RWE4Decisions REAL WORLD EVIDENCE

Webinar Report

Can Endpoints from Digital Technology Provide Meaningful Outcomes for HTA?

Tuesday, 25 June 2024, 15:00-16:30 CEST

Speakers

Rossella Di Bidino
Head of the HTA for AI Unit, ALTEMS; Co-Chair HTAi HB-HTA Interest Group

Andreas Hager
Board Member, Cystic Fibrosis Europe

Anja Schiel
Senior Advisor, Methodologist in Regulatory and Pharmacoeconomic Statistics, Norwegian Medicinal Products Agency

Lara Wolfson
Associate Vice-President & Head HTA Statistics, MSD; Co-Chair, PSI/EFPSI HTA Special Interest Group

Co-moderators

Eric Sutherland
Senior Health Economist, OECD

Alina Pavel
RWE4Decisions Secretariat

The RWE4Decisions 25 June Public Webinar focused on endpoints collected from digital technologies and their role in health technology assessments (HTA). The speakers considered whether the fast-paced digital technologies used by patients and in our healthcare systems may provide Real-World Data (RWD) which can be developed into reliable endpoints to help HTA/Payers understand the benefit of highly innovative technologies.

Dr Rossella Di Bidino discussed **hospital level** strategies for development, governance and assessment of digital health technologies. She emphasised that hospitals are not only *adopters* of digital health, but also act as **collectors, (co-)developers**, and **assessors.**

Firstly, hospitals **collect** a range of data in different ways, through their own bespoke systems and through use of digital health technologies created by a range of developers. The aim is to provide the best possible care for individual patients through personalised care plans and to create a learning health system. For example, the advancement of digital solutions has enabled the early discharge of patients and the remote monitoring of those with chronic conditions. Furthermore, hospitals often participate in the **development** process: they are best placed to identify the needs of clinicians and patients, and can present these findings to digital technology developers who have the expertise to produce the required solutions and make them usable by patients.

The Fondazione Policlinico Universitario Agostino Gemelli IRCCS in Rome is investing in digital health through initiatives like the Gemelli Generator, which uses hospital-collected RWD for AI, and the spin-off Gemelli Digital Medicine & Health, aimed at producing various digital solutions. For example, the hospital co-developed with industry and a technology developer a personalised remote care solution for heart failure patients.

The hospital must also act as an **assessor** of digital health solutions. Digital technologies should be assessed since the piloting phase with a flexible and specific HTA framework. There are currently two relevant European projects: AI-Mind, which is developing and assessing AI-based tools to support early diagnosis of dementia , and EDiHTA, providing a flexible assessment framework adaptable to different digital health solutions and technology readiness levels. Finally, assessment of digital health technologies in the hospital setting requires good-quality evidence from clinical trials and RWD.

Hospital-based HTA (HB-HTAs) systems acknowledge the potential relevance of digital endpoints, but some key questions need to be addressed.

Firstly, are digital endpoints perceived as a source of evidence? Recently, the EU HTA Coordination Group guidance on outcomes for Joint Clinical Assessments (JCA)[1] clarifies that digital endpoints arise from patient-generated data from apps, as automated measures from medical devices and through digital technologies that could be administered in clinical or non-clinical settings. However, to be considered as a clinical outcome they need to be validated to demonstrate validity and reliability against a reference standard. Furthermore, as these technologies can collect data at high frequency, the big data they produce can be challenging to analyse.

In HB-HTAs digital endpoints are still seen as intermediate or surrogate outcomes. Their impact on relevant clinical effects, economic and organizational implications, hospital strategy must be demonstrated to be recognized as primary endpoints in the assessments. Dr Di Bidino outlined that we are more open to consider digital endpoints as a primary outcome when comparing digital solutions amongst each other, rather than when comparing a digital solution with a traditional one. She mentioned the PICOS-ComTec[2] framework for defining digital health interventions, which includes digital endpoint.

Dr Di Bidino concluded that hospitals need digital health technologies and are involved in developing solutions, as they are fully aware of the limitations of traditional endpoints. However, as hospitals are still learning how to fully exploit digital endpoints, their role in relation to hospital decision-making, such as use of highly innovative medicines, still needs to be determined.

Andreas Hager presented his path to becoming a digital technology developer, led by having two children born with cystic fibrosis, working in the intersection between academia and healthcare, and being an entrepreneur. Over the last 20 years, he has been involved with various health ecosystems around the world, while offering knowledge and insights from patients.

As part of his daughter's care plan, he collected data about her well-being and biomarkers, learning the relevance of different measurements for different stakeholders, while also witnessing the influence of data collection on his daughter's care plan. This experience led him to create a platform that enhances communication and understanding between patients, families, healthcare, and researchers.

In 2005, he contributed to the digitisation of the Swedish rheumatology outcomes registry. This system was used for identifying patient-specific needs and tracking group improvements. The data were then utilised not only for patient-clinician conversations,

[1] https://health.ec.europa.eu/document/download/a70a62c7-325c-401e-ba42-66174b656ab8_en?filename=hta_outcomes_jca_guidance_en.pdf
[2] https://www.sciencedirect.com/science/article/pii/S109830152400038X

but also for gaining population perspectives and facilitating collaborations with industry and HTA bodies. Swedish HTA bodies use the rheumatology model as best in class example of how to use RWD for HTA, and the model has been exported to other countries.

In cystic fibrosis the first disease modulating treatments did not become available until 2018. Due to mixed results from patient use of these protein modulators, this expensive drug was not reimbursed in Sweden. However, a cystic fibrosis coalition platform was established that used the rheumatology model to create a cystic fibrosis outcome registry to collect real world data from Swedish patients.

The treatments were reimbursed conditional on data collection, with treatment continuation based on goals relating to healthcare parameters defined by the Swedish HTA authorities. In addition, Mr Hager and the Swedish cystic fibrosis coalition looked at what and how patient-reported outcomes (PROs) could support HTA. This brought an important patient perspective to the HTA decision-making about value, but led to complex questions about data coverage, data quality and potential additional RWD-sets.

New endpoints had to be developed to understand cystic fibrosis-related exacerbations, based on information from registries around the world. They created a conceptual model for capturing data from healthcare provision at home and during clinical practice, creating data flows that lead to learning healthcare systems and research benefitting all stakeholders, including HTA bodies.[3]

Andreas Hager concluded by sharing his goal: working with a personal health information exchange that can empower people living with a long-term illness and can support working together to improve care and generate multipurpose data. There is considerable power in PRO measures and although we speak different languages, we need to come together as patients, providers, payers, and researchers to help systems evolve in new ways.

Lara Wolfson reflected on the potential of these new and emerging technologies, and their use by health technology developers (HTDs) to demonstrate the value of highly innovative medicines. She underlined the important potential of digital technologies to minimise patient burden. They can help obtain accurate data for the safe and efficacious evaluation of a product, in a way that is less burdensome to the patient, compared to traditional data collection in clinical trials, which are done under specialised conditions. Furthermore, digital technologies can offer data-rich, long-term, specialised insights.

The challenge is ensuring that digital technologies fulfil the purpose for which they are being used and developed, and that they provide validity to all relevant stakeholders. However, the **right balance** must be struck digital technologies are fast-evolving, and an

[3] https://www.jmir.org/2021/1/e16842

evaluation process that is too lengthy and burdensome may render them technologically out of date by the time the validation is complete.

Anja Schiel presented the perspective of a statistician working in both regulation and HTA. Her message was that data is data: digital tools are just a more refined version of already-existing tools, giving us access to a larger magnitude of data. As a result, the same old rules, regulations, and frameworks often still apply, albeit these may be context dependent.

Regarding HTAs, she referred particularly to the relative effectiveness and cost effectiveness: if digital tools impact the former, then it will necessarily impact the latter as well. Therefore, there is a shift from the "safe harbour of the clinical study" into the real world, where patients must experience the real-world effectiveness by means of a digital tool. A challenging area for HTAs is represented by the "nice to have" tools, which are not linked to any intervention but might nevertheless benefit the healthcare system – here, the issue lies in reimbursement and in the methods of submission. Overall, it is important that digital endpoints stick to basic validation rules and account for contextual differences.

A lively **panel discussion** followed, where the panellists reflected on the questions below:

- What are the keys to developing a successful digital health technology that can inform HTA/Payers? Who are the most important stakeholders to work with?
- Would using a patient as its own control address some of the contextual differences when measuring real-world outcomes?
- How can we reduce duplication of apps development and ensure that development of apps is a multi-stakeholder process?
- Are there specific guidelines or regulations for HTAs of digital services?
- What are the incentives to improve data coverage and collection, and make these coherent? How do we aggregate data together for broader decision-making?

Several themes emerged from the conversations. Firstly, the panellists agreed on the importance of the **mirror principle:** it is paramount to create feedback loops and ensure that each stakeholder enjoys a clear benefit from their involvement, which also promotes the collection of data. For this, it must also be ensured that the stakeholders involved in a discussion understand each other.

Secondly, **duplication** of digital technologies must be reduced: for example, by defining the necessary strategies or governance, or by modifying the business models of the app. A proposed option was identifying a gap for the technology to fill and setting the

necessary criteria, in the context of a multi-stakeholder dialogue. This would then allow natural competition and collaboration to occur, as developers rush to the “finish line”.

Thirdly, **regulation for HTAs and digital devices** is rather thin: it was not seen as a priority for the EU HTA Regulation or other regulatory frameworks, and current methods may prove unfit to address the rapid changes in digital health technologies. **Regulation of data**, however, has come in the form the EU General Data Protection Regulation and the European Health Data Space, and we are getting to the right level of empowering patients without disclosing too much of their data. **Quality of data** is ensured through implementing the mirror principle reflected above, and from adopting long-term national and regional data standards.

Final reflections focused on the next practical steps to ensure collection of patient-generated data from digital technology sources to provide meaningful and better HTA processes going forward. The following aspects were underscored:

- the importance of tailoring digital tools to specific healthcare decisions
- the potential of RWD in managed entry agreements
- the design and use of digital technologies in both clinical and real-world settings and the inclusion of digital tools in post-launch evidence generation plans.

RWE4Decisions is a payer-led multi-stakeholder learning network, which has developed **stakeholder actions** that will better enable the use of real-world evidence in HTA/payer decisions about highly innovative technologies. The work has been commissioned by the Belgian National Institute of Health and Disability Insurance (NIHDI) and is led by a multi-stakeholder Steering Group with a wider community of contributors including HTA bodies and payers, regulatory agencies, patient groups, clinicians, industry, analytics experts and academic experts/researchers. The RWE4Decisions Secretariat is provided by FIPRA, with sponsorship by the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE), AstraZeneca, Boehringer Ingelheim, Gilead, Novartis, Pfizer, Roche and Takeda.

For further information and to watch the recording of the webinar, visit our website at:

https://rwe4decisions.com/event/public-webinar-can-endpoints-from-digital-technology-provide-meaningful-outcomes-for-hta/

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