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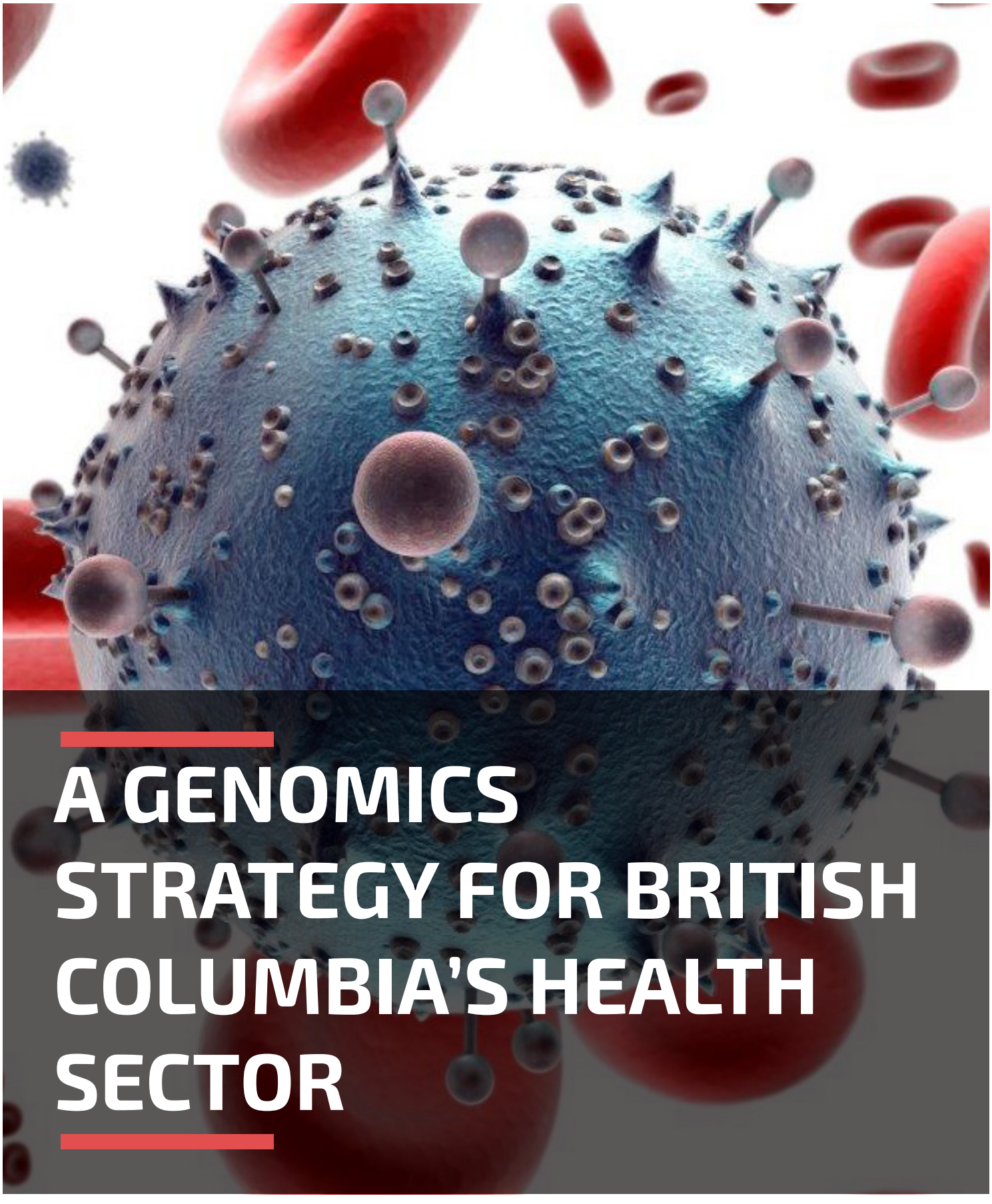

A GENOMICS STRATEGY FOR BRITISH COLUMBIA'S HEALTH SECTOR

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GENOME BRITISH COLUMBIA

Vision

Genomics will revolutionize many aspects of our lives and provide solutions to humankind's challenges.

Mission

Genome British Columbia leads academia, government and industry in the growth of a world-class genomics R&D cluster to deliver sustainable social and economic benefits to British Columbia, Canada and beyond.

This is achieved through:

- Excellent projects and technology platforms,
- Innovative applications for the life sciences cluster,
- Commercialization and translation partnerships for entrepreneurs, SMEs, and other end users in government and society,
- Strategic regional, national & international collaborations, and
- Proactive leadership in exploring societal impacts of genomics.

Genomics is the science that aims to decipher and understand the entire genetic information of an organism (i.e. microorganisms, plants, animals and humans) encoded in DNA and corresponding complements such as RNA, proteins and metabolites.

The knowledge and innovations emerging from this field are finding solutions to complex biological challenges, while at the same time raising questions of societal and economic importance.

Genomics has already brought huge economic and societal gains to Canadians through better healthcare, improving food quality, safety and production and protecting our environment and natural resources.

Looking ahead, genomics will be the foundation of Canada's growing bio-economy (all economic activity derived from life science-based research), which is estimated to be responsible for some 2.25 per cent of GDP, or about $38 billion, by 2017.

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1 Executive summary

- The 'genome' is the complete set of DNA-based blueprints found within all living things.
- Throughout this document, we use a broad definition of genomics, encompassing whole genomes, single genes, and gene products (e.g. RNA and proteins).

What is Genome BC's role in the health sector in British Columbia (BC)?

Genome British Columbia (Genome BC) aims to deliver sustainable social and economic benefits to BC by supporting the use of genomic approaches towards understanding human health and disease, and applying this knowledge in the 'real world'. Genome BC has played an important and catalytic role in the application of genomics to health research (discovery, applied, and translational) for nearly 15 years.

Our strengths include identification, management, and funding of targeted projects and initiatives, as well as brokerage and management of partnerships necessary for success. In the next five years and beyond, we will build on our success in enabling health research to bring tangible health and economic benefits to the population of BC using genomic approaches.

What is the potential for genomics to benefit the health sector in BC?

The potential for genomic knowledge, tools and technologies to deliver benefits to BC is vast, encompassing: (1) improving health outcomes; (2) improving healthcare system efficiency; (3) stimulating economic growth; and (4) fueling scientific discoveries. These benefits stem from the ability of genomics to provide a new type of "microscope" that allows us to understand the role of DNA and related molecules in health and disease. This knowledge can be applied to improve disease prevention, diagnosis, and treatment, as well as to inform our approaches to wellness, nutrition, and public health.

What is Genome BC's strategy to focus its investment in health?

In order to maximize the benefits that genomics can deliver in the next five years, while sowing the seeds for longer term benefits, we analyzed the potential utility and clinical readiness of genomic approaches across a wide range of high burden diseases and genetically driven conditions. This analysis identified three disease areas with strong potential for genomics to deliver near-term benefits to BC: cancer, infectious diseases, and rare diseases/rare mutations[1], as well as an opportunity to use pharmacogenomic[2] tests to guide medication dosing and avoid adverse drug reactions across many diseases. This analysis also demonstrated the need and potential value of a continued broad investment in health research, given the complex role of genetics in many of BC's highest burden diseases. In both research and healthcare delivery, collecting and applying genomic data at a large-scale, ideally at the level of populations, will be critical for realizing maximal benefits.

[1] A rare disease is defined as one that affects fewer than 200,000 people in the United States or fewer than 1 in 2,000 people in Europe. Although individually rare, collectively these conditions affect millions of children worldwide. Most rare diseases are genetic in origin, and best estimates suggest that there are at least 7,000, and possibly many more, rare genetic diseases.

[2] Pharmacogenomics is the study of how genomic variation influences drug response (can be based on the genome of host/human, tumour, or infectious agent).

What is Genome BC's vision for genomics in BC?

Our five-year vision is to demonstrate the benefits of clinical utilization of genomics in BC in selected diseases, by applying genomics in specific patient populations where genomic approaches are poised to deliver healthcare benefits. This vision is a step towards our ten-year vision for genomics to catalyze a transition from symptom-based care to a model based on understanding the underlying disease cause. In this new paradigm, the patient's genome and other molecular data will increasingly inform patient care across the continuum from prevention, through screening, to diagnosis, and treatment of diseases.

How will Genome BC contribute to realizing the promise of genomics in BC?

Realizing our vision will be challenging, and will require time, dedication, and collaboration amongst disparate stakeholders, including medical professionals, health authorities, funders, and health researchers. Genome BC can catalyze success by: (1) uniting the genomic community around a common vision for personalized medicine in BC across and within key application areas; (2) bringing together the necessary partnerships, funding, and operational models to enable clinical application of genomic technologies in BC at the level of populations. At the same time, Genome BC will continue to promote and manage competitive programs in health research (discovery, applied, and translational).

2 Background

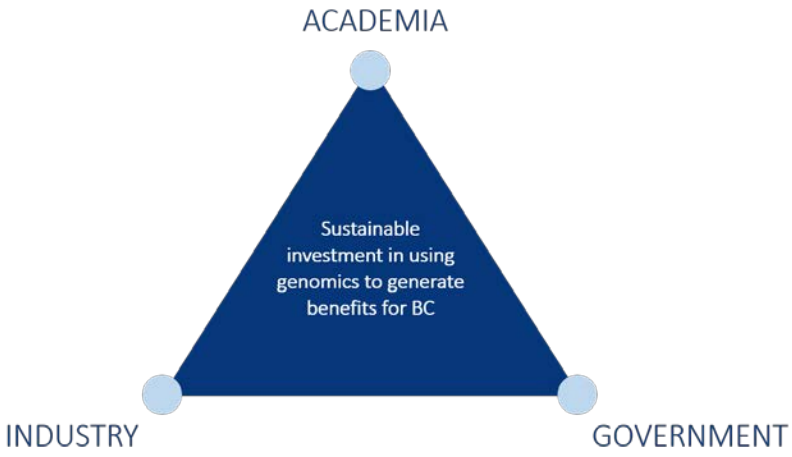
2.1 Role of Genome BC

Genome BC's vision is that:

Genomics will revolutionize many aspects of our lives and provide solutions to humankind's challenges.

Genome BC has been moving towards this vision by supporting world-class genomics research projects (discovery, applied, and translational) and technology platforms, and engaging in strategic partnerships. Over the last 15 years, Genome BC has worked with Genome Canada and other partners to catalyze and manage over 136 projects in health representing an investment of $334.6 million[1] (see Appendix 10.6 for a list of major health programs and projects). In the next five years and beyond, Genome BC will continue to make significant investments in health research but will increasingly assume a mandate to deliver tangible and sustainable health and economic benefits to BC. Satisfying this mandate will require a thoughtful focus on selected application areas, as well as an evolution in Genome BC's roles and interactions with government and industry stakeholders.

FIGURE 1: ROLE OF GENOME BC



Genome BC leverages the following strengths to realize our vision:

- Identification of high priority, impactful projects that support our vision
- Funding and program management (alone or in partnership)
- Acting as a neutral, "honest-broker" in building and managing partnerships/relationships
- Adding value to the whole by enabling the sum of the parts

2.2 Purpose and scope of document

This document provides a strategic framework and a foundation upon which to focus Genome BC's efforts towards maximizing the benefits of genomics on the health sector in BC. Accordingly, the document's scope encompasses the application of genomic tools and technologies both in health research and in 'real-world' clinical applications. Genome BC's programs and projects for 2015-2020 will build upon the foundation laid by this document.

2.3 Development of document

This document was developed with input from a Task Force comprising leaders representing BC's health research organizations and the broader health community (see Appendix 10.1). Genome Canada, other provincial Genome organizations, the BC Ministry of Health, multiple provincial health authorities, and members of the broader community (e.g. biotech and digital health industry) were also consulted in finalizing the document.

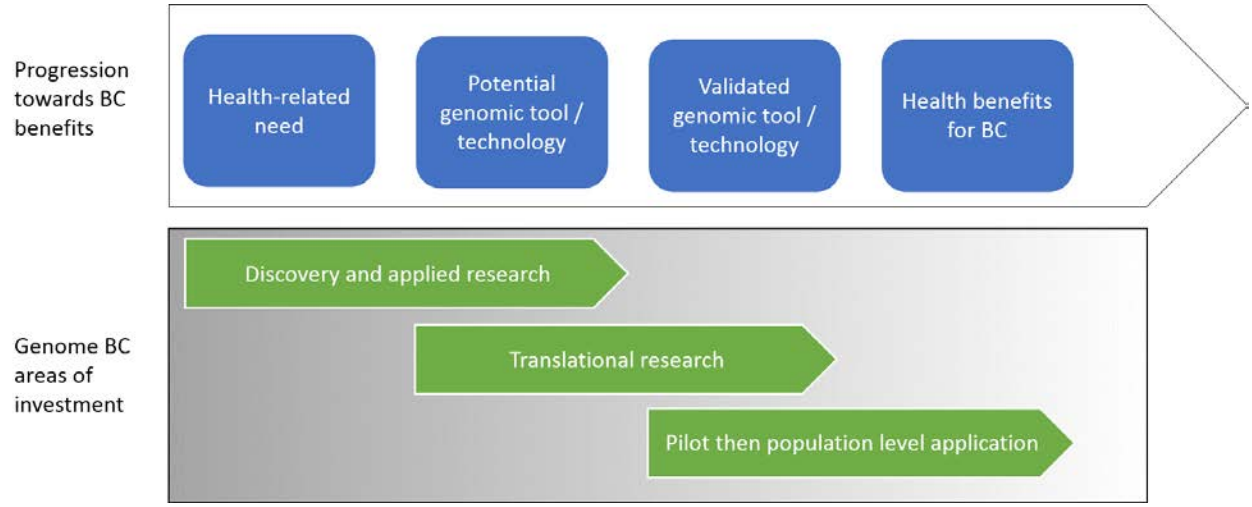
This document builds on Genome BC's initial 2009 '*Towards a Genomics & Health Strategy*', and is aligned with several recent provincial strategies and reports (described in Appendix 10.2), including *Directions for Health Research in BC* (2014)[2], *Setting Priorities for the BC Health System* (2014)[3], and *Findings from the Ontario Personalized Medicine Network's (OPMN's) 2014 Consultations*[4].

3 Introduction

The genome is the complete set of DNA-based blueprints found within all living things. Our genomes and the genomes of the infectious agents that colonize us help determine many aspects of our lives, from our personalities, our eye colour, our weight, our risk of mental and physical diseases, to our response to drugs, and more. As such, the potential for genomic tools and technologies to bring personal and societal benefits is vast, both in terms of health outcomes and economics. In BC and globally, these benefits are now within reach, due largely to significant technological advances in the past decade.

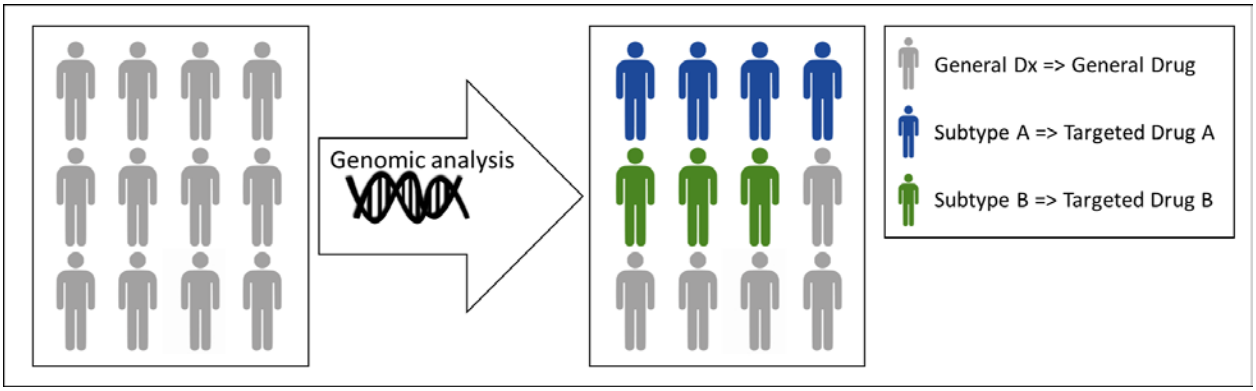
As outlined in Figure 2, the roadmap to realizing the benefits of genomics in healthcare starts with applying genomics to better understand health and disease. Once a genomic discovery/potential product has been technically validated and tested in patients, we must assess the value of the innovation in the clinical context (clinical utility), typically by moving into clinical use at a pilot scale. Once clinical utility is established, we aim to maximize health benefits by bringing genomics to all patients in a specific population (e.g. all cancer patients), and in doing so, fuel the next generation of discoveries.

FIGURE 2: ROADMAP TOWARDS BENEFITS OF GENOMICS



Our five-year vision is to bring genomic approaches to specific populations in BC where we can demonstrate clinical utilization and measure the benefits of genomics, and to do so in several clinical contexts with anticipated near-term benefits. This vision is a step towards our ten-year vision for genomics to catalyze a transition from symptom-based care to a model based on understanding the underlying disease cause. In this new paradigm, the patient's genome and other molecular data (e.g. microbiome, transcriptome, proteome) will increasingly inform patient care across the continuum from prevention, through screening, to diagnosis, and treatment of diseases. As a theoretical example, Figure 3 illustrates the use of genomic analysis to identify distinct disease subtypes, some of which have corresponding targeted drugs with increased efficacy and/or safety.

FIGURE 3: USE OF GENOMICS TO IDENTIFY DISEASE SUBTYPES AND GUIDE TREATMENT



As we look forwards, we recognize that the growing role of individuals and consumers in the acquisition and use of genomic data will be an important element of the landscape. The growing role of consumers in the genomic health landscape is part of an overall trend towards 'patient empowerment', and has been fueled by several related trends, including a dramatic decrease in the cost of DNA sequencing, an increase in consumer-oriented health devices, and an increase in digitization of medical data, all of which are expected to continue and/or accelerate. While it's impossible to predict where consumer involvement will lead, it's clear that Genome BC and other stakeholders in the health sector must prepare themselves for a significant contribution from consumers to genomic applications and data.

In this document, we review the potential benefits for applying genomics in health, the requirements for success, and synthesize our findings into Genome BC's areas of strategic focus in health.

4 Benefits of genomics in the health sector

The broad role of genomics in many aspects of human health underlies the vast and profound potential for genomic tools and technologies to bring benefits to individuals and societies. By incorporating the perspectives of diverse stakeholders (e.g. patients, payers, healthcare professionals, researchers), we identified four major categories of benefits, which vary in their horizon from near to long term.

1. Improving health outcomes
2. Improving healthcare system efficiency
3. Stimulating economic growth
4. Fueling scientific discoveries

4.1 Improving health outcomes

Genomic approaches have the potential to benefit our health outcomes in diverse ways, spanning disease prevention through improved treatment and monitoring. Many of these benefits focus on urgent individual needs (e.g. to increase the proportion of prescriptions that are effective) while others are more forward-looking, and population-based, like reducing the spread of anti-microbial resistance. Table 1 describes the major categories of health outcome benefits with selected examples of each.

Table 1: Health outcomes benefits of genomics

Benefit	Role of genomics	Example
Prevent diseases with genetic predisposition	• Genomics can identify high-risk individuals who can then engage in monitoring and/or lifestyle changes • The longer term role of genomics in prevention includes guiding vaccine development and use, and informing how people respond to food products and the environment	• Individuals that test positive for Lynch syndrome are at increased risk of colorectal cancer and may begin screening colonoscopies in their 20s rather than in their 60s • Individuals that carry a mutation in BRCA1 are at high risk of breast and ovarian cancer and may undergo prophylactic surgery to prevent disease
Rapidly and effectively diagnose genetic diseases	• An estimated 80% of rare diseases have a genetic origin • Specific subsets of common conditions can be caused by rare mutations • Genomics can help to rapidly diagnose many conditions that otherwise require many rounds of testing and may never yield an answer • Genomic testing can be applied prenatally, for newborn screening, and even pre-implantation[5,6,7]	• A single DNA sequencing test can rapidly diagnose any of the conditions covered in hundreds of single gene DNA tests (and avoid dozens of single tests). Even when not treatable, diagnosis is extremely valuable for families • In the FORGE Canada study, disease-causing DNA variants were identified for 146 of 264 patients, in some cases leading to better treatments[8]
Increase the proportion of prescriptions that are effective	• Genomics can categorize disease at a more granular level based on its molecular cause/profile • Selection of a drug can be made based on its efficacy in the relevant disease subset	• Only skin cancer patients whose tumours have a BRAF mutation are highly likely to respond to the drug Vemurafenib®, which targets this defect • Patients whose tumours have mutations in the gene KRAS are unlikely to respond to certain treatments for lung cancer (ie Erbitux®)
Avoid unnecessary treatments	• Genomics can help identify patients who are at low risk of progression and can be spared aggressive treatment	• OncotypeDx® (Genomic Health) is a widely adopted genomic test (gene expression panel) that categorizes breast cancers based

		on risk of recurrence and avoids unnecessary treatments. • Decipher® (GenomeDx) is a genomic test (gene expression panel) that categorizes tumours and identifies patients that may safely avoid additional treatment
Avoid adverse drug reactions	• Genomic testing can prevent adverse reactions based on individual DNA variants • Tests of drug metabolism genes can identify individuals that metabolize the drug more or less extensively, and should have doses tailored accordingly to optimize safety and efficacy	• Genetic testing of the immune gene HLA-B*5701 test can avert adverse reactions to Abacavir® (for HIV)[9] • Genetic testing of drug metabolism genes informs dosing of Warfarin, avoiding adverse events and optimizes dosing of many anti-psychotics[10]
Help prevent, diagnose, and treat infectious diseases	• Infectious agents have small genomes that can be rapidly analyzed to identify and measure the cause (virus, bacteria, parasite) and inform which drugs the agent is resistant to • This knowledge enables targeted and effective treatment with antibiotics/antivirals	• Genomic approaches are routinely used in BC to customize drug treatment for HIV (e.g. testing for CCR5 tropism to guide use of Celsentri®, and testing for resistance to integrases). Effective treatment has been shown to contribute to reduced disease transmission[11]
Reduce spread of drug-resistant infectious organisms	• Containment of drug-resistant organisms depends on rapid detection and effective treatment of cases, as well as public health strategies to prevent and monitor transmission and staunch epidemics • Genomics tools can be rapidly deployed to identify and monitor the spread of resistant organisms	• Genomic approaches can assess most causes of resistance in *Mycobacterium tuberculosis* (TB) in several days[12] compared to 1-2 months for traditional approaches

4.2 Improving healthcare efficiency and value

In BC and globally, healthcare systems are facing onerous costs (41% of the overall BC budget in 2014[13]). Increased healthcare costs in Canada have been driven by a variety of factors including price inflation (wages and services), demographics (population growth and aging), changes in utilization (increased volume and shift to expensive drugs) and use of expensive technologies[14]. Without dramatic changes, costs are expected to continue to rise. In addition, issues like the spread of drug-resistant microbes could become significant drivers of further healthcare costs if steps are not taken to mitigate this risk. Containing cost while maintaining or improving health outcomes will require new approaches, and genomics can play an important role among them.

Each category of health outcome benefit described above also represents an opportunity to improve healthcare efficiency and value. These opportunities are particularly profound in single payer systems – systems like Canada and the United Kingdom (UK) where parties are insured by a single agency for life. Such systems have the benefit of longitudinal accounting, that is, the ability to support short-term investments that yield longer-term dividends (e.g. in risk assessment and tailored early intervention). While data are limited on the cost-effectiveness of specific genomic approaches, our understanding of how to use these technologies to save costs is growing[15]. Table 2 illustrates that genomic approaches, including whole-genome sequencing (WGS), can be cost-effectively delivered.

Table 2: Healthcare efficiency and value benefits of genomics

Benefit to patient	Potential to benefit healthcare system	Example*
Prevent disease	• Improved cost-effectiveness of screening strategies by targeting high-risk individuals	• Cost-effectiveness modeling suggests that testing for mutations in BRCA1/2 is cost-effective in women with a >3.1% likelihood of testing positive (e.g. family history of breast/ovarian cancer), provided testing costs are below $9000 (current costs are less than $5000)[16]
Rapidly and effectively diagnose genetic diseases	• A single DNA sequencing test can rapidly diagnose any of the 7,000 known genetic disorders, replacing dozens of single tests • Widespread screening will become cost-effective as sequencing costs fall further	• Cost-effectiveness analysis of WGS for providing molecular diagnoses for neurodevelopmental delays in children suggests WGS is cost-effective at testing costs of $7000 (based on 40% chance of diagnosis). WGS could also have enabled diagnosis 6-7 years earlier on average[17] • A study of the clinical and economic impact of returning results for 56 medically actionable genes (ACMG-56) suggests this could become cost-effective when the cost of WGS falls to $500[18]
Increase the proportion of prescriptions that are effective	• Diagnostic tests can ensure the patient gets the right drug the first time, reducing need for further treatments • Diagnostic tests typically cost a fraction of the cost of the drug	• Modeling of testing for mutations in the gene KRAS to select patients with colorectal cancer for EGFR inhibitor therapy suggests savings of $7,500-$12,400 per patient in the US[19]
Avoid unnecessary treatments	• Genomics can help identify patients who are at low risk of progression and can be spared aggressive treatment	• A meta-analysis of the use of OncotypeDx® (Genomic Health), a genomic test that categorizes breast cancers based on likelihood of

		recurrence, found that use of this test led to an 18.2% (average) decrease in recommendations for chemotherapy[20]
Avoid adverse drug reactions	• Genomic testing can guide dosing and/or avoid adverse drug reactions	• Use of a drug metabolism genotyping test to guide dosing of Warfarin, used to prevent blood clots, could save the US healthcare system between $100 million and $2 billion per year, largely by avoiding strokes and hospitalizations[21] • Genetic testing for variants in TPMT prior to mercaptopurine treatment is a cost-effective way to avoid life threatening bone marrow suppression in children with acute lymphoblastic leukaemia (ALL)[22]
Improve treatment and diagnosis of infectious diseases	• A single DNA sequencing analysis can replace many serial tests for known bacteria and viruses and identify which antibiotics/antivirals the agent is resistant to • Tailored treatments translate into fewer ineffective prescriptions and fewer complications	• The laboratory costs of genomic sequencing for infectious agents provide more information than tests for single microbes and will soon have a comparable cost • A cost-effectiveness study modeling expanded use of highly-active anti-retroviral therapy in BC was associated with a net benefit of $900 million over 30 years[23]
Reduce spread of anti-microbial resistance	• Containment of drug-resistant organisms is a critical public health issue and depends on rapid detection and effective treatment of cases, as well as strategies to prevent and monitor transmission • Genomic tools can be rapidly deployed to identify and monitor the spread of resistant organisms	• Studies of targeted genomic approaches in the context of multi-drug resistant TB suggest cost-effectiveness, based on a reduction in costly cases of multi-drug resistant infections[24]

*All currencies in United States (US) dollars

4.3 Stimulating economic growth

An investment in bringing genomics into the clinic offers the additional economic benefit of stimulating BC's bio-economy through new scientific discoveries and subsequent development of novel products and services. The breadth of potential economic impact is well illustrated in a recent report: "The Impact of Genomics on the United States (US) Economy"[25], which found that considering all federal investment in human genome project (HGP) related genomics activities through 2012 yields a leverage ratio of 65 to 1 - every dollar of federal HGP and related investment has helped contribute to the generation of an

additional $65 in the US economy. In 2012 alone, the research, development, and commercial activities arising from human genome sequencing projects directly and indirectly generated:

- $US 65 billion in US economic output, $US 31 billion toward 2012 U.S. GDP and $US 19 billion in total personal income
- 152,000 genomics and supplier jobs and supporting more than 125,000 additional jobs in the US economy

Many of these jobs come from new companies centered on personalized medicine products and/or new products from existing companies. In 2014, there were over 113 prominent examples of personalized medicine drugs, treatments, and diagnostic products in the US, up from only 13 in 2006 - (based on 2014 Personalized Medicine Coalition report[26]), and 20% of FDA's new drug approvals included a genomic test to guide use.

Beyond diagnostic and therapeutic products centered on genomics, there are substantial opportunities in e-health (tools and technologies to enable transfer of health resources and health care by electronic means), as well as in devices and applications that tap into the growing consumer interest in collecting, analyzing, and sharing their health-related data. In addition to the potential for generation of new local companies, there is further potential for economic benefit by attracting international companies interested in a Canadian base.

Since inception, Genome BC has had an estimated 1.4 billion dollar economic impact on BC's GDP and created over 21,000 jobs. We have also filed 477 patent applications and contributed to the advancement of 33 companies (companies created, supported, or otherwise advanced by the investments made by Genome BC in industry-relevant projects), which together employ 359 people (as of March 2015).[27]

4.4 Fueling scientific discoveries

The application of genomic tools and technologies in health research has already enabled many major scientific breakthroughs in understanding many diseases. As genomic approaches are applied in patient (and healthy) populations at larger scales, there will be tremendous opportunities to gain insights into many more conditions, including complex, multigenic conditions that are the cause of tremendous disease burden. Major areas of application for genomics in health research are described in Table 3, with examples of BC research in each area. Building a fundamental understanding of disease in turn can provide new targets for therapies, new potential diagnostics, and can enable efficient development of new drugs (e.g. through development of disease models for testing candidate drugs and use of appropriate companion diagnostic biomarkers), ultimately enabling all of the benefits to patients described above in Table 2.

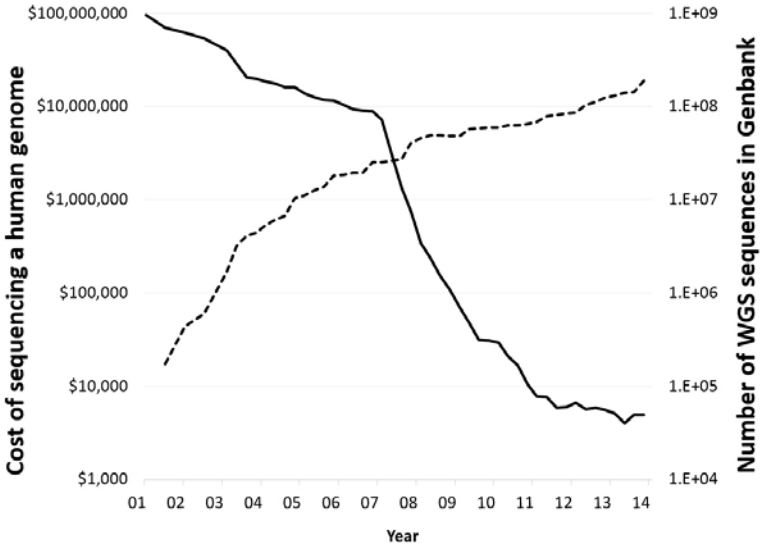
Table 3: Key areas of applications for genomics in health research

Research objective	Role of genomics	BC example
Uncovering the causes of genetic diseases • **New drug targets** • **New disease models for drug development**	• Genomics plays a role in causation of the majority of non-communicable diseases • The role of genomics in most chronic diseases is extremely complex, involving small contributions of many genes • Genomic drivers of disease may provide targets for new drugs • Models of disease that reflect genetic defects are critical for drug development	• Discovery of novel genes associated with familial Parkinson's by genome wide analysis of an affected family[28]
Identifying novel clinically relevant disease subtypes	• Genomics provides a high resolution 'microscope' with which to dissect heterogeneous diseases into distinct subtypes • Molecular subtypes may have better/worse prognosis and/or higher/lower likelihood to respond to a specific treatment	• Identification of novel breast cancer subgroups by genomic and transcriptomic profiling of 2,000 breast tumours[29] • Identification of novel medulloblastoma subtypes by genomic profiling of 1,000 tumours[30]
Uncovering genomic factors that influence drug reactions	• Variations in drug metabolism genes can affect how individuals metabolize a drug, which in turn influences risk of adverse drug reactions. • Variations in immune genes can influence drug safety and efficacy	• Discovery of variants in drug metabolism genes that may be associated with increased risk of cardiotoxic effects following anthracycline treatment[31] • Variants in the TPMT gene may be associated with hearing loss in children receiving cisplatin[32]
Understanding the role of microbes in human health and disease	• DNA sequences serve as a fingerprint for measuring, detecting and classifying microbes (bacteria and viruses) • DNA-based approaches are much faster and efficient than traditional culture-based methods • These approaches can be applied to our naturally occurring resident bacteria (our 'microbiomes') and to invasive, disease-causing microbes	• Mouse models of asthma reveal that early exposure to antibiotics may increase incidence and severity of allergic asthma[33] • The microbes that inhabit the human vagina are different in healthy pregnant women and women with preterm premature rupture of membranes[34]
Understanding mechanisms of drug resistance and transmission in microbes	• DNA sequencing can identify bacteria/viruses carrying genes responsible for drug resistance	• Bacterial WGS was combined with social networking data to understand an outbreak of TB in a BC community[35]

5 Requirements for success

The time is right for BC to realize the benefits of genomic tools and technologies. Only five years ago, cost and limited capacity alone rendered genome analysis impractical for routine clinical use. This barrier has been essentially eliminated over the last decade due to advances in DNA sequencing technologies, which have made rapid clinical use of genomic studies both feasible and increasingly affordable (see Figure 4)[36].

FIGURE 4: DNA SEQUENCING COST AND GROWTH IN GENOMIC DATABASES



However, technical capabilities alone are not enough to ensure success. This section provides a broad overview of the diverse requirements for success in achieving Genome BC's five-year vision to bring tangible benefits to BC, by applying genomics in specific patient populations where genomic approaches are poised to deliver healthcare benefits. These challenges are essentially universal amongst single payer systems, and are consistent with the findings of the Ontario Personalized Medicine Network (OPMN)[37]. While many of these challenges are outside the traditional remit of Genome BC, we play a role in illuminating the challenges and bringing together relevant stakeholders to address them. The broad requirements for successful clinical implementation are described briefly in Table 4 and in more detail in the subsequent sections (in non-prioritized order).

Table 4: Summary of requirements for successful clinical implementation

Requirement	Description	Elements of a solution
Scientific understanding and technical capabilities	• Scientific understanding of role of genomics • Technical capabilities for speed/throughput/quality • Large cohorts needed	• Resources to support discovery, applied, and translational health research • Technical capabilities • Collaborations
Alignment and prioritization	• Resource constraints necessitate focus on selected opportunities across stakeholders	• Alignment on near-term priorities • Education on value of genomic approaches

Health information technology (IT) infrastructure, tools, and governance	• Data infrastructure • Electronic Medical Records • Decision support tools • Consistent, transparent and reliable data access process	• Academic and industry innovation and collaboration • Clinical adoption • Enabling data governance policies
Clinical and laboratory infrastructure and capabilities	• Tissues and bio-banking infrastructure • Laboratory Standard Operating Procedures (SOPs) • Quality assurance mechanism • Training	• Dedicated resources
Regulatory guidelines	• Regulatory guidance can: o Ensure safety and efficacy of Laboratory-Developed Tests (LDTs) o Enable access to international products • Clear regulatory pathways enable local companies	• Clear regulation of LDTs • Clear regulatory policy for genomic products in health
Harmonized ethical consent	• Harmonized consent needed for large scale studies	• Leadership/champion • Collaboration amongst researchers/clinicians
Privacy and anti-discrimination policies and legislation	• Patient and Ministry of Health concerns about misuse of data are limiting and must be addressed through legislation	• Government policy on privacy/data ownership • Anti-discrimination legislation
Reimbursement guidelines	• Lack of clear guidelines • Fear of increased costs limits adoption by healthcare system	• Cost-effectiveness studies • Establishment of evaluation framework for government
Healthcare professional capacity, awareness, training and adoption	• Expansion in key specialties: e.g. molecular pathologists • Practice guidelines • Communication and training for healthcare professionals • Incentives for adoption	• Recruitment and training to fill gaps • Curriculum development by educational and healthcare professional organizations

5.1 Scientific understanding and technical capabilities

A scientific understanding of the role of genomics in disease is a pre-requisite for clinical application. Cancer and certain rare diseases stand out as areas where our understanding of the role of genomics is mature. Indeed, the root cause of some of these diseases can be found in one or a handful of genes. Similarly, we have made great strides in leveraging genomics to understand the biology of infectious diseases, as the small genomes of bacteria and viruses facilitate their genomic profiling for repeated monitoring. In contrast, our understanding of the role of genomics in many other diseases, including common chronic diseases like heart disease and diabetes, is still nascent. Large-scale studies involving tens to hundreds of thousands of patients will be required to tease out the many genes contributing

small effects, as well as the role of environmental factors[38]. Such studies are presently underway in the US and Europe with results impacting clinical care expected within five years (see Appendix 10.3).

In general, scientific discoveries and validation thereof require:

1. Testable models of health and disease as well as access to human bio-specimens with necessary consents (for discovery)
2. Large, comprehensive biobanks of human biospecimens with linked clinical data and necessary consents (for validation)

This can be a major obstacle, particularly for less common diseases, given the large numbers of cases and controls required for discovery and validation studies. Collaborations will be required for success – between clinicians and researchers across and beyond BC and Canada.

3. Technical tools to perform genomic analysis of bio-specimens

Fortunately, the cost of genomic sequencing has now fallen to levels that make large-scale undertakings feasible. A full human genome can be analyzed for roughly $1,000, compared to over $10 million ten years ago[39], and genome analysis is now readily and rapidly available through a variety of commercial and academic service providers.

4. Informatic tools, infrastructure, and capacity to analyze and interpret results

Now that generation of DNA sequence data is no longer a barrier, Eric Green, Director of the US National Human Genome Research Institute (NHGRI) and others have identified data analysis as a critical bottleneck in genomics. We have made great strides in this regard for diseases with more straightforward genetic/genomic bases, but substantial challenges remain in our ability to uncover signals when many genes of small effect are involved. Overcoming this challenge will require an investment in recruiting and training of qualified individuals, who can in turn develop and apply informatics tools and infrastructure.

5. Funding for research and validation

The ability to obtain funding for research, infrastructure, and personnel is an ongoing challenge for health researchers. The old model of an academic researcher obtaining a grant on their own for siloed research is disappearing in favour of funding for interdisciplinary work with clear societal and/or economic impact(s). In Canada, grants tend to be smaller than elsewhere (e.g. the US), thus, obtaining sufficient funding for large projects can be extremely time consuming, and once obtained, the costs of collaboration are substantial. That said, there are many research teams in BC that continue to be successful year after year, often leveraging resources that assist them in competing for funding.

5.2 Alignment and prioritization

Genomic approaches are already becoming standard of care in numerous contexts, and have demonstrated a wide range of benefits to patients and healthcare systems (described in Section 4.0 “Benefits of genomics in the health sector”). However, given the substantial investment required by multiple stakeholders to bring genomics to the level of populations, it’s imperative that stakeholders focus adoption of these approaches on a common set of priorities. The framework that we describe in this document for prioritization is a critical first step in this direction. Our ability to perform this type of

assessment can be greatly improved by an investment in mechanisms to rigorously gather and monitor costs and benefits of genomic (and other) approaches in BC.

5.3 Health information technology infrastructure, tools, and governance

Successful implementation of genomics in the clinic at the level of patient (and healthy) populations requires linking of genomic data to high quality medical history and clinical data. This requirement has several sub-requirements: (1) digitization of medical records in a standardized, high quality manner (implementation of electronic medical records (EMRs)); (2) connecting silos that hold clinical and other relevant data; (3) linking together genomic data with clinical data; (4) development of decision support tools to enable interpretation. The solution must also ensure that data are secure yet searchable with appropriate permissions. Underlying all of this is development and deployment of analytical expertise and appropriate/standardized tools.

The private sector must play a major role in overcoming these challenges. BC companies like PHEMI have demonstrated the feasibility of linking and searching disparate data sources using big data approaches. There are many players in the decision support domain, such as BaseHealth (San Francisco, CA), which offers genomic profiling for individuals, providing online analytical tools for patients and doctors to use together. The "what if" tool allows the doctor and patient to "start playing around" with their disease risk model, seeing how changes to diet, exercise, and lifestyle could lower the risks of, for example, diabetes.

An additional, critical element of success in health information is ensuring a consistent, transparent, and reliable data access process, for data is worthless without access. Developing such processes will require government policy around data ownership and privacy, which is discussed in Section 5.7.

5.4 Clinical and laboratory infrastructure and capabilities

With regards to clinical infrastructure, the key requirements for success are large-scale, centralized collection and storage of specimens and datasets. For laboratories, resources will need to be dedicated towards infrastructure, developing SOPs (standard operating procedures), mechanisms for quality assurance, and training of laboratory personnel.

Province-wide adoption of genomic tools and technologies will require re-balancing of resources. While not trivial, this should be feasible provided the allocation is supported by a clearly stated value proposition.

5.5 Regulatory guidelines

One critical regulatory issue that needs to be addressed is the need to develop regulation of laboratory-developed tests (LDTs), as these tests can impact critical treatment decisions. The importance of this issue is well recognized in the US and elsewhere, as reflected in efforts to develop regulatory frameworks. In October, 2014, the FDA produced a draft guidance document for public comment: "*Framework for Regulatory Oversight of Laboratory Developed Tests*"[40]. The guidance is intended to provide an oversight framework that will assure that devices used in the provision of health care, whether developed by a laboratory or a conventional in-vitro diagnostic (IVD) manufacturer, comply with the appropriate levels of regulatory controls to assure that they are safe and effective.

A second issue that has been the topic of major regulatory efforts in other countries is the need to develop guidance for regulatory approval of companion diagnostics (CDx) products, that is, products where a diagnostic product informs the use of a therapeutic product. In August 2014, after several years and iterations, the FDA published its final guidance on the development, review, and clearance of companion diagnostics (CDx): "*In Vitro Companion Diagnostic Devices Guidance for Industry and Food and Drug Administration Staff*" [41] This guidance is intended to help companies identify the need for these tests during the earliest stages of drug development and to plan for the development of a drug and a companion test at the same time.

Lastly, to ensure that patients in BC have access to the best healthcare options, we must provide a clear and accessible path for regulatory approval of global products.

5.6 Harmonized ethical consent

Informed consent of patients is critical to complete the feedback loop from clinical implementation to discovery. Recognizing that the greatest power for discoveries comes from large scale studies, empowering research to the full extent requires extensive co-ordination and harmonization across the province (and often more broadly). We should strive to achieve a clear governance framework that enables harmonized consent both for initial analysis and for re-contact, to ensure that samples and data can be leveraged to capitalize on technological and scientific advances. A system of harmonized ethical consent would not only be invaluable for advancing research, but would also afford a major opportunity for increased efficiency and time savings.

5.7 Privacy and anti-discrimination policies and legislation

In order for individuals to feel secure in providing data on their genomes, strategies must be developed to: (1) address the potential for misuse of genetic information, particularly the risk of genetic discrimination; (2) provide clarity on ownership of health data (including genomic data); 3) deal with incidental findings. In the US, concerns about genetic discrimination were addressed by The Genetic Information Nondiscrimination Act of 2008, an Act of the US Congress designed to prohibit the use of genetic information in health insurance and employment. Ownership of health data was addressed in the US in 2013, with an update to The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule which improved privacy protections and security safeguards for consumer health data.

These issues have yet to be adequately addressed in Canada and success in these efforts will require extensive public engagement and dialogue among stakeholders.

5.8 Reimbursement guidelines

Widespread adoption of genomics in BC will require establishment of reimbursement guidelines that encompass genomic approaches. Presently, many healthcare payers are leery of adopting genomic approaches (particularly whole genome sequencing (WGS)) for fear of increased costs associated with overuse and associated follow-up. This concern is understandable given the dearth of data on their cost-effectiveness; overcoming this obstacle will require dedicated studies of the patient, health system and economic benefit of potential genomic applications, as well as systems to collect and evaluate these benefits on an ongoing basis. Such analyses are complex, as they require understanding costs beyond those of the genomic test, but also the costs implications for care in the near term (e.g. choice of drug, or number of hospitalizations) and in the long term (e.g. additional screening/monitoring). The

economic cost of genomic tests must also incorporate additional resources needed for interpretation and counseling. Logistical barriers alone, such as connecting silos of the healthcare system, can make it very difficult to get a full picture of the economics of any given product (e.g. genomic diagnostic test). The fact that one's genome only needs to be sequenced once, and that the findings can apply to healthcare decisions across a growing list of conditions (including health maintenance), further complicates the value analysis, while helping to make the case for proactively acquiring this information.

A survey of cost-effectiveness studies is illuminating with regards to the 'tipping point' at which the DNA sequencing approach becomes more cost-effective than existing approaches, from the perspective of laboratory and treatment costs. The examples in Table 2 (Section 4.2 "Improving healthcare efficiency and value") show that this estimate has ranged from $US 500 to $US 7000 depending on the context. Given that current costs of WGS are approaching $1000, we are already in this range in some contexts (e.g. testing for genetic bases of neurodevelopmental delays), while for other applications (e.g. testing healthy individuals) this 'tipping point' is not far off.

5.9 Healthcare professional capacity, awareness, training and adoption

A wide range of medical professionals are, and will be, involved in communicating and interpreting genetic/genomic information. These include molecular pathologists, physicians, nurses, pharmacists, genetic counselors, and medical geneticists. In order to ensure widespread and effective use of genomic information, we must also ensure that these professionals are aware, trained, resourced and incentivized to use them.

Meeting the educational and awareness challenges will require a commitment from each set of professionals to update their practice guidelines, and to develop and disseminate appropriate educational materials.

Resourcing of healthcare professionals will be challenging in BC's cost-constrained environment, and will require re-balancing of existing resources as well as dedicated training or recruitment of key specialists (e.g. molecular pathologists).

Adoption of genomic tests will also depend on the extent to which physicians are motivated to move towards these tests. Adoption may be hampered in cases where a physician may lose out economically when using the test, either because the test replaces a more lucrative procedure, or where results of the test yield a reduction in physician procedures. In some cases, profound clinical merit will over-ride this economic disincentive (e.g. OncotypeDx®), but in others, it could severely impact adoption. In other cases, adoption may be slow if a test has a low likelihood of a positive/actionable result for a given patient (e.g testing for a rare adverse event). Given the potential benefits of such tests when considering the entire population, strategies to encourage adoption should be considered.

6 Identifying focus areas for clinical implementation and health research

The amount of investment required for success grows exponentially as we progress from research, to validation, to pilot and large-scale clinical implementation. The number of stakeholders that must work together grows correspondingly. Achieving meaningful benefits through application of genomics in the

clinic will require substantial dedicated effort and investment from Genome BC and many other stakeholders.

To focus our efforts and ensure a high return on our cumulative investments, we performed a systematic assessment of potential focus areas (diseases/conditions and cross-cutting fields of study). Our candidate focus areas included the top ten disease areas as measured by Economic Burden in Canada and/or Disability Adjusted Life Years, in addition to conditions known to have important genetic drivers. We assessed long-term potential based on characteristics of the relative role of genetics in disease risk, diagnosis, and therapeutic decision making. Our assessment of short-term potential for genomics layered on the availability of readily available tools for the above clinical applications, based on the premise that the genomic approach/tool/technique must be already clinically validated in order to have a high likelihood of tangible impact within five years. Our approach and findings are summarized below (Table 5), with the underlying analysis provided in Appendices 10.4 and 10.5.

Table 5: Summary of evaluation of disease areas and cross-cutting disease area opportunities

Parameter	Time Frame	Characteristics of best opportunities	Conclusions
Need		High disease burden in BC: • Economic cost to BC healthcare system • Disability Adjusted Life Years	• Highest need in chronic diseases (e.g. cardiovascular disease, cancer, cerebrovascular disease)
Potential of genomics to improve risk assessment and diagnosis	Near term	• Readily available and currently used genomic tools/technologies for risk assessment and/or diagnosis	• Leading disease areas: cancer, rare genetic diseases, infectious diseases, newborn screening (highly genetically driven conditions)
	Long term	• High heritability • Moderate number of genes involved • Moderate role of non-genetic factors • Known or potential molecular subsets of disease	• Medium to high long-term potential in most chronic diseases (complex/multifactorial) • Additional opportunities in near-term leading areas: cancer, infectious diseases, rare genetic diseases
Potential of genomics to help select optimally effective treatment	Near term	• Readily available, validated genomic tools/technologies for assessing likelihood of therapeutic benefit (typically for a therapy targeted to a specific disease subset)	• Leading disease areas: Cancer, infectious diseases (treatments tailored to genomics of disease)
	Long term	• Molecular disease subsets with corresponding targeted therapies • High variability amongst patients in response to treatment	• High potential in cancer (molecular subsets with matched therapies) • Med-high potential in areas with emerging molecularly defined subsets (e.g. arthritis, asthma)
Potential of genomics to help guide dosing/avoid adverse events	Near term and long term	• High variability amongst patients in response to treatment • Drugs with narrow therapeutic window • Adverse events with potential genomic causes	• High potential to guide therapy and reduce adverse events across a wide range of diseases (chronic and other)

We found that the majority of opportunities for near-term clinical impact fall within a small number of disease areas:

- Cancer: Tailoring treatments by diagnosis of genetic cause/disease subset
- Infectious diseases: Tailoring treatments; Improving diagnosis and management of drug-resistance
- Rare diseases/Rare mutations: Improving diagnosis and management of rare diseases with genetic basis as well as genetic forms of common diseases

In addition to these targeted disease area opportunities, there is a substantial opportunity to apply pharmacogenomic testing to avoid adverse events and optimize dosing across many diseases, from cardiovascular, to neurological, to infectious diseases. It should be noted that the broadest definition of pharmacogenomics encompasses all interactions between drugs and genetic basis (including host genetics, tumour genetics, and infectious agents), thus, an emphasis on the role of host genetics in informing dosing and avoiding adverse events represents a fraction of the potential applications (some of which are covered in the disease specific opportunities described above).

Our analysis highlights the fact that many of the diseases with greatest need are the most challenging scientifically (due to complex genetics, multifactorial causation). As such, it is clear that we must continue to invest broadly in research and clinical validation across these areas of high unmet medical need. Cardiovascular disease and neuropsychiatric diseases are examples of areas with a high potential for impactful genomic research, given the high burden in BC (economic and disability-adjusted-life-years) and the important yet complex role of genetics in causation.

We will ultimately need to incorporate other factors such as cost-effectiveness and societal impact into this framework, once such data are readily available.

7 The BC context

Developing a strategy for genomics in BC requires us to consider the BC health sector context. In principle, BC and many other Canadian provinces possess many of the important attributes for success in bringing valuable scientific advances into the healthcare system. However, in many cases, these apparent strengths simultaneously present challenges, and our strategy must recognize this. Table 6 outlines both sides of the coin for BC in the context of healthcare.

Table 6: BC opportunities and challenges

The BC opportunity	The BC challenge
Single payer health system	• Acute care model is not aligned to chronic diseases and personalized medicine • Inconsistent drug funding: no catastrophic coverage • 30% healthcare funded privately
Longitudinal population databases (e.g. PopData BC)	• High barriers to access (limited to research, restricted by use, unreliable, labour intensive) and not harmonized across most databases • Privacy considerations not addressed
Single provincial medical school	• Need for curriculum re-design (e.g. in population health, chronic diseases, genomics and primary/community healthcare)
Population–based approach to health care	• Lack of integration of public/population health and health care service delivery
Research infrastructure (and investment)	• Academic incentives not aligned with progress from research to clinical application
Clinical infrastructure (and investment)	Challenges with: • Molecular pathology • Bio-specimen access and 'banking' • Functional imaging • Population genomics and bio-informatics • EMR: linked data-sets
Extensive inter-professional & inter-sector collaboration	• Challenged by health sector financing • Challenges with incentives for collaboration
Private sector/privately-funded health care	• Lack of interface or collaborative relationships between public and private sectors
Investment sector in life sciences	• Limited tolerance for risk and innovation • Small market
Significant intellectual resources	• Gaps and non –alignments • Challenges with industry retention
Privacy legislation that enables research	• Does not address genomic research • Data sharing is challenging in practice • Discrimination concerns

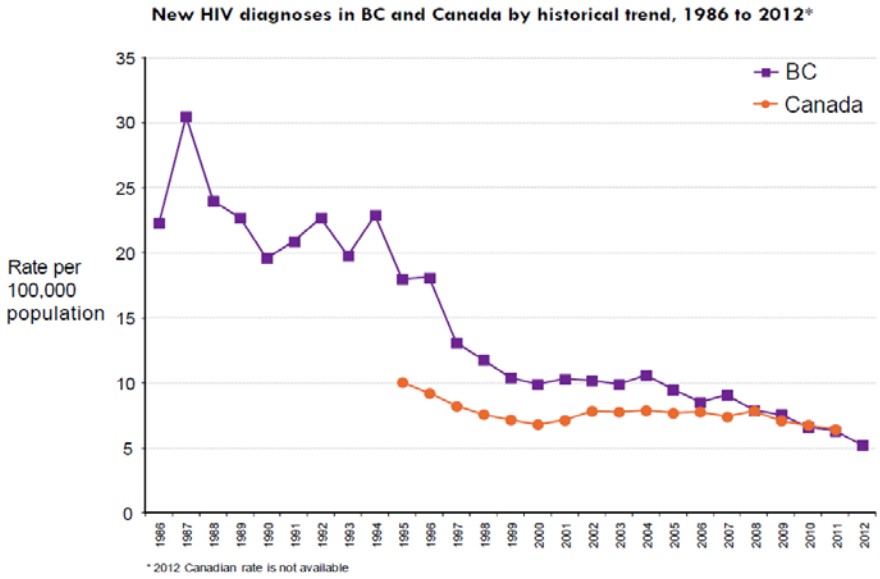
8 Exemplars/Success stories

While the requirements for success in implementing genomics for the benefit of patients are daunting, several examples in BC illustrate that through commitment, collaboration, and sustained investment, success is within reach.

8.1 HIV treatment in BC: Leveraging genomics to achieve better outcomes

One of the best success stories of clinical impact of genomics in health in BC is in treatment and prevention of HIV/AIDS. Since the peak of the epidemic in early 1990s, when a British Columbian was

dying from AIDS almost every day, we have progressed a point where the disease is chronic and manageable. In the same time period, the incidence of new HIV cases has fallen dramatically from over 20 new cases per 100,000 population, to roughly 5 per 100,000 in 2012.[42]



The BC CfE in HIV/AIDS has leveraged genomics significantly in their war against HIV/AIDS. Their first transformative genomically-enabled contribution was to develop tools to monitor viral load. It was through the use of these tools that the academic and clinical communities learned that that treatment with multiple drugs at once was the best strategy, ushering in the era of HAART (Highly Active Anti-Retroviral Therapy). Since that time, the BC CfE in HIV/AIDS has developed additional cutting edge genomic tools to tailor treatments, avoiding ineffective treatments and reducing transmission of resistance. Currently, the centre offers several genomic tests based on the HIV viral genome to guide treatment, as well as one test based on the patient's DNA that predicts the likelihood of adverse reaction to a specific drug (Abacavir®)[43]. In addition, the centre pioneered the "Treatment as Prevention" approach through a BC program called STOP HIV/AIDS. This approach recognizes that the risk of transmitting HIV is substantially reduced by optimizing the treatment of those already infected to minimize their viral load and was recognized as Science Magazine's 'Breakthrough of the Year' in 2011.[44]

In addition to the obvious health benefits of preventing additional cases of HIV/AIDS and tailoring treatments, there are significant health economic benefits. Using genomics to identify the types of drug resistant HIV strains within patients avoids needless exposure to inadequate therapy, wasted expense for failed medications (>$1,300/patient/month) and the risk of further resistance and HIV transmission (estimated to save $15,000 per case of HIV avoided).

One of the BC CfE in HIV/AIDS' greatest assets is a province-wide longitudinal database linking clinical and biological/genomic data. Leveraging this asset, and their genomic expertise, the clinical research team at the centre is now developing an improved HIV drug-resistance test, real-time drug resistance surveillance, and improved methods for personalizing treatment of HIV based on each patient's unique DNA.

8.2 Personalized Onco-Genomics: Using whole genome sequencing to guide cancer treatment

The frontier of cancer treatment is moving beyond directed evaluation of a few selected genes known to be implicated in cancer to more broad surveys of cancer genomes with the dual goal of optimizing treatments for current patients and making discoveries that will help to understand the causes and types of cancers and guide development of future therapeutic strategies. The Personalized Onco-Genomics (POG) experimental treatment program at the BC Cancer Agency exemplifies this approach, and is the first program of its kind in the world. The first phase of POG involved whole genome sequencing of tumours from 70 patients, with each case involving collaborative analysis between scientists and oncologists. The second phase of POG is now underway, aiming to enroll 5,000 patients[45], largely through philanthropic support. This program demonstrates that it is possible to integrate genomic and clinical data, and that scientists and physicians can effectively work side-by-side to guide treatments accordingly. While scaling beyond the pilot phase will bring substantial additional complexities, the pilot phase has been invaluable in illuminating the barriers, solutions, and potential of this approach. Patients' stories like that of Trish Keating[46], whose late stage colon cancer was successfully treated with an unconventional drug based on her tumour's DNA sequence, have led to great optimism, but they are unfortunately not the norm, and we recognize the need to better understand where genomics will offer the best value.

9 Conclusions

The potential for the application of genomics to bring benefits to BC is vast, but the level of investment required is substantial, underscoring the need to focus. This document has been developed as a foundation to focus our collective efforts towards maximizing the benefits of genomics on the health sector in BC.

With an understanding of potential benefits and requirements for success as context, we systematically analyzed high-need diseases and cross-cutting focus areas with respect to the potential for genomic approaches to bring near-term and long-term benefits to BC, emphasizing health outcome benefits. In the long term, the main drivers of potential were need (disease burden) and scientific tractability, based on the extent of the contribution of genomics to disease causation and/or treatment outcomes. In the short term, the main driver was readily available validated genomic tools/technologies with actionable outputs.

This analysis identified three disease areas ripe for near-term clinical application with high potential to impact health outcomes: cancer, infectious diseases and rare genetic diseases. We also see a significant opportunity in a specific category of pharmacogenomics - optimizing dose and avoiding adverse drug reactions – an application which spans many disease areas. The identified focus areas all have strong genetic underpinnings, and, in many cases, genomic information (about tumour, non-tumour, or infectious agent) is valuable as it can be linked to decisions about specific targeted treatments, or, in the case of rare genetic diseases, because it ends a diagnostic odyssey and enables a shift to treatment.

Our analysis of the highest burden disease in BC found that genomics offers great potential to improve diagnosis and treatment in the long term, but that significant investment in health research is still

needed. As described previously, it tends to be very challenging to elucidate the role of genetics in these diseases due to the complexity in their causes, typically involving many genes of small effect, and involving complex interactions between genes as well as between genes and environment. Thus, large-scale discovery and validation studies will be needed to move them into clinical readiness. Given the substantial need, it is imperative that we continue to invest in these areas.

The priority focus areas that we identified for near-term clinical implementation are aligned with the priorities of the UK National Health Services (NHS) *100,000 Genomes Project*. This undertaking aims "to bring the predicted benefits of genomics to NHS patients"[47]. The project will focus on patients with a rare disease and their families, patients with cancer, as well as on infectious diseases. Similarly, the US NHGRI survey of institutions that have begun to use genomic data in clinical practice cites many of the same major areas of application (tumor-genotype based cancer treatment, pharmacogenomics, WGS for unknown disease diagnosis (in addition to risk/susceptibility testing for families)[48]. In addition, the US' recently launched *Precision Medicine Initiative* reinforces the need for large cohorts to uncover the genomic causes of the highest burden diseases, as well as the importance of addressing regulatory and information technology challenges. We have already begun to capitalize on the synergy between these efforts, beginning with extensive discussions with the UK to learn from their implementation strategy, and potentially extending into a deeper collaboration.

Our understanding of the broad requirements for success in achieving clinical implementation at the level of populations provides context for delineating the ways in which Genome BC can contribute. Success will require co-operation amongst many stakeholders – patients, physicians, health authorities, policy makers, payers – whose interests often don't naturally align, and who operate in highly entrenched and resource constrained environments. These stakeholders must unite around a common vision and set of priorities, and engage in dedicated efforts to overcome key challenges. The vision described in this document is already well aligned with the Ministry of Health's high level priorities – most notably, to "Provide patient-centred care", "Provide timely access to quality diagnostics", and "Drive evidence-informed access to clinically effective and cost-effective pharmaceuticals".[49]

Genome BC is well positioned to help BC realize the benefits of genomics. We have a strong foundation in catalyzing health research and growing experience in catalyzing the use of genomics in clinical settings. We have established ourselves as an integral member of the health research community, and have strength in bringing partners and resources together to define and realize a common vision. We will focus our resources on the following:

- Continue to catalyze discovery, applied, and translational research by launching and managing competitive programs in health research. Maximize impact by incorporating elements of successful clinical application into translational research.
- Unite stakeholders around a common vision for clinically implementing genomics in BC and on key application areas.
- Bring together the necessary partnerships (public, private, and not-for-profit), funding, and operational models to enable clinical application of genomic technologies to relevant BC populations

- Our strategy will be informed by partnership models like Genomics England (for realizing 100,000 genomes project in UK) and Accel-Rx (Canada's new health sciences accelerator).

9.1 Next Steps

- Identify individuals representing each of the key stakeholders to collaborate with in building roadmap towards executing our strategy, ensuring clarity on leadership for each requirements for success.
    - E.g. Representation from academia, Ministry of Health, health authorities, privacy, regulatory, health IT, industry, health economics, healthcare professionals, etc
- Define specific sub-goals within each of the identified focus areas, considering near-term impact as well as long-term impact (e.g. ability to inform and enable future investments).
    - E.g. Select a small number of specific opportunities for benefit within infectious disease and develop concrete five year deliverables
- Identify operational models to enable success
    - E.g. Create a Sector Innovation Centre (public-private partnership) focused on a specific subgoal (e.g within infectious disease)

10 Appendix

10.1 Health strategy task force

Name	Affiliation
Marco Marra	BC Cancer Agency Genome Sciences Centre
Doug Nelson	BC Cancer Foundation
Richard Harrigan	BC Centre For Excellence in HIV/AIDS
Mel Krajden	BC Centre for Disease Control
Wyeth Wasserman	Child & Family Research Institute
Simon Sutcliffe	International Cancer Control Congress
Paul Drohan	Life Sciences of British Columbia
Diane Finegood	Michael Smith Foundation for Health Research
Paul Terry	PHEMI Health Systems Inc.
John Andruschak	Provincial Health Services Authority
Martin Dawes	UBC/Family Practice
Pieter Cullis	UBC/Personalized Medicine Initiative
Corey Nislow	UBC/Pharmaceutical Sciences

10.2 Related provincial strategies and reports

- **Directions for Health Research in BC, 2014**[50]
  - *Directions for Health Research in BC* (2014) provides insight into BC's health research landscape and sets out a vision, strategic directions, and actions that are vital to establishing a strong, coherent, and effective research enterprise. It aims to create a road map for building on BC's accomplishments over the past decade while anticipating changes to the evolving health and research landscapes. Development of this document was led by the Michael Smith Foundation for Health Research, and involved consultations with over 1,000 people, including many of the leaders of BC's health research community.
  - While this document does not explicitly discuss the field of genomics, it is clear that many of the actions recommended in this document will benefit the genomics research community, and likewise, that the genomics research community can play a significant role in achieving the broader research community's objectives.
- **Setting Priorities for the BC Health System, 2014**[51]
  - Setting Priorities for the B.C. Health System presents the strategic and operational priorities for the delivery of health services across the province.
- **Findings from the Ontario Personalized Medicine Network's (OPMN's) 2014 Consultations**[52]
  - The Ontario Personalized Medicine Network (OPMN) is an expert panel created to assess the challenges and opportunities presented by personalized medicine, to "ensure Ontario is well positioned to capitalize on this exciting and transformative technology".
  - OPMN surveyed provincial and national experts and identified eight key challenges that must be addressed to enable successful clinical implementation of genomics. These challenges are incorporated into our discussion of Requirements for Success (Section 5).

10.3 Selected large-scale genomic discovery and implementation projects

- **The United Kingdom National Health Services (NHS) 100,000 Genomes Project**[53]: The UK launched the 100,000 Genomes Project in late 2012, "to bring the predicted benefits of genomics to NHS patients". This undertaking has dual aims of research and clinical benefit. Its four main aims are; to create an ethical and transparent program based on consent; to bring benefit to patients and set up a genomic medicine service for the NHS; to enable new scientific discovery and medical insights; and to kick start the development of a UK genomics industry. The project will focus on patients with a rare disease and their families, patients with cancer, as well as on infectious diseases. Genomics England, a company wholly owned and funded by the Department of Health, was set up to deliver this project, and will sequence 100,000 whole genomes from NHS patients by 2017.
- **United States Precision Medicine Initiative**[54]: In the 2016 US budget, President Obama is requesting $US 215 million in new investment a Precision Medicine Initiative, to be distributed to National Institutes of Health (NIH), National Cancer Institute, Food and Drug Administration, and office of the National Coordinator. An important component of the initiative will be a 1 million person cohort that will be fully sequenced.
- Objectives of the Precision Medicine Initiative:
    - More and better treatments for cancer
    - Creation of a voluntary national research cohort
    - Commitment to protecting privacy
    - Regulatory modernization
    - Public-private partnerships
- **Kaiser Permanente Research Program on Gene, Environment and Health (RPGEH)**[55]: The RPGEH program, will link together comprehensive EMRs, data on relevant behavioral and environmental factors, and biobank data (genetic information from saliva and blood) from 500,000 consenting health plan members. They have already built a substantial data resource, linking genomic data (whole genome genotyping/SNP analysis, and telomere analysis) for more than 100,000 individuals to their clinical data. Kaiser Permanente is partnering with academic researchers at University of California San Francisco to analyze this wealth of data. The goal is to use such findings to improve diagnostics, treatment, and prevention of common diseases such as heart disease, asthma, diabetes, and more through improved understanding genetic and environmental factors.
- **Longevity Inc**[56]**:** Craig Venter, who previously led the private effort to sequence the human genome, founded Human Longevity Inc in 2014. It aims to discover and develop life-enhancing therapies, and to build the world's largest genonotype/phenotype database by sequencing more than 40,000 human genomes/year combined with microbiome, metabolome and clinical data
- **Google**[57]**:** In 2014, Google announced their latest project from Google X - Project Baseline. It is partnering with Duke and Stanford medical schools and plan to establish some molecular information about what normal looks like, as an invaluable reference point for understanding disease. Google's plan is to measure the genes and blood chemistry of 175 healthy people in a pilot phase, and eventually scale up to thousands more.

10.4 Analysis of candidate focus areas for risk assessment and disease diagnosis

Candidate Focus Area	Health care Costs in BC (%), 2008	Disability Adjusted Life Years, 2005	Long-term potential for genomic approaches	Available genomic tests for diagnosis
Top 10 Diagnostic Categories by BC Burden (EBIC or DALY)				
Cardiovascular Diseases	13.9%	16.7%	Score = 2 [+] Heritable/some genetic basis [-] Multifactorial causation; Many genes of small effect	Several examples of rare diseases (e.g. long QT syndrome)
Neuropsychiatric Conditions*	13.7%	17.9%	Score = 2 [+] Heritable/some genetic basis [-] Multifactorial causation; Many genes of small effect	
Injuries**	6.7%	10.8%	Score = 0 [-] Non-genetic causation	
Musculoskeletal Diseases	6.2%	3.9%	Score = 2 [+] Heritable/some genetic basis; Emerging molecular disease subsets (e.g. rheumatoid arthritis (RA)) [-] Multifactorial causation; Many genes of small effect	Limited early RA diagnostics (e.g. Augurex, Vancouver BC)
Symptoms, Signs and Ill-Defined Conditions	6.1%	0.2%	Score = 1 [+] Likely some conditions genetic in nature [-] Unclear genetic causation	
Digestive Diseases	6.1%	2.4%	Score = 2 [+] Heritable/some genetic basis; Emerging molecular disease subsets [-] Multifactorial causation; Many genes of small effect	
Infectious Diseases***	5.5%	8.2%	Score = 3 [+] DNA serves as a 'fingerprint' for detection/diagnosis of infectious agents	Routine use of simple genomic tests to detect/classify infectious agents but opportunity to be more comprehensive and broaden to antimicrobial resistance
Respiratory Diseases	4.7%	6.7%	Score = 2 [+] Heritable/some genetic basis; Emerging molecular disease subsets (e.g. asthma) [-] Multifactorial causation; Many genes of small effect	Limited (e.g. Testing of specific IgE antibodies to evaluate if patients have allergic asthma prior to prescribing Xolair®)
Genitourinary Diseases	4.6%	2.6%	Score = 1 [+] Potential genetic contribution [-] Unclear genetic causation	Standard use of relatively simple protein urine tests
Cancer (Malignant Neoplasms)	3.7%	18.1%	Score = 3 [+] Genetically driven disease; Specific subsets are highly heritable	Routine use of genomics for disease classification and risk assessment (specific inherited types)
Diabetes Mellitus	2.5%	5.3%	Score = 2 [+] Heritable/some genetic basis; Emerging molecular disease subsets [-] Multifactorial causation; Many genes of small effect	

Candidate focus areas that span multiple diagnostic categories above				
Rare diseases/Rare mutations ****			Score = 3 [+] Often genetically driven and highly heritable; Value of definitive/early diagnosis	Genetic approaches are standard, moving towards genomic
Tissue/organ transplant			Score = 2 [+] Strong genomic contribution to transplant rejection (especially immune genes) [-] Complex; often involving many genes of small effect	
Prenatal/newborn screening			Score = 3 [+] Genetically driven and highly heritable; Value of definitive/early diagnosis	Widespread use of selected genetic panels, limited use of whole genome sequencing
Adverse drug reactions			Score = 1 [-] Main value is in preventing adverse events rather than in diagnosing those that occur	

*Neuropsychiatric Conditions (DALY figures) includes: Dementia, Mental Disorders and Neurological
**Injuries includes: Injuries of Undetermined Intent; Intentional Injuries; Unintentional Injuries
***Infectious Diseases includes Respiratory Infections and "Certain Infectious and Parasitic Diseases"
****Rare Diseases/Rare Mutations: Economic/DALY figures include the rare disease subsets, but these are 'pulled out' for the purposes of qualitative assessment of genomic opportunities

Cost estimates and Diagnostic Subcategories taken from Economic Burden In Canada online calculator: http://ebic-femc.phac-aspc.gc.ca/custom-personnalise/results-national-resultats.php?year=2008&province=eebb8fcca8ff48c177fe0039ef0c8dc7&agerange=6b257e3c885e430dba2d748775f66754&costsubtype=all&action=province

10.5 Analysis of candidate focus areas for informing treatment decisions

Candidate Focus Area	Healthcare Costs in BC (%), 2008	Disability Adjusted Life Years, 2005	Long term potential for genomic approaches	Available genomic tests for selecting most effective treatment	Available genomic tests for guiding dose/avoiding adverse events
Top 10 Diagnostic Categories by BC Burden (EBIC or DALY)					
Cardiovascular Diseases	13.9%	16.7%	Score = 2 [+] Narrow therapeutic window and role of drug metabolism genes underlie potential to inform dosing/avoid adverse events [-] Current treatments not specific to molecular disease subsets	Limited (e.g. KIF6 for response to statins)	Several drug metabolism tests for dosing (e.g. CYP2C19 variant to guide use of Plavix®)
Neuropsychiatric Conditions*	13.7%	17.9%	Score = 2 [+] Narrow therapeutic window and role of drug metabolism genes underlie potential to inform dosing/avoid adverse events [-] Current treatments not specific to molecular disease subsets		Variants in drug metabolism genes (e.g. CYP2D6) guide dosing for many psychiatric drugs. Immune genotyping can help avoid adverse events (e.g. HLA-B type to guide Tegretol® treatment for epilepsy and bipolar disorder)
Injuries**	6.7%	10.8%	Score = 1 [+] Potential role of 'omics' in variable treatment response [-] Current treatments not specific to molecular disease subsets		
Musculoskeletal Diseases	6.2%	3.9%	Score = 2 [+] Emerging molecular subsets could inform treatment (e.g. RA) [-] Most treatments not specific to molecular subsets	Limited early RA diagnostics for subtyping to guide treatment (e.g. Augurex, Vancouver BC)	Variants in drug metabolism genes inform dosing/avoidance of adverse events (e.g. TPMT genotyping to guide dose/avoid adverse events Imuran® treatment for arthritis)

Symptoms, Signs and Ill-Defined Conditions	6.1%	0.2%	Score = 1 [+] Likely some conditions genetic in nature [-] Unclear genetic causation		
Digestive Diseases	6.1%	2.4%	Score = 1 [+] Emerging molecular disease subsets [-] Current treatments not specific to molecular disease subsets		
Infectious Diseases***	5.5%	8.2%	Score = 3 [+] Drug resistance in bacteria/viruses is genomically driven; Therapeutic choice will depend on drug resistance profile; Small genomes enable rapid turnaround (valuable for impactful decision making)	HIV treatment in BC is tailored based on specific viral genetic factors (e.g. CCR5-tropism testing guides use of Selzentry® for HIV treatment); Treatments avoided/ceased when virus develops resistance	Some immune testing to avoid adverse events (e.g. HLA-B genotype informs Abacavir® treatment for HIV)
Respiratory Diseases	4.7%	6.7%	Score = 2 [+] Some treatments are specific to molecular subsets (e.g. asthma) [-] Most treatments not specific to molecular subsets	Limited (e.g. Testing of specific IgE antibodies to evaluate if patients have allergic asthma prior to prescribing Xolair®)	Limited (e.g. Testing of IgE levels guides dosing of Xolair® in asthma)
Genitourinary Diseases	4.6%	2.6%	Score = 1 [+] Potential genetic contribution [-] Current treatments not specific to molecular disease subsets		
Cancer (Malignant Neoplasms)	3.7%	18.1%	Score = 3 [+] Genetically based disease subsets are known and treatments mechanisms of action are tailored to these types; Host genetics will also play a role in emerging treatment options (e.g. in cancer immunotherapy/vaccines)	Many molecular diagnostics tests for prognosis (e.g. OncotypeDx® to guide use of chemotherapy in breast cancer) and patient selection (e.g. BRAF mutation testing for treatment with Vemurafinib® in melanoma)	Several examples: (e.g. Genotyping of UGT1A1 to guide dosing/avoid adverse events in colon cancer treatment with irinotecan)

Diabetes Mellitus	2.5%	5.3%	Score = 2 [+] Molecular subsets of diabetes are defined in early onset diabetes and have therapeutic implications [-] Type 2 diabetes subsets not well understood; lack of subset-specific treatments	Limited (e.g. Patients with diabetes caused by mutations in the HNF-1α gene are sensitive to the hypoglycaemic effects of sulphonylureas)	
Candidate focus areas that span multiple diagnostic categories above					
Rare diseases/Rare mutations ****			Score = 2 [+] Value of definitive/early diagnosis [-] Limited treatments available for many conditions	Diagnosis can drive treatment in some cases (e.g. enzyme replacement)	
Tissue/organ transplant			Score = 2 [+] Strong potential for genomics to predict transplant rejection and to provide non-invasive alternatives for testing/monitoring [-] Complex genetics; often involving many genes of small effect		Limited (e.g. AlloMap® to assess risk of transplant rejection/avoid biopsies)--
Prenatal/newborn screening			Score = 2 [+] Value of definitive/early diagnosis [-] Limited treatments available for many conditions	Diagnosis drives treatment in some cases (e.g. Phenylketonuria (PKU))	
Adverse drug reactions (ADR)			Score = 2 [+] Strong genetic contribution to some adverse reactions [-] Majority of ADRs not genetically related; Typically the adverse event is very rare		Growing list of examples (see above rows by disease)

*Neuropsychiatric Conditions (DALY figures) includes: Dementia, Mental Disorders and Neurological
**Injuries includes: Injuries of Undetermined Intent; Intentional Injuries; Unintentional Injuries
***Infectious Diseases includes Respiratory Infections and "Certain Infectious and Parasitic Diseases"
****Rare Diseases/Rare Mutations: Economic/DALY figures include the rare disease subsets of common diseases, but these are 'pulled out' for the purposes of qualitative assessment of genomic opportunities

Cost estimates and Diagnostic Subcategories taken from Economic Burden In Canada online calculator: http://ebic-femc.phac-aspc.gc.ca/custom-personnalise/results-national-

resultats.php?year=2008&province=eebb8fcca8ff48c177fe0039ef0c8dc7&agerange=6b257e3c885e430dba2d748775f66754&costsubtype=all&action=province

10.6 Genome BC health projects by program (2004-2014)

*Limited to programs led by Genome BC or Genome Canada

10.6.1 Applied Genomics & Proteomics in Human Health (AHH) [w/Genome Canada]

Dates	Project Title	Primary Investigators
2004 - 2007	Genomic Tools for Diagnosis and Evaluation of Mental Retardation	Jan Friedman, Marco Marra
2004 - 2008	Better Biomarkers of Acute and Chronic Allograft Rejection	Paul Keown, Bruce McManus, Rob McMaster
2004 - 2008	Innovative Genomic Applications to Develop Clinical Biomarkers and Novel Therapies for Common Iron Metabolism Disorders	Paul Goldberg
2005 - 2008	Development and Validation of Comparative Genomic Hybridization Arrays for Clinical Use in Cancer	Doug (Douglas) Horsman, Wan Lam
2005 - 2008	Application of Pharmacogenomics for Rational Chemotherapy of Lung Cancer	Stephen Lam, Victor Ling
2005 - 2009	Genotype Specific Approaches to Therapy in Childhood (GATC)	Bruce Carleton, Michael Hayden

10.6.2 Advancing Technology Innovation through Discovery (ATID) [w/Genome Canada]

Dates	Project Title	Primary Investigators
2011 - 2013	Finding of Rare Disease Genes in Canada (FORGE Canada)	Kim Boycott, Jan Friedman, Jacques Michaud
2011 - 2013	The Canadian Pediatric Cancer Genome Consortium- Translating next-generation sequencing technologies into improved therapies for high-risk childhood cancer	Conrad Fernandez, Cynthia Hawkins, Annie Huang, Nada Jabado, David Malkin, Daniel Sinnett, Poul Sorensen, Michael Taylor

10.6.3 Large Scale Research Program (LSARP2010) [w/Genome Canada]

Dates	Project Title	Primary Investigators
2011 -	Stratifying and Targeting Pediatric Medulloblastoma Through Genomics	David Malkin, Marco Marra, Michael Taylor
2011 - 2014	Orphan Diseases- Identifying Genes and Novel Therapeutics to Enhance Treatment (IGNITE)	Conrad Fernandez, Christopher McMaster, Michel Roberge

10.6.4 Genomics in Personalized Health (GPH) [w/Genome Canada]

Dates	Project Title	Primary Investigators
2013 -	Personalized Treatment of Lymphoid Cancer- British Columbia as Model Province	Joseph Connors, Randy Gascoyne, Marco Marra
2013 -	Viral and Human Genetic Predictors of Response to HIV Therapies	Richard Harrigan, Julio Montaner
2013 -	Reducing Stroke Burden with Hospital-Ready Biomarker Test for Rapid TIA Triage	Christoph Borchers, Shelagh Coutts, Andrew Penn
2013 -	Clinical Implementation and Outcomes Evaluation of Blood-Based Biomarkers for COPD Management	Raymond Ng, Don Sin
2013 -	PEGASUS - Personalized Genomics for prenatal Aneuploidy Screening Using maternal blood	Sylvie Langlois, Francois Rousseau
2013 -	IBD Genomic Medicine Consortium (iGenoMed)- translating genetic discoveries into a personalized approach to treating the inflammatory bowel diseases	Alain Bitton, Megan Levings, John Rioux

10.6.5 Bioinformatics and Computational Biology (BCB) [w/Genome Canada]

Dates	Project Title	Primary Investigators
2013 -	Next Generation Bioinformatics for Clinical Genomics: using de novo assembly in personalized medicine	Inanc Birol, Steve Jones, Aly Karsan
2013 -	A Federated Bioinformatics Platform for Public Health Microbial Genomics	Fiona Brinkman, William Hsiao, Gary van Domselaar
2013 -	Computational interpretation of cancer genomes: Defining mutational landscapes for translational genomics	Paul Boutros, Sohrab Shah
2013 -	Applied Bioinformatics of Cis-regulation for Disease Exploration (ABC4DE)	Wyeth Wasserman

10.6.6 Genomics Applied Partnerships Program (GAPP) [w/Genome Canada]

Dates	Project Title	Primary Investigators
2014 -	Development of Disease Biomarker Assessment Assays and Kits for Targeted Quantitative Proteomics of Mouse Plasma by Mass Spectrometry	Christoph Borchers, Brent Sternig

10.6.7 Strategic Opportunities Fund (SOF 01-06)

Dates	Project Title	Primary Investigators
2009 - 2010	Flow Sorting Facility at BC Cancer Agency	Christoph Borchers, Julian Lum, Brad Nelson, Peter Watson, John Webb
2009 - 2010	Development of Efficient Algorithms and Technologies for Structural Variation Detection by Single Molecule Sequencing	Inanc Birol, Cenk Sahinalp
2009 - 2010	CAE/BC Biolibrary Project- Guidelines, Protocols and Policies	Kieran O'Doherty, Peter Watson
2009 - 2012	PCR-free, Sequence-specific Nucleic Acid Detection	Andre Marziali
2009 - 2011	Splice-Variant Profiling of Voltage-Gated Calcium Channels- Implications for Human Genetic Disorders	Terrance Snutch
2009 - 2011	Novel DNA-Integration Tools for an International Consortium	Elizabeth Simpson
2009 - 2010	Short Sequence Assembly and Finishing of Large Genomes	Inanc Birol, Steve (Steven) Jones
2009 - 2011	High-throughput Bacterial Transcriptome Mapping- A Case Study	Peter Unrau
2010 - 2012	Rapid Evolution of a clinical high-throughput DNA sequencing pipeline to next-generation sequencing	Aly Karsan
2010 - 2012	Functional Characterization of the Transcriptional Network Driving Mammalian Development in Mice	Daniel Goldowitz
2010 - 2011	Using Methods of Chemical Genomics for Developing Potent Androgen Receptor Inhibitors with a Novel Mode of Action	Artem Cherkasov, Paul Rennie
2010 - 2012	Optimization of Pyruvate Kinase Inhibitor Lead Compounds as Novel Therapeutics for the Treatment of Methicillin-resistant Staphylococcus aureus (MRSA) Infections	Neil Reiner, Robert Young
2010 - 2012	Characterizing a bacterial recombinome	Rosemary Redfield
2010 - 2012	Development of a high-throughput proteomics platform for biomarker verification	Christoph Borchers
2010 - 2012	Development of a gene expression-based high-throughput screening platform for human T regulatory cell differentiation	Megan Levings
2010 - 2012	Linking Infectious Agents and Cancer - A Metagenomics Approach	Rob (Robert) Holt, Richard Moore
2010 - 2011	Linking Cholesterol Metabolism, Callousness, and Conduct Disorder	Cornelius Boerkoel, Marco Marra
2011 - 2012	Development of a high-throughput platform to rapidly translate genomic discoveries into therapeutic cancer vaccines	Brad Nelson
2011 - 2013	Antisense PET Imaging of mRNA Expression Using F-18 Labeled CPP-PNA and CPP-Oligonucleotide Radiopharmaceuticals	Paul Schaffer

2011 - 2012	Detecting and Characterizing Chimeric Transcripts in Mouse Tissues	Inanc Birol, Aly Karsan
2011 - 2013	Using Science, Technology, and Society Studies Research to Move Genomics Discoveries from Bench to Bedside- Identification of Data Integration and Sociotechnical Issues Arising in Personalized Medicine & Translational Bioinformatics	Ellen Balka
2013 - 2014	Development of an actionable molecular test for risk assessment of oral precancers	Aly Karsan, Catherine Poh
2013 - 2014	Harnessing cladoniamide biosynthesis for colon cancer therapy	Katherine Ryan
2013 -	Bioinformatic Identification of Optimal Targets and Therapeutic Antibody Development in Oncology	John Babcook, Steve Jones
2013 -	Synergizing -omics to discover treatable intellectual disabilities	Sylvia Stockler, Clara van Karnebeek, Wyeth Wasserman
2013 -	One-Step 18F-Labeling: Development of Clinically Useful PET Imaging Agents	David Perrin
2014 -	Metagenomic analysis of lung infiltrates in patients with leukemia	Raewyn Broady, Rob (Robert) Holt
2014 -	Modeling Human Lymphoma Mutations in Mice	Pamela Hoodless, Keith Humphries, Christian Steidl

10.6.8 Translational Programs in Applied Health (TPAH)

Dates	Project Title	Primary Investigators
2009 - 2011	Genotype-Specific Approaches to Therapy in Childhood- The Canadian Pharmacogenomics Network for Drug Safety (GATC-CPNDS)	Bruce Carleton, Michael Hayden
2009 - 2013	IND Enabling Studies for Antisense Oligonucleotides Targeting Key Regulators of Iron Metabolism, Hepcidin and Hemojuvelin	Paul Goldberg
2009 - 2012	Biomarkers in Transplantation	Paul Keown, Bruce McManus, Rob McMaster, Raymond Ng

10.6.9 Applied Genomics Consortium Program (AGCP)

Dates	Project Title	Primary Investigators
2010 - 2014	CanEuCre- Genomic Resources Advancing Therapies for Brain Disorders	Elizabeth Simpson
2012 - 2013	Development of Novel Biomarker Blood Tests for COPD	Bruce McManus, Don Sin

10.6.10 Strategic Opportunities Fund for Industry (SOFI 01-06)

Dates	Project Title	Primary Investigators
2011 - 2012	Xigris Companion Diagnostic (XCD)	Alexandra Mancini
2012 - 2014	Research and Development of a Novel Treatment for Hypertrophic Scarring and Keloids	Beth Allison, Taryn Boivin, Alistair Duncan
2013 - 2014	Barracuda Technology Port and Application Expansion	Jared Slobodan

10.6.11 Personalized Medicine Program (PMP)

Dates	Project Title	Primary Investigators
2011 - 2014	Genomics applied to the management of high-risk AML/myelodysplastic syndromes	Aly Karsan, Marco Marra
2012 -	Implementation of a Pharmacogenetic ADR Prevention Program in BC	Bruce Carleton, Michael Hayden
2012 - 2014	Clinical Implementation of Diagnostic Biomarker Assays in Heart and Kidney Transplantation	Paul Keown, Bruce McManus, Rob McMaster, Raymond Ng

10.6.12 Proof of Concept (POC 01-06)

Dates	Project Title	Primary Investigators
2011 - 2013	Application of next-generation sequencing technologies to clinical testing in hereditary cancer syndromes	Aly Karsan
2011 - 2013	Signal Detection Development for Sequence Specific SCODA	Andre Marziali
2012 - 2013	Development and commercialization of standardized reagents and guidelines for mass spectrometry-based proteomics	Christoph Borchers
2012 - 2012	Development of expression signatures to improve diagnosis and prognosis for patients with muscle-invasive bladder cancer	Peter Black, Elai Davicioni
2012 - 2013	Commercial development of short interfering RNA-lipid nanoparticles (siRNA-LNP) for in vivo functional genomics	Marco Ciufolini
2012 - 2013	Pre-clinical Development of Pentarix- a therapeutic vaccine for HPV-associated cancers	John Webb
2012 - 2013	Chemogenomics-Driven Advancement of a Novel Class of Anti-Androgen Therapeutics	Artem Cherkasov, Paul Rennie
2012 - 2013	New chemical tools for enriching and analyzing epigenetic signatures	Fraser Hof
2012 - 2013	Identification of Novel Broad-Spectrum Drug Targets and Small Molecule Inhibitors for Antibiotic-Resistant Gram-	Fiona Brinkman, Neil Reiner

	negative Pathogens using a Revolutionary Indel-Targeting Approach	
2012 - 2013	Use of the Ion Torrent Next Generation Sequencing Platform for Rapid and Accurate Diagnosis of Childhood Cancers	Poul Sorensen
2012 - 2014	Minimally Invasive Curved Intramedullary Fixation for the Pelvis	Robin Coope, Robert Meek
2012 - 2014	Novel Influenza Neuraminidase Inhibitors - Development of Orally Bioavailable Agents with Reduced Propensity for Resistance	Stephen Withers
2012 - 2014	Pre-commercial Development of Single Cell Monoclonal Antibody Selection	Carl Hansen
2012 - 2014	New Peptide Therapeutic for Treatment of Addiction	Anthony Phillips, Yu Tian Wang
2013 -	Simultaneous Lung and Cardiac Gated Radiotherapy using Electrical Impedance Technology: Prototype Development	Kirpal Kohli
2013 -	Raman Quantification of Cancer Biomarkers for Early Lung Cancer Detection	Reuven Gordon, Fraser Hof
2013 -	Accelerating the development of a novel outer membrane protein based vaccine against Chlamydia infection	Bob (Robert) Brunham
2013 -	Intravesical Docetaxel Formulation for the Treatment of Ta/T1 Stage Bladder Cancer	Helen Burt
2013 -	Commercial Development of Lipid Nanoparticle Reagents for Functional Genomics in Difficult-to-Transfect Cells In Vitro and In Vivo	Brian MacVicar

10.6.13 User Partnership Program (UPP)

Dates	**Project Title**	**Primary Investigators**
2014 - 2014	Simeprevir screening assay for hepatitis C therapy	Richard Harrigan, Huong Hew, Mel Krajden
2014 -	Genomics for Precision Drug Therapy in the Community Pharmacy	Derek Desrosiers, Corey Nislow, Ron Reid

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