Real-World Evidence in the Context of Health Technology Assessment processes – from Theory to Action

Reflections on the HTAi Global Policy Forum held in Barcelona, Spain on 27 to 29 January 2019

“Real-world data (RWD) is observational or administrative data that provides information on the routine delivery of health care and the health status of the target population, and Real-World Evidence (RWE) is evidence derived from the analysis of RWD” – (Definitions used in the background paper)

Dr. Sean Tunis
President, HTAi

The 2019 HTAi Global Policy Forum (GPF) convened 73 representatives from HTA agencies, industry, the HTAi Board, and invited keynote speakers. The objective was to discuss the challenges and opportunities for using RWE in the context of HTA from a policy perspective.

We had excellent keynote presentations from Amy Abernethy, principal deputy commissioner of the FDA, who was representing Flatiron (a healthcare technology and services company), Andrew Mitchell representing the Pharmaceutical Benefits Advisory Committee (PBAC, Australia) and Andreas Hager as a patient representative.

These enthralling presentations set the scene for a thought-provoking and stimulating GPF. Members left with plenty of food-for-thought and hopefully a desire to take forward the discussions into concrete actions.

Dr. Laura Sampietro-Colom
Chair, HTAi Global Policy Forum

Following the inspiring keynote session, there were case study presentations from members, as well as plenary and group discussions. The case studies focused on identified key challenges and opportunities, as well as visions for the future from key perspectives (HTA agency, industry, provider/payer, patients). The discussions were centred on four themes: quality and acceptability, governance and accountability, transferability, and informing decisions.

Below are some key reflections from the ensuing discussions. For the first time during the history of the HTAi GPF, the opportunities are presented with possible directions/actions for stakeholders to take forward to further develop sustainable HTA systems. One key theme that is apparent is that the tide of change is approaching, regardless of HTA’s readiness, as regulators and other organizations have already signalled a readiness to make more use of RWE.
Discussion Themes

1. Quality and acceptability

*How should the quality of RWD/RWE be guaranteed, so that it can be used for HTA purposes and be acceptable for decision makers?*

Digitalization leads to democratization; i.e. increased availability of RWE will allow more people to contribute and control their own data. Enhanced stakeholder collaboration is therefore needed, and this requires educational transformation and building trust, which will take time. In the short-term, a common understanding regarding the types of RWD needed for HTA use is necessary. Describing and understanding the levels of uncertainty and confidence of these data (noting the significant effort required to obtain and clean RWD) is required.

Electronic health records (EHRs) are the ultimate RWD source for RWE. As such, the implementation, interoperability, ability to link across datasets, and ease of use of EHRs (particularly in clinical care) are critical. Agreement on the definition and prioritization of patient-focused endpoints to allow replication and cross-validation is also needed. A vision for the future is the shift to full acceptance of patient data.

Incentives (including financial) and cultural solutions for timely collection and reporting/use of RWD are needed. Increased transparency is key; registering protocols for RWE studies with minimal confidential (i.e., non-public) data could be a short-term goal. Longer-term actions include establishing an independent accreditation body and encouraging a global initiative for agreeing common data models and developing quality standards for RWD/RWE.

2. Governance and accountability

*RWD is being produced by different stakeholders for different purposes. Guidance on how to improve governance and accountability of RWD for producing RWE to inform HTA is needed.*

The governance and oversight of RWD should be aligned with relevant research questions in the short-term. In the longer term, defining what data can be shared between HTA agencies and regulators (guided by a social contract and a universal vision on the generation and use of RWD/RWE) is needed.

Good practice guidance on multi-stakeholder data ownership and management is important. A global directory of accredited data sources with a key to access is a possible future goal; this could be funded by a transparently operated global public/private partnership. Addressing privacy issues is a recurring theme; the establishment of an ethical framework for collecting and using RWD is a long-term goal. Common privacy laws (harmonization), including data protection and streamlining consent for use of patient data for future research are pre-requisites.

3. Transferability

* Differences in structure, setup and content of databases can lead to challenges in sharing of RWD/ RWE across countries and/or regions. The issues of what, when and how to transfer RWD/RWE across jurisdictions to inform decision-making need to be addressed.*

Stakeholder involvement, especially from patients and clinicians, is important to address transferability in the short-term. Defining meaningful outcomes from the patient perspective is key and can only be achieved with a common understanding of the need for RWD/RWE, as well as the acceptability of using RWD/RWE. Multi-country pilots could be conducted with well-defined patient groups and interactions (e.g. in rare diseases) in the future. PICOTS could potentially also be shared across jurisdictions regarding the same pathologies and interventions.

To enhance transferability, the development of an international or cross-country framework could be a way forward in the longer-term. Such a framework could address legal issues, data security, informed consent, methods for
aligning different data sources to capture core outcomes, open data, and standards to ensure transferability from RCTs to RWD/RWE where applicable. It should also take into account practice variation / standard of care in a specific jurisdiction.

4. Informing decision-making

**Currently there is no clear and widely accepted guidance on when and how to use RWD/RWE to inform decision-making in the lifecycle of a technology.**

The HTA community is currently standing at a cross-roads; more (personalized) RWD is increasingly available and used in learning health systems. Industry and others are already building their own datasets and platforms. However, the current HTA systems, capacity and methods are not fully equipped to address these developments. In moving forward, stakeholders must start to align on framing the relevant (research) problem, on what is the best source of evidence, and on when and how to generate and use RWD/RWE across the lifecycle. The HTA community should take action and become influencers in determining the data that is needed, as well as knowledge brokers, working more closely together, also with groups outside the HTA community and health sector.

As previously outlined, to enhance this alignment, more clarity on methods, standards and data sharing, more streamlining in data collection (a common data model), and integration with health systems is needed. The need for fit-for-purpose repositories across jurisdictions, details on methods/sources and programming codes, and replication of RWD (having sound methods and expert analysis) are immediate collaborative priorities.