Ontario Health

Genetic Testing for Familial Hypercholesterolemia: Recommendation

Final Recommendation

Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding:

- Genetic testing for familial hypercholesterolemia for people suspected to have familial hypercholesterolemia or people who have a diagnosis of familial hypercholesterolemia based on accepted diagnostic criteria (i.e., Canadian Cardiovascular Society, Simon Broome Register, or Dutch Lipid Clinics Network)
- Genetic cascade screening for familial hypercholesterolemia for people who choose to undergo screening and who are biological relatives of people with a genetically confirmed diagnosis of familial hypercholesterolemia

Rationale for the Recommendation

The Ontario Health Technology Advisory Committee has reviewed the findings of the health technology assessment[1] and the recommendation of a subcommittee, the Ontario Genetics Advisory Committee.

The Ontario Health Technology Advisory Committee made its recommendation after considering the clinical and economic evidence and patient preference and values. The clinical evidence supports that people with a genetically confirmed diagnosis of familial hypercholesterolemia (FH) may have increased use of cholesterol-lowering treatments and have lower total cholesterol and low-density lipoprotein cholesterol (LDL-C) blood levels, possibly due to treatment changes or improved treatment adherence. Additionally, genetic cascade screening for FH may help identify people at risk for cardiovascular disease.

The economic evidence supports that genetic testing for FH is cost-effective for people suspected of having, or clinically confirmed to have, FH. While genetic and lipid cascade screening are both cost-effective compared with no screening, the committee weighed in favour of genetic over lipid cascade screening because of its improved accuracy. Genetic testing for FH in people suspected of having or clinically confirmed to have FH would likely result in cost savings to the province. While the province would likely incur additional costs to publicly fund the genetic cascade screening tests for biological relatives, the committee recognized the potential for cost savings to the province if a reduction in cardiovascular disease was realized in those screened.

The evidence regarding patient preferences and values shows that people with high cholesterol levels perceive positive impacts of having a genetically confirmed diagnosis of FH on (1) their medical

management, and (2) their ability to inform family members, who then have the option to discover their own FH status through genetic cascade screening. Similarly, genetic confirmation that a person does not have FH is also a perceived benefit of testing. However, individual desire for autonomy and privacy is an important consideration in the implementation of genetic cascade screening, and a person's choice to undergo screening should guide practice.

Decision Determinants for Genetic Testing for Familial Hypercholesterolemia

Overall Clinical Benefit

Effectiveness

How effective is the health technology/intervention likely to be (taking into account any variability)?

Genetic testing is likely to improve four outcomes measuring treatment change (increased statin dose, initiating statin treatment, adding ezetimibe to existing LDL-C lowering therapy, and remaining untreated with cholesterol lowering drugs), and is likely lead to a reduction in LDL-C blood level and total cholesterol levels (Grading of Recommendations Assessment, Development, and Evaluation [GRADE]: Moderate). Additionally, it may lead to a change in treatment regimen and increased use in cholesterol-lowering drug regimens; it may also allow for LDL-C targets to be reached after using cholesterol-lowering drugs (GRADE: Low).

Safety

How safe is the health technology/intervention likely to be?

Genetic testing for FH requires a blood test. Blood testing is associated with minimal to no harm. Genetic testing for FH provides information to a person about their risk of cardiovascular disease. This information may be helpful to some people. It may also cause anxiety in some people.

Burden of Illness

What is the likely size of the burden of illness pertaining to this health technology/intervention?

About 1 in 250 Canadians have the heterozygous form of FH. FH can increase a person's risk for cardiovascular disease (i.e., heart attack or stroke, or even premature death).

Need

How large is the need for this health technology/intervention?

FH is underdiagnosed and undertreated in Canada. A genetic confirmation of FH can support treatment with publicly funded *PCSK9* inhibitors.

Patient Preferences and Privacy

Patient Preferences and Values

Do patients have specific preferences, values, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment?

Participants valued having a genetically confirmed diagnosis of FH due to their perceived ability to access new and effective treatments and inform family members of the risk of the condition.

Autonomy, Privacy, Confidentiality, and/or Other Relevant Ethical Principles as Applicable

Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles that are relevant to this assessment?

FH genetic testing aligns with current practice of diagnosis through non-genetic tests. Individual preference for autonomy and privacy has implications for cascade testing, as participants may have concerns about confidentiality and may not want to receive genetic information or have it shared with family members.

Equity and Patient Care

Equity of Access or Outcomes

Are there disadvantaged populations or populations in need whose access to care or health outcomes might be improved or worsened that are relevant to this assessment?

Currently, there is only one laboratory in Ontario that provides genetic testing for FH. As a result, there may be inequity in access to the service. Additionally, one laboratory may not be able to meet the additional demand for testing that may result from expanding access to genetic screening.

Patient Care

Are there challenges in the coordination of care for patients or other system-level aspects of patient care (e.g., timeliness of care, care setting) that might be improved or worsened that are relevant to this assessment?

Coordinating care between clinical areas involved in the care and management of people with high cholesterol will be required to enable the successful implementation of both genetic testing and genetic cascade screening of FH.

Cost-Effectiveness

Economic Evaluation

How efficient is the health technology/intervention likely to be?

At commonly used willingness-to-pay values of $50,000 or $100,000 per quality-adjusted life-year (QALY) gained, genetic testing for individuals with a clinical diagnosis of FH would be dominant (less costly and more effective than usual care). Our economic evaluation suggested that, compared to a clinical diagnosis based on lipid testing only, genetic testing for individuals with a clinical diagnosis of FH would reduce the number of FH diagnoses, lead to fewer cases of cardiovascular disease, and improve QALYs, while lowering costs.

When comparing genetic cascade screening strategies to no cascade screening for biological relatives of genetically confirmed FH index cases, our model suggested that the most likely estimate of the incremental cost-effectiveness ratio is between $50,220 and $58,390 per QALY gained.

Feasibility of Adoption Into Health System

Economic Feasibility

How economically feasible is the health technology/intervention?

The cost of genetic testing for FH is $490 per person. We estimated that publicly funding genetic testing for individuals with a clinical diagnosis of FH in Ontario would lead to a total cost saving of $141 million over the next 5 years.

For relatives of genetically confirmed FH index cases, we estimated that publicly funding genetic cascade screening would lead to a total additional cost of $73 million over the next 5 years.

Organizational Feasibility

How organizationally feasible is it to implement the health technology/intervention?

Genetic testing for FH is already publicly funded in Ontario as an out-of- country service. For FH diagnosis, we expect most of the processes to remain the same if the service is to be repatriated to Ontario. There may be costing and ethical challenges in implementing cascade screening.

Reference

(1) Ontario Health. Genetic testing for familial hypercholesterolemia: a health technology assessment. Ont Health Technol Assess Ser [Internet]. 2022 Aug;22(3):1–155. Available from: https://hqontario.ca/evidence-to-improve-care/health-technology-assessment/reviews-and-recommendations/genetic-testing-for-familial-hypercholesterolemia

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