**HDRN CANADA PRAGMATIC TRIALS TRAINING PROGRAM OVERVIEW:**

Pragmatic clinical trials are often embedded in routine care and involve the analysis of routinely collected data (e.g., health registries, electronic medical records, and administrative data). Done well, pragmatic trials yield valid generalizable results faster than explanatory (“traditional”) clinical trials and can be completed at a fraction of the cost.

The **HDRN Canada Pragmatic Trials Training Program** is a Clinical Trials Training Platform funded by the **Canadian Institutes of Health Research** (CIHR). Coordinated by the **Schulich School of Medicine & Dentistry at Western University** and embedded within **HDRN Canada**, this two-year virtual pan-Canadian program will provide training to advanced learners across three streams: (1) future trial leaders, (2) postdoctoral fellows, and (3) highly qualified personnel.

*HQP = highly qualified personnel. HDRN Canada = Health Data Research Network Canada (member organizations).*

Applicants must review this “program overview” document prior to submitting their application.
This diagram illustrates the collaborative, mentorship, and experiential learning aspects of the HDRN Canada Pragmatic Trials Training Program.

All participants will have access to a learning management system.
- Participants will have the opportunity to access educational materials and network with other trainees from all streams.

Future trial leaders will receive external mentorship (e.g., from an experienced pragmatic trialist).
- For the benefit of all participants, external mentors will also contribute educational materials to a learning management system.

Future trial leaders will facilitate experiential learning through collaborations with postdoctoral fellows in the program through the development of a pragmatic trial protocol.
- In the situation when a fellow's primary supervisor is not a trial leader in the program, it must be understood by trial leaders that fellows will be involved in other work directed by their primary postdoctoral supervisor outside of the program.

Public sector HQP employed by HDRN Canada member organizations will engage, when possible, in projects, i.e., a project that furthers HDRN Canada’s ability to support pragmatic trials research (e.g., reducing barriers for analyses of routinely collected data, particularly multi-regional data, that informs trial design and execution).
- Mentorship on projects within HDRN Canada member organizations will come from supervisor(s) at the HDRN Canada member organization.

Private sector HQP and public sector HQP not employed by HDRN Canada member organizations will access a learning management system where they can view educational materials and network with other trainees.
- These HQP will not necessarily engage in a project-based learning experience. However, such opportunities can be discussed after acceptance into the program on a case-by-case basis.

If you have any questions or concerns, contact the Program Manager (Taylor McLinden) at taylor.mclinden@hdrn.ca.

The HDRN Canada Pragmatic Trials Training Program believes Inclusion, Diversity, Equity, and Accessibility (IDEA) is key in fostering a respectful, innovative, and pioneering learning environment. The program’s commitment to IDEA ensures participants will benefit from the full range of skills, perspectives, cultural backgrounds, and experiences needed to learn about the design, implementation, and management of pragmatic trials.

The activities of the HDRN Canada Pragmatic Trials Training Program are taking place on the traditional and ancestral territories of First Nations, Inuit, and Métis Peoples across Canada.
GENERAL INFORMATION:

What are pragmatic clinical trials?

Pragmatic clinical trials are a type of experimental study used to evaluate the effectiveness of interventions, often by randomizing the intervention (e.g., a treatment) under study. These trials are typically conducted in routine care settings with the aim of providing evidence that is applicable to real-world clinical care. Pragmatic trials are often contrasted with explanatory or “traditional” clinical trials, which typically focus on establishing the efficacy of an intervention under ideal conditions. Characteristics of pragmatic trials may include:

- **Real-world settings**: Pragmatic trials are conducted in diverse settings, such as clinics, hospitals, and primary care facilities to reflect the variability and complexities of routine practice.
- **Broad inclusion criteria**: Pragmatic trials often have less strict eligibility criteria compared to explanatory trials, allowing for a wider range of patients to participate. This helps to ensure that the results are generalizable to a broader population.
- **Flexible interventions**: Interventions in pragmatic trials are typically designed to mimic how they would be used in routine care, rather than being highly controlled or standardized. This means that providers may have some flexibility in how they deliver the intervention under study.
- **Patient-centered outcomes**: Pragmatic trials often prioritize outcomes that matter to patients, such as reductions in hospitalizations, rather than focusing solely on surrogate markers or biomarkers.
- **Larger sample sizes**: To detect meaningful differences in clinical outcomes, pragmatic trials often involve larger numbers of participants than explanatory trials. This is often made possible by using routinely collected data (e.g., health registries, electronic medical records, and administrative data) at various stages of the trial.
- **Longer follow-up**: The use of routinely collected data enables pragmatic trials to have longer follow-up periods to assess the effects and sustainability of interventions.

Pragmatic clinical trials are important for bridging the gap between highly controlled clinical research and actual practice. Using randomization, they provide valuable insights into how treatments and interventions perform in diverse settings and populations. Trial results are typically highly generalizable and readily translatable into healthcare policy and clinical care.

What topics may be covered in this training program?

Participants will learn about designing, implementing, and managing pragmatic trials alongside best practices in clinical trial reporting and standards. Topics that may be covered include but may not be limited to:

*Design and analysis:*

- Randomization unit: Individual vs. cluster randomization, level of the intervention (e.g., an intervention may be delivered by a healthcare provider, but the randomization unit may be a hospital).
• Randomization strategy and justification: Cluster-randomized, stepped-wedge, crossover, factorial, adaptive; choice and construction of a comparator group (e.g., active or usual care); choosing a statistically efficient design and ensuring the design is fit-for purpose (see PRECIS-2).
• Randomization method: Simple, covariate-constrained, minimization, pair matched, stratified; randomization schedule for cluster-randomized trials with multiple cluster-periods.
• Blinding and allocation concealment: Who is blinded (e.g., the patient, the provider, the outcome assessor), when does it happen; justifications for blinding; ensuring blinding is maintained through time.
• Endpoints and outcomes: Considerations regarding the outcome distribution (i.e., time to event [including recurrent events, competing risks], binary, continuous, ordinal, count); single vs. composite; cost effectiveness; patient-reported and patient-important outcomes.
• Sample size considerations: Intraclass correlation, unequal cluster sizes, multiple cluster periods, adjustment for small samples (i.e., <30 clusters), treatment-effect heterogeneity, novel trial designs, and planning for sub-group and stratified analyses.
• Analysis: Unit of analysis (individual-level; cluster-level), covariate adjustment, heterogeneous treatment effects; handling missing data.
• Bias: Assessment of selection bias, measurement error/misclassification, residual confounding, and other threats to validity.

Data sources, variables, quality, and linkage: Data for pragmatic trials, including but not limited to baseline characteristics and outcomes, can come from existing routinely collected data sources such as linked provincial administrative health data, disease and healthcare registries, e-health records, and surveillance systems. Topics may include:

• Linking data across systems, regions, and networks; how to assess data quality; how to select and define outcome measures; database coding; and how to conduct validation studies and complete privacy impact assessments.
• Ethical and legal aspects of aggregating data across networks while maintaining privacy rules, how to link externally collected trial datasets to administrative data, and opportunities for data collection outside of the routinely collected data.
• The First Nations principles of OCAP: standing for ownership, control, access, and possession, OCAP is a tool to support strong information governance on the path to First Nations data sovereignty.

Implementation science and trial conduct: Participants will learn about the importance of designing simple, scalable interventions for broad implementation. They will learn about implementation frameworks, theories, and models. Implementation plans ensure successful intervention uptake and help determine the need for a pilot phase. Topics may include:

• How to assess current practice patterns (via surveys and/or routinely collected data analyses), perform qualitative studies to understand potential barriers to intervention uptake, prepare trial roll-out strategies informed by evidenced implementation strategies,
Program Overview

V: 1.0 Date: Nov 6, 2023

Health Data Research Network Canada
Pragmatic Trials Training Program
Coordinated by the Schulich School of Medicine & Dentistry
Western University, Ontario, Canada

• Develop monitoring protocols to assess fidelity, and how to measure and assess implementation outcomes.
• Privacy compliance, quality assurance, contracts, and budgets.

**Partner buy-in and public/patient engagement:** Participants will learn about the importance of engaging and communicating with diverse partners to cultivate a research-ready community (where partners may include healthcare organizations, providers, administrators, and public, patient, and family advisory councils). Topics may include:

- How to liaise with key partners using audience-adapted materials and how to seek feedback through various channels.
- How to create educational websites and brief videos tailored to key partner groups, and how to appropriately use social media to promote the trial and provide updates on recruitment, progress, and knowledge translation.

**Research ethics and regulations:** Existing ethical frameworks were developed primarily in the context of explanatory clinical trials, where the efficacy and safety of interventions for market approval is usually tested in trials of individually randomized patients. In contrast, pragmatic trials of usual-care interventions are often delivered by healthcare staff, using existing data collected in routine care, and these elements can present challenges to existing ethical and regulatory frameworks. Topics may include:

- How randomization, intervention delivery, and existing data collection at the level of the patient, health provider, or health system raises fundamental questions about the process of informed consent, the nature of research participation, and ethical protections.
- In the absence of internationally accepted ethical guidelines, researchers and ethics committees may have no common standard to guide appropriate practices in pragmatic trials. This can lead to variability in ethics reviews across regions. (Contributors to this training program have played leadership roles in advancing a responsible ethical framework for conducting these trials, including developing the first international ethics guidelines for cluster-randomized trials).
- Potential ethical challenges unique to pragmatic trials and appropriate modifications to traditional screening, recruitment, and consent models (e.g., e-consent, integrated consent, short form consent), the role of local gatekeepers, and how to prepare submissions for research ethics boards.
- Equipoise for routine care interventions (e.g., completing a literature review before a trial to demonstrate there is genuine uncertainty within the research community about the effectiveness of the interventions being compared), community engagement and patient-centered outcomes (e.g., demonstrating that the study’s potential results will be meaningful to participants and that they align with their preferences and values), data security, confidentiality, and post-trial data access (e.g., data repositories).

**Inclusion, Diversity, Equity, and Accessibility (IDEA):** By design, pragmatic trials are highly inclusive, as typically all patients who would receive the intervention in practice will be included in the trial. These trials also enable the inclusion of patients and community-based centres in
remote locations, which are often excluded from explanatory trials due to a lack of dedicated research staff.

Participants in the program will consider the following overarching questions in the context of data and its use within a pragmatic trial: (1) Who is the data collected by? (2) For whom and for what purpose is the data being collected? and (3) Who benefits from the data collection?

*Indigenous rights:* Participants will have access to the Wabishki Bizhiko Skaanj Learning Pathway, and other related training, to enhance their knowledge and awareness of racial biases, Indigenous voices and stories, the impact of colonization on Indigenous health, and culturally safe health research practices.

**How does this training program compare to the other CIHR-funded Clinical Trials Training Platforms?**

Currently, the HDRN Canada Pragmatic Trials Training Program is the only CIHR-funded training platform that focuses specifically on pragmatic clinical trials. While more general (“traditional”) clinical trials educational materials will be available in a learning management system, participants in this program will focus on novel and evolving aspects related to pragmatically evaluating interventions in real-world settings.

Specifically, this training program will not focus on a particular disease or content area but rather, there will be an expanded focus on the use of existing data sources in trials, including health registries, electronic medical records, and administrative data. This is one of the reasons why this training program is embedded within HDRN Canada.

Pragmatic trials involve innovative study design choices. (See [here](#) for a list of pragmatic design elements that can be introduced into a trials design). In addition to the rapid evolutions observed in the explanatory clinical trials space, there are many novel pragmatic trial-specific elements to consider as well, including but not limited to multi-regional participant recruitment and data access (with specific considerations around Inclusion, Diversity, Equity, and Accessibility, as well as Indigenous data sovereignty), altered consent procedures and novel ethical considerations, biostatistical and epidemiologic methods complexities, and intricacies of implementing and maintaining interventions in routine care settings.

Lastly, unlike several of the other Clinical Trials Training Platforms, this program focuses solely on advanced learners (e.g., faculty-level trainees, postdoctoral fellows, and highly qualified personnel in the workforce).

**Has this training program been offered before?**

No. The program will launch for the first time in April 2024 and run for two years. Therefore, participants should be prepared for the realities that come with a first-time offering. In light of this, the program will seek routine feedback from participants and adapt to help meet their learning objectives.
What is the language of instruction for this program?

The language of instruction for the program will be English. Therefore, to fully engage with the educational materials and other participants, all applicants must have an adequate level of proficiency in English.

If I am enrolled in another CIHR-funded Clinical Trials Training Platform, can I apply to this training program?

This program does not explicitly prohibit trainees participating in other platforms from applying to this program (albeit other platforms may have such restrictions). From the perspective of this program, the major barrier to involvement in multiple training programs are considerations around time commitments and funding.

For example, in this program, salary awards for postdoctoral fellows may be combined with other awards, up to a combined maximum allowed by the host institution and/or the allowed maximum within the funding conditions of other salary awards currently held by the applicant. To maintain this funding, fellows must need the conditions of this program (as outlined in the application form). Such stipulations may impact one’s ability to be formally involved in multiple CIHR-funded training programs at the same time, many of which also provide financial support (with associated time commitment requirements to maintain that support).

Will there be requirements and/or opportunities to attend in-person events?

There is no funding for in-person events for this training program. However, given that this program is embedded in HDRN Canada and has pan-Canadian partnerships with groups such as the ACT Canada Consortium and other Clinical Trials Training Platforms, there may be ad hoc opportunities for participants to network in person. Such opportunities, while not guaranteed, will be announced to participants, when and if they arise.

How will you accommodate the required attendance at monthly, one-hour virtual meetings in the pan-Canadian context?

To accommodate time zones, these monthly meetings will be scheduled to start between 12:00 PM and 3:00 PM Eastern time; exact day of the month is to-be-determined. Participants will be required to attend 80% of these meetings.

What is the governance structure of this program?

HDRN Canada is a CIHR-funded pan-Canadian network focused on facilitating multi-regional studies (including, but not limited to, clinical trials) using routinely collected data. The training program is embedded within the governance structure of HDRN Canada; the nominated principal applicant and program manager are members of the HDRN Canada Leads Team and the ACT Canada Consortium/HDRN Canada Clinical Trials Working Group. The Leads Team receives input from the SPOR CDP Advisory Committee, as well as HDRN Canada working groups (e.g., Indigenous data, IDEA, and public engagement groups).

As a CIHR requirement, there is also a training program advisory committee that guides and monitors the progress of this specific program. Specifically, this committee advises on the
design, implementation, and high-level operations of the program. As outlined by CIHR, the committee includes trainees, healthcare professionals, clinical research professionals, early career researchers, an IDEA champion, a person with lived/living experience, and an individual who self-identifies as Indigenous (First Nations, Inuit, and/or Métis).

The training program is coordinated by the Schulich School of Medicine & Dentistry at Western University in Ontario, Canada. The nominated principal applicant and program manager are also members of the Pragmatic Trials Scientific Advisory Committee at Western University, where the nominated principal applicant serves as an Associate Dean of Clinical Research and the program manager is an Adjunct Research Professor in the Department of Epidemiology and Biostatistics. Further, the nominated principal applicant is a member of the ACT Canada Consortium Operating Committee and a Co-Chair of the Scientific Committee. The program manager is also a member of the ACT Canada Training Committee.

**How is Inclusion, Diversity, Equity, and Accessibility (IDEA) being considered in this program?**

The training program grant was drafted with the input of HDRN Canada’s IDEA team lead who is also a member of the training program advisory committee. There is dedicated funding from the grant devoted to supporting IDEA initiatives within this program. Further, this training program aligns with CIHR’s goal of creating a more inclusive, diverse, equitable, and accessible Canadian research enterprise. The program staff endorse the statement that this is “essential to creating the excellent, innovative, and impactful research necessary to advance knowledge and understanding, and to respond to local, national, and global challenges.”

**How are Indigenous rights being considered in this program?**

The training program grant was drafted with the input of the Indigenous Peoples’ Engagement and Research Council (IPERC) and program staff have seasonal check-ins with the IPERC. The program also employs a full-time Indigenous Cultural Competency Training Coordinator who is mentored by Indigenous Knowledge Keepers. The training program advisory committee also includes Indigenous representation and HDRN Canada has a team dedicated to Indigenous data in the context of pan-Canadian routinely collected data.

Participants will have access to the Wabishki Bizhiko Skaanj Learning Pathway, and other related training, to enhance their knowledge and awareness of racial biases, Indigenous voices and stories, the impact of colonization on Indigenous health, and culturally safe health research practices.

**How does the time release funding (for HQP employed at public sector organizations) correlate with the required time commitments for HQP in the program?**

As outlined in the application form, to facilitate the involvement of public sector HQP, public sector organizations will receive 150 hours of time release funding, per year, valued at a minimum of $50 per hour (i.e., each public sector employer will receive a minimum of $7,500 per year for each of their HQP in the program). This amount may be adjusted based on the number of successful public sector HQP applications.
It is also noted that, at minimum, HQP must be able to engage with tasks related to the program on a bi-weekly basis (6 hours over a two-week period, ~3 hours per week). Assuming an HQP works ~50 weeks of the year (assuming ~2 weeks of vacation), ~3 hours per week (for ~50 weeks) would equate to 150 hours of time spent on tasks related to the program.

**Why are public sector HQP employed by HDRN Canada member organizations being asked to engage in an experiential project-based learning experience?**

Pragmatic trials are often embedded in routine care and, thus, can leverage routinely collected data. HDRN Canada connects organizations across the country to share expertise, identify opportunities for collaboration, and foster innovation in areas related to routinely collected data (e.g., health registries, electronic medical records, and administrative data).

Therefore, the training program is formally embedded within HDRN Canada and one of its goals is to expand HDRN Canada’s capacity to support pragmatic trials research, particularly multi-regional trials. To help meet this goal, there is a targeted need for HQP employed by HDRN Canada member organizations to expand their ability to support pragmatic trials research (e.g., reducing barriers for analyses of routinely collected data, particularly multi-regional data, that informs trial design and execution).

Unlike other public sector organizations that employ HQP, and unlike private sector organizations, the direct relationship between this training program and HDRN Canada permits the facilitation of potential project-based learning experiences. It would be more challenging to prescribe or support such projects for HQP at other employers, particularly those in the private sector, within this program.

**Can public sector HQP outside of HDRN Canada member organizations, or private sector HQP, get involved in project-based learning experiences?**

The program acknowledges that HQP from, for example, public sector clinical trial organizations may also be well situated to engage in projects that expand their organization’s ability to support pragmatic trials research. However, due to the breadth of host organizations employing these non-HDRN Canada public sector HQP, this will not be assessed at the time of application. As mentioned, the engagement of public sector HQP from outside HDRN Canada in project-based learning experiences will be discussed after acceptance into the program on a case-by-case basis.

Similarly, it is not anticipated that private sector HQP (who will not receive time release funding) will have the capacity to engage in project-based learning. Although, as with non-HDRN Canada public sector HQP, this can be discussed on a case-by-case basis after acceptance into the program.