OCTOBER 4-5, 2016

Genomics and **Precision Health** FORUM

GLOBAL CHALLENGES GENOMIC SOLUTIONS

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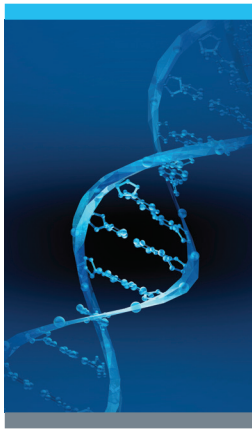
Genomics and **Precision Health** FORUM

Executive summary

The Genomics and Precision Health Forum held in Toronto on October 4 and 5, 2016, brought together international and national stakeholders and key opinion leaders in the field of precision health[1] for a wide-ranging discussion aimed at developing strategies to advance the implementation of genomics[2] into Canada's health-care system.

The forum opened with presentations on international and national initiatives to show current, global state-of-the art efforts around precision health implementation. Participants were informed of the activities of the Global Alliance for Genomics and Health, an international coalition formed to enable the sharing of genomic and clinical data. Participants also learned of precision health initiatives in the U.S., the U.K. and Australia. Although Canada does not yet have a population-level genome sequencing initiative, Genome Canada and the Canadian Institutes of Health Research (CIHR) are showing leadership in this area through funding programs and initiatives designed to move genomics and precision health forward. The main program to date was Genome Canada's 2012 Large-Scale Applied Research Project (LSARP) Competition – Genomics and Personalized Health, launched in partnership with CIHR. The 2012 LSARP competition supported large-scale research projects that demonstrated how genomics-based research can contribute to a more evidence-based approach to health and improve the cost-effectiveness of the health-care system. Important lessons have been learned from the projects funded in the 2012 LSARP competition related to data sharing and interpretation, and clinical validation and integration into the health-care system.



Forum participants were also informed by real world examples of clinical implementation of genomics from across Canada. In all cases, work is proceeding in discrete pilots using clinically validated tests with actionable results, with many of these pilots spearheading best practices around implementation into the health-care system.

Presentations on the patient's perspective demonstrated the pivotal role of patients in the development of precision health approaches. The presentations also highlighted the importance of informing and engaging patients and the public in mutually meaningful ways to support the implementation of genomics into the health-care system. Patients also want to be – and should be – engaged in research projects, knowing how and when their data will be used.

Representatives from provincial health authorities provided their perspectives on the current process by which new technologies are evaluated and put into practice. They described initiatives underway at the provincial level to support the implementation of genomics. Perhaps not surprisingly, given the common barriers to the implementation of genomics into clinical care, most provinces seem to be doing similar things to address challenges. Yet they are often working in isolation.

[1] The term "precision health" is defined here as an approach to improving the health of individuals and populations by harnessing the power of new tools of science and technology, such as genomics and big data, as well as predictive analytics that take into account personal, environmental and social determinants of health.

[2] The term "genomics" is defined here as the comprehensive study, using high throughput technologies, of the genetic information of a cell or organism, and includes related disciplines such as bioinformatics, epigenomics, metabolomics, metagenomics, nutrigenomics, pharmacogenomics, proteomics and transcriptomics.

Forum participants also heard from the former head of a regional health authority who said that the genomic innovations that are advancing into routine care are typically being implemented via existing processes and policy frameworks and, to date, the health-care system has been only marginally transformed by genomics. As we look to scale up the application of genomics and precision health, we can expect a disruptive transformation of the health-care system to be required, necessitating integrated genomics education across the system and new policies to support individual privacy and engagement.

Informed by these plenary presentations, breakout sessions and facilitated discussions, participants proposed the following actions to advance implementation of precision health into the health-care system, and to improve patient and population health and well-being in Canada.

- Develop a national vision for the implementation of genomics into the health-care system. Start with a demonstration project in a targeted area to raise the profile of precision health in Canada and provide a framework to leverage synergies from existing work.

- Incorporate a health technology assessment service in publicly funded research projects, through an organization such as the Canadian Agency for Drugs and Technologies in Health or the Institut national d'excellence en santé et en services sociaux, to ensure a harmonized and proactive pathway for the assessment of new technologies.

- Establish national guidelines for the assessment and evaluation of genomic tests to support a harmonized and streamlined approach to the adoption of genomic tests by each province.

- Develop, and require the adoption of, national standards for the collection, aggregation, integration, storage and governance of data generated with public sector funds, in alignment with the standards articulated by the Global Alliance for Genomics and Health. This would accelerate the validation of new genomic tests and provide a platform for research and development.

- Support the development of appropriate curriculum and tools for the education and training of students and health-care practitioners to ensure the comprehensive and equitable use of genomic tests in clinical care.

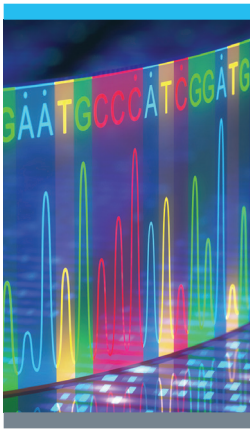
- Consider how elements established by Canada's Strategy for Patient-Oriented Research and related initiatives and platforms can be integrated into existing health-care delivery and research structures to advance efforts to implement precision health within our health-care systems.

- Develop a white paper to articulate the roles and responsibilities of each stakeholder involved in health-care system transformation and help strengthen the precision health research and delivery continuum.

Objective of the Forum

The Genomics and Precision Health Forum brought together scientists, clinical researchers, provincial health authorities, policy makers, funders and key opinion leaders from across Canada, along with select international experts, to develop strategies to advance the implementation of genomics into Canada's health-care system. Supported by Genome Canada, the Canadian Institutes of Health Research (CIHR) and the regional Genome Centres, the forum was informed by plenary presentations from international and national experts, and the outcomes of a satellite workshop the preceding day that sought to identify success stories and best practices in genomics and health projects currently funded by Genome Canada and CIHR.

International Initiatives



- Moderator: Patricia Evans, Patricia Evans & Associates
- Geoff Ginsburg, Duke University & Global Genomic Medicine Collaborative
- James Peach, Genomics England
- Clara Gaff, Australian Genomics Health Alliance
- Peter Goodhand, Global Alliance for Genomics and Health

Participants in the first session summarized initiatives being undertaken in different countries to support precision health, an approach to improving the health of individuals and populations by harnessing the power of new tools of science and technology, such as genomics and big data, as well as predictive analytics that take into account personal, environmental and social determinants of health. A number of countries have launched large-scale (or "population- scale") genome sequencing or cohort creation efforts[3] to gather the evidence required to support the application of genomics in clinical care to improve patient and population health and wellness. The drivers, scope, scale and support for these initiatives vary greatly. They may be national or regional in scope; be wide-ranging or limited to a particular population or patient cohort; have broad or constrained consent conditions; be within or apart from health-care systems; or be publicly, privately or jointly funded. Most initiatives, however, have been driven or catalyzed in a top-down manner and have some sort of national coordination.

These projects are generating considerable data. However, these data, including medically actionable data such as variants to guide the treatment of non-small cell lung cancer, are rarely used to inform routine clinical care. Generally speaking, most countries find barriers around lack of evidence, interpretation of variants, uncertainty in validity, lack of decision support tools, reimbursement questions and often other barriers related to the complexity or fragmentation of health-care systems themselves. Accordingly, work in many countries is expanding to include consideration of key elements of health-care systems. These include workforce education, decision support tools for physicians and other caregivers, health economic studies and the genomic literacy of the public.

[3] Initiatives – U.S.: the National Institutes of Health's Precision Medicine Initiative cohort of one million participants, Geisinger Health System's and Regeneron Pharmaceuticals, Inc.'s 100,000 genomes project, the Department of Veterans Affairs Office of Research & Development's Million Veteran Program; U.K.: Genomics England's 100,000 Genomes Project; Qatar: Genome Qatar's Qatar Genome Programme of 300,000 Qatari genomes; Estonia: the Estonian Genome Center's Estonian Genome Project of 52,000 genomes; Israel: Genomics Israel, 100,000 genomes; Saudi Arabia: Saudi Human Genome Program of 150,000 genomes, focused on cardiovascular disease; Iceland: Iceland's project to sequence 350,000 genomes.

In Australia, genomic literacy, adoption by clinicians and clinical service change are three broad challenges to the implementation of precision health. These challenges are being tackled nationally and at a state level through a number of individual projects designed to support the development of national policies. These challenges are being tackled on a state level through a number of discrete pilots with the hope that outcomes may provide support to develop national policies. In the U.K., work to address barriers is being undertaken on a more comprehensive system level, due in part to the positioning of Genomics England's 100,000 Genomes Project within the National Health System (NHS). Here, work is focusing on the education of health-care professionals through the national body Health Education England and the embedding of genomics within NHS operations so that genomics is requisitioned and used in routine care like any other test. In the U.S., the Implementing Genomics in Practice consortium was established to help develop methods that incorporate genomics information into clinical care, exploring these methods for their effective implementation, diffusion and sustainability in diverse clinical settings. Work is being taken forward in six projects focused on developing implementation and effectiveness outcomes in different areas (e.g., ways to use pharmacogenomics, clinical support for genomics).

As countries wrestle with the challenge of advancing precision health into clinical care, it is becoming clear that implementation is a science in and of itself and that implementation research will be needed.

Initiatives such as the Global Alliance for Genomics and Health (GA4GH) are bringing a multinational approach to large-scale genomics, seeking to unlock the potential of genomic data being generated by different groups around the world through the development of harmonized approaches to data generation, sharing and analysis. The key here is interoperability to facilitate the aggregation of genomics data. This, in turn, will accelerate the potential of genomic medicine to improve human health. GA4GH focuses on research and clinical data, and it is hoped that best practices developed might inform sharing of data that are being collected under clinical protocol or must be maintained in national or health-system databases.

Many countries, facing common challenges, are also recognizing the opportunity to share best practices for implementing precision health as these practices emerge. In 2014, global leaders in the implementation of genomic medicine in clinical care established the Global Genomic Medicine Collaborative (G2MC). The G2MC seeks to identify opportunities and foster global collaborations that demonstrate the value and effective use of genomics in medicine. The G2MC is taking this work forward through seven working groups in areas such as policy, evidence and education. Countries on the leading edge of this work are recognizing that whole system change is needed. They are talking not of the implementation of genomics, but rather the transformation of health-care systems.

Setting the Stage

- Cindy Bell, Genome Canada
- Jane Aubin, CIHR

Although Canada does not yet have a population-level genome sequencing initiative, Genome Canada and CIHR are showing leadership in this area through funding programs and initiatives

designed to move genomics and precision health forward. Genome Canada's flagship investment in genomics and precision health is the 2012 Large-Scale Applied Research Project (LSARP) Competition – Genomics and Personalized Health, launched in partnership with CIHR. The LSARP supports large-scale research projects that will demonstrate how genomics-based research can contribute to a more evidence-based approach to health and improve the cost-effectiveness of the health-care system. Genome Canada also funds precision health research and development (R&D) through the Genomic Applications Partnership Program – a program focused on funding downstream R&D projects that address real world challenges in health and other sectors.

CIHR also offers funding mechanisms to support health research: from creation of new knowledge to its translation to improve health outcomes. In addition to partnering with Genome Canada on the 2012 LSARP, CIHR has developed the Health Research Roadmap, which outlines three strategic directions for investment. One of these strategic directions seeks to mobilize health research for transformation and impact in four priority areas, including initiatives that focus on such topics as chronic diseases and health innovation. Through the Strategy for Patient-Oriented Research (SPOR), for example, CIHR is investing in research and research enablers that engage patients as partners, focusing on patient-identified priorities to improve patient outcomes. This research is conducted by multidisciplinary networks and teams, and supported by CIHR in partnership with relevant stakeholders, including the provinces. SPOR aims to apply the knowledge generated to improve health-care systems and practices, and it provides people and systems that could be utilized to advance precision health implementation efforts.

Canadian Experience: Lessons learned from ongoing projects

- Moderator: Paul Lasko, CIHR – Institute of Genetics

This session focused on a discussion of three areas that were identified as roadblocks to the implementation of precision health at the satellite workshop, which brought together precision health research project teams funded by Genome Canada and CIHR. The three areas were:

- data interpretation and sharing;
- clinical validation; and
- implementation into the health-care system.

Data interpretation and sharing

Although Canada does not have a national genome sequencing initiative, different groups across the country have undertaken large-scale genomics projects. However, as these projects have not been coordinated through a top-down approach, there is a sense that Canada is missing an opportunity to link the reams of data generated by previous investments to generate discoveries and innovations. There is a pressing need to bring together existing data to seed new innovations, but also for Canada to continue to generate and translate new large-scale data sets to remain competitive internationally. However, the quality and interpretation of the data generated are of critical importance if we are to be able to aggregate data and leverage resources.

A key question going forward is how can Canada aggregate existing genomic data and ensure that new data collected are standardized and broadly accessible. Three options were discussed:

- establish a common national data repository;
- create a system of standardized, federated databases with a common language; or
- opt for "data lakes," a method of storing data within a system or repository, in its natural format, to facilitate the collocation of data in various schemata and structural form.

Data lakes were proposed as an alternative to a central repository and federated databases as they could accommodate differences in data, such as quality, standards and architectures, that might be difficult to accommodate in a federated system. This scenario might require a "data steward" to maintain data quality and facilitate access to data in different databases. In fact, such functions may already exist in various bioinformatics hubs and institutions across Canada.

The idea of a (national) chief data officer was also suggested as a way to coordinate and facilitate access to data. One thing is clear: public sector funders of genomics research have a role to play in shaping and mandating the use of an appropriate mechanism for the national collation and use of genomic data such that the data can be leveraged to advance the genomics field as a whole.

Clinical validation

Generating an evidence base to support the validation of genomic tests is a complex task involving significant amounts of well-annotated data. An added complexity often overlooked is the transition from validation in research projects to validation in the real world – that is to say, moving from pilot to scale-up in the clinical setting. Genomic tests, which are often piloted and proven under perfectly controlled conditions, are liable to failure when scaled up. A move to more pragmatic clinical trials where the complexity of the system is taken into account earlier may help generate more robust and clinic-ready genomic tests.

Integration into the health-care system

The integration of genomic tests into routine care is extremely complex. There is a clear role for implementation research in generating new ways of understanding and addressing barriers. For instance, evidence to secure clinical validity and clinical utility is not necessarily the same as evidence that secures regulatory approval. There is a gap to be bridged here and this is not something that one organization can accomplish alone. Strategic relationships between key groups could be used to streamline approaches to evidence generation and use. Disinvestment, the removal of existing technologies from practice, remains a concern and research will be required to determine how best to accomplish this in the face of new disruptive technologies.

The role of education in supporting the integration of genomic tests into routine care was also discussed. Education is seen as critical to changing clinical practices and something that must be ongoing – especially with a field as fast moving as genomics. In Australia, workshops that educate health practitioners about the classification of genomic variants are proving useful. Funders and other stakeholders with an interest in advancing precision health may have a role to play in supporting the development of educational and training curriculum and tools for medical students and health-care practitioners to enable the successful implementation of precision health.

How Are We Doing? Stories on the Path to Implementation

- Moderator: Catalina Lopez-Correa, Genome British Columbia
- Drew Bethune, *'Implementation of a Lung Cancer Genomics Program'*
- Jacques Michaud, *'Using Exomes to Diagnose Rare Diseases'*
- Danielle Andrade, *'Using Genomics to Diagnose Epilepsy'*
- Christian Steidl, *'Personalized OncoGenomics Program'*

This session provided an opportunity to reflect on some real world examples where genomics is being integrated into care across the country. In all cases, work is proceeding in discrete projects using clinically validated tests with actionable results. In most cases, these tests are also being used to study and pilot best practices around implementation into the health-care system.

In Atlantic Canada, Drew Bethune at the Atlantic Canada Molecular Oncology Centre (ACMOC) is introducing EGFR testing for lung cancer as a way to improve patient care and reduce costs. This work is being done in partnership with a multidisciplinary group that brings together molecular biologists, medical oncologists and other local experts with the National Research Council Canada, Capital Health and several pharmaceutical companies. The ACMOC, which is using a panel of 12 markers (across eight genes) to guide the use of two existing drugs, is harnessing the resulting lung cancer tissue bank as a resource for continued R&D. Between 2012 and 2016, 3,000 tests have been performed. This approach has become the standard of care for all of Atlantic Canada.

In Quebec, clinical researchers at the Réseau mère-enfant at the Centre hospitalier universitaire Sainte Justine are using exome sequencing to develop and validate a diagnostic pipeline for rare diseases. Within the pilot, 300 patients were run through a clinical workflow and pipeline. An economic assessment was conducted to understand cost savings using genomics. The group has concluded that the use of genomics as a diagnostic technology is often the most cost-effective option, significantly reducing the time required to achieve a diagnosis. It is hoped that this evidence will lead to genomics becoming the standard of care with respect to diagnosis of a rare disease.

Similar work is occurring in Ontario. A partnership between Toronto Western General Hospital and the Hospital for Sick Children in Toronto is undertaking whole genome sequencing as part of a longitudinal study on epilepsy. This initiative has identified genetic mutations in patients with intractable epilepsy who had not received a diagnosis through standard testing. An accurate diagnosis can apprise treatment options and enables much more informed genetic counselling for siblings. The BC Cancer Agency has had success in implementing genomic tests in routine care and a hereditary cancer panel is now publicly funded. Through the Personalized OncoGenomics Program, the group is also using whole genome sequencing to inform treatment of late stage cancers.

At the moment, the use of whole genome sequencing or whole exome sequencing depends, among other things, on the application. Currently, there is an economic argument to be made for whole exome sequencing (over whole genome sequencing) but the economic case is not likely to exist in the future as the sequencing costs decrease. In both cases, we are generating more information than we can use. There is clearly tension between using a restricted panel of actionable targets to inform clinical decision-making and generating more information (e.g., via whole genome sequencing or whole exome sequencing) that may inform clinical decision-making and fuel new discoveries, too.

These different approaches to the use of genomics in clinical practice will have implications for scale-up and also raise questions around re-interrogation of data (e.g., in the case of epilepsy as the pediatric patient becomes an adult, and reporting). In cancer, the heterogeneity and nature of disease will also be a factor. Going forward, the landscape and options will become even murkier as other 'omics, such as proteomics and transcriptomics, come online and move into the clinic, and as we begin using genomics for prevention.

Why Are We Doing This Anyway? Perspectives on Patient Advocacy and Engagement

- Moderator: Stephen Robbins, CIHR – Institute of Cancer Research
- Louise Binder, Canadian Cancer Survivor Network
- Patrick Sullivan, Team Finn Foundation and PROFYLE Project
- Kym Boycott, CARE for RARE Program
- Nathalie Bolduc, Canadian Association of Genetic Counsellors and LifeLabs

This session provided an opportunity to focus on the recipient of precision health: the patient.[4] The session began by focusing on rare diseases. This is a collection of diseases which, due to their rare and often unknown nature, necessitate a personalized approach to diagnosis and often involve and engender advocacy in family members seeking a diagnosis – and equally often unknown or elusive treatment options – for their loved one. Research undertaken in the CARE for RARE program provided some patient perspectives on the potential and use of genomics in the diagnosis of rare diseases. Patients with rare diseases exemplify the significant role of patients as drivers, co-developers, advocates and educators of precision health. Patients are keen to engage with genetic counsellors to improve their understanding of their conditions and the options available to them. Patients and their families are often highly engaged in the pursuit of a diagnosis and welcome opportunities to connect and share data and experiences with other patients around the world. They are also keen to share their odyssey with the public and, through patient advocacy, play an important role in driving innovation and the uptake of health technology and genomic technologies more specifically. Using particular examples, presentations from the Team Finn Foundation and the Canadian Cancer Survivor Network underscored the important role patient advocacy can play. The importance of an informed and engaged patient cannot be underestimated or taken for granted, and it is critical to ensure patient rights are respected and protected.

While some patients are willing to be "genomically naked"[5] if it can help advance the understanding of a disease and development of a treatment or cure, there is a balance to be struck between the security of data and the usability of data. As diseases become stratified, many common diseases will become rare. It will be necessary to find ways to share data without compromising

[4] We use the term "patient" in this section while recognizing that many of the issues raised here apply equally to the general public – individuals who may, or may not, be or become affected by disease.
[5] A state where an individual's genome is exposed or freely available or accessible to others.

patient privacy or creating opportunities for discrimination. The terms “sharing” and “open” are often used to characterize data, yet there is no general consensus on what is meant by these terms and there is no framework around what should be shared and under what conditions. The potential for discrimination remains perhaps the key driver of approaches to data security, especially in the absence of laws to protect against genetic discrimination in Canada. Patients have a pivotal role to play in the development of precision health approaches in primary care and it will be important to inform and engage patients and the public in mutually meaningful ways to support the development and implementation of genomics into the health-care system. This begins with appropriate and informed consent, and ends with reporting. In terms of stimulating innovation, consent that allows the use of patient samples and data for clinical and research purposes now and in the future may be most useful for researchers. However, patients want to be engaged in the research project and know how, and when, their data are used (e.g., whether to advance public good via a health-care system or to improve profits of a commercial enterprise). Patients may be less inclined to contribute freely to research undertaken by private companies. However, it is important to recognize the role the private sector plays as a funder and developer of diagnostics and therapeutics to improve patient care.

Canadian Context: Overview of Canada’s health-care system

- Ida Goodreau, Board of Genome British Columbia

The presentation in this session provided an overview of the Canadian health-care system with perspectives on its distinctive features, including the research–commercialization pathway for health innovation, the public–private split and the federal–provincial division in responsibility. Advances in precision health are being driven by the promise of genomics, yet despite significant promise and equally significant investment, the implementation of precision health is occurring slowly. Genomics-based trials (pilots) in pharmacogenomics, rare diseases, infectious disease and cancer have been ongoing for several years but it is only recently that applications are beginning to find routine use in standard of care (e.g., hereditary cancer panels). Genomics innovations that are advancing into routine care are typically being implemented via existing processes and policy frameworks and, to date, the health-care system has been only marginally transformed by genomics. As we look to scale up the application of genomics in the health-care system, we can expect that the health-care system will require a disruptive transformation. This will call for integrated genomics education across the system and new policies to support individual privacy and engagement.

For Canada’s health-care system, a system designed to be stable and predictable, transformation to incorporate innovations arising from a fast moving and dynamic research system will be challenging. There is a clear opportunity to bring together our research and health-care delivery systems – aligning stakeholders and finding a mechanism to link the research ecosystem with health-care system needs. Done right, the health delivery system can support research activities (e.g., via links to health data, support for pilots, partnerships for big-data systems and involvement in implementation evaluation). The research system will contribute innovations that address patient needs. The federal–provincial division of responsibility may be an asset here as

successful pilots in some provinces may motivate faster adoption in other provinces. This division of responsibility may also be an asset as provinces trial and share best practices to address barriers to what are essentially common components of provincial health-care delivery. These themes were taken up in the session, "How Can We Work Together? Perspectives from the Health-Care System," and explored in the subsequent "Summary of Discussion and Proposed Actions" panel discussion.

How Can We Work Together? Perspectives from the Health-Care System

- Moderator: Patricia Evans, Patricia Evans & Associates
- Ian Rongve, British Columbia Ministry of Health
- Don Juzwishin, Alberta Health Services
- Jim Slater, Diagnostic Services Manitoba
- Bonnie Reib, Ontario Ministry of Health and Long-Term Care
- Michele de Guise, Institut national d'excellence en santé et en services sociaux (INESSS), Quebec
- Rodney Ouellette, Atlantic Cancer Research Institute

This session explored initiatives being taken forward within a number of provincial health-care systems to support implementation of genomics.

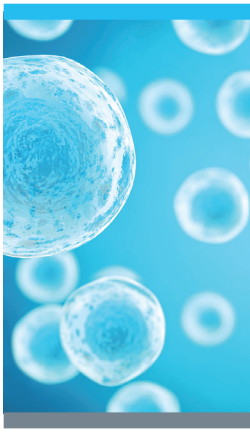
In British Columbia, lab services – including genomic testing – have been considered since 2015 under a single act administered under BC's Agency for Pathology and Laboratory Medicine. The agency is establishing new processes for test evaluation and reimbursement. This work is being done via process and policy-oriented committees that include patient representation. Working groups are also being established to build policy around areas of education for health-care professionals and patients, data sharing, legal and ethical issues, and accountability.

In Alberta, assessing and appraising tests and identifying the next wave of innovations likely to enter the system is the responsibility of the Health Technology Assessment & Innovation Department. The department accomplishes this via three programs:

- Assessment and Appraisal: Novel technologies and processes are identified and developed to improve the access, quality and sustainability of health-care delivery.
- Replacement/Reassessment: Technologies are examined at pre-determined times after their acquisition and toward the end of their life cycle to determine safety, efficacy, cost-effectiveness, obsolescence and appropriate use.
- Innovation: New and innovative technologies are identified and supported in combination with industry.

The Assistant Deputy Minister of Health also recently undertook a consultation with health stakeholders to develop guidelines to support precision health research. The guidelines will help ensure that genomic medicine/precision health research projects being proposed to Alberta Health Services will meet the health needs of Albertans and Canadians, can be effectively integrated into care delivery, and are of the highest scientific merit (see Appendix 3, Alberta Guidelines for Genomic Medicine/Precision Health Applications).

In Manitoba, diagnostic health-care services are provided by Diagnostic Services Manitoba. At present, 16 oncology tests and four genetics tests, all funded by the province, are standard of care. Genomic tests are validated by oncology and genetic working groups and an advisory committee that assesses utility and costs. Tests must demonstrate value for money with a view to replacing existing tests (i.e., divestment). It was noted that Manitoba saved $3 million by replacing existing tests with genomic tests in 2015.



In Ontario, work is focusing on management coordination and the modernization of lab services. A laboratories and genetics branch was established in 2015 in the Ontario Ministry of Health and Long-Term Care. The ministry is looking for a new model for genetic services that would align resources and optimize funding. Currently, there are 11 provincially run genomics centres and two private service providers in the province. The ministry has established a group of ministry-appointed advisors with responsibility and accountability for the work. This group, Health Quality Ontario, recommends and evaluates tests. The Ontario Genetics Advisory Committee (a subcommittee of the Ontario Technology Advisory Committee) and the Office of the Chief Health Innovation Strategist (OCHIS) provide further support for this work. OCHIS is a catalyst to help accelerate health technology commercialization efforts in Ontario. OCHIS works on behalf of health technology innovators to remove barriers and improve access to Ontario's health-care system.

In Quebec, INESSS is also undertaking evidence-based health assessment of health technology and is involving diverse stakeholders in this work. Before inclusion in physician formulary, a multidisciplinary committee composed of experts in the field assesses clinical validity, economic benefit, safety and so on. INESSS is also considering how to assess complex 'multiplex' tests and ways to gather evidence from practice.

In New Brunswick, the population of 750,000 is served by two health authorities (one French and one English) and two corresponding diagnostics facilities under the provincial Department of Health. In contrast to other provinces, there is little, if any, centralized provincial expertise in molecular diagnostics, so selection and adoption of genomic tests is enabled by research centres that identify and develop new technologies. Work is done within global budgets and is clinically driven.

Perhaps not surprisingly, given the common barriers to the implementation of genomics into clinical care, most provinces seem to be doing similar things to address challenges. But they are working in isolation. National coordination does not exist around the evaluation and validation of genomic tests – as tests are reimbursed on a provincial level – yet there is clearly room for better coordination between provinces. Budgetary pressures are a factor in all jurisdictions, as health spending continues to grow. This will force whole life-cycle analysis of tests, looking not just at the test and treatment but at other factors the tests may impact, including timelines for divestment of existing technologies. Economic analysis and best practices to divestment represent opportunities for coordination between provinces. Proactive spending on genetic counselling may provide a different approach to reducing costs, empowering and engaging individuals in behavioural change that can reduce risk of chronic disease.

Summary of Discussion and Proposed Actions

- Moderator: Patricia Evans, Patricia Evans & Associates

Three breakout sessions focused on themes presented throughout the forum took place. These breakout sessions examined:

- a vision for further implementation of genomics into the health-care system;
- the steps required to move forward on the implementation of genomics into the health-care system; and
- the role of key players.

Participants then reconvened for a facilitated discussion and to make the following key recommendations.

Vision for the implementation of genomics into health-care systems

The idea of a national vision with national goals for precision health in Canada was discussed. Many groups across Canada have developed roadmaps for precision health. A national vision may raise the profile of Canada's precision health research ecosystem internationally. It may also help leverage synergies across regional initiatives and accelerate the implementation of genomics into the health-care system. The vision would likely benefit from global foresight that informs emerging technologies or therapeutics that Canada may implement. Vision goals could include the initiation of a large population-scale sequencing initiative but could also be more focused. For example, they could focus on rare diseases, a condition with high prevalence in the population and/or a common screening program.

➥ **Recommendation**: Develop a national vision for the implementation of genomics into the health-care system. Start with a demonstration project in a targeted area to raise the profile of precision health in Canada and provide a framework to leverage synergies from existing work.

Moving forward toward the implementation of genomics into health-care systems

The validation and evaluation of genomic technologies in the health-care setting, and health technology assessment more generally, are challenges across the country that require engagement with a broad stakeholder group. Funders seek to facilitate this work by requiring scientists to consider the entire 'bench to bed-side' implementation pathway and address the appropriate ethical, economic, environmental, legal and social aspects of genomics research (GE^3LS) in their projects to identify barriers and assist in the effective translation of research results into practice and policy. In reality, this is often accomplished in a less than ideal way. For example, health economists are often brought into projects on short notice and without meaningful integration. Also, few research projects address all GE^3LS issues, or generate the comprehensive datasets required for health technology assessment and the integration of genomics into the health-care system.

Earlier engagement with an organization such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or INESSS may help ensure research is well positioned for implementation. Such organizations have clear and well established processes for evaluating clinical effectiveness, cost-effectiveness and the ethical, economic, environmental, legal and social implications of health technologies on patient health and the health-care system. Through such models, researchers would ensure appropriate data are generated and GE^{3}LS research is undertaken. Health technology assessors would benefit from earlier engagement with researchers on innovations in the pipeline. In Quebec, such an approach is already being discussed with INESSS. Incorporating a health technology assessment service like this in research projects would not replace the requirement for GE^{3}LS research needed in one or more of the relevant areas to advance precision health.

➥ **Recommendation**: Incorporate a health technology assessment service in publicly funded research projects, through an organization such as CADTH or INESSS, to ensure a harmonized and proactive pathway for the assessment of new technologies.

Canadian provinces, as payers of genomic technologies, are developing and applying frameworks for the assessment and evaluation of new health technologies. As already noted, this work is occurring in silos. Yet, in many cases, provinces require similar bodies of evidence upon which to base decisions on clinical utility and validity. Provinces may benefit from a harmonized approach to this work through the establishment of national guidelines for the assessment and evaluation of genomic technologies. Using these guidelines, decisions on reimbursement could then be made at a provincial level.

➥ **Recommendation**: Establish national guidelines for the assessment and evaluation of genomic tests to support a harmonized and streamlined approach to the adoption of genomic tests by each province.

Precision health innovations will be accelerated through the better use of existing and future data – both patient data and health-care data. In particular, there is a sense that data generated with public funds should be used to deliver benefits to the public health-care system. Currently, relevant data such as genomics, clinical and administrative data are collected to variable standards and stored on an array of public, private and within-lab servers. The harmonization and accessibility of these data would accelerate new discoveries and reduce redundancies in health research and patient care. This may be most efficiently and effectively accomplished through top-down-mandated approaches – at provincial and/or federal levels (e.g., funders of research or provincial ministries of health).

➥ **Recommendation**: Develop, and require the adoption of, national standards for the collection, aggregation, integration, storage and governance of data generated with public sector funds, in alignment with the standards articulated by GA4GH. This would accelerate the validation of new genomic tests and provide a platform for R&D.

It will be important to ensure that practitioners in health-care systems (physicians, nurses, regulators, pharmacists, etc.) understand the role and application of genomics in precision health. As more, and diverse, genomic tests enter clinical care, it will be important to ensure that student training and programs for continuing education are developed to facilitate uptake into practice.

Education and training should include approaches to informing and engaging patients, the use of emerging decision support tools, and the reporting and interpretation of incidental findings. Genetic counsellors have a role to play as well, educating physicians and other health-care workers on the use of genomics in the clinic and informing patients and patient advocacy groups to support broader education around genomics and integration into clinical care.

➥ **Recommendation**: Support the development of appropriate curriculum and tools for the education and training of students and health-care practitioners to ensure the comprehensive and equitable use of genomic tests in clinical care.

Significant investment by CIHR, the provinces and other partners has been made in genomics research projects, platforms, networks and strategic initiatives such as SPOR. These and other platforms, initiatives and infrastructures are not yet well-integrated but may be tackling, in silos, various barriers to the implementation of genomics.

➥ **Recommendation**: Consider how elements established by SPOR and related initiatives and platforms can be integrated into existing health-care delivery and research structures to advance efforts to implement precision health within our health-care systems.

Roles and responsibilities of key stakeholders

It is becoming increasingly clear that diverse stakeholders must be involved in the development, validation, evaluation and implementation of genomic tests and health-care system transformation. The development of a white paper that aims to articulate the roles and responsibilities of each stakeholder could provide a useful catalyst for discussion and engagement. It may also facilitate the construction of robust research projects.

➥ **Recommendation**: Develop a white paper to articulate the roles and responsibilities of each stakeholder involved in health-care system transformation and help strengthen the precision health research and delivery continuum.

APPENDICES

Genomics and **Precision Health** FORUM

APPENDIX 1

Agenda October 4-5, 2016

STEERING COMMITTEE

Co-Chairs

Cindy L. Bell, Genome Canada

Catalina Lopez-Correa, Genome BC

Members

Jane Aubin, CIHR

Chris Barker, Genome Prairie

Kathryn Deuchars, Ontario Genomics

Karen Dewar, Genome Canada

Peter Goodhand, Global Alliance for Genomics and Health

Robin Harkness, Ontario Genomics

Diana Iglesias, Genome Quebec

Paul Lasko, McGill University CIHR-Institute of Genetics

Stéphanie Lord-Fontaine, Génome Québec

Étienne Richer, CIHR-Institute of Genetics

Stephen Robbins, University of Calgary, CIHR-Institute of Cancer Research

Dan Roden, Vanderbilt University

Gijs van Rooijen, Genome Alberta

Andy Stone, Genome Atlantic

Kate Swan, Genome Canada

DAY 1 – TUESDAY, OCTOBER 4, 2016			
Time	**Room**	**Topic**	**Speaker(s)**
5:00 pm	Tudor 7	REGISTRATION & RECEPTION	
6:30 pm	Tudor 8	Welcome	**Marc LePage**, Genome Canada
6:40 pm	Tudor 8	**International Initiatives** Moderator: Patricia Evans, Patricia Evans and Associates	**Geoff Ginsburg**, Duke University – *Global Genomic Medicine Collaborative (G2MC)* **James Peach**, *Genomics England* **Clara Gaff**, Melbourne Genomics Health Alliance – *Australian Genomics Health Alliance* **Peter Goodhand**, OICR & Global Alliance for Genomics and Health
9:00 pm		Meeting adjourns	
DAY 2 – WEDNESDAY, OCTOBER 5, 2016			
7:00 am	Territories	BREAKFAST AVAILABLE	
8:00 am	Tudor 7 & 8	Welcome	**Patricia Evans**
8:05 am	Tudor 7 & 8	Setting the Stage	**Cindy Bell**, Genome Canada **Jane Aubin**, CIHR
8:30 am	Tudor 7 & 8	**Canadian Experience: Lessons learned from ongoing projects** Moderator: Paul Lasko, McGill University & CIHR-IG	**Genome Centre Representatives**

Time	Room	Topic	Speaker(s)
9:15 am	Tudor 7 & 8	**Panel – How are we doing? Stories on the path to implementation** Moderator: Catalina Lopez-Correa, Genome BC	**Drew Bethune**, Dalhousie University & Nova Scotia Health Authority – *Implementation of a lung cancer genomics program* **Jacques Michaud**, Ste Justine – *Using exomes to diagnose rare diseases* **Danielle Andrade**, Toronto Western General – *Using genomics to diagnose epilepsy* **Christian Steidl**, BCCA – *Personalized Oncogenomics Program*
10:15 am		BREAK	
10:45 am	Tudor 7 & 8	**Panel – Why are we doing this anyway? Perspectives on patient advocacy & engagement** Moderator: Stephen Robbins, University of Calgary, CIHR-ICR	**Louise Binder**, Canadian Cancer Survivor Network **Patrick Sullivan**, Team Finn Foundation & PROFYLE **Kym Boycott**, Care 4 Rare Project, Children's Hospital of Eastern Ontario **Nathalie Bolduc**, Canadian Association of Genetic Counsellors and LifeLabs
11:45 am	Tudor 7 & 8	**Canadian Context: Overview of Canada's health care system**	**Ida Goodreau**, Chair Genome BC Board, former CEO Vancouver Coastal Health
12:15 pm	Territories	LUNCH	
1:00 pm	Tudor 7 & 8	**Panel – How can we work together? Perspectives from the health care system** Moderator: Patricia Evans	**Rodney Ouellette**, Atlantic Cancer Research Institute **Michele de Guise**, INESS, Quebec **Bonnie Reib**, Ontario Ministry of Health and Long Term Care **Jim Slater**, Diagnostic Services Manitoba **Don Juzwishin**, Alberta Health Services **Ian Rongve**, BC Ministry of Health *Ida Goodreau will join panel for discussion
2:00 pm	Tudor 7 & 8 Quebec Confederation 3	**Breakout groups** – How to move forward on implementation of genomics into the clinic	
3:00 pm		BREAK	
3:30 pm	Tudor 7 & 8	**Facilitated Discussion** – Vision for the future	**Patricia Evans**
4:45 pm	Tudor 7 & 8	**Wrap-Up session** Define next steps	**Cindy Bell** & **Jane Aubin**
5:00 pm		**Meeting adjournment**	**Catalina Lopez-Correa**

APPENDIX 2

Participant List

Genomics and Precision Health Forum Participants

October 4 and 5, 2016
Toronto, ON

First Name	Last Name	Affiliation
Danielle	Andrade	Toronto Western General Hospital
Steve	Armstrong	Genome Atlantic
Jane	Aubin	Canadian Institutes of Health Research (CIHR)
Jehannine	Austin	University of British Columbia
Phillip	Awadalla	Ontario Institute for Cancer Research (OICR)
David	Bailey	Genome Alberta
Robert	Balshaw	British Columbia Centre for Disease Control
Shantanu	Banerji	University of Manitoba
Chris	Barker	Genome Prairie
Brendan	Barrett	Memorial University
Cindy	Bell	Genome Canada
Carolyn	Bell	British Columbia Ministry of Health
François	Bernier	Alberta Health Services
Drew	Bethune	Nova Scotia Health Authority
Louise	Binder	Canadian Cancer Survivors Network
Marie-Josée	Blais	Ministère de l'Économie, Science et Innovation (MESI) du Québec
Marco	Blouin	Ministère de l'Économie, Science et Innovation (MESI) du Québec
Nathalie	Bolduc	Canadian Association of Genetic Counsellors / LifeLabs
Guillaume	Bourque	McGill University
Kym	Boycott	Children's Hospital of Eastern Ontario (CHEO)
Natalie	Brender	Genome Canada
Disa	Brownfield & Walker	Alberta Innovates Health Solutions
Mike	Brudno	SickKids
Tania	Bubela	University of Alberta
Dennis	Bulman	Children's Hospital of Eastern Ontario (CHEO)
Christian	Carswell	Genome Canada

First Name	Last Name	Affiliation
Ivana	Cecic	Genome British Columbia
Anna	Chiarelli	University of Toronto/Cancercare Ontario
Tammy	Clifford	Canadian Agency for Drugs and Technologies in Health (CADTH)
Joseph	Connors	British Columbia Cancer Agency
Patrick	Cossette	Université de Montréal
Pieter	Cullis	Personalized Medicine Initiative
Brady	Davis	Illumina
Martin	Dawes	University of British Columbia
Michèle	de Guise	Institut national d'excellence en santé et en services sociaux (INESS)
Kathryn	Deuchars	Ontario Genomics
Karen	Dewar	Genome Canada
Peter	Dirks	SickKids Hospital
Lena	Dolman	Global Alliance for Genomics and Health
Martin	Doyon	Ministère de l'Économie, Science et Innovation (MESI) du Québec
Ian	Dubé	British Columbia Agency for Pathology and Laboratory Medicine
Anick	Dubois	CEPMED/Montreal Heart Institute
Clara	Gaff	Melbourne Genomics Health Alliance
Harleen	Ghuttora	Genome Alberta
Geoff	Ginsburg	Duke University – Global Genomic Medicine Collaborative
Peter	Goodhand	Ontario Institute for Cancer Research (OICR)
Ida	Goodreau	Chair, Genome British Columbia Board of Directors
Ellie	Griffith	Genome British Columbia
Robin	Harkness	Ontario Genomics
Richard	Harrigan	University of British Columbia
Michael	Hillmer	Ontario Ministry of Health and Long Term Care
Diana	Iglesias	Genome Québec
Nada	Jabado	Montreal Children's Hospital / McGill UHCRI
Don	Juzwishin	Alberta Health Services
Suzanne	Kamel-Reid	University Health Network
Agnes	Klein	Health Canada

APPENDIX 2

Participant List *(cont.)*

Genomics and Precision Health Forum Participants

October 4 and 5, 2016
Toronto, ON

First Name	Last Name	Affiliation
Sylvie	Langlois	University of British Columbia
Paul	Lasko	CIHR Institute of Genetics
Marc	LePage	Genome Canada
Jordan	Lerner-Ellis	Ontario Institute for Cancer Research (OICR)
Peter	Liu	University of Ottawa Heart Institute
Catalina	Lopez-Correa	Genome British Columbia
Stephanie	Lord-Fontaine	Genome Québec
Dave	Mack	University of Ottawa
Alex	MacKenzie	Children's Hospital of Eastern Ontario (CHEO)
Darcy	Marciniuk	University of Saskatchewan
Marco	Marra	BC Cancer Agency
Christopher	McCabe	University of Alberta
Joby	McKenzie	LifeLabs
Jacques	Michaud	Université de Montréal, CHU Ste-Justine
Daniel	Mueller	Canadian Association of Mental Health (CAMH)
Raymond	Ng	University of British Columbia
Blaire	O'Neil	Alberta Health Services
Rodney	Ouellette	Atlantic Cancer Research Institute
James	Peach	Genomics England
Andrew	Penn	Victoria General Hospital
Mark	Pereira	University of Toronto
Geoff	Pradella	Alberta Research and Innovation Authority
Trevor	Pugh	University of Toronto
Proton	Rahman	Memorial University
Bonnie	Reib	Ontario Ministry of Health and Long Term Care
Étienne	Richer	CIHR Institute of Genetics
John	Rioux	Université de Montréal & Montreal Heart Institute

First Name	Last Name	Affiliation
Rachael	Ritchie	Genome British Columbia
Stephen	Robbins	CIHR Institute of Cancer Research
Ian	Rongve	British Columbia Ministry of Health
François	Rousseau	Université Laval / Hôpital Saint--François-d'Assise
Denis-Claude	Roy	Université de Montreal / Maisonneuve & Rosemont Hospital
Stephen	Scherer	SickKids Hospital
Anu	Shukla-Jones	Health Canada
Jacques	Simard	Université Laval
Jim	Slater	Diagnostic Services Manitoba
Pascal	Spothelfer	Genome British Columbia
Christian	Steidl	British Columbia Cancer Agency
Lincoln	Stein	Ontario Institute for Cancer Research (OICR)
Alain	Stintzi	University of Ottawa
Andy	Stone	Genome Atlantic
Patrick	St-Pierre	Canadian Institutes for Health Research (CIHR)
Patrick	Sullivan	Team Finn Foundation / PROFYLE
Kate	Swan	Genome Canada
Rachel	Syme	CIHR Institute of Cancer Research
Karl	Tibelius	Genome Canada
Kristin	Tweel	Genome Atlantic
Tibor	Van Rooij	Telus Health
Gijs	van Rooijen	Genome Alberta
Sophie	Veilleux	Université Laval
Kristine	Votova	Vancouver Island Health Authority
Christine	Williams	Ontario Institute of Cancer Research (OICR)
Brenda	Wilson	University of Ottawa
Shannon	Wilson	IBM
Tyler	Wish	Sequence Bio
Michael	Wolfson	University of Ottawa
Jonathan	Yeh	Université de Montréal
Emma	Zheng	University of British Columbia

APPENDIX 3

Alberta Guidelines for Genomic Medicine/Precision Health Applications

The purpose of the following guidelines is to ensure that genomic medicine/precision health research projects being proposed to Alberta Health Services (AHS) will meet the health needs of Albertans and Canadians; can be effectively integrated into care delivery; and are of the highest scientific merit.

The guidelines provide applicants, partners, organizations, and reviewers with important considerations that would lead to potential endorsement by AHS as an end user of the outcomes of the research project.

Benefits to Patients

- The proposal provides a clear line of sight as to how the research outcomes will benefit the health of Albertans and Canadians.
- Patient engagement is recognized and demonstrated; and the patient perspective is integrated throughout the application.

Strength of Evidence

- A systematic and critical review of available pre-clinical or early clinical data is included.
- An analysis of the context demonstrates the relevance for the technology, and that it is coming of age.
- Evidence indicates that this new technology addresses an unmet health need or that it replaces a less effective intervention which would be removed from health services delivery.

System Alignment

- The project clearly outlines the value to the health care system in terms of outcomes, access, safety and quality. Alignment with the health system priorities is articulated.
- AHS capital equipment requirements are taken into account and a life cycle perspective is adopted and aligned including the need for integration into existing and future infrastructure.
- AHS information technology and data requirements and capabilities are considered and aligned including privacy and security factors related to access and sharing of patient/clinical information.
- It is feasible that the technology can be implemented into practice within a five year time frame.

Economic and Financial Implications

- Value for money has been taken into account using appropriate approaches, methods, and economic tools. The headroom component of the Validation Evaluation and Implementation (VET) analysis may be used to demonstrate potential economic viability.

Legislative, Legal, and Ethical Implications

- Consideration is given to ethical and legal implications particularly in cases of new and emerging technologies.
- An approach to risk mitigation is included for equipment that is considered to be “for research only”.

Collaboration

- Alignment and continuity from bench to bedside is critical for successful translation, adoption and implementation as well as the necessary allocation of resources.
- Whenever possible, the project involves a comprehensive membership from across the province, nationally and global centers of excellence.
- A collaborative approach also integrates participation from: Strategic Clinical Networks administrative leaders and clinical end users within AHS setting the stage for transformation of health care in Alberta.

Requests for AHS support on grant applications must be received at least 4 weeks prior to the deadline for submission. Grants received less than 4 weeks prior to the deadline will not be considered.

If you have questions or feedback about these guidelines, please contact:
Don Juzwishin PhD, FCCHL, Director, Health Technology Assessment & Innovation, AHS
Tel: 780.735.0741 Email: don.juzwishin@ahs.ca

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