# Exploring Expanded Carrier Screening in Canadian Genetics Services

by

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## ABSTRACT

Expanded carrier screening (ECS) is a genetic test that can screen an individual for their carrier status for hundreds of genetic conditions. This test is not part of routine healthcare in Canada however is accessible to Canadians as a private pay genetic test. ECS has been available for approximately a decade, during which time studies have explored American and European genetic health professionals' (GHPs) experiences and opinions of ECS and have identified potential challenges and opportunities for ECS in the genetics clinic. The opinions and experiences of Canadian GHPs with ECS has yet to be explored and may be uniquely shaped by working a public healthcare system. This study used a mixed-methods design using both quantitative (survey) and qualitative (interview) data to explore ECS in the Canadian genetics clinic. GHPs recruited to the study included genetic counsellors, geneticists and molecular geneticists currently working in Canada. The majority of survey respondents had experience counselling patients for ECS, did not have an institutional or clinic policy regarding the discussion of ECS and reported that discussions of ECS arose a few times a year. Differences in opinions were observed between respondents with the most ECS experience and those with the least experience with ECS. The majority of survey respondents agreed that with additional training, obstetricians, gynecologists or family physicians are best suited to provide pre-test counselling for ECS. Thematic analysis of the interviews revealed four themes related to GHP experience and opinions: ECS as a reactive option, Canadians should be made aware of ECS, public healthcare barriers to discussing ECS and GHPs as informed healthcare consumers. Overall, the insights gained from this exploratory study provide a foundation for future studies regarding ECS in Canada.

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## LIST OF ABBREVIATIONS

**ACMG:** American College of Medical Genetics and Genomics

**AJ:** Ashkenazi Jewish

**AR:** Autosomal recessive

**CAGC:** Canadian Association of Genetic Counsellors

**CCMG:** Canadian College of Medical Geneticists

**CF:** Cystic fibrosis

**cfDNA**: Cell free DNA

**CFTR:** Cystic fibrosis transmembrane conductance regulator

**CHT:** Canada Health Transfer

**CLIA**: Clinical Laboratory Improvement Amendments

**DTC-GT:** Direct-to-consumer genetic testing

**ECS:** Expanded carrier screening

**GC:** Genetic counsellor

**GECKO**: Genetics Education Canada Knowledge

**GHP:** Genetic healthcare professional

**GP:** General practitioner

**NGS:** Next generation sequencing

**NIPT:** Noninvasive prenatal testing

**NSGC:** National Society of Genetic Counselors

**OB/GYN:** Obstetrician/gynecologist

**PI:** Primary investigator

**PSS:** Professional status survey

**SMA:** Spinal muscular atrophy

**SOGC:** Society of Obstetricians and Gynecologists

**TSD:** Tay-Sachs disease

**WHO:** World Health Organization

# CHAPTER 1: INTRODUCTION & LITERATURE REVIEW

## 1.1 INTRODUCTION

Carrier screening is used to identify couples at risk of having a child with a recessively inherited genetic condition. The current approach to carrier screening in Canada is targeted to those at risk of being a carrier due to their ancestry or family history. Canadians identified as high risk of being a carrier can access publicly funded carrier screening and genetic counselling services. Advancements in DNA sequencing technology have increased the speed and decreased the cost of DNA sequencing, which has made it possible to sequence numerous genes simultaneously for a reduced cost. Applying this technology to carrier screening led to the development of expanded carrier screening (ECS), a test that screens for an individual's carrier status for hundreds to thousands of genes. In contrast to targeted, publicly funded carrier screening, ECS is available as a private pay option that is offered by various diagnostic testing laboratories primarily located in the United States and is available for purchase regardless of baseline carrier risk.

ECS has been available for approximately a decade, during which time certain countries have developed specific guidelines and have studied genetic healthcare providers' (GHP) experiences (Janssens et al., 2017; van der Hout et al., 2017). These studies have identified several challenges such as informed consent during pre-test counselling but also potential opportunities such as equity of access to carrier screening regardless of ethnicity, however the Canadian perspective is missing from this literature. The aim of this study was therefore to develop the literature regarding ECS in Canada by exploring GHP experiences with and opinions toward ECS.

## 1.2 INTRODUCTION TO SCREENING

The purpose of screening is to identify individuals in an apparently healthy population that may be at risk for disease. The results of a screening test are not diagnostic, but rather provide a probability that an individual has a condition (World Health Organization, 2020). Individuals identified through screening to be at increased risk of disease may have further follow-up testing to confirm a potential diagnosis. Two examples of screening programs in Canada include

screening for colorectal cancer in the population aged 50-74 using mailed fecal immunochemical test kits and newborn screening, in which blood is collected via a heel prick of a newborn to identify those at risk of a treatable metabolic/genetic disorder prior to the development of symptoms. The implementation of these screening programs began when the major public health burden in developed nations shifted from communicable diseases to chronic health conditions such as cancer or cardiovascular disease. These conditions may be curable when identified early, but are incurable in later stages (Wilson & Jungner, 1968).

Although there are many chronic health conditions, not all are amenable to screening and a number of criteria must be met before a disease is considered a good candidate for a screening program. One crucial criterion is the sensitivity and specificity of the screening test (World Health Organization, 2020). Test sensitivity (also referred to as the detection rate) refers to how good the test is at correctly identifying those with a condition as screen positive. For example, a test with 95% sensitivity will accurately identify 95% of individuals with the condition (true positive result) but will miss 5% who have the condition (a false negative result). Test specificity refers to how good the test is at correctly identifying healthy individuals as screen negative. A test with 95% specificity will correctly identify 95% of individuals without the condition (true negative result) but will incorrectly identify 5% of healthy individuals as screen positive (false positive result). A test with high specificity will have a low false positive rate (Swift et al., 2020). It is important that the criteria of high test sensitivity and specificity are met since a high rate of false negative and false positive results would potentially cause more harm than benefit both to the patient and to healthcare resources required for follow up.

Advances in medicine and technology in the 1960s increased the capability to screen for disease, however policymakers grew concerned about the lack of strict criteria guiding the development of screening tests. In 1968, the World Health Organization (WHO) published Wilson and Jungner's *Principles and practice of screening for disease* which defined ten principles intended to guide the selection of conditions suitable for screening. These criteria remain the gold standard for screening programs (J. Wilson & Jungner, 1968):

1) *The condition 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 criteria form the basis of any screening program they were developed before it became a reality to screen for genetic disease with a high degree of sensitivity and specificity. The discovery of new genes and advancements in DNA sequencing technology continue to expand genetic screening capabilities, which has outpaced the development of formal criteria specific to genetic screening for disease (Andermann et al., 2011). In the meantime, the Wilson and Jungner criteria continue to be revisited by policymakers in order to guide what diseases constitutes screening candidates in the genomic era.

## 1.3 CARRIER SCREENING

Unlike the original aim of screening programs, which was to identify those at risk of developing a disease, carrier screening aims to identify those at risk of having a child with a genetic condition. Carriers are individuals who themselves are unaffected but are at increased risk of having a child with a genetic condition (usually autosomal recessive or X-linked inheritance). Carrier screening entails comparing an individual's DNA sequence to the DNA sequence of someone who is not a carrier. DNA sequence changes that are associated with an increased risk for disease are referred to as a pathogenic variants (historically referred to as mutations). Carriers therefore are individuals who have one functioning copy of a gene and one gene copy with a pathogenic variant, but are otherwise healthy. Historically, the approach to carrier screening has typically been targeted and condition-driven; only individuals at risk of

being a carrier were offered carrier screening for that specific condition. As with other screening tests, a negative carrier screen reduces the likelihood of being a carrier but does not eliminate the risk completely. Usually, there remains a residual carrier risk, which is the chance that an individual is still a carrier even after a negative carrier screening test. This residual risk depends in part on the sensitivity of the test (Leung et al., 2021). Typically, carrier screening is primarily performed for conditions that are considered to have an early onset with significant morbidity and mortality such as cystic fibrosis (CF) and Tay-Sachs disease (TSD). Reproductive carrier screening for adult-onset diseases or diseases of variable penetrance is not recommended such as hemochromatosis and alpha-1 antitrypsin deficiency (ACOG Committee Opinion No. 69).

### 1.3.1 Autosomal Recessive & X-linked Recessive Inheritance

It is estimated that humans have between 20,000-25,000 genes (Online Mendelian Inheritance in Man, OMIM., 2020). Monogenic or Mendelian disorders occur when one gene is non-functional. Monogenic conditions can be inherited as autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive or Y-linked. Autosomal recessive (AR) and X-linked recessive conditions make up the broader group of inherited genetic conditions. This is in contrast to genetic conditions that are digenic or polygenic which result from the cumulative effect of two or more genes with altered function, for example coronary artery disease and Alzheimer's disease.

The majority of conditions included in carrier screening follow an AR inheritance pattern (Joint SOGC-CCMG Committee Opinion No.335). Everyone inherits two copies of each gene, one that is maternally inherited, and one that is paternally inherited. AR conditions arise only when both genes that are inherited have absent or reduced function due to pathogenic variants in the DNA sequence. An individual who is a carrier for a condition is at risk of having an affected child if their reproductive partner is also a carrier for the same AR genetic condition. For a couple where both partners have a pathogenic variant in the same gene, there is a 25% chance with each pregnancy of having an affected child, a 50% chance of having a child that is also a carrier and a 25% chance of having a child who is unaffected and is not a carrier (Figure 1).

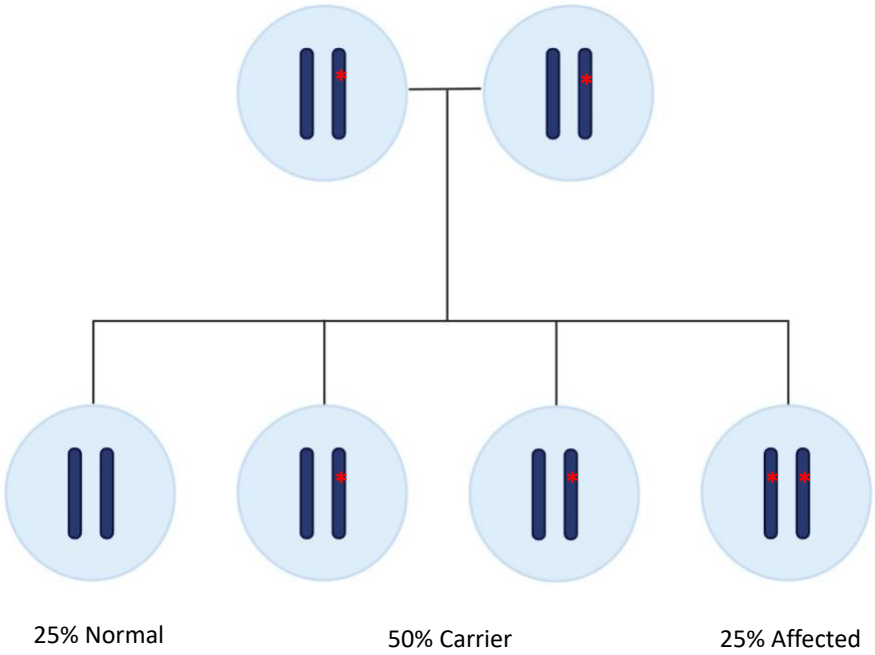



**Figure 1.** Reproductive possibilities for a couple that are carriers for the same AR condition. Each parent contributes one copy of each chromosome (depicted in blue), only one pair of chromosomes is shown for simplicity. The red asterisk denotes a pathogenic variant in a gene associated with an AR condition. With each pregnancy there is a 25% chance that the child will not be a carrier, 50% chance that the child will also be a carrier and a 25% chance that the child will be affected with the AR condition.

The proportion of individuals in a population who are carriers for a pathogenic variant associated with a recessive condition is referred to as the population carrier frequency. Recessive conditions with high disease incidence (the number of new cases over a defined time period) will have a higher carrier frequency than conditions with a low incidence. For example, the incidence of TSD in the AJ population in approximately 1 in every 3,500 newborns (Rozenburg and Pereira, 2001) and has an estimated carrier frequency of 1 in 30 (Joint SOGC-CCMG Committee Opinion No.335), compared to 1in 320,000 births in non-Jewish populations (Online Mendelian Inheritance in Man, OMIM., 2020). It is important to note that the population carrier frequency of an AR condition does not remain static across ethnic groups, as disease incidence varies among ethnic groups so too does the carrier frequency.

While AR conditions make up the majority of conditions screened, a few of the conditions screened exhibit X-linked recessive inheritance. Only genes on the X chromosome can follow this inheritance pattern. Since women have two X chromosomes, they are generally carriers for

X-linked recessive conditions. In this case, if a gene on one X chromosome is non-functional, the other X chromosome can serve as a backup by providing a functioning copy of the gene. Men on the other hand are more likely to be affected with an X-linked recessive disorder since they have only one X chromosome. If a male has a non-functioning gene on the X chromosome, they have no backup that can compensate and they will be affected. A common X-linked recessive condition is color blindness which affects approximately 9% of men and less than 1% of women (Harrison et al., 1977). A woman who is a carrier for an X-linked recessive condition has a 50% chance that each male pregnancy will be affected and a 50% chance that each female pregnancy will also be a carrier.

### 1.3.2 Goals of Carrier Screening

The majority of children with an AR condition are born to unsuspecting parents with no known family history. It is estimated that there are more than 1300 recessively inherited disorders (Bajaj & Gross, 2014) and that 1-2% of couples in the general population are at risk of having a child with an AR condition (Ropers, 2012). The goal of carrier screening therefore is to provide prospective parents with the opportunity for informed reproductive decision making.

In order to maximize reproductive options, it is recommended that carrier screening be done preconception as this provides couples with the most reproductive options– including natural conception followed by prenatal diagnosis, using preimplantation genetic diagnosis, using a donor sperm or oocyte, choosing not to become pregnant or adoption. Carrier screening can also be performed in the prenatal period, however options are limited to prenatal intervention or neonatal care. In cases where treatment and therapy options are available, such as for metabolic conditions for example, advanced awareness of the condition may allow for early intervention and treatment, reducing morbidity and mortality in an affected child. (Chokoshvili et al., 2018).

While reproductive autonomy is the goal of carrier screening in Western societies, the goal of carrier screening varies in other parts of the world. In countries where a high burden of severe AR disease significantly impacts quality of life and healthcare resources, reducing the number of affected births may be the goal of carrier screening. This was the case in the AJ community where there is a high carrier frequency for TSD, which is a fatal condition causing progressive degeneration of the nervous system (Edelson 1997). Recognizing that TSD had a

devastating impact on the AJ community, a premarital carrier screening program called Dor Yeshorim was introduced and today credits itself for "singlehandedly eradicating Tay-Sachs from the Jewish community" (Dor Yeshorim, 2021). In Cyprus, there is a high prevalence of β-thalassemia, a disorder in which infants are unable to make the adult version of hemoglobin, the protein that carries oxygen to the body's organs and tissues. Treatment involves frequent blood transfusions, putting significant demand on blood supply and treatment costs. Left untreated, individuals decline slowly and die in childhood. Beginning in the late 1970s Cyprus mandated premarital carrier screening for β-thalassemia, with the goal of reducing the number of births with β-thalassemia to zero (Cowan, 2009).

### 1.3.3 Development of Carrier Screening Programs

The concept of systematically screening individuals in a population for their carrier status was first initiated in populations with a high burden of AR disease, such as screening for TSD in AJ community (Dor Yeshorim, 2021). Carrier screening in these populations was considered a worthwhile endeavour since the high disease incidence made it likely that carriers would be identified through carrier screening. The approach to identifying individuals at high risk of being a carrier has therefore primarily been based on ethnicity. More recently, the recognition that AR diseases can occur across ethnicities has resulted in the recommendation that carrier screening for specific conditions be offered to everyone in the population, regardless of ethnicity. (ACOG Committee Opinion No.691).

One of the first population carrier screening programs began in the 1970s for TSD in the AJ population using biochemical testing. In 1969 the biochemical basis of TSD was uncovered as the absence of the hexosaminidase A enzyme in the brain and neurons of patients with TSD (Okada & O'Brien, 1969). This allowed for biochemical screening for hexosaminidase A levels to distinguish affected individuals, carriers, and noncarriers (Romero, Biggio, et al., 2017). By the 1970s carrier screening for TSD was offered in the AJ population and led to a greater than 90% reduction in the incidence of TSD (Kaback, 1993).

Two decades later, in 1989, the possibility to perform carrier screening via genetic testing became a reality when the gene causing CF, the cystic fibrosis transmembrane conductance regulator (CFTR) gene was discovered. CF is the most common AR condition in Northern Europeans with a carrier frequency of approximately 1 in 25 (R. D. Wilson et al., 2016). Soon

after, the most common pathogenic variant associated with CF in the Northern European population, referred to as ΔF508 (c.1521_1523delCTT for the DNA change and p.Phe508del for the resulting protein product) was identified, permitting genetic screening for CF (Ioannou et al., 2014). Carrier screening for CF is currently offered to all women considering pregnancy or who are pregnant in the United States (ACOG Committee Opinion No. 691), however is not routinely offered to the general population in Canada.

Carrier screening programs have continued to develop and are now available for individuals of various ethnicities and for a number of different conditions. For example, AJ carrier screening has expanded to include screening for additional AR conditions that are more prevalent in the AJ population than in the general population such as Canavan disease and familial dysautonomia (Joint SOGC-CCMG Committee Opinion No.335). In the United States, carrier screening for spinal muscular atrophy is offered to all women who are considering pregnancy or are pregnant (ACOG Committee Opinion No. 691). Carrier screening for specific AR conditions is also available to individuals of French-Canadian descent, and individuals belonging to groups with a high prevalence of AR disease such as Hutterite and Mennonite communities (Joint SOGC-CCMG Committee Opinion No.335).

### 1.3.4 Carrier Screening Methods

The general approach to carrier screening is to test for the presence or absence of common disease-causing variants present within a population. For example, although there are approximately 2000 variants in the CFTR gene that have been associated with CF, the majority of these variants are rare (Drumm et al., 2012). The most common pathogenic variant associated with CF is the variant referred to as ΔF508, which accounts for 70% of all CF pathogenic variants. (Drumm et al., 2012). The current recommendation is to screen for only the most common pathogenic variants known to cause classic CF which includes at minimum the 23 most common pathogenic variants that will identify approximately 88% of non-hispanic white carriers (i.e. the test sensitivity or detection-rate) (ACOG Committee Opinion No. 691). This approach to screening is inexpensive, has a high detection-rate (can identify the majority of carriers in the at-risk population) and provides results that are generally simple to interpret, as variants on the screening panel have a known association with the disease and a predictable clinical outcome.

While this approach can significantly reduce an individual's carrier risk, it cannot eliminate it completely since only a subset of all pathogenic variants are included in the test. Therefore, the is a residual risk, which is defined as the remaining carrier risk after a negative carrier test (Wilson et al., 2016). For example, an individual of Northern European ancestry without a family history of CF will have a 1 in 25 risk of being a carrier. After a negative test screening for the 23 most common CF variants, this individual will have a residual carrier risk of 1 in 200 (ACOG Committee Opinion No. 691).

Tests with a high detection rate (sensitivity) will have a lower residual risk, while a screening test with a low detection rate will have a higher residual risk. The detection rate of a genetic test can be limited by a number of factors such as the sequencing method used and the individual's ethnicity. Therefore, a test may have a high detection rate in an at-risk population but a lower detection rate in the general population, which may comprise of more rare pathogenic variants that are not included in the screening test. For example screening for the 23 most common CF pathogenic variants has a detection rate of 88% in non-hispanic Whites, but a detection rate of 64% in African Americans. The residual carrier risk for someone of African American descent is therefore higher after a negative CF panel test at 1 in 170 (ACOG Committee Opinion No. 691). The detection rate can be improved in such situations by full gene sequencing, which allows identification of rare pathogenic variants regardless of ethnicity.

### 1.3.5 Carrier Screening in Canada

Currently, carrier screening in Canada is targeted to those who are at high risk due to ethnicity or family history. The *Joint Society of Obstetricians and Gynecologists and the Canadian College of Medical Genetics (SOGC-CCMG) Opinion Statement on Reproductive Carrier Screening* (R. D. Wilson et al., 2016) provides a guideline for carrier screening for Canadian practitioners. The populations and conditions (and their respective carrier frequencies) recommended for carrier screening are summarized in Table 1. The guideline further outlines six criteria for carrier screening:

1) *the condition must have a significant impact on morbidity*
2) *intervention that improves patient outcome must be available*
3) *there must be a high frequency of carriers in the population*
4) *testing must be available that is cost effective and has a high detection rate*

5) *individuals must have the opportunity to access to genetic counselling and provide informed consent*
6) *carrier screening must be a voluntary option for patients.*

**Table 1**. SOGC-CCMG carrier screening recommendations. Adapted from the 2016 Joint SOGC-CCMG Opinion for Reproductive Genetic Carrier Screening No. 335.

| Condition | Carrier Frequency | Screening Recommendation |
|---|---|---|
| **Fragile X syndrome** | 1/148 (female) | Offered to those with a personal or family history. |
| **X-linked hemophilia** | Prevalence in males ranges from 1/5500-1/30000 | Offered to those with a family history. |
| **Thalassemia/hemoglobinopathies** | Variable depending on type and ethnicity | Offered to women/families from ethnic backgrounds with a reported increased carrier frequency (African, Southeast Asian and Mediterranean descent) |
| **Cystic Fibrosis** | Saguenay Lac-St-Jean: 1/15<br>Charlevoix: 1/20<br>1/23-1/25 in Caucasians | French Canadians from the Quebec regions of Saguenay Lac-St-Jean and Charlevoix.<br>Personal or family history, or clinical manifestations of CF in the pregnancy. |
| **Spinal muscular atrophy** | 1/40-1/60 | Offered to those with family history. |
| **Tay-Sachs disease**<br>**Canavan disease**<br>**Familial dysautonomia** | 1/30 (AJ); 1/14 (Bas-St-Laurent and Gaspesie)<br>1/37-1/53<br>1/32 | Individuals of Ashkenazi Jewish heritage*<br>Families orignating from Quebec Bas-St-Laurent (Rimouski) and Gaspesie regions as well as from adjoining New Brunswick territories. |
| **Bloom syndrome**<br>**Cystic fibrosis**<br>**Fanconi anemia group C**<br>**Niemann-Pick type A**<br>**Mucolipidosis type IV**<br>**Gaucher disease**<br>**Glyocogen storage disease type 1a**<br>**Maple syrup urine disease**<br>**Dihydrolipoamide hydrogenase deficiency**<br>**Usher syndrome**<br>**Nemaline myopathy**<br>**Joubert syndrome**<br>**Walker-Warburg syndrome** | 1/104<br>1/28<br>1/89<br>1/90<br>1/100-127<br>1/18<br>1/64<br>1/97<br>1/107<br>1/120<br>1/168<br>1/92<br>1/150 | Recommend offering to individuals of Ashkenazi Jewish heritage*<br>with a positive family history for the condition. |
| **Tyrosinemia type 1**<br>**Leigh syndrome French Canadian type**<br>**Spastic ataxia, Charlevoix-Saguenay type**<br>**Agenesis of the corpus callosum with peripheral neuropathy** | 1/19<br>1/23<br>1/23<br>1/23 | Offered to couples for whom each partner has at least one grandparent originating from Saguenay Lac-St-Jean/Charlevoix region. |

*Ashkenazi Jewish (AJ) heritage is defined as having at least one grandparent of AJ background.

How the SOGC-CCMG recommends identifying individuals with a high carrier risk is outlined in Figure 2. Identification begins with a discussion about carrier screening with the family physician/general practitioner (GP) or obstetrician/gynecologist (OB/GYN) and collecting information on the family history and ethnicity. The guidelines recommend that women should be asked about symptoms in their family such as intellectual disability, muscular dystrophy, bleeding disorders, congenital anomalies and stillbirths. Individuals who are identified to have a family history suspicious of a genetic condition, have a family member with an inherited condition, or if both partners are identified to be carriers for the same condition should be referred to genetics to discuss carrier screening and reproductive or prenatal diagnostic options. For these individuals, carrier screening and genetic counselling services are provincially funded.

Although the SOGC-CCMG guideline provides recommendations for testing, what is actually covered under each provincial carrier screening program is independently determined by each province. For example, in Ontario carrier screening for individuals of AJ ancestry includes seven disorders that have high prevalence in the AJ community, whereas in Quebec, AJ individuals are screened for three conditions (GECKO, 2021).

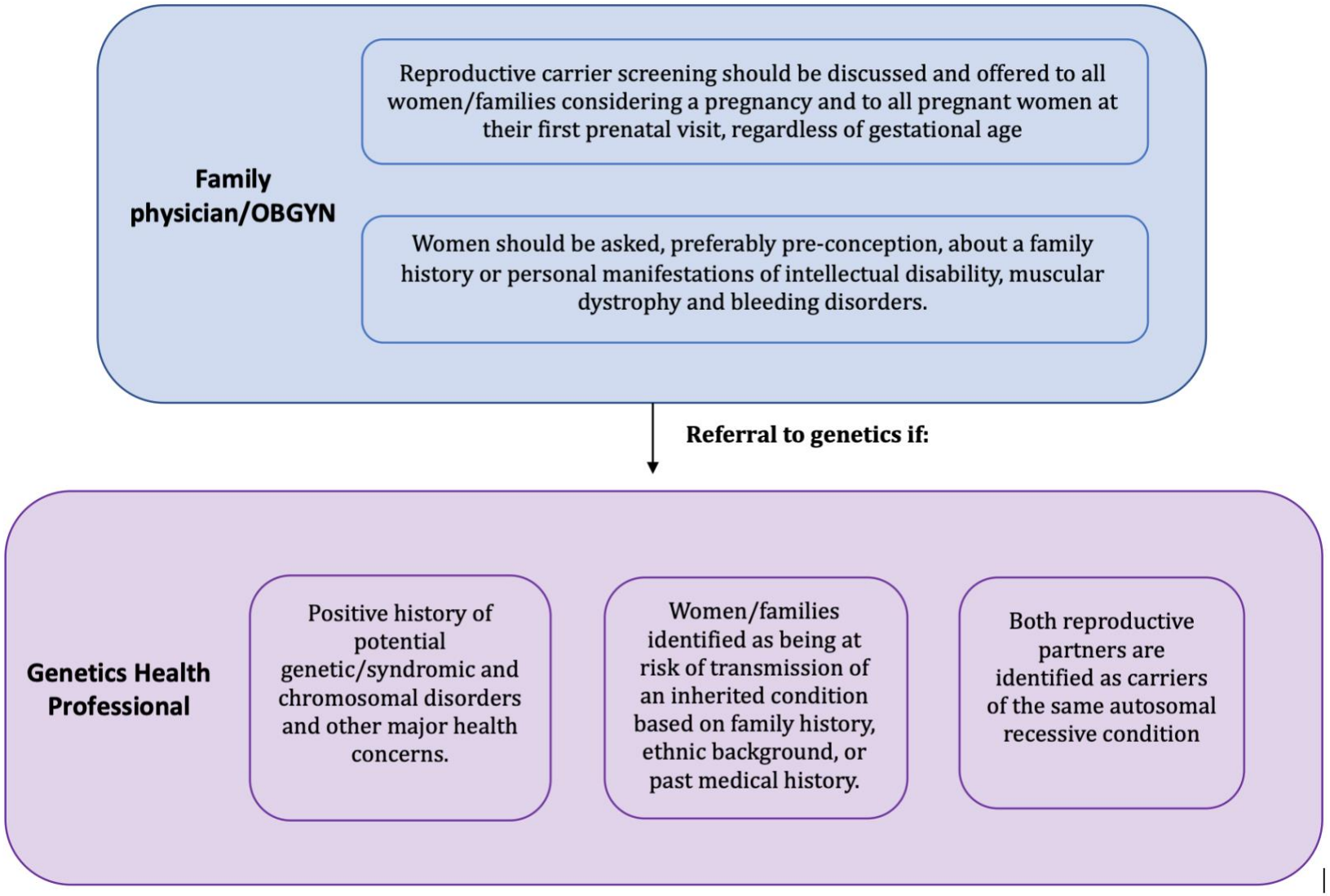



**Figure 2**. Algorithm for the identification of high-risk individuals for carrier screening. Adapted from the 2016 Joint SOGC-CCMG Opinion for Reproductive Carrier Screening No.335

## 1.4 BEYOND ETHNICITY AND FAMILY HISTORY BASED SCREENING

Next generation sequencing has led to a decrease in the cost of genetic testing and the time it takes to sequence DNA (Yohe et al., 2017). Continuous advances in molecular genetics and increasing characterization of genetic disorders has made it easier and cheaper to screen for additional genetic conditions in populations who would otherwise not be screened using the current carrier screening approaches.

### 1.4.1 Expanded Carrier Screening

ECS can test for carrier status for dozens, hundreds, or thousands of genes simultaneously, regardless of the individual's baseline risk for being a carrier (Lazarin et al., 2014). ECS is offered through the private sector by a number of genetic testing companies, the majority of which are based the United States (Chokoshvili et al., 2018). As of 2017, a few hospitals had developed their own ECS panels (Chokoshvilli et al., 2018). The very first ECS panel was available approximately a decade ago through the Silicon Valley start-up genetic testing company COUNSYL and cost approximately $349 USD per individual or $698 USD per couple (Pollack, 2010). With continued advancements in DNA sequencing technology over the last decade, the most cost effective ECS test currently available is offered by Invitae for $250 USD, with partner testing available for an additional $100 USD (Invitae Corporation, 2021). Some companies will offer genetic counselling services, which are either included in the price of the test or for an additional fee.

It is important to distinguish ECS from direct-to-consumer genetic testing (DTC-GT), such as ancestry testing, or 23&me, since test results obtained from DTC-GT are not generally used to make healthcare decisions, whereas ECS testing is a clinical test as it is performed in a Clinical Laboratory Improvement Amendments (CLIA) certified laboratory. A genetic result obtained from DTC-GT would need to be validated by a certified laboratory prior to being used to make healthcare decisions. ECS testing can be used to make healthcare decisions such as those related to preconception or prenatal care, for example, to pursue prenatal diagnostic testing, to conceive using in vitro fertilization with preimplantation genetic diagnosis, or to use a sperm or oocyte donor. While DTC-GT can be ordered by the consumer, ECS must be ordered by a physician or

healthcare provider on the patient's behalf. ECS can be completed via a saliva test that is mailed in or via a blood test drawn at local laboratory.

### 1.4.2 Comparison to traditional carrier screening

ECS has a number of benefits and limitations when compared to traditional carrier screening approaches. This section will compare both ECS and traditional carrier screening in the areas of detection rate, SOGC-CCMG carrier screening recommendations, clinical validity and clinical utility.

#### Detection Rate

The detection rate for traditional carrier screening approaches is generally high for individuals who belong to the target group for which the screening test was specifically designed. In situations where an individual not belonging to the at-risk group requires carrier screening (for example if their partner is identified as a carrier or they are of mixed ethnicity) the detection rate will generally be decreased, and the residual carrier risk will be higher. In these situations it may be appropriate to offer full gene sequencing to increase the detection rate after a negative carrier screening test. Since many ECS tests are performed by full gene sequencing, ECS will provide a higher detection rate, particularly for individuals who do not belong to high-risk populations. However the possibility to detect many variants can potentially complicate patient decision making in scenarios where rare variants with limited information or questionable association to disease are identified or variants associated with more mild disease phenotypes (Zhang et al., 2019). DNA sequencing can also identify secondary findings, for example pathogenic variants in genes known to be associated with a hereditary cancer syndromes (Cronister, A et al., 2019).

#### SOGC-CCMG Recommendations for carrier screening

The SOGC-CCMG criteria for carrier screening programs as outlined above in subsection 1.3.5: Carrier Screening in Canada are used to decide which conditions are good candidates for carrier screening in most provinces. While most ECS panels contain the SOGC-CCMG recommended conditions, there are many more that are beyond this list. One of the SOGC-CCGM criteria is that individuals must have the opportunity to access genetic counselling and

provide informed consent. Since genetic counselling is not always offered by ECS testing companies and pre-test counselling may be provided by a non-GHP provider with limited experience consenting patients to genetic testing, it is possible that the patient may not be fully informed about all the possibilities stemming from ECS test results.

### Clinical validity

Clinical validity refers to the strength of the gene-disease association. Some genes have strong evidence that supporting the association of a pathogenic variant with a particular disease. For other conditions, particularly ones that are very rare, the association may not be as strong (Balzotti et al., 2020). Therefore, it is important that a carrier test has clinically valid associations between pathogenic variants and disease prognosis, since individuals use this information to make reproductive or prenatal decisions. Traditional carrier screening tests are typically thought of as being clinically valid: the conditions screened are relatively common, providing ample evidence of gene-disease association. Furthermore, the subset of pathogenic variants that are selected for carrier screening are associated with a predictable disease phenotype. For example CF carrier screening is limited to the most common pathogenic variants in the CFTR gene because these variants have a clear association with the classic CF phenotype. Meanwhile full gene sequencing is not recommended because there are nearly 2000 variants that have been identified in the CFTR gene, many of which are very rare and may be associated with symptoms that are less severe than classic CF, such as CFTR-related disorders, which can be limited to azospermia with mild lung involvement.

The clinical validity of genes included on ECS panels can vary, since some conditions are very rare and have limited data available to support gene-disease association. Other factors such as reduced penetrance and variable expressivity can further complicate counselling and patient decision making. Conditions with variable expressivity or reduced penetrance decrease the clinical validity of a test (Henneman et al., 2016).

### Clinical utility

Tests that can lead to improved patient outcomes or which can guide treatment and intervention are clinically useful (Lesko et al., 2010). On the other hand, identifying variants without a definitive association with disease limits the clinical utility of a test. The benefit of

screening for common, known pathogenic variants is that the associated phenotype is known, and the clinical utility of the test is explicit. For example follow-up testing may be recommended, testing for family members at risk may be available and there are routine reproductive options or prenatal testing options that can be discussed. For individuals with a negative result, their residual risk is clear (Leung et al., 2021). Full gene sequencing for rare conditions, such as those included on ECS panels, may provide a clinical utility that is less clear since genotype-phenotype correlation may not be established, treatment or intervention options may not be available and residual risks may be difficult to predict for conditions where a carrier frequency is not known (Henneman et al., 2016).

Consent

A limitation of screening for dozens to hundreds of conditions is that it can complicate informed consent. For instance, due to the number of conditions included on some ECS panels, it is not feasible to counsel about each one individually. Rather, a tiered approach to describing the conditions has generally been used. For instance, the first tier of conditions may include those that result in a shortened life span or intellectual disability. The second tier of conditions may decreased quality of life such as impaired mobility, and internal physical malformation. The third tier may be conditions causing sensory impairment, and immunodeficiency. And the final tier includes conditions causing reduced fertility (Lazarin et al., 2014). Patients should broadly understand the types of conditions they are being screened for, which some argue is more time consuming and more difficult for patients to grasp compared to the consenting patients to screen for one genetic condition. In addition, patients may also have to understand concepts such as penetrance (the proportion of individuals carrying a particular variant of a gene who are symptomatic and variable expressivity – the range of symptoms that can occur in different individuals with the same genetic condition.

### 1.4.3 Expanded Carrier Screening in Canada

The SOGC-CCMG guidelines for reproductive carrier screening (No.335) was last updated in 2016 and briefly addresses ECS. The guidelines refer readers to two statements on ECS made by the American College of Medical Genetics (ACMG) in 2013 and 2015 and summarizes the key points. The guidelines also refer readers to the Genetics Education Canada

Knowledge Organization (GECKO) website, which provides tips for providers before and after ordering ECS. Tips before ordering ECS include considering whether the company offers genetic counselling, considering whether the ordering provider would be comfortable handling uncertain results, and ensure that patient has some familiarity with the nature of disorders on the panel, such as modes of inheritance, availability of treatment or management, and age of onset. Points for consideration after ECS is ordered can help providers with results interpretation. For instance, knowing that a negative result does not rule out the possibility of being a carrier (there remains a residual risk, although it is greatly reduced) or other genetic conditions not tested, there may be recommendations for the patient if they have a positive result, and using an infographic aiding the interpretation of variants of uncertain significance (VUS) may be helpful. The guidelines further state that women or families who choose to pursue private-pay ECS and are subsequently found to be carriers have to be made aware prior to ordering ECS that access to formal genetic counselling may be limited (GECKO, 2021).

### 1.4.4 Expanded Carrier Screening in the United States & Europe

The United States and Europe have issued practice guidelines specific to ECS. In 2013 the ACMG issued a position statement on prenatal/preconception expanded carrier screening, which aimed to address the lack of professional guidelines regarding which disease genes and variants should be included on an ECS panel (Grody et al., 2013). According to this statement, in order for a particular disorder to be included in carrier screening it should meet the following five criteria:

1. *Be of a nature that most at-risk patients and their partners identified in the screening program would consider having a prenatal diagnosis to facilitate making decisions surrounding reproduction.*
2. *Patients must provide consent for adult-onset disorders that are included in screening panels, especially when there maybe implications for the health of the individual being screened or other family members.*
3. *For each disorder, the causative gene(s), mutations, and mutation frequencies should be known in the population being tested, so that meaningful residual risk in individuals who test negative can be assessed.*
4. *There must be validated clinical association between the mutation(s) detected and the severity of the disorder.*
5. *Compliance with the American College of Medical Genetics and Genomics Standards and Guidelines for Clinical Genetics Laboratories, including quality control and proficiency testing.*

The statement also states that screening for dozens of hundreds of conditions simultaneously will require a more "*generic consent process than is typically used for single-disease screening because it may not be practical for a clinician to discuss each disease included in multi-disease carrier screening panels*." Lastly, the guidelines state that genetic counselling before testing should be made available and post-test genetic counselling for those with positive screening results is recommended. In 2015, the ACMG issued a joint statement with the American College of Obstetricians and Gynecologists, National Society of Genetic Counselors (NSGC), Perinatal Quality Foundation and Society for Maternal-Fetal Medicine regarding ECS in reproductive medicine (Edwards et al., 2015), which addresses points to consider when offering ECS and outlined the components of consent for ECS.

The European Society of Human Genetics has also issued recommendations regarding responsible implementation of expanded carrier screening (Henneman et al., 2016). The recommendations are similar to those in the American guidelines and address the types of conditions that should be included on ECS panels (severe, childhood onset), timing of ECS, and how to provide informed consent for ECS.

## 1.5 OVERVIEW OF CANADIAN PUBLIC HEALTHCARE

Publicly funded medical insurance in Canada (referred to as Medicare) is federally regulated under the *Canada Health Act* of 1984. Under this Act the primary objective of Canadian health care policy is "*to protect, promote and restore the physical and mental well-being of residents of Canada and to facilitate reasonable access to health services without financial or other barriers*" (Canada House of Commons, 1984). This legislation established the criteria for public healthcare administration and delivery and also prohibited billing and user fees for insured services. Each province/territory must deliver healthcare that meets five criteria of public administration, comprehensiveness, universality, portability and accessibility in order to receive federal funding. These criteria are summarized below:

1) **Public administration** – healthcare must be administered and operated on a non-profit basis by an appointed public authority.

2) **Comprehensiveness** - the health care insurance plan of a province must insure all insured health services provided by hospitals, medical practitioners or dentists, and similar or additional services as applicable under provincial law.
3) **Universality** - the health care insurance plan of a province must entitle one hundred per cent of the insured persons of the province to the insured health services provided for by the plan on uniform terms and conditions.
4) **Portability** – The provincial and territorial plans must cover all insured persons when they move to another province or territory within Canada.
5) **Accessibility** – The provincial and territorial plans must provide all insured persons reasonable access to medically necessary hospital and physician services without financial or other barriers."

The federal government supports the funding of provincial and territorial healthcare programs on a per capita basis cash transfer under the Canada Health Transfer (CHT). The CHT is financed using revenue from federal, provincial and territorial taxation. In 2020-2021, the CHT was an estimated $42 billion (Majoir Federal Transfers Canada, 2021). The CHT funds approximately 70% of Canadians' healthcare, with the remaining 30% paid for through the private sector (Health Canada, 2021).

While public healthcare is unified under national legislation and must meet specific criteria, healthcare administration and delivery is highly decentralized. For example, while the Act states that medically necessary services must be covered by public health insurance, what constitutes a medically necessary service is not defined under the Canada Health Act and individual provinces and territories determine what qualifies as a medically necessary service. While hospital and physician services are universally agreed upon as medically necessary services, the availability of public funding for other health care services such as prescription drugs, home care, long-term care and mental health care may differ by province/territory, which may be financed through a combination of public and private insurance. For example, in Ontario the majority of prescription drugs are covered for anyone under 24 years of age and over 65 years of age who is not covered by private insurance (Get Coverage for Prescription Drugs | Ontario.Ca, 2021). In British Columbia, the amount of prescription drugs covered is based on income (PharmaCare for B.C. Residents - Province of British Columbia, 2021. Healthcare services such as dental care, vision

care for adults and outpatient physiotherapy are financed almost entirely by private insurance or out of pocket (Marchildon et al., 2020) .

## 1.6 PRIVATE HEALTHCARE IN CANADA

Although public healthcare is often a source of national pride and a defining feature of what it is to be Canadian (Canadian Press Poll: Canadians Are Most Proud of Universal Medicare, 2012), Medicare is not without its critics. A prominent concern is whether current levels of healthcare spending are sustainable, particularly when faced with an aging population. Shortcomings of public healthcare such as long wait times and overcrowded hospitals lead some to argue that Canada could benefit from a model in which public health and private insurance for medically necessary services exist in parallel (Flood & Thomas, 2018). Proponents of this model argue that if medically necessary services are accessible through private pay, this could alleviate some pressures of public healthcare and potentially reduce wait times, overcrowding and government spending. Others argue that such a model is a threat to public healthcare that could introduce a two-tiered system that benefits those of a higher socioeconomic status, furthering the gap in health outcomes between the wealthy and the poor. These shortcomings of the public system have been used to challenge the Canada Health Act in court.

In Chaoulli v. Quebec (2005) the Supreme Court of Canada ruled that prohibiting Quebec residents from obtaining in the private sector health care services already available under Quebec's healthcare plan, but subject to long wait times infringed on Quebecers rights to life and security of person under the *Quebec Charter of Human Right and Freedoms*. This decision, only binding in the province of Quebec, supports private-pay access for certain medically necessary services in circumstances where long wait times prohibit reasonable access through public healthcare.

In 2016, Cambie Surgeries Corporation, a private surgery clinic in British Columbia, challenged the Medicare Protection Act (MPA), which prevents privately practicing physicians from charging patients enrolled in public healthcare for services covered by public insurance. The lawsuit argued that long wait times can cause patients prolonged suffering, which is unconstitutional and violates the "right to life, liberty and security of the person" and "equal protection" under the *Canadian Charter of Rights and Freedoms*. The claim was dismissed by the Supreme Court of British Columbia in 2020, which concluded that the benefits of publicly

available healthcare are "*significant and far outweigh any deleterious effects they cause*" because they "*ensure that access to necessary medical care is based on need and not the ability to pay, thereby protecting those with the greatest healthcare needs*" (Attorney General of British Colombia, 2020)

These two cases demonstrate the divide between those with a strong desire and willingness to pay privately for publicly covered services and the equally strong desire of those to preserve a one-tiered healthcare system. With opposing Supreme Court judgements, private healthcare in Canada is a debatable issue that must balance the developing healthcare needs of Canadians, while protecting the interests of the most vulnerable groups.

## 1.7 OVERVIEW OF GENETIC SERVICES IN CANADA

### 1.7.1 Role of the Clinical GHP

GHPs in Canada include medical geneticists, genetic counsellors (GCs) and genetic counselling assistants. Medical geneticists are specialized physicians who assess patients suspected to be affected by a genetic condition, discusses possible testing options and provide medical guidance and recommendations in the management of genetic disorders. Molecular Geneticists typically have a doctoral degree and additional postdoctoral training. They are scientists who work as laboratory directors or as assistants to laboratory directors in laboratories that perform biochemical, molecular or cytogenetic testing on human samples. In Canada, many usually work in a hospital setting (Canadian College of Medical Geneticists, 2020).

GCs are specialized healthcare professionals who provide education and support for patients at risk of inheriting a genetic condition and help individuals adapt and cope with a genetic diagnosis (National Society of Genetic Counselors, 2021). GCs will usually see patients who are at high risk of being a carrier for pre-test counselling to discuss their reproductive risks, risks to other family members and discuss the benefits and limitations of available carrier testing options. GCs will also provide post-test counselling once the carrier screening result is received and may inform the patient if screening of a reproductive partner is warranted (Joint SOGC-CCMG Committee Opinion No.335). GCs frequently work with a medical geneticist, but can also support other specialists in the provision of specialized genetics care.

### 1.7.2 The Public Genetics Clinic

Publicly funded genetic services are provided by geneticists and GCs as a consultation service and are typically housed within hospitals. Patients are usually referred to a genetics clinic by a healthcare provider if there is suspicion of a hereditary condition in the individual or their family. Referral criteria, testing criteria and coverage of genetic testing is determined by the province and therefore likely varies across the country. For example a genetic test that is covered in one province may not be covered in another. Individuals who meet specific institutional/provincial referral criteria are eligible for a genetics appointment in the publicly funded clinic. These patients meeting institutional/provincial criteria can have publicly funded genetic testing, which is typically reserved for those at high risk of an inherited condition. For those patients that do not qualify for publicly funded genetic testing, the option to pursue private-pay genetic testing may or may not be brought up by the GHP, as there is currently no legal obligation to inform patients of this option.

Whether the GHP informs their patient of the option of private-pay genetic testing or helps the patient with selecting and arranging the test is left to the discretion of the GHP/their institution, as there is currently no standard of practice regarding private pay genetic testing in Canada. A 2019 study assessing Canadian genetic health professionals' attitudes toward private-pay testing found that 95% of survey respondents reported discussing private-pay genetic testing with patients (Di Gioacchino et al., 2019). The most frequently discussed tests included multi-gene panels, noninvasive prenatal testing (NIPT) and preimplantation genetic diagnosis.

### 1.7.3 Private Pay Genetic Counselling & Testing in Canada

Several private genetics clinics in Canada offer private pay genetic services for a fee to anyone regardless of their risk status. Individuals may also choose to pay for genetic testing without visiting a private genetics clinic, for example ECS can be ordered by GP and genetic counselling services may or may not be offered by the company offering ECS. Individuals may choose to pursue private pay genetic testing for a variety of reasons, such as avoiding lengthy wait times for an appointment in the public genetics clinic, to protect their privacy, as preventive healthcare or to access a test not available in the public system. It is unknown how many

Canadians have paid privately or would be willing to pay for genetic testing or genetic counselling services.

Private pay testing can gain acceptance within public healthcare as has been the case with maternal plasma cell-free DNA screening (cfDNA), commonly referred to as non-invasive prenatal testing (NIPT). This is a prenatal screening test that uses cfDNA in maternal blood to screen for trisomy 13, 18, 21, in the fetus with high sensitivity (Audibert et al., 2017). Cell-free DNA screening is available for $99 USD (Invitae, 2021) or approximately $500 CAD (Harmony), depending on the laboratory the patient chooses (Dynacare, 2021). Certain provinces may cover the cost of cfDNA screening for women at high risk of having a child with trisomy. Since 2013, it has been recommended that cfDNA screening should be an option available to women at increased risk of having pregnancy with trisomy 21, 18 or 13 (Langlois & Brock, 2013).

Although there is no consensus on how to address private pay in the genetics clinic, a practice guideline addressing private pay genetic counselling and testing in Canada is currently under development by the Canadian Association of Genetic Counsellors (CAGC) (personal communication, Ingrid Ambus, April 2021). This guideline aims to address how to best balance the use of private and public healthcare systems to maximize access to genetic counselling services for all Canadians.

## 1.8 STUDY RATIONALE

Given the unique potential challenges associated with ECS, as outlined in the preceding sections, it is imperative to understand the experiences of healthcare providers with this test. While other countries such as the United States and various European countries have bodies of literature and specific recommendations pertaining to ECS, this body of literature excludes the Canadian perspective. There is also a limited understanding of Canadian GHP attitudes toward private pay genetic testing, which could be shaped by working in a public healthcare system. Practical issues and ethical considerations raised by private pay testing has been voiced by genetic counsellors across the country (di Gioacchino et al., 2019). Given that each healthcare system has its own unique strengths and limitations, Canadian ECS guidelines should be specifically informed by the Canadian perspective.

This study used a mixed methods design to collect both survey and interview data in order to explore GHPs experiences and opinions of ECS across Canada, and to identify related themes. Identifying and qualitatively exploring GHP opinions and experiences with ECS may provide a foundation for future studies into this emerging technology.

### 1.8.1 Research Questions & Aims

Due to the exploratory nature of this study, there were two broad research questions:

1. What are the opinions of Canadian GHPs toward ECS?
2. What are the experiences of Canadian GHPs with ECS?

The aims of this study were to:

1. Describe GHP opinions of ECS. This included understanding professional opinions about whether ECS was beneficial or harmful and how GHPs felt about counselling patients for ECS.
2. Describe GHP experiences with ECS. This included understanding how often GHPs counseled patients for ECS and whether they experienced any ethical or logistic challenges when counselling patients.

# CHAPTER 2:METHODS

## 2.1 RATIONALE FOR A MIXED-METHODS STUDY DESIGN

Mixed methods research involves both quantitative and qualitative data collection, analysis and integration to answer a research question (Creswell & Plano Clark, 2007). Mixed methods incorporates both the positivist research paradigm inherent to quantitative research methods, which aims to discover a measurable and universal truth within the data, and the interpretivist research paradigm of qualitative research, which recognizes multiple truths that are shaped by individual experiences and social contexts (Ravich & Mittenfelner Carl, 2016 ). The rationale for mixing both of these research paradigms into a single mixed methods approach is one of pragmatism. Each method alone is insufficient to answer the research question and the combination of quantitative and qualitative methods will best answer the research question. Incorporating the complementary strengths of each method while supplementing the limitations of each method will expand, strengthen and validate a study's conclusions (Greene & Caracelli, 1997).

The research question that this study aims to answer is: what are Canadian GHPs experiences and opinions of ECS? The rationale for using a mixed methods design to answer this research questions is that part of understanding Canadian GHP experience and opinion of ECS requires a large sample size - a strength of quantitative methods. The generalizable result obtained through quantitative methods however would lack the many nuances that impact a user's experience and opinions. For example, GHPs work in provinces with different provincial healthcare plans, different institutional practices, different sociodemographic patient populations and different personal experiences with working and using public healthcare. Qualitative methods can capture these contextual factors. Directly integrating the quantitative results to the qualitative results allows for data triangulation, which is the concept that if the same result is observed in both quantitative and qualitative data sets, it provides a more valid conclusion (Plano Clark & Ivankova, 2016).

## 2.2 STUDY DESIGN

The study consisted of a survey phase (quantitative data collection) followed by an interview phase (qualitative data collection). Central to a mixed methods research design is the mixing, or integration of both quantitative and qualitative data. There are different strategies for the timing of quantitative and qualitative data integration, depending on the research question and study design. This study followed a convergent strategy, which consisted of separate quantitative and qualitative data collection and analysis phases, followed by integration of both data sets (Creswell & Plano Clark, 2018). Data sets were integrated by comparing and contrasting the qualitative and quantitative results.

GHPs currently working in Canada or GHPs working as a Canadian representative for an American company were eligible to participate in the study. For the purpose of this study GHPs included GCs, medical geneticists, molecular geneticists, and genetic nurses. There was no minimum work experience required to participate. Eligible GHPs were able to complete a survey, an interview or both. An overview of GHP recruitment to the survey and interview is depicted in Figure 3.

This study was approved by the Research Ethics Board at the University of Manitoba (approval number HS23880/H2020:198).

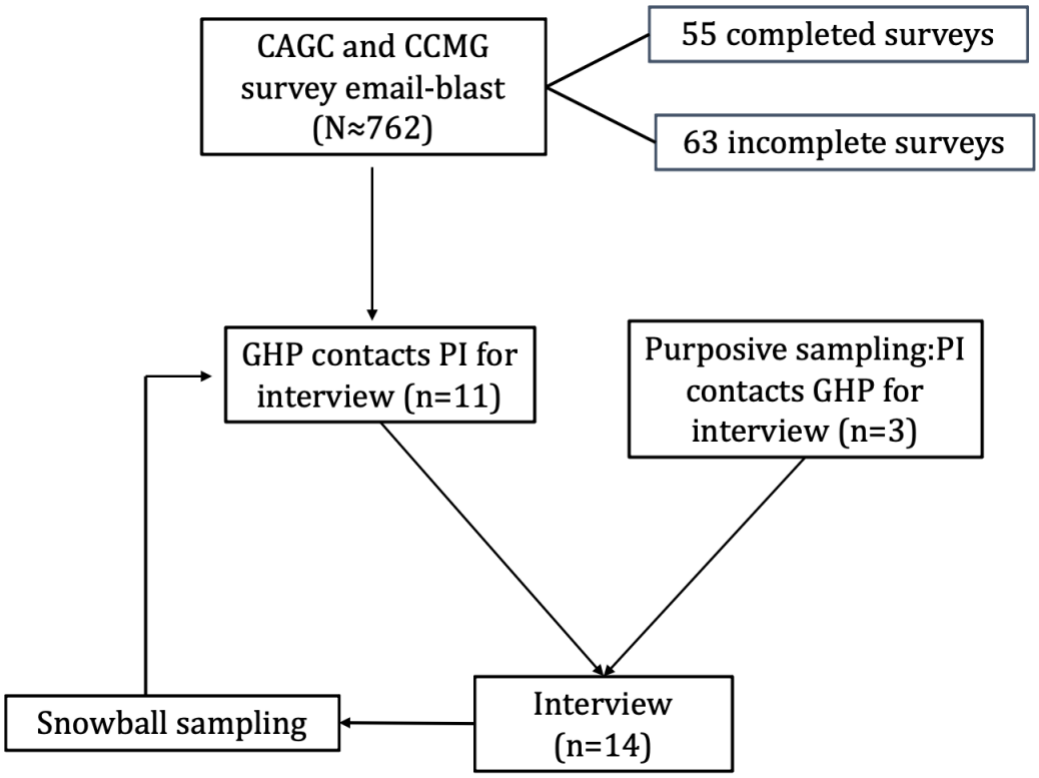



**Figure 3**. Procedure used to recruit GHPs to the survey and interview portions of the study

2.2.1 Survey

The survey was disseminated electronically in July 2020 to Canadian GHPs via an eblast from the Canadian Association of Genetic Counsellors (CAGC) (n~400) and the Canadian College of Medical Geneticist (CCMG) (n~362). A reminder email was sent to the CAGC membership 6 weeks after the initial eblast. Snowball sampling was used to recruit GHPs who were not members of the CAGC or CCMG; the invitation to participate requested that recipients forward the study invitation to their Canadian GHP colleagues. Survey data was collected and managed using the REDCap (Research Electronic Data Capture) tool hosted at the University of Manitoba (Harris et al., 2009). REDCap is a secure, web-based software platform for building and managing online surveys. REDCap only allows anonymous collection of survey data which cannot be linked back to individual participants. Therefore, the number of interview participants who completed a survey is not known. By completing the survey, the participant consented to participate in this portion of the study.

The primary goals of the survey were to 1) obtain demographic information of the Canadian GHP population who had experience with ECS, 2) understand in what context and how much experience Canadian GHPs had with ECS and 3) obtain a general sense of Canadian GHP opinions of ECS. Survey demographic questions were developed using the National Society of Genetic Counsellors (NSGC) annul executive summary to facilitate comparison of study demographics to the Canadian GC population. The remaining survey questions were developed based on a literature review and a limited number of survey questions were adapted from the questionnaire developed by Di Gioacchino et al., (2019). The survey consisted of yes/no, multiple choice and free-text responses and included questions pertaining to how frequently the participant encountered ECS in clinic and in which clinical scenarios, as well as questions regarding ECS benefits/limitations and funding. For the complete survey, see Appendix A. The survey was piloted for content and clarity by three GC students and one maternal fetal medicine resident at the University of Manitoba, and was modified based on feedback. The final version of the survey was conservatively quoted as taking 15 to 20 minutes to complete. Quantitative data collection occurred from July 2020 to November 2020.

### 2.2.2 Interviews

Several strategies were used to recruit GHPs to the interview phase of the study which took place from November 2020 until February 2021. The initial recruitment approach was to inform participants about the interview at the conclusion of the survey, which listed the contact information of the student primary investigator (PI) and invited participants to participate in a one-on-one interview lasting 30-45 minutes. An email recruiting participants to the interview portion of the study was sent to the CAGC membership in late October, 10 weeks after the initial survey email blast. After the survey phase closed in November 2020 and the maximum interview participants were recruited from that route, additional GHPs were purposively recruited to promote provincial and professional diversity among the interview sample. Email invitations were sent by a committee member to colleagues working in genetics clinics in the three provinces not yet represented among the interview participants. Another committee member forwarded the email invitation to colleagues working molecular diagnostic laboratories in the three provinces not yet represented. A final recruitment attempt was made using social media (Twitter) by tweeting during the 2020 NSGC annual conference in November. Lastly, the

recruitment strategy was supplemented using snowball sampling. At the end of each interview, the student PI asked the participant to inform their colleagues of the interview phase of the study. The target number of interviews was approximately 15 based on previous research suggesting that a sample size of 15 is sufficient to reach thematic saturation, at which point no new themes are expected to emerge from the interviews (Guest et al., 2006).

The existing literature was referenced to construct the semi-structured interview guide. The interview guide was reviewed with the co-investigator and thesis committee and adjusted as necessary. The student PI met with Dr. Michelle Driedger, a professor at the University of Manitoba with qualitative research expertise and a member of the student advisory committee, to discuss proper interviewing techniques prior to conducting interviews with participants. The interview protocol explored 1) participants' experience with ECS in their current and/or past roles 2) participants' professional opinion toward ECS and 3) participants' personal opinion of ECS. The semi-structured interview guide can be found in Appendix B. Informed consent was obtained by the student PI prior to the interview using the interview consent form (Appendix C). All interviews were conducted over the phone with the exception of one interview which was conducted over the video communication application, Zoom. Interviews were conducted by the student PI using the semi-structured interview guide that was iteratively amended to address emerging themes as more interviews were completed. Interviews were audio recorded; four interviews were transcribed by the student PI and the remaining 10 were transcribed by a hired transcriptionist from the company TranscriptHeroes, who signed a confidentiality agreement before any data was shared. All transcipts obtained from TranscriptHeroes were audio-verified by the student PI for accuracy.

## 2.3 DATA ANALYSIS

### 2.3.1 Survey Data

Survey data was exported from REDCap into Microsoft Excel and Statistical Package for Social Sciences (IBMM SPSS Version 27). Dr. Depeng Jiang, associate professor in the Department of Community Health Sciences at the University of Manitoba provided statistical consultation. Descriptive statistics were used to summarize demographic data, and all other survey data, which consisted of multiple choice and yes/no questions. Due to a small sample

size, statistical analysis to determine non-random association between categorical variables (province of practice, practice area, years of experience) was not possible. Free text responses were exported into excel, and responses for each question were analyzed for similarities. Responses reflecting similar ideas were grouped together and tagged under a key word or phrase that summarized the idea expressed. Questions 22, 23, 25 and 26 were not included in the survey analysis as the majority response was “not applicable” or “unsure”.

### 2.3.2 Interview Data

Interview data was analyzed by assigning key words or phrases to the interview data that summarized the ideas being expressed, a process referred to as coding. Due to the large volume of data, coding was performed using Dedoose, an application for managing and analyzing qualitative data (Dedoose Version 8.3.45 Web Application for Managing, Analyzing, and Presenting Qualitative and Mixed Method Research Data., 2019). Codes were derived from the ideas expressed by the participants and there were no pre-existing codes that had been established prior to beginning the coding process. During first cycle coding, a combination of descriptive and topic coding was used to generate the initial codebook. Descriptive codes provide contextual information about the participant such as profession, years of experience, practice area and whether they had experience with ECS, while topic codes are words or short phrases that reflect the topic being discussed. The student PI and student supervisor independently coded two transcripts and met to discuss the codebook and resolve discrepancies. The codebook was then revised by the student PI and applied to the coding of all subsequent transcripts and re-coding of previously coded transcripts. Themes emerged from the data by analyzing for patterns and themes and grouping codes reflecting similar concepts. Themes were therefore generated from the data and were not developed prior to coding. The analysis process continued until data saturation was reached.

#### 2.3.2.1 Positionality

In qualitative research it is the researcher who collects, analyzes, interprets, and draws conclusions about the data. It is therefore important that the researcher reflects on their own biases, understanding and assumptions about the research topic. The researcher is a genetic

counselling student and has not paid for private-pay genetic testing or had publicly funded genetic testing. The student researcher does not have extensive experience personally receiving or navigating public healthcare. As a genetic counselling trainee, with limited direct experience working within the public healthcare system and counselling patients for carrier screening, the researcher did not have a strong pre-existing opinion towards ECS or private-pay testing in Canada. ECS in the Canadian genetics clinic was chosen as the research topic due to the interest of the student researcher in the area of prenatal and preconception genetics. It is possible that the power imbalance between the participants and the researcher, as well as the fact that the genetic counselling field is relatively small in Canada influenced whether participants felt more or less comfortable to provide candid responses.

### 2.3.3 Data Integration

Once both data sets had been analyzed independently, they were integrated by comparing the main themes that emerged in the interviews to the results of the survey. Similar results that emerged in both quantitative and qualitative data provided validation for each set of data. The qualitative data was also analyzed to see if context could be given to quantitative results.

# CHAPTER 3: SURVEY RESULTS

## 3.1 PARTICIPANT OVERVIEW & RESPONSE RATE

A total of 118 individuals started the online survey during the data collection period between July 2020-November 2020 and 55 surveys were completed. The remaining 63 surveys were less than half completed and were not included in the analysis. Survey participants included 45 GCs, nine medical geneticists and one molecular (PhD) geneticist. Eleven interview participants were recruited to the study via the survey or snowball sampling, and three participants were purposively sampled. The interview participants included 12 GCs, one medical geneticist and one molecular geneticist. Since survey data was collected anonymously, interview participants could not be linked back to their survey responses, and it is not known how many interview participants also completed the survey.

The survey response rate among GCs was estimated using data from the 2020 NSGC Professional Status Survey (PSS), which is an annual report that includes demographic information for Canadian GCs. According to the 2020 PSS there are approximately 635 GCs working in Canada. Using this information, the estimated survey response rate among GCs is 7% (45/635). Using the 2019 Medical Genetics Profile published by the Canadian Medical Association, it is estimated that there are approximately 111 medical geneticists working in Canada. The response rate among medical geneticists was therefore approximately 8% (9/111). Since there is no data available to suggest the number of molecular geneticists working in Canada, and only one respondent was from this group, this response rate was not calculated.

## 3.2 DEMOGRAPHIC CHARACTERISTICS

The demographic characteristics of survey participants are summarized in Table 2. The majority (82%, 45/55) of survey respondents were GCs and 18% (10/55) of respondents were geneticists (nine medical geneticist and one molecular geneticist). The majority of GCs who completed the survey were primarily in a prenatal or preconception role (53%, 24/45). The roles of the remaining 21 GCs ranged from those working in a clinical specialty other than prenatal/preconception (33%, 15/45), those working in the laboratory (7%, 3/45) or research (7%, 3/45). Geographically, the highest representation GHPs was from Ontario (51%, 28/55).

The number of years of work experience as a GHP ranged from less than one year to more than 20 years, although the majority (35%, 19/55) had between 1-4 years of experience as a GHP. Sixty-nine percent (38/55) of participants worked in a hospital clinic, 11% (7/55) worked in a private clinic, 9% (5/55) worked in a diagnostic laboratory, and 9% (5/55) worked in an academic institution.

The demographic characteristics of this study population are similar to those of the broader GC profession as reported in the 2020 NSGC PSS (summarized in Appendix D). Forty-eight percent of Canadian GCs work in Ontario, (51% of GCs in this study); 37% have between 1-4 years of experience as a GC, (42% of GCs in this study) and 73% work in a hospital clinic (69% in this study). Although the survey sample size is small, it is a reasonable representation of the Canadian GC workforce, however the low response rate did not sufficiently power the survey to allow statistical comparisons (i.e. between provinces, areas of practice, years of experience).

**Table 2.** Demographic characteristic of survey participants (n=55).

| **Demographic variable** | **Genetic Counsellor (n=45) n (%)** | **Geneticist (n=10) n (%)** |
|---|---|---|
| Specialty | | |
| Prenatal/Preconception | 24 (53.3) | - |
| Non-prenatal | 21 (46.6) | - |
| Province | | |
| British Columbia | 6 (13.3) | 1 (10) |
| Alberta | 2 (4.4) | 0 |
| Saskatchewan | 3 (6.7) | 0 |
| Manitoba | 2 (4.4) | 1 (10) |
| Ontario | 23 (51.1) | 5 (50) |
| Quebec | 7 (15.5) | 3(30) |
| Nova Scotia | 1 (2.2) | 0 |
| Newfoundland & Labrador | 1 (2.2) | 0 |
| Prince Edward Island | 0 | 0 |
| Yukon | 0 | 0 |
| Years of experience | | |
| Less than 1 year | 1 (2.2) | 0 |
| 1-4 | 19 (42.2) | 0 |
| 5-9 | 12 (26.7) | 3 (30) |
| 10-14 | 6 (13.3) | 2 (20) |
| 15-19 | 7 (15.6) | 1 (10) |
| 20 or more | 0 | 4(40) |
| Work setting | | |
| Hospital clinic | 31 (68.9) | 7 (70) |
| Diagnostic lab | 4 (8.9) | 1 (10) |
| Private clinic | 5 (11.1) | 1 (10) |
| Academia | 3 (6.7) | 1 (10) |
| Other | 2 (4.4) | 0 |

## 3.3 GHP EXPERIENCE WITH EXPANDED CARRIER SCREENING

To better understand the experience of Canadian GHPs with ECS, the survey included several questions related to ECS counselling, institutional or clinic policy, and frequency of clinical encounter (refer to Appendix A for survey). GHPs were eligible to complete the survey regardless of whether or not they had experience with ECS in order to gain broad perspectives and some results below pertain only to those who indicated they had experience with ECS (n=31). In addition, one respondent did not answer each question, and therefore totals may add up to less than 55.

The majority (57%, 31/54) of survey respondents had experience counselling patients for ECS, while 31% (17/54) did not have ECS counselling experience and 11% (6/54) responded that ECS counselling was not relevant to their practice area (Figure 4). Among those participants who had counselled patients for ECS, just over half (52%, 16/31) had counselled more than 7 cases. The majority had experience with both pre- and post-test counselling (71%, 22/31). Slightly over half of those with experience counselling ECS were prenatal GCs (52%, 16/31), followed by non-prenatal GCs (29%, 9/31) and medical geneticists (19%, 6/31) (Table 3). When examined by profession and practice area, 66% (16/24) of prenatal GCs had experience in counselling for ECS as well as 66% (6/9) of geneticists and 45% (9/20) of non-prenatal GCs.

**Table 3.** Number of ECS cases counselled by GCs and geneticists (n=31).

| Number of ECS cases | Genetic Counsellor (n=25) n(%) | Geneticist (n=6) n(%) |
|---|---|---|
| 1-2 | 8 (32) | 0 |
| 3-4 | 4 (16) | 3 (50) |
| 5-6 | 0 | 0 |
| 7 or more | 13 (52) | 3 (50) |

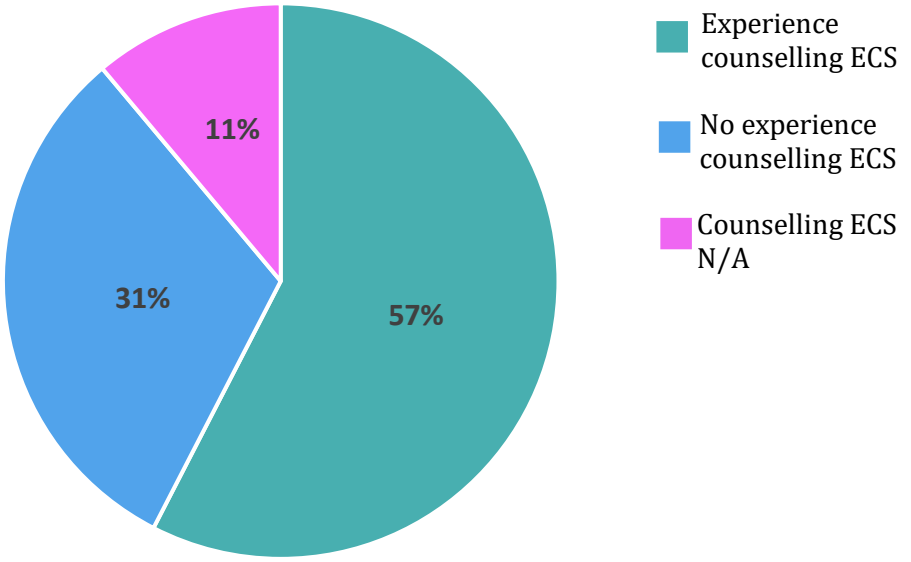



**Figure 4**. Proportion of GHPs with experience counselling patients for ECS. GHPs with experience counselling patients for ECS (green), GHPs with no experience counselling for ECS (blue) and GHPs who did not find counselling for ECS applicable in their current role (pink)(n=54).

The majority (54%, 29/54) of participants in this study worked in a clinic or institution that did not have a policy regarding ECS and 24% (13/54) were unsure whether their institution had a policy specific to ECS. Twenty-two percent (12/54) of participants' clinic or institution had a policy regarding ECS, 50% (6/12), of which were hospitals, 25% (3/12) were private clinics, 17% (2/12) were research institutions (2/12) and 8% (1/12) was a diagnostic laboratory. Participants with an institutional policy were prompted to answer follow-up questions to get a better sense of the nature of this policy (Figure 5). Of the participants with an institutional policy, most (58%, 7/12) had an informal agreement or unwritten understanding and the remaining 42% (5/12) had a formal, written policy. For most participants (83%, 10/12), this policy permitted the discussion of ECS with patients and for two participants their institution did not allow discussion of ECS. Most policies (70%, 7/10) permitted the provider to initiate discussion of ECS, while 20% (2/10) only permitted patient-initiated discussion of ECS (two of the 12 participants with an institutional policy did not provide an answer regarding whether their policy permitted provider or patient-initiated discussion of ECS so total is out of 10). Nearly all participants (83%, 10/12) agreed with their institution's policy, one participant whose institution did not permit discussion

of ECS disagreed with the policy and one participant whose institution permitted discussion of ECS was unsure.

Nine of the 12 participants included a free text response asking them to elaborate on whether they agree or disagree with their institution's policy. The participant who disagreed with their institution's policy to not discuss ECS wrote that "*It is our role to educate and inform. Many times, patients are not aware of the options that may be available and appropriate*." (P76-Survey, medical geneticist*)*. While the participant who agreed with their institution's policy not to discuss ECS with patients wrote that:

> *We are an OHIP covered clinic, and as such, I don't agree with us spending time/clinic resources discussing self-pay testing options with every patient who walks through the doors. But I think it is absolutely appropriate to discuss this with patients of ours who are consanguineous*. (P07-Survey, prenatal GC)

In total, four participants wrote that they felt it was their duty to inform patients that ECS is an option that is available. Two participants mentioned that they only discuss ECS with patients if there is a reason to do so and used the example of consanguinity. One participant mentioned that leaving the discussion of ECS to the discretion of the GHP introduces variability in the care patients receive, one participant indicated that they only bring up ECS if the patient asks, and one participant working in private fertility clinic indicated that patients are routinely made aware of ECS.

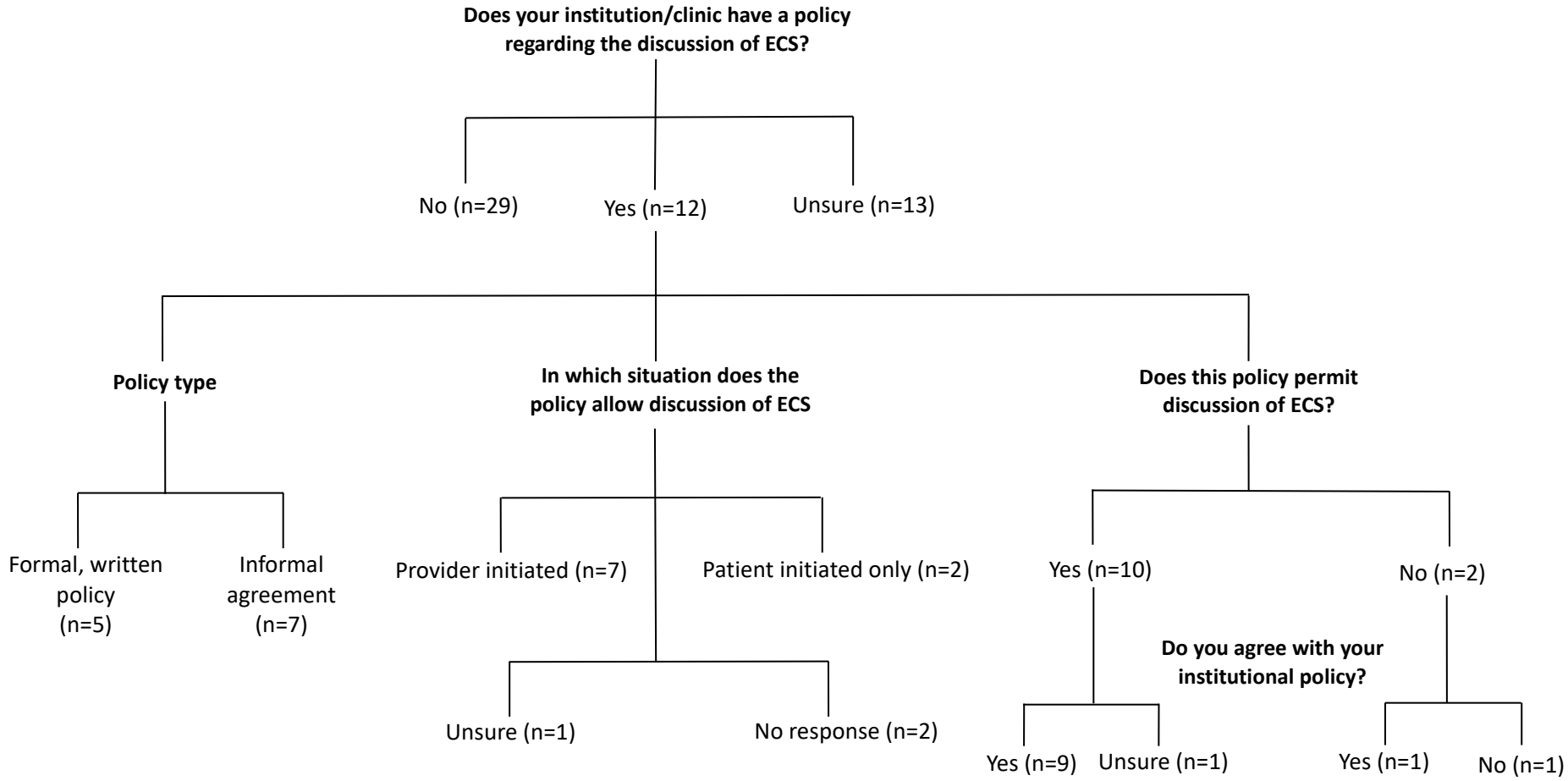



**Figure 5.** Institutional/clinic ECS policy characteristics and GHP opinions regarding their institutional policy (n=12).

Several survey questions were related to how often the discussion of ECS arises in clinic, which can include how often the subject of ECS is raised with patients, without necessarily providing full counselling (Figure 6). The majority (59%, 32/54) had discussed ECS with their patients, and for most (56%, 18/32) these discussions arose a few times a year. Interestingly, 5 of the 6 participants who worked in the private sector reported in their free-text response that they routinely discussed ECS with their patients. Just over half (53%, 17/32) of participants who discussed ECS with patients did not discuss ECS as frequently as other private-pay tests such as NIPT, while 44% (14/32) discuss ECS as frequently. Participants were split on whether discussion of ECS presented logistic or ethical challenges, with 41% (13/32) believing that it did, 41% (13/32) believing that it did not, and 19% (6/32) were unsure. Seventeen of the 32 respondents submitted free-text responses describing the logistic/ethical challenges related to ECS. The most common response, raised by 6 respondents was that of unequal access to ECS due to cost or due to patients with a higher education level being more likely to inquire or be aware of other testing options. Other responses related to the clinical challenges related to ECS. Four participants stated that ordering and arranging the test was time consuming and they would leave this to the family physician. The remaining free-text responses that related to clinical challenges included who should pay for the test, if it is indicated enough to warrant recommendation, difficulty getting a partner tested through the provincial system and reclassification of VUSs.

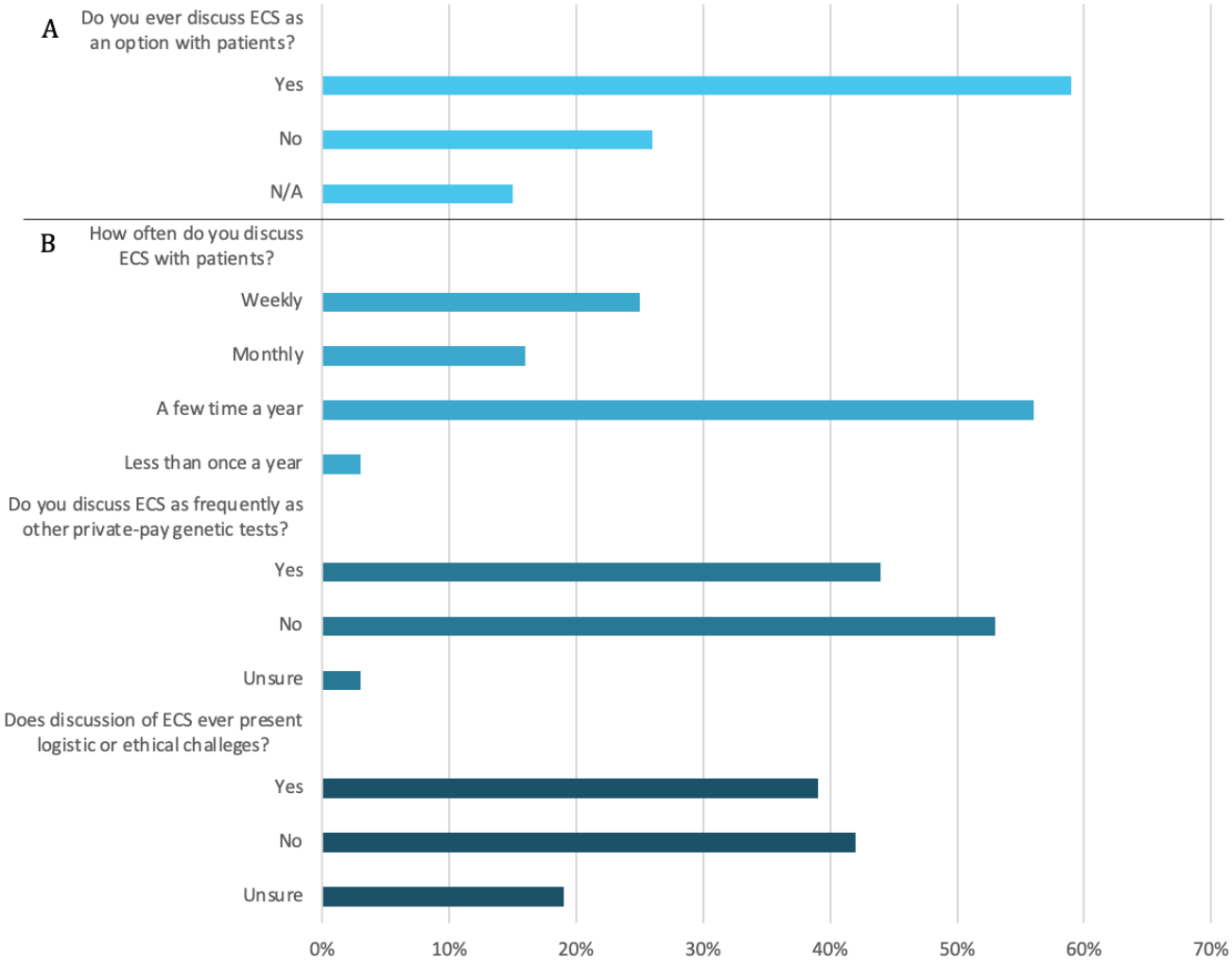



**Figure 6.** GHP experience discussing ECS in clinic. A) Proportion of participants in this study who had discussed ECS with patients (59%, 32/54). B) Follow-up questions regarding GHP experiences with discussing ECS with patients (n=32).

## 3.4 GHP OPINIONS OF EXPANDED CARRIER SCREENING

GHP opinions are presented in the following section among three groups: total survey respondents, survey respondents with the most ECS experience (those who had counselled seven or more ECS cases; n=16) and those who had the least ECS experience (counselled zero ECS cases; n=17). Differences in opinions emerged between those with the most and least experience with ECS, and although the number of responses per cell is not large enough to be measured statistically, the similar sample size of these two groups allows easy visual comparison. Survey questions explored opinions of ECS compared to targeted carrier screening, funding and discussion of ECS in Canadian healthcare, and which healthcare providers should inform patients about the option of ECS.

### 3.4.1 Targeted carrier screening compared to ECS

The majority of survey respondents (43%, 23/54) agreed that they prefer to offer targeted carrier screening over ECS to their patients, while 17% (9/54) disagreed with this statement and 19% (10/54) were neutral. There was a difference in agreement with this statement between GHPs with the most and least ECS experience, with the majority (38%, 6/16) of GHPs experienced with ECS disagreeing with the practice to offer targeted carrier screening over ECS, and the majority (47%, 8/17) of GHPs least experienced with ECS agreeing with this statement (Figure 7A).

Participants were then asked whether ECS presents more benefits, limitations or a balance of the two for patients in comparison to targeted carrier screening. Over half (54%, 30/55) of all participants thought that ECS presents a balance of benefits/limitations for the patient and 38% (21/55) thought that ECS presented more advantages for the patient. None of the respondents thought that ECS presented more limitations for the patient. Sixty two percent (10/16) of GHPs with the most ECS experience thought that ECS presented more benefits for the patient, while 71% (12/17) of GHPs with the least ECS experience thought that ECS presented a balance of benefits and limitations for the patient (Figure 7B).

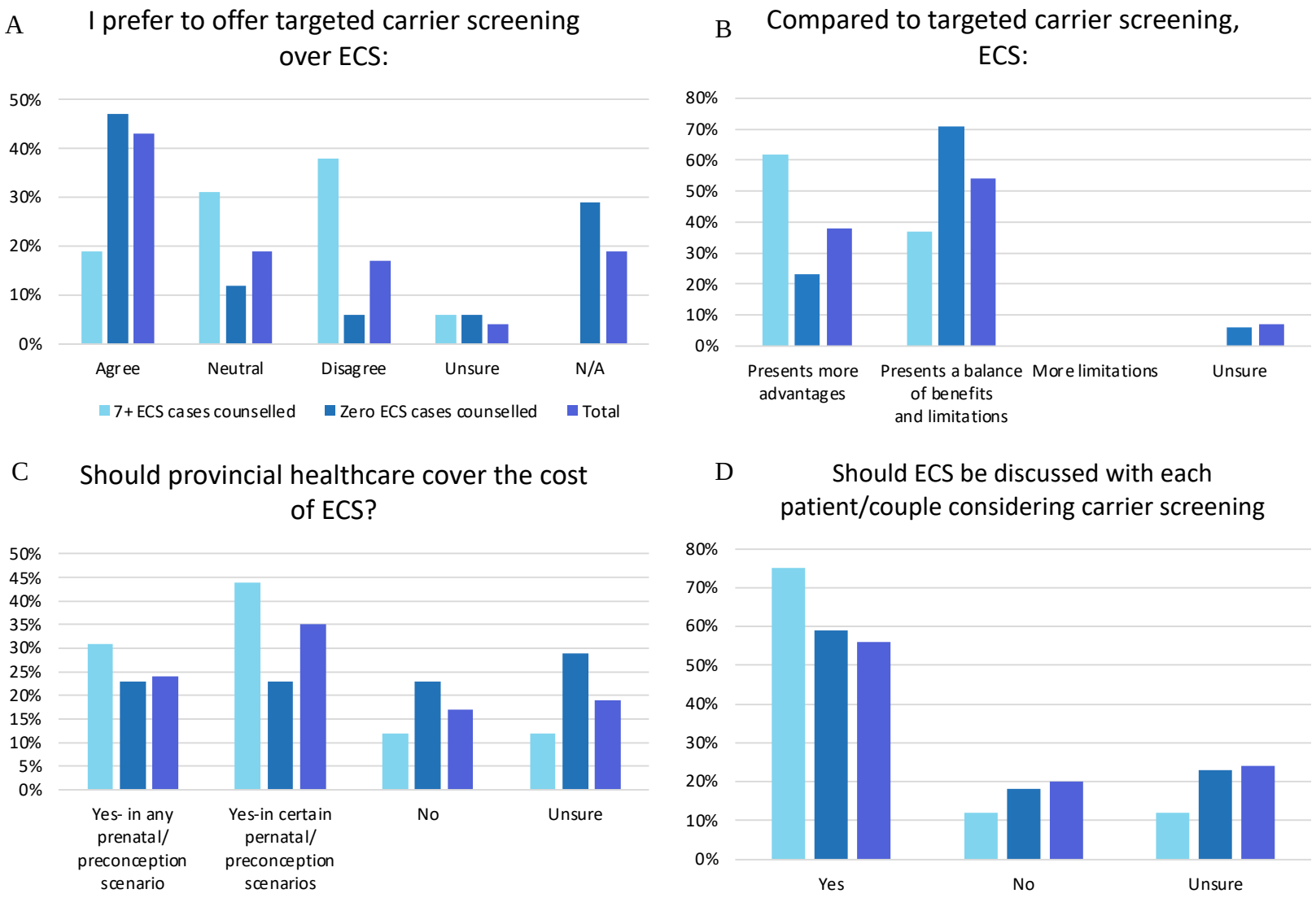


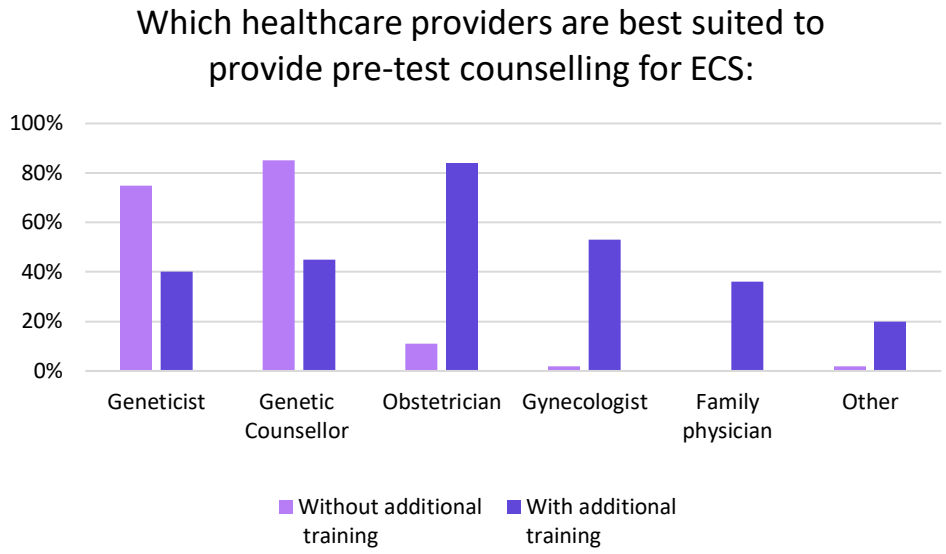

**Figure 7.** Opinions of ECS among survey respondents. Three groups are shown: GHPs who counselled more than 7 ECS cases (n=16; light blue), GHPs who counselled zero ECS cases (n=17; dark blue), and total survey responses (n=55; purple). Opinions of ECS compared to targeted carrier screening (A and B). Opinions related to ECS in Canadian healthcare (C and D).

### 3.4.2 ECS in Canadian healthcare

In response to whether ECS should be provincially funded, the most common option selected by 36% (20/55) of *all* survey participants was that ECS should be funded in certain prenatal/preconception situations, followed by 25% (14/55) selecting that ECS should be covered in any prenatal/preconception scenario. The majority of participants with the most ECS experience believed that ECS should be provincially funded, with 44% (7/16) believing it should be covered in certain prenatal/preconception scenarios, and 31% (5/16) believing it should be covered in any prenatal/preconception scenario. Opinions among GHPs with the least ECS experience were more varied, with 29% (5/17) being unsure and 23% (4/17) selecting each of the remaining three options of funding in any scenario, certain scenarios, and ECS should not be funded respectively. The majority of respondents (56%, 30/54) thought that ECS should be discussed as an option with each couple considering carrier screening, whether or not the couple qualified for provincially funded carrier testing, and this was the majority response among participants in both the most and least experienced group.

When it came to ECS pre-test counselling, 84% (46/55) of GHPs agreed that obstetricians were the healthcare provider best suited to perform this task with additional training, while without additional training, participants believed that GCs and medical geneticists were best suited to provide pre-test ECS counselling selected by 85% (45/55) and 75% (42/55) of respondents respectively (respondents were able to select more than one healthcare practitioner) (Figure 8A). Interestingly, 94% (15/16) of GHPs with the most ECS experience had concerns about non-GHPs providing counselling, compared to 41% (7/17) of participants in the least experienced group (Figure 8B). The majority of participants thought that pre-test counselling could be accomplished by methods other than through a healthcare provider. Participants were able to select which method they believed could be used for pre-test ECS counselling. Ninety-three percent (51/55) chose online videos, followed by website modules (93%) and informational pamphlets (71%, 39/55) as an alternative to an appointment for pre-test counselling for ECS. Only 20% (11/55) of participants selected “other” and indicated in the free text response that pre-test counselling could be accomplished with a genetic counselling appointment or group counselling session (data not shown, participants were able to select more than one response).

A




B

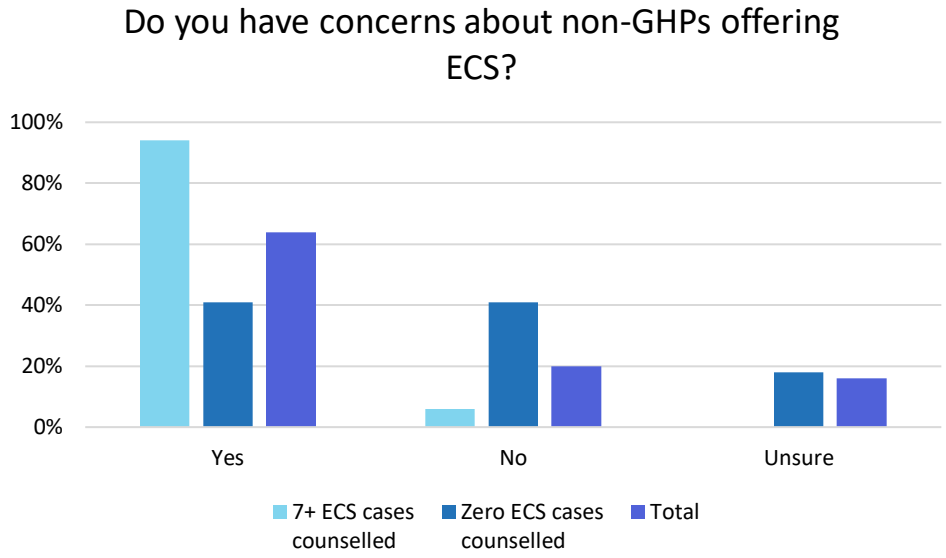



**Figure 8.** GHP opinions regarding pre-test ECS counselling by non-GHP providers. A) GHP opinions regarding which healthcare professionals are best suited to provide pre-test counselling for ECS without additional training (light purple) and with additional training (dark purple). Participants were able to select more than one healthcare provider. B) Opinions regarding non-GHPs offering ECS among participants who counselled more than 7 ECS cases (n=16; light blue), zero ECS cases (n=17; dark blue), and total responses (n=55; purple).

Participants were able to submit a free-text response regarding their opinion of ECS and 19 participants provided a response. The most common opinion submitted by four participants was that non-GHPs are in the best position to offer ECS:

> *It makes sense for it to be offered by non-genetics, and only if positive be referred to genetics for more detail and discussion of options. Also, most ECS labs have a team of GCs able to speak with the patients about results, so I think that's also very helpful and eases pressure on local GC clinics.* (P97-Survey, Diagnostic Laboratory GC)

Three participants expressed why they had concerns about non-GHPs providing pre-test ECS counselling. As one participant described her experience with non-GHPs providing pre-test counselling for other tests which did not make her confident that pre-test counselling for ECS would be better:

> *I think the pre-test counselling won't be great in many scenarios, as I see how the pre-test counselling currently fails with regards to NIPT and MSS when non-genetics professionals discuss it. I think this will be the same.* (P114-Survey, Medical Geneticist)

Another participant was specifically concerned about non-GHPs being able to counsel about the limitations of ECS:

> *I think non-genetics healthcare professionals are capable of ordering expanded carrier screening, my only concern would be them appropriately counselling the limitations. For example, if there's a family history of an unknown condition, emphasizing to the patient that a negative result does not necessarily rule out this condition in them.* (P05-Survey, Prenatal GC)

Another participant recognized the need to strike a balance between accessibility vs a thorough consent process:

> *I do believe that the consent process would be much more complete with a genetics professional but I feel that it needs to be accessible without specialist involvement and feel that informational resources provided through a GP could do an adequate job.* (P117-Survey, Diagnostic Laboratory GC)

Four other participants submitted comments that non-GHPs would require additional education in order to understand the limitations of ECS.

In summary, the majority of survey participants held a positive or neutral view of ECS. However those who had more experience with ECS were more likely to have a positive opinion than those with no experience with ECS, who were more likely to have a neutral opinion or were unsure about their opinion on certain topics. The majority of participants believed that with

additional training, obstetricians would be the healthcare provider in the best position to inform Canadians of the option of ECS. The majority of participants expressed concerns about non-GHPs providing pre-test counselling for ECS, and this opinion was particularly prevalent among GHPs with the most ECS experience.

# CHAPTER 4: QUALITATIVE FINDINGS

A total of 14 participants were interviewed. Interviewees were purposively sampled for variability in participant demographics (province of practice, practice area, years of experience). Thirteen participants contacted the student PI and one participant was contacted by the student PI in order to include the perspective of a GHP working in industry for a private-pay genetics company. Thirteen semi-structured interviews were conducted over the phone and one interview was conducted over Zoom. Interviews lasted on average 46 minutes (range 31 to 51 minutes), were audio-recorded, transcribed and analyzed. Field notes were documented before and after each interview to practice reflexivity throughout the data collection process.

Participant descriptive characteristics are summarized in Table 4.1. Participants consisted of twelve GCs, one molecular geneticist and one medical geneticist. Eleven of the participants worked in the public sector in a hospital clinic, one participant worked in private-pay laboratory, one participant worked part-time in a private-pay clinic and part-time in a hospital clinic and one worked in academia. At least one participant was interviewed from each province with a medical genetics unit. This included five participants working in Ontario, three working in British Columbia, and each of the remaining six participants working in either Manitoba, Saskatchewan, Alberta, Quebec, Nova Scotia or Newfoundland. Three genetic counsellors had previous experience working in the United States, including two who worked part time as GCs in the United States and Canada at the time of the interview. Years of experience ranged from 1 year to 28 years. Individual participant demographics are summarized in Table 4.2. Half of the 12 genetic counsellors interviewed worked primarily in a prenatal role (50% or more of their role), two genetic counsellors worked in a laboratory role, two worked primarily in a pediatric role, one was in academia and one in industry. Nine participants had experience counselling ECS and experiences ranged from pre-test, post-test counselling or both. The majority of participants had counselled less than 10 patients for ECS throughout their career. The five participants who did not have experience counselling ECS included a GC in academia, a laboratory GC, two GCs primarily in a pediatric role, and the molecular geneticist and medical geneticist.

The goal of this study was to explore Canadian GHPs experience with ECS and their opinions regarding ECS. Interviews were conducted to provide a nuanced understanding of GHP experiences and opinions, which may be impacted by a number of factors such as provincial

healthcare funding, accessibility of genetic testing within the province, institutional policies regarding discussion of private-pay testing and individual experiences and opinions regarding public healthcare.

Four main themes emerged related to the professional/personal opinions of ECS and GHPs experience with ECS (Figure 9). Themes 1 and 3 are related to GHP experience with ECS in their professional role, theme 2 is related to GHP professional opinions and theme 4 is related to GHP personal opinions and experiences with ECS. The first theme: ECS as a reactive option, is related to when and with who GHPs discussed ECS. Theme 2: Canadians should be made aware of ECS, reflects GHP general positive opinion regarding ECS. Theme 3: Public healthcare barriers, provides further insight into the GHP experience with ECS and why it is not routinely discussed despite participants believing that Canadians should be made aware of ECS. The fourth theme: GHPs as informed healthcare consumers, demonstrates the impact knowledge and awareness can have on healthcare consumerism

**Table 4**. Interview participant descriptive characteristics

| Demographic variable | Total number of participants (%) |
|---|---|
| Role | |
| Genetic counsellor | 12 (86) |
| Medical geneticist | 1 (7) |
| Molecular geneticist | 1 (7) |
| Province | |
| British Columbia | 3 (21) |
| Alberta | 1 (7) |
| Saskatchewan | 1 (7) |
| Manitoba | 1 (7) |
| Ontario | 5 (36) |
| Quebec | 1 (7) |
| Newfoundland | 1 (7) |
| Nova Scotia | 1 (7) |
| Years of Experience | |
| <10 years | 7 (50) |
| >10 years | 7 (50) |

**Table 5.** Individual interview participant demographics

| Participant ID | Practice Area | Counselled ECS |
|---|---|---|
| P01 | Prenatal | Yes |
| P02 | Laboratory | No |
| P03 | Pediatric/preconception | Yes |
| P04 | Cancer/Peds | No |
| P05 | Prenatal | Yes |
| P06 | Academia | No |
| P07 | Prenatal/general | Yes |
| P08 | Laboratory | Yes |
| P09 | Prenatal/fertility | Yes |
| P10 | Prenatal/general | Yes |
| P11 | Prenatal/general | Yes |
| P12 | Industry | Yes |
| P13 | Laboratory | No |
| P14 | Metabolic/peds/cardiac | No |

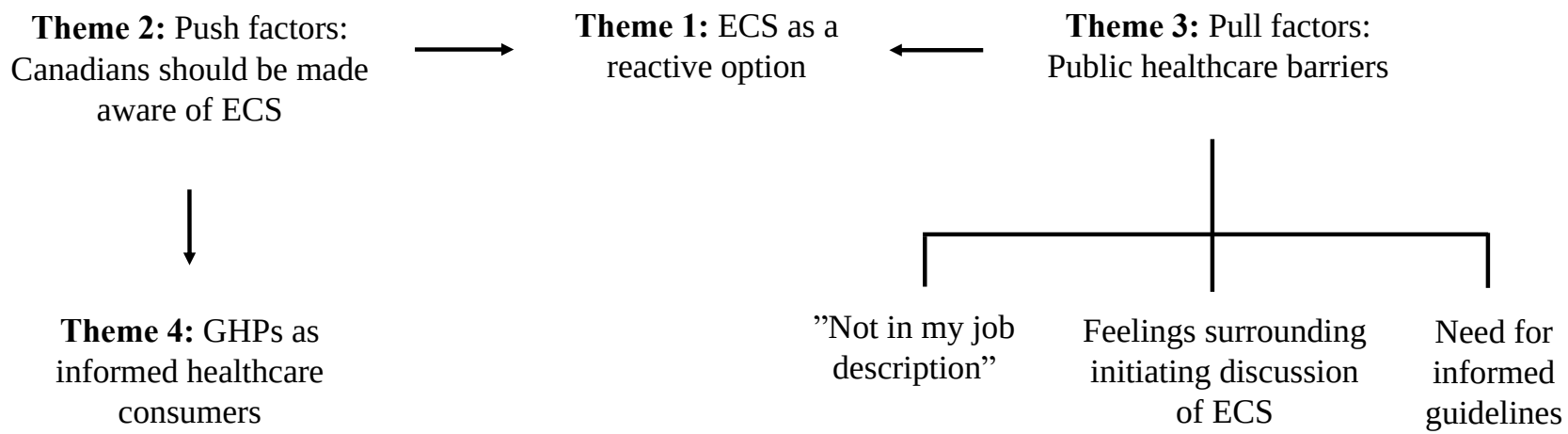



**Figure 9**: The thematic framework derived from an in-depth qualitative analysis of the interview transcripts.

## 4.1 THEME 1: ECS AS A REACTIVE OPTION

Participants were asked about their professional experience with ECS in their current or any previous roles held in Canada. The majority of GHPs in this study had experience counselling patients for ECS, although most acknowledged that their experience was limited. Most participants indicated that they had counselled patients for ECS less than 10 times in their current or any previous roles.

Approximately half of ECS counselling experiences occurred with patients referred from the fertility clinic to discuss the ECS test result of an intended donor sperm or egg and to discuss carrier screening options for the other biological parent. A GC in a preconception role described:

> *Right now the context where I see the most amount of expanded carrier screening is actually for my patients who have used an egg or a sperm donor and so the companies that they obtain those donor samples from of course are always doing at least some expanded carrier screening. I think most cases I've dealt with have come from American companies that Canadian individuals have obtained the specimens from*. (P03)

The remaining ECS experiences occurred outside of the fertility context. Since participants in this study indicated that their clinic would likely decline a referral for ECS counselling alone, the remaining experiences included discussion or counselling for ECS that had been initiated during the appointment with patients who had been referred to genetics for some other indication. None of the GHPs in this study discussed ECS on a routine basis with their patients who were seen in the publicly funded genetics clinic. A theme emerged regarding when GHPs chose to discuss ECS with their patients. ECS discussion came up in one of two scenarios: the GHP initiated the discussion due to a perceived increased risk that the patient could be a carrier, or if the patient initiated the discussion.

Many participants described introducing the option of ECS when they perceived the patient to be at higher risk of being a carrier such as in the case of consanguinity, a previous stillbirth or child with a congenital anomaly.

> *I had a couple of people that part of their indication peripheral was consanguinity. And so there was no specific thing in their family, but we said, well, we could potentially offer (ECS). So, that was the context that I had offered it in.* (P07)

Another participant described that she perceived patients to be at high risk if they were consanguineous and had a positive family history of an undiagnosed condition.

> *I would say consanguinity with some sort of family history suggestive of an autosomal recessive condition. So if it was a family history and everybody was well and this couple was consanguineous we probably would not consider it. Let's say it was a consanguineous couple and there was a family history of an undiagnosed condition that appeared to be inherited that would be more so when we would consider.* (P11)

Several participants had initiated discussion of ECS with patients who had a previously affected child with an unknown diagnosis.

> *I remember seeing a couple that had a child die shortly after birth from a metabolic condition in another country; it was never quite identified what it was. And although we didn't necessarily facilitate expanded carrier screening through our clinic, I did counsel them that (ECS) was an option that might be of interest to them.* (P08).

Another participant described offering ECS under similar circumstances to "somebody that has a family history of something, but they don't know what the condition is and there is no way to find that out" (P05). Similarly, the participant also described how in her experience, those with an unknown diagnosis in the family were often patients from other countries.

> *We see a lot of patients here that are from other countries originally and a lot of their family is still in their home countries. And so in a lot of these kinds of developing countries they don't really have the ability to do very much genetic testing or diagnosis of things; so sometimes I'll bring it up to those people.* (P05)

One participant worked as a prenatal GC in a hospital clinic and as a preconception GC in a semi-private fertility clinic. She described different experiences regarding when ECS is discussed in these two clinics. Her experience with discussing ECS in the prenatal clinic was similar to that of participants who worked in public healthcare:

> *In the prenatal genetics clinic we don't offer expanded carrier screening to all couples, but it is more on a case by case basis. So if a couple has had pregnancies resulting in stillbirth and there's not a diagnosis and there happens to be consanguinity or something that would indicate expanded carrier screening then we are offering that testing, but we're not able to offer it to every patient that we see.* (P09)

Interestingly, on her experience in the fertility clinic she described:

> *We've made a decision at (our) fertility that any patients that are meeting with the genetic counsellor and discussing PGT-A (pre-implantation genetic testing for aneuploidy) sort of pre-test counselling then we would offer them or at least inform them of the option of expanded carrier screening.* (P09)

In the participants' experience, it was uncommon for their patients to initiate discussion of additional or more genetic testing options. As one participant described, "I've only really had patients ask me about it or kind of looking for similar options a handful of times" (P11). Patients tended not to ask for ECS specifically however, if patients initiated discussion by inquiring about the availability of other testing options, GHPs would inform patients of the option of ECS.

> *(Patients) almost never bring (ECS) up specifically asking about this test but if they bring up the concept of wanting more information, wanting a really complete analysis or they're worried about something in the family then yeah, we bring it up*. (P05)

Participants described the circumstances when patients would initiate discussion of more testing options. A couple participants described that some couples were "just seeking information" (P08). One participant mentioned how in her experience some patients had become aware to seek more information.

> *Some instances I can think of we know individuals who have siblings who maybe live in the US and who have had more extensive testing, and so that, I can think of that as an example where individuals have asked for the testing or who've pursued testing.*(P09)

A few participants described that in their experience some of the couples that had inquired about more testing were couples with a previously affected pregnancy or child.

> *Yeah, usually the ones who ask for expanded carrier screening, they're not referred for a family history of a condition. Usually it's couples who have had a fetus or a child with significant malformation.* (P10)

> *Many couples perhaps have a child with a recessive condition and worry that they're at risk for other recessive conditions, I would say that's the majority of couples, they're either concerned about a condition because they have a child already with a recessive condition or they just want as much information as possible as they embark on their family planning and having a child.* (P09)

One participant highlighted the consequence of being reactive rather than proactive.

> *Regardless of patient request and who can pay, maybe this is something we should be considering, to help prevent disease. Are we going to keep on adding newborn screen after newborn screen or do we actually have to start thinking about doing expanded carrier screening and prevent these things in the first place? It's a lot of heartache for some families*. (P14)

Another participant did not think it was fair that ECS was being routinely discussed in private fertility clinics but not in public healthcare.

> *I have issue with the fact that individuals if they're planning a pregnancy through a fertility clinic are almost always offered expanded carrier screening. But if you conceive or plan to conceive naturally you don't have that discussion. And to me that's an access issue. It should be the same. If it's fair for the individuals that are paying for fertility treatment, and we think that's ok, then I don't understand why there's not that same discussion.* (P12)

In summary, approximately half of participants' experience with ECS was with patients who had been referred from the fertility clinic to genetics. The remaining experiences with ECS were those that had been initiated by the provider or by the patient during the appointment. A theme emerged in regard to when and with who GHPs discussed ECS. In many situations, whether provider or patient initiated, ECS was offered reactively –after a couple had an affected child or pregnancy. Some discussions of ECS arose in more proactive situations, such as in the case of consanguineous couples or when patients had the forethought to inquire about more testing options. Interestingly, the subset of patients seen in genetics who might routinely be using ECS in a proactive manner were those accessing private-pay fertility treatment.

## 4.2 THEME 2: PUSH FACTOR: CANADIAN COUPLES SHOULD BE MADE AWARE OF ECS

The GHPs in this study had generally positive opinions regarding ECS. The majority of participants thought that ECS could provide Canadians with useful information and those who had counselled patients for ECS commented that they perceived their patients were happy they had the test.

> *I think for the most part the results are informative or helpful or reassuring which is often what patients are looking for, that additional information and I think in general I feel as if the patients I've worked with are quite satisfied that they've done the testing. I feel as if surely the majority of couples seem happy that they did the testing and happy that they have this additional information.* (P09)

> *I do see the value in having this option available. I think it is important and I think for my patients, my two patients who did the test, I don't think they regret doing the test. I think this was useful information for them. So I think this is important that this is an option that's out there.* (P01)

> *I can only speak to the one couple that I've counselled and it did find that they were carriers but they were not carriers for the same thing. So it did find something, it did not impact their ongoing pregnancy. I remember this couple telling me it might be helpful for their relatives because they came from a large family.* (P11)

Although the general opinions toward ECS were positive, each participant recognized limitations to ECS. One of the most frequently cited limitations was that of accessibility, which was discussed in terms of patient awareness of the test and affordability. Many participants recognized that ECS may only be available to patients belonging to a certain demographic.

> *It's not really reasonable that it's only the people who are educated enough are able to ask about this and get access to it… It shouldn't be up to people to have the means and the money to make sure that they get equitable care.* (P01)

The GHPs in this study prioritized patient awareness and the majority thought that Canadian couples who are planning a pregnancy should be made aware of ECS.

> *I do feel like (ECS) should be offered. I've always felt that way. I'm not saying that everybody should have it. I just think everyone should be made aware that it is an option*. (P12)

> *In general I think like it's good for people to be aware of their options, and again for some people this would be very helpful information to know.* (P04)

Two participants expressed that although ECS was not affordable for all, patients should still be made aware of the option.

> *I think it should still be an option for people. It can be quite devastating, some of the conditions and I think that people should be made aware of that possibility. I recognize that some people just won't be able to afford it which is unfortunate. But I don't know if that's enough of a reason to not offer it to people.* (P04)

> *I think that care should be equitable. You know I suppose that at some level that unfortunately is how care is provided in Canada and across different jurisdictions and I'm not sure that we can fix that, but I agree that in a perfect world I think I would have this test readily available and covered so that it was available for patients if they wish to proceed with the testing always with informed choice of course, but I don't know that I see reasons for it not to be available.* (P09)

Participants recognized the potential for ECS to be inaccessible due to cost and acknowledged that the decrease in cost of ECS over the last 10 years (from thousands of dollars to hundreds of dollars) has made it more affordable, but it likely still remains unaffordable to some Canadians. Cost was acknowledged as a limitation and most participants agreed that in an ideal world they would like ECS to be publicly funded, however in reality believed that healthcare dollars could be better spent on other healthcare services.

> *It would be wonderful to be able to offer this to everybody it's just there's such a shortage (of GHPs). Also we're provincially funded so like I totally understand that side*

> *of it. As someone who is a clinician I want to be able to offer this for my patients. And I know I don't always really have to worry about the price and all the dollar signs. I get there has to be a level of risk that's high enough to make the price worth it*. (P03)

> *I recognize that as a healthcare system, we do have to prioritize all of our needs, and that might not be the biggest impact for our money at this point in time. You know, I don't think that somebody should be denied their cancer treatment because we're spending our money on universally screening for those things. And so, although I would like to see us maybe move in that direction, I think it does have to be balanced with the needs of the healthcare system at a much like higher level.* (P08)

One participant thought it was appropriate that ECS remain private pay, as long as it did not provide its users with an advantage.

> *If these are more common conditions and it is something that I feel like will be worthwhile for more people to have, then it probably would become a problem for me if it remained private pay*. (P10)

Another participant did not support publicly funding ECS because in her opinion, more testing does not necessarily improve patient healthcare outcomes or lead to "fairness" in public healthcare.

> *What is fair? Does more testing equal fair? I don't think so. Because if the testing is useless, or not really getting you anywhere and the outcomes aren't what you need. The best service for the least amount of effort and cost to get the best outcomes, is fair. So we have to be careful about the more is better thing*. (P14)

Not all GHPs thought couples should routinely be made aware of ECS. One participant felt that there was not enough information about the benefit of ECS for the patient and the healthcare system in order to warrant routinely making patient's aware.

> *I think we are still missing some of the information on the clinical utility of the test. So if we are routinely offering it you know, is it really having a positive impact on patient's and healthcare systems.* (P11)

Another participant who was a strong proponent of public healthcare was reluctant to accept its implementation in the absence of demonstrated overall benefit to healthcare and to patients before she could support ECS.

> *I believe very strongly in a one-tier, strong public healthcare system and I recognize that sometimes you have to make difficult decisions in terms of there are going to be people and things that are missed to have higher quality care for everyone else in a lot of other areas. So, without evidence that it's worth the cost to the healthcare system, it's hard for me to support it one way or the other. If there was evidence that was like, this is how the*

> *public healthcare system could support it, here's how decision making is better, here is how we save money in terms of different treatments, and the diagnostic odyssey and this in the NICU, and based on even say certain literature of how many people are terminating. If it makes sense in the context of our healthcare system then I would be the first one out there advocating so hard for it.* (P02)

In advocating for awareness of ECS, many participants were cognizant of the potential of further stigmatizing disability and expressed that the goal of making couples aware of ECS was not to prevent disease, but rather to promote informed decision making among Canadians.

> *Every time there's a baby born with one of those conditions they're like well how did I not know about this in advance? And that's that heartbreaking question which I think is harder to answer as a prenatal or pediatric counsellor now. I think carrier screening is one of those missed opportunities. That's not to say people should have prenatal diagnosis. It just shouldn't be a surprise when a baby is born with a condition vs an awareness, a planning for, a real appreciation for that condition, what therapies might be available, etc ,etc.* (P12)

In summary, GHPs recognized awareness and affordability as major limitations to ECS. Participants seemed to prioritize patient awareness and the majority thought that all couples planning a pregnancy should be made aware of ECS as an option. Most participants described that ideally ECS would be publicly funded for any individuals that wanted it, however in reality did not think this would be the best use of healthcare resources, and generally felt that it was appropriate that it remain a private-pay test.

## 4.3 THEME 3: PULL FACTORS: PUBLIC HEALTHCARE BARRIERS

Although the majority of participants expressed that they believe Canadian couples should be aware of ECS, many participants in this study discussed ECS on a case-by-case basis (explored in theme 1 "ECS as a reactive option"). The following theme provides further insight into the reasons participants do not discuss ECS, each of which is related to the realities of working in public healthcare and may represent barriers. Three subthemes emerged "Not Part of the GHP role", "GHP feelings surrounding initiating discussion of private-pay testing" and "unclear institutional/professional carrier screening and ECS guidelines".

### 4.3.1Not Part of the GHP Role

While most participants felt that patients should be made aware of ECS or that it could provide individuals with useful information, the majority did not feel that it was their responsibility to routinely make their patients aware of ECS. Participants expressed a number of reasons why they believed routine discussion of ECS was not part of their role. These reasons included that the discussion was more suitable to other healthcare settings, resource limitations and providing equitable care to patients.

Some participants felt that they were not the most appropriate healthcare provider to initiate discussion of ECS because they are typically seeing patients for some other specific indication, which is the focus of the appointment. Participant 12 reflected on her previous experience as a prenatal genetic counsellor:

> *I wasn't the right individual to be talking about carrier screening because I'm dealing with individuals who are pregnant with an anomaly.* (P12)

Similarly, other participants felt that their main role was to answer the referral indication, and discussion of ECS may not be relevant.

> *I normally would not talk about (ECS) because it's not relevant to the referral indication, even if they are preconception age or whatever. In the context of a clinical setting, I'm still going to be focused primarily on the reason for referral. Which is probably not going to be expanded carrier screening.* (P01)

The majority of participants thought that other healthcare providers such as GPs and OB/GYNs were better positioned to discuss ECS with patients primarily because patients would have more time to make an informed decision regarding whether or not they want ECS, and it would provide individuals with more reproductive options if ECS was done before the patient was seen in genetics.

> *I think the ideal time is GP level prior to conception. It should be part of "hey, we should start talking about prenatal vitamins and we should start talking about carrier screening." Same dialogue…. It really needs to be more primary care and maternity care, because by the time they get to me and they're 20 weeks, carrier screening is less useful. There is so much more power to do genetics and if it's just held in medical genetics departments there's less, there's just so many more people who could be advantaged by using genetic testing.* (P12)

One of the most commonly cited reasons that GHPs did not believe routine discussion of ECS should be part of their role was that they did not have enough clinic resources in the form of manpower and time.

> *We have been told not to routinely bring it up due to resource limitations. Because there's not enough of us just to do our regular work*. (P10)

> *I look at my workload and I don't have time to help facilitate this. Like there's already so much paperwork we have to do and things like that, and I really, I just know I don't have time for it*. (P03)

Another participant felt that she did not have enough time during the appointment to discuss ECS given everything she already had to discuss.

> *I think it's just getting harder and harder to inform people about every single testing option now. When we meet people we have to talk about first trimester screening, we have to talk about NIPT, CVS, amnio, they already get confused between those. It can get very time-consuming fast. (P05)*

One participant described that although she would want to routinely inform her prenatal patients about the option of ECS, resource limitations prevented her from doing so.

> *Certainly we all realize it's not standard of care, that we don't have a legal obligation at this point to offer it. I think the only hesitation is resources and I think you know coming back to our public healthcare system I feel as if we're all limited from a resource point of view to assist couples. But I think taking resources out of the equation and time and what have you then I think that the majority of myself and my colleagues I think are in favor of the testing. I think resources, at least in my experience, is the limiting factor*. (P09)

While some participants spoke about a lack of resources in a very practical manner such as lack of time for routine discussion/counselling for ECS, for many other participants a lack of resources meant ensuring equitable distribution of their time by providing counselling for those at highest risk. It seemed that for many a defining feature of their role was that of a public healthcare employee.

> *If you look at my job description (discussion of ECS) is not one of my roles that I am supposed to be doing. I am supposed to facilitate care for provincial patients within the constructs that we're given.* (P03)

> *The time spent counselling/arranging is disproportionate compared to people who have specific risks. So if you think about expanded carrier testing, people who are requesting expanded carrier testing are at a population risk for various things. They're not requesting it because they are at high risk. It seems silly that arranging the test takes way*

> *more time than it takes to arrange a test for somebody who actually is identified to be at risk, right? So I feel like that's not a good use of my time as somebody who is working in the public healthcare system*. (P01)

> *You probably hear this a lot but, resources. Lots of genetics clinics already have pretty long wait lists and so to see people for this when it's probably a pretty low risk in the first place, like, maybe that ends up taking away spaces from people that maybe need to be seen more urgently for things that are more high risk.* (P07)

> *If we are routinely offering it, is it really having a positive impact on patient's and healthcare systems. And I think too balancing it with limited resources - is that where we could have the most impact*? (P11)

Other participants expressed feeling no obligation to routinely discuss a test with their patients that was not funded by public healthcare.

> *If it wasn't a provincial program, we didn't see that we had a responsibility to make sure that patients knew about these other options. But we would address them if patients brought them up. I feel like it's still the case that prenatal genetic counsellors don't feel obligated to mention it to all of their patients routinely, because it's not available in the public system.* (P06)

> *I don't necessarily think that it should be an expectation for us to discuss things that are not provincially funded. So if we as a healthcare system aren't willing to pay for it, why am I expected to tell somebody oh this exists but you can't afford it. So no they shouldn't have to pay me to tell patient about it if they're not going to pony it up. It shouldn't be an expectation if we're not willing to do something with it.* (P02)

A couple of participants expressed that the reason they would not discuss a test that was not publicly funded related back to fair distribution of resources. One participant felt that if the test was not funded, then perhaps it's because patients are not at high-risk: "If it's not being offered publicly then I don't know how necessary it is" (P01).

Another participant chose not to volunteer information about ECS "because it wasn't accessible to everybody" (P07). This participant described offering the test only when it had been provincially funded.

> *I think the only time I've really mentioned that was… a couple years ago when Life Labs still had that carrier screening panel and, again, the Ministry of Health stopped approving these a couple years ago.* (P07)

While participants almost unanimously agreed that discussion of ECS was not part of the role of a public healthcare GHP, there was uncertainty expressed over whose role it is to make

patients aware of ECS: "It's just a problem of whose responsibility is it" (P01). "I don't know whose role it is…I don't know whose responsibility it should be" (P05).

As previously mentioned, many participants thought that informing individuals about ECS should be left to the GP or OB/GYN, although a number of participants expressed some level of concern towards non-GHPs providing pre-test counselling for ECS.

> *No, honestly, I don't think a family doctor generally would understand expanded carrier screening and the limitations of it. I'm sure some could but I've had experiences where family doctors don't understand very simple genetic tests and I'm just like 'oh boy'. But I … I know if I spent too much time doing that that would not be good...I'm really conflicted honestly. No, I don't trust family doctors to do it but maybe they can help guide the patient in some sort of way of like at least where to look that might be good.* (P03)

In summary, participants in this study unanimously felt that routine discussion of ECS was not part of their role. Participants thought that other non-GHP such as GP and OB/GYNs were better suited to discuss ECS which could provide patients with time for informed decision making regarding ECS and could maximize patient reproductive options. Participants frequently cited resource limitations, and the vast majority of participants felt that their responsibility as a public healthcare employee was to provide care to those at highest risk, rather than spending their limited resources discussing options that are not publicly funded.

### 4.3.2 GHP Feelings Surrounding Initiating Discussion of ECS

A number of participants considered how initiating discussion of ECS and private-pay testing in general would be perceived by their patients. Some GHPs expressed feeling uncomfortable or worried and perceived that there were barriers to discussing private-pay testing in public healthcare.

Two participants described feeling uncomfortable suggesting a private-pay test to their patients, especially when they perceived that the patient could not afford the test.

> *I feel a little bit uncomfortable bringing up ECS. I do feel a little bad bringing it up when I'm almost positive that none of my patients can afford it or feel like I'm almost certain there's no way they're going to do this test but maybe that's not necessarily true*. (P05)

> *This is a test that isn't covered, so it does feel weird to offer this saying that you have to pay. In a situation where I knew people couldn't afford it I think that I would feel a little bit uncomfortable.* (P04)

A few participants expressed that when they initiated discussion of ECS, they felt worried about how the patient would feel if they could not afford a test a healthcare provider was perhaps seemingly suggesting.

> *People take what the healthcare provider is saying. You know they might say, "Oh well I feel like I need this test" and then feel guilt that they can't afford it and things like that. So I guess that would be my only issue is if I'm working in an area where there's a low socioeconomic population I would find it hard to discuss a test that I know people can't afford.* (P04)

> *I've really struggled personally if it's something the patient would have to pay for and not receive genetic counselling from a clinical perspective than if we were to bring it up and leave some patients feeling like they were unable to fund tests that they might appear recommended because they were brought up by a healthcare provider. But then just balancing that in terms of making sure the patient is as informed as possible. (P11)*

For participant 5, initiating discussion of a private-pay test raised concern about the client-patient relationship.

> *When I bring up self-paid testing I usually say "Just so you know I get no commission on this" [laughs]and I'm not making any money by mentioning this" because I don't want them to think that I'm trying to sell them something.* (P05)

Other participants worried that just bringing up the option of ECS might raise the patient's anxiety. Participant 9 articulated this worry well:

> *I don't want to make any assumptions, but I think once you put it out there, I do wonder sometimes if we're sort of raising anxiety or that patients worry when we start talking about the risk for these recessive conditions and that we're all carriers for some conditions. I can't really say for sure, but I wonder sometimes if couples worry and if it's a higher perception of risk than what truly is.* (P09)

Participant 5 who worked in the United States as well as Canada shared her experience with bringing up private pay testing with Canadian patients compared to American patients. She perceived that a barrier to initiating discussion of self-pay testing with Canadians was that Canadian patients do not expect to pay for their healthcare.

> *I do think there is sort of this barrier. People are used to having their healthcare for free and I do think that once you start talking about paid options a lot of people are like, "Ah no" -not that they say this but I kind of perceive it like 'I don't pay for healthcare, like no we don't pay for healthcare here, we're not doing that." So, I think there is a barrier here. It's not just that they can't afford it. They're not used to paying for it as well I think.* (P05)

Another participant raised a similar point, finding it difficult to justify discussing a private-pay option with Canadians who are used to receiving healthcare in a single-tier system.

> *… I guess I just kind of think about in terms of like other things in healthcare, and I can't think of any off the top of my head but is there anything where a doctor would say, "Oh well you can do this but you have to pay for it". I'm trying to think. I don't know if I can think of anything off the top of my head that fit in that. If I did then I would feel more justified in doing that [offering ECS]*. (P04)

The dialogue among participants was noticeably different when discussing patient-initiated discussion of ECS. Many expressed that "*if a patient brings (ECS) up then I am happy to talk about it*" (P02). As described above, this could be because provider-initiated discussion raised uncomfortable feelings or worry for the patient and perhaps these feelings did not surface when the patient initiated the discussion.

Perhaps another reason why participants were hesitant to initiate discussion of ECS was that they might feel an added responsibility depending on who initiated the discussion. Participants usually described that if the discussion was patient initiated, they could draw a line with how far the discussion went. Whereas if the discussion was provider initiated, participants seemed to feel more responsibility to help the patient through the process.

> *If patients are interest in carrier screening outside their reason for referral, expanded carrier screening is something that we could mention to them on a patient pay basis and as much as we can't provide the counselling for it but it is an option and maybe review some of the benefits and limitations*. (P11)

> *I mean it doesn't hurt to [mention expanded carrier screening], it's just like how far do you take it. I'm kind of conflicted. You can mention it but, you know, some patients are really autonomous. Like they can go out there, they can advocate for themselves, they know where to look, and some patients don't. And based on how autonomous that patient is or savvy I guess I don't have to help that much. But maybe for some people that aren't as savvy I would have to help more*. (P04)

In summary, when initiating discussion of private-pay testing some participants described feeling uncomfortable, worried about raising patient anxiety and the potential impact it might have on the client-patient relationship. Some participants described being particularly aware of these feelings when discussing private pay with patients who they perceived could not afford the test. Others perceived that there was a barrier to discussing private pay with patients who were used to receiving public healthcare. Although not explicitly stated by participants, perhaps a reason why GHPs appeared more receptive to patient-initiated discussion was that they felt more

comfortable removing themselves from helping patients with further steps of the ECS process. It appears that there might be additional factors that might make GHPs hesitate to initiate discussion of ECS and private-pay testing in general.

### 4.3.3 Need for More Informed Guidelines

Many participants acknowledged that the SOGC-CCMG guidelines regarding reproductive carrier screening are recommendations and not standards of practice, however many turned to the guidelines to help them make practice decisions.

The majority of participants did not frequently encounter ECS in clinic and therefore admitted to not looking too much into the current guidelines regarding ECS, although did express that some guidance would be helpful. Two participants who were familiar with the SOGC-CCMG recommendation regarding ECS did not find them helpful when applied in practice because they were too "vague" and open to interpretation.

> *The SOGC-CCMG guidelines are kind of vague with respect to expanded carrier screening. Anyway, so I don't find it particularly useful for that purpose. (* P01)

> *In my opinion they [SOGC-CCMG guidelines] are very vague as to really what the message is there in terms of offer or not offer. I feel like it's misinterpreted. The language of those guidelines do not say you need to speak to all of your primary care patients about expanded carrier screening options. And I feel like if they said that, and I don't think they say that, they are pretty close but they don't quite say that. So I feel like they need to be stronger. (*P12)

Many participants spoke more broadly to the carrier screening guidelines in general. One participant felt that the reason carrier screening in Canada has not been further developed is due to a lack of clear and helpful guidelines.

> *Like carrier screening in general. I'm not sure that that's been as highly developed as maybe it could be. Because there's no real guidance on what to do. As far as I can tell, our counsellors are like, well should we be testing for this or should we be testing for that? And where's the guidance and what's the guideline? (P14)*

Another participant provided an example of why she finds the guidelines unclear.

> I *feel like sometimes we're offering carrier screening to a partner this person's a carrier of this rare condition, and there's a one in 40,000 chance their partner's a carrier, and we're still offering that to them. So why would we not offer CF carrier screening to all Caucasians, like, one in 25? That's relatively high in comparison. I know it's all based on funding and all that kind of stuff, but it just doesn't seem like it makes a whole lot of sense sometimes.* (P07)

A number of participants felt that carrier screening guidelines needed to be revisited to reflect technological advancements that have provided the ability to screen for more conditions for decreased cost. For one participant, this meant analyzing the economics of more testing, while for another this meant adapting the basic principles of screening to technology advancements.

> *We've never done a pilot study looking at 3 vs 10 vs 40 vs 300 carrier testing in our population. I think a lot of that can be revisited given the lower cost of some of those tests now compared to when maybe some of those economic studies were done 10 years ago, 20 years ago. So I think it's a question that needs to be revisited as our technology gets better and I don't know if it is. So our guidelines are limited based on lack of studies done in terms of the benefits of carrier testing in the Canadian population and in the information that can be used to make the guidelines.* (P02)

> *We have these principles of screening but the thing is, how do you actually translate those previous principles into current state with the technology interpretation results, ease of getting really rare stuff. Back in the day we only had a certain hard number of things that you could actually test for. But now with next gen sequencing, we have to ask ourselves, is this really applicable the way that it used to be to current state. But it's so hard with all these layers of the past and what people used to do and why.* (P14)

A theme emerged among the more experienced GHPs (12+ years in their role) who had seen genetic testing technology advance over the course of their careers. These participants felt that they had not seen these advancements applied to prenatal practice.

Participant 6 observed *"carrier screening – population-based carrier screening in Quebec actually hasn't changed that much even since those years* (early 2000s)".

For these participants, prenatal practice seemed to be stuck in the past. Three participants specifically questioned why "*in the prenatal world there's been so much focus on Down syndrome*" (P12). Participant 14 found the focus on Down syndrome outdated.

> *The reasons why we did something often is because we could, because the technology was available at the time, but now things have changed and we keep doing the same thing. Originally we were just doing all this MSS for Down syndrome because the test was available. But why are we still picking on Down syndrome? It's like we have to rethink what's the purpose of things, like all of it. It all needs to be rethought. All of the screening. What are we trying to achieve and why? And then how are we going to get there?* (P14)

Another participant felt that because we now have the ability to screen for hundreds of conditions at once, this collective risk outweighed the risk of Down syndrome and perhaps justified a more expanded approach to carrier screening.

> *Here in Ontario we do first trimester screening to find out Down syndrome chances, and if it's higher than one out of 350 that's considered positive. That's a third of 1%, so they consider that worth it but then they don't consider expanded carrier screening worth it when something like maybe 1% or 2% of couples will find that helpful in the long-term. That's another problem I have with all this stuff is just like 'why are we prioritizing down syndrome and screening for down syndrome when that is like not nearly the worst condition that people could have and face…. It frustrates me that like, 'why are our prenatal screening programs always all about Down syndrome, when we have the ability to screen for a whole bunch of other conditions through expanded carrier screening and we're not doing that. That bothers me a lot actually*. (P05)

Some participants raised the concern that if policy cannot keep up with technological advancements, there is the risk of private-pay tests entering public healthcare before adequate safeguards and regulatory frameworks are in place.

> *It means that the private sector is driving our healthcare. It's driving the healthcare that we end up having to deliver, rather than it being a rational public decision-making process*. (P06)

> *I would say perhaps we're getting close to when guidelines are needed. Just to kind of be prepared that if demand say were to rise that you know we are going about this in a controlled and educated way. (P11)*

In summary, participants spoke to several limitations in the current carrier screening guidelines which included vague recommendations regarding ECS, at time confusing recommendations regarding carrier screening and guidelines that were perhaps not as informed from the perspective of newer technological carrier screening capabilities. More updated and explicit guidelines could help GHPs recognize in what situation discussion of ECS may be appropriate. Furthermore, guidelines may help encourage more uniform practice of ECS across the profession.

## 4.4 THEME 4: GHPS AS INFORMED HEALTHCARE CONSUMERS

In order to gain further insight into participants' opinion of ECS, participants were asked whether they would personally pursue ECS. Most participants indicated that they would consider pursuing ECS. Seven participants indicated that they either would have ECS if they were in a

reproductive situation or would have had ECS had it been available when they were of reproductive age. In addition, five participants disclosed that they had some form of preconception carrier screening. Two participants were not interested in personally pursuing ECS.

Of the five participants who had some form of preconception carrier screening, two had paid for ECS, and another had paid for CF carrier screening only. Two participants were able to access genetic testing for free - one participant had whole exome sequencing as a healthy volunteer for a research study and another had publicly funded carrier screening for CF, SMA and Fragile X.

A theme emerged that GHPs are informed healthcare consumers when it comes to accessibility and awareness of reproductive carrier screening.

The two other participants who had accessed carrier screening for free had done so due to their knowledge of genetic testing availability. Participant 7 who wanted to have ECS shared the unique way that she was able to access whole exome sequencing due to her awareness of a research study.

> *I actually signed up for that (PGP Exome Canada Project) to do my whole exome as a healthy participant because I essentially wanted expanded carrier screening.* (P07)

Participant 12 also had not paid for carrier screening, but admitted to accessing publicly funded carrier screening by using the knowledge gained as a prenatal GC. This participant suggested that this may be a broader practice among GCs.

> *Before getting pregnant, I had carrier testing for CF, SMA and Fragile X. Did I have a family history? I did on the requisition. Because I have the knowledge that I do, I know that I could have that testing if I provided certain information on the requisition. And I'm not alone. I don't even think I came up with that idea. I think there were other genetic counsellors before me who might have suggested that you just extrapolate a little on your family history*. (P12)

This participant had many years of experience as a prenatal GC and further commented that in her experience she was aware of many GCs accessing some form of preconception carrier screening.

> *For those of us who have been in prenatal for a long time, we have seen this evolve and have seen all the genetic counsellors that come out of the woodwork when they're planning a pregnancy and want to have this test...* (P12)

Participants shared why they had chosen to have carrier screening, or why they would or would choose not to pursue ECS. For a number of participants, experiences directly related to their GHP role had influenced their decision. For a couple of participants, routinely working with high risk patients had changed their risk tolerance, as expressed by participant 7 when sharing her reasoning for having whole exome sequencing as a research participant:

> *I'm not planning a family anytime soon and I know that 98% of pregnancies are fine, but we kind of are skewed to seeing the 2%, 3% of things that are so, so rare and can sometimes be so, so devastating. So, I thought I kind of want to know what I carry. So, yes, I would probably do expanded carrier screening.* (P07)

Conversely, for participant 11, it was a similar experience that made her not want ECS, as she perceived that she would be more anxious if she had a positive test result.

> *I guess I'm not all that interest to know about all the rarer potentially things that I might be a carrier for. And I also think that if I put myself in that situation, I don't think I would want to make myself more anxious than being a pregnant genetic counsellor with the information I already possess. I don't think I would want any additional knowledge. I think it's also in the context, I do not have siblings who might also benefit from that information so it could be say of limited utility if I was a carrier of something. I'm also just a bit of a risk adverse person.* (P11)

Participant 9 expressed that she would have pursued ECS had it been available due to the experience of seeing patients who would have benefited from ECS had they been aware it was an option.

> *I have seen too many couples come through who have had a child pass away from SMA for example. Or who have had a child affected with cystic fibrosis and are furious to know that they could have been screened and it wasn't offered to them or that they went through a fertility clinic and they were not offered expanded carrier screening even though that same fertility clinic is affiliated with an expanded carrier screening lab. I guess I've heard too many of those stories or seen couples come through for PGTM after learning, you know after the death of a chid for whatever condition.* (P09)

Another participant who did not have ECS prior to her first pregnancy but decided to have preconception ECS with her second pregnancy described that she had become convinced after attending a presentation by a leader in the field of prenatal genetics.

> *…And one of the speakers this year was [expert in prenatal]. And he's a pretty big name in prenatal genetics. And his presentation was on – I think it was on expanded carrier screening, but I remember him giving a pretty impressive statistic that – I forget exactly now, I want to say it was 80 percent of the babies that they see with genetic conditions in the NICU would have been picked up on expanded carrier screening. And I feel like that*

> *was the straw that convinced me. That I was like yeah, OK. I think this time around maybe we'll do (ECS).* (P08)

For others, it was their confidence in their specialized knowledge and training in genetics that perhaps made them perceive that there were fewer risks associated with the test than for the average patient, such as unnecessary stress or anxiety.

> *Part of me would say sure because I know I trust my ability to interpret those results. It's interesting. I don't know but – and then like emotionally I don't know if something came back if I could handle it. Maybe one day when I'm thinking about having children I'll know what I want to do but I have no idea right now. I just know that if I did do it I trust my abilities to be able to logically look at the results and know what to worry about what not to*. (P03)

> *I think that's purely from like a I'm a curious person that knows a little bit more about the science and I can rationalize it as well. I know enough that I would be comfortable with those results, but I don't know if that's representative of the average person.* (P14)

Although participant 4 would not pursue ECS, she was comfortable with her decision because it was an informed one.

> *I don't know that I would get expanded carrier screening which is funny because I was advocating for it. For me – but I mostly advocated because I feel people should be aware that that's an option not that people should have it. And I'm aware of the option and I think that I kind of lean towards not doing that.* (P04)

While the theme centered around GHP awareness of testing options and informed decision-making, one participant did raise cost as an accessibility issue.

> *I have not had (ECS), but yes, I'm the type of person that would love to know more about my genetics. So I would do it if it was free. I don't think that I would pay for it, because I'm not at that point where I feel like I can spend that type of money for that reason.* (P10)

Interestingly, a few participants recognized the discordance in their hypothetical or real choice to have ECS and their views on public healthcare.

> *I'm a bit of a hypocrite because I've paid for…in 2009 before carrier screening was really a thing, I paid out of pocket for CF testing for myself. I never paid for expanded carrier testing because my kids are already born. But if I were starting to have my babies now, I probably would pay for it. So as somebody who truly does believe in a one-tier system I haven't been very good at living that life.* (P02)

> *I'm going to be a huge hypocrite for a second. Ya, as much as I espouse all this stuff about like everybody should get it equally, we shouldn't have a two-tiered health care system, etc, etc. As much as I espouse that, it's super interesting isn't it?! Like, it is super*

> *interesting and it would be interesting to know what I'm a carrier for. If hypothetically I was expecting a pregnancy, maybe not for medical reasons but just for fun.* (P01)

Participant 5 expressed feeling guilty for paying for ECS out of pocket. Her perception of the healthcare system as fair and equal was different than her reality using healthcare. She also expressed struggling to consolidate what she felt were her healthcare needs and her healthcare beliefs.

> *I mean even when I did it myself I was pregnant at the time and we did expanded carrier screening for me and my husband. And at the time I did feel guilty about it because I was like "We can afford to do this" and at the time it was much more expensive …we spent almost $2000 on this, out-of-pocket. And so I did feel like here I am, thinking that we have this great, fairly equal system and I really want testing to be accessible to everyone and here I am paying like $2000 out of pocket to do this test [laughs]…as someone from a middle to upper income like I want to know about those tests. I don't know how to resolve that in my mind.* (P05)

In summary, the majority of participants in this study would pursue ECS. Some participants had already pursued ECS or had accessed preconception carrier screening through other avenues. Participants' accounts of how they accessed carrier screening and what factors influenced their decision making demonstrated the importance of awareness of one's options and knowledge required to make an informed decision. Several described unique opportunities that allowed for accessibility and knowledge that may not be available to the general population such as awareness of a research study, attending a presentation by a leader in the field, and knowledge of how to access publicly funded genetic testing. A minority of participants recognized the discordance between their personal decision regarding ECS and their belief of equitable healthcare delivery. While this theme cannot be extrapolated to the broader profession, it is perhaps a striking example of the impact that knowledge and awareness has on healthcare consumerism among healthcare providers.

# CHAPTER 5: SYNTHESIS OF QUALITATIVE & QUANTITATIVE FINDINGS

The rationale for using a mixed methods design was that one method alone would be insufficient; a combination of quantitative and qualitative methods would best answer the research question. The goal of combining both quantitative and qualitative research data strengthens the validity and comprehensiveness of the research conclusions.

## 5.15.1 GHP OPINIONS OF ECS

The majority of survey participants held a positive or neutral view of ECS, evidenced by the fact that the majority (56%) of survey respondents believed that ECS should be discussed as an option with each couple considering carrier screening, whether or not the couple qualified for provincially funded carrier testing. In addition, over half of survey participants (54%) thought that ECS presented a balance of benefits and limitations for the patient, and 38% thought that ECS presented more advantages for the patient. None of the survey respondents thought that ECS presented more limitations for the patient. This was also supported by the qualitative findings, in which a theme emerged among participants that Canadian couples should be made aware that ECS is an option. The majority of interview participants thought that ECS provide Canadians with useful information and those who had counselled patients for ECS, they perceived that their patients were happy with the test as illustrated by the following quote:

> *I think for the most part the results are informative or helpful or reassuring which is often what patients are looking for, that additional information and I think in general I feel as if the patients I've worked with are quite satisfied that they've done the testing. I feel as if surely the majority of couples seem happy that they did the testing and happy that they have this additional information*. (P09- Interview)

While both survey and interview participants thought that Canadians or patients should be made aware of ECS, both data sets also found that GHPs did not think they were the best healthcare provider to initiate discussions of ECS. Among survey respondents, 85% of GHPs agreed that obstetricians were the healthcare provider best suited to provide ECS pre-test counselling providing they received additional training, whereas in the absence of additional training only 6% of GHPs felt obstetricians were best suited to provide pre-test counselling. Free text responses asking participants to comment on their opinion of ECS also supported the idea

that more training for non-genetics healthcare providers would be required if they were to routinely discuss ECS with their patients.

> *Family doctors/ fertility specialists need info and training as most women don't see OB until late in pregnancy*. (P108-Survey)

> *I can see it working well in the practice of a general OB but we would have a significant hurdle in making sure all the appropriate education is there prior to initiation.* (P68-Survey)

> *Additional training and support should be provided by industry to family physicians to offer this test*. (P58-Survey)

Although the interviews did not explore which health care provider was best suited to provide pre-test counselling for ECS, interview participants did not routinely discuss ECS with their patients and the qualitative findings provided context for why this was the case. Three sub-themes emerged related to why the GHPs did not discuss ECS which included not seeing it as part of their role as a public healthcare employee, feeling uncomfortable bringing up a private pay test, and the need for informed guidelines related to ECS in order to better judge when ECS should be discussed as an option.

Both survey and interview data found that GHPs in this study had some reservations when it came to non-GHP counselling patients for ECS. Several participants expressed this concern in the free-text response in the survey:

> *I think the pre-test counselling won't be great in many scenarios, as I see how the pre-test counselling currently fails with regards to NIPT and MSS when non-genetics professionals discuss it. I think this will be the same*. (P41-Survey)

> *I saw a patient once who had ordered expanded carrier screening through a non-genetics provider. The provider had not specified ethnicity on the test order, therefore the detection rates and reproductive risks were not accurate. I had to request amendments to the report and the patient was very grateful that I had reviewed for her. Makes me concerned about what else might get missed with other providers.* (P31-Survey)

> *I think non-genetics healthcare professionals are capable of ordering expanded carrier screening, my only concern would be them appropriately counselling the limitations. For example, if there's a family history of an unknown condition, emphasizing to the patient that a negative result does not necessarily rule out this condition in them*. (P15-Survey)

Similar concerns were raised among interview participants when considering non-genetics healthcare providers counselling ECS as expressed by one interviewee:

> *No, honestly, I don't think a family doctor generally would understand expanded carrier screening and the limitations of it. I'm sure some could but I've had experiences where family doctors don't understand very simple genetic tests and I'm just like 'oh boy'…. No, I don't trust family doctors to do it but maybe they can help guide the patient in some sort of way of like at least where to look that might be good.* (P03-Interview)

### 5.25.2 GHP EXPERIENCE WITH ECS

The proportion of GHPs who had experience counselling ECS was similar among both the survey and interview participants, with 57% (31/54) of survey respondents having counselled ECS and 64% (9/14) of interview respondents.

Six survey participants worked in a private clinic and one participant worked in industry. In the free-text response asking participants to comment on the carrier screening practices at their institution, three participants working in private pay, and one working in industry commented that they routinely discuss the option of ECS and/or private pay carrier screening with their patients. Although only one interview participant worked part time in a private pay fertility clinic, this participant also reported routinely offering ECS as an option. This participant suggested that resources were perhaps one of the reasons why ECS is not discussed in the public genetics clinic.

> *Certainly we all realize it's not standard of care, that we don't have a legal obligation at this point to offer it. I think the only hesitation is resources and I think you know coming back to our public healthcare system I feel as if we're all limited from a resource point of view to assist couples. But I think taking resources out of the equation and time and what have you then I think that the majority of myself and my colleagues I think are in favor of the testing. I think resources, at least in my experience, is the limiting factor*. (P09-Interview)

# CHAPTER 6: DISCUSSION

## 6.1 PUSH AND PULL FACTORS KEEP ECS AS REACTIVE OPTION IN PUBLIC HEALTHCARE

In this study, the general positive opinion among participants toward ECS was a "push" factor, one that would promote the use of ECS in healthcare. The majority of interview and survey participants believed Canadians of reproductive age should be made aware of ECS, and that ideally ECS should be funded for those interested. This was balanced by pull factors related to working in public healthcare, which were reasons why GHPs did not routinely discuss ECS.

The balance of push and pull forces resulted in GHPs using ECS as a reactive option of providing healthcare based on need rather than ability to pay. GHPs usually initiated discussion of ECS similarly to how they would targeted carrier screening – by offering it to couples who they perceived were at higher risk of being a carrier, although in the case of ECS it was due to previous clinical history and/or consanguinity, rather than ethnic background. A similar finding was reported in a study assessing the attitudes of Canadian GHPs toward private pay testing, in which the most common circumstance for discussing private-pay testing, reported by 85% of participants was when a test was clinically indicated (e.g., but funding was denied) (di Gioacchino et al., 2019). A different study exploring ECS among European geneticists (who likely worked in a public healthcare system) found that participants agreed that ECS was most appropriate to offer in the context of consanguinity, a family history of a rare recessive disorder, or if there was a family history of an undiagnosed condition (Janssens et al., 2017).

Interview participants in this study expressed a number of pull factors as to why they only discussed ECS in certain clinical scenarios, rather than routinely. One of these reasons was that participants felt that discussion of ECS was not part of the GHP role. The majority of participants saw their role as providing publicly funded care to those at "high risk". They also expressed that their time spent routinely counselling patients for ECS would be better spent counselling patients who were at the highest risk, particularly given limited resources. Participants expressed similar reasoning for why ECS should not be funded- due to higher priorities for the healthcare system than universal reproductive screening, which would likely not be the best use of healthcare dollars. Similar perspectives were expressed in several qualitative studies exploring attitudes among European GHPs toward ECS (Janssens et al., 2017). GHPs in

Sweden, a country with public healthcare, expressed concerns relating to ensuring that programs such as ECS are worthy of spending resources and emphasized the importance of maximizing benefit to society (Matar et al., 2019). In a separate study the author found that GHPs in Sweden believed that ECS should not be a healthcare priority and that money should be allocated toward more essential services such as cancer treatment (A. Matar et al., 2016).

The majority of interview participants in this study were happy to discuss ECS when the discussion of private pay testing was patient-initiated. Although it was not explicitly discussed why they were happy to do so, perhaps this alleviated some of the "pull" factors such as GHP feelings of worry when initiating discussion of ECS. Interview participants expressed feeling worried that initiating a discussion about ECS would make patients more anxious or they were worried about how it would affect the client-provider relationship. Presumably, GHPs may not have these feelings if the patient initiated the discussion. Additionally, perhaps the patient-initiated discussion demonstrated patient motivation and initiative, and GHPs perceived that they would not have to spend their time helping these patients facilitate and organize the test, as a lack of resources/time was mentioned by a number of GHPs as a reason why they did not see routine discussion of ECS as part of their role.

## 6.2 PUSH AND PULL FACTORS IN THE PRIVATE SECTOR

Notably, although the sample size was limited, all of the participants who worked in private pay (the majority of who worked in a fertility clinic) reported an experience with ECS that was different than their public sector counterparts. These participants reported that they routinely made their patients aware of ECS, with a few indicating that their private-pay institution had a policy regarding discussion of ECS. Further supporting the notion that ECS may be routinely discussed in the private pay sector, approximately half of study participants' experiences with ECS in this study was with patients referred from fertility clinics. More frequent use of ECS in the private sector was also found in a study from New Jersey which identified differential utilization of expanded carrier screening tests in patients from private and academic practices. The rate of unconventional carrier screening (screening above what is recommended by the American carrier screening professional guidelines) was 10-fold higher among patients referred to genetics from a private practice than those referred from an academic practice (Schoen et al., 2015).

Although why ECS was routinely discussed in the private pay sector was not explored in this study, some inferences can be made based on the opinions expressed in this study and in the literature. The majority of participants thought that discussion of ECS would be more appropriate in other healthcare settings since the optimal time for any carrier testing is preconception. Perhaps timing is a push factor for why private-sector GHPs choose to discuss ECS routinely. In a study among European GHPs, participants cited that since fertility patients are already paying out of pocket, this made it easy to initiate the discussion of ECS. This could perhaps remove the cost as a barrier and reduce provider discomfort, as the cost of ECS is significantly less than fertility treatments. On the other hand, in the same study, some geneticists felt that it was their obligation to prevent the birth of an affected child in the fertility setting (Janssens et al., 2017). A push factor for ECS in the private sector might be defensive policy making, which is policy that stems from fear of physician liability rather than the evaluation of benefits and limitations of the technology for the patient. Interview participants working in public healthcare expressed that when deciding to discuss ECS, they factored in the patient's ability to afford ECS or how they would be perceived by the patient for initiating discussion of a private pay test. For a number of interview participants, these were factors that prevented them from discussing ECS. In the private healthcare setting, patient affordability and perception of private healthcare is less of a concern since presumably these are patients with the means and willingness to pay for private healthcare. Without some of the barriers that exist in public healthcare, ECS may simply be easier to discuss with patients in the private clinic.

One of the themes identified through interviews was a lack of ECS specific guidelines and concerns that the private-pay sector will drive healthcare, rather than it being a rational public decision-making process. In a study that used focus groups to interview 40 geneticists working in the United States, participants expressed similar concerns that increased uptake of ECS by clinicians may result in a defensive approach to risk identification (McGowan et al., 2013). Public discourse and patient expectation can undoubtedly lead to defensive policy making. For instance, a lawsuit was launched by seven families against Canada's largest sperm bank after 5 of 7 children born using the same sperm donor had Charcot-Marie-Tooth disease, a hereditary condition that causes progressive loss of muscle tissue and sensation. Among their claims is that the sperm bank did not perform "adequate genetic testing of the donor" (Sperm Bank Misled Families about Donor's Genetic Disorder, $30M Lawsuit Claims | CBC News, 2020). In other

instances, wrongful birth claims have been successful in Canada. These are claims in which a parent of a child with a congenital condition can take legal action against a physician for failing to recommend appropriate prenatal testing, resulting in the birth of child that would otherwise have been terminated. For example, a 35-year-old woman was not offered prenatal screening as per the standards of practice and gave birth to a child with Down syndrome. She asserted that if not for this this negligence, she would have chosen to abort the fetus (Toews & Caulfield, 2014). While defensive policy making may be more relevant among a patient population that is highly motivated to ensure they have a healthy child such as those seeking fertility treatment, it does have the potential to shape public discourse and expectations, particularly when those in the private sector are perceived as receiving more or better care than those accessing public healthcare, which could drive policy making in the public sector.

Interestingly, while GHPs in this study aimed to provide equitable healthcare by offering ECS to those at high risk, they were happy to provide information to those who asked about ECS or those who were accessing ECS via a private pay fertility clinic, and who were perhaps more likely to be using ECS proactively. There are perhaps differences in how ECS is used depending on the healthcare setting, whether private or public, which may have their own respective push and pull factors that promote or discourage use of ECS.

## 6.3 THE COST OF ECS IN THE CANADIAN GENETICS CLINIC

One of the arguments in favour of private pay healthcare in Canada is that it can potentially alleviate pressure from public clinics such as reducing patient wait times and decrease healthcare costs. The most common scenario in which interview participants were encountering ECS was as a referral from a fertility clinic, which are largely only accessible through private pay. In contrast to the argument of private pay healthcare reducing the public healthcare burden, the cost of ECS to Canadian healthcare was one of the reasons why GHPs working in public healthcare did not view discussion of ECS as part of their role, as explored in theme 3. GHPs in this study described that in their experience ECS took time away from patients who were at high risk and felt that this was an issue given the long wait lists in many genetics clinics. Whether initiated in a private clinic or a public clinic, ECS has the potential to create downstream costs to public healthcare but also has the potential to provide cost savings in other areas such as lower

frequency of affected births or early diagnosis leading to reduced lifetime morbidity and mortality (Cernat et al., 2021).

### 6.3.1 Considering the Cost-Benefit of ECS

The majority of survey respondents believed that ECS should be provincially funded in any preconception/prenatal scenario or only in certain preconception/prenatal scenarios. However, a number of interview participants indicated that they did not have an opinion about whether ECS should be funded without a cost-benefit analysis of ECS. In addition, a number of interview participants believed that a cost-benefit analysis was warranted given the outdated focus of prenatal screening on Down syndrome and vague guidelines pertaining to ECS. While a detailed cost-benefit analysis of ECS in the Canadian population is beyond the scope of this thesis, a simplified analysis can provide an appreciation of the resources needed if ECS were to become a routine test and how many individuals would benefit.

As discussed in subsection 1.3.4, the goal of carrier screening in Western countries is to provide opportunities for informed reproductive decision making. For example, one of the primary outcome measures of Mackenzie's Mission, an Australian project piloting universal ECS, is to ascertain the reproductive choices made by increased-risk couples (Mackenzie's Mission: The Australian Reproductive Carrier Screening Project, 2020). One of the potential impacts of ECS among the Canadian population can therefore be thought about in terms of opportunities for informed decision making among the population. Carrier screening programs such as Dor Yeshorim in the AJ population, where the carrier frequency for a specific AR condition is high, can impact the reproductive decision making of a comparatively large number of couples. Using TSD as an example, with a carrier frequency of 1 in 30 (Willson et al., 2016), a couple where both partners are of AJ descent have a 1 in 900 chance of both being carriers for TSD (1/30 x 1/30). In other words, 899 couples would need to be screened before one increased risk couple is identified. Similarly, carrier screening for CF in Northern Europeans would identify an at-risk couple for every 624 couples screened (1/25 x 1/25). Individuals with early detection of CF have been shown to have reduced morbidity and mortality, particularly for cases of severe CF (Tridello et al., 2018).

The success of screening programs in high-risk populations have perhaps fueled the development of ECS. While ECS provides the opportunity to screen for more recessive

conditions, this does not necessarily correlate with equally increased opportunities for decision making by couples. The majority of conditions included in ECS panels are rare in the general population, with a low carrier frequency, and even lower likelihood that both partners will be carriers. For example, for a condition with a carrier frequency of 1 in 300, 89,999 couples would need to be screened before one at-risk couple is identified. In this scenario, the resources required to provide counselling and testing to identify one at risk couple are greater than the resources needed to identify one at risk couple for an AR condition in a high risk population.

A study by Guo & Gregg, (2019) analyzed the difference of the number of at-risk couples identified by carrier screening a population for 415 genes vs 40 genes. Screening using the 40 gene panel, where each condition had a carrier frequency greater than 1 in 100, identified 76.4 to 96.8% of the at-risk couples that had been identified by screening using the 415 gene panel. Increasing the number of genes screened may not lead to identifying many more carrier couples, however will likely lead to the identification of many carriers, since most individuals are carriers of at least one condition (Beauchamp et al., 2020).

A measured and thoughtful approach to carrier screening, perhaps expanding current carrier screening criteria to include conditions with the highest incidence in a specific population could make an almost equally large impact. On the other hand, although it may seem insignificant to miss a percentage of carrier couples through screening, the effect is often significant for those who fall into the missed percent. For example, interview participant 05 shared that she and her partner were identified as an at-risk couple through ECS. She shared how thankful she was to have had ECS because it afforded the couple early awareness and intervention for her child who was affected with an AR condition.

ECS has the potential to reduce costs in other areas of healthcare. For example, sometimes establishing a genetic diagnosis can require numerous diagnostic test (imaging, biochemical, genetic, among others), and multiple appointments with various healthcare providers. Some individuals, particularly those with a rare disease, may find themselves in a “diagnostic odyssey”, which can sometimes be solved by genetic testing. ECS may identify at risk couples for a rare condition, which could provide an early diagnosis and avoid costly “diagnostic odyssey”, even if there is not treatment for the diagnosis (Monroe et al., 2016; Tan et al., 2017).

### 6.3.2 Cost to Patients

One area in which ECS could have a downstream cost to patients is in the form of patient anxiety. Screening an individual for a large number of conditions increases the likelihood that they will be identified as a carrier since most individuals are carriers for at least one condition. At a population level, ECS introduces the possibility of identifying many carriers.

Learning that one is a carrier could potentially cause anxiety compared to the unscreened couple, even if it is short lived. For example, if a woman has ECS prenatally and is identified to be a carrier, there can be anxiety in the period in which she waits for the results of her partner's carrier test. In addition, there is the chance that lack of understanding of the risks associated with being a carrier, particularly if the patient did not have formal genetic counselling to explain their ECS result could cause individuals to experience anxiety due to being misinformed. Lastly, since ECS is not a diagnostic test, a subset of patients with a negative test result may still worry about residual risk.

Some of the interview participants mentioned that they did not talk about ECS with their patients specifically because they recognized the potential for ECS to increase anxiety. Reports in the literature have found that ECS can heightens patients' anxiety temporarily until they receive their result or until their partner has carrier testing (Beard et al., 2016, Kraft et al., 2018). On the other hand several interview participants in this study mentioned that their patients found the information they learned from ECS helpful, even if they were not identified to be carriers for the same condition. Some studies have found that in order to minimize anxiety patients should be offered ECS preconception (Dijke et al., 2021).

### 6.3.3 Cost to Healthcare

Many participants indicated that since the resources for public genetics clinics are finite, ECS took genetic counselling time away from the most at-risk patients. Participants cited that their clinic already did not have enough GCs to perform their regular work and this resulted in long patient waitlists. Many viewed counselling for ECS as time that could be better spent counselling higher risk patient. The most common clinical scenario in which GHPs had encountered ECS, (encountered by half of interview participants) was due to a referral from a fertility clinic, where patients usually accessed ECS through private pay.

Downstream costs can also come from prenatal diagnosis, as some couples who are known to be at risk of having a child with an AR condition may choose to conceive naturally and have prenatal diagnosis, while others may not have carrier screening until already pregnant. Additional downstream costs can also come up preconception, for example if one partner is identified to be a carrier through private pay ECS, the logical next step is to offer carrier screening to their partner. In addition, at-risk family members of reproductive age may also want carrier testing. The cost of this testing may or may not be shouldered by provincial healthcare system.

ECS also presents the opportunity for cost saving to the healthcare system by reducing the number of affected births or by reducing morbidity and mortality of an affected child. For example, couples may choose to terminate an affected pregnancy or may choose to conceive using a donor sperm/ egg or can pursue preimplantation genetic diagnosis. An early diagnosis can also ensure that affected individuals receive appropriate and targeted treatment as early as possible, potentially improving morbidity and mortality and reducing the burden on healthcare services.

## 6.4 SUMMARY OF RECOMMENDATIONS FOR ECS IN CANADA

The overall significance of this study was to provide a starting point for ECS research in Canada. Many participants expressed feeling unsure of what other centres were doing and turned to search for a guideline or recommendation. Below is a summary of the main recommendations and opinions shared by study participants from both the survey and interviews. Where possible points are compared and contrasted to practice guidelines and the existing literature regarding private-pay genetic testing in Canada.

1. **GHPs in the public healthcare clinic are discussing ECS when referred from fertility, when the GHP perceives the patient to be at increased risk of being a carrier, or when the patient initiates the discussion. GHPs in private clinics routinely discuss ECS.**

Similar to the clinical scenarios in which participants in this study discussed the option of ECS with their patients, Di Gioacchino et al., (2019) found that the three most common circumstance in which GHPs discussed private pay testing was when a clinically appropriate test

was not funded, or funding was denied, when patients initiated the discussion and whether the GHP perceived that the patient could afford to pay. A similar finding emerged among interview participants, where the second most common scenario in which ECS was discussed was when the GHP perceived ECS to be a clinically appropriate test in the absence of publicly funded testing options and the third most common scenario was when the patient initiated the discussion of private pay testing options.

The CAGC is in the process of publishing a practice guideline regarding discussion of private pay genetic testing (personal communication, Ingrid Ambus, April 2020). One of the aims of publishing this guideline is to encourage uniformity in practice. There appeared to be some uniformity in when GHPs discussed private-pay genetic testing in this study and in the Di Gioacchino study. However, a discrepancy was observed between GHPs working in the public genetics clinic and those in the private genetics clinic. Five out of six survey participants who worked in a private clinic mentioned that they routinely discuss ECS with their patients, and one interview participant who worked in both a public clinic and private clinic reported routinely discussing ECS in the private clinic and not in the public clinic.

GHPs in this study shared similar reasons as to why they do not routinely discuss ECS with patients, each of which were factors related to working in public healthcare. For example GHPs viewed their role as providing service to those at high risk and described considering how the patients perceive GHP initiated discussion of private pay testing in a public clinic. GHPs working in a private clinic may not encounter the challenges that arise in public healthcare which may enable routine discussion of ECS. As discussed in the preceding section, private pay clinics may also be more likely to develop formal policies addressing ECS, which can facilitate discussion by the GHP.

### 2. Canadian individuals of reproductive age should be aware of ECS in order to make fully informed reproductive decisions.

Participants in both the survey and interviews believed that Canadians should be aware that is ECS is an option. Although differences in opinion regarding ECS were observed between survey participants with the most ECS experience and those with the least ECS experience, both groups agreed that Canadians should be made aware of ECS. This is perhaps unsurprising given the focus on informed decision making in genetic counselling.

### 3. With additional training, obstetricians, gynecologists and family physicians are best suited to inform individuals of ECS.

The majority of study participants agreed that without additional training, GHPs are the best provider to conduct pre-test counselling for ECS, however the majority (85%) believed that with additional training obstetricians would be best suited to perform pre-test counselling for ECS, followed by gynecologists (53%) and family physicians (36%). It is interesting that 85% of survey respondents chose obstetricians as the best suited healthcare providers since the ideal time for ECS is preconception, as this allows the full range of reproductive choices to be considered. However, it is important to mention that most women do not see an obstetrician until they are already pregnant (McGowan et al., 2013). This could be because GHPs consider obstetricians as the most genetics-literate among non-GHPs, as they are already responsible for pre-test counselling for non-invasive prenatal testing (NIPT) and in some provinces counselling for NIPT. In comparison, discussions about genetic testing and disclosure of genetic testing results may not come up routinely in family medicine (Benn, et al., 2014).

A number of participants in both the interviews and survey expressed concerns about non-GHPs providing pre-test counselling for ECS and were specifically concerned that consent would not be as informed as it would be with pre-test counselling by a GHP. Which healthcare provider conducts pre-test counselling for genetic testing could potentially influence patient decision making. A 2019 study found that Canadian pregnant women's preferences regarding the use of NIPT were associated with who informed them of their testing options. Being informed by a GC correlated with an equal likelihood of choosing amniocentesis or NIPT, whereas not being informed by a GC correlated with being more than three times as likely as prefer amniocentesis (Birko et al 2019). This difference was perhaps due to GHPs having a more nuanced understanding of NIPT benefits/limitations.

In addition, pre-test counselling for ECS can be potentially more challenging for non-GHPs than other genetic tests such as NIPT, or carrier testing for a single disorder. The survey participants with the most ECS experience almost unanimously agreed that they had concerns with non-GHPs offering ECS. Although this study did not explore why GHPs had concerns, this finding suggests that complex situations can arise when offering ECS or that those experienced

with ECS had witnessed first-hand what can go wrong when ECS is offered by a non-GHP provider.

### 4. ECS should be funded by public healthcare in certain scenarios.

Over half (61%) of participants believed that ECS should be funded by public healthcare in any prenatal/preconception scenario or in certain prenatal/preconception scenarios. One of the themes that came out in the study was that participants were uncomfortable initiating discussion of a private pay genetic test in the publicly funded genetics clinic, worrying about how it would be perceived by the patient. These feelings could be mitigated in certain scenarios if ECS was publicly funded.

Although the cost of ECS has decreased, it likely still remains inaccessible for many. Two Canadian studies found that socioeconomic status was correlated with how much patients would be willing to pay for genetic testing, while other factors such as gender and education level were not correlated (Ries et al., 2010, Birko et al.,2019). Birko et al., (2019) also found that single mothers in Ontario were less likely to pay for NIPT than married women. As a private pay option ECS is likely to remain accessible to a certain demographic. Perhaps providing further evidence to this claim is that the majority of survey respondents indicated that they either already had or would pay for private pay carrier screening. Based on the 2020 PSS, the average GC belongs to the demographic of an educated, white female with an above average income.

### 5. More explicit guidelines about carrier screening and ECS would be helpful.

Only 22% (12/54) of survey participants had an institutional or clinic policy regarding ECS and of these, 80% of policies permitted the discussion of ECS. This result is similar to the report by Di Gioacchino et al., (2019) in which 22% of Canadian GHPs reported working in a clinic that had a policy on discussing private pay genetic testing options. The majority of policies permitted discussion of private pay options. The lack of formal policy could potentially cause inconsistencies in patient access to ECS.

In this study, a number of participants expressed that they found the SOGC-CCMG recommendations regarding ECS vague and found that these recommendations did not help them make decisions regarding integrating ECS in their clinical practice. Several participants in this

study called for more explicit guidelines that can help GHPs address challenges they may face in clinic regarding the discussion/counselling of ECS.

## 6.5 PROFESSIONAL VS PERSONAL OPINIONS

There was a notable discordance among interview participants professional values and personal values. On a professional level GHPs discussed ECS only in specific situations as described in Theme 1. On a personal level however GHPs almost unanimously would pursue ECS or had paid privately for some type of carrier screening. Although GHPs personal experience or opinions on private pay genetic testing has not been explored, there is literature exploring GC experiences with receiving genetics services, which similarly put GCs in the role of healthcare user rather than provider.

A number of GHPs in the interview mentioned that they would pursue ECS because working as a prenatal GC had skewed their perspective, even though they knew that the majority of pregnancies are unaffected. Menezes et al. (2010) observed a similar finding among pregnant prenatal GCs, who described finding it difficult to maintain a realistic viewpoint due to the frequency of witnessing fetal abnormalities among their patients.

Interestingly, almost all GHPs interviewed expressed that they felt like they had to uphold Canadian healthcare goals by providing service to those at highest risk, however would also personally pursue ECS. Two participants recognized this discordance and referred to themselves as being hypocritical. However, participants also felt that because they were GHPs, they could interpret the results themselves and perhaps would not require services from the public genetics clinic. Although it did not come out in interviews, GHPs could still use other services such as prenatal testing if both partners were carriers or their ECS result might lead other at-risk family members to seek genetic testing through a public clinic.

## 6.6 STUDY LIMITATIONS

This study aimed to recruit participants across Canada in various roles in order to compare opinions and experiences between demographic groups, such as GHP role (GC, geneticist), practice area or province of practice. The survey portion of the study was limited by a small sample size, which did not allow for statistical comparisons between these groups or generalizability of the quantitative results to the broader GHP population. Consequently, this did

not play to the strengths of the quantitative component of a mixed methods study. In addition, the study population consisted overwhelmingly of GCs, particularly for the interview participants. The opinions of Canadian geneticists are largely missing from this study, which could have yielded different result, particularly since the CAGC private pay practice guideline was not supported by the CCMG, indicating that there are perhaps differences in opinions regarding discussion of private pay genetic testing between the two groups (Palma, 2021).

It is also possible that participants self-selected based on specific preferences that are not necessarily representative of the GHP population in Canada as a whole. For example, four out of the 14 interview participants had paid privately for carrier screening and one participant had accessed carrier screening as a study volunteer. Seven other participants indicated that if they were in a preconception situation, they would choose to have ECS. Given the interest by the interview participants to use ECS personally, such volunteerism may have been driven by their personal interest in this topic, potentially skewing the results in favour of ECS.

Similarly, it is possible that participants self-selected based on their professional opinions of ECS, whether strongly in favour or strongly against the use of ECS. For example, the survey portion of the study found that GHPs with more ECS experience had more positive opinions of ECS. It is possible that GHPs with positive opinions toward ECS would be more likely to discuss ECS with their patients. Therefore, rather than GHP experience with ECS influencing their opinion, pre-existing positive or negative opinions of ECS may have influenced participamts' level of experience with ECS.

## 6.7 FUTURE DIRECTIONS

This study was the first to explore ECS in the Canadian genetics clinic and identified several interesting points that warrant further exploration. The majority of participants in this study believed that obstetricians, gynecologists and family physicians were best suited to provide pre-test counselling for ECS. Future studies are needed to understand whether there is buy-in from these non-GHP providers to discuss ECS/private-pay testing, as well as their comfort level with discussing ECS. Further assessing their knowledge may guide the design of training or educational opportunities or the design of patient counselling materials.

There was also an observed difference in opinions between GHPs with lots of ECS experience and those without ECS experience. The most striking difference in opinion between

these two groups was related to concerns with non-GHPs offering ECS. Almost all of those in the experienced group expressed concern with non-GHPs offering ECS, while the less experienced group was split. Future studies could focus on understanding the challenges among the more experienced GHPs with ECS or with other providers offering ECS in order to better characterize the challenges that may arise with pre-test ECS counselling. This could then help identify the ways that these challenges can be mitigated, and identify areas for educational and training for non-GHPs.

The focus of this study was on provider opinions of ECS, however historically public opinion towards carrier screening for specific conditions has been collected prior to the implementation of a carrier screening program. Similarly, prior to NIPT becoming widely offered in Canada, public opinion was collected. Understanding the opinions of the Canadian population towards ECS and whether it is something they would be interested in learning about or pursuing is an important next step.

# CHAPTER 7: CONCLUSION

ECS is a relatively new genetic test that is available through private pay, with limited literature reflecting ECS from the Canadian healthcare perspective, where the perceived benefits and limitations of ECS may be unique to a public healthcare system. This study aimed to explore Canadian GHPs experience with and opinion towards ECS. GHPs across Canada were recruited to participate in a survey and/or interview. Survey and interview results revealed that ECS was most frequently discussed by prenatal/preconception and pediatric GCs but is not routinely discussed by other GHPs in the public healthcare setting. The majority of participants in this study reported that they did not have an institutional or clinic policy regarding ECS. Interview participants provided further insight into when ECS is discussed as an option with patients in public clinics, with the three most frequent scenarios being a fertility clinic referral, the GC perceives the patient to be at increased risk of being a carrier, or the patient initiates the discussion. Participants had a positive or neutral opinion towards ECS, with the majority of survey respondents believing that ECS presented a balance of benefits and limitations and that ECS should be funded in certain situations. The majority of interview participants would personally pursue ECS and believed that ECS could provide certain couples valuable information, and thought that all Canadians of reproductive age should be made aware that ECS is an option. Both survey and interview participants believed that with additional training other healthcare providers such as obstetricians or family physicians are best suited to make Canadians aware of ECS. Interview participants raised several reasons as to why they thought GHPs should not routinely discuss ECS, such as not seeing it as part of their role as a public healthcare employee, their feelings of discomfort surrounding initiating discussion of a private pay test in a public healthcare setting and the need for more ECS or private pay specific guidelines. The results from this study provide evidence that there is general support among Canadian GHPs for ECS, however also identified several tensions that limit or prevent discussion of ECS in the publicly funded genetics clinic. The experiences and perspectives shared in this study provide insight into current Canadian practice with ECS, which can be helpful in striving towards consistent genetics practice across Canada. This study identified barriers to discussing ECS in the public genetics clinic, which can be informative when establishing guidelines or deciding which healthcare provider should inform Canadians of ECS. Furthermore, this study highlights

the need for GC to explore their personal biases and feelings regarding private pay testing options within their public healthcare setting. Overall, the insights gained from this exploratory study provide a foundation for future studies regarding ECS in Canada.

## REFERENCES

American College of Obstetricians and Gynecologists. (2017). Committee Opinion No. 691: Carrier Screening for Genetic Conditions. *Obstetrics and gynecology*, *129*(3), e41–e55. https://doi.org/10.1097/AOG.0000000000001952

Andermann, A., Blancquaert, I., Beauchamp, S., & Costea, I. (2011). Guiding policy decisions for genetic screening: Developing a systematic and transparent approach. Public Health Genomics, 14(1), 9–16. https://doi.org/10.1159/000272898

Attorney General of British Colombia (2020). *Cambie Surgeries Corporation v. British Columbia*. https://www.bccourts.ca/jdb-txt/sc/20/13/2020BCSC1310.htm

Audibert, F., De Bie, I., Johnson, J., Okun, N., Wilson, R.D., Armourm C., Chitayat, D., & Kim, R. (2017). Joint SOGC-CCMG Guideline: Update on Prenatal Screening for Fetal Aneuploidy, Fetal Anomalies, and Adverse Pregnancy Outcomes. Journal of Obstetrics and Gynaecology Canada, 39(9):805-817. Doi:10.1016/j.jogc.2017.01.032

Bajaj, K., & Gross, S. (2014). Carrier Screening: Past, Present, and Future. *Journal of Clinical Medicine*, *3*(3), 1033–1042. https://doi.org/10.3390/jcm3031033

Beauchamp, K. A., Johansen Taber, K. A., & Muzzey, D. (2020). Clinical impact and cost-effectiveness of a 176-condition expanded carrier screen. *Genetics in Medicine*. https://doi.org/10.1038/s41436-019-0455-8

Ben-Shachar R, Svenson A, Goldberg JD, Muzzey D. A data-driven evaluation of the size and content of expanded carrier screening panels. *Genetetics in Medicine.* 2019;21(9):1931-1939.

Benn P, Chapman AR, Erickson K, Defrancesco MS, Wilkins-Haug L, Egan JF, Schulkin J. (2014). Obstetricians and gynecologists' practice and opinions of expanded carrier testing and noninvasive prenatal testing. *Prenatal Diagnosis*, doi: 10.1002/pd.4272.

Canadian College of Medical Geneticists (2020). Frequently asked questions. https://www.ccmg-ccgm.org/training/frequently-asked-questions.html#FAQ3

Canadian Medical Association *(2019). Medical Genetics Profile*. https://www.cma.ca/sites/default/files/2019-01/medical-genetics-e.pdf

*Canadian Press Poll: Canadians are most proud of universal medicare*. (2012). CTV News. http://www. Ctvnews.ca/91anada/poll-canadians-are-most-proud-of-universalmedicare-1.1052929#

Cernat, A., Hayeems, R.Z. & Ungar, W.J. (2021). Cascade health service use in family members

following genetic testing in children: a scoping literature review. *European Journal of Human Genetics* **29,** 1601–1610. https://doi.org/10.1038/s41431-021-00952-4.

Chokoshvili, D., Vears, D., & Borry, P. (2018). Expanded carrier screening for monogenic disorders: where are we now? *Prenatal Diagnosis, 38*(1), 59–66. https://doi.org/10.1002/pd.5109

Creswell, J. W., & Plano Clark, V. L. (2018). *Designing and Conducting Mixed Methods Research* (3rd ed). Sage Publications, Inc.

Cronister, A, Wallace, F., Heckman, L., Cheney, S., & Fissell, K. (2019). Counseling Complexities of Expanded Carrier Screening: an ATM Case Report. Poster presented at the 2019 ACMG Annual Clinical Genetics Meeting. Seattle, Washington. https://cslide-us.ctimeetingtech.com/acmg_19/attendee/eposter/poster/531

Dedoose Version 8.3.45 web application for managing, analyzing, and presenting qualitative and mixed method research data. (2019). SocioCultural Research Consultants, LLC.

Di Gioacchino, V., Langlois, S., & Elliott, A. M. (2019). Canadian genetic healthcare professionals' attitudes towards discussing private pay options with patients. *Molecular Genetics and Genomic Medicine, 7*(4). https://doi.org/10.1002/mgg3.572

Dor Yeshorim. *History and achievements*. Retrieved October 2021 https://doryeshorim.org/history-achievements//

Drumm, M. L., Ziady, A. G., & Davis, P. B. (2012). Genetic variation and clinical heterogeneity in cystic fibrosis. *Annual review of Pathology, 7*, 267–282. https://doi.org/10.1146/annurev-pathol-011811-120900

Dynacare (2021). *Harmony Prenatal Test (NIPT), the proven option for safe, early, accurate prenatal testing*. https://www.dynacare.ca/news/harmony-prenatal-test-(nipt).aspx#:~:text=In%20addition%2C%20women%20who%20want,test%20from%20Dynacare%20for%20%24495.

Edelson, P. J. (1997). The Tay-Sachs disease screening program in the U.S. as a model for the control of genetic disease: An historical view. Health Matrix (Cleveland, Ohio: 1991), 7(1).

Edwards, J. G., Feldman, G., Goldberg, J., Gregg, A. R., Norton, M. E., Rose, N. C., Schneider, A., Stoll, K., Wapner, R., & Watson, M. S. (2015). Expanded carrier screening in reproductive medicine-points to consider. *Obstetrics and Gynecology* (Vol. 125, Issue 3, pp. 653–662). https://doi.org/10.1097/AOG.0000000000000666

Elliott, A. M., Radecki, J., Moghis, B., Li, X., & Kammesheidt, A. (2012). Rapid Detection of

the ACMG/ACOG-Recommended 23 CFTR Disease-Causing Mutations Using Ion Torrent Semiconductor Sequencing. *Journal of Biomolecular Techniques 23*(1) https://doi.org/10.7171/jbt.12-2301-003

Flood, C. M., & Thomas, B. (2018). A successful Charter challenge to medicare? Policy options for Canadian provincial governments. *Health Economics, Policy and Law, 13*(3–4) https://doi.org/10.1017/S1744133117000469

GECKO Reproductive Genetic Carrier Screening in Canada. 2020. Retrieved June 18, 2021, from https://geneticseducation.ca/point-of-care-tools-2/preconception-and-prenatal-genomics/reproductive-genetic-carrier-screening-in-canada/

Get coverage for prescription drugs. Retrieved June 18, 2021, from https://www.ontario.ca/page/get-coverage-prescription-drugs

Government of Ontario. *Newborn Screening – Health Care Professionals.* Retrieved June 3, 2021, from https://www.health.gov.on.ca/en/pro/programs/newborn/

Grody, W. W., Thompson, B. H., Gregg, A. R., Bean, L. H., Monaghan, K. G., Schneider, A., & Lebo, R. v. (2013). ACMG position statement on prenatal/preconception expanded carrier screening. *Genetics in Medicine*, *15*(6), 482–483. https://doi.org/10.1038/gim.2013.47

Guo, M. H., & Gregg, A. R. (2019). Estimating yields of prenatal carrier screening and implications for design of expanded carrier screening panels. *Genetics in Medicine, 21*, 1940–1947. https://doi.org/10.1038/s41436

Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*, *42*(2). https://doi.org/10.1016/j.jbi.2008.08.010

Health Canada (2021) *Canada's Health Care System* https://www.canada.ca/en/health-canada/services/health-care-system/reports-publications/health-care-system/canada.html#a3 Retrieved June 16, 2021

Henneman, L., Borry, P., Chokoshvili, D., Cornel, M. C., van El, C. G., Forzano, F., Hall, A., Howard, H. C., Janssens, S., Kayserili, H., Lakeman, P., Lucassen, A., Metcalfe, S. A., Vidmar, L., de Wert, G., Dondorp, W. J., & Peterlin, B. (2016). Responsible implementation of expanded carrier screening. *European Journal of Human Genetics*, *24*(6), https://doi.org/10.1038/ejhg.2015.271

Invitae (2021). *Billing* https://www.invitae.com/en/providers/billing Date accessed: November 12 2021.

Ioannou, L., Mcclaren, B. J., Massie, J., Lewis, S., Metcalfe, S. A., Forrest, L., & Delatycki, M.

B. (2014). Population-based carrier screening for cystic fibrosis: A systematic review of 23 years of research. In *Genetics in Medicine*, *16 (3)* https://doi.org/10.1038/gim.2013.125

Janssens, S., Chokoshvili, D., Vears, D., de Paepe, A., & Borry, P. (2017). Attitudes of European Geneticists Regarding Expanded Carrier Screening. *JOGNN – Journal of Obstetric, Gynecologic, and Neonatal Nursing*, *46*(1), 63–71. https://doi.org/10.1016/j.jogn.2016.08.012

Jaswal, A. (2013). *Valuing health in Canada Who, how, and how much?* www.canada2020.ca

Johansen Taber, K. A., Beauchamp, K. A., Lazarin, G. A., Muzzey, D., Arjunan, A., & Goldberg, J. D. (2019). Clinical utility of expanded carrier screening: results-guided actionability and outcomes. *Genetics in Medicine*, *21*(5). https://doi.org/10.1038/s41436-018-0321-0

Kaback, M. M. (2000). *Population-based genetic screening for reproductive counseling: the Tay-Sachs disease model*. *European journal of pediatrics*, 159 https://doi.org/10.1007/pl00014401

Kraft, S. A., Duenas, D., Wilfond, B. S., & B Goddard, K. A. (2019). The evolving landscape of expanded carrier screening: challenges and opportunities. *Genetics in Medicine*, https://doi.org/10.1038/s41436

Langlois, S., & Brock, J. (2013). Current Status in Non-Invasive Prenatal Detection of Down Syndrome, Trisomy 18, and Trisomy 13 Using Cell-Free DNA in Maternal Plasma. *Journal of Obstetrics and Gynaecology Canada*, 35(2), 177-181. 10.1016/S1701-2163(15)31025-2

Lazarin, G., Hawthorne, F., Collins, N., Platt, E., Evans, E., & Haque, I. (2014). Systematic Classification of Disease Severity for Evaluation of Expanded Carrier Screening Panels. *PLOS ONE*.

Leung, M. L., McAdoo, S., Watson, D., Stumm, K., Harr, M., Wang, X., Chung, C. H., Mafra, F., Nesbitt, A. I., Hakonarson, H., & Santani, A. (2021). A Transparent Approach to Calculate Detection Rate and Residual Risk for Carrier Screening. *The Journal of molecular diagnostics*, *23(1)*, 91–102. https://doi.org/10.1016/j.jmoldx.2020.10.009

Major federal transfers – Canada.ca. Retrieved June 18, 2021, from https://www.canada.ca/en/department-finance/programs/federal-transfers/major-federal-transfers.html

Marchildon GP, Allin S, & Merkur S. (2020). Canada: Health System Review. *Health Systems in Transition*, 22(3).

Martin, D., Miller, A. P., Quesnel-Vallée, A., Caron, N. R., Vissandjée, B., & Marchildon, G. P. (2018). Canada's universal health-care system: achieving its potential. *The Lancet, 391(10131)* pp. 1718–1735. https://doi.org/10.1016/S0140-6736(18)30181-8

Matar, A., Kihlbom, U., & Höglund, A. T. (2016). Swedish healthcare providers' perceptions of preconception expanded carrier screening (ECS)—a qualitative study. *Journal of Community Genetics, 7*(3), 203–214. https://doi.org/10.1007/s12687-016-0268-2

Matar, A., Hansson, M. G., & Höglund, A. T. (2019). Values and value conflicts in implementation and use of preconception expanded carrier screening – An expert interview study. *BMC Medical Ethics, 20*(1). https://doi.org/10.1186/s12910-019-0362-1

McGill University (2018*). Health Care in Canada Survey*.https://www.mcgill.ca/hcic-sssc/hcic-surveys/2018

Mcgowan, M. L., Cho, D., & Sharp, R. R. (2013). *The Changing Landscape of Carrier Screening: Expanding Technology and Options? Health Matrix* https://scholarlycommons.law.case.edu/healthmatrix/vol23/iss1/4

Menezes, MA., Hodgson, JM., Sahhar, MA., Aitken, M., Metcalfe, SA. (2010). "It's challenging on a personal level"--exploring the 'lived experience' of Australian and Canadian prenatal genetic counselors. *Journal of Genetic Counseling* 19(6):640-652. DOI: 10.1007/s10897-010-9315-z.

Monroe, G. R., Frederix, G. W., Savelberg, S. M., de Vries, T. I., Duran, K. J., van der Smagt, J. J., Terhal, P. A., van Hasselt, P. M., Kroes, H. Y., Verhoeven-Duif, N. M., Nijman, I. J., Carbo, E. C., van Gassen, K. L., Knoers, N. V., Hövels, A. M., van Haelst, M. M., Visser, G., & van Haaften, G. (2016). Effectiveness of whole-exome sequencing and costs of the traditional diagnostic trajectory in children with intellectual disability. *Genetics in Medicine 18(9),* 949–956. https://doi.org/10.1038/gim.2015.200.

National Society of Genetic Counselors. (2020). *Professional status survey 2020: Demographics & methodology*. Chicago, IL. Retrieved from https://www.nsgc.org/Policy-Research-and-Publications/Professional-Status-Survey.

National Society of Genetic Counselors (2021). *About Genetic Counselors* https://www.nsgc.org/About/About-Genetic-Counselors Date accessed: November 5 2021.

Okada, S., & O'Brien, J. S. (1969). Tay-Sachs Disease: Generalized Absence of a Beta-D-N-Acetylhexosaminidase Component. *Science, 165*(3894). https://doi.org/10.1126/science.165.3894.698

Online Mendelian Inheritance in Man, OMIM®. (2020). Johns Hopkins University, Baltimore, MD. https://omim.org/

Palma, L. (2021). Growth of private pay genetic counselling and testing services in Canada: Can we responsibly navigate these uncharted waters? Presented at the CAGC Annual Education Conference. Sep 29-Oct 2 2021.

PharmaCare for B.C. Residents - Province of British Columbia. Retrieved June 18, 2021, from https://www2.gov.bc.ca/gov/content/health/health-drug-coverage/pharmacare-for-bc-residents

Pollack, Andrew. (Jan 28 2010). *Firm Brings Gene Test to Masses*. The New York Times. https://www.nytimes.com/2010/01/29/business/29gene.html

Raphael, D., Bryant, T., Mikkonen, J., & Raphael, A. (2020). *Social Determinant of Health the Canadian Facts*. http://www.thecanadianfacts.org/

Romero, S., Biggio, J. R., Saller, D. N., & Giardine, R. (2017). Committee Opinion Number 691. *Committee Opinion Number*, *129*(3).

Romero, S., Rink, B., Biggio, J. R., & Saller, D. N. (2017). *Carrier Screening in the Age of Genomic Medicine Committee on Genetics* (Vol. 129, Issue 3).

Ropers, H.-H. (2012). On the future of genetic risk assessment. *Journal of Community Genetics*, *3*(3). https://doi.org/10.1007/s12687-012-0092-2

Schoen, C., Santolaya-Forgas, J., Genc, M., & Ashkinadze, E. (2015). Differential utilization of expanded genetic screening tests in patients of reproductive ages from private and academic practices. *Journal of Perinatal Medicine*, *43*(6), 689–693. https://doi.org/10.1515/jpm-2014-0160

Supreme Court of Canada (2005). *Chaoulli v. Quebec*. https://scc-csc.lexum.com/scc-csc/scc-csc/en/item/2237/index.do

Swift, A., Heale, R., & Twycross, A. (2020). What are sensitivity and specificity? Evidence-Based Nursing, 23, 2-4. http://dx.doi.org/10.1136/ebnurs-2019-103225

Tan, T. Y., Dillon, O. J., Stark, Z., Schofield, D., Alam, K., Shrestha, R., Chong, B., Phelan, D., Brett, G. R., Creed, E., Jarmolowicz, A., Yap, P., Walsh, M., Downie, L., Amor, D. J., Savarirayan, R., McGillivray, G., Yeung, A., Peters, H., Robertson, S. J., … White, S. M. (2017). Diagnostic Impact and Cost-effectiveness of Whole-Exome Sequencing for Ambulant Children With Suspected Monogenic Conditions. *JAMA pediatrics*, *171*(9), 855–862. https://doi.org/10.1001/jamapediatrics.2017.1755

Toews, M., & Caulfield, T. (2014). Physician Liability and Non-Invasive Prenatal Testing. *Journal of Obstetrics and Gynaecology Canada* (Vol. 36, Issue 10, pp. 907–914). Elsevier Inc. https://doi.org/10.1016/S1701-2163(15)30441-2

Tridello, G., Castellani, C., Meneghelli, I., Tamanini, A., Assael BM. (2018)

*ERJ Open Research* 4: 00109-2017; DOI**:** 10.1183/23120541.00109-2017

Van der Hout, S., Holtkamp, K., Henneman, L et al. (2017). Advantages of expanded universal carrier screening: what is at stake? *European journal of human genetics*, 25. Doi: 10.1038/ejhg.2016.125

Wilson, J., & Jungner, Y. (1968). *Principles and practice of mass screening for disease*. World Health Organization

Wilson, R. D., Bie, I. D., Armour, C. M., Brown, R. N., Campagnolo, C., Carroll, J. C., Okun, N., Nelson, T., & Zwingerman, R. (2016). Joint SOGC–CCMG Opinion for Reproductive Genetic Carrier Screening No.335 : An Update for All Canadian Providers of Maternity and Reproductive Healthcare in the Era of Direct-to-Consumer Testing. Journal of Obstetrics and Gynaecology Canada, 38(8), 742-762.e3. https://doi.org/10.1016/j.jogc.2016.06.008

World Health Organization(2020). *Screening programmes: a short guide*. https://apps.who.int/iris/bitstream/handle/10665/330829/9789289054782- eng.pdf

Yohe, S., & Thyagarajan, B. Review of Clinical Next-Generation Sequencing. (2017). *Archives of pathology & laboratory medicine*, *141*(11), 1544–1557 https://doi.org/10.5858/arpa.2016-0501-RA

Zhang, T., Madeira, J., Lu, Y., Sun, Y., Mertes, H., Pennings, G., & Lindheim, S. R. (2019). Expanded Preconception Carrier Screening in Clinical Practice: Review of Technology, Guidelines, Implementation Challenges, and Ethical Quandaries. Clinical Pbstetrics and gynecology 62(2). DOI: doi: 10.1097/GRF.0000000000000437

# APPENDIX

## APPENDIX A. SURVEY

**Survey Instrument**

1. What is your profession? (Check all that apply)
   - ☐ Clinical Geneticist (MD)
   - ☐ Genetic Counsellor
   - ☐ PhD Geneticist
   - ☐ Obstetrician
   - ☐ Gynecologist
   - ☐ Midwife
   - ☐ Nurse practitioner
   - ☐ Other: _____

   If clinical geneticist or genetic counsellor:
   1b) In what area(s) of genetics do you primarily practice?
   - ☐ Prenatal
   - ☐ Cancer
   - ☐ Adult
   - ☐ Metabolic
   - ☐ Cardiology
   - ☐ Laboratory
   - ☐ Pediatric
   - ☐ Psychiatric/Neurogenetics
   - ☐ Newborn Screening
   - ☐ Other: _____

2. With which gender to you identify?
   - ☐ Male
   - ☐ Female
   - ☐ Non-binary

3. In what language(s) do you primarily practice? (Check all that apply)
   - ☐ English
   - ☐ French
   - ☐ Other (specify):_____

4. For how many years have you been working in your profession?
   - ☐ Less than 1 year
   - ☐ 1-4 years
   - ☐ 5-9 years
   - ☐ 10-14 years
   - ☐ 15-19 years
   - ☐ 20-24 years

- ☐ 25+ years
- ☐ I am not currently working in the genetics or maternity field

5. In which province/territory do you currently practice? (Check all that apply)
   - ☐ Alberta
   - ☐ British Columbia
   - ☐ Manitoba
   - ☐ New Brunswick
   - ☐ Newfoundland and Labrador
   - ☐ Northwest Territories
   - ☐ Nova Scotia
   - ☐ Nunavut
   - ☐ Ontario
   - ☐ Prince Edward Island
   - ☐ Quebec
   - ☐ Saskatchewan
   - ☐ Yukon

6. Which of the following best describes your role?
   - ☐ Direct patient care
   - ☐ Non-direct patient care
   - ☐ Mixed

7. In what type of institution do you practice? (Check all that apply)
   - ☐ Academic
   - ☐ Diagnostic laboratory
   - ☐ Hospital clinic/ university health sciences centre
   - ☐ Private clinic
   - ☐ Industry
   - ☐ Government agency
   - ☐ Other: _____

**Current Carrier Screening Guidelines**

The following questions will ask about targeted carrier screening, defined as a molecular, enzymatic or biochemical test used to confirm carrier status for a specific condition in individuals identified to be at increased risk due to family history of a specific condition or belonging to an ethnic group with known increased incidence of particular genetic condition(s).

The Joint Society of Obstetricians and Gynaecologists (SOGC) and the Canadian College of Medical Geneticists (CCMG) Opinion for Reproductive Genetic Carrier Screening Guidelines recommends offering targeted carrier screening in individuals of reproductive age who are identified as having an increased carrier risk of an inherited condition based on family history, ethnic background, or past medical/obstetrical history.

The Joint SOGC-CCMG guidelines make specific recommendations for targeted carrier testing for thalassemia/hemoglobinopathies, Fragile X, hemophilia A, cystic fibrosis, spinal muscular atrophy, as well as Ashkenazi Jewish and founder populations.

For full recommendations please see Wilson, D.R., De Bie, I., Armour, C.M. et al. 2016 doi:10.1016/j.jogc.2016.06.008.

8. In relation to these guidelines, the offering of provincially funded targeted carrier screening in your centre:
   - ☐ Is consistent with the SOGC guidelines
   - ☐ Is lesser than what is recommended by the SOGC guidelines
   - ☐ Is greater than what is recommended by the SOGC guidelines
   - ☐ Unsure

   COMMENTS:

9. Please describe in which circumstances targeted carrier testing is covered in your province? (ie: a certain disease frequency, where there is a provincial lab which tests for it, anyone with a family history of an AR condition). Feel free to cut/paste specific guidelines used at your institution.

10. When discussing carrier screening options with a patient, how often does the option of expanded carrier screening arise?
    - ☐ Every time
    - ☐ Most of the time
    - ☐ Occasionally
    - ☐ Never
    - ☐ Unsure
    - ☐ N/A

11. Do you have any comments about the above questions or this topic in general that you would like to share?

**Professional Opinions Surrounding Expanded Carrier Screening**

The following questions will ask you about your professional opinion regarding expanded carrier screening. Expanded carrier screening uses next generation sequencing to test an individual's carrier status for hundreds of genetic conditions.

Expanded carrier screening is distinct from direct-to-consumer testing in that it must be ordered by a physician and can provide diagnostic information.

The 2016 SOGC-CCMG guidelines recommend that expanded next generation sequencing screening panels should be discussed with the patient for a complete informed consent process.

12. In your opinion, as compared to targeted carrier screening, expanded carrier screening:
- ☐ Presents more advantages **for the patient**
- ☐ Presents more limitations **for the patient**
- ☐ Presents a balance of benefits and limitations **for the patient**

13. Do you think expanded carrier screening should be discussed as an option with each patient/ couple considering carrier screening (whether or not they qualify for provincially funded testing)?
- ☐ Yes
- ☐ No
- ☐ Unsure

14.Do you think provinces should cover the cost of expanded carrier screening? In which scenario?
- ☐ Yes – for all pregnant women
- ☐ Yes – for all pregnant women and women planning a pregnancy
- ☐ Yes – for some pregnant women in specific scenarios
- ☐ Yes – for some pregnant women and women planning a pregnancy in specific scenarios
- ☐ No

15. Do you foresee expanded carrier screening being routinely incorporated into your clinical practice?/clinical genetics
- ☐ Yes
- ☐ No
- ☐ Unsure

16. In your current practice region, which healthcare professionals are best suited to provide pre-test counselling (i.e. education about the risks/benefits/limitations and possible results) for expanded carrier screening **without** additional training and education? (Check all that apply)
- ☐ Clinical geneticist (MD)
- ☐ Genetic counsellor
- ☐ PhD geneticist
- ☐ Obstetrician
- ☐ Gynecologist
- ☐ Midwife
- ☐ Nurse practitioner
- ☐ Other (specify):

17. In your current practice region, **with additional training and education**, which professional(s) are better suited to provide pre-test counselling (i.e. education about the risks/benefits/limitations and possible results) for expanded carrier screening? (Check all that apply)
- ☐ Clinical Geneticist (MD)
- ☐ Genetic Counsellor

- ☐ PhD Geneticist
- ☐ Obstetrician
- ☐ Gynecologist
- ☐ Midwife
- ☐ Nurse practitioner
- ☐ Other (specify):

18. Patient pre-test counselling (education about the benefits, limitation and outcomes of this test) for expanded carrier screening can be accomplished through the following (check all that apply):

- ☐ Informational pamphlets
- ☐ Online video (i.e. YouTube)
- ☐ Website module
- ☐ Other (specify):

18.b) Do you have any comments about educational materials related to expanded carrier screening:

**The following questions relate to your professional experience with expanded carrier screening.**

19.Does your clinic/program have a policy regarding the discussion of expanded carrier screening for genetic testing with your patients?

- ☐ Yes
- ☐ No
- ☐ Uncertain

19. b) If **YES** to #19: Is it a formal policy or an unwritten understanding?

- ☐ Formal, written policy
- ☐ Informal agreement/unwritten understanding
- ☐ Unsure

19.c) If **YES** to #19: This policy:

- ☐ Permits discussion of expanded carrier screening
- ☐ Does not permit discussion of expanded carrier screening
- ☐ Unsure

19.d) If your clinic/ program permits discussion of expanded carrier screening, what are the situations when this discussion occurs: (Check all that apply)

- ☐ Permits discussion initiated by the provider
- ☐ Permits discussion only if initiated by the patient
- ☐ Discourages this discussion being initiated by the provider
- ☐ Comments regarding the details of this policy: _____

19. e) Do you agree with your institution's policy? Why?

- ☐ Yes
- ☐ No
- ☐ Unsure

20. When counselling a patient about carrier screening, I prefer to offer targeted carrier screening over expanded carrier screening. Why?

- ☐ Agree
- ☐ Neutral
- ☐ Disagree
- ☐ Unsure

COMMENTS:

21. Do you ever discuss expanded carrier screening options for genetic testing with patients?

- ☐ Yes
- ☐ No

21. b) If **YES** to #21: Approximately how often do these discussions arise?

- ☐ Weekly
- ☐ Monthly
- ☐ A few times a year
- ☐ Once a year
- ☐ Less than once a year

21. c) If **YES** to #21: Do you discuss expanded carrier screening as frequently as other private-pay tests (e.g. private-pay NIPT)

- ☐ Yes
- ☐ No
- ☐ Unsure

21. d) If **YES** to #21: When discussing expanded carrier screening I tend to: (Choose all that apply)

- ☐ Discuss both benefits and limitations of the test
- ☐ Focus on the limitation of the test (VUSs, carrier status for rare conditions, etc.)
- ☐ Discuss why expanded carrier screening is not relevant for the patient
- ☐ Discuss the benefits of expanded carrier screening
- ☐ Other: _____

21.e) If **YES** to #21: After discussion of expanded carrier screening, patients tend to proceed with the test:

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time (50/50)

- ☐ Some of the time but most choose not to proceed
- ☐ Never

21. f) If YES to #21: Does discussion of expanded carrier screening ever present any logistic or ethical challenges?

- ☐ Yes
- ☐ No
- ☐ Unsure

COMMENTS:

21. g) If **NO** to #21: Why is expanded carrier screening not discussed?

- ☐ It is not relevant to the patient (i.e. patient of non-reproductive age)
- ☐ Other carrier testing options are available
- ☐ I leave it up to other healthcare professionals/clinic subspecialties to discuss expanded carrier screening
- ☐ It does not come up during the appointment
- ☐ Other:

22. Compared to 5 years ago, is there a difference in how often you **offer and/or discuss** expanded carrier screening with patients (either patient initiated or health professional initiated)?

- ☐ Yes – Increase
- ☐ Yes– Decrease
- ☐ No difference
- ☐ Unsure

23. Compared to 5 years ago, is there a difference in how often you are **counselling** patients about their expanded carrier screening results?

- ☐ Yes – Increase
- ☐ Yes– Decrease
- ☐ No difference
- ☐ Unsure

24. Do you believe that expanded carrier screening uptake will increase in the future?

- ☐ Yes
- ☐ No
- ☐ Unsure

25. To your knowledge, which other health professionals in your region are offering expanded carrier screening?

- ☐ Clinical geneticist (MD)
- ☐ Genetic counsellor
- ☐ PhD geneticist
- ☐ Obstetrician
- ☐ Gynecologist
- ☐ Midwife
- ☐ Nurse practitioner

- ☐ Family physician
- ☐ No other health professionals are offering expanded carrier screening in my region
- ☐ Other (specify):

26. In your experience, what is the most common way patients access expanded carrier screening? Check all that apply.

- ☐ Clinical geneticist (MD)
- ☐ Genetic counsellor
- ☐ PhD geneticist
- ☐ Obstetrician
- ☐ Gynecologist
- ☐ Midwife
- ☐ Nurse practitioner
- ☐ Family physician
- ☐ Unsure
- ☐ Other (specify):

26. b) Do you have any concerns about non-genetic healthcare professionals offering expanded carrier testing?

- ☐ Yes
- ☐ No
- ☐ Unsure

Comments: _____

27. Do you have experience managing/counselling patients who are interested in or have received expanded carrier screening?

- ☐ Yes
- ☐ No

27. b) If **YES** to #28: Approximately how many cases have you managed/counselled?

- ☐ 1-2
- ☐ 3-4
- ☐ 5-6
- ☐ 7 or more

27. c) If **YES** to #28: Which components do you have experience counselling?

- ☐ Pre-test only
- ☐ Post-test only
- ☐ Both

27.d) If Y**ES** to #28: In what context?

- ☐ Preconception
- ☐ Prenatal
- ☐ Other: _____

28. Are you being asked to see patients who have positive expanded carrier screening results?

- ☐ Yes
- ☐ No

28. b) If **YES** to #28: In what context?
    - ☐ Preconception
    - ☐ Prenatal
    - ☐ Other: _____

Part of our research study includes conducting a 30-60 minute long telephone interview in order to further explore opinions and experiences with expanded carrier screening. If you are interested in participating in a telephone interview or have any questions about the telephone interview, we ask that you contact the student principal investigator (Dorothy Michalski) at xxx-xxx-xxxx or xxx@xx.xx.

## APPENDIX B: SEMI-STRUCURED INTERVIEW GUIDE

**Genetic and Maternity Health Professionals' Opinions of Expanded Carrier Screening**

1. Tell me about your role.
2. Do you ever see patients for carrier screening in your role?
    a. Thoughts on SOGC-CCMG guidelines for carrier screening
3. Have you ever counselled patients for expanded carrier screening?
    a. What was the scenario in which you were discussing ECS.
    b. Were there challenges? Logistic? Ethical?

4. Do you discuss ECS with your patients? In what situation?
    a. Why or why not?
    b. Any moral or ethical dilemmas related to discussing ECS?

5. Do you think expanded carrier screening might be preferable to more targeted approaches to carrier screening?
    a. What are some of the benefits/limitations of ECS? For the patient? For healthcare system?

6. Would you pursue ECS if in a preconception situation?
    a. Why or why not?

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 C. INTERVIEW CONSENT FORM

## RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

**Title of the study:** *Exploring expanded carrier screening in Canadian genetics services*

**Supervisor:** Claudia Carriles, MS, CGC, Certified Genetic Counsellor, Genomics, Diagnostic Services, Shared Health Manitoba.

**Student Principal Investigator:** Dorothy Michalski, MSc, Genetic Counselling Student, 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 professional opinions and experiences with expanded carrier screening in Canadian genetics services. This study defines expanded carrier screening as a genetic, next-generation sequencing test for an individual's carrier status for a number of genetic conditions regardless of ethnicity or family history. Please take your time to review this consent form and discuss any questions you may have with the study staff. Do not sign this consent form unless you understand the information in it and have had your questions answered to your satisfaction.

**Purpose of this Study:** Canadian genetic health professionals' and maternity care professionals' opinions and experiences with expanded carrier screening have yet to be explored in Canada. Canadian genetic and maternity health professionals may have opinions and experiences that are uniquely shaped by the Canadian healthcare system. In the future, the results from this study may contribute to the development of informed expanded carrier screening recommendations for Canadian practitioners.

**Participant Selection**: You are being asked to participate in this study because as a genetic or maternity health professional currently working in Canada your professional opinions and experience is valuable in exploring expanded carrier screening within the Canadian healthcare system. A total of 15-20 participants will take part in the study.

**Study procedures**

- The interview will be conducted over the phone by the student researcher.
- Participation in the study will consist of one interview session which will take up to one hour.
- During the interview, you will be asked questions relating to your thoughts, opinions and experience with expanded carrier screening.
- The sessions will be audio recorded and transcribed by either the student researcher 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 recording with anyone other than the researchers.
- Your name will not be revealed during the individual interview. If your name is

mentioned during the recording, it will be excluded from the transcription.
- The results of the study will be available to you upon request.

**Risks:** Participation in this study presents no more than minimal risk. Questions will pertain to your professional opinion and experience and are unlikely to evoke strong emotions. You do not have to answer any questions that make you feel uncomfortable or that you find too upsetting. Should you need any additional help or support we will refer you to counselling services or help you to find other counselling support in your province.

**Benefits:** Participation in this study will not provide any direct personal benefit. We hope that in the future, the professional opinions and experiences identified in this study can contribute to the development of informed expanded carrier screening recommendations in Canada which may benefit professional and personal practice.

**Costs:** There is no cost to you to participate, other than the time it takes to conduct the interview.

**Payment:** You will receive no payment or reimbursement for any expenses related to taking part in this study.
**Confidentiality:** All records containing identifying information, such as names, email addresses, or telephone numbers will be kept strictly confidential during the study. All study related documents and materials (including eligibility questionnaires, interview transcripts and audiotapes) will be kept in a locked filing cabinet or office located in the Department of Biochemistry and Medical Genetics or the Program of Genetics and Metabolism. Digital material and documents containing participant consent and contact information will be stored in a secure electronic document on a password secured University of Manitoba computer in a locked office. Any databases containing identifiers will be protected using a password known only to the Principal Student Investigator and supervisor.

Transcripts, interview notes, and audiotapes will be labeled with a coded ID number, which will be assigned to you upon enrollment into the study. If you are quoted or referred to in any written or oral reports of the study, you will be given an alternate name. You will never be referred to by your real name or any other identifying information in any written or oral reports based on the interview.

Written material will be destroyed (by shredding) seven years following the completion of the study in the fall of 2021. Digital materials (transcripts, demographic information and audio files) will be permanently deleted from the computer hard drive two years following the completion of the study in the fall of 2021.

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.

**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 Dorothy Michalski (Student Researcher) at xxx-xxx-xxxx or Claudia Carriles (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 xxx-xxx-xxxx.

**Consent Signatures:**

1. I have read all 3 pages of the consent form.
2. I have been given the opportunity to ask questions, which have been answered to my satisfaction.
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 participation is voluntary. I am free to discontinue or refuse to participate in this study at any time, and for any reason.
5. 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.
6. I understand that I may withdraw from the study at any time and my data may be withdrawn prior to publication.
7. I understand I am providing verbal consent to the researcher.
8. I understand I will be provided with a copy of the consent form for my records.
9. I agree to participate in the study.

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

**Participant phone number: _____**

**Relationship (if any) to study team members**: **_____**

**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**

**Student Researcher Name: _____Date _____**
**(day/month/year)**

**Student Researcher Signature: _____**

## APPENDIX D: 2020 PROFESSIONAL STATUS SURVEY DEMOGRAPHICS

| Demographics | % (n=245) |
|---|---|
| **Practice Area*** | |
| Prenatal | 31 |
| Preconception | 25 |
| Cancer | 45 |
| Pediatric | 25 |
| Adult | 35 |
| Metabolic | 9 |
| Laboratory | 12 |
| **Province** | |
| British Columbia | 19 |
| Alberta | 11 |
| Saskatchewan | 1 |
| Manitoba | 4 |
| Ontario | 48 |
| Quebec | 11 |
| Nova Scotia | 4 |
| Newfoundland & Labrador | 1 |
| Prince Edward Island | <1 |
| Yukon | <1 |
| **Years' Experience** | |
| <1 year | 18 |
| 1-4 years | 37 |
| 5-9 years | 18 |
| 10-14 years | 15 |
| 15-19 years | 6 |
| 20-24 years | 4 |
| 25+ years | 2 |
| **Work setting** | |
| Hospital clinic | 73 |
| Diagnostic lab | 11 |
| Private clinic | 5 |
| Academia | 6 |
| Other | 1 |

*Participants were able to choose more than one option; total adds up to greater than 100%.