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Development of the Ontario Hereditary Cancer Research Network, a unified registry as a resource for individuals with inherited cancer syndromes: an observational registry creation protocol

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ABSTRACT

Introduction In Canada, care for individuals with hereditary cancer is fragmented across the provinces and territories, with carriers of pathogenic variants in cancer-susceptibility genes seeing multiple doctors and often advocating for their own management plans. The need for a national registry of carriers has been well established. While other cancer consortia exist, barriers in clinical and genomic data sharing limit the utility of the information gathered.

Methods and analysis Within the province of Ontario, the Ontario Hereditary Cancer Research Network (OHCRN), funded by and located at the Ontario Institute for Cancer Research, is being developed to fill this gap. The registry will hold clinical, genomic and self-reported data from consented carriers and will make this data available to qualified researchers in anonymised and aggregated form. Individuals must agree to certain components to participate in OHCRN; there are also optional consents participants can agree to without impacting their involvement in OHCRN. We plan to open the registry for participant enrolment in mid-2025.

Ethics and dissemination Ethics approval for registry creation was obtained from the Ontario Cancer Research Ethics Board, a centralised body that streamlines reviews for cancer research studies in Ontario. Registry data will be disseminated to participants and researchers as aggregate data through the OHCRN website and presented at scientific conferences, made available to Ontario Health (Cancer Care Ontario) to inform policy and evidence-based practice, as well as be available to the scientific community for further analysis and answering relevant questions.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Facilitation of collaborations with siloed existing specialised carrier clinics and administrative health databases, as well as harmonising different clinical and research programmes across institutions and geographic regions.
⇒ Ability to consolidate clinical and genomic information for individuals with all types of hereditary cancer (not disease or gene-specific) in one secure, online registry.
⇒ Inconsistent electronic medical records and laboratory information systems at participating sites limit automating the data ingestion processes.
⇒ The registry is limited by its focus on Ontario-specific cancer data, with no inclusion of information from deceased patients.

INTRODUCTION

Individuals with hereditary cancer syndromes (HCSs) have inherited pathogenic/likely pathogenic (P/LP) variants in genes associated with an increased risk of cancer development. These variants are diagnosed through germline genetic testing, which looks for P/LP variants in relevant genes from DNA derived from peripheral blood leucocytes. Individuals who harbour P/LP variants in one of >100 predisposition genes have a heightened risk of cancer and often describe themselves as a 'cancer ticking time bomb'.[1] Due to an increased risk of developing cancer,[2] those with HCS undergo intensive surveillance and/or risk-reducing surgeries tailored to their genetic predispositions. After the sentinel case is identified in a family, first-degree relatives have up to a 50% chance of carrying the same familial variant, making

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early diagnosis of an HCS through genetic testing crucial to the successful management of these individuals.

In 2021, genetic testing criteria were first established in Ontario, Canada, for *BRCA1/2*, familial adenomatous polyposis and Lynch syndrome[3]; these guidelines were recently updated and expanded in 2023 to include a larger range of HCS and a broader set of eligibility criteria.[4] There are still some issues surrounding genetic testing criteria, such as not accommodating transgender people, not taking into consideration the multicultural population of Canada,[5] and the under-representation of Indigenous communities in genome-wide association studies and reference population variant data sets.[6 7] This leads to underdiagnosis of HCS, underscreening and higher rates of variants of uncertain significance (VUS) in these populations.

Moreover, there is inequity of care for HCS carriers in Ontario, a province with a population of 14.57 million individuals (2019). For example, individuals who live in northern, rural or remote regions of Ontario do not have equitable access to the specialised genetics and oncology clinics that are more commonly located in larger cities. Few centres in the province offer specialised surveillance for newly diagnosed patients with HCS and many lack access to cancer genetics expertise related to diagnosis and follow-up. As such, the care of individuals diagnosed with HCS may fall to the local primary care physician. This is problematic, as in many communities, there is a shortage of primary care physicians, and these general practitioners may lack the specialised knowledge needed to guide the management of their patients and families.

There is long-standing recognition of the potential benefits of a registry of HCS carriers to inform research and aid patient care. These carriers are a valuable population of patients on whom to study cancer surveillance, early detection, prevention and precision therapy. A registry could facilitate research involving novel imaging techniques and genomics-based biomarkers as potential alternatives to costly conventional surveillance in HCS, bridging the gap between *omics* discovery and unmet clinical needs. Aggregation of the data across centres will be very useful in defining the clinical characteristics of carriers for rare gene variants. Developing an HCS registry can improve health services for HCS carriers, decrease inequities in access and accelerate precision medicine research and translation.

A partial list of some prominent HCS registries is summarised in online supplemental appendix A table S1. These registries serve as sources of real-world evidence for regulatory purposes and clinical trials, support care delivery, help identify participants eligible for trials and other therapeutic interventions and have a positive impact on our understanding of cancer biology and healthcare delivery for patients and families with HCS. There are diverse methodologies employed by hereditary cancer registries; not all registries contribute to both research and clinical care. For example, the International Hereditary Cancer Centre and Roswell Park Familial Ovarian Cancer Registry contribute broadly to cancer research, while others, such as the Dutch Hereditary Cancer Registry, focus on ensuring appropriate surveillance of its participants. Additionally, certain registries limit participation exclusively to adults, which in turn may trigger the need for establishing a distinct registry for paediatric cases. While some registries can collect de-identified information for clinical benefit, privacy limitations often prevent the inclusion of identifiable information and contact with patients,[8] with participant feedback about registry consent captured in detail by the Inherited Cancer Connect database.[9] Other challenges relate to funding, governance, legal and privacy issues, inability to integrate into national systems, issues with patient representation[10] and requirements for physicians to consent patients with no option for self-registration.[11] Most hereditary cancer registries focus on specific types of cancer, while only a few, such as the Inherited Cancer Registry, have attempted to capture all hereditary cancers.[12] This trend is consistent with current hereditary cancer registries in Ontario (table 1).

Since its inception in 1980, the Familial Gastrointestinal Cancer Registry, a national Canadian database, has provided collaborators with access to demographic, genetic and medical data from patients with familial gastrointestinal cancers. Since 1998, two population registries in Toronto, OFBCR and the Ontario Familial Colon Cancer Registry, which collect information on family history, epidemiologic data and blood/tumour samples from patients with/families with colorectal cancer,[13] have been involved in genetic data sharing with participating sites and individuals who applied for data access.

While creating large cohorts of rarer HCS continues to be a challenge due to fragmentation and inclusion restrictions, genomic data-sharing efforts are increasing both in Ontario and across Canada. In 2013, the Canadian Open Genetics Repository was developed with the aim of standardising variant assessment procedures, extracting and transferring data from Canadian clinical laboratories into a centralised repository and improving data access through a publicly available database.[14] Each participating laboratory received a variant assessment tool and guidelines were implemented for data sharing between clinical laboratories to enhance interpretation of human genetic variants.[14] In November 2022, the Canadian Institutes of Health Research announced a funding opportunity to support the development of a Pan-Canadian Human Genome Library, a federated framework for national genomic data sharing. In July 2023, the Canadian Partnership Against Cancer and the Canadian Cancer Society announced the launch of the pan-Canadian Cancer Data Strategy, which provides a guidance framework to enhance the collection, integration and use of cancer data to improve access to care and cancer prevention.[15] Finally, the pan-Canadian All for One precision health initiative through Genome Canada is developing a common platform to enable the direct sharing of variant and case-level data between sites for

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Table 1 List of hereditary cancer registries and provincial screening programmes in Ontario

Consortium	Aims	Institution
Ontario Breast Screening Programme[17]	Breast cancer screening programme for patients at increased risk of developing breast cancer.	Ontario Health (Cancer Care Ontario)
The Ontario Familial Breast Cancer Registry[18]	A population-based National Institute of Health-funded registry that provides infrastructure for research, identified and follows up on patients at high risk of breast cancer as well as populations that could benefit from enrolment in the preventive and therapeutic interventions.	Sinai Health System
The Familial Gastrointestinal Cancer Registry[19]	Provides specialty care to families affected with rare forms of inherited gastrointestinal cancer, contributes to prevention of cancer through early diagnosis and treatment and educates patients and caregivers.	Sinai Health System
The Familial Breast Cancer Research Unit[20]	Explores strategies for prevention and management of cancer in *BRCA1/2* and *PALB2* carriers.	Women's College Hospital
The Paediatric Cancer Genetics Program[21]	Early detection and increased survival in children and families who are at an increased genetic risk for cancer.	The Hospital for Sick Children

All research centres are located in Toronto.

rare diseases to address barriers to data sharing and to promote equitable uptake of precision health.

Thus far, there has not been a comprehensive research HCS registry developed either across Canada or in any Canadian province or territory that allows researchers access to linkable genetic and genomic data. Even in cases where hospitals have agreements in place with existing HCS registries, agreements are often limited to academic institutions and may exclude community-based participants, which potentially deepens disparities of care. In this report, we describe the design, methodology and development of the Ontario Hereditary Cancer Research Network (OHCRN). We aim for OHCRN to be the provincial model for hereditary cancer registry development in Canada, with a framework that can be expanded nationally. OHCRN will be unique from other registries in its broader inclusion criteria, ability to reidentify and technical infrastructure that supports improved interoperability and linkage. Although the reidentification of personal information creates logistical issues from a privacy standpoint, this will improve patient-reported outcomes and access to clinical trials and enable longitudinal research studies. In addition, OHCRN supports participant autonomy through a dynamic e-consent process, giving individuals control over their involvement.

METHODS AND ANALYSIS

Survey of existing Ontario genetics clinics and laboratories

In February 2020, the Ontario Institute for Cancer Research (OICR) held a collaborative meeting with stakeholders across Ontario, including clinicians, laboratory scientists, genetic counsellors, patient partners/advocates and leadership of existing Ontario cancer registries, to discuss the provincial HCS knowledge gaps. Supported by the enthusiasm of this group, we applied for funding through OICR's Adaptive Oncology programme to address the fragmentation of care for HCS carriers across Ontario by creating OHCRN to identify more carriers, better define clinical characteristics of carriers of different P/LP variants, resolve VUSs and discover novel genetic mechanisms in gene-negative families with extensive cancer histories.

Beginning in April 2021, a standardised set of 76 clinically relevant HCS genes became available in Ontario, promoted and supported by a strong collaboration between nine Ontario cancer-focused genetics laboratories and oversight by Ontario Health (Cancer Care Ontario), a provincial government agency that aims to connect and coordinate Ontario's healthcare system to improve patient care.

In addition to the nine cancer-focused genetic laboratories, there are approximately 30 genetics clinics across Ontario, with 20 of these routinely testing for HCS through germline genetic analysis. Historically, these clinics have varied infrastructure, with patient specimens sometimes sent for testing to laboratories outside the province or country (with Ministry of Health approval). In 2022, we undertook an informal environmental scan of genetics clinics in Ontario to survey the current successes and gaps in HCS care, which highlighted common issues with the current state:

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1. Clinicians across the province do not have equivalent knowledge of existing HCS research registries; therefore, information regarding self-enrolment in existing HCS registries is not always provided to eligible patients.
2. A lack of permission and/or agreements to share patient contact information with existing HCS registries further reduces eligible patient access.
3. A lack of readable electronic medical records and in-house databases results in data being stored in paper charts, often in PDF format, which limits some hospitals from identifying and tracking patients with HCS within their own hospitals.
4. Clinicians do not always request comprehensive HCS multigene panel tests; instead, they may select smaller subpanels relative to a patient's history. Therefore, most patients with HCS will only have a subset of HCS genes tested.
5. Clinical genetic testing laboratories store comprehensive HCS patient molecular data, but these data are inaccessible to researchers.
6. A lack of unified reporting format/software systems for reporting means that the location and naming of data fields differ between the genetic testing laboratory reports, making it difficult to capture this data into a unified structured database.
7. The registry consent process relies on paper consent forms and the use of fax to share consent with existing HCS registries, resulting in manual data entry for the registry. Manual data entry of patient enrolment data into existing registries is an error-prone, time-consuming process and busy clinical staff do not have extra time to devote to this process.

Registry design

OHCRN is designed to be an Ontario-wide registry that collects clinical and genomic information derived from individuals of all ages who have had germline genetic testing for a known or suspected HCS. OHCRN has collaborators at the nine clinical genetics laboratories, as well as 20 of the 30 genetics clinics in Ontario, including two paediatric centres, to identify participants and provide relevant information. The genetics laboratories are located in Ottawa, Hamilton, Toronto area (five), London and Kingston; between 1 April 2021 and 31 March 2022, these sites performed 10 564 genetic tests,[4] and 17 076 genetic tests between 2023 and 2024. Additionally, we will partner with non-genetics specialists who offer genetic testing to capture all patients newly diagnosed with HCS. The implementation of the OHCRN registry is comprised of three stages. Stage 1, the focus of this paper, began in October 2021 and centres on the design of the registry architecture and specifications of the minimum requirements for individuals to consent to join the registry. Stage 2, set to begin in mid-2025, will involve participant enrolment, harmonisation of data sets and data sharing with existing cancer registries, supported by participant consent. Stage 3 will allow researchers to analyse de-identified data from OHCRN, link to external data sets, educate and empower participants and improve access to clinical trials.

Registry inclusion criteria

OHCRN uses broad inclusion criteria to ensure anyone in Ontario who may benefit from having their clinical and genetic information consolidated in a centralised registry can participate. Any individual who has had germline genetic testing for a known or suspected hereditary cancer predisposition syndrome, regardless of cancer status or genetic test result, is eligible to enrol in OHCRN. There are no age restrictions. Individuals (or legal guardians) must be able to consent on their own or provide consent through a substitute decision-maker. Translation services with a paper consent form will be used as needed.

Identification of eligible participants

Multiple strategies will be used to identify eligible participants:

1. A member of the circle of care at participating institutions may identify eligible patients by reviewing relevant clinical charts, including genetic testing results. In addition, contact forms will be provided to genetic counsellors, physicians and genetics laboratories for patients to complete at the time of their clinical appointments. The circle of care team will contact patients to obtain verbal consent for a member of the OHCRN study team to contact them for consent to review their charts for registry eligibility.
2. Eligible patients from genetics clinics who have previously consented to recontact for research purposes and meet study criteria will be contacted directly by a member of the study team to provide information regarding consent to OHCRN.
3. Participants may be recruited through existing specialised registries, supported by the existing study's consent for participant recontact. Study team members involved in the existing registry will review the database for eligibility. A member of the patient's circle of care or an existing registry study team member will first approach the participant regarding consent to OHCRN.

We have identified five existing Ontario registries (specialised carrier clinics; table 1) that recruit specific patient populations, including those with hereditary cancer and register their information into a database. To preserve the autonomy of existing registries, these clinics will continue to be a hub for their respective syndromes, but there will be a two-way data transfer agreement between OHCRN and existing registries to form a cohesive registry. While these hereditary cancer registries exist in Ontario, a unified registry is hindered by differences in data formats, expertise, access processes and challenges in standardising and linking them to other health databases. Additionally, given that most registries exist in one region (Toronto), institutional approval in other regions of the province was not incorporated into their architecture and

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therefore not able to encompass the entire breadth of the Ontario population.

OHCRN consent process

We determined that access to clinical records is mandatory for enrolment in OHCRN. Medical records will be directly accessed by OHCRN study team members with hospital privileges at the participating sites. The release of information forms will be used at non-participating sites if needed. Online supplemental appendix B table S2 outlines the patient data that will be collected as part of OHCRN. There are multiple levels of consent in OHCRN, where participants must agree to the release and update of clinical and genomic data obtained from applicable institutions and/or provided by the participant to be stored within OHCRN for de-identified research. While any future research involving linkage to provincial administrative health databases requires an Ontario Health Insurance Plan (OHIP) number, the lack of an OHIP number will not be an exclusion criterion for participation.

Additionally, OHCRN will have four optional consents. Participants can choose to consent to none, all, or any combination of these consents without any impact on their participation in OHCRN.

1. Contact the next of kin or secondary contact for updates to health information if attempts to reach the participant have been unsuccessful.
2. Release of contact information and genetic test results to existing approved cancer registries, where appropriate.
3. Recontact about future research studies, surveys and release of contact information to relevant clinical trials.
4. Access and use of previously collected archival tissue/biospecimens and associated clinical data by approved researchers as part of unknown future ethics- and OHCRN-approved research studies.

Since consent is required for participation in the registry, OHCRN is a prospective study. Existing registries and clinics are able to notify previous patients and participants about OHCRN; however, once they enrol in OHCRN, they will be considered prospective participants for the registry, even though their germline variant was identified in the past. Deceased individuals will not be enrolled in OHCRN due to the consent requirement.

Participant portal

Although there will be an option for paper consent into OHCRN, the main method of consent will be participant self-identification and e-consent through an online portal. The development of the consent process required multiple discussions with patient partners, the ethics board and those who treat individuals who require an SDM (eg, genetic counsellors at paediatric hospitals) to determine feasibility. The initial OHCRN ethics submission is through the Ontario Cancer Research Ethics Board (OCREB), a centralised and streamlined process for approval. Site-specific applications for all participating sites are also submitted through OCREB to accelerate approval; some applications may also require additional approval at the local participating site. Provincial applicant approval has been granted for the University Health Network in Toronto (OCREB/4221), with supporting site-specific applications in progress.

Each individual participant will have their own unique account and profile with a unique ID accessible only to the study team. Duplicate entries coming from genetics clinics or laboratories will be flagged by the registry software and removed by the study team by cross-checking OHIP numbers. The home page will include basic patient and personal health information, consent for participation and release/link health data, as well as copies of the consent form and an option to withdraw from OHCRN. To prevent inadvertent health information disclosure to participants, most health information will not be visible to participants. Participants can update their account information as needed. If the participant has agreed, the next of kin will be contacted if the participant is deceased.

Registry enrolment process

All participants (or individuals completing the consent process) will create a personal participant account, with account creation, verification and access anchored to an email address. Multiple pathways of entry for participants to enrol in OHCRN have been developed (figure 1).

If the participant is identified by a member of their circle of care, verbal consent will be obtained of the participant's interest in joining OHCRN and their consent to be contacted. A member of the circle of care will connect their patients by providing OHCRN with the patient's full name, phone number, email address and consent to be contacted by a member of the study team. This information will be collected through the clinician-identified link in the online portal. Institutional email domains will be whitelisted to identify the circle of care as a registered member of the clinical community.

Self-identified adults (≥18 years of age) can register themselves online through the participant portal. Participants <18 years of age require a capacity assessment by a member of their circle of care prior to registration in OHCRN. Participants will be registered through a parallel stream of the clinician-identified link in the online portal, indicating age constraints and requirements. When a participant turns 18, they will be contacted to reconsent into OHCRN as an adult.

We expect a small subset of the HCS population will require an SDM, including some individuals with Tuberous Sclerosis Complex, Beckwith-Wiedemann syndrome or Gorlin syndrome, as well as some individuals in the general population. Individuals with an SDM or power of attorney have typically already been assessed by a medical doctor; therefore, a second assessment specifically for OHCRN enrolment will rarely be needed. This process will follow the same workflow as for participant enrolment through the self-identified link, with the SDM creating the account on behalf of the individual

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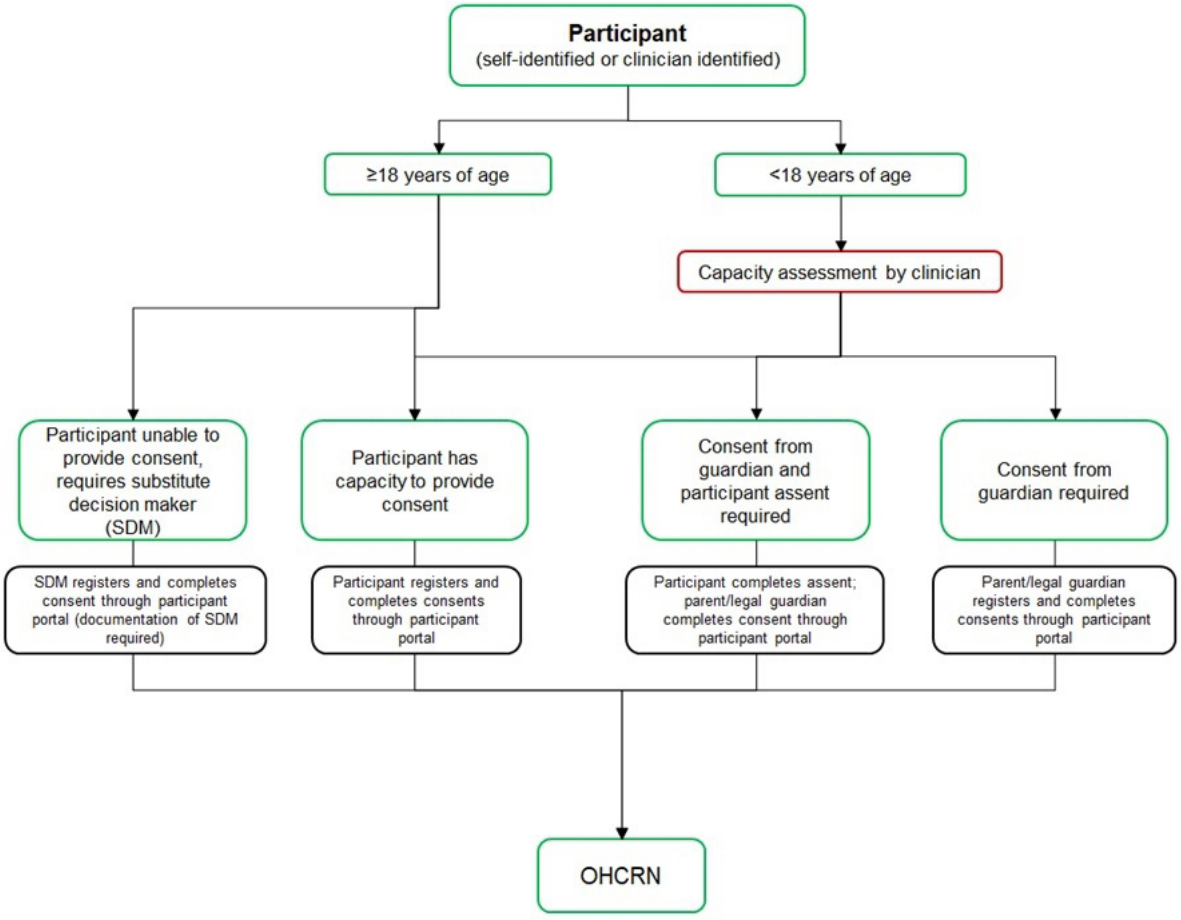

Figure 1 Various workflows for participant enrolment into the OHCRN registry through the participant portal. OHCRN, Ontario Hereditary Cancer Research Network.

but indicating that an SDM was used and providing their details. Following the completion of the consent process, a member of the OHCRN study team will contact the SDM to verify the primary care physician who has a record of the SDM.

Withdrawal process

Participants may withdraw their consent to participate in the registry without providing a reason to the study team. Participants can choose to either pause or delete their accounts. If the account is paused, OHCRN will not collect new data or link to administrative databases; however, unaggregated data will still be available to researchers. If the account is deleted, OHCRN will no longer contact the participant, information will be removed, and access to the portal will be deactivated. It will not be possible to destroy derived data or information already provided to researchers.

Acquiring diagnostic genetic test results

In Ontario, data related to genetic testing resides in the medical records of patients and does not exclusively reside under the auspices of the genetics clinic. Many oncologists order genetic testing.[4] Furthermore, most clinics give the patient the genetic testing report directly or through patient portals.

Genetic test results will be collected during the initial stage of the OHCRN registry through a manual process. The OHCRN has various mechanisms to obtain genetic testing reports. This can be through the medical record of the institution encompassing all clinics (genetics, oncology and others), by the patient themselves or by the laboratory that conducted the genetic testing. The study team will contact the institution(s) where participants had their testing performed to obtain the completed genetic test report. A PDF report will be uploaded to the registry. Preliminary work has been conducted using optical character recognition on the germline reports to accurately extract most data from the reports. In the future, we also aim to streamline this process by exploring electronic file transfer protocols with laboratories and hospitals to facilitate automated data entry.

Participants will reside in Ontario and may have undergone genetic testing in a lab either within or outside the province. In Ontario, the types of genetic panels are determined by hereditary testing criteria,[4] with further testing managed by the clinical genetics service that

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initially assessed the patient. Typically, patients return to the genetics clinic that conducted the original testing for additional, more comprehensive tests. While OHCRN does not directly coordinate genetic testing, it will provide educational resources and raise awareness about genetic testing in general. Additionally, specific research projects developed from the OHCRN cohort may invite participants to undergo further testing.

Linkage to existing Ontario platforms

An important component of OHCRN is the identification of administrative provincial databases that provide the most comprehensive and relevant data sets for our population. We are exploring linkage with the Institute for Clinical Evaluative Sciences (IC/ES), a non-profit corporation that receives funding from Ontario's Ministry of Health.[16] IC/ES allows researchers to use data collected from the healthcare system ('administrative data') for population-based health research. External research databases such as OHCRN can be linked to IC/ES; however, only highly de-identified data can be used. We are exploring storing OHCRN data within IC/ES as either a Project Specific Data set, used only for the purposes of our project, or as a Controlled Use or General Use Dataset, governed by a data sharing agreement between IC/ES and OICR. IC/ES Data and Analytic Services can share highly de-identified linked data following a data sharing agreement, but individual-level data cannot be downloaded. In its current state, the IC/ES platform has limitations to consider before supporting OHCRN data linkage long-term. While IC/ES can link data using OHIP, no genomic sequencing data or clinical genetic test reports are stored, which are critical data sets for OHCRN to enhance research collaborations. Consideration is being given to using OHCRN as a test registry for an updated version of IC/ES that does accommodate genomic data. In addition, a researcher cannot directly access IC/ES data and must work through an IC/ES staff member, which can lead to significant time delays. It is expected that IC/ES will maintain a copy or partial copy of the OHCRN registry, linking it with their data at regular intervals. Researchers will use OHCRN registry data to generate cohorts and then link them to additional administrative health datasets. Researchers will be allowed to analyse and work with data within the secure IC/ES research environment.

The Ontario Health Data Platform (OHDP) is emerging as another potential solution to support the linkage of genomic data sets with healthcare system data. OHDP links large health data sets upon agreement with each of the dataset holders, offering the opportunity to track patients' testing, clinical encounters and surgeries. The ability of OHDP to collect data and link genomic data was facilitated for COVID-19 research during the height of the global pandemic. Laboratories were compelled to share specific data with OHDP; it is anticipated that OHCRN may benefit from a similar process, whereby molecular laboratories share genetic test results and/or genomic sequencing information. Currently, OHDP is not authorised to hold hereditary cancer genomic sequencing information.

We are also exploring the possibility of linking to the data holdings of the Ontario Cancer Registry (OCR), which contains health information from Ontario residents diagnosed with cancer. OCR holds some synoptic pathology data and plans to also capture key fields from narrative reports from germline molecular testing in the province. However, OCR does not currently hold genomic information and genetic test reports. Data sharing details are being defined with Ontario Health, as the governing body of the OCR. It is most likely that Ontario Health will request that researchers generate a cohort within OHCRN and then apply directly to them for access to data they hold required for the project.

Facilitating linkage to external databases and datasets is an important component of registry sustainability. This linkage, along with only storing core data, allows for lower long-term carrying costs. As OHCRN is funded on a 5-year cycle by the provincial government, we will further support and maintain the registry by liaising with other foundations that focus on hereditary cancer, co-funding with researchers who will use OHCRN as a data portal and data utilisation fees for industry-led clinical trials involving OHCRN participants.

Future stages of OHCRN

Broadening the scope of recruitment

Initially, most participant recruitment will involve prospective identification through the genetics clinics and laboratories. However, we anticipate that carriers may hear about the registry through their affected relatives or participation in existing studies. In addition, genetic testing laboratories may be able to include information about the OHCRN registry in reports through a centralised reporting system. We also anticipate partnering with the Ontario Tumour Bank to expand recruitment by identifying potential HCS cancer samples using their existing database.

Further acquisition of genetic test results

Further integration with laboratory systems may allow OHCRN to collect results in an automated way. Through OICR's Ontario Molecular Pathology Research Network, which drives innovations in cancer research by supporting molecular pathology education and resourcing, we are engaging with all 9 genetic testing laboratories across Ontario. OHCRN study team members from OICR Genome Informatics surveyed where and how genetic test results and genomic data are being stored in the province. We met with each laboratory, including their IT and bioinformatics teams, to discuss what resources are required for the automated transfer of data into OHCRN and are developing recommendations for the integration of OHCRN with the respective molecular laboratory interfaces. We will ascertain the laboratory processes for identifying carriers of P/LP variants in cancer-causing genes, including communications with laboratory directors, to

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increase the participation of Ontario laboratory medicine departments in research.

To facilitate future integration, the OHCRN data model is aligned with international standards, such as mCODE and health level-7, to enhance direct field mapping and ensure our data schema and elements are consistent with globally recognised models. Additionally, we are using standardised terminologies and ontologies to ensure interoperability across different systems.

OHCRN is also closely following the data harmonisation efforts in the genetics and genomics community in Ontario for future integration into centralised systems, such as the Ontario Laboratory Information System, which is integrated into the IC/ES infrastructure.

Development of the researcher portal

The researcher portal will house anonymised data, cohorts and linked data. Researchers will be required to apply to OHCRN to access specific data, which will undergo review by the appropriate OHCRN subcommittee and will require institutional ethics review prior to approval. Information will be de-identified prior to being provided to researchers. Researchers will be able to filter between affected and unaffected populations with germline (P/LP) variants; depending on the research protocol, authorised researchers will be able to filter by many different fields outlined in the data model (online supplemental table S2), for example, carriers affected with cancer and those unaffected. The data collected for OHCRN is not site-specific, and OHCRN study team members will have the ability to reidentify any coded data. Access for researchers to de-identified data for approved research projects is a mandatory part of the participant consent. A summary of all approved projects involved in OHCRN will be published on the OHCRN website.

Genomics and gene discovery for patients with HCS in Ontario

For HCS carriers who have had tumour biopsies or samples, OHCRN will capture somatic information (in addition to germline) to facilitate research into links between somatic and germline variants. OHCRN is also exploring ways to eventually collect and share sequencing data from laboratories to support future research.

As gene panel testing evolves into genomic testing in Ontario, OICR's CAP-accredited Genomics Programme will be central to informing a comprehensive genomic, epigenomic and circulating tumour DNA analysis strategy, scalable across all HCS. Over time, we aim to genomically sequence as many HCS carriers as possible. To support this, OHCRN is exploring collaboration with other projects, including the Ontario Tumour Bank. These collaborations will facilitate tumour whole genome sequencing and methylome analysis, followed by liquid biopsy-based whole transcriptome sequencing, whole genome sequencing and methylation analysis, leading to earlier detection, diagnosis and cancer treatment.

Summary

OHCRN will contribute to an improved understanding of HCS and, consequentially, better cancer care that will place Ontario on the international stage for hereditary cancer research. OHCRN differs from other international registries and existing hereditary cancer registries in Ontario due to its ability to enrol participants with all types of hereditary cancer (including rarer syndromes), clinician or self-enrolment of both adults and children, linkage to administrative health databases, and contribution to both research and clinical care. HCS carriers are a valuable population of patients to study cancer surveillance, early detection, prevention and precision therapy. The impact of precision cancer therapies based on germline variants in patients with HCS is vast, and we plan to enhance precision cancer therapy and chemopreventative trials for participants by expanding recruitment across all HCS populations and geographical reach to increase the power of clinical trials. We aim for OHCRN to be the provincial model for hereditary cancer registry development in Canada, with a developed framework that can be expanded nationally.

Patient and public involvement

Representatives of advocacy groups across Canada, including Ovarian Cancer Canada, My Gut Feeling—Lynch syndrome, the Canadian Von Hippel Lindau Alliance and the Canadian Li-Fraumeni Syndrome Association, as well as individuals who are carriers of a P/LP variant for HCS, have participated in the design of the OHCRN registry since the initial application for funding. These individuals are remunerated for their time and have provided feedback on OHCRN conferences/workshops, the online participant portal, the website and ethics documents (eg, consent forms and study protocol). Members of our patient team have also presented their stories during OHCRN conferences, and we have patient representatives on all OHCRN governance committees. We are exploring opportunities to connect with Indigenous patient navigators who provide care at provincial cancer centres. Any results generated using data from OHCRN will be shared with stakeholders, including patient advocacy groups, policymakers, healthcare organisations and the general public, according to patient consent and ethical data sharing principles (OCAP—First Nations principles of ownership, control, access and possession).

ETHICS AND DISSEMINATION

We will disseminate our findings from OHCRN in peer-reviewed cancer genetics journals and present them at relevant conferences worldwide to describe

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our process of creating an Ontario hereditary cancer registry.

Study governance

OHCRN is governed by a steering committee and three subcommittees (Laboratory, Data Management and Research and Ethics). Each committee includes scientists, healthcare providers, patient partners and members of the OHCRN study team.

Ethics statements

Ethics approval for registry creation was obtained from the Ontario Cancer Research Ethics Board, project ID 4221.

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