Living health technology assessments: how close to living reality?

Grammati Sarri [ID],[1] Anna Forsythe,[2] Jamie Elvidge,[3] Dalia Dawoud[3]

[1]Real World and Advanced Analytics, Cytel Inc, London, UK
[2]Real World and Advanced Analytics, Cytel Inc, Miami, Florida, USA
[3]Science, Evidence and Analytics Directorate, National Institute for Health and Care Excellence, London, UK

Correspondence to:
Dr Grammati Sarri, Cytel Inc, Waltham, London, UK; grammati.sarri@cytel.com

Check for updates

Introduction

Healthcare decision-makers are exploring more responsive, innovative processes in the wake of the COVID-19 pandemic, including a 'living' approach to health technology assessment (HTA).[1] Even before the pandemic, the use of real-world data (RWD) and the advent of mobile and digital health technologies were transforming HTA decision making.[2]

These developments coincided with a broad recognition that keeping pace with rapid publication of new evidence and variation/inefficiencies in review can lead to HTA decisions based on out-of-date evidence.[3] These challenges hinder timely patient access to promising, innovative health technologies when decision-makers are asked to accept higher uncertainty in the evidence base, especially in populations with substantial unmet need.[4] More reactive and flexible 'living' approaches to HTA should be explored.

This commentary outlines challenges of current, 'static' HTA approaches, offers solutions provided by a 'living' HTA approach, and considers implementation of this method.

Are current HTA approaches optimal to address ongoing evidence generation?

HTA processes have remained largely unchanged, but innovative study designs (eg, pragmatic and adaptive clinical trials, single-arm trials) are transforming evidence generation, while regulatory decisions are increasingly being based on surrogate endpoints rather than primary outcomes.[5] This introduces uncertainties which require supplemental data to validate additional assumptions in the analyses.[6 7]

Recently, managed entry arrangements were developed to regulate reimbursement of new technologies with promising but uncertain benefits. For example, coverage with evidence development (CED) schemas grant patients temporary access to novel treatments while additional evidence is systematically collected.[8] Decision making based on CED, however, largely ignores a technology's 'lifecycle' in the context of evolving evidence. A 2019 review of CED decisions in Netherlands highlighted how systematically identifying uncertainty can guide the feasibility of follow-up evidence generation.[9] A 2022 review of economic models from National Institute for Health and Care Excellence (NICE) technology appraisals in England showed how uncertainty caused by unsupported predictors, use of surrogate outcomes and lack of a model's transparency can be overcome by regular technology reassessment.[10] In Sweden, evidence generated from the CED for a novel treatment for advanced Parkinson's disease was unconvincing during HTA reassessment, causing it to be withdrawn from clinical practice; reimbursement was reinstated after a re-evaluation of follow-up data.[11]

The lack of periodic re-evaluation of technologies unnecessarily strains overburdened healthcare systems which miss opportunities to disinvest in technologies that do not maintain their value or reconsider the value of approved technologies in light of new evidence.

Is 'living' HTA a viable solution to accommodate continual evidence generation, assessment and decision making?

Living HTA is a real-time, dynamic approach that uses explicit methods to determine the value of a health technology at different points in its lifecycle from the point of use (market access) through continued evidence generation[12] (figure 1). This can resolve some common uncertainties and evidence gaps seen in initial HTA submissions (especially close to product launch) related to the target population, disease, costs or the new therapy (eg, adding subgroups, real-world effectiveness and safety, validating surrogate outcomes, survival extrapolations and economic data). New safety evidence can also inform updated decision making. Living systematic reviews (LSR) which combine contemporaneity and rigour to enhance the data accuracy and utility for decision making are now widely accepted as an alternative to traditional single, static reviews[13] and living, adaptable whole-disease pathway economic models can inform pricing renegotiations.[1]

There has been an explosion of technological applications in evidence synthesis, data analysis and economic modelling,[5] and the integration of automation is central to this living process. Methods to trigger systematic review updates have been proposed[14] and artificial intelligence tools (eg, machine learning algorithms) were tested in specific applications in comparative effectiveness research.[15] These tasks are resource intensive but can be significantly streamlined through automation. Similar developments have been proposed in economic modelling.[16]
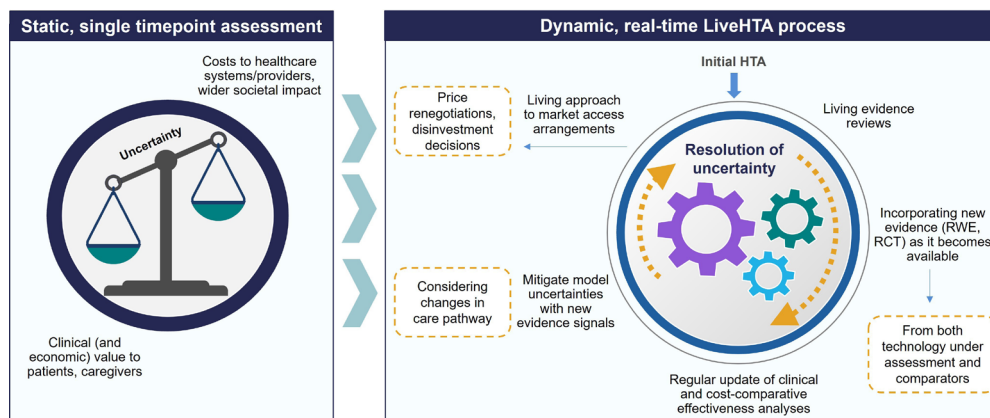
Figure 1 Moving from a static HTA To a dynamic living HTA Process. HTA, health technology assessment; RCT, randomized clinical trial; RWE, real world evidence.

How can 'living' HTA be implemented?

Pre-existing conceptual frameworks for lifecycle HTA processes[17] can provide the basis for living HTA implementation by incorporating: (1) transparent processes on safe integration of digital tools (eg, frequency of and trigger for review); (2) presentation of updated LSR and modelling results; and (3) updated reporting guidance. Fundamentals for automation, continuous improvement and maintaining high-quality standards have been covered in the emerging literature on this topic.[18] One study determined LSRs were a suitable approach during a pandemic, and outlined methodological challenges that may inform future research.[19] Other structured frameworks for integrating RWD in evidence synthesis can help implementation of a living HTA approach.[20 21] Technological aversion—a long-standing obstacle to innovations in healthcare decision making—can be overturned by open dialogue, collaboration and standardisation of processes, as well as targeted training by HTA agencies to upskill their staff. Issues around data privacy, transparency, access and validation of operational procedures are key to support development of living HTA frameworks.

A living HTA process may standardise search strategies, data extraction templates, review methodologies and modelling approaches, and will help eliminate duplication of efforts across HTA agencies.[22] An online platform (MAGICapp) used during the recent pandemic for uploading living guidelines and encouraging evidence reuse in different contexts demonstrates how international healthcare organisations can collaborate to inform public policy. Such examples demonstrate that speed does not come at the expense of certainty in the evidence.[16 23]

Cost implications of HTA must be proportionate to the expected societal benefit including the cost of potentially inappropriate commissioning decisions. Automation of evidence retrieval, screening, data collection and analyses can minimise any economic burden of a living HTA approach. The Australian Living Stroke Clinical Guidelines found a 99% reduction in time from research to point of care with significant savings to multiple stakeholders.[24] However, the living HTA approach should be piloted to assess its pros and cons. Health system resources and country-specific priorities will determine if a living appraisal framework is more appropriate in certain cases, such as high-cost or high-impact technologies, innovations that are CED candidates or in diseases with rapidly evolving treatment landscapes.

Next steps?

HTA bodies can embrace a living approach by enhancing their technological capabilities and framework structures. Recent efforts to harmonise and streamline HTA processes at a regional and cross-border level (eg, the proportionate approach to HTA in the UK by NICE, the European Union (EU) Joint Clinical Assessments, the Access Consortium, The Innovative Licencing and Access Pathway and Project Orbis) will help HTA bodies to manage workloads and reduce duplicative efforts, allowing living HTA to become a living reality.

ORCID iD
Grammati Sarri http://orcid.org/0000-0001-5536-8038

References

1 Elvidge J, Summerfield A, Knies S, *et al*. Best-practice guidance for the health technology assessment of diagnostics and treatments for COVID-19. *Zenodo* 2021. Available: https://zenodo.org/record/5530468

2 Facey KM, Rannanheimo P, Batchelor L, *et al*. Real-World evidence to support payer/HTA decisions about highly innovative technologies in the EU-actions for stakeholders. *Int J Technol Assess Health Care* 2020:1–10.

3 **O'Rourke B**, Werkö SS, Merlin T, *et al*. The " top 10 " challenges for health technology assessment: INAHTA viewpoint. *Int J Technol Assess Health Care* 2020;36:1–4.

4 **Vogler S**, Haasis MA, Dedet G, *et al*. Medicines reimbursement policies in europe [internet]. WHO regional office for europe. 2018. Available: https://jasmin.goeg.at/421/

5 **Nicod E**, Annemans L, Bucsics A, *et al*. Hta programme response to the challenges of dealing with orphan medicinal products: process evaluation in selected European countries. *Health Policy* 2019;123:S0168-8510(17)30084-2:140–51.:.

6 **Schneeweiss S**, Eichler H-G, Garcia-Altes A, *et al*. Real world data in adaptive biomedical innovation: a framework for generating evidence fit for decision-making. *Clin Pharmacol Ther* 2016;100:633–46.

7 **Briggs AH**, Weinstein MC, Fenwick EAL, *et al*. Model parameter estimation and uncertainty analysis: a report of the ISPOR-SMDM modeling good research practices Task force working group-6. *Med Decis Making* 2012;32:722–32.

8 **Dabbous M**, Chachoua L, Caban A, *et al*. Managed entry agreements: policy analysis from the european perspective. *Value Health* 2020;23:425–33.

9 **Pouwels XGLV**, Grutters JPC, Bindels J, *et al*. Uncertainty and coverage with evidence development: does practice meet theory? *Value Health* 2019;22:799–807.

10 **Daly M-J**, Elvidge J, Chantler T, *et al*. A review of economic models submitted to NICE's technology appraisal programme, for treatments of T1DM & T2DM. *Front Pharmacol* 2022;13:887298.

11 **Willis M**, Persson U, Zoellner Y, *et al*. Reducing uncertainty in value-based pricing using evidence development agreements. *Applied Health Economics and Health Policy* 2010;8:377–86.

12 **O'Rourke B**, Oortwijn W, Schuller T, *et al*. The new definition of health technology assessment: a milestone in international collaboration. *Int J Technol Assess Health Care* 2020;36:187–90.

13 **Elliott JH**, Turner T, Clavisi O, *et al*. Living systematic reviews: an emerging opportunity to narrow the evidence-practice gap. *PLOS Med* 2014;11:e1001603.

14 **Shekelle PG**, Motala A, Johnsen B, *et al*. Assessment of a method to detect signals for updating systematic reviews. *Syst Rev* 2014;3:13.

15 **Thomas J**, McDonald S, Noel-Storr A, *et al*. Machine learning reduced workload with minimal risk of missing studies: development and evaluation of a randomized controlled trial classifier for cochrane reviews. *J Clin Epidemiol* 2021;133:140–51.

16 **Smith RA**, Schneider PP, Mohammed W. Living HTa: automating health economic evaluation with R [Internet]. *Wellcome Open Res* 2022;7:194. 10.12688/wellcomeopenres.17933.2 Available: https://wellcomeopenresearch.org/articles/7-194

17 **Kirwin E**, Round J, Bond K, *et al*. A conceptual framework for life-cycle health technology assessment. *Value Health* 2022;25:1116–23.

18 **Beller E**, Clark J, Tsafnat G, *et al*. Making progress with the automation of systematic reviews: principles of the International collaboration for the automation of systematic reviews (ICASR). *Syst Rev* 2018;7:77.

19 **Iannizzi C**, Dorando E, Burns J, *et al*. Methodological challenges for living systematic reviews conducted during the COVID-19 pandemic: a concept paper. *J Clin Epidemiol* 2022;141:82–9.

20 **Mikati IKE**, Khabsa J, Harb T, *et al*. A framework for the development of living practice guidelines in health care; 2022. *Ann Intern Med*, Available: https://www.acpjournals.org/doi/10.7326/M22-0514

21 **Sarri G**, Patorno E, Yuan H, *et al*. Framework for the synthesis of non-randomised studies and randomised controlled trials: a guidance on conducting a systematic review and meta-analysis for healthcare decision making. *BMJ Evid Based Med* 2022;27:109–19. 10.1136/bmjebm-2020-111493 Available: https://ebm.bmj.com/content/early/2020/12/09/bmjebm-2020-111493

22 **Créquit P**, Trinquart L, Yavchitz A, *et al*. Wasted research when systematic reviews fail to provide a complete and up-to-date evidence synthesis: the example of lung cancer. *BMC Med* 2016;14:8.

23 **BMJ**. Trustworthy and living guidance for covid-19: time to join forces in the evidence ecosystem. *The BMJ* 2020. Available: https://blogs.bmj.com/bmj/2020/09/04/trustworthy-and-living-guidance-for-covid-19-time-to-join-forces-in-the-evidence-ecosystem/

24 **Elliott J**, Lawrence R, Minx JC, *et al*. Decision makers need constantly updated evidence synthesis. *Nature* 2021;600:383–5.