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Building capacity for clinical exome sequencing: a comparative case study of Canadian provinces

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Research Article

Keywords: Case study, healthcare delivery, exome sequencing, implementation, genome diagnostics, Canada

Posted Date: November 12th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11148101/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

As genome diagnostics advance, health systems face growing pressure to implement complex and resource-intensive technologies like exome sequencing (ES). Understanding how implementation varies across health systems is critical for informing the organization, delivery, and sustainability of advanced genome diagnostics. We explored how Canadian provincial health systems and key stakeholders have approached clinical ES implementation to guide ongoing efforts to improve access to genome diagnostics for Canadians.

Methods

Using an embedded multiple-case study design informed by Rogeres' Diffusion of Innovation theory and the Consolidated Framework for Implementation Research, a comparative analysis was conducted to understand the provincial landscape of genetic service delivery and the implementation strategies used to support clinical ES in four Canadian provinces: Alberta, British Columbia, Manitoba, and Ontario. Semi-structured interviews with informants from clinical genetics, diagnostic laboratories, government and genomics research organizations were conducted between August 2023 and August 2024, and relevant documents published up to January 2026 were reviewed. Interview and document review data were integrated using qualitative thematic analysis.

Results

Forty-one participants were interviewed. Results revealed a shared provincial motivation to enhance local capacity for clinical ES, with an emphasis placed on the importance of centralized clinical ES infrastructure. A centralized implementation strategy appears to be essential to supporting the complexity of this intervention that requires significant resources (e.g., sequencing infrastructure, informatic, data storage), specialized expertise, and coordination among clinical and laboratory groups. Provincial differences in the delivery of genome diagnostics services were identified. These related primarily to the variable eligibility criteria across provinces, leading to inconsistencies in patient access to clinical ES.

Conclusion

Within the context of Canada's decentralized health system, the findings emphasize the need for standardization of structures and processes to support the adoption, delivery, and ongoing evaluation of existing and emerging -omics technologies. Interprovincial collaboration and resource sharing may provide opportunities to strengthen implementation capacity and support access to genome diagnostics across Canada. These findings are also relevant to other countries with decentralized or regionally distributed health systems, where standardized approaches to the delivery of complex health interventions can facilitate improved access for patients.

Background

Canada's publicly funded healthcare system is an example of a decentralized system consisting of ten provincial and three territorial healthcare systems.[1] The provincial and territorial governments are primarily responsible for delivering health and other social services.[1] Aligned with the Canada Health Act, clinical genetic services are publicly funded when deemed medically necessary.[2] Within each province or territory, various genetic tests are available through local labs or through out-of-province or out of country special access programs.[3, 4] Most genetic tests are covered by provincial health plans for patients who have coverage if they meet test-specific criteria and when the test is ordered by a physician.[5, 6] When these conditions are not met, some individuals choose to access testing through out-of-pocket payment or through private or employer-based insurance programs.[6] As with other health services, regional variations exist in the availability and scope of genetic tests that are offered across provinces and territories.[2]

Exome sequencing (ES) enables comprehensive analysis of an individual's genetic makeup.[7] Since ES demonstrates high diagnostic yields compared to conventional genetic tests, its clinical use has increased globally.[8, 9] Despite its role in early diagnosis, local implementation of clinical ES within the Canadian health systems has been slow. Until the last few years, clinical ES has been largely outsourced to US-based laboratories through out-of-country exceptional access programs, leading to significant interprovincial variability in patient access, costs, and missed opportunities for local discovery research.[10–12]

Challenges to implementation have been well documented globally and include the complexity of existing systems for genetic service delivery, workforce shortages, limited investment in infrastructure, and gaps in evidence on clinical utility, cost-effectiveness, and optimal implementation approaches.[13–17] However, evidence on how health systems organize and implement complex genome diagnostics such as clinical ES remains limited in the Canadian context. As provinces and territories are at different stages of adopting and implementing clinical ES, understanding what processes are in place for implementing clinical ES at the provincial level may offer valuable insights into strategies well-suited to a range of provincial settings. The learnings may also offer insights for other decentralized health systems that face similar challenges in implementing resource-intensive complex health interventions.[18] Informed by Rogers' diffusion of innovation theory and the Consolidated Framework for Implementation Research, we conducted an in-depth comparative analysis to understand the landscape of provincial genetic service delivery and the implementation strategies in place to support clinical ES in four provinces.[19, 20]

Methods

Study design

This study used an embedded, multiple-case study design.[21] Since healthcare services are administered at the provincial level, a case study design enabled an in-depth understanding of the implementation context for clinical ES in selected Canadian provinces and a comparative analysis across provinces to inform best practices for ES implementation.[21]

Case selection

Applying Rogers' Diffusion of Innovation (DOI) theory, we selected cases based on provincial readiness for clinical ES implementation.[19] Rogers' theory describes the five-stage innovation decision process (i.e., Knowledge, Persuasion, Decision, Implementation, and Confirmation) through which a decision-making unit (i.e., provincial health authority) reaches the decision to adopt and implement an innovation (i.e., clinical ES). At the Knowledge stage, the decision-making unit becomes aware of the innovation and gains an understanding of its function. At the Persuasion stage, the decision-making unit develops a favourable or unfavourable attitude toward the innovation. The Decision stage is reached when the decision-making unit engages in activities that lead to a decision to adopt or reject the innovation. Implementation occurs when the innovation is put to use. At the Confirmation stage, the decision-making unit seeks support for the decision that was made. The decision may be reversed if conflicting information about the innovation becomes available. We used the stages of the innovation decision process to characterize provincial readiness and selected provinces that were considered to be in the Implementation stage for clinical ES. Selection criteria included: 1) access to out-of-province clinical ES as a reimbursed test, and 2) presence of a provincial process for health technology assessment (HTA) in genomics. Four provinces – Alberta, British Columbia, Manitoba, and Ontario – met the selection criteria. At the time of study conception, no publicly funded Canadian molecular diagnostic laboratory offered ES as a clinical service. Within each case, key interest groups were identified, comprising three embedded units: 1) clinics that deliver genetic services, 2) molecular diagnostic laboratories that offer clinical genetic testing, and 3) provincial organizations involved in the oversight and evaluation of genetic service delivery and/or translational genomics research funding.

Data Collection

Key informant interviews

Eligible participants from each embedded unit in each province included 1) clinical geneticists and genetic counsellors with experience ordering out-of-country clinical ES, 2) molecular diagnostic laboratory directors, technologists, and genetic counsellors, and 3) policymakers involved in developing, evaluating, or implementing provincial genetic services. In addition, individuals in leadership roles within relevant national research funding organizations, patient advocacy organizations, or professional associations or policy committees were eligible to provide broader contextual insights into the Canadian landscape. For each province, a list of potential participants for each of the four groups was created using publicly accessible websites (e.g., professional societies, hospitals offering clinical genetic services in each province). Purposeful and snowball sampling methods were used to recruit participants, ensuring diversity in years of work experience, practice setting (i.e., urban or rural) and gender. To protect participant anonymity, participant age and ethnicity were not collected.

The interview guide was developed specifically for this study, informed by Rogers' Diffusion of Innovation Theory and the Consolidated Framework for Implementation Research (CFIR v2)(Supplementary file 1).[19, 20] Specific topics were queried at the provincial level and included the structure for genetic service delivery, process for adopting novel genetic tests, ES implementation climate, and ES implementation approach. All interviews were conducted in English on video conferencing software or by telephone between August 2023 and August 2024.

Document review

Documents were collected through a targeted search of relevant websites using Google. Only English content with a publication date up to January 15, 2026 were reviewed. The search focused on websites of provincial governments, professional societies, regional funding organizations, clinical genetics services, and molecular diagnostic laboratories in each province. Websites were reviewed for information on delivery of genetic services within the province, including documents on the adoption and implementation of ES. Data extraction was guided by CFIR v2, with a focus on content related to three domains: *Outer Setting*, *Inner Setting* and *Implementation Process*.

Data analysis

Interviews were audio-recorded, transcribed verbatim, and deidentified. Key informants were categorized as clinical, laboratory, and other (Table 1). Documents were categorized by province or assigned to the national context. Documents and interview data analyses were iterative and guided by the three aforementioned CFIR v2 domains.[20, 22] Interview data were coded and thematically analyzed following a mixed, deductive-inductive approach. Domain-based and inductively generated codes from documents and interviews were consolidated to generate a case description of genetic service delivery in each province, including its current landscape for delivering clinical ES. Specifically, for each province, data were synthesized under the following headings within the three CFIR domains: *Outer setting* (1) health system structure, (2) process for adopting new tests, *Inner setting* (3) organization and delivery of clinical genetic services, (4) organization and delivery of molecular diagnostic services, and *Implementation process* (5) clinical ES implementation, including eligibility criteria, available test options, and motivation and approach for building in-province capacity. Once case descriptions were constructed, similarities and differences among the provinces were identified. Following preliminary data analysis, member checking was conducted to verify that the study findings

accurately reflected participants' perspectives.[23] Given that key interest groups had been actively working to build in-province capacity for clinical ES over the course of this study, member checking enabled respondents to share insights they had gained since their initial interview.

Results

Participant characteristics

Forty-one key informants participated (response rate: 53%; Tables 1 and 2). Thirty-seven of 41 (90%) participated in member checking. A complete list of reviewed documents is provided in supplementary file 2. Table 3 compares the results across the four provinces.

Table 1. Participant characteristics (N = 41)	**N (%)**
Gender	
Female	26 (63)
Male	15 (37)
Province	
Ontario (ON)	12 (29)
Alberta (AB)	9 (22)
British Columbia (BC)	9 (22)
Manitoba (MB)	8 (20)
Other (i.e., national context)	3 (7)
Professional Setting*	
Genetics Clinic	21 (51)
Molecular Diagnostic Laboratory	10 (24)
Other (e.g., policy, provincial government, health research, genomics funding organization)	10 (24)
Current Professional Role	
Medical geneticist (MG)	13 (32)
Genetic counsellor (GC)	11 (27)
Other (e.g., director, program manager, chief scientific officer, researcher) (OT)	11 (27)
Laboratory director (LAB)	6 (15)
Years of work in current role	
1–5	6 (15)
6–10	8 (20)
11–15	5 (12)
16–20	9 (22)
>21	13 (32)

Table 3
Genetic service delivery and clinical ES across provinces

CFIR domain		Alberta	British Columbia	Manitoba	Ontario
Outer setting	Healthcare system structure	Centralized	Regionalized	Regionalized	Decentralized
	Support for the adoption of new diagnostic tests	Alberta Precision Laboratories is the sole provider of lab services and review requests to adopt new publicly funded laboratory tests The Lab Formulary Committee is dedicated to reviewing and approving requests	Provincial Laboratory Medicine Services oversees and coordinates laboratory medicine across the province and is accountable for implementing policies and processes related to laboratory services A provincial advisory committee exists to make recommendations specific to genetics and genomics laboratory services	No formal process for assessing and adopting new diagnostic tests was identified Utility and cost-effectiveness of novel genomic tests are reportedly assessed by ad hoc working groups and advisory committees	Formal adoption of and funding recommendations for new health technologies are adjudicated by the Ontario Health Technology Assessment Committee (OHTAC) A subcommittee of OHTAC, the Ontario Genetics Advisory Committee, conducts health technology assessments for new genetic and genomic tests
Inner setting	Health system structure for clinical genetic service delivery	Centralized – Clinical and Metabolic Genetics program	Decentralized – clinical genetic services operate independently at major healthcare centres located in Vancouver and Victoria	Centralized – Winnipeg Regional Health Authority Genetics and Metabolism services	Decentralized with Provincial Genetics Program oversight Hospital-based genetics clinics operate independently
	Referral for clinical genetic services	Required	Required	Required	Required
	Number of physician medical geneticists	16 (0.4 per 100,000 population)	11 (0.2 per 100,000 population)	6 (0.4 per 100,000 population)	39 (0.3 per 100,000 population)
	Number of genetic counsellors	45 (1.2 per 100,000 population)	90 (1.76 per 100,000 population)	14 (1,03 per 100,000 population)	235 (1.60 per 100,000 population)
	Health system structure for molecular diagnostic service delivery	Centralized – the Genetics & Genomics Program within Alberta Precision Laboratories provides diagnostic services for acquired and inherited genetic diseases	Centralized – the division of Genome Diagnostics at BC Children's and BC Women's Hospital is the only laboratory that provides molecular genetic testing for inherited diseases except for inherited cancer testing	Centralized – the molecular diagnostic laboratory within the Genomics discipline of the provincial diagnostic services is the sole provider of genetic testing services for inherited diseases	Decentralized – most molecular diagnostic laboratories based in major hospitals across the province operate independently
Implementation process	Availability of clinical ES				
	Postnatal, non-urgent	OOP and In-province	OOP and In-province	OOP and In-province	In-province
	Prenatal	OOP	OOP	OOP	OOP
	Urgent	OOP	OOP	OOP	OOP
	Criteria for clinical ES	- A baseline evaluation has been completed by a medical geneticist or appropriate specialist, including a physical examination, family history evaluation, and any relevant preliminary investigations such as chromosomal microarray - The results are anticipated to directly impact clinical decision making and care for the patient and/or their family members - A genetic etiology is the most likely	- Known existence of genetic cause for the condition being tested - Submission by the physician specialist with the appropriate expertise to adequately obtain informed consent and scope of practice to interpret and follow up on the results of testing - Involvement of a genetic counsellor or medical geneticist - Clear benefit for the patient (e.g., alters treatment)	- Test must be for the purpose of diagnosis, prevention, and/or treatment - Will a positive molecular test result change therapy or clinical management of the patient and/or family member? - Will a positive molecular test result stop further clinical investigation for the patient?	Genome-wide sequencing eligibility criteria (must meet ≥ 1 items) 1. Neurodevelopmental indications* (to be ordered by geneticists or physician specialists as per PGP guidance) - Global developmental delay and age 0 to 5 years - Intellectual disability (moderate, severe, or profound) - Autism or mild intellectual disability and one or more clinical features suggestive of a genetic syndrome

CFIR domain		Alberta	British Columbia	Manitoba	Ontario
		explanation for the patient's phenotype, supported by a clinical presentation which includes: severe to profound intellectual disability in the absence of known risk factors OR at least two of the following: - Moderate to severe developmental or functional impairment - Multisystem involvement - Progressive clinical course - Differential diagnosis which includes two or more well-defined conditions requiring evaluation by multiple targeted gene panels - Suspected severe undiagnosed genetic syndrome for which multiple family members are also affected, or where parents are consanguineous	- Completion of the appropriate consultations and initial in-province tests		2. Medical or congenital indications* (to be ordered by geneticists or physician specialists as per PGP guidance) - 2 or more congenital anomalies - Suspected neuromuscular disease onset between 0 and 24 months - Suspected ataxia onset between 0 and 5 years - One or more cardiac conditions meeting eligibility as per Cardiogenetics Recommendations* - One or more neurologic conditions meeting eligibility as per Neurogenetics Recommendations* 3. Indications to be ordered or recommended by geneticists (recommended through consultation, assessment or e-consultation) - Suspected severe genetic syndrome NYD for which multiple family members are also affected, or where parents are consanguineous - Suspected genetic condition with multisystem involvement, progressive clinical course and/or severe developmental or functional impairment - A broad genetic differential diagnosis that would otherwise require two or more separate targeted genetic investigations - Uninformative targeted panel where a genetic syndrome is still highly suspected - Clinical judgement, clinical rationale to be specified
	Who can order clinical ES	Medical geneticists with a designation of Fellow of the Canadian College of Medical Geneticists (FCCMG) and/or a Royal College of Physicians of Canada certification in Medical Genetics and Genomics, OR specialist physicians working with a certified genetic counsellor	Medical geneticists and certain designated non-genetics specialists	Medical geneticists or non-geneticist specialists (e.g., neurologists, immunologists) working with a certified genetic counsellor	- Physician specialists with sufficient expertise in genetics to provide pre- and post-test counselling and to safely manage results - Examples of physician specialists include: geneticists, cardiologists, cardiac surgeons, neurologists, developmental pediatricians, child psychiatrists
	Approval process for clinical ES	- Reviewed by the GRC	- Reviewed by the molecular diagnostics laboratory based on eligibility criteria	- Review by a provincial committee comprised of clinical geneticists and non-genetics specialists	- Reviewed by a laboratory staff (e.g., genetic counsellor) at SickKids or CHEO
	Local sequencing infrastructure for clinical ES	- Molecular Genetics Laboratory within the Genetics & Genomics program at Alberta Health Services	- BC Children's Hospital Genome Diagnostics BC - Genome-wide Sequencing BC (GSBC) pilot, where sequencing performed at SickKids and interpretation performed at Genome Diagnostics BC	- Shared Health Diagnostic Services Genomics Lab	- Sequencing performed at SickKids - Interpretation performed at SickKids and CHEO

CFIR domain		Alberta	British Columbia	Manitoba	Ontario
	Funding for clinical ES	- GRC has an allotted budget for OOP tests - Genetics & Genomics program has a separate budget for in-province diagnostic tests	- No funding structure established for in-province clinical ES - OOP testing is funded through a separate government funding source	- Genomics Lab receives an allotted budget from Shared Health Manitoba for both in-province and OOP tests	- An allotted budget for OOP tests - The GSO program receives volume-based funding for clinical ES
	Outcomes ascertained or planned for in-province ES implementation	- Diagnostic yield and turnaround time	- Diagnostic yield and turnaround time	- Diagnostic yield and turnaround time	- Preliminary outcome data on diagnostic yield and turnaround time available for ES and GS - Diagnostic yield is comparable to rates reported in the literature - Turnaround time improved compared to turnaround time for clinical ES conducted out of country

Abbreviations:

AB = Alberta; BC = British Columbia; MB = Manitoba; ON = Ontario

OOP: out-of-province

ES: exome sequencing

GWS: genome-wide sequencing

GRC: Genetic Resource Centre

CHEO: Children's Hospital of Eastern Ontario

SickKids: The Hospital for Sick Children

*Five participants worked in more than one professional setting: two worked in the clinic and the laboratory, three worked in clinical and policy settings.

Table 2
Participants across cases

Professional setting	Case				National[d]
	AB	BC	MB	ON	
Clinical	5	5	5[b]	6[c]	
Laboratory	2	1	3	4	
Other[a]	2	3	-	2	3
Total	9	9	8	12	3

Abbreviations: AB = Alberta; BC = British Columbia; MB = Manitoba; ON = Ontario

[a]Other: Policy, provincial government, health research or genomics funding organization

[b]Two participants with their primary role in the clinical setting also worked in the policy setting

[c]Two participants worked in both clinic and laboratory, and one worked in clinical and policy settings

[d]The professional setting of three participants were not tied to a specific province (e.g., health systems leader in a national organization)

Outer Setting

Support for the adoption of new diagnostic tests

Available information on the governance and processes supporting the adoption of new genetic tests varied across provinces. In Ontario, Ontario Health (OH), a single health agency, oversees healthcare planning and delivery across the province. Within OH, funding recommendations for new health technologies are adjudicated by the Ontario Health Technology Assessment Committee (OHTAC). A subcommittee, the Ontario Genetics Advisory Committee, conducts HTAs to advise OHTAC on the validity, clinical utility, cost-effectiveness, and patient preferences related to new genetic tests.[24, 25] Despite these formal processes, a key informant noted that, historically, laboratories developed new tests in response to growing clinician demand through a *"bottom-up approach."* (ONLAB001) To improve the quality of and standardize genetic services in the province, OH established the Provincial Genetics Program (PGP) in 2021.[26, 27] An equivalent program does not exist in the other three provinces. In addition, OH established the Ontario Laboratory Medicine

Program (OLMP) in 2023 to "provide strategic and operational coordination and oversight for lab services across the province."[28] The OLMP and the PGP are part of the province's effort to improve the delivery of genetic services in Ontario.

In British Columbia, Provincial Laboratory Medicine Services (PLMS), within the Provincial Health Services Authority (PHSA), oversees laboratory medicine.[29] PLMS, which is analogous to the OLMP, is accountable for implementing policies and processes related to laboratory services, including making recommendations to the Ministry of Health for publicly funded laboratory tests. These recommendations are made with the support of provincial advisory committees, including the Genetics & Genomics Advisory Committee.[30] British Columbia has an established HTA process through which decisions on the provincial adoption of devices, diagnostic services, medical procedures, and programs are made. However, the list of completed assessments between 2016 and 2024 does not include any genome diagnostic technologies.[31, 32]

In Alberta, Alberta Precision Laboratories (APL) is the sole provider of lab services. APL's Lab Formulary Committee reviews and decides whether to adopt and fund new laboratory tests.[33, 34] APL applies the 'Rapid HTA Prioritization Framework' to ensure tests demonstrate strong clinical and economic value. Physicians or laboratory staff can submit a request for a new test, but not all tests require review and approval by this committee.[34] A participant (ABLAB001) shared that *"recently, the formulary is used only if it's a test that's going to have a wide impact, like pharmacogenomic testing, that would impact many, many patients in the province."* For tests that impact a small number of families, the decision is made at the laboratory level.

Manitoba's Shared Health is the provincial health authority responsible for province-wide programs and specialized health services, including diagnostic services. Available documents did not identify information on the process for assessing and adopting new diagnostic tests in Manitoba.[35] Instead, novel genomic tests are assessed by ad hoc working groups and advisory committees.[36] In the case of ES, a participant (MGMG002) shared that access to ES was initially approved in response to an exceptional patient case rather than through an established process. This unique case led the Department of Health to authorize out-of-province access to ES for all patients who met specific criteria.

Inner Setting

Organization and delivery of clinical genetic services

In all provinces, clinical genetics is divided into distinct subspecialties, although the availability of specialized clinics varies. In Alberta, despite the 2025 restructuring of Alberta Health Services (AHS) into four priority sectors, clinical genetics remains centralized and part of AHS's Clinical and Metabolic Genetics Program.[37, 38] Similarly, Manitoba's services are delivered through the Genetics and Metabolism Program of Winnipeg Regional Health Authority, which serves the whole province.[39] In British Columbia, clinical genetic services operate independently at major centres in Vancouver and Victoria, as part of the PHSA and the Vancouver Island Health Authority.[40, 41] Ontario employs a decentralized model, with hospital-based genetics clinics operating independently.[42] Data on the clinical genetics workforce are limited. However, long wait times for genetics services were reported across provinces and may reflect ongoing workforce capacity challenges.[43, 44] Current wait times for non-urgent, non-cancer genetics appointments across the provinces range from six months to six years, posing a significant barrier to timely and equitable access for patients.[43, 45]

Organization and delivery of molecular diagnostic services

Molecular diagnostic services fall under the provincial health authority in Alberta, British Columbia, and Manitoba. In Alberta, APL is the sole provider of laboratory services.[46, 47] The APL Genetics & Genomics Program provides diagnostic services for genetic diseases. For any test performed out-of-province, the Genetic Resource Centre manages approval and sample coordination. Similarly, in British Columbia, Genome Diagnostics at BC Children's and BC Women's Hospitals is the sole provider of molecular genetic testing for inherited diseases, except for inherited cancer testing (BCLAB001). In Manitoba, the provincial laboratory provides genetic testing for inherited diseases and adjudicates requests for genetic tests.[48–50] In contrast, Ontario's laboratory services are decentralized, with most laboratories operating independently within major hospitals.[5, 51–54]

Implementation Process for clinical ES

Clinical ES has been available as an out-of-province test in all four provinces for a decade prior to the onset of this work. Recently, a movement to develop in-province capacity for ES has taken place. For non-urgent postnatal ES, Ontario transitioned to in-province ES for all eligible cases as of April 1, 2021.[10, 55] In Alberta, British Columbia, and Manitoba, the volume of in-province ES has been gradually increasing.

Motivation for building in-province capacity

Participants across provinces highlighted several motivations for developing in-province ES capacity (e.g., BCMG003, ONLAB002, ABLAB001, ONMG005, MBMG001). While it takes time to build infrastructure and expertise, local capacity would ultimately enable faster turnaround times, especially for urgent cases. Retaining genomic data within the province supports comprehensive analysis and interpretation of results through close collaboration between the clinics and the laboratory, as well as opportunities for secondary research on and reanalysis of undiagnosed cases. Pressure from providers to access testing locally was also highlighted. Ultimately, in-province genome diagnostics ensures that healthcare investments remain within the province, supporting local infrastructure, training, and innovation. Many participants noted that relying on external commercial laboratories presents challenges, including limited control over available services and limited opportunities to tailor testing to individual patient needs.

Clinical ES eligibility criteria for postnatal, non-urgent cases

Eligibility criteria for clinical ES vary across provinces, leading to differences in patient access (Table 3). Alberta and Ontario's criteria are more prescriptive, including defined clinical presentations. In Ontario, the criteria have evolved and are now further subdivided into cardiogenetic, neurodevelopmental, and neuromuscular disorders. Additionally, both clinical geneticists and non-geneticists specialists can order ES. Participants highlighted that the interprovincial variability in eligibility criteria contributes to inequitable access to ES across the country. A participant from Manitoba (MBGC001) shared that Ontario residents who receive care in Manitoba clinics would qualify for ES through Ontario's program, but Manitoba residents with a similar clinical presentation would not.

Implementation approach for in-province clinical ES

Across provinces, implementation of in-province ES occurred in a bottom-up manner, with implementation leads securing external funding to initiate the process. Ontario was the first to offer publicly funded clinical ES, effective April 1, 2021. This began as a 2-year pilot project (Genome-wide Sequencing Ontario - GSO), which was funded by the Ontario Ministry of Health and Genome Canada.[10, 26, 27] The implementation included a centralized approach for sequencing and informatics at The Hospital for Sick Children (SickKids) and a multi-institutional model for test approval, variant interpretation, and reporting at both SickKids and Children's Hospital of Eastern Ontario.[55] This hub-and-spoke model enabled province-wide delivery of clinical ES.

In contrast to Ontario's approach, which offered in-province ES to all eligible cases from inception for all sequencing strategies (e.g., trios – patient and biological parents, duos – patient and one biological parent, singletons – patient-only), British Columbia's in-province ES was launched as a pilot in 2023 through a collaboration between the Medical Genetics program and the BC Children's Hospital Division of Genome Diagnostics with funding from Genome Canada, Genome British Columbia, the PHSA, and other funding sources.[56] Genome Diagnostics also collaborates with SickKids on another clinical pilot, Genome-wide Sequencing BC (GSBC). Through this pilot, trio cases undergo sequencing at SickKids, with variant interpretation at the BC Genome Diagnostics laboratory, while singleton and duo cases are performed by BC Genome Diagnostics.[57, 58]

Alberta's implementation similarly began with a Genome Canada-funded project launched in 2020. The TIGeR (Translational Implementation of Genomics for Rare diseases) project is a collaboration between the University of Calgary and APL, with the goal of establishing local ES.[59] Effective June 16, 2025, Alberta has begun offering in-province ES.[46] In Manitoba, the Shared Health molecular diagnostic laboratory launched in-province ES in the fall of 2024 with financial support from Shared Health and external sources. Local evidence of ES's clinical utility, generated through translational research initiatives such as the Canadian Prairie Metabolic Network, played a key role in Shared Health's decision to invest in local ES capacity (MBMG001).

Across provinces, similar service-level outcomes are measured (e.g., diagnostic yield, turnaround time). Data from Ontario's GSO pilot indicate a diagnostic yield that is comparable to rates reported in the literature, along with significantly improved turnaround times compared to out-of-country testing.[60] Outcome data from other provinces are limited due to the early stage of implementation.

[Insert Table 3]

Discussion

The Canadian landscape of genome diagnostics is evolving, with provinces demonstrating a shared motivation for in-province ES. This study presents a comparative analysis of the provincial landscape of genetic service delivery and identifies interprovincial variability in the delivery of clinical and laboratory services. Despite these differences, a centralized approach for clinical ES implementation was consistently observed in the four provinces studied. This approach was supported by significant resources, specialized expertise, and coordination between clinical and laboratory services.

In Alberta and Manitoba, centralized service delivery for specialized health services likely emerged organically due to the smaller patient population size and greater connectivity among members of the genetics workforce. In contrast, Ontario's move toward centralizing sequencing and informatics was more deliberate. A centralized approach was expected to be the most efficient way to implement a complex intervention involving many types of experts and resources. While provincial health structures vary, their influence on the implementation of clinical ES may be less critical than the characteristics of the intervention itself and the groups responsible for its implementation.

A 2023 study identified Alberta and Quebec as being in a better state of readiness for genomic medicine, partly due to the establishment of a single laboratory service organization and programs that provide the necessary infrastructure for coordination and planning.[5] In contrast, Ontario was noted as being at a disadvantage due to its highly decentralized healthcare system.[5] However, the centralized approach adopted by GSO for the laboratory component of ES implementation demonstrates that establishing or leveraging centralization is feasible, even within a decentralized healthcare delivery system. This may serve as a precedent-setting model for Ontario and for the delivery of future genomic technologies in Canada and internationally. Other countries with publicly funded health systems have successfully implemented genome diagnostics through harmonization and standardization across jurisdictions. In Australia, the federated model developed by Australian Genomics has guided the harmonization of state and federal government policies to integrate genomics, reducing siloing of implementation efforts and improving patient access to genomic medicine.[61]In England, the Genomic Medicine Service – a network of seven regional genome laboratory hubs – was established to deliver standardized genomic testing services.[62]

Outcomes evaluation of clinical ES implementation

While early service-level outcomes are promising for provincial clinical ES in Ontario[60], the long-term sustainability of this approach must be evaluated. Evaluation should consider whether the current GSO structure can accommodate the anticipated increase in demand, or if structural adaptations and additional infrastructure investments will be necessary to support future scalability. Furthermore, the evaluation of clinical ES is warranted in all provinces and should not be limited to diagnostic yield and turnaround time, but also include implementation outcomes such as acceptability and penetration, as well as patient- and system-level outcomes. Specifically, these evaluations should assess whether local capacities for ES have meaningfully improved patient access to diagnostic services compared to ES accessed through out-of-province programs, and whether reduced out-of-country spending and enhanced local data assets have strengthened the quality of genomic medicine overall. Such evaluations are already underway in other jurisdictions, including Australia and England.[61, 63, 64] In Australia, outcomes from the first five years of the Australian Genomics initiative have provided important insights into the impact (e.g., economic, policy, ethical, workforce) of incorporating genomics within the Australian health system context, resulting in evidence-based policy and practice changes.[61]

Consolidation and standardization of structures and processes to support the adoption, delivery, and evaluation

Implementing genome diagnostics for rare disease remains challenging and continues to rely, in part, on a bottom-up approach that often depends on securing external research funding. The absence of a clear pathway poses a barrier to specialized genomic tests and other emerging “omics-based” diagnostic tests.[65]

Across provinces, both formal and informal systems are used. Formal processes, such as Alberta’s Lab Formulary Committee and Ontario’s Genetics Advisory Committee, promote consistency and transparency but are often time- and resource-intensive, resulting in delays in the adoption of novel technologies. Genomic technologies may also be deprioritized when decision makers emphasize investment in technologies or services with broader population impact. These processes cannot keep pace with the rapidly changing field of genomics, partly due to the time-consuming nature of HTA processes. Innovative approaches to HTA may offer greater flexibility and facilitate more responsive uptake of emerging technologies.[66] However, they also present challenges, such as lack of standardization.

This analysis identified inconsistencies in patient access to clinical ES, with the eligibility criteria varying considerably across provinces. This highlights a pressing need to standardize clinical genome diagnostic services across Canada, a need that a pan-Canadian oversight body could help address. Internationally, countries with universal healthcare systems, such as the United Kingdom and Australia, have successfully implemented clinical ES through centralized genomic testing infrastructures and national oversight.[61, 67] While implementing a fully centralized sequencing infrastructure for the entire country may not be feasible, desired, or even necessary given Canada’s decentralized structure, aligning laboratory and clinical standards of care could ensure equitable access and reduce interprovincial disparities in genome diagnostic services. The launch of the Canadian Genomics Strategy in February 2025 reflects federal commitment to advancing genomics.[68] Although the strategy emphasizes federal-provincial and international collaboration to advance genomics applications, clear plans for a national governing body to oversee service delivery and quality do not yet exist.

Limitations

We were unable to include a participant from Manitoba whose primary role was in policymaking. However, policymaking perspectives may still be reflected in the views of clinical participants who have served on advisory committees that inform genomics-related services in the province. Document analysis was limited to publicly available data. As a result, internal policy documents or unpublished reports that may contain relevant insights were not included. The exclusion of for-profit diagnostic laboratories and patient partners is a limitation of this study. These groups may have provided distinct insights into the implementation of clinical ES within provincial contexts. These exclusions were made primarily due to feasibility constraints, and future research should consider their inclusion. This study was focused on clinical ES implementation. However, the lessons identified may also be relevant for Canada and other jurisdictions considering genome sequencing as an emerging approach to advancing genome diagnostics for patients.

Conclusion

A comparative case study of four Canadian provinces revealed a shared motivation to strengthen local capacity for clinical ES. The substantial resource requirements, including specialized expertise and coordination needed to implement a complex health intervention, consistently led to a centralized approach to clinical ES implementation, despite varying health system contexts. The provincial differences identified in genome diagnostics indicate a need for pan-Canadian support for the standardization of processes to ensure timely adoption, delivery, and ongoing evaluation of existing and emerging genome diagnostics across Canada. The learnings from this work may inform other countries with decentralized health systems, where centralized approaches to the delivery of resource-intensive complex health interventions can facilitate improved access for patients.

Abbreviations

AHS
Alberta Health Services
APL
Alberta Precision Laboratories
CFIR
Consolidated Framework for Implementation Research
ES

Exome Sequencing
GSO
Genome-wide Sequencing Ontario
GSBC
Genome-wide Sequencing British Columbia
HTA
Health Technology Assessment
OH
Ontario Health
OLMP
Ontario Laboratory Medicine Program
OHTAC
Ontario Health Technology Assessment Committee
PGP
Provincial Genetics Program
PLMS
Provincial Laboratory Medicine Services, within the Provincial Health Services Authority (PHSA)
SickKids
The Hospital for Sick Children
TIGeR
Translational Implementation of Genomics for Rare Diseases

Declarations

Ethics approval and consent to participate

This work was approved by the Research Ethics Boards of The Hospital for Sick Children (REB #1000079064) and University of Toronto (REB #42672) and conducted in accordance with the ethical standards and principles of these institutions. All participants provided informed consent prior to the interview.

Consent for publication

Not applicable

Funding

This work was supported by the Canadian Institutes of Health Research's Doctoral Research Award, awarded to W Lee. RZ Hayeems is supported by a Canada Research Chair in Genomics and Health Policy (Tier 2).

Author Contribution

All authors (WL, RZH, MB, MD, JMF, CRM) contributed to the conceptualization and methodology of the study. WL collected, analyzed, and interpreted data with RZH and MB. WL and RZH were responsible for funding acquisition. WL wrote the original draft, and all other authors were major contributors in editing and finalizing the manuscript.

Acknowledgements

Not applicable

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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