompensation, especially during periods of increased metabolic demand including illnesses. Management of MSUD involves a strict diet with minimal consumption of branched chain amino acids, with low protein medical foods and supplementation of other amino acids. The carrier frequency of the c.595delAG mutation in BCKDHB gene in Hutterites is unknown.

Methylmalonic acidemia [MIM:251000]

Methylmalonic acidemia (MMA) is an organic acidemia disorder caused by mutations in the MMUT gene that typically presents in the neonatal period with failure to thrive, poor feeding, vomiting, hypotonia, metabolic acidosis, and secondary hyperammonemia. If untreated, infants develop progressive encephalopathy which can be fatal. There are several subtypes of MMA which differ in the amount of residual enzymatic activity, with variable ages at onset and response to treatment. Management of MMA involves avoidance of catabolism with aggressive metabolic, fluid, and nutritional support during intercurrent illness, as well as a high calorie, low protein diet with carnitine supplementation. The carrier frequency of the c.1420C>T mutation in MMUT is estimated to be 1/63 among S-leut Hutterites (Triggs-Raine et al., 2016).

Morquio syndrome (mucopolysaccharidosis type 4A) [MIM: 253000]

Morquio syndrome is a lysosomal storage disorder caused by biallelic mutations in the GALNS gene, characterized by intracellular accumulation of the glycosaminoglycans keratansulfate and chondroitin-6-sulfate. Affected individuals are normal at birth, but in childhood present with progressive skeletal dysplasia, disproportionate short stature, coarse facial features, and corneal clouding. The skeletal abnormalities lead to significant morbidity, including pain, respiratory complications, and obstructive sleep apnea. Other organ systems can be involved resulting in hearing loss, vision loss, and heart disease. Enzyme replacement therapies are available and may help to improve quality of life. Management of Morquio syndrome involves supportive care by multiple specialists, physical therapy, and surgery. The carrier frequency of the c.1139+1G>A GALNS mutation in Hutterites has not been determined.

Nephronophthisis, type 1 [MIM:256100]

Nephronophthisis is a typically juvenile onset ciliopathy caused by mutations in the NPHP1 gene and characterized by medullary cystic kidney disease that leads to end stage renal disease (ESRD) in childhood or adolescence. This condition can also present with liver disease, situs inversus, and cardiac defects. Onset can be variable including in the prenatal period where it can present with polyhydramnios and renal failure in infancy, and later onset with ESRD occurring before the age of 30. Juvenile nephronophthisis has been observed in D-leut Hutterites although the carrier frequency of the c.1918delA mutation is unknown.

Nonsyndromic deafness (DFNB1) [MIM: 220290]

Biallelic mutations in GJB2 are associated with congenital, nonprogressive mild to profound sensorineural hearing loss. GJB2 encodes a transmembrane connexin protein that anchors cells together and is especially important for cochlear development (Iossa et al., 2011, p. 2). Affected individuals can benefit from hearing aids and cochlear implants if profound. The carrier frequency of the c.35delG mutation in S-leut Hutterites is approximately 1/28 (Chong et al., 2012).

Oculocutaneous albinism, type 1A [MIM:203100]

Biallelic mutations in TYR cause oculocutaneous albinism (OA) type 1A. The gene product of TYR

is essential for the production of melanin from tyrosine, so affected individuals have decreased or absent pigmentation in the hair, skin, and eyes. Melanin is also an essential signalling molecule during development of the visual structures, so patients are born with foveal hypoplasia, abnormal optic nerve connectivity, and decreased gyrification of the visual cortex (Federico & Krishnamurthy, 2020). Combined with the absence of pigment in the retinal epithelium, these abnormalities result in severely decreased visual acuity, impaired binocular vision, and nystagmus. Additionally, the skin of OA1A patients cannot tan, and exposure to solar radiation over time predisposes these patients to cutaneous malignancies. The carrier frequency of the c.272G>A mutation in TYR among S-leut Hutterites is 1/7 (Chong et al., 2012).

Odontoonychodermal dysplasia [MIM: 257980]

Odontoonychodermal dysplasia (OODD) is a type of ectodermal dysplasia caused by biallelic mutations in the WNT10A gene. Patients present with sparse dry hair, dysplastic or absent nails, severe hypodontia, keratoderma, hyperhidrosis, and a smooth tongue. Management of patients with OODD may include dental implants for severe hypodontia. The carrier frequency of the c.321C>A mutation in WNT10A has not been determined.

Restrictive dermopathy [MIM:275210]

Restrictive dermopathy (RD) is a lethal condition affecting the skin caused by mutations in the ZMPSTE4 gene. ZMPSTE4 encodes a protein essential for normal development of the skin's extracellular matrix. Prenatally, RD causes decreased fetal movement, lung hypoplasia, polyhydramnios, and arthrogryposis. Affected infants have thin, translucent, tightly adherent skin that tears easily. Infants can also present with diverse congenital anomalies and dysmorphic features. Death usually occurs in the first week of life due to respiratory failure. The carrier frequency of the c.1085dupT mutation in ZMPSTE4 gene in S-leut Hutterites is 1/15.5 (Chong et al., 2012).

Segawa syndrome [MIM: 605407]

Segawa syndrome is an inborn error of metabolism caused by biallelic mutations in the TH gene which encodes tyrosine hydroxylase. Tyrosine hydroxylase is required for the production of dopamine and other catecholamines, and deficiency in this enzyme results in infancy-onset

dystonia. Infants with Segawa syndrome present with progressive, abnormal jerky movements and decreased spontaneous movements. The movement disorder present in this condition responds to treatment with L-dopa. The carrier frequency of the c.1481C>T mutation in TH among Hutterites has not been determined.

Sitosterolemia type 1 [MIM: 210250]

Sitosterolemia type 1 is a childhood onset metabolic disorder caused by biallelic mutations in the ABCG8 gene. Affected individuals have impaired metabolism of plant sterols resulting in hypercholesterolemia and premature atherosclerosis in childhood. This condition may also present with tuberous or tendon xanthomas as well as hemolytic anemia. Management of sitosterolemia involves maintaining a low-fat diet, and especially avoiding plant sterols which are found in foods like vegetable oils, nuts/seeds, avocados, and chocolate. Additionally, therapies are available that decrease the absorption of sterols from the gut. Atherosclerosis can be minimized, and existing xanthomas can regress by maintaining plasma sterol levels at an appropriate level with these therapies. The carrier frequency of the c.320C>G mutation in ABCG8 is approximately 1/12 in S-leut Hutterites (Chong et al., 2012).

Thyroid dyshormonogenesis [MIM:274400]

Thyroid dyshormonogenesis is caused by mutations in the SLC5A5 gene which encodes an iodide transporter that is essential for thyroid hormone synthesis. Affected individuals present with congenital hypothyroidism resulting in growth retardation, gastrointestinal dysfunction, thyroid goiters or nodules, and intellectual disability if untreated. Drug therapy is effective at normalizing thyroid hormone levels and if managed well, cognitive impairment and other morbidities can be avoided. The carrier frequency of the c.1183G>A mutation in SLC5A5 among Hutterites has not been determined. In the Manitoba NBS program.

Usher syndrome types 1B, 1F [MIM: 276900, 602083]

Usher syndrome type 1 is a genetically heterogeneous disorder affecting the development and function of sensory cells in the inner ear and retina (Kremer et al., 2006). Mutations in the MYO7 (type 1b) and PCDH15 (type 1F) genes associated with Usher syndrome have been observed in the Hutterite population. This condition is characterized by congenital profound

sensorineural hearing loss and progressive vision loss due to retinitis pigmentosa. Type 1 Usher syndrome also results in vestibular dysfunction, so patients have difficulty with balance and children have delayed motor development. Cochlear implantation should be considered in children with Usher syndrome and without it, most do not develop speech. Onset of visual impairment usually takes place in adolescence and may result in complete blindness. Vitamin A and omega 3 supplementation may help to slow the progression of vision loss and multiple gene therapies are under investigation to treat this condition. The carrier frequency of Usher syndrome type 1F (PCDH15) is approximately 1/40 in S-leut Hutterites (Chong et al., 2012).

APPENDIX B. Survey instrument

1. Please select your age:
    - Under 18
    - 18-25
    - 26-35
    - 36-45
    - Above 45

2. Please select your gender:
    - Male
    - Female
    - Other/Prefer not to say

3. Please select your relationship status:
    - Married, with children
        - If you selected this option, how many children do you have? _____
            - Are you planning on having more children? (Circle one) Yes No
    - Married, without children
        - Are you planning on having children? (Circle one) Yes No
    - In a longer-term relationship or engaged
    - Dating
    - Single

4. Carrier screening is the blood test that checks your DNA to see if you are a carrier of any genetic disorders that have previously been found in people of Hutterite descent. Have you ever heard about carrier screening before? (Choose all that apply)
    - Yes, from my PCP (circle one)
      Doctor Nurse practitioner Physician's assistant
    - Yes, from a previous Town Hall presentation
    - Yes, from a teacher at school
    - Yes, from someone else (please specify) _____
    - No, this is the first time I have heard of carrier screening

5. Do you have a family member or know someone else with a genetic condition? (Choose all that apply)
    - Yes, my child/sibling/parent
    - Yes, a different family member
    - Yes, someone not in my family
    - No

6. If you answered YES to Question 5, do you feel that any of the condition(s) your family member(s) or friend(s) have are severe or life-limiting? (Select one)

Not at all severe or life-limiting		Somewhat severe and/or life-limiting		Extremely severe and life-limiting
○	○	○	○	○

7. I think that carrier screening for genetic conditions is…

Good		Neutral		Bad
○	○	○	○	○
Important				Unimportant
○	○	○	○	○
Alarming				Reassuring
○	○	○	○	○
Sensible				Unwise
○	○	○	○	○
Undesirable				Desirable
○	○	○	○	○
Harmful				Beneficial
○	○	○	○	○

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
8. I want to be reassured about whether I am at risk of having a child with a severe genetic condition	○	○	○	○	○
9. I feel that carrier screening has the potential to help my community	○	○	○	○	○
10. I am feeling worried about being a carrier of a genetic condition	○	○	○	○	○
11. I am feeling worried about having a child with a genetic condition	○	○	○	○	○

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
12.I think there is a high chance that I am a carrier of a genetic condition	○	○	○	○	○
13. I think that offering these carrier tests will cause anxiety	○	○	○	○	○
14. I think that by offering these carrier tests people will be burdened with unwanted information	○	○	○	○	○
15. I would feel unhealthy if I were a carrier	○	○	○	○	○
16. I would consider using the results of the carrier test to help me in choosing a partner	○	○	○	○	○
17. I would make different decisions about having children if I were a carrier	○	○	○	○	○
18. I would choose not to have more children if my partner and I were both carriers of the same condition	○	○	○	○	○
19. I would choose to test the baby during pregnancy if my partner and I were both carriers of the same condition	○	○	○	○	○
20. I would consider ending a pregnancy if the unborn child was affected with one of the conditions	○	○	○	○	○
21. I would want to have information about assisted reproduction if my partner and I were both carriers of the same condition	○	○	○	○	○

22. The carrier test could be offered by several different providers. Please rate your interest in accessing carrier screening from the following providers and write the reason in the box to the right:

	Not interested	Interested	Reason
PCP (local doctor, nurse practitioner, physician assistant)	○	○	
Clinical Geneticist or Genetic Counsellor in Person (at Health Sciences Centre)	○	○	
Clinical Geneticist or Genetic Counsellor via Telehealth (video appointment)	○	○	

23. The carrier test could include all the genetic conditions that have been identified in the Hutterite community, or only some of them. Please indicate your interest in knowing your carrier status for the following:

	Not interested	Interested
A test screening for all of the genetic conditions that have been identified in the Hutterite community	○	○
A test screening for severe genetic conditions that start in childhood and benefit from early detection and treatment	○	○
A test screening for severe, untreatable genetic conditions that start in childhood	○	○
A test screening for treatable or untreatable genetic conditions that start later in life	○	○

Thank you for completing the survey. We invite you to also participate in the next phase of our study which will consist of individual interviews with the student researcher, Cassie McDonald. If you are willing to be contacted for an individual interview, please write your name and telephone number below.

Name: _____

Telephone number: _____

APPENDIX C. Interview guide

Introduction:

Thank you so much for taking the time to speak with me today. My name is Cassie McDonald and I'm a student doing my master's degree in genetic counselling at the University of Manitoba. For this research project, we are trying to understand how people in the Hutterite community think and feel about carrier screening for genetic conditions – if you aren't familiar with this term I will explain in a moment. Your participation in this research project will help us to make recommendations for how genetics providers like physicians and genetic counsellors can provide the best care for people in the Hutterite community.

A bit of information before we go on - there are about 30 genetic conditions that occur in families of Hutterite descent, including muscular dystrophy and cystic fibrosis. For a person to be affected by these conditions, they need to have both copies of the gene not working. Usually, when a child has one of these conditions, they inherited 2 genes that don't work, one from their mother and one from their father. Their parents are what we call "carriers". Carriers do not have any symptoms of disease. Research shows that everyone is a carrier for something, and most people are carriers for several different conditions.

There is a genetic test called carrier screening which is a simple blood test that can tell whether a person is a carrier of genetic conditions. If a couple are carriers of the same genetic condition and they have children together, there is a 25% chance of each child having the condition. There is a carrier screening test being developed at Health Sciences Centre right now, which will give people in Hutterite communities the option of learning if they are carriers any of the 30 conditions that affect Hutterite families.

We are conducting this research study to learn how people in the Hutterite community feel about this carrier screening test, what they would do with information about their carrier status, and to understand what the most helpful way would be to offer this service.

Review informed consent. Ask participant if they would like more time to think about whether to participate in the interview and if they do, set up another time to check in with them.

If participant would like to continue, request permission to start recording.

During this interview, I am going to ask you a range of questions about what you think and feel about the carrier screening test. You can let me know if you prefer not to answer a question or if you would like to take a break as it's important that you feel comfortable.

1. What do you think of when you hear the words "carrier screening"? (What feelings or thoughts does that bring up for you?) Probes:

   a. How would it impact someone to have knowledge about their carrier status? In what ways would this be helpful? In what ways would this be harmful?
   b. Who should be able to make decisions about whether carrier screening is available? [Prompt: some people might say that people shouldn't be allowed to know this information and others might say it's a personal decision]
   c. How do you think others in your community feel about carrier screening?

2. Do you have experience with genetic conditions, have one yourself, or know anyone who is affected with one?
   a. How does having the condition impact their (your) life?
   b. How does it affect the lives of their (your) family?
   c. How does this impact the way you view carrier screening?

3. Would you like to know your carrier status for genetic conditions? Why/why not?
   a. What is the most important factor you would consider when deciding about whether to get carrier screening? [Prompts: some might say that they would only get carrier screening if they have genetic conditions in their family. Others might say that they would get carrier screening just because they want to know. Or if they were planning on getting married or having children.]
   b. Would you want to know your carrier status for all the genetic conditions on the panel or just a subset? [Prompts: only severe conditions that benefit from early treatment, only severe untreatable conditions, adult-onset conditions]
   c. How would you like to learn about your carrier status?

4. If you had carrier screening and found out you were a carrier for a severe genetic disorder, how would this impact you in your life?
   a. How do you think you would feel?
   b. How would this information change the way you make life decisions? [Prompts: wanting to know partner's carrier status]
   c. If your partner was a carrier for the same condition, how would this change the way you make life decisions? [Prompt: choose not to have children/stopping a pregnancy if affected/assisted reproduction]

5. When the carrier screening panel is available, we want to make sure that it is offered in a way that is helpful to the Hutterite community.
   a. What information do you think people will need in order to decide whether to get carrier screening?
   b. What would be a good way for people to get this information? [Prompt: through town halls, sending out a brochure, in schools, at doctor visits]
   c. When should education about carrier screening be available to people in the Hutterite community?
   d. In terms of life stages, when is the best time for carrier screening to be offered to people in your community?

Examples of probes:

Clarification:
What do you mean by…?

Asking for more detail:
Can you tell me more about that?
Can you give me an example?

Probing for feelings/thoughts/rationale:
Why is that important to you?
What did that mean to you? What did it mean to others close to you?
How did that impact you? Others close to you?
How do you feel about that?

APPENDIX D. Survey participant information and consent form

Title of the study: *Attitudes, decision-making processes, and preferences regarding preconception carrier screening among Hutterites in Manitoba*

Principal Investigator: Cassie McDonald, BSc, Genetic Counselling Student, Department of Biochemistry and Medical Genetics, Rady Faculty of Health Sciences, University of Manitoba.

Supervisor: Dr. Patrick Frosk, PhD, MD, FRCPC, FCCMG
Assistant Professor, Department of Pediatrics and Child Health, Department of Biochemistry and Medical Genetics, Rady Faculty of Health Sciences, University of Manitoba.

Study Description: You are being invited to participate in a survey study about attitudes toward genetic carrier testing in the Hutterite community in Manitoba. This survey is being conducted to understand the perspectives of people in Hutterite communities toward genetic carrier testing, in order to inform doctors and genetic counsellors about the most helpful way to offer this service. This is important because there is a new carrier testing panel that will be available to Hutterites in the next year.

Your role: Your feedback will be collected through completion of a survey which will ask you a series of questions and should take about 20 minutes to complete. Your participation is completely voluntary. You should only answer the questions you feel comfortable answering. You are **not** required to provide any **personal information such as your name, address or telephone number**. Your responses will be anonymous as we will not know who has completed the survey or questionnaire(s) and it will not be linked to any other information about you.

Risks: The risks of participating in the study are minimal. Thinking about your experiences with genetic conditions in order to answer the questions may cause you to feel upset or emotional. The information you provide is confidential.

Benefits: Participation in this study may not provide any personal benefit to you but the findings of the study may help people in the Hutterite community who want to access genetic carrier testing. **Your participation is important to us and may help us to provide tailored genetics services to people in the Hutterite community.**

Questions: If any questions come up during or after the study contact Cassie McDonald (Lead Researcher) at xxx-xxx-xxxx or Dr. Patrick Frosk (Principal Investigator) at xxx-xxx-xxxx.

For questions about your rights as a research participant, you may contact The University of Manitoba, Bannatyne Campus Research Ethics Board Office at 204-789-3389.This study is funded by the University of Manitoba. This study and survey have been approved by the University of Manitoba Health Research Ethics Board. Completion and return of this survey imply your consent for the purposes stated above.

APPENDIX E. Interview participant information and consent form

Title of the study: *Attitudes, decision-making processes, and preferences regarding preconception carrier screening among Hutterites in Manitoba*

Principal Investigator: Cassie McDonald, BSc, Genetic Counselling Student, Department of Biochemistry and Medical Genetics, Rady Faculty of Health Sciences, University of Manitoba.

Supervisor: Dr. Patrick Frosk, PhD, MD, FRCPC, FCCMG
Assistant Professor, Department of Pediatrics and Child Health, Department of Biochemistry and Medical Genetics, Rady Faculty of Health Sciences, University of Manitoba.

You are being invited to participate in an interview study about attitudes toward genetic carrier testing in the Hutterite community in Manitoba. Please take your time to review this consent form and discuss any questions you may have with the study staff, your friends or your family before you make your decision. This consent form may contain words that you do not understand. Please ask the study staff to explain any words or information that you do not clearly understand.

Purpose of this Study: This study is being conducted to understand the perspectives of people in Hutterite communities toward genetic carrier testing, in order to inform doctors and genetic counsellors about the most helpful way to offer this service. This is important because there is a new carrier testing panel that will be available to Hutterites in the next year.

Participant Selection: You are being asked to participate in this study because as a member of the Hutterite community, your opinions and perspectives can help to shape the way that carrier screening is offered and delivered in your community. A total of 15-20 participants will be asked to participate.

Study procedures

- The method of data collection for this study will be individual interviews conducted over the phone or in person.
- Participation in the study will consist of one interview session which will take up to one hour.
- The student researcher, Cassie McDonald, will be conducting the interview.
- You will be asked some questions relating to your feelings about carrier screening, how you would make the decision to get carrier screening or not, and how this service should be delivered to your community.
- The sessions will be audio taped, and the audiotapes will be transcribed by either Cassie or a professional transcription service to ensure accurate reporting of the information that you provide.

- Transcribers will sign a form stating that they will not discuss any item on the tape with anyone other than the researchers.
- Your name will not be revealed during the individual interview. However, if your name is mentioned during the recording, the transcriber will be instructed to exclude this from the transcription.
- The results of the study will be available to you upon request.

Risks: There are very few risks associated with participating in this study. However, you may find talking about your experiences with genetic conditions to be upsetting or emotional. You do not have to answer any question that makes you feel uncomfortable or that you find too upsetting. Should you need any additional support we can refer you for counselling services or help you to find other help.

Benefits: Participation in this study may not provide any personal benefit to you but the findings of the study may help people in the Hutterite community who want to access genetic carrier screening.
Your participation is important to us and may help us to provide tailored genetics services to people in the Hutterite community.

Costs: There is no cost to you to participate in the individual interview.

Payment for participation: You will be thanked for your time with a $5 gift card for Tim Hortons.

Confidentiality: We will do everything possible to keep your personal information confidential. Your name will not be used at all in the study records. A list of names and addresses of participants will be kept in a secure file so we can send you a summary of the results of the study if requested. If the results of this study are presented in a meeting, or published, nobody will be able to tell that you were in the study. Please note that although you will not be identified as the speaker, your words may be used to highlight a specific point. The collection and access to personal information will follow provincial and federal privacy laws.

Audiotapes of the interview will be typed and used to prepare a report. The audiotapes and typed notes will be kept in a locked file cabinet in a secure office for 18 months following completion of the study. Only the research staff will have access to them and know your name. Some people or groups may need to check the study records to make sure all the information is correct. All of these people have a professional responsibility to protect your privacy. These people or groups are:

- The Health Research Ethics Board of the University of Manitoba, which is responsible for the protection of people in research and has reviewed this study for ethical acceptability.
- Quality assurance staff of the University of Manitoba who ensure the study is being conducted properly.

All records will be kept in a locked secure area and only the research staff and those persons identified above will have access to these records. If any of your research records need to be copied to any of the above, your name and all identifying information will be removed. No information revealing any personal information such as your name, address, or telephone number will leave the University of Manitoba.

Permission to Quote:
We may wish to quote your words directly in reports and publications resulting from this. With regards to being quoted, please check yes or no for each of the following statements:

Researchers may publish documents that contain quotations by me under the following conditions:	
☐ Yes ☐ No	I agree to be quoted directly if my name is not published (I remain anonymous).

Voluntary Participation/Withdrawal from the Study: Your decision to take part in this study is voluntary. You may refuse to participate, or you may withdraw from the study at any time.

Questions: If any questions come up during or after the study contact Cassie McDonald (Lead Researcher) at xxx-xxx-xxxx or Dr. Patrick Frosk (Supervisor) at xxx-xxx-xxxx.

For questions about your rights as a research participant, you may contact The University of Manitoba, Bannatyne Campus Research Ethics Board Office at 204-789-3389

Consent Signatures:

1. I have read all 3 pages of the consent form.
2. I have had a chance to ask questions and have received satisfactory answers to all of my questions.
3. I understand that by signing this consent form I have not waived any of my legal rights as a participant in this study.
4. I understand that my records, which may include identifying information, may be reviewed by the research staff working with the Principal Investigator and the agencies and organizations listed in the Confidentiality section of this document.
5. I understand that I may withdraw from the study at any time and my data may be withdrawn prior to publication.
6. I understand I am providing verbal consent to the researcher.
7. I agree to participate in the study.

Participant printed name: _____ Date _____
(day/month/year)

Participant phone number: _____

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their verbal consent.

Printed Name: _____Date _____
(day/month/year)

Signature: _____

Role in the study: _____