Canada's Drug and Health Technology Agency

Special Report

Optimizing the Integration of Real-World Evidence as Part of Decision-Making for Drugs for Rare Diseases

What We Learned

The Need for Better Evidence

In October 2021, CADTH collaborated with the Canadian Institutes of Health Research, the Canadian Organization for Rare Disorders, Health Canada, and the RWE4Decisions international initiative to hold a Best Brains Exchange about the optimal integration of real-world evidence (RWE) for decision-making about drugs for rare diseases.

CADTH has been reviewing drugs for rare diseases through its reimbursement review processes since 2004 and has developed strong relationships with patient groups, care providers, and other stakeholders involved in decision-making. Through this experience, CADTH has recognized the need to develop knowledge, capabilities, and competencies related to RWE to meet the challenge of evaluating drugs for the treatment of rare diseases.

CADTH's value assessment considers not only clinical effectiveness and safety, but also the wider implications for the patient, family, caregivers, and the Canadian population at large; the economic implications and implementation considerations, such as ethical, social, cultural, and legal issues; as well as organizational and environmental impact. Much of this information is collected outside the context of a randomized controlled trial and requires engagement and collaboration with a wide variety of stakeholders.

The value of RWE was highlighted in a joint Health Canada–CADTH publication early in 2020. An RWE Steering Committee co-chaired by CADTH and Health Canada with representation from key pan-Canadian-level stakeholders has been meeting regularly to support the development of a framework to integrate RWE into regulatory and reimbursement decision-making (Appendix 1).

In the past year, the RWE Steering Committee has focused its efforts on drugs for rare diseases. In parallel, CADTH has been participating in several Canadian and international initiatives concerning standards, methods, guidance, and processes related to the use of RWE in the domain of health care decision-making.

"This is a watershed moment."
— Best Brains Exchange attendee

The 2-day Best Brains Exchange was attended by 137 participants from 12 stakeholder groups who were split into 5 breakout groups to discuss issues related to decision-making and real-world data for a fictitious case study.

The objectives of the Best Brains Exchange were to learn the value of RWE to fill evidence gaps, exchange different perspectives on the role of RWE, identify next steps in using RWE in decision-making, and identify and understand the challenges and opportunities related to multistakeholder collaboration.

The lessons learned through the Best Brains Exchange will guide CADTH to integrate evidence through a collaborative process to enhance decision-making throughout the life cycle of drugs for rare diseases.

Best Brains Exchange

During this event, participants, in multistakeholder breakout groups, discussed issues related to decision-making and real-world data for a fictitious case study concerning a gene therapy about to be submitted for regulatory approval for treatment of a rare pediatric condition.

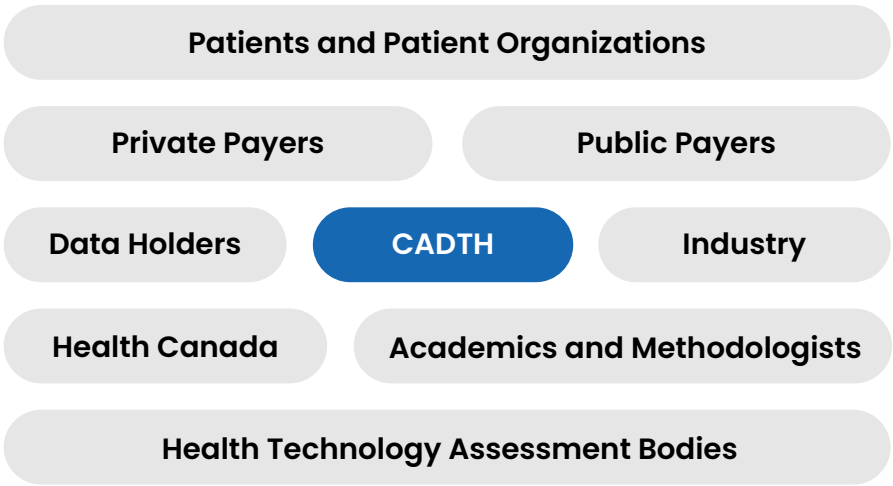
Objectives

- Learn about the potential value of generating RWE to fill gaps in evidence about the treatment of a rare disease
- Identify next steps toward strengthening RWE for decision-making about drugs for rare diseases in Canada (the highest priority objective for 41% of attendees)
- Hear and exchange different perspectives on the role of RWE in decision-making about drugs for rare diseases
- Identify and understand the challenges and opportunities related to multistakeholder collaboration that would successfully streamline processes for decision-making

What We Learned About RWE Stakeholders

In bringing together key stakeholders to participate in the Best Brains Exchange, we learned that to optimize integration of RWE in decision-making about drugs for rare diseases, we need to hear perspectives from a variety of different stakeholders.

Figure 1: Stakeholder Groups at the Best Brains Exchange



Post Best Brains Exchange

In addition to meetings with Health Canada, CADTH has held meetings with individual stakeholder groups to learn how to enhance and streamline multistakeholder engagement within the decision-making process for drugs for rare diseases.

Lessons Learned

Stakeholder Input

"Have the patients as key stakeholders; bringing the patient's voice can help identify the best outcomes to track."

Plan Real-World Data Generation Through Early and Iterative Multistakeholder Dialogue

What Data Are Needed to Resolve Uncertainties?

- Consider patient and caregiver perspectives by collecting data on what is a clinically meaningful change for them; their values, preferences, unmet needs, and key milestones; and burden on caregivers
- Collect qualitative data as well as quantitative data
- Collect disease-based outcomes rather than drug-specific outcomes
- Assess the comparative value of new therapies using data generated from single-arm studies and epidemiological data from a Canadian context concerning natural history and/or burden of disease
- Collect real-world data that includes important subgroups such as Indigenous Peoples and patients not included in trials
- Collect quality of life with standardized measures
- Measure economic outcomes (e.g., health care resource utilization data, cost-effectiveness, and cost-utility)

Stakeholder Input

"Even in rare diseases, there are rare subgroups of those rare diseases. We'd have a much better understanding of which patients benefit from the treatment versus the ones who don't if we had a disease registry that had been running for 10 or 20 years."

"Canada must collaborate internationally as it doesn't have the patient population size for rare diseases."

Canada Is Rich in Real-World Data Resources, But We Lack Awareness and Coordination

How to Find the Data We Need to Resolve Uncertainties

- Use data from existing disease-based registries to augment or complement existing information from other Canadian data sources (e.g., administrative data)
- Leverage existing data sources, data linkage infrastructure, and expertise (e.g., health care resource utilization data, claims data, industry and private datasets, electronic medical records, chart reviews, and other hospital data)
- Leverage international registry data and published scientific literature
- Collaborate with multiple stakeholders to develop new pan-Canadian–level registries:
  - one national rare disease registry (with both common and disease-specific data elements) OR
  - disease-specific registries that can be accessed through a single national platform

Stakeholder Input

“There is not a lot of robust data in rare disease, and RWE is not structured in the same way as clinical trials. So, we should consider establishing guidelines for clinicians and evaluators on how we should be analyzing RWE and what level of evidence is acceptable.”

Stakeholder Input

"[We] need a better spectrum, a better scope of natural history data…a way to get that is to have a registry that is independent of pharmacy."

"It is critical that a multistakeholder team comes together right at the inception of the design to say what kind of data is needed and what are going to be the caveats around the quality of that data."

We Need to Build Confidence in RWE for Decision-Making

How to Increase Multistakeholder Confidence in RWE

- Generate data that meet stakeholders' information needs for decision-making
- Develop an independent data generation process in which data are collected prospectively according to clear definitions
- Provide guidance on how to collect and analyze real-world data to ensure it meets standards for use in decision-making
- Use international data that are harmonized with Canadian data and contextualized to the Canadian health care setting
- Develop a multistakeholder consensus on the definitions of *high-quality*, *robust*, and *decision-grade* data
- Build in measures of safety (e.g., early warning signals) from the outset of data generation

Stakeholder Input

"Without trust, we can't go anywhere; we are profit-oriented organizations, but our intent most often than not is to really impact patients positively."

Successful Collaboration Requires Trust and Transparency

Develop a Framework for Multistakeholder Dialogue

- Involve all stakeholders as early as possible and continue iterative dialogue throughout the decision-making life cycle
- Involve regulators, health technology agencies, industry, clinicians, provincial payers, patient organizations, and academics as well as international partners by invitation
- Increase trust between different stakeholders through the development of collaborative relationships and transparent processes for generation of RWE
- Increase coordination between pan-Canadian health organizations to streamline the decision-making process
- Identify learning projects that could benefit from multistakeholder collaboration
- Develop a multistakeholder learning network

Stakeholder Input

“One of the biggest barriers in Canada is that some jurisdictions require informed consent of patients to capture their data. We have to recognize that data collection is not a medical intervention.”

Stakeholder Input

"Have 1 entity (arms-length organization) to manage the collaborations between people which is neutral and have common goals."

"It's very important to have that middle body of investigators that oversee collecting the data, analyzing the data, owning the data, and delivering those insights to payers or HTA authorities."

"[We] need a unique pathway for drugs for rare diseases."

Responsibilities of Stakeholders and the Role of RWE in the Decision-Making Process Need to Be Defined

Develop Governance for RWE

- Have a neutral arms-length organization with expertise in real-world data and multistakeholder collaboration to provide guidance and governance on integration of RWE for decision-making
- Require a clear governance structure for multistakeholder dialogue, including a standing office for patient and clinician engagement
- Establish multistakeholder agreement on information and choice of data elements, data collection protocol, and data analyses before data collection begins
- Define the different roles of each stakeholder group and how they can contribute to the generation and use of RWE
- Develop training tools to improve stakeholders' ability to participate in decision-making through a better understanding of the process and the role of RWE

Stakeholder Input

"The cost for the infrastructure for collection, integration, processing, even for providing platforms for collaborative analysis, are dropping with the standardization of the processes. The pain points are finding where those data are and gain access, striking those legal agreements, governance, setting standards, and figuring out the analysis. They need help from external partners to gain access to those datasets to do analysis and figure out what things can be teased out of the data which is the major cost point."

"Data needs to be used to full potential. In Canada, and especially with rare diseases, need to make sure full sample size across jurisdictions; this will require the political will to get there and starting upstream to ensure data holdings are designed in a way that they can be linked with administrative data that are routinely collected."

"Boots on the Ground" Needed in a National-Level Approach

Build an Infrastructure for Real-World Data Generation

A national-level approach is needed to leverage existing data infrastructure, overcome existing barriers to data access and interoperability of data from different sources, and address privacy issues to:

- learn from successful infrastructure models in other parts of the world and collaborate with those engaged in efforts to collect and use RWE
- explore funding models that use public-private partnerships
- develop pan-Canadian-level collaboration to increase the number of patients included in Canadian datasets
- build on existing "secure access environments" to facilitate sharing of data because privacy is a high priority due to the small number of patients with rare diseases
- consider the possibility of creating patient portals for patient-reported outcome measures and link these portals to registries.

Stakeholder Input

“[We] could have a multistakeholder group agree upfront at the time of approvals on what are the minimum outcomes to be studied. And then different groups could do their own studies, or it could be done collaboratively and then pick a body to own the data that is an expert. And then, in terms of who could act as the oversight body, it could be CADTH or another.”

Next Steps

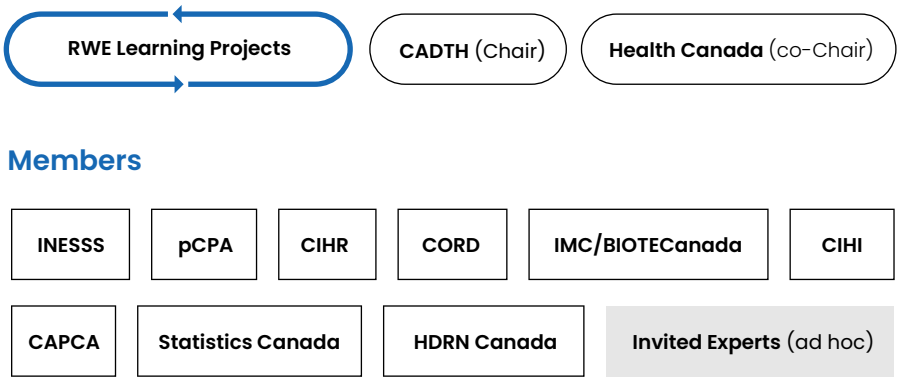
Based on these learnings, CADTH will integrate evidence within a collaborative process to enhance decision-making throughout the life cycle of drugs for rare diseases. CADTH has the necessary capacity, skills, and relationships to successfully enhance its role in health technology management to optimize the integration of different types of evidence into decision-making about drugs for rare diseases. To this end, CADTH will learn to:

- create a framework for continued evidence building
- engage with patient groups, care providers, data holders, academic methodologists, and industry representatives to give them more opportunity to work with regulators, health technology assessment organizations, and payers, and collaboratively plan and generate evidence that better supports decision-making throughout the life cycle of a drug
- enhance and expand its early scientific advice program to include requests after phase III for drugs for rare diseases
- enhance and expand the application of RWE in the review of initial submissions and reassessments for drugs and technologies
- use national and international guidance, tools, and initiatives to develop appropriate RWE guidance and tools for the Canadian context
- leverage relationships with rare disease registries and pan-Canadian data holders to enhance Canada's capacity to generate real-world data to inform decision-making
- apply the existing strengths of Canada's health care decision-making system and its established partnerships with other pan-Canadian health organizations, policy-makers, and payers to collaboratively address current limitations in infrastructure, governance, and processes.

A proposed framework to achieve these goals will be shared with stakeholder groups as well as members of the RWE Steering Committee.

Appendix 1: Real-World Evidence Steering Committee (Last Updated)

Figure 2: Steering Committee Membership



CAPCA = Canadian Association of Provincial Cancer Agencies; CIHI = Canadian Institute for Health Information; CIHR = Canadian Institutes for Health Information; CORD = Canadian Organization for Rare Disorders; IMC = Innovative Medicines Canada; HDRN = Health Data Research Network; INESSS = Institut national d'excellence en santé et en services sociaux; pCPA = Pan-Canadian Pharmaceutical Alliance; RWE = real-world evidence.

CADTH was established by Canada's federal, provincial, and territorial governments to be a trusted source of independent information and advice for the country's publicly funded health care systems. Health administrators and policy experts rely on CADTH to help inform their decisions about the life cycle management of drugs, devices, and services used to prevent, diagnose, and treat medical conditions.

CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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