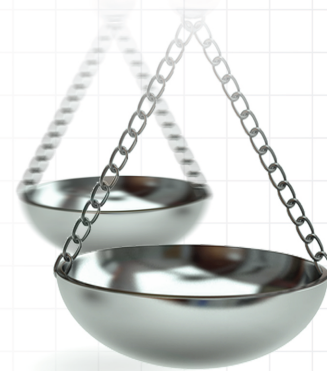




RWE ready for reimbursement? A round up of developments in real-world evidence relating to health technology assessment: part 6

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In this latest update we highlight recent publications from the US FDA and a Canadian Health Technology Assessment collaboration which provide insights into the future role of real-world evidence in market access in terms of health technology management.

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CanREValue is a collaborative multi-stakeholder initiative focused on developing a framework for the generation and use of real-world evidence (RWE) for cancer drug funding decisions in Canada [1]. In late 2021, the group published two articles based on work carried out by their reassessment working group [2,3]. The articles describe their key considerations in developing a framework for a Canadian health technology reassessment process and the findings of a subsequent project in which they tested the proposed framework with key stakeholders by simulating a reassessment with a case study.

It is clear from the considerations paper that RWE was seen to play a pivotal role in the proposed reassessment process with data on real-world utilization, indication creep, patient experience, clinical outcomes, cost–effectiveness and treatment sequencing all highlighted as relevant evidence for reassessment [2]. The importance of RWE on patient reported outcomes and patient experience in particular was strongly highlighted during the simulated reassessment, with stakeholders noting the importance of such data in providing a complete economic assessment and in allowing for comparison with initial assessments [3]. Stakeholders also noted the importance of patient outcomes being obtained from Canadian patients as the transportability of such evidence is typically limited [3]. For other types of RWE (e.g., clinical outcomes) stakeholders were more open to the use of real-world data from other geographies; with the caveat that such cases must be justifiable (e.g., rare diseases) and appropriate methodologies must have been utilized to minimize bias [3].

Beyond the specific insights provided in the articles, the two publications also serve to highlight the increasing interest in health technology reassessment (HTR) and health technology management (HTM); whereby, the value of health technologies is assessed throughout their lifecycle. While there has been much recent discussion of the role RWE can play in regulatory decisions and health technology assessments (HTA), its most natural role is likely to lie in the HTR/HTM setting. Finally, while their work focused specifically on the reassessment of oncology drugs within the Canadian health system, the findings are applicable in areas outside oncology and should broadly support other bodies currently adopting or modifying their approaches to include HTR/HTM, or bodies such as the National Institute for Health and Care Excellence (NICE) who are broadly considering the place of RWE in their processes [4].

Meanwhile, in the USA, a number of recent publications provide us with interesting insights into the developing views of the US FDA on RWE. In December, the FDA published their latest draft guidance relating to real-

world data (RWD)/RWE in regulatory decision-making [5]. This guidance builds on the three previous guidance documents on data sources and standards published earlier in 2021 [6–8], and describes expectations regarding the transparency of data source selection, study design and study conduct. Broadly, the document points to the need to ensure RWD are handled and reported with the same degree of rigor applied to clinical trials but highlights a number of considerations not always executed in non-interventional studies including the importance of clearly distinguishing and documenting early work to establish feasibility of a data source from the main analysis, accurately documenting protocol and analysis plan development, publicly registering protocols and ensuring FDA access to data are feasible. The value of early engagement to discuss noninterventional study plans is also highlighted. Many of these views were echoed in a recent ‘Annals of Oncology’ article on external controls authored by a group of FDA employees. The researchers outline a number of external control case studies used to support marketing applications to the FDA. While the case studies demonstrate the relatively peripheral and supporting role external controls have played in oncology to date, the article nevertheless provides a generally positive view on external controls. The potential for them to play a more pivotal role in future submissions when using high quality data sources and appropriate study design and analysis is noted [9]. A very recent article summarizes a lot of the guidance called out by regulators and other best practices (such as the target trial approach for analysis, assessment of unmeasured confounding, etc.) as a guide to use when conducting studies to drive regulatory acceptance [10].

Overall, these recent publications highlight the continuing, positive progress of the FDA and wider regulatory community in defining an expanded role for RWE, and the commensurate need for continued work to do the same in market access. Evidence submitted to regulators typically forms the main body of evidence used to support subsequent market access activities. As a result, the operational and methodological expectations and standards set by the FDA will strongly influence the type, quality and magnitude of RWE encountered by decision-makers focused on access and reimbursement. While the draft guidance produced by the FDA thus far appears prudent and relevant to access, it will be interesting to see what concerns are raised by external stakeholders during consultation and to observe the extent to which regulators address any concerns related to access and reimbursement; we hope that pragmatism prevails in the service of patients.

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