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Journal of **Comparative Effectiveness Research**

Access in all areas? A round up of developments in market access and HTA: part 5

Alice Beattie[1], Francisco Olivença[1], Catrin Treharne[1] & Sreeram V Ramagopalan*[,1,2]

[1]Lane Clark & Peacock LLP, London, W1U 1DQ, UK

[2]Centre for Pharmaceutical Medicine Research, King's College London, SE1 9NH, UK

*Author for correspondence: sreeram.ramagopalan@lcp.uk.com

In this latest update, we explore the recent announcement by Canada's Drug Agency (CDA-AMC, formerly CADTH) on their pilot to include the societal perspective in the evaluation of certain new medicines; a recent Office of Health Economics (OHE) report on the evaluation of HTA agency methods over time; and publications examining the impact of Project Orbis on patient access to oncology treatments.

First draft submitted: 3 September 2024; Accepted for publication: 13 September 2024; Published online: 1 October 2024

Keywords: Canada's drug agency • health technology assessment • market access • Office of Health Economics • oncology • patient access • Project Orbis • societal perspective

Earlier this year, Canada's Drug Agency (CDA-AMC, formerly CADTH) announced they will pilot a new approach to include the societal perspective in economic evaluations for certain new drugs from December 2024 [1]. Until now CDA-AMC's Drug Reimbursement Review program has required that the healthcare payer perspective be adopted in the base-case analysis [2]. This pilot will additionally consider costs that fall outside of the healthcare system, such as productivity loss due to inability to work [1]. These new considerations will apply for drugs reviewed by CDA-AMC through the complex review process from December 2024 [1]. New medicines that will be eligible for the complex review process include cell and gene therapies, first-in-class medicines, drugs reviewed through Health Canada's expedited pathways and drugs that have an as-yet undefined place in therapy [1]. CDA-AMC will take a 'test and learn' approach to explore ways of ensuring the results of the societal perspective analyses are robustly validated [1].

Inclusion of the societal perspective in economic evaluations may increase the likelihood of reimbursement as compared with a healthcare payer perspective alone as it provides a more holistic assessment of a medicine's value [3]. A previous exploratory analysis of the impact of including a societal perspective on cost–effectiveness estimates for nivolumab as second-line treatment of patients with advanced squamous non-small-cell lung cancer (NSCLC) in Canada showed that the healthcare payer perspective yielded an incremental cost–effectiveness ratio (ICER) of just over $151,000 CAD; a traditional societal perspective (incorporating productivity losses) reduced this to just over $141,000 CAD and finally a broader societal perspective (including caregiver burden and insurance value) lowered the ICER to $80,645 CAD [4]. Therefore, while considering a societal perspective is likely to be helpful, exactly what the societal perspective covers is also going to be important. The biggest driver of the ICER reduction under the broader societal perspective was insurance value – i.e., the value that healthy individuals place on nivolumab. Empirical estimates from other diseases also show that a large share of treatment value may be due to insurance value and therefore health technology assessment (HTA) agencies in the future should try to include this in their value assessment [5]. While the fact that CDA-AMC is looking to use a societal perspective is a welcome step forward, it will be interesting to monitor how this impacts their decision making.

In April 2024, the Office of Health Economics (OHE) published their report, "How Have HTA Agencies Evolved Their Methods Over Time" [6]. The report explored the variation in processes of HTA agencies in 14 countries since 2010 (or since establishment of the agency if more recent) and focused on five key topics: discount rates, modifiers, patient involvement, real-world evidence (RWE) and surrogate end points [6]. Reporting on these

five key topics, the OHE found that discount rates for HTA agencies ranged from 1.5 to 5%, with most discount rates lying between 2.5 and 3.5% [6]. Where changes have been made since 2010, HTA agencies have tended to reduce discount rates, e.g., from 5 to 2.5–3% in France and Taiwan. Cohen has recently suggested that the discount rates used by HTA agencies tend to have no supporting rationale; he noted that with projected declines in consumption growth and observed declines in real interest rates HTA agencies should be recommending a discount rate of 1.5–2%, which would make therapies with long-term benefits more cost-effective [7]. In terms of modifiers, the OHE found that all 14 HTA agencies used modifiers either in an explicit framework or implicitly to value health gains differently depending on disease or patient characteristics [6]. For example, in Australia, the Pharmaceutical Benefits Advisory Committee (PBAC) guidance notes three factors which are particularly influential in favor of listing (called the 'rule of rescue') which are: no alternative treatment exists; the condition is severe, progressive and expected to lead to premature death; and the condition only affects a very small number of patients [8]. Eight of the 14 HTA agencies changed their position on modifiers since 2010, with these changes resulting in additional modifiers being explicitly considered in guidelines [6]. Modifiers can be considered quantitatively or qualitatively, however for a qualitative modifier the report notes that it is very hard to determine how it is being applied. For patient involvement, the report highlighted that the majority of HTA agencies now have an explicit position on patient involvement and since 2010 nine HTA agencies moved from no consideration of patient involvement in guidelines to clarification of their position or implementing informal opportunities. CDA-AMC, IQWiG (Institut fur Qualitat und Wirtschaftlichkeit im Gesundheitswesen) and NICE (National Institute for Health and Care Excellence) provide multiple opportunities for patient engagement throughout the HTA process, with the possibility for patient input in decision-making. Only the Italian Medicines Agency (AIFA) currently has no position in its guidelines for patient involvement [6]. This data overall suggests a positive move toward increased inclusion of patients in HTA, which benefits patients and has the potential to improve decision making. In terms of the use of RWE, the general trend over time across most HTA agencies was toward an increased consideration of RWE as evidence for HTA but with notable differences in acceptance [6]. For example, IQWiG notes a preference for randomized controlled trials and AIFA prefers the use of RWE from local sources [6]. Finally, the majority of HTA agencies used surrogate end points to some degree, although their level of acceptance is variable [6]. Six of the 14 HTA agencies have changed their position on the acceptance of surrogate end points since 2010, and six agencies have introduced guidance on consideration of surrogate end points [6]. While the report concludes that generally HTA agencies have become more explicit, adaptable and pragmatic in methods and processes over time, approaches by HTA bodies remain variable leading to differing evidence requirements and appraisals, ultimately resulting in differential patient access to treatments [6]. The report suggests that international collaboration is a route to accelerate having more consistent HTA methods across the globe [6].

Project Orbis, launched by the FDA in 2019, is a global initiative designed to streamline regulatory reviews of promising cancer drugs across multiple countries, including Canada, Australia, Singapore, Brazil, Israel, Switzerland and the UK [9]. Although all partner countries collaborate in the review process, a central feature of the program is that each regulator maintains its independence in the final decision and drug label. Given that drugs are often launched first in the USA, the rationale was that international collaboration with the FDA could facilitate faster regulatory reviews and earlier patient access in other countries. Initial analyses from Swissmedic showed that the time between submission to the FDA and Swissmedic and Swissmedic review time was significantly reduced by participation in Project Orbis, suggesting that participation could lead to faster patient access to drugs [9]. However, patient access is dependent not only on regulatory approval but also on reimbursement. A recent study provides insight into whether Project Orbis also leads to quicker reimbursement through HTA in Canada, England and Scotland [10]. The study found that in the UK, only 33% of Project Orbis drugs received routine reimbursement recommendations from NICE, although 72% were recommended by the Scottish Medicines Consortium (SMC) [10]. Similarly, in Canada, 72% of Project Orbis drugs became available after HTA and price negotiations [10]. While Project Orbis aims to harmonize regulatory processes and potentially speed up patient access to new cancer treatments, this study highlights the complex interplay between regulatory approval and HTA. Notably discordant value assessments between countries have resulted in variable patient access to treatment. As Project Orbis continues to expand, potentially including more countries and therapeutic areas, this study highlights the need for a comprehensive collaboration between regulatory agencies and HTA bodies.

In conclusion, Canada's pilot to include societal perspectives in economic evaluations, the evolution of HTA agency methods as reported by the OHE and the analysis of Project Orbis' impact on patient access all point to efforts to improve and streamline drug evaluation processes. However, challenges remain in harmonizing approaches across

different countries and agencies. As the landscape evolves, there is a growing need for international collaboration to develop more comprehensive and consistent HTA methods globally.

Financial disclosure

SV Ramagopalan has received an honorarium from Becaris Publishing for the contribution of this work. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Competing interests disclosure

The authors have no financial and/or nonfinancial competing interests or relevant affiliations with any organization/entity to declare that are relevant to the subject matter or materials discussed in this manuscript. This includes employment, grants or research funding, consultancies, membership on scientific or other advisory boards, honoraria, stock ownership or options, paid expert testimony, patents received or pending, or royalties.

Writing disclosure

No writing assistance was utilized in the production of this manuscript.

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