Preparing for Precision Medicine in Ontario: A Current State Assessment

A report evaluating Ontario's current data sources and infrastructure to implement Precision Medicine initiatives

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EXECUTIVE SUMMARY

The healthcare system is experiencing and transforming from the *'one-size-fits-all'* approach of evidence-based medicine to *'Precision Medicine'* (PM) approach that is defined as "An emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle."

PM also known as personalized or individualized medicine, is a rapidly evolving field in healthcare in which physicians can use various data sources to determine and provide the right clinical intervention to the right person at the right time. By moving away from a reactive medicine approach towards more targeted, accurate diagnoses and treatment, people should be able to live longer, and healthier lives and social outcomes should improve. This is what medicine has always aspired to but has not yet been able to deliver. To achieve this goal, all healthcare-related stakeholders need to be involved, associated, and aligned to capture, share, store, and analyze all necessary data in a very well-defined holistic PM approach.

This PM white paper reviews the various data sources and the current infrastructure to implement the PM approach in Ontario. Through examining the diverse data generation, data sharing and data storage components required for PM, this report outlines the barriers associated with its more comprehensive implementation in Ontario's healthcare system, as well as offers high-level recommendations to key stakeholders, healthcare decision-makers, clinicians, and policymakers to help guide clinical adoption efforts of PM.

KEY FINDINGS

Building the necessary infrastructure

PM relies on data (health, omics, lifestyle and environment) that is often fragmented and not readily useable, yet. Varying data structures and scales across municipal, provincial, and federal datasets is a considerable barrier to implementing a PM solution. A PM approach in Ontario probably requires new infrastructures (align with the PM ecosystem), with the simultaneous upgrades of legacy systems that facilitate collecting, storing, and analyzing high-quality data needed.

Precision Medicine is beyond genomics

Presently, most PM initiatives focus on the genetic aspect of data gathering, focusing on a focus for patients with certain cancers and rare diseases. This emphasis on a single gene or sequence results in the limited requirement for collateral clinical data and minimal dependence on lifestyle or environmental data. The focus on the genetic data of PM might be due to the feasible and accessible nature of data collection relative to collecting environmental and lifestyle data.

Shifting from physician-patient engagement toward patient-centred care.

Patient-centricity is entirely aligned with the PM model. In a patient-centred care model, patients are treated from a clinical perspective and from an emotional, mental, spiritual, social, and financial perspective. For this precision approach, all required data are needed to be shared fully and promptly; then, healthcare providers, patients, and their families can make informed decisions.

RECOMMENDATIONS

Stronger focus on the social determinants of health (SDOH)

The SDOH are the social and economic factors that influence an individual’s health. It is recommended that the fifth data domain should strictly focus on the SDOH and how they are obtained to influence patient care and contribute to a PM ecosystem.

Building a precision medicine ecosystem

To implement a holistic PM solution, building a data platform capable of storing, processing, and analyzing continuously and dynamically capturing large-scale data is essential. This platform would need to acknowledge the various nuances at different healthcare system levels. Developing, implementing, or updating each part of the Ontario health system should align with the PM ecosystem that prioritizes data generation, sharing, and analysis usability and efficiency.

Overall, this report aims to open the doors to a more critical conversation amongst crucial stakeholders on implementing a PM solution in Ontario. As technological advancements continue to transform the delivery of patient care, together with genomic sequencing, increased data storage capacities, and bioinformatics capabilities, Ontario can now push towards precision medicine interventions.

INTRODUCTION

The introduction of evidence-based medicine at McMaster University in 1991 heralded a new age of clinical practice across the Globe [1]. By combining the rigours of biomedical research, especially the double-blind, randomized controlled trial, and the statistical rigour of clinical epidemiology, evidence-based medicine changed the face of medicine within a brief period of time. Through the power of evidence-based medicine disseminated systematically, heart disease in Canada has moved from being the number one killer to being the number 2 killer. This has been due to excellent population education efforts that ensured that Canadians understood the causes of heart disease and took the medications that were prescribed for them. Medicines for the treatment of high blood pressure (hypertension) and high cholesterol have been especially effective in preventing heart attacks and strokes and allowing people to live longer.

However, evidence-based medicine is not without its drawbacks. Clinical epidemiology is a science of populations, not a science of individuals. Medications don't benefit individuals; they benefit populations. This subtle distinction is not lost on patients. They had understood that when a medication was recommended to them, there was a chance that they personally would not benefit. There has been growing dissatisfaction with evidence-based medicine by both patients and clinicians. They are looking for more precise predictions of risk (will I get it or not?) and are looking for more personalized recommendations for treatments that are much more likely to benefit individuals. This new field of greater precision and greater personalization is called Precision Medicine.

While the dissatisfaction with evidence-based medicine has been brewing, digital health has been advancing rapidly. With the vast amount of health data now available (although still locked up in silos), maturing medical knowledge, and health technology developments, a transition from the *'one-size-fits-all*' approach of evidence-based medicine to *'Precision Medicine*' approach is entering the realm of possibility [2].

Multiple definitions for precision medicine exist, depending on the authors' perspective. However, President Obama's *Precision Medicine Initiative (PMI)* provides a comprehensive definition: "An emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle." [3]

Precision Medicine is often used interchangeably with personalized medicine and precision health. Throughout this report, we follow President Obama's preferred term and definition of Precision Medicine (PM) to describe individualized care using gene, environmental, and lifestyle data to treat and prevent diseases.

PM is an approach to the practice of medicine that provides the right clinical intervention to the right person at the right time; or in other words, offers a personalized, proactive, predictive, and precise care plan to treat and prevent disease, which meets the ultimate goal in medicine. [4] [5]

When implementing a PM approach in clinical care settings, there are many factors to consider. The most effective approach in providing effective treatment and prevention intervention is when large amounts of clinical, molecular, phenotypic, and lifestyle data are collected, linked, and reused, made possible from large populations. To achieve this goal, lots of internal – healthcare system - and external stakeholders should be involved, associated, and aligned in order to capture, share, store and analyze all necessary data in a very well-defined holistic PM approach.

In this regard, all potential stakeholders working within the various phases, including data capturing, sharing, storing, and analyzing, should be identified and their maturity level explored based on a holistic PM perspective.

This study explores the availability and accessibility of all required data to implement a holistic PM approach in Ontario. Respective to the data domains needed, this study solely focused on data generation, data sharing and data storage components. Furthermore, this study identified potential gaps or challenges in implementing a PM approach. As PM is the intersection between individuals, their environments, changes in their markers of health/illness and behavioural factors over time, in this study, four data domains have been identified and considered:

1. **Patients' Health**: health/clinical data and demographic information,
2. **Genomics (biomarkers)**: related biological data such as genomics, metabolomics, phenomics, pharmacogenomics (omic platforms),
3. **Lifestyle (behavioural)**: related data of numerous life choices which can affect individuals' health, and
4. **Environmental factor (exposome)**: focusing on related data of any potential exposures or environmental influences on individuals and populations.

This study focused on Ontario's health, genomic, lifestyle, and environmental data domains. Although the level of complexity in implementing a PM solution is relative to the number of data domains available, other data domains that are not listed, techniques, and potential related analytic solutions were considered out of the scope of this study.

METHOD

A multimethod approach was used in this study, including semi-structured interviews and an 'Exponential Non-Discriminative Snowballing Sampling' method. In addition to the interviews, an environmental scan was conducted through literature reviews, whitepapers, and related articles published on precision medicine, preventative care, and patient-centred care.

To understand the current data climate of PM in Ontario, 80 in-depth semi-structured interviews were conducted with key stakeholders and decision-makers from private and public health organizations, academic institutions, and consulting firms in Ontario. The main objectives of these interviews were to obtain a richer understanding of how Ontario's healthcare system may adopt a holistic PM approach, understand the challenges associated with the integration of PM, and develop a perspective on the range of PM adoption in different levels of data flow.

To find our interview subjects, we identified one key subject matter expert (SME) in each setting and utilized the 'Exponential Non-Discriminative Snowball Sampling' method to identify other SMEs then interviewed. [6]

These interviews served as a foundation to identify the parameters that institutions valued at the leading edge of PM. Based on these interviews, we redefined and tuned evaluation criteria for the environmental scanning. We considered health, genomics, lifestyle and environment data as the four main data domains, and for each one, we considered three phases: data generation, data sharing and data storage. The 80 SMEs were interviewed separately and virtually, and the interview data were thematically analyzed.

A team of health informatics students from the University of Toronto, Ryerson University and George Brown College, as well as health informatics researchers, reviewed related articles and reports and conducted an environmental scan of any potential affiliated organizations, companies, individuals, or solutions related to the objective of this study.

RESULTS

Patients' Health Data

Data Generation

Seven major patients' health data generators in Ontario have been identified: (Figure 1)

- Hospitals: hospital data is generated, captured, and stored by different Hospital Information Systems (HIS), such as EPIC, Cerner, Meditech, amongst others;
- Community clinics: Patient's primary care information generated, captured, and stored by various Electronic Medical Record (EMR) systems – certified or uncertified EMRs -, [7] namely TELUS PS Suite, QHR-Accuro, OSCAR Pro (these three are the majority of primary care EMRs in Ontario), amongst others;
- Medical laboratories which are using specific lab information management systems to capture and store related lab tests results;
- Pharmacies that capture prescription data and dispense related data in their pharmacy practice management systems (PPMS);
- Medical imagining facilities generate visual and textual data regarding different imaging diagnostic procedures, such as X-rays, CTs, MRIs, Ultrasounds, mammograms, Angiography, Fluoroscopy, PET Scan, Nuclear Medicine, Bone Mineral Density which are managed by different information management systems;
- Registries/databases (including disease-related data or administrative data) would be the other origin of specific disease/disorder related data which are managed by the Ministry of Health (MOH), Ontario Health (OH), or Public Health Ontario (PHO), which are holding personalized and valuable clinical and demographic data for a holistic PM approach.
- Long-term care facilities, Home and Community-Care Support Service organizations, and other allied healthcare professionals (26 Ontario Regulated Health Professions) [8] hold important data to potentially support PM. The necessary data may find in their health information systems - electronically or through traditional communication methods (such as paper faxes). They may use some EMR versions or other information management systems such as PointClickCare. [9]

Data Sharing and Data Storage

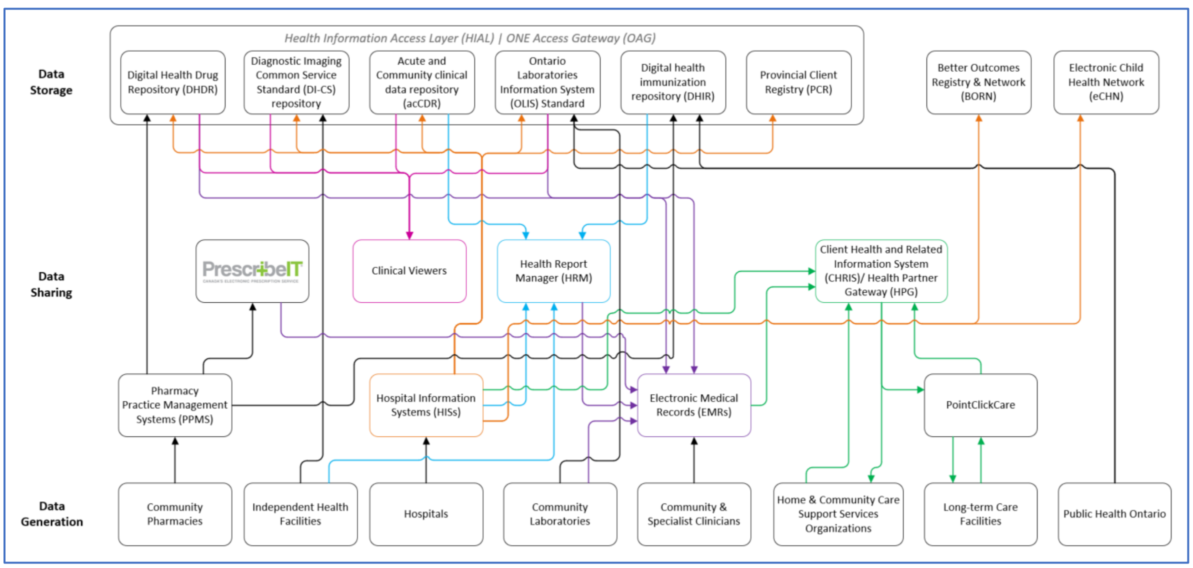
Six local repositories have been identified in obtaining health data from data generators mentioned above through Health Information Access Layer (HIAL), which is being replaced with the ONE Access Gateway (OAG):

- Acute and Community Care Clinical Data Repository (acCDR) [10]

- Diagnostic Imaging Common Service Standard (DI CS) Repository [11]
- Digital Health Drug Repository (DHDR) [12]
- Digital Health Immunization Repository (DHIR) [13]
- Ontario Laboratories Information System (OLIS) [14]
- Provincial Client Registry (PCR) [15]

Most hospitals in Ontario share clinical data through OLIS, PCR, DHDR, acCDR and DI-CS. Pharmacies share information through the DHDR - only if the information is related to Ontario Drug Benefit (ODB) or Narcotics Monitoring System (NMS) and share vaccination information with DHIR. OLIS obtains data from hospitals, Public Health Ontario (PHO) and community laboratories (hematology, pathology, chemistry, microbiology, and the blood bank). The provincial DI-CS receives diagnostic imaging data from hospitals and independent health facilities. DHIR data is accessible to all healthcare providers through a designated portal, and it is the only repository/portal in which the data is available for Ontarians to update their immunization information.

Home & Community-Care Support Services organizations and Long-term care facilities in Ontario share their data through the Client Health and Related Information System (CHRIS)[16] and Health Partner Gateway (HPG) with PCR and acCDR. (Figure 1)



Ontario healthcare providers access a part of the warehoused clinical data in the local repositories through one-way viewer solutions, including ConnectingOntario ClinicalViewer, ClinicalConnect, and eHealth Portal. [17] [18] [19]

The Institute for Clinical Evaluative Sciences (ICES) and the Canadian Institute for Health Information (CIHI) are considered as the provincial and national organizations, respectively. Both organizations receive health-related data from the Ministry of Health (MOH), Ontario Health (OH), or hospitals for secondary data use, including research and analytics.

Challenges

Data Generation/Collection: Findings from semi-structured interviews suggested that the complexities at the level of data generation will cause further and subsequent challenges, particularly in interoperability. Some critical health data are generated by allied healthcare professionals (psychology, dentistry, optometry, physiotherapy, etc.) and even some primary care physicians in a traditional method (paper); or they may use some information management systems which can not communicate with other systems and just work as a silo of health data.

Data Sharing: Complete access to all required clinical data for a holistic PM approach is not yet possible in Ontario. For example, data collected by allied healthcare professionals or even some primary care physicians are required for the holistic PM approach but are not yet easily accessible as the data is siloed.

The complexity in data governance in different health system levels and data sharing agreements is a critical challenge that has caused information blocking. In addition, the complexity of privacy rules and privacy acts, such as the Personal Health Information Protection Act (PHIPA) and the Freedom of Information and Protection of Privacy Act (FIPPA), creates challenges in linking health data (under PHIPA) and non-health data. Navigating the various privacy regulations is another significant challenge decelerating Ontario's clinical/health data sharing. Currently, no provincial solution is available to efficiently share clinical data between Ontario hospitals and primary care providers (PCP) who use different EMRs. Although existing local systems such as ConnectingOntario ClinicalViewer and ClinicalConnect, show hospital data (currently stored in provincial repositories), they are not integrated within EMRs, restricting users to adding, removing, or updating patient data.

Data Storage: Clinical data gathered in local repositories is not accessible for all authorized stakeholders. OLIS and DHDR data are available in selected, certified EMRs [7], not all of them yet. Also, the two main provincial viewers - ConnectingOntario ClinicalViewer, ClinicalConnect - do not provide the same information. Community laboratories share the lab test results with OLIS, which the OHIP only covers, excluding other test results. A similar situation can be seen within the DHDR, which receives drug dispensed information that is publicly funded, such as the ODB or NMS.

Genomics data

The term ‘omics’ refers to several areas of study within biology at different levels, including the molecular gene level (genomics), the protein level (proteomics), and the metabolic level (metabolomics). All different levels of omics data are required for a holistic PM approach, but for the scope of this study, only genomic data was considered.

Data Generation

Genomics data is generated using DNA sequencing in various spaces in Ontario, including:

- Community laboratories, such as LifeLabs or Dynacare based on primary care or specialist physician requisition,
- Hospital laboratories which might be for diagnostic, treatment, or research purposes, and
- Private laboratories operate under private companies for diagnostic, treatment, or research purposes.

Data Sharing and Data Storage

We identified no provincial system that shares and stores genomics data in Ontario through the environmental scan. Community laboratories share DNA sequencing results with physicians in a paper/PDF format (not as discrete data/unstructured data) and do not share genomic test results with the provincial repositories (i.e., OLIS).

Due to the sensitive nature of genomics data, many privacy regulations exist to limit sharing and storage. Genomics data is not shared between different healthcare stakeholders for any reason (diagnostic, treatment, or research purposes). Several research centers producing, analyzing, or using genomics data in Ontario have been identified:

- Ontario Institute for Cancer Research (OICR)
- Terry Fox Research Institute (TFRI)
- UHN-Princess Margaret (PM) Cancer Centre
- Children's Hospital of Eastern Ontario, Ottawa
- Credit Valley Hospital, Trillium Health Centre
- Hamilton Health Sciences
- Kingston General Hospital
- Mount Sinai Hospital
- Women's College Hospital
- Centre for Addiction and Mental Health (CAMH)

DNA sequencing within these research centers occurs in hospital laboratories or is sequenced in other advanced labs such as the Centre for Applied Genomics (TCAG) [20] at SickKids Hospital. TCAG usually sends genomics data as structured data (raw or analyzed) to the research centers that sent patients' samples.

Challenges

Genomic data sharing is hindered by an absence of framework/standards about patients' data privacy, agreement principles, and data characterization. [21] Genomic data custodians may be concerned about genomic data sharing to a data breach, which results in public harm. [22]

Lifestyle Data

A study by WHO concluded that over 60% of related factors to individual health are associated with lifestyle. [23] There is no consensus within the academic literature on a principal definition of the use of 'lifestyle data,' specifically from a PM standpoint. Davies et al. define it as "the key ingredients that make up a person's health and well-being, including (but not limited to) relationships, employment status and accommodation." [24] Lifestyle data includes the behavioural factors that can influence health and disease. PM may start at home by focusing more on what is on our plate, how much we move, and how to rest and sleep properly. [25]

Ten lifestyle-related factors have been identified by reviewing recent (after 2010) related articles and reports which describe the features of lifestyle data required to develop a holistic PM approach:

- Precision nutrition[1]
- Diet[2]
- Activity/Exercise
- Sleep pattern
- Sexual behaviour
- Substance use/abuse
- Medication use/abuse
- Emotional well-being
- Leisure time
- Spiritual/religious behaviour

Data Generation, Sharing and Storage

Some structured and unstructured lifestyle data are generated individually via the Internet of Things (IoT), including wearables (i.e., smartwatches), smartphones, and mobile applications. Also, this data is increasingly being captured through some systems such as remote monitoring programs (i.e., Ontario Telemedicine Network: CHF and COPD patients' remote monitoring programs). Provincial surveys like Ontario Health Study (OHS), [26] national ones, like CanPath [27] or Statistics Canada surveys might capture some lifestyle data. Patients' portals and EMRs may also obtain some lifestyle-related information. A larger contributor to lifestyle-related data has been social media. As a public tool, in order to be used for a PM solution, the use of social media must be paired with advanced analytics and big data to capture lifestyle/behavioural patterns. Lifestyle data is mainly stored by owner/technical companies, such as Samsung, Apple, Fitbit, or other personal devices, and are not usually shared with healthcare professionals to make a clinical decision.

Challenges

Hundreds of studies have demonstrated the influence of lifestyle factors on health status in two ways: an imbalanced lifestyle which can cause several mental and physical disorders, and secondly, a balanced lifestyle that can prevent chronic health issues or reduce related risk factors. [28] However, these scientific correlations between lifestyle and health status are available; we do not have a well-defined catalogue of all lifestyle factors as well as how to define each one and calibrate it to capture standard data.

The inaccessibility of lifestyle-related data is considered as a challenge in creating a holistic PM approach. Due to privacy concerns, companies such as Samsung, Apple, and Fitbit, hesitate to share the captured data for clinical use. Subsequently, there is no defined standard in capturing lifestyle-related data between the various devices or applications. The lack of standardization diminishes the reliability of

[1] Each person may have a different response to specific foods and nutrients, so the best diet for one individual may look very different than the best diet for another. Precision nutrition evaluates one's genome, microbiome, and metabolic response to specific foods or dietary patterns to determine the most effective eating plan to prevent or treat disease. https://www.hsph.harvard.edu/nutritionsource/precision-nutrition/

[2] Includes a variety of foods from the major food groups (i.e., fruits, vegetables, grains, protein, healthy fats, etc.) and how much food to choose from each group (based on the guidelines) that might fit individual's tastes, lifestyle and budget. https://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/basics/healthy-diets/hlv-20049477

lifestyle data, as clinicians or researchers may not trust the accuracy of the measuring device (i.e., smartwatch).

Environmental Data

Clinical studies have supported the impact of environmental factors, such as air, water, land, or any potential source, on population health or disease status. The 'Exposome' is the proper terminology to refer to this complex interplay and is defined as "a systematic approach to acquiring large data sets corresponding to environmental exposures of an individual along with her/his life." [29]

It was raised in 2015 that the environmental factors/exposomes are the primary required data in the PM framework. Still, there have not been definitions on variant exposomes until the International Medical Informatics Association (IMIA) created a working group in 2017 on more investigation on diverse exposomes, particularly by focusing more on informatics aspects related to the exposome. [29]

> Dr. Christopher Wild -Director of WHO-International Agency for Research on Cancer (IARC)- stated *"There is a desperate need to develop methods with the same precision for an individual's environmental exposure as we have for the individual's genome. I would like to suggest that there is a need for an 'exposome' to match the 'genome'."* [30]

In this study, we have identified some exposomes, along with their related data, that are beneficial in informing a precise clinical decision (holistic PM approach): [31] [32] [33]

- Chemical
    - Air pollutants (Outdoor, Indoor)
    - Heavy metals (Arsenic, Mercury, Lead, etc.)
    - Pesticides
    - Toxin/Contaminant (Carcinogen, Teratogen, Mutagen, Neurotoxin, Endocrine disruptor)
    - Other chemicals (Radon, Asbestos, Polychlorinated Biphenyls, Bisphenol A, Phthalates, etc.)
- Physical
    - Radiation (infrared radiation, visible light, ultraviolet light, radio waves, and microwaves)
        - Sun exposes (UV)
        - Ionizing radiation
    - Noise pollution
    - Electromagnetic fields
    - Temperature extremes
    - Mechanical
        - Vibration
        - Repetitive motion
        - Lifting
- Biological
    - Pollen
    - Bacteria/Viruses/Parasites

Also, they might be categorized in another format: [34]

Water quality	•	Contamination by human waste
	•	Oil and chemical spills in waterways
	•	Pesticide/herbicide contamination of groundwater and runoff to local waterways
	•	Aquifer contamination by industrial pollutants
	•	Toxic contamination of fish and seafood
Housing	•	Rodent and insect infestations
	•	Particulates from wood-burning stoves
	•	Houses and buildings with poor ventilation systems—sick building syndrome
	•	Off-gases from carpets and plastics used in home construction
Food quality	•	Bacterial contaminants
	•	Pesticide residues on fruits and vegetables
	•	Disruption of food chain by pollutants
	•	Chemical food additives
	•	Hormone supplements and antibiotic residues in animal food products
Radiation	•	Nuclear facility emissions
	•	Radioactive nuclear waste
	•	Radon gas seepage in homes and schools
	•	Nuclear testing
	•	Excessive exposure to X-rays
	•	Ultraviolet radiation (UV-B) due to global depletion of stratospheric ozone

Occupational health – a subcategory of environmental health - would be a promising field for the development of PM approaches; however, it will need to overcome a variety of legal, economical, ethical and socio-political concerns, particularly for preventive approaches. [35] [36] [37]

Main potential occupational exposomes/stressors which their data are required for a PM framework: [35] [37] [38] [39]

- Chemical: exposure to chemicals in the workplace, including neurotoxins, immune agents, dermatologic agents, carcinogens, reproductive toxins, systemic toxins, asthmagens, pneumoconiotic agents, and sensitizers.
- Biological: include samples of a microorganism, virus or toxin (from a biological source)
- Physical: include radiation, heat and cold stress, vibration hazards, and noise hazards
- Ergonomic: conditions that may pose the risk of injury to the musculoskeletal system, including awkward postures, static postures, large forces, repetitive motion, or short intervals between activity
- Psychosocial & Psychological: any occupational hazard that affects the psychological well-being of workers, including their ability to participate in a work environment

Data Generation, Sharing and Storage

Currently, there is no standard framework or coordinated approach to assess and collect environmental data required for a holistic PM approach within Ontario. [40] Some private sectors and public organizations have collected environment-related data via mobile environmental sensors, satellite, IoT (mobile applications or wearables) and questionnaires/surveys, such as Ontario Health Study (OHS) or Statistics Canada.

The Public Health Ontario (PHO) is less active in collecting environment data directly, but mainly uses others' data to provide some statistical and scientific report about: [41]

Daily exposures & environmental carcinogens:

  - UV radiation in sunlight
  - Breathing indoor and outdoor air
  - Eating food
  - Drinking water
  - Ingesting indoor dust
- Water quality
- Air quality
- Food safety
- Health hazards:
  - Biological
  - Chemical: indoor and outdoor
  - Physical: noise, temperature, vibration and radiation

In Ontario, regarding occupational health-related data, the Ministry of Labour inspects workplaces to monitor compliance with occupational health and safety legislation and regulations. [42] [43]

Challenges

The semi-structured interviews suggested imbalances and inefficiencies in capturing environmental-related data for PM. Data collection is sporadic and geographical-based, not individualized, which requires more time, energy, and resources to prepare the data. The key features of using environmental-related data for PM require statistical analysis, record linkage, derivation of indicators, computer modelling, and subject-matter analysis. [40] Ontario does not have a proactive provincial data strategy that collects the required environmental factors/exposome data to inform and address emerging issues and concerns.

The challenge in obtaining primary environment data is not only limited to the collection yet extends to the data workflows from which primary data is obtained. There would need to be appropriate data infrastructure to support interoperability of the data to ensure insight optimization. This review found a varying data structure and scale across municipal, provincial, and federal datasets, which is a considerable barrier to integration. Privacy laws and ethical guidelines are unclear. Incompatibilities between data management systems across institutions are barriers to sharing, linking, or harmonizing data. [44]

DISCUSSION

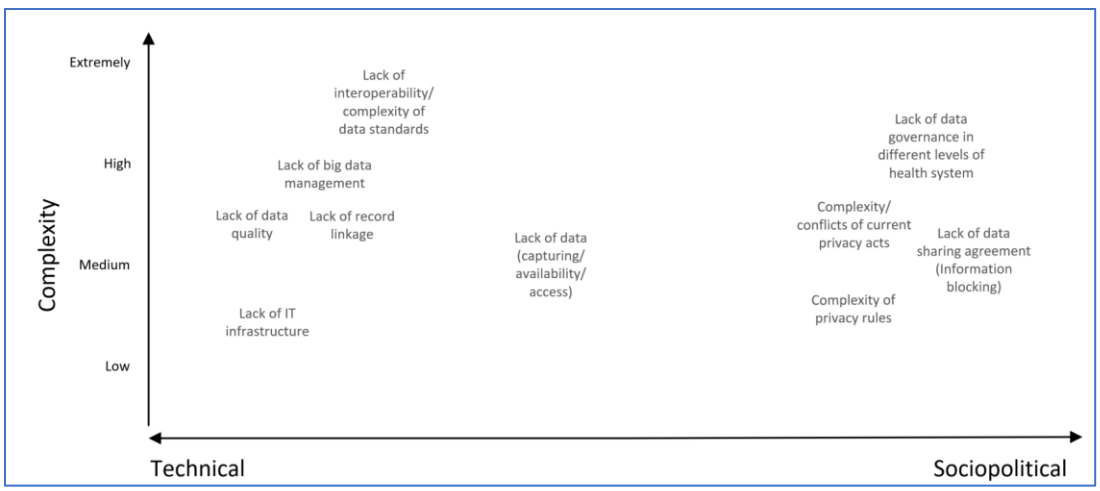
Ontario Challenges

In Ontario, required data from a PM point of view are fragmented, often unavailable, and inconsistent. [44]

Through reviewing various related articles and reports and results from the semi-structured interviews, we identified the main challenges in different levels of Ontario's healthcare system from a PM perspective. We grouped similar challenges/gaps into the following categories:

- Lack of data governance in varying levels of the health system
- Complexity of current federal and provincial acts (PHIPA – FIPPA)
- Lack of data sharing agreement (Information blocking)
- Complexity of organizations privacy rules
- Lack of record linkage
- Lack of interoperability/complexity of data standards
- Lack of data (capturing/availability/access)
- Lack of data quality
- Lack of Big data management
- Lack of IT infrastructure

Figure 2 identifies the challenges for achieving a PM approach. The challenges are ordered horizontally based on being technical or sociopolitical in nature, and the vertical scale describes the complexity required to address the challenge. This graph is based on a qualitative analysis from the survey results by participants in semi-structured interviews.



Canadian PM related assets

Some individual solutions, regardless of being provincial or national, are bridging some gaps mentioned above:

Ontario's Health Report Manager (HRM) is a digital health solution that allows clinicians to receive patient reports electronically in their EMR from participating hospitals and specialty clinics. HRM receives data from hospitals, independent health facilities (which provide imaging study), CoVaxON, and CHRIS referral system (only eNotifications) to deliver them as text-based medical record reports (e.g., Discharge Summary) directly into patients' chart, within the clinician's EMR. [45]

CANUE [46] is a Canadian organization that has developed sharable environmental data and data processing tools. They have built a unique repository of standardized metrics of urban, suburban, and rural characteristics, along with the tools used to produce them by focusing on national and global datasets. CANUE is focused on compiling and deriving standardized environmental exposure data about aspects of the urban and suburban environment for linking to human health research platforms:

- Greenness
- Neighbourhood
    - Active Living Environments
    - Canadian Access to Employment
    - Proximity to Roads
    - Green Roads
    - Building Density
    - Noise
- Air Quality
    - Ozone (O3)
    - Sulphur Dioxide (SO2)
    - Nitrogen Dioxide (NO2)
- Weather
    - Climate Metrics
    - Water Balance Metrics
    - Local Climate Zone
    - Ultraviolet

Digital Health Discovery Platform (DHDP), a pan-Canadian approach, will deliver a cutting-edge technological infrastructure through the application of big data (mostly genomics data about cancer and neurodegenerative disease) and artificial intelligence to improve health outcomes using PM. The main DHDP goal is creating a federated data ecosystem and governance. [47]

The Canadian Distributed Infrastructure for Genomics (CanDIG) is Canada's solution to enable data sharing. CanDIG is a driver project of the Global Alliance for Genomics and Health (GA4GH), an international effort setting standards for genomics and health data looking to improve interoperability across the genomics landscape worldwide. The CanDIG platform was developed to address Canada's province-based healthcare and privacy legislation, building a federation of datasets simplifying the challenges of sharing across provincial borders. CanDIG is also a vital component of the upcoming Digital Health and Discovery Platform (DHDP). [48]

PrescribeIT® (national e-prescribing service) as a medication management system connects community-based prescribers (such as physicians and nurse practitioners) to community retail pharmacies, enabling the digital transmission of prescriptions. Right now, PrescribeIT is not a PM solution, indeed; but its enhanced version might potentially manage prescribed and dispensed information. [49]

Precision Medicine is beyond only Genomics

However, Lichtenstein et al. stated that the attributable risk from the genome for chronic disease was only less than 30%, and the behaviour, environmental and sociodemographic (i.e., poverty, housing, race etc.) factors were responsible for the other over 70% [50]; presently, most PM initiatives focus on the genetic aspect with relatively narrow applications, mainly for people with certain cancers and rare diseases. This emphasis on a single gene or sequence resulted in the limited requirement for collateral clinical data and minimal dependence on lifestyle or environmental data. [51] [52]

Specifically, the focus on the genetic data of PM might be due to the feasible and accessible nature of data collection relative to collecting environmental and lifestyle data. Secondly, environmental and lifestyle data is not well defined and does not hold a specific standard in data collection. Behavioural data – lifestyle modification - is often embedded in clinical data. For example, behavioural interventions are the significant interventions in most chronic diseases such as diabetes prevention and treatment (i.e., weight loss and diet and activity) but have no standards.

Precision Medicine is a Patient-Centred Care model

Quality of patient care is the primary goal of any healthcare system, and defined patient-centred care is a model that is totally matched and aligned with the holistic PM approach. In the patient-centred care model, patients are treated from a clinical perspective and from an emotional, mental, spiritual, social, and financial perspective. The main element of patient-centred care is providing the right care at the right time in the right place. For this precision approach, we need all required data to be shared fully and promptly; then, healthcare providers, patients, and their families can make informed decisions. [53]

By reviewing the mentioned identified barrier categories in the Ontario healthcare system, we can't provide patient-centred care unless all related stakeholders make the right effect to resolve those barriers. The healthcare system's mission, vision, values, leadership, and quality-improvement drivers should align with patient-centred goals.

RECOMMENDATIONS

The promise of PM is more significant than this; it is time to expand the thinking about this evolving approach to medicine. Through this report, we hope that the collection of expertise sharing, ideas, criticism, diverse but with common aspects and objectives, will serve the reader to assess the importance of addressing clinical data-driven initiatives that integrate clinical, genetic, behavioural, and environmental information, all necessary for the development of holistic PM approach. The era of precision medicine is nigh.

> "Ten years from now, with the benefit of years of data contributed by more than 1 million people, we are going to know even more about what actions each person can take to keep themselves healthier," Eric Dishman, director of the All of Us Project says. "My vision is, ultimately, that everyone has that information, and nobody will have to suffer through trial-and-error care." [4]

SDOH, the 5th PM required data domain

The social determinants of health (SDOH) are the social and economic factors that influence an individual's health. The SDOH may impact health in many positive and negative ways. This is the recommended list by the Canadian Mental Health Association (CMHA) [54] and the Canadian Public Health Association [55]:

- Aboriginal status
- Disability
- Early life
- Education
- Employment and working conditions
- Food insecurity

- Health services
- Gender and gender identity
- Housing
- Income and income distribution
- Race
- Sexual orientation
- Social exclusion
- Social safety net
- Unemployment and job security

However, there are some overlapping between these socio-economic factors and lifestyle or environmental factors in PM perspective, some of them are exclusive and can be categorized separately, and their related data would be necessary for a PM framework. We recommend that SDOH factors be considered the fifth data domain required for a comprehensive PM initiative. [56]

Precision Medicine Ecosystem

Building secure, interoperable, and scalable back-end platforms that provide real-time information for PM data-driven framework is expected. A holistic PM solution cannot be achieved without massive efforts demanding extensive multidisciplinary collaboration, encompassing genetics, healthcare, engineering, human ethics and business. [57]

To implement a holistic PM approach, building a data platform capable of storing, processing, and analyzing large-scale data which is continuously and dynamically captured is essential. This platform would need to acknowledge the various nuances at different healthcare system levels. To implement a holistic PM approach in future, we need to co-design a “Precision Medicine Ecosystem” in our healthcare system. Developing such a PM ecosystem will require new infrastructures or upgrading legacy systems that facilitate collecting, storing, and analyzing high-quality data needed. [58-66]

This would also require government and policymakers to address the privacy, ethical, and technological challenges in integrating a PM framework into the healthcare settings. Government stakeholders must heavily invest in the PM ecosystem to accelerate PM's inclusion in areas of workforce, infrastructure, technology, and strategic planning.

Developing, implementing, or updating each part of the Ontario health system should align with a PM ecosystem that prioritizes data generation, sharing, and analysis usability and efficiency.

As we work towards building a holistic PM approach in Ontario, it is imperative we use international development in PM as an example. The World Economic’ Forum's Platform for Shaping the Future of Health suggests a development framework for governments to design and implement targeted and personalized approaches to screening, preventing, diagnosing, and treating diseases: [67]

1- the aspirational metrics of health decision making agencies to incorporate PM approaches into care;
2- the steps and partnerships outlined to achieve such targets within a specific time frame;
3- Follow the **FAIR** Guiding Principles in PM required datasphere: to be **F**indable, **A**ccessible, **I**nteroperable and **R**eusable;
4- Multistakeholder collaborations enabling PM innovation; and
5- PM innovation financing strategy.

Furthermore, the Organisation for Economic Co-operation and Development (OECD) recommended a Health Data Governance framework that encourages greater availability and processing of health data within countries and across borders for health-related public policy objectives while ensuring that risks to privacy and security are minimized appropriately managed. This multi-stakeholder consultation process advises governments to develop and implement national health data governance frameworks according to high-level principles (collection limitation, data quality, purpose specification, use limitation, security safeguards, openness, individual participation, and accountability), setting the conditions for greater harmonization to benefit the ultimate uses of data.

It is hoped that this study informs the development of partnerships, guidelines, and practical attempts to investment in PM. By understanding the current state of data, this report can support healthcare systems in adopting the most scientifically and technologically appropriate approaches to achieve PM. [68] [69]

Next step, lay out the PM Puzzle

More research activities are required to define and illustrate the 'Precision Medicine Ecosystem' and identify and distinguish all related actors, stakeholders, and elements in different levels of healthcare and society flawlessly and clearly. A magnificent giant puzzle with numerous pieces.

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