THE STATE OF HEALTH TECHNOLOGY ASSESSMENT

BY MICHELE CLEARY

AS NEW DRUGS AND HEALTH TECHNOLOGIES EMERGE, often with exceedingly high price tags, health payers and other decision makers are increasingly reliant on health technology assessment (HTA) to navigate the balance between access and affordability. Health payers, hospitals, doctors, medical groups, and more are wrestling with the same basic questions of how to make the best use of limited resources, and how to try to make sure that prices align with the benefits for patients.

Healthcare decision makers are increasingly reliant on HTA as a way to evaluate clinical and economic evidence to help improve cost containment and quality, guide more effective delivery of care, and decrease the use of programs or treatments that are ineffective. This month's feature article examines differences in how HTA has been implemented globally, highlighting common concerns and future objectives.

Canada: CADTH and Beyond

Brian O'Rourke, BSc (Pharm), PharmD, president and CEO of the Canadian Agency for Drugs and Technologies in Health (CADTH), summarized his view of HTA organizations around the world, "If you've seen one HTA, you've seen one HTA. We all differ based on our governance, whether we're part of government or not-for-profit, how we're funded, the transparency that we have, and the scope of work. Some are specifically focused on devices and some are specifically focused on drugs and some have a much broader portfolio covering both and even public health interventions."

O'Rourke considers CADTH to be more of a full-service HTA agency, evaluating pharmaceuticals, medical devices, medical, dental, surgical devices, procedures, programs and diagnostics—basically, any clinical intervention where there is a need for evidence to support a reimbursement of that particular intervention.

Established in 1989 as the Canadian Coordinating Office for Health Technology Assessment (CCOHTA), CADTH originated as an independent, not-for-profit government organization aimed at improving coverage decisions to ensure appropriate and cost-effective healthcare for all Canadians.

Canada's Common Drug Review

In the 1990s, CCOHTA expanded its scope to include pharmaceuticals, incorporating economic methodologies to its clinical evaluations. CADTH created the Common Drug Review in 2003, providing a pan-Canadian approach to reviewing new drugs and new drug indications. The Common Drug Review is firmly established as part of Canada's drug review process. Upon receiving market approval from Health Canada, manufacturers make a submission to the Common Drug Review for an HTA recommendation. Public drug plans across Canada use these recommendations in making their coverage decisions, with the Common Drug Review recommendation often forming the basis for drug price negotiations by its pan-Canadian Pharmaceutical Alliance.

Patient input is sought for each drug that is reviewed by the Common Drug Review. This input is discussed during expert committee deliberations and reflected within the final reimbursement recommendations. The final recommendations are published in full so patients can understand how their input was incorporated into the process.

Commitment to transparency

Today, CADTH's recommendations extends beyond traditional assessments of new drugs and technologies and now advances a life-cycle approach to HTA, providing early scientific advice to industry, undertaking reassessments of drugs after they are listed, conducting condition-level reviews, and integrating real-world evidence into drug reviews.

"One of the things we learned very early on as the agency evolved through the years was the need to provide methodology guidelines and be very transparent about the work we do," O'Rourke said. CADTH publishes its assessment guidelines (now in its 4th edition), outlining how it conducts its economic evaluations for all of the technologies, including orphan drugs. O'Rourke noted that these are downloaded 10,000 to 12,000 times every year in Canada.

Expanding stakeholder engagement

To expand transparency, CADTH launched its patient engagement program for its drug reviews in 2010 to ensure that patient perspectives regarding orphan drugs, gene and cell therapies, and other disruptive technologies were captured.

CADTH now includes patient and community advisory committees with broad representation from different disease areas, as well as different cultures from across Canada to identify "patient-important" outcomes and expectations for new treatments and to inform the development of research protocols. "We engage patients to help better understand the outcomes that are important to them, and that data need to be captured in that clinical trial," O'Rourke said. "They also provide good advice on how we can best engage with the patient community."

However, going forward, he wants CADTH to expand involvement of other stakeholders, namely clinicians, physicians, pharmacists, nurses, and physiotherapists. "If the policy and the clinical practice go hand in hand, it's a much smoother transition into the reviews and the reimbursement recommendations," said O'Rourke.

Other Canadian approaches: HTA in British Columbia

HTA in Canada extends beyond CADTH, as a recent survey identified 44 different HTA organizations within Canada. One such example is the University of British Columbia's Therapeutics Initiative. In 1994, the British Columbia Ministry of Health, concerned about both the increased use of prescription medications and the introduction of new (and often expensive) drugs, partnered with independent, academic researchers at University of British Columbia to establish the Therapeutics Initiative.

Therapeutics Initiative created an outcomes-based, decision-making framework that supports responsible funding decisions in the province, using published literature, Cochrane Collaboration meta-analyses, and scientific material presented by the pharmaceutical industry. Mitch Moneo, BA, Assistant Deputy Minister, Pharmaceutical Services Division, noted, "The key consideration of public coverage in British Columbia is quality and published evidence of comparative mortality or morbidity benefit."

Prioritizing patient voices

British Columbia's Drug Benefit Council reviews evidence generated by CADTH and Therapeutics Initiative, while also considering input garnered from patients, caregivers, and patient groups submitted through an online questionnaire called Your Voice. Input from these critical stakeholder groups helps contextualize the national CADTH recommendations for British Columbia.

As with many HTA organizations, orphan drugs pose a significant challenge to Moneo's organizations. The evidence associated with the regulatory approval of most orphan drugs is very sparse, creating a lot of uncertainty for public and private payers. Yet, evaluation of how these types of drugs and disruptive technologies support patient outcomes is consistent with the core values of the Canadian system.

Opportunities and challenges of real-world evidence

British Columbia has joined other Canadian jurisdictions to explore wider use of real-world evidence for their HTA evaluations. "The methods for selecting candidates and assessing the real-world evidence are being explored," Moneo said. "For example, methods for rapid expected value-of-partial-perfect-information are used to determine (at an early analytic stage) if there is a positive social value to real-world evidence generation through research-oriented market access; methods for simulation models for drug uptake and real-world evidence generation are being constructed to identify the optimal design and terms of a market access agreement; and methodologies to facilitate iterative Bayesian updating of prior parameter distributions (including bias adjustment and advanced evidence synthesis components) are being explored.

However, Moneo sees limits to the use of real-world evidence in his organization. "The concept of using pragmatic trials and patient registries and routine administrative databases to assess the impact of therapy may have some merit, but what it means in terms of scientific rules of evidence isn't clear." He continued, "It's a bit troubling that there is a growing expectation that HTA organizations and payers will now undertake work that has essentially been the domain of traditional phase III clinical trials."

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> – Brian O'Rourke

Regulatory changes on the horizon

Moneo did highlight upcoming regulatory changes in Canada. On July 1, 2020, a newly amended Patented Medicines Regulations will come into effect, establishing new value thresholds.

Canada's Patented Medicines Review Board is proposing a guideline that sets a pharmacoeconomic value threshold of $60,000 per quality-adjusted life year, adjusted by market size. Also noteworthy, for patented medicines with an estimated total prevalence no greater than 1 in 2000 across all approved indications, the allowable drug price will be set at 50% above the threshold (but further adjusted for market size if the patented medicine realizes annual revenues in excess of $12.5 million). In theory, this national value threshold may mitigate the burden of risk associated with orphan and other high-cost drugs, but not without controversy. Industry and patients have expressed fear that regulatory value thresholds will impede Canadians' access to important medicines.

Taiwan

Taiwan has been conducting HTAs since 2007 following the creation of the Division of Health Technology Assessment within the Center for Drug Evaluation. The HTA findings support the National Health Insurance Administration's reimbursement and drug coverage decisions (the group is not directly involved in price determination). "The ultimate goal of the HTA program is to support the health authority to maximize public health benefits," noted Churn-shiouh Gau, PhD, Executive Director of the Center for Drug Evaluation.

The HTA team primarily assesses the clinical comparative effectiveness and economic evaluation of new drugs and medical devices, providing pre- and postmarket evaluations to support the National Health Insurance program's decision making. The team also conducts various HTA-related research projects commissioned by other health authorities under the Ministry of Health and Welfare. The HTA program was extended to include medical devices in 2011, medical services in 2014 , and social care in 2016.

Patients views have long been a national priority

Gau stated that patient engagement has been a priority since 2013, when the National Health Insurance Act mandated that patient participation in its insurance coverage decisions. Patient participation in HTA began in 2015. The online platform, Patient

Opinions for New Drugs and New Medical Devices, allows patients and advocacy groups to provide opinions about drugs and medical devices currently being evaluated.

Since 2016, more than 20 face-to-face talks or focus groups have been hosted by the Center for Drug Evaluation HTA team, with more than 300 patient participants sharing their perspectives. Participating groups have included the Chinese National Association of Deaf, Taiwan MPS Society, the Rheumatoid Arthritis Aid Group of the Republic of China, and the Hemophilia Association of Taiwan.

United States: ICER

As with much of its healthcare system, the United States has taken a different approach to HTA. No formal health technology assessment body resides in the United States to evaluate the value of new drugs. Instead, the United States relies on multiple stakeholders (eg, pharmacy benefit managers, payers, providers, and manufacturers), each using different measures to determine the value of new products. However, as payers and policy makers have begun to scrutinize prescription drug prices, Steven D. Pearson, MD, MSc, founder and president of the Institute for Clinical and Economic Review (ICER), has filled the void of a designated HTA in the United States.

Like previously mentioned HTA organizations, ICER uses publicly available information, clinical trials data, and other manufacturer-provided information to conduct pharmacoeconomic analyses to inform payers and policy makers.

> In our common quest to find the ideal in fair pricing, fair access, and future innovation, we have to learn from each other. –Steven D. Pearson

HTA in United States mirrors its decentralized health system

However, it is also a reflection of the US health system. Pearson noted, "In the United States, with a very chaotic or pluralistic insurance system and with a generally higher distrust of centralized decision making over markets, it's been more natural for the system not to evolve towards having a centralized kind of federal process for evaluating evidence, whether you want to call it comparative clinical effectiveness or cost-effectiveness." He continued, "I think we're on our own unique, distinctive journey. The United States is a very different system and we can't just copy and paste what other countries do."

Addressing the question of "fairness"

ICER was founded as a laboratory to experiment with methods to determine and discuss value so that the public could participate in creating a higher value health system. Pearson spoke of the "great eternal question" of HTA, that is, Is it fair to everybody? Sensitive to the issue of fairness, ICER adheres to a very formal process of introducing their methods to public comment.

However, Pearson noted the challenge with engagement in HTA is when and how long to engage. "It's still been a learning process for them and for us, ensuring that we make that engagement as meaningful as possible. We have to start out saying that we really don't know the diversity of experience with this condition, what value really feels like to patients and to their families and what do we, and what can we learn from that?"

Pearson continued, "We almost always find that some of the most important aspects of value aren't captured in the clinical data from the trials that are done before FDA (US Food and Drug Administration) approval. And so we're trying to figure out how to either qualitatively or quantitatively build that into our assessments so that ultimate decision makers can really keep that in view. So, we really need the patients, and as time goes on, we need to continue to find ways for their input to be tangible, visible, and very influential."

Importance of transparency

Pearson highlighted ways he felt ICER is distinctive, stressing transparency and stakeholder engagement. "Our approach allows end users to feel confident that our reports have gone through a rigorous scientific process, as well as a full public engagement process. I think that's the key to our being distinctive rather than the kind of cost-effectiveness modeling that we do, which others can do as well." He continued, "We do have some distinctly different methods for looking at treatments for ultra-rare disorders, as well as ones that we've just announced this past year on high-impact single- or short-term therapies, things that some people would call potential cures."

Pearson noted that ICER uses state-of-the-art cost-effectiveness methods, embedded in a kind of "distinctive approach to public deliberation that acknowledges other dimensions of value and contextual issues." ICER publishes its formal list of criteria on its website, noting how it prioritizes those technologies where there will be a paradigm shift in care. He said that he finds few groups doing that kind of constellation of approaches, creating trustworthy, publicly available research. And that was by intent. "We really wanted our work to be the starting point for a public kind of deliberation on value." He continued, "I think we've gained a stature through our experience and through people's view of the scientific rigor of our work. That means that there really aren't other groups that are doing work for applied health technology assessment in the same way."

Future applications of real-world evidence

Pearson stated that ICER tries to keep its ears open and respond honestly to a criticism. He added, "Criticism is very healthy, and we don't seem to ever be short of it. That's one of the benefits to us not being a governmental agency. We certainly feel like we can be flexible and listen and experiment in ways that hopefully can be quick and responsive to the needs of the, the communities that we hope to, to help."

Like Moneo, Pearson expects real-world evidence to play a larger role in HTA despite its challenges. "It's going to be a challenge for us in terms of how often we update our reviews, what data sources are used, and how do we do it in a way that is transparent and trustworthy. But my gut tells me we are going to continue to innovate and have exciting new platforms for treatment that are going to challenge us to figure out how to use them clinically and how to pay for them is going to increase the need."

"Ultimately it does serve everyone's interest to have good evidence, to have high bars for good evidence, to really reward good science, good innovation, and to reward it in proportion to the ability to help patients," he concluded.

Future challenges

With a consistent stream of innovative new therapies, HTA organizations are challenged to determine ways that health systems can pay for new technologies in a sustainable way. And the pressure for HTA will grow with the threat of economic recessions. These market forces will increase the pressure for HTA organizations to figure out how to align the prices better with the benefits to patients and to make sure that this continues to provide enough incentives for robust innovation.

"How we are going to pay for all of these technologies in a sustainable way? That's going to require new ways of thinking, new managed entry agreements, new assessments across the life cycle of technology," said O'Rourke. "No one agency is going to be able to do this themselves."

Many international jurisdictions have developed and implemented new approaches to assess value with various degrees of success. We need to learn from others' experience and share knowledge. Pearson summed up things this way, "In our common quest to find the ideal in fair pricing, fair access, and future innovation, we have to learn from each other. I think the positives can certainly outweigh the short-term contest that we often feel that we're engaged in when we're talking about one specific drug or one specific other kind of intervention."

About the Author

Michele Cleary is a HEOR researcher and scientific writer with more than 15 years of experience in the healthcare field.

Suggested reading:

Value in Health Themed Section: HTA Around the World: Influences of Culture, Values, and Institutions [January 2020]

- HTA Around the World: Broadening Our Understanding of Cross-Country Differences
  Aleksandra Torbica
- The Emerging Social Science Literature on Health Technology Assessment: A Narrative Review
  Olga Löblová, Trayan Trayanov, Marcell Csanádi, Piotr Ozierański
- Differences in Health Technology Assessment Recommendations Among European Jurisdictions: The Role of Practice Variations
  Rick A. Vreman, Aukje K. Mantel-Teeuwisse, Anke M. Hövels, Hubert G.M. Leufkens, Wim G. Goettsch
- Do Social Values and Institutional Context Shape the Use of Economic Evaluation in Reimbursement Decisions? An Empirical Analysis
  Aleksandra Torbica, Giulia Fornaro, Rosanna Tarricone, Michael F. Drummond
- Economic Evaluation for Pricing and Reimbursement of New Drugs in Spain: Fable or Desideratum?
  Juan Oliva-Moreno, Jaume Puig-Junoy, Marta Trapero-Bertran, David Epstein, Carme Pinyol, José Antonio Sacristán
- Increasing the Legitimacy of Tough Choices in Healthcare Reimbursement: Approach and Results of a Citizen Forum in The Netherlands
  Leon Bijlmakers, Maarten Jansen, Bert Boer, Wieteke van Dijk, Stef Groenewoud, Jacqueline Zwaap, Jan-Kees Helderman, Job van Exel, Rob Baltussen
- Role of Culture, Values, and Politics in the Implementation of Health Technology Assessment in India: A Commentary
  Shilpi Swami, Tushar Srivastava
- Formal Implementation of Cost-Effectiveness Evaluations in Japan: A Unique Health Technology Assessment System
  Masataka Hasegawa, Shigekazu Komoto, Takeru Shiroiwa, Takashi Fukuda