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Access to genetic testing for rare diseases: Existing gaps in public-facing information

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Abstract

Genetic testing plays an increasingly important role in the diagnosis and potential treatment of inherited and rare conditions, such as aniridia—a disease that leads to abnormal eye development, as well as in health research on these conditions. As genetic testing is increasingly sought for accurate and early diagnosis of rare genetic disorders and in the context of direct-to-consumer genomics, it is critical to examine the public-facing information about access to these services and reimbursement policies. We conducted a targeted policy and public-facing resource search. Our analysis of resources available for the patient community revealed that there is very little practical guidance available about access and reimbursement for genetic testing for rare diseases. Greater clarity in public-facing resources about genetic testing would be beneficial to the patient community as it would promote informed choices about the procedure, mitigate potential harms associated with lack of information and enable patient engagement in their own health care.

KEYWORDS

aniridia, genetic testing, patient information,

Key points

- Genetic testing is crucial for diagnosis and treatment of inherited and rare conditions.
- Information about access to genetic testing and reimbursement for it is not easily available in public-facing resources.

- The patient community would benefit from greater clarity in available information about genetic testing, because it would facilitate informed decision-making and promote patient engagement in their care.

KEYWORDS
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INTRODUCTION

Although the term "rare disease" implies low prevalence, there are currently over 10,000 monogenetic inherited disorders that combined affect millions of individuals worldwide (Priori et al., 2009). Aniridia is one such rare condition: a genetic eye disorder that involves abnormal development of the iris and other parts of the eye, with long-term complications including vision loss and associated gene syndromes. Aniridia occurs one in 40,000–100,000 births, therefore it is not a part of routine neonatal or prenatal screening programs. It is diagnosed by an ophthalmological examination, however, *PAX6* mutation must be detected to confirm diagnosis, as the clinical phenotypes vary between patients (Richardson et al., 2016). Additionally, while some symptoms of aniridia are present at birth, other symptoms develop later in life and genetic testing can help determine the patient's prognosis (Richardson et al., 2016). In this paper, we will use the term *genetic testing* when referring to the *PAX6* gene sequencing, which is crucial for aniridia diagnosis. We use the terms *whole-genome* or *whole-exome sequencing* when referring to the comprehensive analysis of the entire genome or exome which are significantly more costly and less accessible than the previously mentioned methods.

Aniridia is a progressive disease, involving multiple vision pathologies that vary in severity (Orphanet: Isolated aniridia, n.d.). Current treatment for patients with aniridia includes the management of symptoms associated with the condition, as well as progressive complications. Among interventions for aniridic eyes are monitoring and relieving high eye pressure and light sensitivity, treatment of cataracts, glaucoma and keratopathy (Lee et al., 2008). These treatments can only slow the progression of the disease—however research is underway to address the underlying causal mutations in the transcription factor *PAX6*. For aniridia as well as many other inherited conditions, genetic testing is playing an increasingly significant role in diagnosis and management of the disease. Two in three individuals diagnosed with aniridia have inherited the condition from their parent and specific mutations can be associated with various clinical outcomes (Richardson et al., 2016). Specific gene mutations may also be inclusion criteria for participation in health research and as such may determine eligibility for specific research opportunities (Hingorani & Moore, 1993) and potential future therapy.

In Canada, access to genetic testing varies greatly across health conditions and even between provinces and territories. The aim of this project was to characterize the landscape of public-facing information about access and reimbursement policies for genetic testing for aniridia in Canada.

MATERIALS AND METHODS

We conducted a targeted search of Canadian policies and public-facing information about access and reimbursement for genetic testing for aniridia. Our search strategy (Table 1) targeted freely accessible, English-language information available in the following resources:

TABLE 1 Search strategy

Provincial and territorial policies or guidelines	Provincial/territorial health authorities' websites
Federal policies or guidelines	Health Canada
Private insurance coverage	Sun Life
	Manulife
	The Great West Life Assurance Company
	Desjardins Insurance
	SSQ Insurance
	Green Shield Canada
	Pacific Blue Cross
	Medavie Blue Cross
	Industrial Alliance
	Alberta Blue Cross
Private companies' offers	Life Labs
	23andMe
	GenomeMe
	Molecular You
Non-profit foundation information	Canadian Aniridia Foundation
	Choosing Wisely Canada
	Genetics Education Canada
	Canadian Association of Genetic Counsellors
	The Foundation Fighting Blindness

1) Des Libris, an online database of Canadian policies;
2) Federal (e.g., Health Canada) and provincial (e.g., BC Ministry of Health) government websites;
3) Regional health authorities in Canada (e.g., Vancouver Coastal Health);
4) The top ten private health insurance companies (Benefits Canada.com, n.d.),
5) Private genetic testing companies (e.g., 23ande); and
6) Non-profit organizations related to aniridia (e.g., the Canadian Aniridia Foundation).

The search terms used were “aniridia,” “genetic,” and “rare diseases”. All pages of search results were examined. When a search returned over 1000 results, we narrowed the search to include the exact word or phrase, combined keywords or refined the results by theme (e.g., health). Where there was no search option available on the website, we manually evaluated the website for information related genetic testing for aniridia. Provincial/territorial health department websites were also manually mined to determine medical benefits covered under the provincial/territorial plan. For insurance websites, we assessed the most basic individual insurance plan if the policy was available. A full summary of the websites visited, search results and dates of access can be found in Table S1.

RESULTS

The search of DesLibris yielded two documents relating directly to our research question (Gauvin & Wilson, 2012; Waddell, n.d.). An evidence brief from 2012 ("Coordinating the Use of Genetic Tests and Related Services in British Columbia") provides a comprehensive overview of genetic testing in BC, Canada. At that time, the authors found no information on which specific genetic tests are covered by the Medical Services Plan (Gauvin & Wilson, 2012). The second publication, "Examining the Public Provision and Funding of Clinical Genetic Tests," is from 2017 and aimed at investigating the availability of genetic tests in different jurisdictions across Canada, Australia, New Zealand, UK, and United States as well as examining the factors taken into account when deciding which genetic tests will be covered (Waddell, n.d.). Regarding the access and reimbursement for genetic testing, the synthesis reports that there is little information available for each jurisdiction, with most places subsidizing or covering the service when the test can advance treatment or is considered a medical necessity, but there is a lack of a formal list of available/covered tests (Waddell, n.d.). The American Academy of Ophthalmology Task Force on Gene Sequencing (Stone et al., 2012) offered specific recommendations on when to offer genetic testing, that is, to "patients with clinical findings suggestive of a Mendelian disorder whose causative gene(s) have been identified."

The search of Canadian federal and provincial government websites yielded similar results. None of the health agencies' publicly available content in the 85 websites we consulted included mentions of genetic testing for rare diseases. Information regarding access and coverage of genetic testing is limited to a description that physicians need to provide a referral for laboratory tests and services. Health Canada resources referred to Orphanet (www.orpha.net/consor/cgi-bin/index.php), an online portal for rare diseases. This site lists laboratories from around the world that conduct genetic testing for rare diseases. According to our search on Orphanet (conducted in November 2018) only one laboratory in Canada (Alberta Children's Hospital) does sequencing only for the *WT1* mutation (WAGR syndrome), not for the *PAX6* mutation. Eight other laboratories in Canada offer cytogenetics/FISH services for WAGR syndrome, but not sequencing. Manual search of laboratory service providers such as LifeLabs showed, however, that complete genome sequencing as well as specific *PAX6* tests are available at any of their locations (with a referral from a physician). Samples are drawn at LifeLabs locations and then are shipped to Germany for testing.

Of the top 10 insurance companies in Canada (Benefits Canada.com, n.d.) Sun Life, the Great West Life Assurance Company, Desjardins Insurance, and Green Shield Canada cover laboratory/diagnostic services. Pacific Blue Cross covers services that are not included in the government plan. None of the private insurers' websites mentions genetic testing, rare diseases, or aniridia.

Direct-to-consumer genetic testing companies (23andMe, Molecular You, Genome Me) did not include tests for aniridia/*PAX6* at the time of search (November 2018).

The Canadian Aniridia Foundation website does not provide details on access or reimbursement for genetic testing. The Fighting Blindness Canada website has a section that addresses questions about genetic testing. It provides information about access to genetic testing services via a genetic counselor and acknowledges that there is a limited number of ocular genetics specialists available in Canada. Information about coverage of the tests is limited, as the conditions for coverage differ between the provinces and territories.

The full data set extracted from the consulted websites is available in Table S1.

DISCUSSION

Our policy and public-facing resource search revealed that the information available on access to and reimbursement of genetic testing for rare diseases like aniridia is scarce. This finding is consistent with the North American literature on genetic testing for rare diseases. Chiang et al. contrast the rapid development and increased availability of genetic testing with the lack of legislative efforts and the need for introduction of specific guidelines (Chiang et al., 2015). Somerville and Allingham-Hawkins (2010) point out that because of the division of responsibility for health services among provincial and federal institutions there are no unified guidelines about the delivery of genetic testing in Canada. The authors report that while the *Canada Health Act* protects the access to hospital and diagnostic services across Canada, the federal/territorial governments regulate whether and how genetic testing is funded, which results in varied access and pricing of these services in the country.

The lack of clear information and guidance on public health authorities' websites may result in patients relying on information available in the media. Benjaminy and colleagues (2015) point out that in popular broadcasting of research about gene therapy for ocular disease, research is often presented as therapy which may result in initial confusion when making decisions to take part in research trials (Benjaminy et al., 2015). The authors mention organizations that contribute to the communication and education about genetic ocular diseases, such as Fighting Blindness Canada (www.fightingblindness.ca), which among other services connects patients to clinical trials and specialists that focus on their condition (Benjaminy et al., 2015). Patient registries and natural history studies increasingly play a role in bringing together patients with rare diseases and building a sense of support and community (Boulanger et al., 2020). Once the patients obtain their diagnosis, they get the opportunity to connect with other individuals with the same condition and engage in peer support (Doyle, 2015). Participating in patient registries and research efforts can be empowering, as the patients get actively involved in their care and contribute to better understanding of their specific condition (Smith et al., 2021). One potential challenge for patients with rare diseases is distinguishing between legitimate clinical trials and trials that do not meet safety or ethics standards but are still searchable in databases like clinicaltrials.gov. Fighting Blindness warns against attempts to abuse patients' hope for a cure to gain financial profit (Fighting Blindness Canada, n.d.).

The lack of information about access to and reimbursement for genetic testing may prevent patients from seeking these potentially beneficial services. Some benefits from genetic testing for inherited eye diseases include diagnostic confirmation, medical surveillance for complications, reduction of anxiety and medical costs, more treatment options, such as gene therapy, participation in clinical trials and better family planning (Chiang et al., 2015; Drack et al., 2010; Gillespie et al., 2014; Stone, 2007; Wiggs & Pierce, 2013; Zanolli et al., 2014). For instance, the presence of *PAX6* mutations in an individual may affect person's reproductive decisions, as two in three aniridia patients have an affected parent, or it could inform a predictive prenatal test (Richardson et al., 2016). While there are many potential benefits of genetic testing, it is also critical that the risks and ethical issues of these diagnostic tests are communicated to the patients. Thus, easily accessible genetic counseling is crucial for patients considering and undergoing genetic testing. One potential solution to address some of the access barriers, especially in rural and remote areas, is to expand the availability of telehealth and online counseling solutions (Cohen et al., 2019). The transformation of healthcare systems due to the COVID-19 pandemic accelerated the introduction of telehealth services across different settings (Wosik et al., 2020). As a result, it is likely that accessibility of virtual counseling will also increase. Some other known issues explored in the literature regarding genetic testing decision-making include applicability of genetic testing to complex disorders, predictive testing for untreatable conditions, genetic

discrimination, prenatal sequencing, and abortion (Combs et al., 2013; Mezer & Wygnanski-Jaffe, 2009; Zanolli et al., 2014).

While there have been efforts to develop guidelines for providing genetic test coverage in Canada in fields such as oncology and epilepsy (Butts et al., 2013; Jain et al., 2019; Petit et al., 2008), we found a clear gap in the lack of unified policy in public-facing sources and of detailed policies for relevant jurisdictions (e.g., provinces). This issue is further compounded by the challenge of providing patients with information that is up-to-date. It is also important to note that while there are gaps in information about access to and reimbursement for sequencing of specific genes or gene panels, some individuals with rare diseases require more comprehensive testing, such as whole-genome or whole exome-sequencing. This type of testing which is crucial for identifying a number of diseases, obtaining a diagnosis and planning treatment is currently not reimbursed in Canada under any health plan.

An additional barrier to whole-genome and whole-exome sequencing, as well as targeted sequencing tests is a limited number of laboratories in Canada with the appropriate expertise and equipment to perform these types of tests. As revealed by our search, many laboratories (such as LifeLabs) outsource the tests to other countries which increases the overall costs. Consequently, organizations such as Genome Canada are working on developing a national strategy to make whole-genome sequencing more accessible to Canadian patients (Genome Canada, Genome Canada launches national initiative to bring precision health to patients, n.d.). The rapid pace of development of genetic testing for rare diseases may result in frequent guideline changes that would have to be captured by public-facing resources. Ensuring current information is easily available to patients requires commitment to ongoing updates and oversight.

LIMITATIONS

This study is not without limitations. Due to the gap in publicly available policies regarding access and reimbursement of genetic testing for rare diseases, the focus of our research question shifted to consider public-facing information about genetic testing. Additionally, we limited our search to public-facing information extracted using keyword combinations and targeted types of resources (Table 1)—as such, our sample may exclude items returned when doing a query in a search engine. Finally, our sample is limited to English-language resources—future work in this area will benefit from expanded inclusion criteria.

CONCLUSION

Overall, our search yielded very little practical guidance at the policy level for members of the patient community who may have questions about genetic testing for aniridia. We found that there is a need for clearer and more easily accessible information about genetic testing, especially on public-facing health authorities' websites. It would not only benefit the aniridia patient community, but also other patients with rare diseases and those who have not yet been diagnosed. In 10 out of the 13 provinces and territories, we found that genetic testing was covered by provincial or territorial plans if it was considered medically necessary. However, no information was available about how these terms are defined and whether sequencing for *PAX6* is considered a medical necessity by physicians. We also found conflicting evidence about access to genetic testing for aniridia, which may cause confusion for aniridia patients when debating taking the test. Faced with lack of resources and confusing information, patients with aniridia may feel limited in their choices, which in turn may result in them enrolling in research studies specifically to obtain access to genetic

sequencing. Clarity around access and reimbursement would help address some of the ethical issues associated with genetic testing, including access to genetic counseling, empowerment of patients by greater awareness of treatment options and prognosis, as well as better personal planning.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

No human participants were involved in this study.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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