Carrier Screening for Cystic Fibrosis, Fragile X Syndrome, Hemoglobinopathies, and Spinal Muscular Atrophy: Ethics Analysis

Angel Petropanagos
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Background

Carrier screening, a type of non-invasive genetic testing, is used to determine whether a person carries a recessive gene for a genetic condition and the likelihood they would produce a genetically-related child affected by that condition. The global market for carrier screening is expected to grow rapidly over the next few years due to the increased frequency of genetic disorders, improved early treatment interventions, growing social awareness and acceptance of genetic testing, and advancements is genetic screening technologies (Research Dive, 2021; Terdale & Sumant, 2021).

There are several approaches to carrier screening. These approaches are described in a recent health technology assessment (HTA) report by Ontario Health titled "Carrier Screening Programs for Cystic Fibrosis, Fragile X Syndrome, Hemoglobinopathies and Thalassemia, and Spinal Muscular Atrophy: A Health Technology Assessment" (Ontario Health, 2023). To summarize, carrier screening may be used by individuals at the preconception or prenatal phases and it may be offered only to individuals at increased of carrying pathogenic recessive genes due to family history or ethnicity or offered universally to anyone planning to have a child. Carrier screening testing methods may be targeted for select genetic disorders or employ comprehensive or expanded screening panels that test for a number genetic variants.

In British Columbia (BC), carrier screening for certain conditions (including cystic fibrosis, fragile X syndrome, hemoglobinopathies, and spinal muscular atrophy) is publicly funded through BC Medical Services Plan (MSP) for persons who meet eligibility criteria and are considered to be high risk of producing a child with a particular genetic condition. Population-based carrier screening for the purposes of reproductive planning is not covered by MSP. Individuals who do not meet the eligibility criteria may still access carrier screening, but must pay through private insurance or out-of-pocket. At this time, expanded carrier screening is not funded through provincial health insurance.

The purpose of this health technology assessment (HTA) ethics report is to help inform decision making about whether to implement a universal, a publicly-funded carrier screening program for cystic fibrosis, fragile X syndrome, hemoglobinopathies, and spinal muscular atrophy.

Purpose and Scope of Ethics Analysis

This HTA identifies and explores key ethical issues related to the implementation, provision, and use of universal publicly-funded carrier screening program for cystic fibrosis, fragile x syndrome, hemoglobinopathies, and spinal muscular atrophy, with the aim of supporting ethical deliberations about carrier screening programs in BC. It considers substantive and procedural values from a variety of perspectives including prospective parents, family members, future offspring, clinicians, policy makers, and the public. The following questions are considered in this HTA ethics analysis:

1. *What are the relevant ethical considerations (principles and values) related to preconception and/ or prenatal reproductive carrier screening programs for testing for specific genetic conditions and expanded carrier screening panels?*

2. *What are the ethics-related barriers or opportunities for implementation, provision, and use of carrier screening at the individual, social, and systemic levels?*
3. *What are the ethical issues and considerations in employing cost-benefit and cost-utility analyses in assessing carrier screening programs?*
4. *Are there any ethics considerations for the implementation, provision, or use of carrier screening that are specific to the BC context?*

This ethics report was conducted at the request of the British Columbia Health Technology Assessment Committee (BCHTAC) as part of a collaboration to support OHTAC's HTA on Carrier Screening.

Methodology

The methodology for this ethics report is twofold, as it employs both descripted and normative ethical analyses. First, a descriptive ethical analysis was conducted. The relevant literatures were reviewed to identify ethical issues related to the implementation, provision, and use of carrier screening. A non-exhaustive, informal review of the relevant clinical and bioethical literatures was conducted in August 2022 with the help of the librarians supporting the British Columbia Health Technology Assessment Committee (BCHTAC). Targeted searches were completed using JSTOR, PubMed, Google Scholar and Google and Bing searches. Included articles and sources made explicit or implicit mention of an ethical issue related to the context reproductive carrier screening and grey (non-commercially published) literature including relevant laws, policies, guidelines, and websites.

The BCHTAC librarians were provided with the following key terms for the literature search: ethic*; moral*; carrier screening; genetic screening; autonomy; informed consent; parental or reproductive rights; well-being; harm; justice; equity; access; disability rights; genetic counselling; preimplantation genetic diagnosis; eugenics; and ableism. A targeted literature search was also conducted to help identify ethical issues related to the use of a cost-benefit/ cost-utility analysis for the economic report in this HTA. The key words for this second search included the following: quality adjusted life years; QALY; disability; reproduction; ethic*, disability rights; social conception of disability; social determinants of health; methodological issues with QALY analysis; lived experiences of disability; monetary value of life; resource allocation; and ableism.

BCHTAC Librarians also conducted targeted searches for the following bioethics journals: *The Canadian Medical Association Journal*; *Canadian Journal of Bioethics*; *American Journal of Bioethics*; *Journal of Medical Ethics*; *Clinical Ethics; Bioethics*; *Journal of Bioethical Inquiry*; *Kennedy Institute of Ethics Journal; Theoretical Medicine and Bioethics*; *Hastings Centre Report*; *Medicine*, *Health Care and Philosophy*; *Cambridge Quarterly of Healthcare Ethics*; *The Journal of Law*, *Medicine, and Ethics*; *The Journal of Medicine and Philosophy*; *International Journal of Feminist Approaches to Bioethics*; *Public Health Ethics; Medical Humanities*; *Journal of Health Politics, Policy and Law*; *Ethics*; *Health Care Analysis*; *Science, Technology, and Human Values*; and *Social Science and Medicine*. Sample journal articles were provided to the BCHTAC librarians to help ensure that the search results captured the relevant ethics literature. Initial searches were for articles published within the past five years, but the publication date was

expanded to capture some articles from the targeted bioethics journals listed here. Non-English articles were excluded from this review.

Ethical issues explicitly named in the literature were identified from the primary literature review (supported by BCHTAC) and the HTA draft report including clinical, economic, and stakeholder analyses (provided by OHTAC), and targeted searches of the grey literature. Explicit ethical issues include issues that are describe as "ethical", appear in an ethics section, journal publication, or named as relating to an ethical principle or value.

Second, a normative ethical analysis was conducted. This methodological approach was informed by expertise in feminist bioethics and analytic philosophy with the aim of identifying implicit or novel ethical issues related to the implementation, provision, and use of carrier screening programs, as well as discerning potential gaps in the literature. This ethical analysis considered both substantive and procedural values. Additional targeted internet searches were conducted to support this normative analysis.

Findings: Summary of Ethical Issues

Carrier screening falls within the broader bioethics literatures exploring assisted reproduction, disability, genetic testing, and funding of healthcare services. Common ethical issues identified in the literature include the value of and challenges with autonomous reproductive decision making, the nature and meaning of disability, access to genetic information and genetic privacy, and just resource allocation. There are also a number of articles that focus on the ethical considerations raised in the context of testing for specific genetic conditions, such as cystic fibrosis, fragile X syndrome, hemoglobinopathies, and spinal muscular atrophy. For the purposes of this report, more than 150 journal articles were reviewed, including 105 articles that were provided by the BCHTAC librarians. Select grey literature was also reviewed, including government websites, professional guidelines, and commercial websites. Seventy are referenced in this report. A systematic and comprehensive ethics literature review is well beyond the scope of this report, but it is worth noting the ethics literature relevant to carrier screening is exceptionally large.

Two dominant rationales for the implementation of carrier screening programs are evident in the literature, namely to promotion of reproductive autonomy and the pursuit of public health goals. The benefits and challenges of justifying carrier screening programs in relation to the goals of promoting reproductive autonomy and public health are described below.

i. Reproductive Autonomy Rationale

The general principle of respect for autonomy—the right or condition of self-government—is a foundational principle in Canadian bioethics. It is often expressed through the model of informed consent in British Columbia's Health Care (Consent) and Care Facility (Admission) Act, and is a central feature in many healthcare professionals' guidelines, and practices. Reproductive autonomy is a

person's ability to make their own decisions about their reproductive health and body and to do so in accordance with their own values and interests and without manipulation by external forces. Reproductive autonomy includes choices related to contraception, pregnancy, abortion, and parenthood. While reproductive autonomy is about individual choice, these choices are fundamentally embedded in social contexts. In response to traditional, individualistic theories of autonomy, many theorists define autonomy as relational, such that social contexts shape and influence an individual's ability and power to decide and act according to their own values and interests (Dove et al., 2017; Gómez-Vírseda et al., 2019; Mackenzie & Stoljar, 2000; Romero, Rink, et al., 2017).

The Society of Obstetricians and Gynaecologists of Canada and the Canadian College of Medical Geneticists have stated that the option of reproductive genetic carrier screening should be part of the informed consent process (Wilson et al 2016). Carrier screening programs are often described as promoting and enhancing the reproductive autonomy of prospective parents (de Jong & de Wert, 2015; G. de Wert et al., 2021; G. M. W. R. De Wert et al., 2011a; Edwards et al., 2015; Henneman et al., 2016a; Plantinga et al., 2016; van der Hout et al., 2019). This rationale is dominant in Western arguments in favour of carrier screening programs (Henneman et al., 2016b) and it was also employed the OHTAC's HTA report to motivate the potential implementation of a universal, publicly-funded carrier screening program. Unpacking the ethical issues related to reproductive autonomy and carrier screening draw attention ethical issues affecting prospective parents, offspring, family, and clinicians supporting the provision of carrier screening.

Ethical Benefits

Carrier screening programs support reproductive autonomy by giving people access to information that can help them to make reproductive choices align with their own values and interests (G. M. W. R. De Wert et al., 2011a; L Dive & Newson, 2021; Plantinga et al., 2016; van der Hout et al., 2019). At the preconception phase, carrier screening allows individuals and couples to determine if they carry recessive genes for any conditions that could be inherited by their future child and the likelihood of passing along that condition to their child. This information allows prospective parents to prepare and plan for a child with a particular genetic condition or affords them an opportunity to use in vitro fertilization (IVF) and pre-implantation genetic diagnosis (PGD) in an attempt to avoid passing certain genetic condition to their future offspring. Other reproductive options following preconception carrier screening include natural conception, the use of donor eggs or sperm, adoption, refraining from having genetically-related children, choosing not to become a parent; or choosing a different reproductive partner. Individuals or couples who use carrier screening during pregnancy (prenatal carrier screening), can use genetic information to help them to prepare and plan to parent a child with a particular genetic condition. Alternatively, they might choose to terminate the pregnancy through an elective abortion. Their reproductive options following carrier screening are prenatal diagnostic testing to confirm whether the fetus has the genetic condition in question, and the choice to continue or to terminate the pregnancy. Carrier screening used in the preconception phase allows for more family planning options and more time to consider the available options. Carrier screening can be especially empowering for people who are or plan to become pregnant and help to support their bodily autonomy (Stoll & Jackson, 2020). Improvements to carrier screening technologies that allow for faster or more comprehensive

testing (e.g., expanded screening panels or whole genome sequencing) might further support reproductive decision making.

By supporting reproductive autonomy, carrier screening can positively impact the emotional, psychological, and physical well-being of prospective parents. For example, one study found that prospective parents found value in knowing genetic information because it helps to give them a sense of control, reduces anxiety (J. L. Schneider et al., 2016). The knowledge that one does not carry certain pathogenic genes can improve psychological well-being, reduce feelings of stigmatization, and improve the perceptions of one's own health, and reduce emotional distress (AJMC, 2018). The clinical summary in this HTA also found that for some people, the use of carrier screening may lower anxiety and stress related to pregnancy or parenting. Children whose parents have undergone carrier screening may benefit from the knowledge of their genetic risks. Those who have particular genetic conditions might also benefit from their parents' decisions to access early interventions for their genetic condition or from having parents who were become well-prepared to manage their condition.

Some theorists argue that parents have a responsibilities to minimize harms to (future) children (Clarkeburn, 2000) or to maximize the well-being their offspring (Savulescu & Kahane, 2009). They maintain that having a child with a disability can be different (and arguably more challenging) than raising a child without a disability (Gyngell et al., 2020). Others argue that there is an obligation to prevent the births of children with disabilities in order to prevent suffering, which they assume is a necessary component of disability (Harris, 2000). Messaging about parental obligations and well being are also echoed in advertising for privately funded carrier screening services (CADTH, 2021) and implied in the value that is put on reproductive autonomy and the ability to choose what 'type' of child one wants to parent.

Given that in BC publicly-funded carrier screening is only available for high risk individuals and at the discretion of physicians, not everyone can access carrier screening and exercise or enhance their reproductive autonomy. Out-of-pocket costs for carrier screening are more than $600 and may be prohibitive for some individuals/ couples. One benefit of a universal, publicly-funded carrier screening program would be to help remove financial barriers to carrier screening and to promote equality in access to genetic information. If there is a right to know one's genetic information (De Jong et al., 2010), the ability to access this information may be a matter of reproductive justice.

Ethical Challenges

Despite the ways in which carrier screening can promote reproductive autonomy, there are several aspects of carrier screening that present challenges for informed decision making. Informed decision making includes both the ability to provide informed consent to carrier screening/ IVF and PGD/ abortion and the ability to make an informed refusal for these options. One concern is that the genetic information related to carrier screening is complicated or confusing, and difficult to understand or appreciate. Although screening tests can help to identify the likelihood of genetic risk, they are not diagnostic and this can be misinterpreted by prospective parents (Lisa Dive & Newson, 2021c). There can also be a large degree of variability is the way that genes are expressed, so it the extent of the genetic

condition experienced by future offspring may be uncertain (Kihlbom, 2016). The results of carrier screening tests can yield false positives or false negatives. Test accuracy, trust in the results, or confusion about the test information can making it difficult for prospective parents to discern what the information about genetic risk means for them and any future offspring. Expanded carrier screening panels or whole genome sequencing can exacerbate challenges with understanding and appreciated information. Genetic sequencing is complex and the misinterpretation of information can result in harm (Silver & Norton, 2021). Calculating the given genetic risks to future offspring can be difficult because test results can yield information about more than one recessive (Kihlbom, 2016). Poor genetic literacy by patients or clinicians supporting them can also hinder informed decision making related to carrier screening (Ghiossi et al., 2018; Henneman et al., 2016b).

Many people maintain that genetic counselling is essential for helping to alleviate some of the challenges related to informed decision making (Clarke & Wallgren-Pettersson, n.d.; Li. Dive & Newson, 2020; Gbur et al., 2021; Kater-Kuipers et al., 2020; Michie & Allyse, 2022; Silver & Norton, 2021; van den Berg et al., 2006). Some studies note that participation, particularly by male partners in heterosexual relationships, can be limited (J. L. Schneider et al., 2016). Genetic counselors can help individuals and couples to understand the test results and to explore what this information means to them. The availability of genetic counselling might also be important in the context of secondary disclosures of unexpected findings from genetic testing. For example, one might learn information that can impact their own health. Or, like in other types of genetic testing, one might receive genetic information that challenges their understanding of existing familial relationships (e.g. someone might inadvertently learn that they are not related to their genetic parent).

The Canadian Medical Association supports increased genetics training for physicians to help them build an appreciate for the complexity of genetics (Canadian Medical Association, 2017). Such training may help physicians become better prepared to support their patients who consider the use of carrier screening. However, the majority of clinicians lack the training to be able to adequately provide counselling for carrier screening patients (Fakih & Spector-Bagdady, 2019), so there remains a need for patient access to professional genetic counselors. The number of genetic counsellors in Canada, although growing, remains limited. The Canadian Association of Genetic Counsellors recently administered a professional status survey to 702 of its members who work in Canada working in a variety of practice areas including pediatrics, prenatal, cancer, metabolic disease, neurology, cardiology, infertility, pharmacogenetics, genomic medicine, and others (Canadian Association of Genetic Counsellors 2022). Of the 251 survey respondents, 36 genetic counsellors reside in BC, however the data on the total number of reproductive genetic counsellors in BC was not found at this time. Data from Ontario shows that the majority of genetic counsellors are practicing in larger cities, suggesting access issues in rural and remote areas (Shugar et al., 2022). It is likely that in BC, genetic counsellors would also be more likely to reside in large cities, such as Vancouver and Victoria. Of note, counselling services, in general, are not covered by BC MSP (Services Not Covered by the Medical Services Plan (MSP) - Province of British Columbia (gov.bc.ca)). These two factors suggest that if a universal, publicly-funded carrier screening program is implemented, some patients may encounter barriers in accessing genetic counselling. Similar challenges may also exist with respect to accessing genetic testing, IVF, or abortion, particularly in rural or remote areas of BC.

When discussing carrier screening, Ainsley Newson and Lisa Dive (2021) emphasize that that social norms influence individual choices and individual choices influence social norms. Informed decision-making about carrier screening and reproduction can also be challenging because of social norms, pressures, and biases such as ableism, pronatalism, geneticism, and other expectations related to reproduction (L Dive & Newson, 2021; Petropanagos, 2017; Thomas & Rothman, 2016). Stigma pertaining to disability can influence people's perceptions about which options are most valuable or responsible (Kihlbom, 2016) and it can make the carrier screening an attractive option for reducing the likelihood of having a child with a disability (Lisa Dive & Newson, 2021b). Stigma surrounding disability. In addition to social biases, existing services, family and social supports can also influence decisions about carrier screening (Thomas & Rothman, 2016). Because of difficulties related to social context and decision making, some people recommend against mass-screening programmes and argues in favour of more targeted, individualized approaches, while emphasizing the importance of supporting and including people with disabilities (Munthe, 2015).

If carrier screening becomes normalized and a routine part of the preconception or prenatal care, opportunities for deliberation may be limited and decisions might be uninformed (Henneman et al., 2016a; Nakou, 2021; Seavilleklein, 2009). Similarly, decisions to use IVF or have an elective abortion could become more routine and the perceived normalization of these options can undermine people's abilities to think critically about their reproductive options and ensure that the choices they make reflect their own personal values and interests (Li. Dive & Newson, 2020; Henneman et al., 2016b; Perrot & Horn, 2022). There are some concerns in the literature that the routinization of carrier screening and of procedures such as IVF or abortion that can follow may undermines the moral status of human embryos and foetuses (G. M. W. R. De Wert et al., 2011a). Some prospective parents might experience emotional harms related to carrier screening, IVF, or abortion, such as feelings of blame, regret, and anxiety (De Jong et al., 2010). Further, decisions to pursue IVF, PGD, or abortion each come with their own set of physical, psychological, and financial risks to patients.

Finally, there are significant ethical concerns related to the collection, use, and disclosure of genetic information. While genetic information can be de-identified by removing health information, anonymized DNA could be still be re-identified using genetic databases and this is concerning for privacy and confidentiality of genetic information (Parobek et al., 2021). Privacy risks are higher for private or direct-to-consumer tests, where privacy policies may be unclear or insufficient (Office of the Privacy Commission of Canada, 2017).

In terms of disclosing genetic information, there are ethical questions about whether individuals are morally obligated to disclose the results of genetic testing to family members that may also be a carrier for a genetic condition. The American College of Obstetricians and Gynecologists recommends that patients be encouraged to inform relatives of the risk and the availability of carrier screening (Romero, Biggio, et al., 2017). Ethical questions also arise concerning whether there is an obligation to disclose genetic information to future offspring. Canada recently passed legislation to help protect individuals against genetic discrimination (Genetic Non-Discrimination Act, 2017). However, there may still be risks related to the storage or use of one's genetic information (CADTH, 2019).

Different reporting models can also raise concerns about the right to access one's genetic information. For example, some carrier screening programs only disclose information if there is a risk to the couple planning to have a child. In some places, carrier screening programs only report the results where both individuals in a couple are carriers for particular genetic conditions (Romero, Biggio, et al., 2017). This means that some individuals who are carriers of a recessive or x-linked condition may not learn about their carrier status if their partner is not a carrier. Some argue that genome sequencing that is administered through the health system can benefit society and people who use it have an ethical obligation to share their health information. They argue that the use of genomic data for the advancement of medical knowledge should be permitted without explicit consent and that international and other bodies should be granted access to data set.(Johnson et al., 2020)

A related concern with carrier screening, particularly with whole-genome sequencing, is that individuals might also experience harm from secondary or incidental findings from carrier screening. For example, they might learn information that could impact their own health or the health of their relatives. Some people maintain that clinicians and laboratory personal have fiduciary duties to prevent harm and warn patients in the consent process about the possibility of incidental findings from screening tests (Green et al., 2013). Test results that report a variation in a gene that has uncertain or unknown significance can leave individual and/or their future offspring in state of "genetic purgatory" which can cause suffering or anxiety (Hoffman-Andrews, n.d.)

ii. Public Health Rationale

Public health is defined as "organized efforts to keep people healthy, prevent injury, illness, and premature death" and it includes a variety of services, programs and policies aimed and promoting and protecting the health of a population (Feinleib, 2001). On the surface, public health aims to address the health or groups or populations, but, as Newson and Dive 2021 argue, public health interventions are interdependent with the individuals who belong to a given population. They suggest that public health ethics is grounded in the values of equity, reciprocity, and solidarity. Equity refers to fair opportunities for each person to access and attain health resources for genetic, socio-environmental and economic determinants of health varying according to individuals, families and social or societal groups. Reciprocity refers to obligations due to others or expected from others are taken into account and acted upon by individuals, groups, or public authorities. Solidarity describes a relationship between individuals or health authorities who recognize a commitment to similar values or goals. Each of these values draws attention to relational and social aspects of public health.

Supporting public health goals, including the reduction of the prevalence or severity of disease within a given population, is the second rationale given in support of carrier screening programs (G. M. W. R. De Wert et al., 2011b; Lisa Dive & Newson, 2021c; Henneman et al., 2016a; Kihlbom, 2016). The public health framing of carrier screening helps to highlight broader social and systemic ethical issues that can arise in the context of carrier screening.

Ethical Benefits

In the literature, carrier screening is described as benefitting public health efforts in three distinct ways: the reduction of disease prevalence; the reduction of disease severity; and cost-effectiveness. First, the reduction of disease prevalence means that the implementation of carrier screening may reduce the number of people who produce a genetically-related child with genetic conditions. The value placed on reducing disease will depend how prevalent a particular genetic condition is within a given community and the harms associated with that condition. In some communities with high burden of disease, population level prevention is the primary aim of carrier screening (Henneman et al., 2016a). Some authors argue that there are moral obligations to use carrier screening to help reduce the incidence of certain genetic conditions, such as spinal muscular atrophy, so that suffering or harm can be prevented (Gyngell et al., 2020).

Second, a public health approach to carrier screening aims to reduce the severity of or harm from a disease or condition by increase opportunities for earlier interventions or planning (Li. Dive & Newson, 2020). If information about a recessive genetic condition is obtained through carrier screening, prospective parents can plan and prepare for a child with a disability. For example, they can arrange access to early treatment or interventions that can reduce the severity of the genetic condition. Carrier screening can extend the benefits of treatment and intervention for certain genetic conditions and also help to reduce the time to diagnosis for children born with certain genetic conditions (Henneman et al., 2016b; Kingsmore, 2012). Because some diseases are more prevalent in certain populations, the benefits of carrier screening use for early detection and treatment may have a greater benefit for certain ethnic groups.

Third, there are potential costs savings or efficiencies related to carrier screening programs. The economic analysis in this HTA found that universal carrier screening programs are associated with cost savings. Cost-effectiveness of long-term carrier screening programs exceeded the rate of cost savings for short-term programs. Continued increases in cost savings may be expected as DNA sequencing technologies improve and the cost of carrier screening is reduced and the costs of novel therapies for treating rare genetic diseases increase (Chokoshvili et al., 2018). In addition, carrier screening can help to reduce the cost of diagnosis for certain disease by implementing carrier screening to help with early detection instead of using more expensive types of testing (Kingsmore, 2012).

Ethical Challenges

There are several ethical concerns that emerge in the context of public health rationales for carrier screening programs. One set of challenges relate to the individual and social meanings and values ascribed to "disability" in general and to particular genetic conditions or diseases. Some people suggest that carrier screening can serve to mark certain lives as either valued or devalued. (Kirk et al., 2021; Thomas & Rothman, 2016). A key concern with public health justifications for the implementation of carrier screening programs is related to the messaging about the value of the lives of persons with particular disabilities the particular genetic condition that is screening for. Decisions about which genetic conditions are included in carrier screening testing raise ethical issues. Although criteria for included genetic conditions have to do with the severity and early childhood onset of the diseases, there are disagreements about what should be included and who decides. Some disability theorists suggest that carrier screening and related practices "express" negative views of people with disabilities (expressivist argument) (Kaposy, 2022). Although this HTA considers a carrier screening program for four types of recessive genetic conditions, there are considers about "specification creep" whereby more genetic conditions are added to testing panels (De Jong et al., 2010). Whole-genome sequencing raises additional ethical challenges for the meaning and value ascribed to genetic information or conditions. Kirk et al 2021 argue that gene selection for carrier screening panels should be a dynamic process with ongoing review and refinement.

Others disability theorist argue that carrier screening aimed at the reduction of disease prevalence is a type of eugenics. "Eugenics" is defined as "practices and policies designed to promote the reproduction of people with desired attributes—and, thus, avert the reproduction of people with undesired attributes (e.g., people with disabilities)" (Thomas & Rothman, 2016). Some theorists are concerned that cultural eugenics could occur within populations that have higher rates of carrier screening (L Dive & Newson, 2021). Many disability rights activist believe that public support for carrier screening and subsequent abortions based on disability are fundamentally in tension with the goals of the disability rights movement (Parens & Asch, 2003). However, some disability theorists suggest that being able to specify the genetic bases of disability, and distinguish them from other causative factors, will contribute to a fuller understanding of disability and a better response to disabled people (Scully, 2008). Concerns related to eugenics and ableism may be further complicated by the intersection of oppressive social forces, such as racism. A recent CADTH report on carrier screening for cystic fibrosis, fragile X syndrome, hemoglobinopathies, and spinal muscular atrophy, describes the racist history of carrier screening programs (CADTH, 2021). Attention to the social context and biases around disability and other axes of identity is important for understanding the potential implications of carrier screening. This might be especially true in the context of BC where there is a long history of eugenic politics and practices and mistrust of medical systems within Indigenous, Asian, Black and other communities (Claxton et al 2021). This social context can influence the perception and impact of carrier screening programs. Newson and Dive 2021 suggest that it is important to address the perceived eugenic potential of carrier screening and to pay attention to both individual freedoms and social context.

The cost-analysis calculations to determine cost savings or effectiveness of carrier screening programs also raises ethical concerns. Specifically, some economic analyses, such as the one in this report, use

QALY (quality adjusted life years) or DALY (disability adjusted life years) as outcomes of cost-utility analyses. QALY aim to measure the value of particular health outcomes that include both the length of life and the quality of life (Prieto & Sacristán, 2003). A common belief is that disability is bad for the person who is disabled and that it has a negative effect on their well-being on well-being. However, some theorists assert that disability is has little or no impact on how well a person's life goes and the most negative aspects of life with a disability are caused my societal attitudes and practices (Stramondo, 2021). Individuals living with a disability and those living without that disability would probably place different values on the quality of life when living with a disability, yet there is debate about which perspective should take priority when adopting a QALY framework (Whitehurst & Engel, 2018) People suggest that the use of QALY in cost-utility evaluations is problematic and ableist and may lead to the systematic underestimation of the value of life-extending treatments (P. Schneider, 2022).

Another ethical concern evident when looking at carrier screening from a public health rationale are challenges related to Big Data. Carrier screening, especially whole genome sequencing necessarily involves huge amounts of genetic information about individuals and populations. This genetic information has considerable value in the medical and genetic research contexts and there are important questions related to the ethical collection, use, and transfer of this information, especially with respect to private carrier screening or direct-to-consumer programs. CADTH recently published report on ethical considerations related to genome-wide sequencing (CADTH, 2019). While a robust discussion of the ethical issues related to whole genome sequencing is beyond the scope of this report, identifying ethical issues that are relevant to carrier screening and implementing strategies to address these concerns would be important for the ethical implementation and provision of a carrier screening program.

A further consideration related to the public health rationale for carrier screening relates to the broader impact on a province's healthcare system. One example of this is the relationship between carrier screening and medical tourism. Provinces such as Ontario and BC see a large number of medical tourists, including many who travel to Canada for the purposes of giving birth or as intended parents entering into surrogacy arrangements. Canada is an attractive destination for reproductive tourism because of citizenship rules that allow babies born in Canada to easily receive Canadian citizenship regardless of the citizenship of their parents (Favaro & Flanagan, 2019). It is also a top destination for surrogacy (Motluk, 2018) and cost-savings related to pregnancy might be attractive for some intended parents. It is possible that a universal publicly-funded carrier screening program might become an additional benefit of reproductive tourism.

Discussion and Concluding Remarks

In this ethics report, two rationales for the implementation of carrier screening that dominate the literature on this topic were explored. While these aims were considered separately, ethical benefits and challenges at the individual, social, and systemic levels are interrelated. The ethics of carrier screening programs should consider the benefits and challenges related to *both* reproductive autonomy and public health goals (Lisa Dive & Newson, 2021a; Plantinga et al., 2016). The identification and understanding of these benefits and challenges can highlight opportunities and strategies for the ethical implementation and provision of carrier screening programs. From an ethics perspective, it is important

to include and prioritize the voices and perspectives of the people impacted by decisions about carrier screening in the recognition of opportunities and the development of strategies to address ethical issues. In terms of engagement, a mixed-methods strategy to support informed debate and participation of a large number of people can supporting meaningful public participation in the decisions about a publicly-funded carrier screening program (Lopes et al., 2020). There is ethical and practical value in being transparent about the reason for funding the program. Transparency about the reasons or goals related to a publicly-funded health program can help to build and maintain public trust and government accountability. Clearly articulating the goals of a carrier screening program will help to set corresponding measures for success and establish and maintain government accountability for the success of the program.

In addition, it is important for decision makers to keep the following ethical obligations in mind.
First, social context matters. It is important to recognize the current pressures, norms, biases, and ideologies that can shape, support, or hinder individual and collective decision-making. For example, increasing social awareness and understanding about disabilities, as well as supporting the availability and access of related health and social services can make it easier (or possible) for people to make decisions that align with their own values and interests. These efforts can also help to address concerns related to disability critiques of carrier screening.

Second, healthcare stewardship, meaning a broad over-arching responsibility over the functioning of the health system as a whole and ultimately, over the health of the population, should be part of decision making about a carrier screening program. This means that decisions about carrier screening are necessarily within the context of decisions about healthcare funding more generally and decisions about short or long-term public funding for a carrier screening program should consider the current healthcare system pressures and priorities.

Third, the ethical development, implementation, and provision of carrier screening programs should align with relevant provincial and federal laws. For example, this might include the Health Care (Consent) and Care Facility (Admission) Act; the Freedom of Information and Protection of Privacy Act; the Personal Information Protection Act; The Genetic Non-Discrimination Act; and the Assisted Human Reproduction Act. Decisions and actions should also align with relevant organization policies, and professional guidelines.

Finally, ethical decision making about the implementation of a public carrier screening program should adopt a framework for ethical decision making, such as Accountability for Reasonableness (A4R). A4R is a procedural framework for ethical and fair decision making that helps to guide ethical and fair decisions about priority setting. Four conditions are included in this framework: relevance, publicity, appeals, and enforcement. This framework supports decision makers and stakeholder to establish an explicit, defined, and an agreed upon process for making decisions, even when they may not agree on the substantive values related to the options they consider (Daniels & Sabin, 2008; Faden et al., 2022).

This ethics analysis has identified several substantive and procedural values related to the implementation, provision, and use of universal publicly-funded carrier screening program for cystic fibrosis, fragile x syndrome, hemoglobinopathies, and spinal muscular atrophy, with the aim of supporting ethical deliberations about carrier screening programs. The information is intended to support ethical deliberations about publicly-funded carrier screening programs across Canada but with particular emphasis on British Columbia and Ontario.

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