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Environmental Scan of Genetic and Genomic Biomarker Testing Assessment Frameworks, Processes, and Inventories in Cancer Care

Key Messages

What Is the Issue?

- Precision medicine is rapidly emerging and increasingly being adopted in cancer care. Precision medicine relies on testing for biomarkers, such as genes or proteins, to provide information about disease status and likely response to treatment. However, approaches to evaluating and implementing testing for various biomarkers are not standardized and vary between jurisdictions in Canada.

What Did We Do?

- This Environmental Scan included a literature review and consultations to identify and summarize existing assessment frameworks, processes, and guiding principles that inform the implementation of or funding decisions for biomarker testing in cancer care.
- We summarized and compiled key concepts from the frameworks, literature from within and outside of Canada, and consultations for guiding principles, assessment criteria, and decision-making processes.
- We also identified and described existing inventories, databases, and lists of genetic and genomic biomarkers for which testing is currently available or is being funded in cancer care in jurisdictions across Canada.

What Did We Find?

- Four guiding principles were identified through the literature and consultations:
  - health rights of individuals and communities
  - transparency and accountability
  - collaboration, cooperation, and engagement
  - social justice and equity.
- Three categories of assessment criteria were identified:
  - evidentiary (i.e., clinical condition, test considerations, characterization of available evidence, and personal considerations)
  - implementation (i.e., health system context, health care context, and social and ethical values)
  - decision-making (i.e., deliberation and recommendations, and priorities for future research).
- Five categories or steps within a decision-making process were identified:
  - test nomination
  - evidence reviews and impact assessment

Key Messages

    - deliberation and recommendations
    - communication and engagement
    - implementation.
- Biomarker assessment and decision-making processes vary substantially across jurisdictions in Canada, with some implementing structured systems that emphasize reviews of evidence and clinical guidelines through a centralized evaluation process, while other jurisdictions operate a more decentralized process that may be driven by clinical demand.
- In some jurisdictions, there are key distinctions between decision-making for companion diagnostic testing (in support of targeted drug therapies) and other biomarker testing (used for prognostic or predictive purposes or in support of nondrug therapies).
- Funding approaches vary, with some jurisdictions allocating specific budgets for biomarker tests, while others integrate requests into broader laboratory or health budgets.
- Many provinces in Canada maintain inventories or lists of available biomarker testing, with some more comprehensive and current than others, and some intended for internal use by health providers requesting tests and others also intended for access by members of the public.

What Does This Mean?

- The guiding principles, assessment criteria, and decision-making processes we compiled through our literature review and consultations can support and inform the development of a consistent and efficient approach to assessment and decision-making for biomarker testing in Canada. A consensus assessment framework could help to establish standardized assessment criteria and help to reduce inequities in availability and access to timely biomarker testing in cancer care.

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Background and Context

With the rapidly emerging field of precision medicine, more complex and promising biomarker tests are being used to identify genes, proteins, or other molecules that can help inform treatment and care, most prominently in the field of oncology. Health decision-makers across Canada make decisions about implementing or funding tests for various biomarkers that may inform cancer diagnosis, treatment, prognosis, prediction, and recurrence monitoring typically based on an assessment of which biomarkers bring the most value to patients and health systems. Nonetheless, approaches to evaluation and decision-making are variable, inconsistent, and lack transparency across several of Canada's provincial and territorial health systems,[1] which has introduced inequities in availability and access to biomarker testing and precision medicine technologies in cancer care across Canada.

To establish an understanding and begin addressing some of the inconsistencies and challenges around the assessment and implementation of precision medicine approaches in cancer care, experts and interested parties in the fields of genetic and genomic oncology were convened for a survey and round table discussion led by Canada's Drug Agency (CDA-AMC) in November 2022. The aim was to initiate discussions around the concept of a pan-Canadian framework to inform the evaluation, funding, and use of genetic and genomic health technologies, with an overall objective to identify approaches that could enable more equitable and efficient decision-making related to the implementation of genetic and genomic tests for cancer diagnosis, prognosis, and prediction of therapeutic response.

To advance this work, there is both a need and an opportunity to understand the features and characteristics of existing assessment frameworks, criteria, checklists (and other relevant tools), processes, and guiding principles that are currently being used to inform decisions about funding and adoption of biomarker testing in cancer care as well as what biomarker testing is currently available or funded in cancer care across Canadian jurisdictions.

Objectives

The key objectives of this Environmental Scan are as follows:

1. To identify and describe existing assessment frameworks, criteria, checklists (and other relevant tools), processes, and guiding principles that inform the implementation of or funding decisions for biomarker testing in cancer care, including features, characteristics, and other relevant information.
2. To identify and describe existing inventories, databases, or lists of genetic and genomic biomarkers for which testing is currently available or being funded in cancer care in jurisdictions in Canada.

The results of this Environmental Scan will be summarized and used as input for a time-limited Advisory Panel led by CDA-AMC that will be tasked with developing a standardized, consensus-based assessment framework to support consistent, efficient, and equitable assessment and access to genetic and genomic testing for biomarkers in cancer care.

Methods

An Environmental Scan was conducted to identify and synthesize existing information related to frameworks and processes that currently inform the assessment, implementation, and funding decisions for genetic and genomic biomarker testing as well as what biomarker testing is currently available or being funded in cancer care across Canada. This information was collected using a staged and iterative approach. Stage 1 comprised a limited search and review of grey literature and other published literature sources. Stage 2 focused on information collected during consultations with key informants and interested parties involved in the assessment, implementation, and funding decisions for genetic and genomic biomarker testing in cancer care in Canada. The intent was to summarize available information — not to evaluate or draw any conclusions about existing frameworks and processes or what characteristics should inform a more standardized approach. Details describing the methods are reported in Appendix 1.

Findings

Overview of the Literature Review Results

Twenty-five relevant sources were identified and included in the scan for addressing both key objectives,[1-25] with 14 addressing the first key objective (Appendix 2)[1-14] and 11 addressing the second key objective (Table 4).[15-25]

Overview of the Consultations Results

We consulted with 13 representatives from 11 jurisdictions in Canada (all provinces in addition to Nunavut) who are responsible for assessment, implementation, or funding decisions for genetic and genomic biomarker testing. Participant expertise ranged from medical oncology, community pathology, anatomic pathology, molecular pathology, and health care administration. Consultation questions focused on assessment approaches (frameworks, criteria, checklists, processes, decision-making, funding), features (including guiding principles), and inventories.

Key Objective 1: Guiding Principles, Assessment Criteria, and Decision-Making Processes for Genetic and Genomic Biomarker Testing in Cancer Care

Of the 14 relevant literature-based sources addressing the first key objective of this scan,[1-14] 5 originated from Canada[1-5] and 9 were produced outside of Canada.[6-14] One foundational source was published in 2019 (across 2 documents) and proposed a new framework for the evaluation of genetic tests, using a systematic review of frameworks for the evaluation of genetic tests as well as a Delphi process including public health experts in Italy.[10,11] The frameworks captured within this foundational source were not included or summarized individually within this Environmental Scan report; rather, the data and information reported in the 2019 publication and supplemental file were included and summarized.

Relevant data were grouped by concept (i.e., guiding principles, assessment criteria, and decision-making processes) and were abstracted from each included source, as reported. We conceptualized the

relationship between guiding principles, assessment criteria, and decision-making processes by their interconnected roles in shaping decisions about genetic and genomic biomarker testing in cancer care. Guiding principles set the foundation for what should be prioritized when making decisions, assessment criteria operationalize these principles by defining measurable factors for evaluating biomarker tests, while decision-making processes apply these criteria to ensure that test evaluations translate into policy actions in a fair and systematic way. This interconnected framework could help balance scientific evidence, ethical considerations, and resource allocation in biomarker testing decisions.

Guiding principles were identified in 6 included literature sources,[2-4,6,8,9] 2 of which described guiding principles for the same program[2,3] and were identified by 10 jurisdictions during the consultations. Criteria relevant to the assessment of genetic or genomic biomarker testing were described by 11 jurisdictions during consultations and within 10 literature sources that described 8 sets of criteria;[2-4,7,8,10-14] 4 of the sources described duplicate or supporting information for 2 relevant sets of criteria.[2,3,10,11] Processes relevant to the decision-making for the implementation or funding of genetic or genomic biomarker testing were described by 6 literature sources[1-3,5,8,13] and by 9 jurisdictions during the consultations. Details describing the included literature sources are presented in Appendix 2.

Synthesized Results

On review of the identified literature sources, 1 foundational literature source was selected for each of the 3 key concepts identified (i.e., guiding principles, assessment criteria, decision-making processes) based on relevance, breadth and comprehensiveness, and data were abstracted and tabulated from each foundational source.[5,6,10,11] The concepts from all other included literature were then mapped alongside and added to those from the foundational sources. Data from the consultations were then reviewed and integrated within the mapping exercise using the same approach. These data and information were then used to inform a set of compiled guiding principles (Table 1), compiled assessment criteria (Table 2), and compiled decision-making processes (Table 3) to represent available information and approaches. No attempt was made to appraise existing frameworks or processes or infer what characteristics should inform a more standardized approach. These compiled features and descriptions are outlined in Table 1. Additional details describing the methods for synthesis are reported in Appendix 1, and the mapping exercise results are presented in Appendix 5.

Compiled Guiding Principles

Four guiding principles were synthesized from literature: the health rights of individuals and communities; transparency and accountability; collaboration, cooperation, and engagement; and social justice and equity. A description for each compiled principle is presented in Table 1.

Table 1: Guiding Principles for Genetic and Genomic Biomarker Testing Assessment in Cancer Care

Compiled guiding principles[a]	Description
Health rights of individuals and communities	To affirm the value and fundamental right of every individual, families, and communities to the highest attainable standard of health.
Transparency and accountability	To ensure effective, reasonable, transparent, and accountable stewardship, including clarity, efficiency, consistency, timeliness, quality, value, affordability, and adaptability.
Collaboration, cooperation, and engagement	To build and foster trust, integrity, solidarity, and reciprocity among health system partners.
Social justice and equity	To promote equitable opportunities to achieve health, well-being, and the fair distribution of benefits.

[a]Guiding principles were identified in 6 included literature sources,[2-4,6,8,9] 2 of which described guiding principles for the same program.[2,3] These findings were supplemented with data collected during the consultations.

What We Heard in Canada

Equity in access, transparency, and efficiency emerged as common guiding principles in our consultations across jurisdictions in Canada. Some larger jurisdictions emphasized transparency, contributing parties' engagement, and the operational feasibility of proposed testing, while some smaller jurisdictions emphasized affordability and collaboration with referral centres or larger jurisdictions to ensure testing availability.

Compiled Assessment Criteria

Assessment criteria were selected and adapted from the mapping exercise into a set of 9 criteria across 3 domains: evidentiary considerations (including the clinical condition, test considerations, characterization of available evidence, and personal considerations), implementation considerations (including the health system context, health care context, and social and ethical values), and decision-making considerations (including deliberation and recommendations, and priorities for future research). The compiled domains, criteria, and accompanying descriptions synthesized from the literature are outlined in Table 2.

Table 2: Assessment Criteria for Genetic and Genomic Biomarker Testing Assessment in Cancer Care

Complied criteria[a]	Consideration	Description
Evidentiary considerations		
Clinical condition	• Biological plausibility • Public health benefit	Key considerations regarding the clinical condition of interest include evidence demonstrating biological plausibility of the association between the biomarker of interest and available treatment or management for the condition and public health benefit of the available treatment.

Complied criteria[a]	Consideration	Description

Test considerations	• Test effectiveness and appropriateness
	  ◦ analytic validity
	  ◦ clinical validity
	  ◦ clinical utility
		The effectiveness and appropriateness of the test, including consideration of analytic validity (i.e., the accuracy with which the test identifies the biomarker of interest), clinical validity (i.e., the accuracy with which the test identifies the condition of interest), and clinical utility (i.e., the likelihood that the test informs clinical decision-making and impacts patient outcomes).

Characterization of available evidence	• Critical appraisal	Consideration of the quantity and quality of available evidence (i.e., internal and external validity), level(s) of available evidence, and the clarity and comprehensiveness of reporting.
Personal considerations	• Indicators of health and well-being • Patient anxiety • Other considerations	The personal effects of genetic or genomic biomarker testing and the downstream impacts on health and well-being (e.g., anxiety, satisfaction) of patients.
Implementation considerations		
Health systems context	• System partner engagement • Cooperation, communication, and coordination • Economic considerations	The health systems context comprises the regulatory environment(s), decision-makers, care providers (and relationships between these parties), and health economic considerations (e.g., cost-utility, cost-effectiveness) within which testing for the genetic or genomic biomarker is being assessed for implementation.

Health care context	• Delivery models
	  ◦ level(s) of care
	  ◦ health care interventions
	  ◦ patient care pathway
	• Organizational considerations
	  ◦ alignment with organizational goals
	  ◦ demand
	  ◦ capacity
	  ◦ resource and operations management
	  ▪ information dissemination
	  ▪ education and training
	  ▪ clinical endorsement
	  ▪ clinical integration
	  ▪ quality assurance, monitoring, and control
	• Barriers and facilitators to implementation
		The health care context within which testing for the genetic or genomic biomarker is being assessed for implementation. This includes the delivery models within which testing will be provided, organizational considerations for implementing testing, and barriers and facilitators to implementation.

Social and ethical values	• Ethical, legal, and social implications • Patients' and public perspectives	Relevant considerations include equity, autonomy, privacy, and confidentiality, as well as the values and perspectives of patients and the public.

Complied criteria[a]	Consideration	Description
Decision-making considerations		
Deliberation and recommendations	• Net benefit • Cost-effectiveness • Feasibility	An evaluative process is required to weigh the evidence regarding potential benefits and harms of testing in the context within which testing is being considered for implementation.
Priorities for future research	• Evidence gaps • Research questions that require further investigation	Where evidence is lacking or is of insufficient quality to inform decision-making, priorities for future research should be outlined and proposed, including the need for real-world data.

[a]Criteria relevant to the assessment of genetic or genomic biomarker testing were described by 10 sources describing 8 sets of criteria,[2-4,7,8,10-14] with 4 of the sources describing duplicate or supporting information for 2 relevant sets of criteria.[2,3,10,11] These findings were supplemented with data collected during the consultations.

What We Heard in Canada

Some of the common assessment criteria that emerged in our consultations with jurisdictions include clinical utility, feasibility, cost-effectiveness, patient impact, and alignment with organizational goals.

Compiled Decision-Making Process

Decision-making processes were selected and adapted from the mapping exercise to inform a set of steps that could inform the assessment and decision-making process for genetic and genomic biomarker testing in cancer care. The sequential steps in the process, as compiled from the literature, include test nomination, evidence reviews and impact assessment, deliberation and recommendations, communication and engagement, and implementation. These compiled processes and their steps are outlined and described in Table 3.

Table 3: Decision-Making Process for Genetic and Genomic Biomarker Testing Assessment in Cancer Care

Compiled process[a]	Compiled process stages	Description

Test nomination	• Nominations are made through submissions from
	  ◦ either a single or multiple point(s) of access
	  ◦ either broadly and/or publicly available or limited and/or targeted access
	• Nominations may also be initiated by horizon or environmental scanning activities
	• Nominations are reviewed
	• A decision is rendered regarding an assessment
	• Tests approved for evidence review are prioritized
		The process for proposing testing for a new genetic or genomic biomarker would begin with a nomination. Each nomination would propose biomarker(s) for testing and would include supportive information and evidence to justify the nomination, describing why testing for the biomarker(s) should be implemented. The nomination process would demonstrate alignment with the compiled guiding principles, ensuring that due consideration be afforded to all nominations that are complete and meet prespecified criteria.

Compiled process[a]	Compiled process stages	Description
Evidence reviews and impact assessment	• Scoping work is completed • Experts are assigned • Data necessary to inform the review are assessed • Literature searches are completed • Additional data sources are sought, as necessary ◦ unpublished sources, consultations, surveys • Data analyses and synthesis are undertaken • If evidence is scarce and/or complex, it may be collected using a living-review approach until greater certainty can be established • An evidence review report and impact assessment are drafted	Once a decision to make an assessment has been made, an evidence review and impact assessment are initiated to ensure that available evidence and any other relevant information for the nominated biomarker are identified, summarized, and reported, and a comprehensive review is conducted. The completed evidence review and impact assessment then inform the steps that follow (i.e., deliberation and recommendations concerning whether to implement testing for the biomarker).
Deliberation and recommendations	• The evidence review and impact assessment inform recommendation committee deliberation • Recommendations for or against implementation of testing are drafted	Once the evidence review and impact assessment are complete, the reports are used to inform deliberations and the development of a recommendation or recommendations concerning whether or not to adopt testing for the biomarker.
Communication and engagement	• Recommendations report is posted for public feedback • Recommendations are finalized and published with an accompanying report outlining implementation guidance, advice, and priorities for future research, if relevant	The steps for communication and engagement follow the development of the recommendation(s) and are intended to provide an opportunity for broad engagement with interested parties and members of the public.
Implementation	• Implementation plans are developed collaboratively with regional partners	Support for the implementation of biomarker testing that is recommended for adoption may be provided to jurisdictions with the provision that implementation plans may be developed collaboratively with regional partners.

[a]Processes relevant to decision-making for the implementation or funding of genetic or genomic biomarker testing were described by 6 sources.[1-3,5,8,13] These findings were supplemented with data collected during the consultations.

What We Heard in Canada

Through our consultations across jurisdictions, it is clear that each jurisdiction varies in their approach to biomarker assessment and decision-making. Some jurisdictions have structured systems that emphasize reviews of evidence and clinical guidelines through a centralized evaluation process, while other jurisdictions operate a more decentralized process that may be driven by clinical demand. Some jurisdictions use committees to guide decision-making, while others adopt more streamlined or resource-limited approaches and collaborate with larger jurisdictions for expertise (Appendix 4).

In some jurisdictions, there are key distinctions between decision-making for companion diagnostic testing (in support of targeted drug therapies) and other biomarker testing (used for prognostic or predictive purposes or in support of nondrug therapies). Companion diagnostics associated with targeted drug therapies may undergo rapid evaluation and approval due to their direct link to drug treatment. Non-companion biomarker decision-making follows varied and sometimes ad hoc processes, depending on the jurisdiction's capacity and expertise. Some jurisdictions use health technology assessments in some cases to inform decisions and some also rely on other trusted resources, including national and international clinical practice guidelines or recommendations such as the CDA-AMC and National Comprehensive Cancer Network (NCCN) recommendations.

Funding approaches vary, with some jurisdictions allocating specific budgets for biomarker testing, while others integrate requests into broader laboratory or health budgets. Timelines for decision-making and implementation are often influenced by budget cycles, infrastructure readiness, and the complexity of the tests.

Support for developing a standardized assessment framework to harmonize processes for making decisions about biomarker testing in cancer care was recommended by participants across consultations. Participants described that such a framework should ideally address equity, transparency, and efficiency while ensuring standardized criteria and resource optimization. They emphasized an opportunity to leverage existing jurisdictional expertise, foster collaboration, and incorporate evidence-based guidelines to influence decision-making and improve access to biomarker testing.

Key Objective 2: Inventories, Databases, and Lists of Genetic and Genomic Biomarker Testing in Cancer Care Available or Funded Across Canada

Synthesized Results

A variety of features and characteristics of inventories, databases, and lists of genetic and genomic biomarkers for which testing is currently available or being funded in cancer care across Canada were identified from the included literature sources and the data collected from the consultations. These features and characteristics included availability, access, funding, indications, limitations, and other details specific to genetic or genomic biomarker tests in cancer care.

The literature review identified 10 Canadian sources, with representation from Newfoundland and Labrador, Prince Edward Island, Nova Scotia, New Brunswick, Quebec, Ontario, Manitoba, Alberta, British Columbia, and Yukon. No sources were found from Saskatchewan, the Northwest Territories, or Nunavut. Consultations revealed an additional French-language source, and more insight into the nature and use of the inventories or lists of available biomarker testing maintained in different jurisdictions. In summary:

- British Columbia with its Cancer Genetics and Genomics Laboratory at BC Cancer has a publicly accessible resource that identifies testing available to cancer patients in the province.
- Alberta is working on developing a single system for all testing requests that will integrate the existing laboratory test formulary, a test directory, and the related guide to laboratory services.
- Manitoba's Lab Information Manual by Shared Health Manitoba identifies most tests available in the province, but not all. Although not yet publicly accessible, an inventory specific to cancer biomarkers is in development in Manitoba.
- Yukon maintains a directory that lists all referred-out tests.
- Ontario maintains a publicly accessible list of funded biomarkers that clinical sites and members of the public can reference. Ontario Health also collaborates with clinical programs to maintain internal records of biomarkers used within specific disease areas.
- Quebec maintains the Répertoire québécois et système de mesure des procédures de biologie médicale that is updated annually and lists publicly funded tests. New additions can also be captured in midyear updates, but these are not publicly available until the annual update.
- In New Brunswick, some available biomarker tests are listed in the Laboratory User Manual for the Horizon Health Network Regional Health Authority, although it is not comprehensive and does not include testing availability for the Vitalité Regional Health Authority.
- Prince Edward Island is working to develop a directory of all laboratory tests performed in the province or referred out of province, which currently lists some but not all relevant cancer biomarkers.
- Nova Scotia does not maintain a list for the province; however, there is an existing list of genes covered by next-generation sequencing in the province and all tests performed in the Central Zone of Nova Scotia or referred out of province.
- Newfoundland and Labrador maintain a provincial laboratory formulary that is currently out of date and undergoing transition to be more accessible.
- Saskatchewan and Nunavut do not maintain a public inventory of funded cancer biomarkers, although Saskatchewan maintains an internal list.

Additional details for each source, including features of included sources, is reported in Table 4 and Appendix 3.

Table 4: Characteristics of Inventories, Databases, and Lists of Genetic and Genomic Biomarkers for Which Testing Is Currently Available or Funded in Cancer Care Across Canada

Source citation jurisdiction of origin	Title	Source description	Feature(s) of interest	Consultation input
Newfoundland and Labrador Department of Health and Community Services (2021)[21] Newfoundland and Labrador	Provincial Laboratory Formulary[a]	Searchable registry of funded tests available in Newfoundland and Labrador Not specific to cancer (but includes information relevant to cancer care)	• Turnaround time, testing sites, other testing considerations	• The Provincial Laboratory Formulary is undergoing transition to be more accessible.
Health PEI (2024)[18] Prince Edward Island	Health PEI Department of Laboratory Medicine Online Lab Test Catalogue	Work-in-progress directory of all laboratory tests performed in Prince Edward Island or referred out of province Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Turnaround time, testing sites, other testing considerations	• Generic list of some relevant cancer biomarkers but Prince Edward Island does not maintain a public inventory of funded biomarkers.
Nova Scotia Health Authority (2024)[23] Nova Scotia	Department of Pathology and Laboratory Medicine Central Zone Laboratory Test Catalogue and Gene Panels Available for NGS	Directory of all laboratory tests performed in the Central Zone of Nova Scotia or referred out of province; Complete list of genes covered by NGS panels offered in Nova Scotia Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Testing sites	—
Horizon Health Network (2024)[19] New Brunswick	Saint John Area Laboratory User Manual, Version 23.0[b]	Directory of all laboratory tests performed in Saint John, New Brunswick or referred out of province Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Turnaround time, testing sites, other testing considerations	• Some biomarkers are listed in the Laboratory User Manual for Horizon Health Network, not including Vitalité Regional Health Authority.

Source citation jurisdiction of origin	Title	Source description	Feature(s) of interest	Consultation input
Centre universitaire de santé McGill (2024)[24] Quebec	Test directory for CUSM sites[c]	Directory of all laboratory tests performed through the CUSM Health Network in Montreal, Quebec, or referred out of province Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Turnaround time, testing sites, other testing considerations	—
Gouvernement du Québec (2022)[26] Quebec	Répertoire québécois et système de mesure des procédures de biologie médicale	Repository of all publicly funded tests across Quebec. Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Testing sites, turnaround time, other testing considerations	• The Répertoire is updated annually listing publicly funded tests. • New additions are also captured in midyear updates but are not publicly available.
Cancer Care Ontario (2024)[17] Ontario	Comprehensive Cancer Biomarker Testing Program	Database of funded biomarker testing in Ontario Specific to cancer	• List of targeted genes by disease site • Testing sites	• Publicly accessible list of funded biomarkers where clinical sites and the public can reference is maintained.
Ontario Health (2024)[20] Ontario	Ontario Genetic Testing Registry[d]	Registry of funded genetic germline panels available in Ontario; currently in development Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Testing sites	• Ontario Health collaborates with clinical programs to maintain internal records of biomarkers used within specific disease areas.
Shared Health Manitoba (2014)[22] Manitoba	Shared Health Manitoba: Lab Information Manual v2.9.2	Directory of all laboratory tests performed in Manitoba or referred out of province Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Turnaround time, other testing considerations	• Lab Information Manual by Shared Health Manitoba oversees all labs in the province and identifies most covered tests. • Inventory specific to cancer biomarkers under development but not publicly available.

Source citation jurisdiction of origin	Title	Source description	Feature(s) of interest	Consultation input
Alberta Precision Laboratories (2024)[15] Alberta	Alberta Precision Laboratories Test Directory	Interim directory of all laboratory tests performed in Alberta Not specific to cancer (but includes information relevant to cancer care)	• List of targeted genes by panel • Turnaround time, testing sites, other testing considerations	• Interim test directory and not a formulary. • Multiple lists exist to serve different purposes. • Working on a single system for the intake of all test requests across the province.
BC Cancer (2024)[16] British Columbia	BC Cancer: Cancer Genetics and Genomics Laboratory	Website for the centralized laboratory providing molecular genetic diagnostic services to patients with cancer in British Columbia Specific to cancer	• List of targeted genes by panel and cancer type • Turnaround time, other testing considerations	• Cancer Genetics and Genomics Laboratory identifies testing available to cancer patients. • BC website on laboratory services shows turnaround time and tests.
Yukon Hospitals (2024)[25] Yukon	Laboratory Guide to Services, version 7.0	Directory of all laboratory tests performed in Yukon; to be used in conjunction with resources from various BC laboratories for out-of-province testing needs Not specific to cancer (but includes information relevant to cancer care)	• Out-of-province testing	—

CUSM = Centre universitaire de santé McGill; NGS = next-generation sequencing.

[a]This source may be outdated and is undergoing updates to improve accessibility and relevance.

[b]Horizon Health Network is one of 2 regional health authorities in New Brunswick.

[c]The Centre universitaire de santé McGill health network is 1 of 5 laboratory "clusters" servicing the province of Quebec.[1] The Ministère de la Santé et des Services sociaux in Quebec published a provincial-level test directory: the Répertoire québécois et système de mesure des procédures de biologie médicale – Édition 2022-2023.[26] This source was issued in French only.

[d]The Ontario Genetic Testing Registry[20] provides links to the laboratory website and relevant requisitions for each panel. Features classified here may be available from these additional sources.

Limitations

Limitations of this report include a limited literature search and broad selection criteria that did not rely on systematic review methods and may not have captured all sources of relevance to the key objectives of the scan. Following from this, the reliance on 1 reviewer to identify and summarize sources from the literature may have introduced bias.

For key objective 1, there were multiple sources describing assessment criteria and decision-making processes that demonstrated relevance and generalizability to the Canadian context and to the assessment of genetic or genomic biomarkers in cancer care.[1-5,7,8,10-14] For guiding principles, there were 6 sources identified that described 5 sets of guiding principles relevant to objectives of this scan,[2-4,6,8,9] with 3 of them (describing 2 sets of guiding principles) originating from Canada.[2-4] However, 2 of them (describing 1 set of guiding principles) were program-specific,[2,3] limiting their relevance and generalizability. None of the guiding principles identified were specific to cancer care, and most were broader in scope than genetic or genomic biomarker testing, which limited relevance and generalizability as well. In addition, the approach to synthesis relied on the format and presentation of the selected foundational sources, which may not align with the way that others might group and organize the various domains and themes for the 3 concepts compiled. For example, health economic considerations in the compiled assessment criteria were considered under “implementation considerations” rather than “evidentiary considerations,” and “deliberation and recommendations” appeared in the compiled assessment criteria as well as in the compiled decision-making process. Knowledge users of this Environmental Scan, including the Advisory Panel led by CDA-AMC that will be tasked with developing a standardized, consensus-based assessment framework, could use the compiled concepts as a starting point and adapt them to fit their contexts and needs.

We consulted with 13 individual experts from 11 jurisdictions in Canada (excluding Yukon and Northwest Territories) and recognize that this might not have provided a sufficiently comprehensive view. In particular, the individual experts may not represent the diversity of contributing parties (e.g., policy-makers, lived experience and patient-centred perspectives, caregivers and families, regulatory agencies, industry, and drug payers) from each jurisdiction. Hence, the differences in the structure, resources, and other information collected across jurisdictions may mean that the findings are not universally applicable. We also acknowledge that our scan cannot provide a comprehensive view of assessment processes across jurisdictions in Canada with input from Yukon and Northwest Territories missing. It is also possible that some features of the decision-making processes, frameworks, and assessment criteria from some jurisdictions were highlighted more than others and are therefore more prominent in the results. Hence, it is possible that some nuances are missing depending on the participants’ involvement in various processes. We worked to mitigate this potential by having each consultation participant review and validate the information before being included in this report. We also acknowledge that these are complex processes that have been summarized in a succinct format for the purposes of this report, and it is likely that some features of the processes are underrepresented or not represented in our summaries.

For key objective 2, there were no literature sources identified from some of the jurisdictions, limiting an understanding of what genetic or genomic testing is currently available or funded in these jurisdictions.

Although the Répertoire québécois et système de mesure des procédures de biologie médicale was identified as a key inventory during the consultations, the literature review was limited to English-language sources. Therefore, otherwise-eligible French-language source(s) were not included, limiting an understanding of testing availability and funding in some jurisdictions (e.g., Quebec, New Brunswick). For provinces for which eligible inventories, databases, or lists were identified, there was variability in the features and characteristics reported,[15-23] which limits an understanding of what genetic or genomic testing is currently implemented and funded within and across these jurisdictions. This may have been a function of the variability in the purposes of the included sources (e.g., where a source was describing information in support of health providers requesting or ordering tests, information on test availability and public funding may not have been prioritized or included). Limitations of reported features and characteristics of testing were observed, with some overarching limitations including sources that were described as interim or incomplete.[15,18,19] General limitations observed across all of the included sources were key features that were either not reported, or not clearly or consistently reported.[15-23] Observations from the consultations also pointed to some limitations, noting sources with additional or key information reported in supplementary or separate sources only.[15,16,19] Finally, the sources may not be updated, or updated regularly, which may have also limited the currency of the available information.

Conclusions and Implications for Decision- or Policy-Making

This Environmental Scan sought to address 2 key objectives. The first objective was to identify and describe existing assessment frameworks, criteria, checklists (and other relevant tools), processes, and guiding principles that inform the implementation of or funding decisions for genetic and genomic biomarker testing associated with health care interventions and technologies in cancer care, including features, characteristics, and other relevant information. The second objective was to identify and describe existing inventories, databases, or lists of genetic and genomic biomarkers for which testing is currently available or being funded in cancer care in jurisdictions in Canada. These objectives were pursued using a limited literature search and review of sources from within and outside of Canada as well a series of consultations with decision-makers and involved parties in Canada.

Data and information relevant for key objective 1 included sources describing guiding principles, assessment criteria, and decision-making processes related to the assessment of genetic or genomic testing in cancer care. Although a variety of features and characteristics were described, there was considerable concordance across the included sources to enable the synthesis and compilation into single sets of guiding principles, assessment criteria, and decision-making processes. The guiding principles identified in the literature were limited, with few specific to the Canadian context or to genetic and genomic testing or cancer care. However, the information from the consultations, which was specific to the Canadian context, supplemented these findings. The findings from consultations across jurisdictions in Canada highlight diverse approaches to integrating genetic and genomic biomarker testing within health systems. The consultations also underscore an opportunity — and a desire — for pan-Canadian collaboration to harmonize testing assessment practices,

optimize resources, and ensure equitable access to genetic and genomic biomarker testing for cancer care across Canada.

For key objective 2, 12 inventories, databases, and lists of genetic and genomic tests were identified for multiple jurisdictions in Canada through the literature review and through our consultations; however, no sources were identified for Saskatchewan, the Northwest Territories, or Nunavut. Many Canadian provinces maintain inventories or lists of available biomarker testing, with some more comprehensive and current than others and some intended for internal use by health providers requesting tests and others also intended for access by members of the public. Although there were gaps and limitations in the reported information identified from the literature review, the information gathered from the consultations supplemented these findings. However, there is likely an opportunity for increased clarity and standardization of data and information in the public domain.

Similar work as this Environmental Scan was carried in another Environmental Scan in 2012, in an Environmental Scan of evaluation frameworks for genetic tests.[27] That earlier report identified and summarized similar criteria as those that have been identified and described in this report, including an overview of diseases of interest and their underlying genetics, the target population and intended use of the test(s), laboratory information, analytic validity, clinical validity, economic considerations, clinical utility, and ethical, legal, and social implications.[27] A 2017 report from the McMaster Health Forum reviewed the public provision and funding of clinical genetic tests, which identified similar criteria as identified in this report, including analytical validity; clinical validity; clinical utility; ethical, social, and legal implications; and economic considerations.[28] Similarly, many of the insights and findings generated by the round table led by CADTH in 2022 are also corroborated by this report. The survey conducted and discussions at that time suggested some key features of a potentially consistent and efficient approach to the assessment of genetic and genomic health technologies, including standardization, transparency, rigour, efficiency and timeliness, collaboration across the jurisdictions, adaptivity to rapid change (e.g., a life cycle HTA approach or consideration for reassessment), and a focus on value, clinical utility, equity, and health economic impacts. Additional features that were suggested included a coordinated process for the evaluation of drugs and any companion diagnostic testing, the use and incorporation of real-world evidence, information that can support laboratories in the implementation of genetic and genomic testing, consideration of impacts to clinical care, and guidance to support evaluation and implementation. These data and information were also considered in the preparation of this report, which provides a broadened, synthesized, and updated scope on the topics of those earlier reports and engagements, identifying and compiling guiding principles, assessment criteria, and decision-making processes, as well as providing an updated scan of inventories, databases, and lists of genetic and genomic tests currently available in Canada.

Given the rapidly developing field of precision medicine, and the associated landscape of genetic and genomic biomarker testing in cancer care, the results of this Environmental Scan will be a foundational source for the consideration and development of a standardized assessment framework to support coordinated, efficient, and equitable assessment and access to genetic and genomic testing for biomarkers in cancer care.

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Appendix 1: Methods

Note this appendix has not been copy edited.

Literature Review

Literature Search Methods

An information specialist conducted a literature search on key resources including MEDLINE, ECRI, UpToDate, and the International HTA database, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevance. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the objectives of this scan and criteria for literature screening and information gathering (Table 5). The main search concepts were genetics, genomics, biomarkers, and cancer, focusing on assessment frameworks, programs, tools, checklists, criteria, inventories, databases, and policies. The search was limited to English-language sources but not limited by publication date. The search for frameworks, criteria, checklists (and other relevant tools), and processes (i.e., for key objective 1) was not limited geographically, while the search for inventories, databases, and lists (i.e., for key objective 2) was limited to Canada. The focused internet search was completed on June 28, 2024, while the database literature search was run on July 4, 2024. Database search alerts were maintained until January 3, 2025.

Screening and Study Selection

One reviewer screened and selected relevant publications from all sources of information retrieved in the literature searches. Literature that provided information related to the objectives of this scan was screened for eligibility, and those that met the criteria for literature screening (Table 5) were summarized within the report.

Publications that were not specific to cancer care but included information that may be applicable to cancer care (e.g., descriptions of funding decision-making processes for all molecular genetic testing) were included. Preclinical and clinical research studies considered too early for implementation or funding decision-making or publications focused on specific tests or testing platforms (e.g., comparisons of different technologies) or methodologies (e.g., economic modelling) were excluded. For key objective 1, eligible sources that were included within systematic reviews or other sources which were more comprehensive or recent were not included or summarized individually in this report, with the more recent or comprehensive source included and summarized, instead.

Table 5: Criteria for Literature Screening and Information Gathering

Criteria	Objective
Concepts	1. Assessment frameworks, criteria, checklists (and other relevant tools), processes, and guiding principles that inform the implementation or funding decisions for genetic and genomic biomarker testing in cancer care. 2. Inventories, databases, or lists of genetic and genomic biomarkers for which testing is currently available or being funded in cancer care.
Context	1. Health care policy-making, decision-making, and health technology assessment contexts 2. Health care/cancer organizations/agencies, hospitals, and laboratories in Canada.
Types of information	1. Features, characteristics, and other relevant information 2. Features, characteristics, and key data points.

Abstraction of Data and Information

Collection of data and relevant information was performed by 1 reviewer for each key objective. The data were abstracted to tables in Microsoft Word, including bibliographic details (i.e., authors, year of publication, and jurisdiction of origin) of the included reports, websites, or other sources of information, and a description of the features and components that are relevant for addressing the key objectives of this scan was generated for each source. For the included publications that were broader than cancer care or genetic and genomic biomarker testing, only information applicable to the key objectives of this scan were abstracted.

Synthesis of Data and Information

For key objective 1, characteristics and features of assessment frameworks, criteria, checklists (and other relevant tools), processes and guiding principles were summarized and synthesized using an iterative approach. On review of the included literature sources, key concepts were identified and foundational sources were selected based on relevance (including that to the key objectives of the Scan as well as the Canadian context), breadth and comprehensiveness (i.e., the extent to which concepts captured those from other included sources), and recency of publication. One foundational source was identified for each of 3 categories of relevant concepts: guiding principles, assessment criteria, and decision-making processes. Data were abstracted from the foundational source for each of the 3 categories of relevant concepts, with additional guiding principles, assessment criteria, and decision-making processes abstracted from the remaining sources using a cumulative approach, with synonymous or similar features and characteristics mapped alongside those of the foundational source, and with the addition of unique features and characteristics to the data from the foundational source as they were identified, citing all relevant sources. For key objective 2, features and characteristics of the included inventories were summarized and synthesized, with a focus on the types of information of relevance to the assessment of genetic and genomic biomarker testing in cancer care.

Consultations

The consultations were conducted in the form of interviews, with representation sought from each of Canada's provincial and territorial health systems. Potential participants were identified in consultation with

the Canadian Association of Provincial Cancer Agencies (CAPCA), and a snowball sampling approach was also applied by asking the participating interviewees to identify additional candidates who would likely have unique and relevant insights within their respective jurisdiction.

Invitations were distributed by email. Invitees were asked to participate in a 1-hour virtual meeting to discuss assessment and decision-making processes for genetic and genomic testing for biomarker in cancer care within their jurisdiction, including their role in making these decisions and about any guiding principles, assessment criteria, and decision-making processes that are used to support these decisions. Interviews were conducted by team members using a semistructured interview guide (refer to Table 6) whose development was informed by the literature review component of this Environmental Scan. Interviews were recorded to support data analysis and summary for this scan but were not transcribed to be reported verbatim. Participants were given the opportunity to review a summary of the information gathered during their consultation before publication and were informed that only information that was approved to be shared would be included in the summary.

Table 6: Questions Used in the Consultations

Information sought	Question
Role of informant	What is your role in assessing or decision-making around the implementation or funding of genetic and genomic tests for biomarkers in cancer care?
Assessment approach(es)	What frameworks, criteria, checklists (or other relevant tools), or processes do you use to assess or make decisions about the implementation, funding, or use of genetic and genomic tests for biomarkers in cancer care? Please describe. • How are the biomarkers identified for assessment? • How is the framework, criteria, checklist (or other relevant tool[s]), or process applied? • Who applies it/them? • How/from where is the information sourced? • How long does the process take? • Where does the decision go? What next steps does it inform? • Are decisions ever revisited or reconsidered? If so, why and how?
Guiding principle(s)	What are the guiding principles that: • currently characterize frameworks, criteria, checklists, and processes for assessing genetic and genomic tests for biomarkers in cancer care? • should characterize a national framework for assessing genetic and genomic tests for biomarkers in cancer care?
Inventories	Do you know of inventories, databases, or lists of genetic and genomic biomarkers in cancer care for which testing is currently available or funded: • in your jurisdiction?
Other	Who else in your jurisdiction should we talk to for further information?

Synthesis and Reporting

Literature review findings were supplemented using the data gathered and summarized from the consultations. A descriptive analysis was conducted, summarizing and synthesizing the information in

support of the objectives of this scan. Findings from the analyses were reported narratively, including a distinction between the frameworks, criteria, checklists (and other relevant tools), processes, and guiding principles published or in use within Canada versus those published or in use outside of Canada.

Appendix 2: Characteristics and Features of Literature and Information Sources for Key Objective 1

Note this appendix has not been copy edited.

Characteristics of Included Sources

Guiding Principles

Of the 6 sources describing guiding principles,[2-4,6,8,9] there were 3 Canadian sources which originated from the Institute of Health Economics[3] and Alberta Precision Laboratories[2] describing 1 program in Alberta and from the Institut national d'excellence en santé et en services sociaux (INESSS)[4] describing another program in Quebec. The remaining 3 publications were from non-Canadian sources, including WHO,[6] National Health Service England,[8] and the Global Alliance for Genomics and Health.[9]

None of the sources reporting on guiding principles were specific to cancer care.[2,3,6,8,9] All but 1[8] of the sources described principles that were broader in scope than genetic or genomic testing but included principles of relevance to genetic or genomic biomarker testing assessment.[2,3,6,9]

Assessment Criteria

Of the 10 sources describing criteria relevant to the assessment of genetic or genomic biomarker testing,[2-4,7,8,10-14] 3 were produced in Canada: 1 from INESSS[4] in Quebec, and 2 sources which described 1 set of criteria from the Institute of Health Economics[3] and Alberta Precision Laboratories,[2] both in Alberta. Seven sources were from outside of Canada, including 1 from the Medical Services Advisory Committee in Australia;[7] 1 from the National Health Service England in the UK;[8] 2 from Italy, funded by the Italian Ministry of Health, and describing 1 set of criteria;[10,11] 1 from a group of authors based in France;[12] 1 from the National Academies of Sciences, Engineering, and Medicine in the US;[13] and 1 from the Ludwig Boltzmann Institute for Health Technology Assessment in Austria.[14]

One of the sources reporting on criteria was specific to cancer care,[7] whereas the other 9 were broader in scope than cancer, but reported on criteria relevant to genetic and genomic biomarker testing in cancer care.[2-4,8,10-14] Seven of the sources described 6 sets of criteria that were specific to genetic or genomic biomarker testing assessment,[7,8,10-14] whereas 3 sources (describing 2 sets of criteria) were broader in scope, but reported on criteria relevant to genetic and genomic biomarker testing.[2-4]

Decision-Making Processes

Of the 6 sources describing processes relevant to the decision-making for the implementation or funding of genetic or genomic biomarker testing,[1-3,5,8,13] 2 described 1 process from Alberta,[2,3] and 1 of the sources described processes from 5 provinces in Canada.[1] The remaining sources described processes from Ontario,[5] the UK,[8] and the US.[13]

None of the processes were specific to cancer care, but all described steps relevant to the assessment of genetic and genomic biomarker testing in cancer care.[1-3,5,8,13] Three of the sources described processes specific to genetic or genomic testing,[1,8,13] whereas the remaining 3 sources were broader in scope, but described processes that bore relevance to genetic and genomic biomarker testing.[2,3,5]

Table 7: Characteristics of Included Literature Sources for Key Objective 1

Source and citation	Title	Search method used	Jurisdiction of origin	Specific to cancer?	Source description	Feature(s) of interest
Sources from Canadian jurisdictions						
Alberta Precision Laboratories, 2024[a,2]	Process for adding and removing tests to/from the Formulary	Handsearch	Alberta	No (but includes information relevant to cancer care)	Unpublished overview of the guiding principles and process informing the assessment and implementation of tests in Alberta's health care system	• Guiding principles • Processes
Health Quality Ontario[5]	Health Technology Assessments: Methods and Process Guide	Handsearch	Ontario	No (but includes information relevant to cancer care)	A description of the methods and processes used to conduct health technology assessments at Ontario Health	• Processes
Husereau, 2023[1]	Progress toward Health System Readiness for Genome-Based Testing in Canada	Database search strategy	Pan-Canadian	No (but includes information relevant to cancer care)	Mixed methods (literature review and interviews) assessment of current features and processes for informing implementation and reimbursement of genomic testing across 5 designated regions in Canada	• Processes
Institute of Health Economics, 2023[a,3]	Alberta Lab Formulary Committee Rapid HTA Prioritization Framework	Handsearch	Alberta	No (but includes information relevant to cancer care)	A framework to support decision-making concerning the implementation of laboratory tests	• Guiding principles • Criteria • Process
Institut national d'excellence en santé et en services sociaux (INESSS)[4]	Statement of Principles and Ethical Foundations	Handsearch	Quebec	Yes	Criteria and principles used within the Framework for the Appraisal of the Value of Interventions in Health and Social Services	• Guiding principles • Criteria

Source and citation	Title	Search method used	Jurisdiction of origin	Specific to cancer?	Source description	Feature(s) of interest
Sources from non-Canadian jurisdictions						
WHO, 2024[6]	Draft WHO principles for human genome data access, use and sharing	Grey literature search	International	No (but includes information relevant to cancer care)	An overview of guiding principles for the use and sharing of human genome data	• Guiding principles
Medical Services Advisory Committee, 2020[7]	Discussion paper on pan-tumour biomarker testing to determine eligibility for targeted treatment	Grey literature search	Australia	Yes	Guidance on the evidence needed to evaluate biomarker testing to determine eligibility for access targeted therapy using a companion diagnostic case example (i.e., immunohistochemistry testing for mismatch repair deficiency in colorectal cancer to access pembrolizumab treatment) to discuss the broader requirements for pan-tumour biomarker testing assessment	• Criteria (i.e., recommendations for required information)
National Health Service England, 2020[8]	Updating the National Genomic Test Directory	Handsearch	UK	No (but includes information relevant to cancer care)	Processes and criteria used to update the National Genomic Test Directory	• Guiding principles • Processes • Criteria
Global Alliance for Genomics and Health, 2019[9]	Framework for Responsible Sharing of Genomic and Health-Related Data	Grey literature search	International (US-based)	No (but includes information relevant to cancer care)	A framework providing guidance for the sharing of human genomic data	• Guiding principles
Pitini, 2019[a,10]	A proposal of a new evaluation framework toward implementation of genetic tests	Grey literature search	Italy	No (but includes information relevant to cancer care)	A framework for the evaluation of genetic and genomic tests that includes an assessment of service delivery	• Framework and criteria for decision-making
Pitini, 2019[a,11]	Evaluation Framework Handbook	Handsearch	Italy	No (but includes information relevant to cancer care)	Supporting information for the framework proposed by Pitini et al.[10]	• Definitions and elaboration of the criteria proposed in the framework

Source and citation	Title	Search method used	Jurisdiction of origin	Specific to cancer?	Source description	Feature(s) of interest
Barna, 2018[12]	Evidence Required by Health Technology Assessment and Reimbursement Bodies Evaluating Diagnostic or Prognostic Algorithms That Include Omics Data	Database search strategy	France	No (but includes information relevant to cancer care)	Scoping review of methods and criteria used by HTA/ regulatory bodies to inform reimbursement decisions concerning multianalyte assays with algorithmic analyses (MAAA)	• Criteria used by multiple HTA bodies to evaluate 1 technology specific to breast cancer
National Academies of Sciences, Engineering, and Medicine[13]	An Evidence Framework for Genetic Testing	Handsearch	US	No (but includes information relevant to cancer care)	A framework for decision-making regarding the use of genetic tests in clinical care	• Process • Criteria
Kisser, 2014[14]	Procedural guidance for the systematic evaluation of biomarker tests	Grey literature search	Austria	No (but includes information relevant to cancer care)	Broad review and framework* for the assessment of biomarker tests (not specific to genomic/ genetic testing) **Note that this source is relatively dated*	• Framework for decision-making and reimbursement

ACCE = Analytic validity, Clinical validity, Clinical utility and associated Ethical, legal and social implications; AI = artificial intelligence; HTA = health technology assessment; IHC = immunohistochemistry; NCCN = National Comprehensive Cancer Network; NGS = next-generation sequencing; WGS = whole exome sequencing.

[a]Alberta Precision Laboratories (2024), Institute of Health Economics (2023), and Pitini (2019) describe the same guiding principles, assessment criteria, and decision-making processes; both were included because complementary information was available from each source.

Relevant Features of Included Sources

The features of relevance describing the 3 key concepts identified (i.e., guiding principles, assessment criteria, and decision-making processes) reported in the included literature sources were abstracted and tabulated and are presented in Table 8.

Table 8: Relevant Features From Literature and Information Sources for Key Objective 1

Source and citation	Relevant features
Guiding principles	
WHO, 2024[6]	• To affirm and value the right of individuals and communities to make decisions • Social justice • Solidarity • Equitable access to, and benefit from, human genome data

Source and citation	Relevant features
	• Collaboration, cooperation, and partnership • Transparency • Accountability • Stewardship of human genome data

Institute of Health Economics, 2023[3] (supported by a supplementary source describing additional detail on Guiding Principles: Alberta Precision Laboratories[2])	• **Evidence-informed, fair, consistent, transparent, deliberative, and timely** decision-making and consensus concerning
	  ○ Test appropriateness
	  ○ System stakeholder engagement
	  ○ Economic impact
	  ○ Equity
	• **Sustainable** use of all laboratory tests while maximizing **effectiveness, safety, and quality of care** for patients
	• **Accountability** for the inclusion, elimination, or substitution of clinical laboratory tests, including guidelines

Institut national d'excellence en santé et en services sociaux (INESSS)[4]	• **Relevance of objects and adaptation of evaluation modalities**
	  ○ "Relevant and appropriate evaluation modalities are those that adapt methods to the intervention in a way that allows developing recommendations aiming at value creation in a timely and efficient manner." (p. 4)
	• **Knowledge mobilization and integration**
	  ○ "Knowledge is mobilized through a diversity of sources using appropriate methods, followed by analysis and synthesis. Knowledge integration involves organizing the data from these different sources for each evaluation dimension." (p. 5)
	• **Multidimensional deliberation**
	  ○ "Deliberation is when a group of diversified individuals aiming for the common good come together to appraise and weigh the arguments for and against introducing an intervention or changing existing practices. Multidimensional deliberation is organized around the dimensions of evaluation (clinical, population, economic, organizational and sociocultural)." (p. 6)
	• **Fair, reasonable, and value-adding recommendations**
	  ○ "Recommendations reflect the transformation of knowledge and deliberation into concrete proposals for action. A fair and reasonable recommendation aims to balance diverging views and mitigate ethical tensions in the pursuit of the common good." (p. 7)
	• **Support for value creation and re-evaluation**
	  ○ "Value creation refers to the beneficial effects of an intervention in health or social services, in terms of clinical, population and economic aspects, as well as regarding the organization of care and services and socio-cultural dynamics. Support includes all actions that INESSS can take to promote this value creation. Reassessment is the re-evaluation of an intervention." (p. 8)

National Health Service England, 2020[8]	**Principles informing amendments to the Test Directory:** • "Proposed amendments are **evaluated** by test evaluation working groups based on across several domains" (p. 14) (refer to Assessment Criteria section) • "Evaluation and scoring informs test evaluation working groups **holistic review, discussion and decision** on each proposed amendment, allowing recommendations made" (p. 14) • **"Clear and transparent** process for allocating NHS spending. Funding will be allocated based on the recommendations from the test evaluation working groups following evaluation" (p. 14)

Source and citation	Relevant features
Global Alliance for Genomics and Health, 2019[9]	• Respect individuals, families, and communities • Advance research and scientific knowledge • Promote health, well-being, and the fair distribution of benefits • Foster trust, integrity, and reciprocity
Assessment criteria	

Institut national d'excellence en santé et en services sociaux (INESSS)[4]	• **Dimension 1: Populational**
	  ○ "Contributes to a better state of health and well-being for the population in keeping with equity considerations" (p. 2)
	• **Dimension 2: Clinical**
	  ○ "Improves the health and well-being of its users" (p. 2)
	• **Dimension 3: Organizational**
	  ○ "Fits into the organizational context of care and service delivery in a manner that contributes to strengthening the health and social services system" (p. 2)
	• **Dimension 4: Economic**
	  ○ "Optimizes the use of resources to support their responsible and sustainable management" (p. 2)
	• **Dimension 5: Sociocultural**
	  ○ "Fits into the societal context in such a way that it promotes its evolution towards the common good" (p. 2)

Institute of Health Economics, 2023[3] **(with duplicate information provided in a supporting source: Alberta Precision Laboratories**[2]**)**	• **Domain 1: Test appropriateness**
	  ○ Efficacy and effectiveness
	  ○ System-Level Need
	  ○ Alignment with APL Goals
	• **Domain 2: System Stakeholder Engagement**
	  ○ System capacity
	  ○ Clinical Endorsement
	• **Domain 3: Economic Impact**
	  ○ Affordability
	  ○ Cost-effectiveness
	  ○ Financial risks
	• **Domain 4: Equity**
	  ○ Equity
	  ○ Other considerations

Medical Services Advisory Committee, 2020[7]	**Required considerations:**
	• ***Types of evidence***
	  ○ Direct evidence:
	  ○ i.e., RCTs that that have been specifically designed to prove a linkage between the test and the therapeutic outcome
	  ○ Linked evidence:
	  ○ evidence to determine the test's impact on clinical management and health outcomes
	• ***Biological plausibility***
	  ○ Detailed analysis of the biological plausibility of the relationship between the biomarker and

Source and citation	Relevant features

	treatment is required
	• ***Alternative predictive biomarkers***
	  ◦ Any other biomarkers that may have predictive value for treatment outcomes should be considered
	• ***Prevalence of the biomarker in the population to be tested***
	  ◦ The prevalence estimate should include the biomarker prevalence in the overall population and the prevalence among those with the condition(s)
	  ◦ The prevalence rate of the biomarker should be considered in the specific stage(s) of disease being targeted for testing and treatment (i.e., across time)
	• ***Diagnostic performance***
	  ◦ Identification of a reference or evidentiary standard
	  ◦ Analytical validity (i.e., sensitivity and specificity)
	  ◦ Test reliability
	  ◦ Concordance with the reference/evidentiary standard
	  ◦ Clinical validity (i.e., positive/negative predictive values)
	• ***Clinical evaluation***
	  ◦ Prognostic value
	  ◦ Clinical utility
	  ◦ Therapeutic effectiveness
	• ***Comparative costs***
	  ◦ Cost-effectiveness

National Health Service England, 2020[8]	**Evaluation and scoring criteria for new clinical indications proposed for addition to the Test Directory:**
	• Test method considerations:
	  ◦ Proposed use of test
	  ◦ Any concerns over the test method proposed
	  ◦ Opportunities for the generation of further evidence to support decisions
	• Scored criteria[a]:
	  ◦ Clinical utility:
	  ▪ Evidence of clinical utility
	  ▪ Benefit to patient
	  ▪ Evidence of unmet diagnostic need
	  ▪ Strength of scientific evidence base
	  ▪ Evidence of appropriate diagnostic yield
	• Health economic case
	  ◦ Level of additional investment required
	  ◦ Cost-effectiveness
	• NHS implementation:
	  ◦ Alignment with an NHS England and NHS Improvement clinical priority
	  ◦ Practicality of implementation in the GMS
	  ◦ Technical feasibility
	• Evaluation outcomes considered:

Source and citation	Relevant features
	○ Whether to recommend for implementation ○ Whether the proposed eligibility criteria are accepted ○ Whether the application is recommended for discussion by the Test Evaluation Group ○ Any legal, ethical, or social implications ○ Other comments **Evaluation and scoring criteria for amendments to the Test Directory for existing clinical indications:** ● Scored criteria[b]: ○ Impact on clinical management or outcomes ○ Benefit to patient ○ Impact on existing testing pathways ○ Impact on existing clinical pathways ○ Impact on existing activity figures/testing volumes ○ Financial impact ○ Laboratory operational impact ● Evaluation outcomes: ○ Whether the proposed change is accepted ○ Whether the application is recommended for discussion by the Test Evaluation Group ○ Reason for discussion by the Test Evaluation Group (e.g., new area not currently included in the Test Directory; emerging scientific evidence) ○ Any legal, ethical, or social implications ○ Other comments
Pitini, 2019a[10] (with supporting information reported in a supplementary source: Pitini, 2019b[11])	**Evidence Collection** ● ***Test and clinical condition overview*** ○ Clinical condition: ▪ Clinical presentation and pathophysiology ▪ Genetic background ▪ Public health impact ○ Genetic test: ▪ General features ▪ Technical features ▪ Clinical context ● ***Analytic validity*** ○ Analytic sensitivity and specificity ○ Accuracy ○ Precision ○ Robustness ○ Laboratory quality control ● ***Clinical validity*** ○ Scientific validity ○ Test performance: ▪ Clinical sensitivity and specificity ▪ Positive and negative predictive value

Source and citation	Relevant features
	▪ Modifiers ● ***Clinical utility*** ○ Available interventions ○ Efficacy ○ Effectiveness ○ Safety ● ***Personal utility*** **Delivery Models** ● ***Health care programs*** ● ***Level of care*** ● ***Patient pathway*** ● ***Organizational aspects*** ○ Expected demand ○ Resources management ○ Other organizational requirements: ▪ Education of professionals, patients, and citizens ▪ Information dissemination to professionals, patients, and citizens ▪ Cooperation, communication, and coordination ▪ Quality assurance, monitoring, and control ○ Barriers to implementation ● ***Economic evaluation*** ● ***Ethical, legal, and social implications*** ● ***Patient perspective*** **Research Priorities** ● Evidence gaps **Reporting and Decision-Making** ● Net benefit ● Cost-effectiveness ● Feasibility
Barna, 2018[12]	● **Clinical utility** ○ Prognostic ability ○ Clinical validity ○ General ○ Impact on clinical decision-making ○ Impact on patient anxiety ○ Chemotherapy-associated benefits ○ Patient outcomes ● **Health economic** ○ Cost-effectiveness ○ Economic Impact

Source and citation	Relevant features

National Academies of Sciences, Engineering, and Medicine[13]	**Analytic Validity**
	● ***Technical efficacy***: whether the test accurately detects the target biomarker in the lab
	  ○ Accurate detection of genetic variants
	  ○ Analytic sensitivity and specificity
	Clinical Utility
	● ***Patient outcome efficacy***: whether patients derive benefits and harms from use of the test i.e.,
	  ○ Morbidity
	  ○ Mortality
	  ○ Other clinical end points (hospitalizations, procedures)
	  ○ Quality of life
	  ○ Options for prevention or therapy
	  ○ Ability to avoid adverse outcomes of ineffective treatments
	  ○ Options for reproductive planning
	  ○ Improved ability to plan for future events
	● ***Therapeutic and management efficacy***: whether the test impacts the selection of treatment
	  ○ Adherence to therapeutic regimen
	  ○ Planning surveillance, prevention, or treatment plans
	  ○ Targeted treatment or avoiding harms of treatment
	Clinical Validity
	● ***Diagnostic-thinking efficacy***: whether the test supports diagnosis
	  ○ Ending diagnostic odyssey and preventing expensive or invasive diagnostic tests
	  ○ Improved accuracy of prognosis
	● ***Diagnostic accuracy***: whether the test accurately detects the target disorder in patients
	  ○ Accurate molecular diagnosis
	  ○ Clinical sensitivity and specificity
	Ethical, Legal, Social Implications (ELSI)
	● ***Societal efficacy***: whether there is evidence of efficacy or adverse effects of the test at the health system or societal levels
	  ○ Effect on health disparities
	  ○ Cost of health care
	  ○ Population-health intervention
	  ○ Perceptions of disabilities, eugenics
	  ○ Perspectives of genetic determinism

Kisser, 2014[14]	1. **Analytical validation**
	  ○ Accuracy of the biomarker test, including:
	  ▪ limits of detection
	  ▪ limits of quantitation
	  ▪ reference value cut-off concentration
	  ▪ reliability
	  ▪ reproducibility
	2. **Qualification**
	  ○ Evidentiary assessment of:

Source and citation	Relevant features
	▪ the association between the biomarker and disease ▪ the impact of targeted interventions on health outcomes 3. **Utilization** ◦ Evidentiary assessment of the proposed use of the biomarker in context, including: ▪ population ▪ setting ▪ purpose
Decision-making processes	
Health Quality Ontario[5]	• **Topic identification** ◦ Open application process • **Scope development and literature searches** ◦ Develop clinical, economic, and patient preferences and values review plans ◦ Complete literature searches • **Evidence development and reporting** ◦ Complete analyses ◦ Prepare draft HTA report ◦ Present draft HTA findings to OGAC ◦ OGAC develops draft recommendation ◦ Draft recommendation presented to OHTAC for approval • **Production** ◦ Edit HTA report and draft recommendation document ◦ Notify the Ontario Ministry of Health of draft recommendation ◦ Post HTA report and recommendation for public feedback ◦ OGAC finalizes genetic test recommendation, which is then reviewed by OHTAC • **Final ministry notification and web posting** ◦ Share approved HTA report and funding recommendation with the Ontario Ministry of Health ◦ Post finalized HTA report and recommendation on Ontario Health's website
Husereau, 2023[1]	**Process-relevant information described by province/region:** • **British Columbia** ◦ The PLMS test review process provides a single-entry point for new testing ◦ The test review process is not open to the public ◦ The test review process and rationale for the test recommendations are not publicly available ◦ The review process results in recommendations and advice regarding funding to the Ministry of Health. ◦ Service coordination for testing is provided centrally by the PLMS; regional coordination (e.g., for referral and sampling) is provided by individual health authorities • **Alberta** ◦ The APL test review process provides a single-entry point for new testing ▪ The intake form to consider use of a new test is open to the public ▪ The review process may also look at the decommissioning of tests

Source and citation	Relevant features
	◦ The test review process, timelines, and criteria are under development, but not yet publicly available ◦ The review process results in recommendations and advice being provided to the AHS regarding funding ◦ The APL works with the AHS to provide provincial coordination for testing • **Ontario** ◦ There is no single-entry point for the assessment of new testing ◦ The current process through HQO allows commercial manufacturers and researchers to apply for assessment of novel testing ▪ the process for topic prioritization is not clear/publicly available ◦ Other proposals for new testing may be made by clinicians, pharmacy services and other internal parties ◦ Other proposals for new testing may be evaluated through multiple processes and evaluative frameworks that are not formally coordinated • **Quebec** ◦ The DBBM test review process provides an entry point for new testing ◦ The test review process is not publicly available ▪ Only public laboratories can submit requests for assessment of new testing ▪ Assessment of new companion diagnostic testing can be submitted by drug manufacturers as part of the drug review process ◦ Tests are evaluated using a single evaluative framework ◦ The review process results in recommendations and advice being provided to the Ministry of Health regarding funding ▪ recommendations are made public ▪ there is limited engagement with stakeholders • **Nova Scotia** ◦ There is no single-entry point for the assessment of new testing ◦ The test review process is conducted through a provincial advisory committee ▪ the test review process, timelines, and criteria are not publicly available
Institute of Health Economics, 2023[3] (with duplicate information provided in a supporting source: Alberta Precision Laboratories[2])	1. Physician or lab staff identifies test 2. Physician or lab staff completes intake form and submits to LFC secretariat 3. Form reviewed by LFC secretariat 4. Decision is made whether to review by LFC ◦ Tests not approved to proceed are assessed for additional information 5. Tests approved to proceed are reviewed by LFC 6. Decision is made whether to add to the lab formulary ◦ Tests not approved are not added to the formulary ◦ Tests for which information is unclear undergo Rapid HTA and are considered for a second LFC review 7. Tests approved for addition to the formulary are assessed for cost ◦ Tests not exceeding the cost threshold established by the LFC are added to the formulary ◦ Tests exceeding the cost threshold established by the LFC are reviewed by a budgetary review committee of the AHS

Source and citation	Relevant features
National Health Service England, 2020[8]	**Process for annual updates to the Test Directory:** 1. An application to amend the Test Directory is received 2. Internal review of the application is carried out to determine whether additional information is required 3. Applications are assigned to the relevant test evaluation working group and group members with the appropriate expertise are appointed to review the application 4. A full evidence review is undertaken to assess the clinical and scientific basis for the amendment 5. An impact assessment to consider the practical implications of implementation is conducted 6. The working group makes recommendations to the Genomics CRG 7. The Genomics CRG prioritizes the tests and makes recommendations to NHS England and NHS Improvement on an annual basis (October) 8. For changes to the Test Directory which will impact patients, public consultation is undertaken (October to December) 9. An equalities and health inequalities impact assessment is conducted 10. A formal decision on any amendments to the Test Directory is made 11. The updated Test Directory is published to support implementation (December) 12. The updated Test Directory is fully implemented by April each year **Processes for in-year updates to the Test Directory** **Process for informing NICE Technology Appraisals:** 1. Horizon scanning is carried out to identify potential candidate genomic tests for addition to the Test Directory 2. Confirm whether the test is already available through the National Genomic Test Directory 3. The data required to carry out an impact assessment for implementing the test are determined 4. An impact assessment is conducted with the relevant working group 5. Results of the impact assessment are fed into the NICE technology appraisal to inform their recommendations 6. If approved, a detailed implementation plan is produced in collaboration with the GLHs **Process for responding to NHS England and NHS Improvement urgent policy statements:** 1. NHS England and NHS Improvement are notified of any policy involving or requiring genomic testing 2. Confirm whether the test is already available through the National Genomic Test Directory 3. The data required to carry out an impact assessment for implementing the test are determined 4. An impact assessment is conducted with the relevant working group 5. If approved, a detailed implementation plan is produced in collaboration with the GLHs
National Academies of Sciences, Engineering, and Medicine, 2017[13]	1. Development of a genetic testing scenario, including definitions of: ◦ clinical setting ◦ purpose of the test ◦ population ◦ outcomes of interest ◦ comparable alternative test methods 2. Prioritization of topics for evaluation and triage

Source and citation	Relevant features
	3. Evidence review 4. Structured decision process to inform whether or not to adopt use of the test 5. Retain decisions for evaluated genetic test scenarios in a publicly available repository 6. Timely review and revision of decisions as new data are available 7. Identify evidence gaps to be addressed by research

AHS = Alberta Health Services; APL = Alberta Precision Laboratories; CRG = Clinical Reference Group; DBBM = Direction de la biovigilance et de la biologie médicale; GLH = Genomic Laboratory Hub; GMS = Genomic Medicine Service; HTA = health technology assessment; INESSS = Institut national d'excellence en santé et en services sociaux; LFC = Lab Formulary Committee; NHS = National Health Service; NICE = National Institute for Health and Care Excellence; PGP = Provincial Genetics Program; PLMS = Provincial Laboratory Medicine Services.

[a]Each criterion is scored on a scale from 1 to 5, with 1 indicating weak evidence for implementation, and 5 indicating strong evidence for implementation. Scores for each criterion are summed to an overall score, with overall scores between 0 and 20 indicating a weak overall case for implementation, and overall scores > 30 indicating a strong overall case for implementation. It is noted that scoring alone does not determine the outcome of an application but is used to inform the test evaluation working groups in their holistic review, discussions, and decisions on each proposed amendment.

[b]Each criterion is scored on a scale from 1 to 5, with 1 indicating weak evidence for implementation, and 5 indicating strong evidence for implementation. Scores for each criterion are summed to an overall score, with overall scores < 15 indicating a weak overall case for implementation, and overall scores > 20 indicating a strong overall case for implementation. It is noted that scoring alone does not determine the outcome of an application but is used to inform the test evaluation working groups in their holistic review, discussions, and decisions on each proposed amendment.

Appendix 3: Features of Included Sources for Key Objective 2

Note this appendix has not been copy edited.

Features of Included Sources

Eleven of the included 12 inventories, databases, or lists described in-province testing.[15-24] The source from Alberta (as well as a supplementary source),[15,29] 1 from Manitoba,[22] 2 from Quebec (as well as a supplementary source),[24,26,30] 1 from Prince Edward Island,[18] 1 from Nova Scotia,[23] and 1 from Yukon (as well as a supplementary source)[25,31] also described information regarding out-of-province testing. Three of the sources described information regarding the current status of funding for tests, as well.[17,21,26]

With regard to indication, 10 of the 12 included sources described information on tumour location,[15-22] whereas 2 did not.[23,25] Testing indications were differentiated as adult or pediatric in 7 of the inventories, databases, or lists,[15-17,20,22] though this distinction was not included in 5 of the sources.[18,19,21,23] For the purposes of testing, predictive, prognostic, or diagnostic was described by 6 of the included sources,[15,17,18,21,22] and 6 did not report this information, or did not report it clearly or consistently.[16,19,20,23] Information describing reflex testing was reported by 1 source from British Columbia[16] and 1 from Ontario;[17] though the other 10 included sources did not describe this information.[15,18-23]

Ten of the included sources described the biomarkers for which testing is conducted,[15-17,19,20,22,23] whereas 2 sources, 1 from Prince Edward Island[18] and 1 from Newfoundland and Labrador,[21] did not. The testing method(s) used were described by 7 of the included sources[15-19] (with 1[17] reporting this information in a supplementary source[32]), and the test assay(s) used were described by 2 sources.[16,23] Turnaround times for the processing of tests were described by 6 of the sources,[15,16,18,21] but not included, or not clearly and consistently reported, in the remaining 6 sources.[17,19,20,22,23] Information to support test interpretation was included by 1 source from Quebec,[26] 1 source from British Columbia[16] and 1 source from Alberta,[15] but was not included, or not clearly or consistently reported, in the other inventories, databases or lists.[17-23] Finally, the need for repeat testing was described in 3 of the included sources,[16,21] but was not reported, or not clearly or consistently reported, in the remaining 7 sources.[15,17-20,22,23]

The key features of included sources are presented in Table 9.

Table 9: Features of Included Sources for Key Objective 2

Inventory, database, or list Source	Features				
	Availability, access, and funding	Testing indication	Testing details	Limitations	Input from consultations
BC Cancer, 2024[16]	• In-province testing site(s)	• Tumour location and stage • Adult / pediatric • Reflex testing	• Biomarkers • Turnaround time • Need for repeat testing • Testing method • Test assay used • Interpretation	Not consistently reported: • Predictive / prognostic / diagnostic • Reflex testing Not reported or unclear: • OOP testing information • Funding status • Costs	This Cancer Genetics and Genomics Laboratory website at BC Cancer identifies testing available to cancer patients in the province. A BC Cancer website on Laboratory Services shows turnaround times (under the About tab) and tests (under the Test request forms tab in individual requisition forms).
Alberta Precision Laboratories Test Directory Alberta Precision Laboratories[15]	• In-province testing site(s) • OOP testing information[29]	• Tumour location • Predictive / prognostic / diagnostic • Adult / pediatric	• Biomarkers • Turnaround time • Testing method • Interpretation	Reported to be an interim test directory Unable to filter by genetic or genomic testing category: need to know specific keywords associated with the test of interest Some details are only found by accessing linked requisition forms Not consistently reported: • Tumour stage • Test assay used Not reported or unclear: • Funding status • Costs • Reflex testing • Need for repeat testing	Multiple lists exist to serve different purposes (e.g., as a guide to lab services or parts of requisition forms for physicians to request testing). This is an interim test directory and not a formulary (i.e., listing all covered tests). Alberta is working on a single system integrating the lab test formulary, a test directory, and the related guide to lab services.

Inventory, database, or list Source	Features				
	Availability, access, and funding	Testing indication	Testing details	Limitations	Input from consultations
Lab Information Manual Shared Health Manitoba, 2014[22]	• In-province testing site(s) • OOP testing information	• Tumour location • Predictive / prognostic / diagnostic • Adult / pediatric	• Biomarkers	Some details are only found by accessing linked requisition forms Not consistently reported: • Turnaround time • Need for repeat testing • Testing method Not reported or unclear: • Funding status • Costs • Tumour stage • Reflex testing • Testing assay used • Interpretation	This Lab Information Manual by Shared Health Manitoba, which oversees all labs in the province, identifies most covered tests but not all. An inventory specific to cancer biomarkers is in development but not publicly available.
Laboratory Guide to Services, Version 6.0 Yukon Hospitals, 2024[25]	• OOP testing information[31]	• Adult / pediatric	• Biomarkers	Some details are only found by accessing linked requisition forms Not consistently reported: • Predictive / prognostic / diagnostic • Testing method Not reported or unclear: • Funding status • Costs • Tumour location and stage • Reflex testing • Turnaround time • Need for repeat testing • Testing assay used • Interpretation	NR

Inventory, database, or list Source	Features				
	Availability, access, and funding	Testing indication	Testing details	Limitations	Input from consultations
				Not applicable: • In-province testing site(s)	
Comprehensive Cancer Biomarker Testing Program Cancer Care Ontario, 2024[17]	• In-province testing site(s) • Funding status	• Tumour location and stage • Predictive / prognostic / diagnostic • Adult / pediatric • Reflex testing	• Biomarkers • Testing method[32]	Not consistently reported: • Need for repeat testing Not reported or unclear: • OOP testing information • Costs • Turnaround times • Test assay used • Interpretation	ON maintains this publicly accessible list of funded biomarkers where clinical sites and the public can reference. Ontario Health also collaborates with clinical programs to maintain internal records of biomarkers used within specific disease areas.
Ontario Genetic Testing Registry Ontario Health, 2024[20]	• In-province testing site(s)	• Tumour location • Adult / pediatric	• Biomarkers	Not consistently reported:[a] • Testing method Not reported or unclear:[a] • OOP testing information • Funding status • Costs • Tumour stage • Predictive / prognostic / diagnostic • Reflex testing • Turnaround time • Need for repeat testing • Testing assay used • Interpretation	NR
Clinical Laboratory Test Directory for CUSM sites Centre universitaire de santé McGill, 2024[24]	• In-province testing site(s) • OOP testing information[30]	• Tumour location	• Biomarkers • Turnaround time • Testing method	Site-specific[b] • Some details are only found by accessing linked requisition forms Not consistently reported: • Predictive / prognostic / diagnostic	NR

Inventory, database, or list Source	Features				
	Availability, access, and funding	Testing indication	Testing details	Limitations	Input from consultations
				• Testing assay used • Interpretation Not reported or unclear: • Funding status • Costs • Tumour stage • Adult / pediatric • Reflex testing • Need for repeat testing	
Répertoire québécois et système de mesure des procédures de biologie médicale 2022-2023[26]	• In-province testing site(s) • OOP testing information • Tests categorized by complexity and ensured coordinated access • Funding status	• Tumour location • Therapeutic / prognostic • Adult / pediatric	• Biomarkers • Testing method • Sample type • Turnaround time • Need for repeat testing • Interpretation	• Clinical relevance • Limited access to certain biomarkers in some regions • High costs associated with some biomarker tests • Technical challenges	Quebec maintains the Répertoire de biologie médicale 2022-2023 (available in French only) that is updated annually listing publicly funded tests. New additions can also be captured in midyear updates, but these are not publicly available.
Saint John Area Laboratory User Manual v23.0 Horizon Health Network, 2024[19]	• In-province testing site(s)	• Tumour location	• Biomarkers • Testing method	Region-specific[c] • Some details are only found by accessing linked requisition forms Not consistently reported: • Tumour stage • Predictive / prognostic / diagnostic • Adult / pediatric • Need for repeat testing Not reported or unclear: • OOP testing information	Although some biomarkers are listed in this Laboratory User Manual for the Horizon Health Network regional health authority (serving a third of the population [i.e., anglophone]), it is not comprehensive and does not include the Vitalité regional health authority (serving the remaining 2 thirds of the population [i.e., francophone]).

Inventory, database, or list Source	Features				
	Availability, access, and funding	Testing indication	Testing details	Limitations	Input from consultations
				• Funding status • Costs • Reflex testing • Turnaround time • Testing assay used • Interpretation	
Health PEI Department of Laboratory Medicine Test Catalogue Health PEI, 2024[18]	• In-province testing site(s) • OOP testing information	• Tumour location • Predictive / prognostic / diagnostic	• Turnaround time • Testing Method	Reported to be a "work in progress" Not consistently reported: • Biomarkers Not reported or unclear: • Funding status • Costs • Tumour stage • Adult / pediatric • Reflex testing • Need for repeat testing • Testing assay used • Interpretation	This is a generic list that does not comprehensively list relevant cancer biomarkers. Reflex testing is available for lung, breast, and colon cancers, such as MMR, and some hematopoietic tumours, but PEI does not maintain a public inventory of funded biomarkers.
Department of Pathology and Laboratory Medicine Central Zone Laboratory Test Catalogue and Gene Panels Available for NGS Nova Scotia Health Authority, 2024[23]	• In-province testing site(s) • OOP testing information	• NA	• Biomarkers • Testing assay used	Not consistently reported: • Tumour location • Testing method Not reported or unclear: • Funding status • Costs • Tumour stage • Predictive / prognostic / diagnostic • Adult / pediatric • Reflex testing	NR

Inventory, database, or list Source	Features				
	Availability, access, and funding	Testing indication	Testing details	Limitations	Input from consultations
				• Turnaround time • Need for repeat testing • Interpretation	
Provincial Laboratory Formulary Newfoundland and Labrador Department of Health and Community Services[21]	• In-province testing site(s) • Funding status	• Tumour location • Predictive / prognostic / diagnostic	• Turnaround times • Need for repeat testing	Last updated in 2021 Unable to filter by genetic or genomic testing category: need to know specific keywords associated with the test of interest Some details are only found by accessing linked requisition forms A process is reported for OOP testing, however specific tests or reference laboratories are not described[33] Not consistently reported: • Costs • Biomarkers • Testing method • Interpretation[34] Not reported or unclear: • Tumour stage • Adult / pediatric • Reflex testing • Test assay used	Newfoundland and Labrador maintain this provincial lab formulary, but it is outdated and undergoing transition to be more accessible.

NA = not applicable; NR = not reported; OOP = out of province.

[a]The Ontario Genetic Testing Registry[20] provides links to the laboratory website and relevant requisitions for each panel. Features classified here may be available from these additional sources.

[b]The Centre universitaire de santé McGill health network is 1 of 5 laboratory "clusters" servicing the province of Quebec.[1] The Ministère de la Santé et des Services sociaux, Quebec, published a provincial-level test directory, the Répertoire québécois et système de mesure des procédures de biologie médicale – Édition 2022 to 2023.[26] This source was issued in French only.

[c]Horizon Health Network is one of 2 regional health authorities in New Brunswick.

Appendix 4: Consultations Results

Note this appendix has not been copy edited.

Table 10: Findings From the Consultations Relevant to Key Objective 1

Jurisdiction	Features
Framework, Processes and Criteria	
Alberta	The Alberta Laboratory Formulary Committee (LFC) is accountable for evidence-informed, transparent, and timely decision-making regarding the inclusion of, and indications for, laboratory tests included on the AHS laboratory formulary. The LFC comprises members representing leadership roles within laboratory medicine, genetics and genomics, public health, molecular pathology, clinical end-users, HTA, finance, ethics, and includes patient and family advisors. LFC reviews and considers endorsement of the appropriate context of use of a test, while implementation is operationalized by Alberta Precision Laboratories (APL) typically within various disciplinary programs. The LFC makes funding recommendations, which are subsequently reviewed by Alberta Health Services (AHS) in consideration of the budget and in the context of the organizational core values (e.g., equitable access, use in adults or pediatric populations). Criteria used to inform recommendations for funding include test appropriateness (i.e., efficacy and effectiveness of the test, system-level need, alignment with APL goals and values), system stakeholder engagement (i.e., clinical endorsement, system capacity), economic impact (i.e., affordability, cost-effectiveness, financial risks) and equity are other related considerations.
British Columbia	Funding pathways for companion diagnostic tests are aligned with the process for drug funding. Other biomarker tests that are not associated with a targeted therapy are steered through the same pathway but steps in that process are sometimes not as clearly aligned. On funding for companion diagnostics, BC Cancer manages a life support budget (which is ring fenced by BC government to fund lifesaving cancer medications.) It is primarily used for drugs but in recent years has been expanded to include companion diagnostics associated with these drugs. For other processes, the labs receive requests for testing from clinicians or tumour groups directly. Or manufacturers work with the lab and clinician champion to implement a test though seed or grant funding. Tests may also be done by the labs in the context of a clinical trial. In these latter situations, there is sometimes not a clear path for HTA review and funding decision-making and the testing is continued to be performed by the lab through its ongoing operating budget.
Manitoba	There are different assessment and decision-making processes and funding pathways for companion diagnostic tests vs. other biomarker tests that are not associated with a targeted therapy. For companion diagnostics, Manitoba has an Oncology Working Group, which includes key clinical and laboratory decision-makers who meet monthly to review needs for testing tied to drug reimbursement recommendations from CDA-AMC. Biomarkers are typically identified based on knowledge of drugs with companion diagnostics that are undergoing CDA-AMC reimbursement review. Decisions about tests, including whether they should be done in Manitoba or sent out, are largely based on anticipated volume and resources. For other biomarkers –There's reliance on environmental scans and reports from other jurisdictions to align testing practices, with emphasis on the economic impact of testing and ensuring consistency with other jurisdictions to avoid duplication of work. Biomarkers are identified through requests from Disease Site Groups, or specific clinician requests, often driven by immediate patient needs. The Oncology Working Group and a smaller core committee assess requests for biomarker tests. The Oncology Working Group, consisting of pathologists, oncologists, and finance/technical team members, reviews new drug-related biomarker requests, while the core committee handles case-by-case requests for non-drug associated tests.

Jurisdiction	Features
New Brunswick	New Brunswick Cancer Network (NBCN) works with the Regional Health Authorities (RHA) to implement biomarker testing. Currently, there is no standardized assessment framework, as testing decisions are typically made at the physician or pathologist level. Testing is included as part of the global budget at the RHA level. Biomarkers are identified based on clinical need; centralized tracking and oversight are limited. NBCN is making efforts to establish a more coordinated provincial approach, but some structural challenges remain.
Newfoundland and Labrador	Newfoundland and Labrador's Provincial Laboratory Formulary Advisory Council (PLFAC) reviews biomarker test applications. Applications are initiated primarily by oncologists, with support from pathology and other lab disciplines, and reviewed in Advisory Council meetings. The application process includes details on clinical utility, required human and other resources, and cost implications as well as details about the disease and test, whether conducted in-house or sent out, and information about the algorithm/evidence (e.g., if available from CDA-AMC).Approval involves a consensus-based decision, with larger funding requests forwarded to the government when necessary. Implementation depends on funding availability. The process may be prolonged in some instances due to resource constraints and the government's annual budget cycle.
Nova Scotia	NS has an Impact Committee that is tasked with assessing the anticipated impact of new drugs and tests in the pipeline. Impact is considered across a range of potential consequences including infrastructure, educational and human resource requirements across a range of medical specialties, and anticipated health system utilization. For drugs or tests that are anticipated to have substantial impact, a business case is developed and submitted to the hospital or Department of Health for additional funding. The Impact Committee usually meets weekly. Currently, there is no standardized assessment framework to help determine which biomarker tests are implemented or funded, as testing decisions are typically made at the physician or pathologist level. When a test is ordered, it may be processed onsite or sent out of province if local facilities cannot perform the test. A report from the Impact Committee's discussions is prepared every 6 months for presentation to the Cancer Council and Cancer Care program, in addition to being shared with labs and diagnostic imaging teams for awareness and to support readiness. Funding decisions are escalated to the Cancer Care Program leadership and ultimately to hospital executives.
Nunavut	Nunavut has an appointed individual that makes funding recommendations for people in Nunavut that may require genetic testing. The process relies on medical experience and expertise in addition to reference to external resources like those available through the province of Alberta, Ontario, and Manitoba, and their genetic services. Tests for tumour markers with an associated drug treatment may be requested from time to time and would require prior approval through the same mechanism. Decisions require detailed criteria on a checklist, including patient information, clinical diagnosis, and reason for testing. Approvals are made for tests based on clinical need, clinical evidence, and alignment with processes that occur within other jurisdictions. All requests for genetic tests must have included a genetic consultation that is documented on the decision-making checklist. The decision-making is primarily supported by the Medical Consultant, who makes recommendations for funding. Larger jurisdictions like Alberta, Manitoba and Ontario provide guidance on request, and their genetic external committees in these jurisdictions. Tissue biomarkers for solid tumours may be requested in the future to individualize drug treatments for patients based on the choice of the 'best' treatment options, based on a biomarkers' presence (precision medicine). A similar process like that for genetic testing for prior approvals will be in place. Final decisions are approved by Nunavut's health insurance program. Clinical utility and need are priority criteria used to inform recommendations. Access to genetic testing for Nunavummiut that is equitable to other Canadians is vitally important.

Jurisdiction	Features
Ontario	Cancer Care Ontario's (CCO) Pathology and Laboratory Medicine Program is responsible for oversight and funding of genetic testing. A biomarker assessment program develops recommendations for funding and implementation (e.g., for reflex testing). There is a different process and funding pathways for companion diagnostic tests vs. other biomarker tests that are not associated with a targeted therapy. On the process for funding companion diagnostics, tests that are tied to drugs that have positive reimbursement recommendations from CDA-AMC are prioritized. As funding comes from the Ministry of Health (MOH), companion diagnostics are included as part of OH's funding request to the MOH. Companion diagnostics are flagged as a priority item, but actual funding within the province cannot occur until funding is provided by the MOH. As a result, there can be a lag between the recommendation of the CDA-AMC and the implementation of funding. For other biomarkers, decisions are informed by evidence of clinical utility, guidelines in other jurisdictions, and turnaround time. Cost and implementation feasibility are considered once clinical utility has been established. For more complex decisions, working groups may be established that include clinical and laboratory professionals. The process involves annual feedback gathering, and iterative updates as new evidence emerges. Decisions on biomarker testing are implemented through collaborations with clinical sites that help to assess the clinical context to confirm biomarkers' feasibility in Ontario. Clinical utility, feasibility, cost-effectiveness, equity, efficient use of resources and rapid turnaround times are some of the criteria used for existing assessments. Funding is provided by CCO to sites that demonstrate the capability to support cancer care programs with testing capacity at a level that allows sites to test using a panel approach. Sites are responsible for implementation and infrastructure, which is funded at the site (e.g., hospital) level.
Saskatchewan	Saskatchewan has a Molecular Biomarker Prioritization Committee, which includes anatomic pathologists, geneticists, and lab directors, and that assesses biomarkers through a tiered prioritization framework. The process includes 3 priority levels: Category 1: for biomarkers linked to a funded drug (i.e., companion diagnostics and for monitoring); Category 2: for prognostic or predictive markers, and Category 3: for all others; lower priority. The process is applied through a simplified request form to capture clinical utility, logistical needs, disease information, volume, and cost. Funding requests are submitted to the Saskatchewan Cancer Agency, which manages the biomarker budget separately from the drug budget.
Prince Edward Island	Prince Edward Island does not currently have an assessment framework. Decisions about what tests to use and implement are typically driven by requests from oncologists, and pathologists. All testing is currently being conducted out of province, typically in Halifax. Prince Edward Island's pathologists facilitate this process but are not responsible for informing which tests are appropriate in the context of the province. Requests are generally accepted without restriction, with all testing costs covered by the annual lab budget. The process is informal, with no strict budgetary tracking of testing costs, which has not been a significant issue given PEI's population size. PEI relies on referral centre capabilities for testing options and does not have a formal decision-making or evaluation framework.
Quebec	Quebec uses the Répertoire québécois et système de mesure des procédures de biologie médicale (catalogue of available tests) as an inventory of available tests in Quebec. Tests are classified by complexity and volume (local, regional, or super-regional levels) and must be included in the Répertoire to be offered in the public health system. There are different processes for companion diagnostic tests and other biomarker tests. Funding for companion diagnostic tests is typically automatically recommended following a positive reimbursement recommendation by (Institut national d'excellence en santé et services sociaux [INESSS]). Funding for other biomarker tests is assessed by the Ministry and always includes an assessment by INESSS and are additionally informed by feasibility, cost, and clinical importance.

Jurisdiction	Features
Guiding Principles	
Alberta	• Affordability • Equity • Appropriate use • Feasibility
British Columbia	• Consistency • Transparency • Clinical value • Cost-effectiveness • Equity
Manitoba	• Equity • Efficiency • Evidence-based decisions • Patient impact
New Brunswick	• Equity • Efficiency • Affordability • Clinical utility • Appropriateness of testing
Newfoundland and Labrador	• Standardization across provinces to optimize resource use and ensure equitable access
Nova Scotia	• Patient outcome improvement • Equity • Alignment with clinical needs • Early awareness of emerging tests • Cost-effectiveness • Resource feasibility • Regional collaboration to address resource disparities
Nunavut	• Collaboration with larger jurisdictions to maintain consistency and equity in access • Fairness and streamlined decision-making to reduce disparities in smaller regions
Ontario	• Equity • Transparency • Cost-effectiveness • Adaptability • Standardized guidelines across jurisdictions to mitigate disparities and improve access to biomarker testing
Saskatchewan	• Equity • Efficiency • Evidence-based decision-making to align practices and reduce duplication in biomarker evaluation
Prince Edward Island	• Affordability • Timeliness

Jurisdiction	Features
Quebec	• Equity • Efficiency • Cost-effectiveness • Standardized procedures to minimize interlab competition and optimize testing infrastructure

Appendix 5: Map of Relevant Features for Key Objective 1

Note this appendix has not been copy edited.

Identification of Foundational Sources

On review of the data, the source from the WHO was selected as the foundational source for guiding principles based on its relevance and breadth that captured many of the guiding principles described in the other included sources.[6] For the assessment criteria, the 2 sources from Italy (funded by the Italian Ministry of Health) were selected as the foundational sources for their comprehensiveness, relevance, and recency of publication, which also captured many of the criteria outlined in the other included sources.[10,11] For the decision-making processes, the source from Health Quality Ontario was selected for its relevance to the Canadian context, comprehensiveness, and breadth, which also captured many of the process steps described in the other included sources.[5] The guiding principles, assessment criteria, and decision-making processes identified, as reported, from all other included literature and information sources (including those from the consultations) additional to the foundational sources were mapped and added to those from the foundational sources and are presented in Table 11.

Table 11: Map of Relevant Features Across Included Data and Information Sources for Key Objective 1

Foundational literature source	Relevant features from the foundational literature source	Similar, relevant features identified from other sources	Additional relevant features identified from other sources
Guiding principles			
WHO, 2024[6]	To affirm and value the right of individuals and communities	Respect for individuals, families and communities[9]	• Relevance of evaluation modalities[4] • Knowledge mobilization and integration, evidence-informed, test appropriateness, value creation[3,4,8,a] • Timely[3,a] • Advance research and scientific knowledge[9]
	Social justice	NR	
	Solidarity	NR	
	Equitable	• Fair, equitable[3,4,a] • Promote health, well-being, and the fair distribution of benefits[9]	
	Collaboration, cooperation, and partnership	• System stakeholder engagement, deliberative[3,a] • Foster trust, integrity and reciprocity[9,a] • Holistic review, discussion and	

Foundational literature source	Relevant features from the foundational literature source	Similar, relevant features identified from other sources	Additional relevant features identified from other sources
		decision[8,a] • Multidimensional deliberation[4]	
	Transparency	• Transparent, clear[3,8,a]	
	Accountability	• Accountability, consistency[3,a]	
	Stewardship	• Reasonable, feasibility, efficiency, cost-effectiveness, adaptability[4,a]	
Assessment criteria			

Pitini, 2019[10]	**Genetic Test**
	Test and clinical condition overview
	• Clinical condition:
	  ○ Clinical presentation and pathophysiology
	  ○ Genetic background
	  ○ Public health impact
	• Genetic test:
	  ○ General features
	  ○ Technical features
	  ○ Clinical context
	Analytic validity
	• Analytic sensitivity and specificity
	• Accuracy
	• Precision
	• Robustness
	• Laboratory quality control
	Clinical validity
	• Scientific validity
	• Test performance:
	  ○ Clinical sensitivity and specificity
	  ○ Positive and negative predictive value
	  ○ Modifiers
	Clinical utility
	• Available interventions
	• Efficacy
	• Effectiveness
	• Safety
	Personal utility
		Clinical condition considerations
		• Improved health and well-being of populations and benefit to patients[4,8,12-14]
		Test considerations
		• Test effectiveness[2,3,a]
		• Analytic validity[13,14]
		• Clinical validity[12,13,a]
		• Clinical utility[8,12,13,a]
		• Diagnostic performance, clinical evaluation[7]
		Personal considerations
		• Impact on patient anxiety[12]
			• Biological plausibility, qualification, prevalence of the biomarker in the population to be tested, actionability[7,14,a]
			• Impact on clinical decision-making[12,13]

Foundational literature source	Relevant features from the foundational literature source	Similar, relevant features identified from other sources	Additional relevant features identified from other sources

	Delivery models
	Health care programs
	Level of care
	Patient pathway
	Organizational aspects
	• Expected demand
	• Resources management
	• Other organizational requirements:
	  ○ Education of professionals, patients, and citizens
	  ○ Information dissemination to professionals, patients, and citizens
	  ○ Cooperation, communication, and coordination
	  ○ Quality assurance, monitoring, and control
	• Barriers to implementation
	Economic evaluation
	Ethical, legal, and social implications
	Patient perspective
		Organizational considerations
		• System-level and organizational need and capacity[2-4,8,a]
		• Alignment with organizational goals; system stakeholder engagement; clinical endorsement[2,3,8]
		• Impacts to clinical and testing operations[8,a]
		Economic considerations
		• Affordability, cost-effectiveness, financial impacts and risks[3,8,12,13,a]
		• Responsible and sustainable management of resources[4,7]
		ELSI considerations
		• Equity, effects on health disparities[2,3,13,a]
		• Sociocultural, societal efficacy[4,13]
			NR

	Research priorities ***Evidence gaps***	• Levels/quality of available evidence[7] • Consideration of real-world data[7,14]	NR
	Reporting and decision-making ***Net benefit*** ***Cost-effectiveness*** ***Feasibility***	Sources reporting on information of relevance to this criterion described these features as part of their processes for decision-making [1-3,8,13]	NR
Decision-making processes			

Health Quality Ontario[5]	**Topic identification**
	• Open application process
		• Tests proposed for assessment can be identified by:
		  ○ A publicly accessible application process is available in Alberta[1,a]
		  ○ A limited, closed, or unclear application process was described by all other sources[1,3,8,13,a]
			• The application process may or may not be initiated at a single point of entry[1,a]
			• Tests proposed for assessment can be identified by a horizon or environmental scanning process[8,a]
			• Different assessment processes may or may not exist for companion diagnostic biomarker tests vs. other biomarker tests not associated with a drug therapy[a]

Foundational literature source	Relevant features from the foundational literature source	Similar, relevant features identified from other sources	Additional relevant features identified from other sources
			• Proposed tests are reviewed for novelty and completeness and a decision whether to review or not is made[2,3,8] • Proposed topics are prioritized[13,a]
	Scope development and literature searches • Develop clinical, economic, and patient preferences and values review plans • Complete literature searches	• An evidence review is undertaken[2,3,8,13]	• Experts are assigned to the review process[8] • Data required to conduct an impact assessment are assessed[8]
	Evidence development and reporting • Complete analyses • Prepare draft HTA report • Present draft HTA findings to OGAC • OGAC develops draft recommendation • Draft recommendation presented to OHTAC for approval		• An impact assessment is completed, including appropriate expert input[8,a] • Various individuals, groups and/or committees oversee the evidence review and assessment[a] • Evidence for complex reviews may be gathered on an ongoing basis, as newer evidence emerges, allowing for updated assessment[a] • Deliberations may rely on consensus-based or other methods[a]
	Production • Edit HTA report and draft recommendation document • Notify the Ontario Ministry of Health of draft recommendation • Post HTA report and recommendation for public feedback • OGAC finalizes genetic test recommendation, which is then reviewed by OHTAC	• The test review process results in (a) recommendation(s) and/or advice being provided to decision-makers concerning adoption of the test[1-3,8]	• Smaller jurisdictions may rely on information and/or support from larger jurisdictions[a] • Various individuals, groups and/or committees oversee the deliberation and development of recommendation(s)[a] • Various reporting mechanisms and approaches are used to issue recommendations(s) and/or decisions[a] • The impact assessment is considered in development of recommendations[8] • A deliberative/evaluation process informs the development of recommendations[1,13]
	Final ministry notification and web posting • Share approved HTA report and funding recommendation with the Ontario Ministry of	• Decisions are made available in a publicly available repository[13]	• A decision is rendered as to whether or not to adopt the test[1,8,13] • An implementation plan is produced collaboratively with

Foundational literature source	Relevant features from the foundational literature source	Similar, relevant features identified from other sources	Additional relevant features identified from other sources
	Health • Post finalized HTA report and recommendation on Ontario Health's website		regional stakeholders[1-3,8] • Evidence gaps are identified to inform future research[13] • Implementation support may be available to clinical sites through collaborative arrangements[a]

AHS = Alberta Health Services; APL = Alberta Precision Laboratories; CRG = Clinical Reference Group; DBBM = Direction de la biovigilance et de la biologie médicale; GLH = Genomic Laboratory Hub; GMS = Genomic Medicine Service; HTA = health technology assessment; LFC = Lab Formulary Committee; NHS = National Health Service; NICE = National Institute for Health and Care Excellence; NR = not reported; PGP = Provincial Genetics Program; PLMS = Provincial Laboratory Medicine Services.

[a]Findings generated from the consultations.

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