

CADTH Health Technology Review

Genetic Carrier Screening for Cystic Fibrosis, Fragile X Syndrome, Hemoglobinopathies, and Spinal Muscular Atrophy

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Abbreviations

CF	cystic fibrosis
FXS	fragile X syndrome
GP	general practitioner
HbP	hemoglobinopathy
OB-GYN	obstetrician-gynecologist
SCD	sickle cell disease
SMA	spinal muscle atrophy

Key Messages

- People generally describe wanting access to carrier screening because knowing about the risk of passing along a genetic condition is considered important and supportive of their desires to be prepared. In the context of expanded carrier screening programs, this could mean that an increased number of people would want to access these programs.
- Supporting people who are considering carrier screening can be challenging and is likely to be more involved than simply sharing high-level descriptive information about testing details and potential outcomes. Descriptive information is important to help people understand the screening process and the types of results that could emerge from testing; however, programs might be more supportive of informed decision-making if the providers take a proactive role and are open to facilitating speculative conversations about potential ramifications in people's actual lives. This is challenging given the expressed desire by health care providers, clinical geneticists in particular, to provide "neutral information" that patients would not experience as prescriptive.
- Given the challenge of supporting people making decisions about whether or not to pursue carrier screening, and the likely increase in people who would consider carrier screening if targeted programs were expanded to population-level screening, it is important to ensure that health care providers are both aware of jurisdictional carrier screening programs and competent in what carrier screening can offer their patients in terms of clinical actionability. Although this is particularly true for general practitioners who are often the primary point of contact with the health care system for their patients, it is also important for people who work in family planning clinics and women's health clinics.
- Having the option to engage with carrier screening at the preconception stage was universally preferred by participants across the included studies. Compared with prenatal carrier screening, preconception carrier screening was seen as providing prospective parents with more reproductive options. Health care providers were concerned that offering carrier screening during pregnancy might lead pregnant people and their partners to confuse it with other prenatal testing which would limit people's ability to be truly informed before deciding whether or not to pursue screening. However, if offered as a prenatal option, most people consider it important to do so as early as possible because it could be paired with other prenatal tests. Although not referred to specifically by any of the included studies, we note that offering carrier screening prenatally rather than at preconception, could place the responsibility to make the decision on cisgender women and non-binary or transgender people with uteruses.
- Sequentially designed carrier screening programs were the most common across the included studies; however, people moving through programs with this design found the interim period between receiving their positive carrier results and receiving their partners' results difficult. This was particularly true for people who were already pregnant because this interim period forced them to reimagine both their relationship with the fetus and the future they had imagined with that child. Of course, this reimagining might be necessary if both partners' screening results came back positive for the condition in question, but to stagger the return of the results could put undue anxiety on potential parents.
- Carrier screening will not affect everyone in the same way, and reproductive decision-making will still be complex and difficult. As such, the opportunity to engage with genetic counsellors on reproductive options following positive carrier status result is considered valuable.

Context and Policy Issues

Since their emergence in the 1970s, carrier screening programs have offered people the opportunity to learn about the likelihood of passing along inheritable autosomal or X-linked conditions to their children.¹ Given its focus on inheritable genetic conditions, a primary aim of carrier screening is to support people considering pregnancy, or who are already pregnant, make informed reproductive decisions.^{1,2} Although this is closely related to newborn screening or prenatal genetic testing of the fetus, carrier screening is focused on screening the reproductive partners rather than the fetus or child.

Historically, carrier screening programs have been oriented toward identifying the presence of gene mutations for specific conditions within deliberately targeted populations. Target populations have been identified on the grounds of both ethnicity and family history with the condition of interest. Conditions commonly screened for based on ethnicity include 2 hemoglobinopathies (HbPs) among people of African, Mediterranean, Middle Eastern, or Asian descent (i.e., sickle cell disease [SCD] and thalassemia) and cystic fibrosis (CF) among people of European descent.³ One of the earliest ethnicity-based, targeted carrier screening programs in North America was introduced by the Black Panthers in 1971 and focused on screening Black Americans for SCD.⁴ This was originally intended as an act of Black empowerment meant to force the US government to fund further research on effective treatments for a condition of particular relevance to Black lives in the US,⁴ historical and ongoing anti-Black racism in North America has meant that policy and practice around SCD genetic testing has instead been “disempowering and potentially disabling and racist (p. 185).”⁵

One of the proposed solutions to the potentially stigmatizing and discriminatory effect of targeted, ethnicity-based carrier screening has been the development and implementation of expanded testing panels provided at a population-based level.¹ Expanded carrier testing is not proposed simply as an attempt to limit the stigmatizing effects of some targeted screening programs; it has also been promoted as being more cost-effective than single-disease, hereditary, or ethnicity-based testing, and more commonly as “maximizing the opportunity for couples to make autonomous reproductive decisions.”¹ The Society of Obstetricians and Gynaecologists of Canada (SOGC) and Canadian College of Medical Geneticists (CCGM) jointly recommend that all people considering pregnancy (or who are already pregnant) should be offered the opportunity to discuss the value and risks of genetic carrier screening; however, only those who are known to be at an elevated risk of carrying genetic conditions such as CF, fragile X syndrome (FXS), spinal muscle atrophy (SMA), or HbPs are recommended for screening.⁶

The purpose of this review is to support policy-makers faced with a decision of whether to expand current targeted carrier screening programming beyond these recommendations to population-based programming. Our aim is to provide a better understanding of how people considering pregnancy (or who are already pregnant), and the health care providers working with them, might engage with carrier screening programs or tests. Given that the expansion in question would involve people who do not currently have a known elevated risk of being a carrier for the condition being screened for (e.g., through family history or ethnicity), we have paid particular attention to the early stages involved in making an “informed decision” of whether or not to pursue screening. Although we focused particularly on carrier screening for CF, HbPs such as thalassemia or SCD, FXS, and SMA, we also included with literature focused on expanded carrier screening programs more broadly.

Research Question

- What are the expectations, experiences, and perspectives on preconception and prenatal genetic carrier testing programs and tests for cystic fibrosis, fragile X syndrome, hemoglobinopathies, and spinal muscular atrophy of adults and their reproductive partners, related family members, and health care providers, in terms of:
 - accessing and deciding to undergo or offer testing
 - the process of testing, including the communication, interpretation, and use of test results
 - affecting people's reproductive decision-making?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, CINAHL, Scopus, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were preconception care, genetic testing, and genetic carrier screening. Search filters were applied to limit retrieval to qualitative studies. When possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2016, and April 29, 2021.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, were duplicate publications, or were published before 2016.

Critical Appraisal of Individual Studies

The critical appraisal was conducted by the primary reviewer who followed Krefting's⁷ approach for assessing trustworthiness in qualitative research. The trustworthiness of the study results was evaluated by asking questions about how the research methods shaped how the research team arrived at their findings or results. This was done with a particular focus on 4 guiding questions⁷:

- Were the study authors true to their participants (credibility)?
- Does the analysis make sense in light of the data presented (confirmability)?

- Is the analysis consistent across study findings (dependability)?
- Is the analysis relevant to the research question of this review (transferability)?

Results of the critical appraisal were used to understand the methodological and conceptual limitations of the included publications specifically in relation to the research questions.

Data Analysis

A “rapid best-fit” framework synthesis approach⁸ was used to analyze data relating to the expectations of, experiences with, and perspectives on preconception and prenatal genetic carrier screening of adults and their reproductive partners, related family members, and health care providers. The rapid best-fit framework synthesis is an adapted framework synthesis approach to accommodate reviews under time constraints.⁸ The traditional framework synthesis approach draws on existing relevant models or theories to guide data extraction and analysis.⁹ The rapid best-fit approach allows using the review objectives as guiding principles to develop an initial framework to categorize and interpret the findings from the included studies.⁸ We developed our initial framework based on 3 sensitizing categories drawn from our research question:

- accessing and deciding to undergo or offer testing
- the process of testing, including the communication, interpretation, and use of test results
- how testing affects people’s reproductive decision-making.

The primary reviewer conducted the analysis, accompanied by a joint focused dialogue with a second reviewer. The analysis followed a staged analytical process passing through 3 stages: familiarization with the included literature and development of the initial framework, a deductive extraction and analysis of the data informed by the initial framework, and the

Table 1: Selection Criteria

Criteria	Description
Sample	Adults and their reproductive partners engaging with preconception and prenatal carrier screening testing programs and tests and their related family members Health care providers who order, interpret, and consult people on the use of preconception and prenatal carrier screening tests or are part of a testing program (e.g., family physicians, geneticists, genetic counsellors)
Phenomenon of interest	Expectations and experiences of preconception and prenatal genetic carrier screening testing programs and tests (including single genes tests for conditions of interest and panel tests that include a condition of interest and other condition) for cystic fibrosis, fragile X syndrome, hemoglobinopathies, and spinal muscular atrophy
Design	Any qualitative design
Evaluation	Expectations and experiences of access to genetic carrier testing program and tests; pretest counselling and process of informed consent; decision-making around undergoing (or not) testing; understandings and expectations of testing and the value of test results; experiences of the process of testing and in communicating, interpreting, and using test results; impact of test results on peoples’ reproductive decision-making; disclosure and communication of test results to family members; health inequalities and the experiences of racialized persons related to genetic carrier screening
Research type	Primary qualitative studies; qualitative component of mixed-methods studies (excluding surveys)

refinement of the framework to reflect inductively identified content and relationships among data and themes.

First, the primary reviewer began by reading and rereading eligible studies multiple times. Throughout this stage, the primary reviewer made marginal notes on electronic copies of the included publications that reflected preliminary thoughts and impressions about how key findings could be mapped onto the framework. During this preliminary stage, the primary reviewer also built the initial framework in a memo document using Microsoft Word. The reviewer then extracted the data from the included studies directly into the Word document. As the memo document filled up with more data and the primary reviewer began noticing more connections within the primary data, the first and second reviewers were able to identify and add subcategories to the larger framework.

These connections formed the basis of an outline of descriptive themes and served as a skeleton for the final synthesis. Drawing on the primary reviewer's growing familiarity with the dataset as built through iterative readings, this outline was expanded and developed by returning to the primary reviewer's memos and the original papers. Conversations with and reviews of written preliminary findings by the second reviewer helped focus and draw out the analysis and articulate connections within the data and across themes and refine the framework.

Summary of Included Literature

Quantity of Research Available

A total of 1,257 citations were identified in the literature search. Following screening of titles and abstracts, 1,230 citations were excluded and 27 potentially relevant reports from the electronic search were retrieved for full-text review. No potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 16 publications were excluded for various reasons, and 11 publications met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)¹⁰ flow chart of the study selection.

Summary of Study Characteristics

Additional details regarding the characteristics of included publications and their participants are provided in Appendix 2.

Study Design, Data Collection, and Method of Analysis

Eleven publications representing 10 studies were included in this review. One publication described using a mixed-methods study design but did not describe the design used for the qualitative component.¹¹ Of the 10 remaining primary qualitative publications, 2 were described as using a grounded theory approach,^{12,13} 1 was described as following a narrative approach,¹⁴ and the remaining 7 did not describe a study design or approach.¹⁵⁻²¹

Of the 10 primary qualitative publications, 8 used interviews to collect data,^{12,14-20} 1 used both interviews and focus groups,¹³ and 1 used focus groups only.²¹ The qualitative portion of the mixed-methods study used interviews to collect data.¹¹

Four primary qualitative publications representing 3 studies described using content analysis,^{16,18-20} 4 publications described using thematic analysis,^{13,15,17,21} 1 publication described using narrative analysis,¹⁴ and the qualitative portion of the mixed-methods study used content analysis.¹¹ One study described using grounded theory as a mode of data analysis.¹²

Location of Study

Of the 11 publications, 3 each were conducted in the US^{11,20,21} and Australia,¹³⁻¹⁵ 2 each in the Netherlands^{16,17} and Belgium,^{18,19} and 1 in the UK.²²

Study Participants

Of the 10 studies composed of 11 publications, 8 included 135 people identified as women who were participating in interviews or focus groups without their reproductive partners.^{11-14,16,17,20,21} Another 66 people making up 33 male/female couples participated together in 2 studies.^{11,15} A further 36 participants were identified as members of the general public in 1 study.¹³ No people identified either as male or men, currently pregnant, or considering pregnancy participated without their reproductive partners.

Across 2 studies involving 3 publications, there were 97 health care providers, including a range of clinical and molecular geneticists, obstetrician-gynecologists (OB-GYNs), and general practitioners (GPs).^{13,18,19}

Summary of Critical Appraisal

The publications included in this review were assessed to be of a moderate to high degree of trustworthiness overall.

The majority of the studies presented a moderate degree of trustworthiness because they had limited transferability.^{17-19,21} This limited transferability was not so much a shortcoming of the results themselves but rather these studies focused on expanded carrier screening rather than the targeted screening for CF, SMA, hemoglobinopathies, or FXS, the focus of this rapid review. Although most studies maintained a high degree of credibility, confirmability, and dependability, it was sometimes difficult to know if participant comments or concerns would translate to the conditions of interest in this review.

The 1 study identified as of moderate trustworthiness¹⁶ was placed in this category because of the limited amount of time the study authors spent with study participants. This study was identified as an interview study and had a robust presentation of primary data; however, it was concerning that the average time spent interviewing the participants was 14 minutes. Although this did not affect how often we used this study, it did affect its credibility and our engagement with the study findings.

Three studies stood out as of particularly low trustworthiness overall and have been used with limitation throughout the review. Two^{11,20} were graded as low primarily because of the limited presence of data to support the authors' analyses. Although this may be a result of pressures to meet journal word limits that prevent authors from fully elaborating the connections between data and analysis in the text, their confirmability (i.e., whether an analysis makes sense in light of the presented data) was difficult to assess. The links

between data and analysis were clear at times, although this was not consistent across the entirety of either publication. For these reasons, both publications were considered to be of moderate credibility. The third¹⁵ was categorized of low trustworthiness because there seemed to be a mismatch between the articulated intent of the study and the presentation of study findings. Although this study was meant to explore the acceptability and perceived utility of carrier screening among consanguineous couples, the presentation of data and analysis seemed much more oriented toward making consanguineous coupling strange and providing genetic reasons for this.

Results

Accessing and Deciding to Undergo or Offer Testing

The Right to Know and Be Prepared

Most study participants felt that having access to carrier screening was important for people who are either considering pregnancy or who are already pregnant.^{13,14,16,18-21} Having the opportunity to know one's carrier status and the potential risk of passing along a genetic condition to their child was considered supportive of their desires to be prepared and make autonomous reproductive decisions.^{13,14,16,18-21} Some people thought access to carrier screening qualified as a "right." Courtney, who had been identified as a carrier of CF through a targeted screening program, felt this access was included within "a woman or a couple's *right* to find out this information [about their carrier status]...people should be informed and have the choice (p. 2056, our emphasis)."¹⁴

People viewed the right to know as part of the expectational script of carrier screening – that is, the necessity (the "should") of becoming informed, of knowing ahead, and of being prepared. Courtney was not alone in this sentiment. Although other study participants may not have put that pressure "to know" or "to become informed" on all prospective parents, this pressure or desire existed for themselves was evident. One pregnant woman who had been offered (and accepted) targeted, ethnicity-based HbP carrier screening felt that "it's good that at least you have the choice if you want to know it. And, for myself, I'm kind of a control freak, and, yeah, I can imagine that it would be nice if you know in advance (p. 638)."¹⁶ Knowing in advance could, for this woman and some others,²¹ fulfill a need to have some control.

However, one does not have control over individual gene mutations or whether one is a carrier of some genetically inherited condition. In the context of carrier screening, people described control and its assertion as coming directly through reproductive decision-making. Another pregnant woman who had been offered (and accepted) targeted, ethnicity-based HbP carrier screening clearly articulated this movement from a desire for control to imagining how that control becomes asserted (or could be asserted) by noting that having that foreknowledge of carrier status is "...only a good, right? Probably it's not the case [being a carrier], the chances are really small, at least that is what the midwife told us. But when you have that knowledge, you can make a better decision (p. 639)."¹⁶ Knowing in advance might offer a sense of control and put one in the position of making a "better decision."

This idea of being in the position to make a better decision feeds into what made carrier screening so desirable for many study participants – preparation.^{11,14,20,21} What this preparation, or expectation for preparation, looked like differed based on previous life experiences. However, the underlying common idea was that this knowledge would become actionable. To some women who lived through past difficult pregnancies or had previous miscarriages, the offer or availability of carrier screening was imagined as allowing them

to look at, and become prepared for, their current (or future) pregnancy a bit differently by (hopefully) coming to know what might have affected that previous pregnancy.^{14,16}

For others, like Maria, who had been identified as a carrier of FXS through targeted carrier screening, the desire to become prepared through carrier screening stemmed from previous experiences with family members living with various, potentially unrelated, conditions. Maria described being “happy to participate” in carrier screening because “my partner’s cousin has a mental disability [so] we wanted to make sure we weren’t carrying anything... (p. 2055)”¹⁴ Preparation was becoming “sure we weren’t carrying anything” so that they could, perhaps, ensure they were only carrying a healthy child.

Genetic carrier screening was also described as having the added benefit of becoming prepared to live in a family, defined as a long-lasting couple with healthy children. Gulsen tied the importance of learning one’s carrier status to the foundation of what qualified as family and wanted to know how carrier screening might work within the context of possible consanguineous marriages. For her, children were central to marriage, and carrier screening could help identify potential partners who would be able to have healthy children. Not having children was out of the question if both potential partners were found to be carriers of the same mutation because “you want to feel like a family (p. 6).”¹⁷ In this case, to feel like a family is to have children — healthy children — in a long-lasting relationship. When timed appropriately, carrier screening can help identify with whom one is more likely to have healthy children to prepare to feel like a family.

Finally, in a few instances, some participants showed less interest in carrier screening, giving reasons such as the offer came too late (i.e., during pregnancies in which abortion was not an option),^{15,21} feeling as though the knowledge gained through screening was not likely to offer anything actionable,^{16,21} or not feeling that they were at risk of having an affected child.¹⁶

These are some of the ways in which participants across the included studies conceptualized the meaning of having access to carrier screening — and the types of expectations that could be included within those conceptualizations — and we have identified 3 key dimensions of access to carrier screening. First, people generally want access to carrier screening, although with a few exceptions. Second, for those who wanted access, this was often described as combined with the desire to “know ahead of time.” For these people, knowing their own carrier status was considered an indiscriminate good because it could help put them in the position to make a better decision. This was closely tied to the third point that being in a position to make a “better decision” meant being prepared. Carrier screening was expected to have fallout, but that fallout was also possible without screening, so “he and I would want to know... even if I couldn’t prevent it from happening...so we could be as prepared to deal with it as possible (p. 139).”²¹

Providing Information to People Eligible for Carrier Screening

Participants generally felt that people who were offered screening needed to be provided with information and the opportunity to make an informed decision about whether to proceed with screening or not.^{13,14,18,19} As a woman who had been offered FXS carrier screening put it, “... it would be really important to fully educate [people] so that they know exactly what they’re dealing with...[and] all the possible implications... (p. 163).”¹³

For some, this education began outside the clinical encounter — even as early as high school.¹³ This was front of mind for geneticists reflecting on population-level carrier screening programs and the importance of providing the public with “neutral information” about the

presence of carrier screening as an option. As a clinical geneticist noted, “If you are going to offer it, there must be some public campaign, saying that it’s there, but...if you are making a very big campaign, then people would think ‘Oh, I should do that, because otherwise I’m stupid and it’s my own choice to have a baby with a handicap.’ And that’s not the message I want to bring across (p. 4).”¹⁹

This view is connected with another clinical geneticist’s concern with combatting direct-to-consumer marketing in expanded carrier screening. Direct-to-consumer marketing was seen as placing too much responsibility for having a healthy child on the prospective parents. Pointing out the language from a private company, this geneticist noted that it “is just awful. It’s like ‘who doesn’t want to prevent the birth of a child with a genetic disease?’ And ‘it’s your responsibility.’ And it’s a very coercive way of informing the people (p. 4).”¹⁹ Too overt messaging about the presence and importance of carrier screening will diminish people’s freedom to choose on their own terms. Too little messaging, and no one will access the program.

One way considered by health care providers to be both informative and avoid the risk of being too prescriptive when presenting carrier screening as an option was to build distance and time between the presentation of information on carrier screening and the patient’s decision about whether to undergo carrier screening.^{18,19} Their solution included using leaflets and online educational resources as tools for providing factual, but not leading, information to those considering carrier screening. As a clinical geneticist put it: “I could well imagine a system where you have a written leaflet and a very well, carefully constructed YouTube 5- to 10-minute educational video clip that people will be asked to access before testing... It’s [important] that people have leaflets, something web-based educational, information-giving resource (p. 4).”¹⁹

GPs are often people’s primary point of contact with the health care system, and they were seen as having a pivotal role (particularly during preconception) to play in informing their patients of the availability of carrier screening.^{13,18} Geneticists in particular noted how important it was for GPs or other nongenetic health care professionals to be well-informed on program offerings and be competent and confident in their ability to walk through the features and potential outcomes of carrier screening with their patients.¹⁸

Making the Decision to Proceed With Screening or Not

Even with the effort of providing educational resources and tools, some health care providers were still concerned that people undergoing carrier screening might consider it routine pregnancy testing and not fully understand the implications of carrier screening.¹³ What qualified as an “informed choice” was called into question. One OB-GYN put it this way: “... [informed decision-making is] a great theory, and in practice it doesn’t happen, and Down syndrome is a classic example of that... I get women all the time who say, ‘My GP (general practitioner) told me to have this test’...they often have no concept of what the test actually is...haven’t thought through any of those issues...people will end up making uninformed choices... (p. 165).”¹³ The concern is that people who have been referred to (and accepted) carrier screening may not truly understand the implications of their decisions based on a single conversation with their GP, and that physicians may suggest screening tests as part of routine clinical care without more fully informing their patients on the ongoing process of managing carrier status results.

It is possible that some people engaged with carrier screening may be unsure about its purpose and sometimes equate it to other prenatal tests, as was demonstrated by some

study participants.²⁰ However, even when people understand the purpose of screening, they may not accept its value and choose to undergo testing simply because it is available to them. As a woman who had been offered screening for HbP based on her ethnicity and had originally refused but later changed her mind put it: “Actually, it doesn’t say anything, so basically, what do you really know in the end? So, in that case I don’t want to test. But why shouldn’t I do it as I’m already having my blood drawn for another test anyway (p. 639).”¹⁶

This woman considered herself well-informed and originally decided to refuse screening. Yet, offering carrier screening at a time when other prenatal tests were occurring made it difficult to follow through with that refusal. Informed decision-making is about making an informed choice; that is, the ability to give informed consent and to give informed refusal. The convenience of directly accessing carrier screening through other screening tests can be experienced as pressure to consent even if one does not think it has value. Not only could an informed refusal be difficult for those contemplating testing (particularly for people who might already be pregnant), it could also be challenging for them to determine whether making informed decisions is truly just about having the right amount of information.

That this woman had tied her decision to undergo screening directly to the ease of looping it in with other (routine) prenatal tests might have implied to our OB-GYN that there was a risk that she had ultimately made an uninformed decision because of the offer of carrier screening in proximity to other (routine) prenatal tests. Although there were no more details about this woman’s decision, we see this woman’s “why shouldn’t I?” as a way of relating to a possible future in which something *might* come of screening.¹⁶ There is a potential at play in her “why shouldn’t I?” that cannot be known in advance but must, instead, be understood as a part of an unfolding process.¹⁶

Georgia, who had been identified as a carrier of FXS through a population-based, targeted screening program (looking for CF, SMA, and FXS mutations specifically), helped unpack this further. Although she described receiving “everything that I needed” to make the best decision, she and her partner “didn’t really feel the need to get down into a level of detail about each of the conditions because we couldn’t really relate and didn’t really think there was going to be...a large chance of us having to deal with that...” (p. 2054).¹⁴ In other words, Georgia and her partner expected to pass the test unscathed – to come out on the other end without “having to deal with that.”¹⁴ Given that neither she nor her partner were known to have an elevated risk of carrying any of the conditions being screened for, this expectation was not unfounded, and they could comfortably make their decision without intensive details about the potential conditions because they “couldn’t really relate” to them anyway. Nonetheless, they chose to pursue screening.

As previously illustrated, people connect their desires to know their carrier status to hopes of becoming prepared to live their best (reproductive) life, so accepting carrier screening in the context of other prenatal (routine) tests can be expected. Yet, people contemplating carrier screening seem to struggle to “really relate” to the conditions being screened for.¹⁴ This, as we understand it, is a crucial point of decision-making around potential carrier screening and the ramifications of undergoing (or not) that screening. Aameena and Sadeed, who had been identified as carriers of thalassemia through a publicly provided, HbP-targeted prenatal carrier screening program in the UK, described a similar experience of not being able to “really relate.” They decided not to undergo further prenatal diagnostic testing when they found out they were carriers of thalassemia. At the point of the interview, they had 4 children, at least 2 of which were carriers of thalassemia (first 2) and another had thalassemia. Here is how

Ameena described their early engagement with their own carrier status and the challenge of “relating” to what it might mean outside of themselves:

I’ll be honest, you know when I got pregnant and they were saying, “You’re a carrier, and he’s [Sadeed, husband] a carrier and you might have a chance of having a major” [affected child], at that point in time I just didn’t realise how severe it was or how it would affect me or my child, you know. I just fobbed it off like, “oh you know, they say a lot of things...” and I didn’t think much of it... And then my first two [children] were carriers, so I was like, “oh it’s okay, you know, so like...” and then he [Taysir, third child] turned out to be the major. And they told us when he was little... And even then it didn’t sort of click to me and I thought, you know, okay, because I’d never read about it, I didn’t know exactly what it was, I’d never seen anybody with thalassemia, I didn’t even know it ran in the families at all. Because some of them were abroad and I wasn’t too much in contact with my dad, so I didn’t know much about it. And then they did a blood test about two months old and they said he’s really low in iron, we need to do his first blood transfusion, and I cried my eyes out. And that’s when it hit me, yeah,...that there’s something severely wrong here (p. 148).¹²

To relate to the reality of what their status as carriers of thalassemia could mean for their family, Ameena and Sadeed needed 2 children who carried the condition and a third who was affected by it. Only then did the severity of what living with thalassemia could mean “hit” them.¹² Only then could they relate to the condition that was screened for so many years earlier.

These reflections from Ameena, Georgia, and the unnamed woman share a need to understand that “becoming informed” and making decisions about carrier screening is something that is always in process. During this process, there are moments in which decisions to proceed with screening (or not) are made and become concrete actions that are taken. Yet thinking that these decisions are absolutely right or absolutely wrong (informed or not) would set up a false binary that assumes these decisions happen in a vacuum. We find this particularly well noted in a woman’s explanation for why she chose to accept the offer for carrier screening: “At this moment, I’ll just see what happens, and we do this test, and it turns out that I’m a carrier, then I would like to proceed with other tests of course. In the end, it’s all about my little one (p. 640).”¹⁶ For this woman, her decision to undergo carrier screening was explicitly couched within an ongoing process of “just see[ing] what happens.”¹⁶ For those contemplating testing, this decision is neither right nor wrong (informed or not), but rather oriented toward allowing them the ability to relate to the condition being screened for to unfold through time, and to unfold around their “little one[s].”¹⁶

Therefore, becoming informed is not just about having comprehensive information on carrier screening and its potential consequences, but also having facilitated deliberations that help people think through the sorts of potential ramifications involved with this particular decision. The focus is not just on the knowledge that carrier screening can provide, but also on the types of decisions it implies once results come back. This puts more responsibility on health care providers than simply sharing leaflets with their patients¹⁹ or hoping they have thought through “any of those issues” that might emerge from screening on their own.¹⁴ Instead, allowing their patients to change how they might relate to the conditions being screened for while centring on their potential (or existing) fetus might involve more deliberative thinking than refined information sharing. One woman who had been offered screening sums this up well:

It'd be good to speak to someone that could tell you, "Look this is a bit about it, these are the potential issues. Are you prepared to have the test? Because if you do carry this particular gene, you need to think about these other issues. Are you ready to perhaps know about that? Do you want time to think about it, or perhaps go away and discuss it with your partner, or to think about how you'll cope with the results if they come back adverse to what you were hoping?" (p. 165).¹³

How one relates to the information given was described as affecting peoples' decisions to proceed (or not) with carrier screening, but this was not the sole factor affecting decision-making. As shown in the following section, how one proceeds through carrier screening due to things like the form of program (e.g., targeted ethnicity based or broad population based), who it is offered to, and at what time points it is offered can similarly affect people's experiences with carrier screening.

The Process of Testing, Including the Communication, Interpretation, and Use of Test Results

What is the Program and Who Can Access It?

The process of undergoing carrier screening and the related experiences with carrier screening are closely tied to the way screening programs are structured and offered (e.g., targeted ethnicity based or broad population based). For this review, while not always explicitly explored by study participants, there were a few different ways that people could engage with carrier screening. The majority of our studies focused on population-based expanded carrier screening^{11,15,17-21}; however, a few were population-based but only for specific conditions¹²⁻¹⁴ and 1 was ancestry-based and targeted for specific conditions.¹⁶ For those studies that described how people might be screened and in what order, they were predominately sequential with female partners being screened first and then, if they were found to be carrying a genetic mutation of interest, their male reproductive partner would be screened.^{11,14,16,20,21}

This sequential process affected how people experienced carrier screening and the timing of the offer. Among studies investigating when carrier screening could be offered, there was a general consensus among participants that, when possible, it was desirable to have that offer at preconception.^{13,14,16-19,21} Although offering preconception screening to people could be tricky given that people do not always seek medical care for family planning (e.g., sometimes pregnancies just happen), the idea is that there are more reproductive options available at this time.^{13,16,19} Given this trickiness, some people suggested that it would be possible to offer screening at the same time as other checkups with one's primary care provider.¹³ For FXS in particular, some health care professionals suggested that screening could be offered to females at the same time as other relevant interventions such as contraception and Pap smears. It was thought that people coming in for these interventions would already be focused on "thinking about 'my health'... And so, I think you piggy-back it at a good time when they're already a captive audience about good health, I think that's perfect (p. 166)."¹³

This does not mean that people who are already pregnant should not be offered carrier screening, just that a positive carrier status might lead to different types of fallout at this stage.^{13,14,16,19} Additionally, once people are pregnant and need to pay attention to other routine prenatal tests, some may find it overwhelming to add carrier screening to the mix.^{16,21} However, if already pregnant, people consider it helpful to be offered screening at a regularly scheduled appointments.^{14,16,21}

A geneticist went so far as to say that by the time “you have a pregnancy it’s too late (p. 3)”¹⁹; however, most other participants did not describe feeling it was too late even if it made the screening process more anxiety provoking than it might have been at preconception. As Chloe, who was identified as a carrier of CF while pregnant, put it: “It definitely made it more stressful for us because we were already pregnant...had we had the test done...a year ago...I think we still probably would have gone through similar emotions but not with the same gravity... (p. 2057).”¹⁴ Although the feeling of being a carrier might have been the same had she been identified at preconception, the gravity once there was already a fetus involved made it and the attached decision of what to do much more stressful. This could particularly be the case for pregnant people undergoing a sequential screening process.¹⁴

With these timing challenges, people, particularly geneticists, also commented on who should be screened and for what purpose.^{18,19} Although there was general agreement that carrier screening programs, at least those that are publicly provided, should be reserved for couples considering pregnancy or who are already pregnant, some people indicated there could be some value in offering screening to single individuals as well given this information might help other family members learn about their own status. However, geneticists included in this review were committed to the idea that “the goal of screening is to find carrier couples. It’s not interesting to find individual carriers because this doesn’t have any consequences. Any medical consequences (p. 3).”¹⁹ The utility or importance of carrier screening for clinical geneticists is its clinical actionability.

There also could be other goals of carrier screening. As another geneticist noted, it is possible that an individual may want to undergo carrier screening even if their partner does not because it may be useful to other family members considering having children or, if already pregnant, they may no longer be with that partner.^{16,18,19} For example, a pregnant woman who was no longer with the father of her unborn child indicated that if she could undergo screening without him, “I would choose to do that, as long as it’s not too complicated (p. 640).”¹⁶ While uncertain if undergoing screening alone was an option for the carrier screening program she was offered, this was desirable as it might still offer some information as to the risks her child might carry.

There were also discussions about whether test results should be separated out by partner and returned even if only one member carried the genetic variant or if they should return results of genetic variants both partners carry as only these are actionable. For example, the majority of geneticists included in the studies by Janssens et al.^{18,19} felt that it was important to return individual results – even if they had previously objected to screening individuals alone. One of the ways this was rationalized was by noting how common it is for people to change reproductive partners throughout life.

This was not supported by all geneticists involved in this study as at least 1 argued that:

If you are trying to set up a public health exercise and to identify couples at increased risk of a child with a severe recessive condition, then you should stick to that [goal] and not communicate things that are not [relevant] to that ... [You should] make it very clear that even if they say, “I want my individual results,” that’s not something...that you feel is justified in your public health exercise. If your aim is something else altogether, then you might say differently (p. 5).¹⁹

In the following section, we will further draw out how sequential program design might affect experiences with carrier screening – particularly those who already pregnant.

Surprise at “My Own” Status and Anxiety Throughout Partners’ Testing

Given that the majority of study participants were offered screening as part of a population-based program rather than a targeted program based on family history or ethnicity, people often expressed surprise at being identified as carriers of some condition.^{14,20} As Julia, a woman who had been identified as a carrier of SMA, put it, “Neither of us had any sort of family history or anything that would have indicated there could have been a problem. I guess I was a bit shocked actually, at the time [of receiving the result]... (p. 2055).”¹⁴

Paired with this shock was now the question of what to do. As discussed previously, it is possible that people make their decision about carrier screening with a sense of ambivalence and the expectation, as Georgia put it, that nothing would be found. Although this question of what to do could be challenging for all prospective parents regardless of program design, it could be particularly so for those undergoing screening as part of a sequential program.

Between the shock of receiving a positive carrier status result and the reception of a partners’ carrier status result, there seems to be a sort of temporal effect at play for these sequential programs.^{11,14} For example, Karen, who had just been identified as a carrier of SMA, called herself a “doer” and described how thankful she was for the speed with which the genetic counsellor set up her partners’ screening because “it would have been a long night had [they] said I can’t test your husband until next week (p. 2055).”¹⁴ This person described anxiety building up if they were not able to be tested right away.

Not only might this temporal effect lead to serious anxiety and restlessness, but it could also, for those who are already pregnant, disrupt the growing relationship between pregnant person and the fetus they are carrying. Grace, who was also identified as a carrier of SMA, had previously terminated a pregnancy due to fetal abnormality and this period of waiting for her partners’ results required a sort of pivot in which she “...tried to not even think that I was pregnant for that week ‘cos I tried to get myself mentally prepared for going through what I went through last year...just to make it easier on myself... I was trying to...not even think about the baby as much and not to talk about it as much in that week... (p. 2055).”¹⁴ For Grace, the period between the return of her own test results and those of her partner involved passing in and out of different time frames, including “what she went through last year” to protect herself from what she might be going through under these new circumstances.

Georgia, who we have already met and was identified as a carrier of FXS, could relate to not wanting to imagine a future: “At this stage, I was viewing this pregnancy as temporary, like a temporarily maybe kind of thing, I didn’t want to commit to the pregnancy...like I didn’t want to look [at] any baby clothes, I didn’t want to start planning for the future, or like planning too seriously for this baby because I didn’t know whether or not we were going to have it... (p. 2055).”¹⁴

Sally, who had been identified as a carrier of CF, said something similar about this interim period, but with slight nuance. Grace and Georgia both described their response during this time as a way of not “thinking” about or “committing” to the pregnancy, but Sally pointed toward the already existing attachment between her, her partner, and the fetus. At that point, it was too late, as the geneticist might have said, because the future had already been imagined: “It was scary to get a [carrier] result because then we had to...have the discussion of, well, what happens if my husband came up positive and we would then decide what to do, that was obviously really scary to...have to consider abortion... I was well and truly attached and so the thought of having to abort was really devastating (p. 2055).”¹⁴

Sally articulated a sense of responsibility or “having to” during this interim period and just how devastating this could be. Even before knowing whether their fetus was at risk of being a carrier of or having CF, Sally and her partner were forced to consider abortion. Ultimately, her partner might not have been a carrier of the same mutation, but the sequential design of the program forced them to already live in the possibility of “having to” abort the fetus.

Although none of the study participants directly spoke about a desire to have screening programs in which both partners were screened simultaneously, it is possible that the anxiety and the devastation caused by needing to think through difficult decisions to abort (when already pregnant) could be potentially avoided with simultaneous screening programs. It is possible that both partners could be found to be carriers of the same mutation and they would need to think through their options accordingly but avoiding unnecessary anxiety and devastation is likely desirable by people undergoing carrier screening – particularly if they are already pregnant.

Regardless of when screening happens or in what order, people who have been screened will ultimately be faced with how to proceed with that new information. In the following section, we briefly describe how challenging it can be to work through the results of carrier screening and apply them to one’s reproductive decision-making.

Affecting People’s Reproductive Decision-Making

The Challenge of Working Through What the Results Mean

Sally’s struggle with what to do and the deliberation while waiting on the results of her partners’ screening were typical of study participants who had undergone carrier screening prenatally. Although some noted that an abortion was not an option,^{17,20,21} for the majority this remained on the table. Coming to that decision was difficult and required input – particularly from geneticists who could help make sense of what the results might mean.

People described truly appreciating the opportunity to speak to a geneticist upon receiving their result. For example, once Georgia had been identified as a carrier of FXS, she described finding her conversation with a geneticist as helpful in coming to understand what FXS “is”:

When I got the call from [the genetic counsellor], she was extremely informative and I got a really good grasp of what it actually is and what my chances were of, or what the baby’s chances were of, actually having a full mutation of the condition...we probably sat on the phone for 40 to 45 minutes or so as she explained to me what it actually was, so that was extremely helpful... (p. 2055).¹⁴

When coming to an informed decision about whether to pursue carrier screening or not, Georgia’s conversation here fits with an understanding of decision-making and consenting to screening as situated within a process that requires ongoing contact with health care providers – in this case, geneticists. Georgia and the earlier examples indicate that simple high-level informational sharing (leaflets) is not enough; information about carrier screening requires an appropriate level of resources to provide counsel and as a foil for deliberation. As such, it is possible that providers and counsellors might need to be more involved than they feel comfortable given they are not simply sharing “neutral information.”¹⁹

People did not necessarily turn to genetic counsellors to make their decisions or deal with the news. Rather, they described also turning to partners, family members, friends, colleagues, and the internet for support at this point.¹⁴ Although a genetics counsellor might be able to help make the “difficult process as easy as it can be (p. 2056),” if they are empathetic,

reassuring, and non-judgmental,¹⁹ many participants expressed that they might be able to help know what it's like to live with the condition. Although a specialist working in the field of the potential condition might be helpful in this regard,¹⁹ many people described resorting to the internet for this support.^{11,14}

Georgia also described watching YouTube videos of “what it's actually like to live with a child who has the fully mutated fragile X gene...[and] seeing that I kind of thought oh goodness this isn't just a small disability, this is severe... (p. 2056).”¹⁴ Much like previous challenges of not “really relat[ing] (p. 2054)”¹⁴ to the conditions being screened for, we read this perusal of YouTube as an attempt to relate. This could help or, as seen with Ameena and Sadeed, Georgia and her partner might not be able to truly relate to the severity of FXS (in their case) until they have a child with the condition.

Limitations

One of the most challenging limitations of this review was the difficulty of addressing such an expansive research question in a such a limited amount of time. For this reason, it has been challenging to provide the same level of depth across all components of the review. As such, there are some sections that are less analyzed than others. The sections in which we went into greater depth were chosen given our understanding of how they might be particularly relevant to people making decisions on whether to expand from targeted carrier screening to population-based screening for some conditions.

Similarly, although we originally hoped that we would be able to hone in on issues of race and racialization around carrier screening, none of the included literature focused on this aspect. There were at least 3 included studies that involved racialized populations, but none of these explicitly engaged with issues of race or racism. This is not because literature exploring how racialized people experience genetic testing does not exist, just that none specifically met our inclusion criteria. However, although we may not have an analysis in our synthesis specific to racialized populations, we discuss the importance of the interplay between structural racism and genetic testing in the Conclusions and Implications for Decision- or Policy-Making section.

Conclusions and Implications for Decision- or Policy-Making

This review used a rapid best-fit framework synthesis approach to describe and explore some of the ways people who are considering pregnancy (or who are already pregnant) and health care providers understand and engage with carrier screening for genetic conditions. There were 11 publications representing 10 studies that were included and synthesized in this review within a framework that focused on 3 a priori categories drawn from our research question: accessing and deciding whether to undergo, or offer, testing; the process of testing, including the communication, interpretation, and use of test results; and how those results might affect people's reproductive decision-making.

In general, people described wanting access to carrier screening during preconception or, at the very latest, prenatal stages. The opportunity to know their risk of passing along a genetic condition was considered to be important and supported their desire to be prepared

and to make autonomous reproductive decisions. This is well situated within an extensive body of literature that both explores and critiques peoples' experiences under health care regimes in which individuals are imagined as rational actors who are considered responsible if they cultivate an abundance of self-knowledge on both lifestyle and genetic health risks that they then monitor and respond to accordingly.²³ We saw study participants, primarily cisgender women in heteronormative couplings, accept and describe their desire to enact this responsibility to cultivate a deeper knowledge of their genetic risks. Some participants also described coming to know about their risks as more than a simple opportunity. Rather, it was conceptualized as a "right"¹⁴ – they expected to acquire this genetic risk knowledge so that they could proceed to make responsible decisions.

The goal, and indeed responsibility, is to not only cultivate knowledge about the genetic risk, but to act upon this knowledge.²⁴ Acting upon this knowledge meant being able to make decisions and become prepared. For many of our participants, having the ability to know their risk ahead of time was considered empowering and fulfilled a need to have some sort of control over their life's narrative. They imagined their foreknowledge of genetic risk as being able to prepare themselves to have more than just children – they could have healthy children. And with their healthy children, they could have good and lasting relationships with their reproductive partners. As such, the opportunity to understand one's genetic risks through genetic testing technologies such as carrier screening can be a powerful component of reproductive planning.

But this opportunity, or this responsibility, to cultivate knowledge and then act upon this knowledge and become prepared was not without its concerns. From the findings in our review, it was evident that at least some health care providers understood that the availability of carrier screening potentially placed the responsibility for creating healthy children on the shoulders of parents themselves. Providers, particularly geneticists, wanted to ensure that information on carrier screening as a reproductive option remained neutral and non-directive. However, although descriptive information helps people understand the screening process and the types of results that could emerge from testing, our findings point to the importance of having more involved health care providers when deliberating over whether to engage with carrier screening or not. This does not mean that people wanted their providers to make decisions for them. Instead, for those participants, supporting an "informed decision" was more than information sharing and could involve the facilitation of speculative conversations about the potential ramifications of carrier screening in people's lives. As such, we understand the process of becoming informed to be a moving target that requires ongoing support from health care providers rather than a simple knowledge exchange supporting a one-time decision. Ensuring a carrier screening program has the capacity and resources to support people in the process of becoming informed and making decisions would seem to be an important component of any carrier screening program.

However, it may be that this "responsibilization" could move beyond the desires or goals of the people who might engage with a carrier screening program and instead be experienced as a burden or outright discrimination. Although our goal was not to pronounce whether carrier screening or expanded carrier screening programs are ethically acceptable (a further ethics analysis could support decision-makers directly in this assessment), we note how this push toward knowing could be simultaneously disempowering or even restrictive. As previously noted, 1 of the earliest examples of carrier screening programs in North America was developed for SCD in 1971 by the Black Panthers in an effort to force the US government to begin funding research on effective treatment options for SCD.^{4,25} Although this screening program may have originally been intended to empower African Americans by demanding

research dollars for the development of effective treatments, by the 1980s several Black activists equated these programs with things like “unethical medical experimentation.”⁴ This may not be the experience or perspective of all Black people called on to engage with carrier screening for (or other genetic tests associated with) SCD, but it does demonstrate that it is possible for testing to be understood both as “a call to moral action for greater awareness... [that] could be empowering” and “framed within policy and practice was disempowering and potentially disabling and racist (p. 186).”⁵ This particular example is especially pertinent within the context of the current political movement focused on anti-Black racism across the US and Canada and worth highlighting even though none of our studies spoke to this directly. Similarly, we expect that this possibility for carrier screening to be experienced as discriminatory or disempowering to also be present for people living with the conditions being screened for (e.g., FXS, CF or SMA).

Given the challenge of supporting people making decisions of whether or not to pursue carrier screening and the likely increase in people who will consider it if targeted programs are expanded to population-level screening, it is important to ensure that health care providers are both aware of jurisdictional carrier screening programs and competent in what carrier screening might be able to offer their patients. Although this is particularly true for GPs who are often the primary point of contact with the health care system for their patients, this was also considered important for people who work in family planning clinics and women’s health clinics. In Best et al.’s systematic review, the authors noted that carrier screening is complicated.²⁶ In Best et al.’s study, many health care providers felt some form of training was necessary to build their confidence in returning the results to their patients. If these results were positive (indicating their patient was a carrier), having access to genetic counselling was also considered beneficial.

Having the option to engage with carrier screening at the preconception stage was universally preferred by participants across the included studies. Participants viewed preconception carrier screening as providing prospective parents with more reproductive options than when screening was offered prenatally. Health care providers were concerned that offering carrier screening during pregnancy might be confused with other prenatal testing and limit people’s ability to truly be informed before deciding whether or not to pursue screening. However, if it were offered as a prenatal option, most people considered it important to do so as early as possible because it could be paired with other prenatal tests. Although no studies spoke to this specifically, we would also note that offering carrier screening prenatally, rather than at preconception, could place the responsibility to make the decision on cisgender women and non-binary or transgender people with uteruses.

Sequentially designed carrier screening programs were the most common across the included studies, although people moving through programs with this design found the interim period between the reception of their positive carrier results and their partners’ results difficult. This was particularly true for people who were already pregnant. This interim period forced them to reimagine both their relationship with the fetus and the future they had imagined with that child. Of course, this reimagining might be necessary if both partners’ screening results came back positive for the condition in question, but a staggered return of the results could put undue anxiety on potential parents.

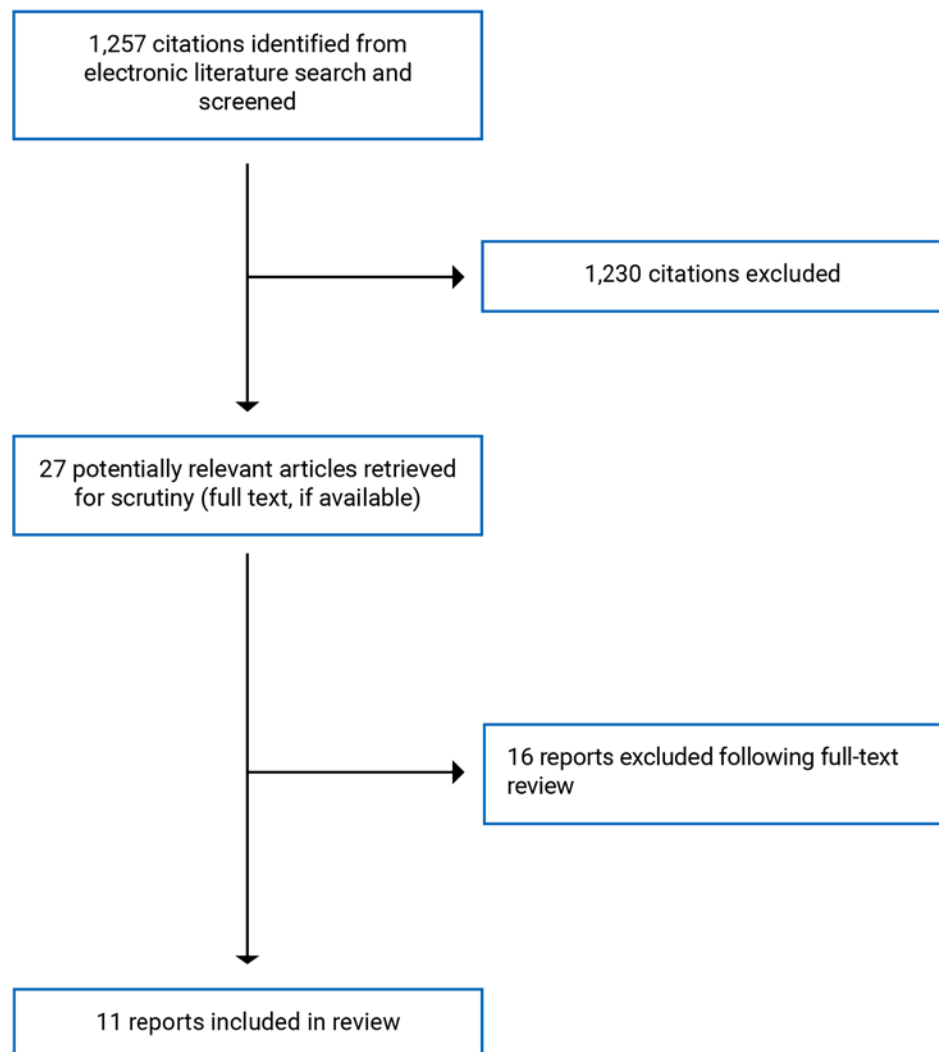
Carrier screening will not affect everyone in the same way, and reproductive decision-making will still be complex and difficult with carrier screening. As such, the opportunity to engage with genetic counsellors about reproductive options following positive carrier status result was considered valuable.

References

1. Kraft SA, Duenas D, Wilfond BS, Goddard KAB. The evolving landscape of expanded carrier screening: challenges and opportunities. *Genet Med*. 2019;21(4):790-797. [PubMed](#)
2. Henneman L, Borry P, Chokoshvili D, et al. Responsible implementation of expanded carrier screening. *Eur J Hum Genet*. 2016;24(6):e1-e12. [PubMed](#)
3. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Genetic carrier screening. 2019: [https://ranzocg.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical-Obstetrics/Genetic-carrier-screening\(C-Obs-63\)New-March-2019_1.pdf?ext=.pdf](https://ranzocg.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical-Obstetrics/Genetic-carrier-screening(C-Obs-63)New-March-2019_1.pdf?ext=.pdf). Accessed 14 Jun 2021.
4. Paul DB. Norm Change in Genetic Services. How the Discourse of Choice Replaced the Discourse of Prevention. *Varia Historia* 2017;33(61):21-47.
5. Berghs M, Dyson SM, Atkin K. Resignifying the sickle cell gene: Narratives of genetic risk, impairment and repair. *Health (Lond)*. 2017;21(2):171-188. [PubMed](#)
6. Wilson RD, De Bie I, Armour CM, et al. Joint SOGC-CCMG Opinion for Reproductive Genetic Carrier Screening: An Update for All Canadian Providers of Maternity and Reproductive Healthcare in the Era of Direct-to-Consumer Testing. *JOGC*. 2016;38(8):742-762.e743. [PubMed](#)
7. Krefting L. Rigor in Qualitative Research: The Assessment of Trustworthiness. *Am J Occup Ther*. 1991;45(3):214-222. [PubMed](#)
8. Shaw L, Nunns M, Briscoe S, Anderson R, Thompson Coon J. A "Rapid Best-Fit" model for framework synthesis: Using research objectives to structure analysis within a rapid review of qualitative evidence. *Res Synth Methods*. 2021;12(3):368-383. [PubMed](#)
9. Booth A, Carroll C. How to build up the actionable knowledge base: the role of "best fit" framework synthesis for studies of improvement in healthcare. *BMJ Qual Saf*. 2015;24(11):700-708. [PubMed](#)
10. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*. 2009;62(10):e1-e34. [PubMed](#)
11. Kraft SA, Schneider JL, Leo MC, et al. Patient actions and reactions after receiving negative results from expanded carrier screening. *Clin Genet*. 2018;93(5):962-971. [PubMed](#)
12. Boardman FK, Hale R. "I didn't take it too seriously because I'd just never heard of it": Experiential knowledge and genetic screening for thalassaemia in the UK. *J Genet Couns*. 2019;28(1):141-154. [PubMed](#)
13. Archibald AD, Hickerton CL, Wake SA, Jaques AM, Cohen J, Metcalfe SA. "It gives them more options": preferences for preconception genetic carrier screening for fragile X syndrome in primary healthcare. *J Community Genet*. 2016;7(2):159-171. [PubMed](#)
14. Beard CA, Amor DJ, Di Pietro L, Archibald AD. "I'm Healthy, It's Not Going To Be Me": Exploring experiences of carriers identified through a population reproductive genetic carrier screening panel in Australia. *Am J Med Genet A*. 2016;170(8):2052-2059. [PubMed](#)
15. Josephi-Taylor S, Barlow-Stewart K, Selvanathan A, et al. User Acceptability of Whole Exome Reproductive Carrier Testing for Consanguineous Couples in Australia. *J Genet Couns*. 2019;28(2):240-250. [PubMed](#)
16. Holtkamp KCA, Lakeman P, Hader H, et al. Experiences of a High-Risk Population with Prenatal Hemoglobinopathy Carrier Screening in a Primary Care Setting: a Qualitative Study. *J Genet Couns*. 2018;27(3):635-646. [PubMed](#)
17. Verdonk P, Metselaar S, Storms O, Bartels E. Reproductive choices: a qualitative study of Dutch Moroccan and Turkish consanguineously married women's perspectives on preconception carrier screening. *BMC Womens Health*. 2018;18(1):79. [PubMed](#)
18. Janssens S, Chokoshvili D, Vears D, De Paepe A, Borry P. Attitudes of European Geneticists Regarding Expanded Carrier Screening. *JOGNN*. 2017;46(1):63-71. [PubMed](#)
19. Janssens S, Chokoshvili D, Vears DF, De Paepe A, Borry P. Pre- and post-testing counseling considerations for the provision of expanded carrier screening: exploration of European geneticists' views. *BMC Med Ethics*. 2017;18(1):46. [PubMed](#)
20. Rothwell E, Johnson E, Mathiesen A, et al. Experiences among Women with Positive Prenatal Expanded Carrier Screening Results. *J Genet Couns*. 2017;26(4):690-696. [PubMed](#)
21. Schneider JL, Goddard KA, Davis J, et al. "Is It Worth Knowing?" Focus Group Participants' Perceived Utility of Genomic Preconception Carrier Screening. *J Genet Couns*. 2016;25(1):135-145. [PubMed](#)
22. Boardman FK, Young PJ, Griffiths FE. Population screening for spinal muscular atrophy: A mixed methods study of the views of affected families. *Am J Med Genet A*. 2017;173(2):421-434. [PubMed](#)
23. Sharon T. Healthy citizenship beyond autonomy and discipline: Tactical engagements with genetic testing. *BioSocieties*. 2015;10(3):295-316.
24. Novas C, Rose N. Genetic risk and the birth of the somatic individual. *Econ Soc*. 2000;29(4):485-513.
25. Markel H. *Scientific advances and social risks: historical perspectives of genetic screening programs for sickle cell disease, Tay-Sachs disease, neural tube defects, and Down syndrome, 1970-1997. Promoting Safe and Effective Genetic Testing in the United States*. Bethesda (MD): NIH-DOE Working Group on Ethical, Legal and Social Implications of Human Genome Research; 1997.
26. Best S, Long J, Theodorou T, et al. Health practitioners' perceptions of the barriers and enablers to the implementation of reproductive genetic carrier screening: A systematic review. *Prenat Diagn*. 2021;02:02.

Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications and Their Participants

Table 2: Characteristics of Included Publications and Their Participants

Author, year, country	Study objectives	Type of carrier screening (e.g., condition specific, expanded panel, population level)	Description of study participants ^a	Study design, method of data collection and analysis	Judgment on trustworthiness and transferability (i.e., low, moderate, high)
Boardman and Hale (2019) ¹² UK	To examine and provide critical analysis of the potential differences in reproductive decision-making between people with foreknowledge that they have an elevated risk of passing thalassemia onto their children (i.e., based on family history or as a person with thalassemia themselves) and those who have been identified as carriers through prenatal carrier screening	Targeted, population-level carrier screening for thalassemia	Total of 15 study participants, but only those discovering carrier status through the prenatal carrier screening program are included in this review (n = 3) All 3 of these participants were women who currently had at least 1 child living with thalassemia that was born after they were identified as a carrier	Described as a qualitative interview study that used a modified approach to grounded theory for analysis	High
Josephi-Taylor et al. (2019) ¹⁵ Australia	To explore the acceptability and perceived utility of reproductive carrier genomic screening in consanguineous couples	Expanded carrier screening	Total of 42 participants making up 21 couples who were related as at least second cousins	Interview study using inductive thematic analysis	Low
Holtkamp et al. (2018) ¹⁶ The Netherlands	To explore how pregnant women at an elevated risk of being carriers of HbPs experience the offer of carrier screening for HbPs by their primary care midwife	Targeted, ancestry-based carrier screening for HbPs	Total of 26 participants who were all described as pregnant women at risk for HbPs based on ancestry	Interview study using thematic content analysis	Moderate

Author, year, country	Study objectives	Type of carrier screening (e.g., condition specific, expanded panel, population level)	Description of study participants ^a	Study design, method of data collection and analysis	Judgment on trustworthiness and transferability (i.e., low, moderate, high)
Kraft et al. (2018)¹¹ US	To explore how people who have undergone expanded carrier screening experience receiving negative results and how this impacts their reproductive decision-making	Expanded carrier screening	Total of 36 participants made up of 12 male/female couples and 12 females alone	Mixed methods Qualitative component analyzed interview data using content analysis	Low
Verdonk et al. (2018)¹⁷ The Netherlands	To explore Dutch, Moroccan, and Turkish women's perspectives on preconception carrier screening and how it impacts reproductive decision-making	Expanded carrier screening	Total of 10 participants who were all described as women in a consanguineous marriage	Interview data were analyzed using thematic analysis	Moderate
Janssens et al. (2017)¹⁹ Belgium	To explore European geneticists' thoughts on and attitudes toward expanded carrier screening with a focus on the development of recommendations	Expanded carrier screening	Total of 16 participants made up of 13 clinical geneticists, 2 molecular geneticists, and 1 geneticist with experience in both clinical and molecular genetics	Interview data analyzed using inductive content analysis	Moderate
Janssens et al. (2017)¹⁸ Belgium	To explore attitudes of clinical and molecular geneticists about the implementation of multi-disease or expanded carrier screening for monogenic recessive disorders	Expanded carrier screening	Total of 16 participants made up of 13 clinical geneticists, 2 molecular geneticists, and 1 geneticist with experience in both clinical and molecular genetics	Interview data analyzed using inductive content analysis	Moderate
Rothwell et al. (2017)²⁰ US	To explore the experiences of women who received positive results from expanded carrier screening in the context of obstetrics care	Expanded carrier screening	Total of 17 participants all of whom were described as women who had received carrier screening tests during pregnancy	Interview data analyzed using content analysis	Low

Author, year, country	Study objectives	Type of carrier screening (e.g., condition specific, expanded panel, population level)	Description of study participants ^a	Study design, method of data collection and analysis	Judgment on trustworthiness and transferability (i.e., low, moderate, high)
Archibald et al. (2016) ¹³ Australia	To explore a variety of stakeholders' perspectives about the offer of population-based genetic carrier screening for FXS	Targeted, population-based carrier screening for FXS	Total of 188 "stakeholders" including health care providers (n = 81), relatives of people living with FXS (n = 29), pregnant women who had been offered screening (n = 11), non-pregnant women who had been offered screening (n = 31), and members of general community (n = 36)	Described as a qualitative approach using a grounded theory framework and thematic analysis; data were collected via semi-structured interviews and focus groups	High
Beard et al. (2016) ¹⁴ Australia	To explore the experiences of women identified as a carrier of either CF, SMA, or FXS through a newly expanded population screening program	Targeted population-based carrier screening for CF, SMA, FXS	Total of 10 study participants who were described as women who had recently undergone carrier screening and had been identified as a carrier of CF, SMA, or FXS	Described as a qualitative study following a narrative approach and using narrative analysis; data collected through semi-structured interviews	High
Schneider et al. (2016) ²¹ US	To explore peoples' perspectives of the advantages and disadvantages of genomic carrier screening	Expanded carrier screening	Total of 16 study participants who were all identified as women with the exception of 1 male partner who showed up at the focus group unrequested All female participants were described as having experience with some form of targeted preconception carrier screening	Described as a qualitative focus group study using thematic analysis	Moderate

CF = cystic fibrosis; FXS = fragile X syndrome; HbPs = hemoglobinopathies; SMA = spinal muscular atrophy.

^aFor mixed-methods studies, we will only be reporting on the qualitative components.