Meeting Report

Second Canadian Cancer Treatment Hackathon

International Comparison

December 14, 2022

Virtual Meeting

Executive Summary

Colorectal Cancer Canada (CCC) held its second *Canadian Cancer Treatment Hackathon* on December 14th, 2022, to explore ways to improve public access to new medicines aimed at improving cancer survival and quality of life.

Twenty-four participants, from patient groups, industry, government, and government agencies, examined health technology assessment (HTA) processes from five jurisdictions (England / Wales, France, Germany, Italy, and Australia), and explored the applicability of key elements within the Canadian context.

The following success factors were identified from these jurisdictions as potentially applicable and relevant to the Canadian context:

- *International collaboration with Project Orbis*
- *Canadian Personalized Healthcare Innovation Network (CPHIN) in Canada to support real-world evidence (RWE)*
- *Best practices from the Canadian Agency for Drugs and Technologies in Health's (CADTH's) "learning projects"*
- *Transparency of pricing*
- *The "innocent before proven guilty" concept of medicine adoption*
- *Requirement for the collection of data across clinicians and patients; cancer system collection versus manufacturer collecting*
- *More interaction between the HTA bodies and the payers/negotiators*

Outcomes from this second Hackathon are building blocks for the development of tangible actions to create an ideal model for a new drug review process in Canada.

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1.0 Introduction

Canadians with public drug coverage continue to have restricted or delayed access to new therapies due to the multi-layered sequential review processes, which inform public drug plans' decisions on whether to provide access and reimbursement to new medicines.[1]

On December 14, 2022, Colorectal Cancer Canada (CCC) held its second *Canadian Cancer Treatment Hackathon,* which aimed to ideate an improved drug review process, by identifying critical success factors and effective guiding principles of the health technology assessment (HTA) in five other jurisdictions:

1. England / Wales – NICE (National Institute for Health and Care Excellence)
2. France - HAS (*Haute Autorité de santé*)
3. Germany – IQWIG / G-BA (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen;* Institute for Quality and Efficiency in Healthcare)
4. Italy - AIFA (*Agenzia italiana del farmaco* / The Italian Medicines Agency)
5. Australia – PBAC (Pharmaceutical Benefits Advisory Committee)

The Hackathon participants, including patient groups, industry, government, and government agencies, brainstormed in breakout sessions, and shared their views in a plenary session (Appendix A – Second Hackathon Agenda).

For each jurisdiction, the following questions were explored:

- *What are the critical success factors and guiding principles for each jurisdiction?*
- *How could these be applied in the Canadian context?*
- *Identify questions or issues for further exploration.*

To encourage inclusive and open dialogue, the ***Chatham House Rule*** was used, its guiding spirit is to share the information received, but not to reveal the identity of who said it.[2]

1.1 Background

It is estimated that two in five Canadians will receive a diagnosis of cancer in their lifetime and that one in four Canadians will die of cancer.[3] New and often precision medicines are helping patients with early stages of cancer and have improved overall survival and quality of life. Beginning in 2019, uncertainties surrounding new regulations to change the way the Patented Medicine Review Board assesses drug prices led to delays in planned launches of new medicines inCanada, according to a survey of the industry conducted by Life Sciences Ontario (LSO).[4]

As in many other countries, the processes of reviewing drugs for public reimbursement are complex; however, Canada's system is more complicated with several levels and jurisdictions regulating, reviewing, negotiating, and funding medicines.[5] Unfortunately, Canada ranks third worst when it comes to public reimbursement of drugs. Health Canada approval time averages approximately 248 days after the first global approval. It then takes 199 more days for the drug to be launched in Canada, with access only through out-of-pocket payment or through private insurance only. Most importantly, it then averages 559 more days (1.5 years) for the drug's public reimbursement in Canada, which enables access for most Canadians.[6] Therefore, Canadians who rely on public health payers to access medicines must wait significantly longer compared to individuals in other countries around the world,[7] and Canadians who rely on private insurance plans.[1]

In recent years, there has been an increase in global regulatory alignment through Project Orbis (https://www.canada.ca/en/health-canada/services/drugs-health-products/international-activities/project-orbis.html) with the Food and Drug Administration (FDA) and other regulatory agencies. These collaborations are welcomed because they are designed to improve efficiency and timely access for patients.[8] Similar collaborations can be explored amongst Canadian HTA agencies to optimize performance standards and reasonable timeframes from Health Canada approvals to provincial reimbursement listings and patient access (Time to Patient).

The world only required one year to develop COVID-19 vaccines, but it takes 12 years on average to bring effective cancer drugs from discovery to approval and even longer to reimbursement.[5] A study showed that there was an average of 80,000 years of life lost for every year of delay in drug approval.[9] Therefore, the regulatory framework must innovate to find strategies to safely speed access as the number of potentiallife-years lost during the drug regulatory and funding process in Canada is substantial.

1.2 International HTA Bodies

In terms of HTA organizations and processes, some are more centralized – England / Wales, Italy, and Australia – while others are more decentralized – France, Germany, and Canada (Table 1). Not all countries require a cost-effectiveness model to be submitted by the manufacturers; however, most of them have an economic component to their evaluation (e.g., a budget impact analysis). Most of the countries that were analysed focus on clinical benefit. Data from RCT remain the gold standard; however, real-world evidence (RWE) studies may be necessary as additional evidence to be collected in the process of price negotiation.

Table 1. International HTA Bodies[10]

Country	HTA body	HTA Process	Willingness to Pay Threshold
England/ Wales	NICE	NICE conducts the HTA and requires the cost-per-QALY threshold be met for a recommendation to list.	£20,000 to £30,000 per QALY*
France	HAS	HAS conducts an HTA on all new drugs. A pricing committee negotiates the price and health insurers (UNCAM) decide reimbursement rate.	No threshold
Germany	IQWIG/ G-BA	IQWiG typically conducts an HTA on all new drugs and G-BA decides level of added benefit. Exception is orphan drugs where G-BA conducts HTA. Following G-BA decision, health insurers (GKV-SV) negotiate price.	No threshold
Italy	AIFA	AIFA conducts HTA and price negotiations.	No threshold

Country	HTA body	HTA Process	Willingness to Pay Threshold
Australia	PBAC	PBAC conducts the HTA, and Department of Health conducts the price negotiation (typically in alignment with PBAC recommendation on pricing)	No threshold
Canada	CADTH	CADTH conducts HTA for all provinces and territories apart from Quebec. pCPA conducts price negotiation. Federal/ provincial drug plan decides reimbursement	$50,000 CAD per QALY
	INESSS	INESSS conducts HTA for Quebec. pCPA conducts price negotiation	No threshold

*NICE published an incremental cost-effectiveness ratio (ICER) threshold for orphan medicinal products at **£100,000** per QALY gained, in addition to a QALY weighting dependent on the QALY gain offered by the new treatment (2017).

Canadian HTA overview:

- CADTH conducts HTA for all provinces and territories apart from Quebec, which is conducted by the *Institut national d'excellence en santé et en services sociaux* (INESSS)
- Priority review processes are available for regulatory and HTA review, but no public coverage (funding) is available for new medicines before the completion of the HTA review
- Innovative market access agreements, such as performance-based and outcomes-based agreements, have been negotiated in Canada post-HTA
- Canada has ranked 18 of the 20 Organisation for Economic Co-operation and Development (OECD) countries in terms of access to oncology drugs[11]
- INESSS is looking at the "promise of therapeutic value" ("*promesse de valeur*") but no results yet[12]
    - Another opportunity includes the manufacturer-funded Patient Support Programs (PSPs) similar to compassionate access schemes in other countries to facilitate access during the pre-listing period
    - PSPs have rapidly increased, with approximately 175 oncology PSPs reported in Canada.

2.0 England / Wales – NICE

2.1 Hackathon Outcomes

The England / Wales HTA process was discussed among the hackathon participants, and the following comparison points were highlighted.

Guiding Questions	England / Wales (NICE)
What are the critical success factors and guiding principles?	• Early access drug funds – various ways that do not exist in Canada yet. • Patient organization in the UK is real-time involved in the HTA decision-making process. • Stakeholders are willing to engage and lead efforts to break down silos. • Managed entry agreements. • RWE frameworks are established.

How could these be applied in the Canadian context?	• Is there a made-in-Canada version of early access funds? Rare Disease Drug Strategy funding?
	• Explore and consider managed entry agreements:
	  ○ An older agreement exists (e.g., INEESS)
	  ○ How can we learn from what we are doing to unpack how they are working?
	• Incorporate leadership from all stakeholders to manage conflicts.
	• Additional collaboration is needed across agencies, organizations, etc.
	• Innovative methods for replacing previously implemented approaches.
	• Building on the success of Project Orbis
	  ○ Help move through prioritized files
	• Fund / financing opportunity to start access earlier→ addresses financial risk.
	• Potential trusted organizations such as CPHIN and Exactis Innovation could support RWE.
	• Registries → consider how data is collected, validated, and verified.
	  ○ Establish collaborative approach in Canada.
	  ○ Build on CADTH's "learning projects" / "learning systems" approach Attempt to learn and recalibrate.
	• Incorporate to CADTH's RWE framework consultation
	  ○ Due early January 2023 → phase two on policy/approach.

Questions for research / further exploration	• Await feedback from pCPA office to clarify the structure and opportunities of managed entry agreements.
	• Examine opportunities within CADTH framework:
	  ○ Are we going to re-define the entire approach or include other sources (e.g., hospitals records; AI, PSPS, etc.) for real-world data?
	  ○ What type of data is required for this framework?
	  ○ Can this data be collected beginning with clinicals trials?

2.1 Additional Discussion Points

Most of the points discussed in sub-groups and the plenary session are conveyed in the above table. One participant added that Canada should consider making a statement similar to that from the National Health Service (NHS) below:

"*Make the UK the best place in the world to discover, develop, test, trial, launch and adopt new treatments and technologies, by creating a forward-thinking commercial environment where the NHS can strike flagship deals and where proven, clinically, and cost-effective innovations are rapidly adopted and spread across the country to bolster the health of the nation, deliver greater value for the taxpayer and stimulate economic growth*."

3.0 France – HAS

3.1 Hackathon Outcomes

The discussion comparing France HAS to Canada led to the following main points.

Guiding Questions	France (HAS)

What are the critical success factors and guiding principles?	• Pathway for early access:
	  ○ Selective about the type of drugs that go through the early access program
	  ○ Establish clear list of five criteria to access faster pathways
	  ○ Recognition of the necessity for faster pathways for patients → especially when there are fewer alternatives for promising therapy

How could these be applied in the Canadian context?	• Better define which medicines could be put through an early access program • Project Orbis could be the source for defined criteria for faster access • Federal government leadership in this area →shift from national pharmacare to this approach • Assess how CADTH could shift to a "managed 'yes' → allow more evidence while it's being collected- what is the risk that industry is willing to take on in the interim?
Questions for research / further exploration	• Assess the challenge of FDA and US developers not respecting the requirements of evidence development with faster approvals • Recognize resource constraints in the system across approvals, evaluations, negotiations ○ How are those jurisdictions handling those capacity restrictions? • What was the political motivation to develop the health innovation plan in the UK?

4.0 Germany – IQWIG / G-BA

4.1 Hackathon Outcomes

Germany - IQWIG / G-BA, in comparison to Canada HTA bodies, was assessed as follows.

Guiding Questions	Germany (IQWIG / G-BA)

What are the critical success factors and guiding principles?	• Cost certainty and sustainability factors:
	  ○ The concept of "fund all drugs at full freight" especially with the challenge of de-listing plus sustainability (affordability across Canada variable)
	• Lack of embracing of RWE may make it less applicable
	• Lack the challenges associated with algorithms
	• Receive funding from German sickness funders:
	  ○ Fund patient organizations that do not have funding from pharmaceutical companies – if you want to participate in HTA you get funding from the German sickness funds
	• Negotiation takes place after six-month period is completed:
	  ○ Assess data versus comparator, with a required price reduction
	  ○ The manufacturer may leave the market and abandon the patient (is this a critical failure factor?)

How could these be applied in the Canadian context?	• The context is not as applicable as other regions. • The general concept of accelerating access is valid → need to pick which aspects to pull into Canada. • Transparency of pricing → list price is public and that's what's paid (could make it hard to pull in). • The "innocent before proven guilty" concept of medicine adoption in Germany: ○ Six-month automatic access, as opposed to waiting in our legal system. • The significance of time-frames → if we receive a positive funding recommendation from HTA→good time-point to do a short conditional approval(note: most of the medicines do get an approval).

Questions for research / further exploration	• Match the programs to patient outcomes → holistic model that includes rehab, etc.
	  ○ How have the outcomes changed? Get to the best outcomes in the world.
	• Assess how many medicines are de-listed or pulled out of the country (11%? – research further 7% oncology; remainder in non-oncology)
	  ○ Are these numbers super problematic?
	  ○ The concept that patient groups at large would not accept patient access may need to be validated - who is that outlier patient and how?

4.2 Additional Discussion Points

- A coverage rate of 80% has been reported for oncology drugs.
- Faster access is not always better for patients. The focus is to be kept on better trials, better comparisons, and better data.
    - The goal is not to improve the rating; it is to get the best comparative therapy, at the soonest possible time.
- Most steps are completed at the national level, but crucial listing decisions are made in siloes.

5.0 Italy – AIFA

5.1 Hackathon Outcomes

The discussion about Italy AIFA led to the following considerations.

Guiding Questions	Italy (AIFA)

What are the critical success factors and guiding principles?	• Incredible data collection:
	  ○ Registries for every indicator for every drug
	  ○ Captures RWE to address some of the uncertainties
	  ○ Funded by manufacturers but administered by government.
	• Value-based assessments are conducted.
	• Attention on the patient registries, in that they are not the solution:
	  ○ Rebates are difficult to achieve, and delisting is challenging if the data doesn't hit the metrics
	• Online registries
	• Acceptance of some uncertainties
	• Exceptional patient approaches
	• National funding dedicated for equitable access
	  ○ Caution: facilitated through hard revenue caps

How could these be applied in the Canadian context?	• Uncertainties are a challenge → can be addressed through manufacturers in their CT designs
	  ○ RWE is not meant to replace RCTs
	  ○ RWE addresses uncertainties around the demographic of the drug, not to replace RCTs
	• Canadian RWE development through PSPs versus Italy where it's administered by government
	• The collection of data across clinicians and patients:
	  ○ Cancer system collection in addition to manufacturer collecting (PSPs)
	• Online registries could be incorporated in Canada
	• Note: Italy allows for regional decisions and hospital-based funding opportunities (second level formulary management, equity can be an issue)

Questions for research / further exploration	• Emphasize attention on patient access – not just faster access → how can this be utilized in a Canadian paradigm?
	• Assess how "exceptional patients" can be included – beyond the HTA recommendation:
	  ○ When a patient doesn't fit into the algorithm or approach, Canada has a policy of "if you don't fit, we deny"
	  ○ Similar issues are not seen in other countries → there isn't a "one-size fits all drug"
	• Consider the GRADE framework – has it made a difference in Italy – is it a barrier / enabler?
	• Consider surrogate endpoints are utilized within performance-based agreements

5.2 Additional Discussion Points

In addition to the points identified above, the following was also discussed:

- Italy has web-based patient registries where patients can directly input their outcomes. This is something that patients in Canada have identified as potentially good to have.
- With regards to registries, for example for rare diseases, national-based registries are governed by the public sector and utilization to inform access may be more well-received.
- In relation to RWE, Italy does not have a threshold of cost-effectiveness, like Canada and UK. CADTH focuses on a cost-effectiveness model, which are based on assumptions, whereas Italy considers clinical effectiveness. Italy has a performance-based agreement.

6.0 Australia – PBAC

6.1 Hackathon Outcomes

Australia PBAC may be compared to Canada HTA bodies as follows.

Guiding Questions	Australia (PBAC)
What are the critical success factors and guiding principles?	• Access to medicines data sharing and transparency • More interaction between the HTA bodies and the payers / negotiators • Priority review opportunity at HTA is good, as long as it's based on specific criteria. • Provisional approval process • Increasing patient involvement
How could these be applied in the Canadian context?	• Each of the aforementioned ideas should be considered for adoption in Canada • Performance-based agreements discussion is similar in Canada as with Australia, even if it's not explicit; it's a "last straw" to get to an agreement – consider how to proactively facilitate access • Establish a catalogue of what data is available and useable and guidelines around that

Questions for research / further exploration	• How does Australia and other countries support the data collection and use that allows them to administer early access schemes?
	  ○ Potentially challenging in CDA because of how dispersed we are
	  ○ Examine how to organize in Canada around a "proxy" framework for some jurisdictions to represent the rest of the country
	• How do we share the cost of RWE studies?

6.2 Additional Discussion Points

The attendees shared the following additional considerations:

- Australia is similar to Canada in terms of timelines, as well as the use of evidence. However, Canada has more innovative agreements, such as performance or outcome-based agreements.
- The negotiation should be built on a guiding principle that will allow for equities in how the funds are being treated. Better guidelines are needed on how provisional approval would work –similar to project Orbis.
- A lot of Australian accountability and responsibility around the data collection does fall on the manufacturers. Some manufacturers have had an unpleasant experience with how much it costs. However, Canada's ability to collect data is very fragmented.

7.0 Hackathon Additional Comments

We aim to **collectively come one step closer to creating an ideal model for a new drug review process in Canada:**

- Improving patient outcomes is the priority.
- If Canada were to have a cancer drug fund, operating at the national level would have to be defined.
- A link is needed between NOC/c program and HTA reviews to ensure the NOC/c is a practical tool to facilitate access, with a proper risk-sharing mechanism to be put in place.

Follow-up discussions are needed in this Hackathon series to continue to develop concrete actions/innovations to improve cancer patient outcomes.

Appendices

Appendix A – Second Hackathon Agenda

10:30 am	**Welcome remarks**	**Barry Stein, Colorectal Cancer Canada**
10:35 am	Roundtable introductions & Review agenda	Bill Dempster, 3Sixty Public Affairs
10:45 am	Overview of selected international HTA agencies and Real-World Evidence	Tara Cowling, President, and Managing Principal, Medlior Health Outcomes Research Ltd.
11:00 am	Breakout groups • Small, facilitated group sessions to identify and develop a list of critical success factors and guiding principles in two pre-assigned jurisdictions, and discuss their applicability in Canada.	Facilitated by Bill Dempster, Kerry Allerton, Gerry Jeffcott, and Robert Bick
11:40 am	Plenary • Each group to present the contents of their discussion. Goal is to create one master list of critical success factors and guiding principles.	Bill Dempster, 3Sixty Public Affairs
12:25 pm	Summary and next steps	Bill Dempster, 3Sixty Public Affairs
12:30 pm	Session adjourns	

Appendix B – Links to Pre-Reads

1. The Pathway for New Cancer Drug Access in Canada: https://www.mdpi.com/1718-7729/29/2/41
2. Review of HTA outcomes and timelines in Australia, Canada and Europe 2017-2021: https://cirsci.org/download/cirs-rd-briefing-86-review-of-hta-outcomes-and-timelines-in-australia-canada-and-europe-2017-2021/
3. Procedures for CADTH Reimbursement Reviews, September 2022: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.cadth.ca/sites/default/files/Drug_Review_Process/CADTH_Drug_Reimbursement_Review_Procedures.pdf

[1] https://www.frontiersin.org/articles/10.3389/fphar.2019.00196/full

[2] https://www.chathamhouse.org/about-us/chatham-house-rule#:~:text=The%20Rule%20reads%20as%20follows,other%20participant%2C%20may%20be%20revealed.

[3] Canadian Cancer Statistics Advisory Committee in collaboration with the Canadian Cancer Society, Statistics Canada and the Public Health Agency of Canada. Canadian Cancer Statistics 2021.
Toronto, ON: Canadian Cancer Society; 2021. Available at https://cdn.cancer.ca/-/media/files/research/cancer-statistics/2021-statistics/2021-pdf-en-final.pdf

[4] https://lifesciencesontario.ca/wp-content/uploads/2021/09/Cast-Our-Pebble-Rare-Disease-Paper-Final.pdf

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6964142/#onco13086-bib-0001

[6] https://www.youtube.com/watch?v=PA9yOI_-IE4

[7] Millson, B., Thiele, S., Zhang, Y., Dobson-Belaire, W., and Skinner, B. (2016). Access to New Medicines in Public Drug Plans: Annual Report 2016. Ottawa, ON: Innovative Medicines Canada

[8] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8947363/

[9] Stewart, David. Short Primer on Why Cancer Still Sucks. Tellwell Talent, 2022.

[10] Tara Cowling, Founder, President, and Managing Principal, Medlior Health Outcomes Research Ltd. Passcode: ^rG7tL.A
https://3sixtypublicaffairs.zoom.us/rec/share/mp6SBYab8uI8O5I6QuBJ04kFzUTL60cdf9Pk2zilOy_oenyzTSu0zbAkSCff9ek.VbotoEhODWXIIYXD

[11] CADTH-TTL-8.5x11 (innovativemedicines.ca)

[12] CAPSULE PHARMACOTHÉRAPEUTIQUE (inesss.qc.ca)