THE VALUE AND IMPACT OF HEALTH TECHNOLOGY ASSESSMENT

HTAi Global Policy Forum 2023 Background Paper

Contents

Introduction

The purpose of this background paper is to inform discussions at the HTAi Global Policy Forum (GPF) meeting being held in the Hague, The Netherlands from the 26th to 28th March, 2023. The topic is "The Value and Impact of Health Technology Assessment". The topic was chosen and refined through engagement with the GPF membership during 2022.

This topic was chosen because while health technology assessment (HTA) programs are often directed at answering questions of "value for money", they are under increasing pressure to demonstrate that they are a cost-effective use of finite resources themselves, with a demonstrated impact on health expenditure and wider public health (1). As noted in the 2020 update to the definition of HTA, its purpose is to "inform decision-making to promote an equitable, efficient and high-quality health system" (2). Therefore, the ultimate value of HTA in a health system may depend in part on its contribution to improved health status, reduced inequities, and increased efficiencies within, as well as contributions to, a sustainable health system (3).

The benefits of the roles that HTA brings may be under-recognized by the wider public. Evidence of the effectiveness and achievements of HTA programs are of strategic importance to defend against funding cuts or other challenges (such as in times of political change where the support for HTA may be questioned). In the current climate, HTA is potentially at risk of being perceived as an unnecessary barrier or hurdle to access for important, innovative treatments. Given the increasing pace of innovation and the continued efforts by regulatory authorities to accelerate drug and device approvals, the future of HTA may be under threat without action, particularly as the world moves to a post-pandemic setting. Highlighting the strengths and benefits that come from conducting HTA, and concerted efforts to ensure that HTA is viewed as an essential tool for promoting efficient resource use and supporting innovation is warranted.

The background paper collates information available in the published literature obtained using a targeted literature review. This was supplemented by expert interviews with GPF members, HTAi interest group Chairs, academics and others to identify additional issues pertinent to the topic. The interviews included representatives of HTA bodies from 11 countries (both members and non-members of the GPF for a global perspective on the issue); see the Acknowledgements for further details. Finally, review and further input from the HTAi GPF Organizing Committee, the wider HTAi GPF membership, and members of the HTAi Board was also considered during the development of this background paper.

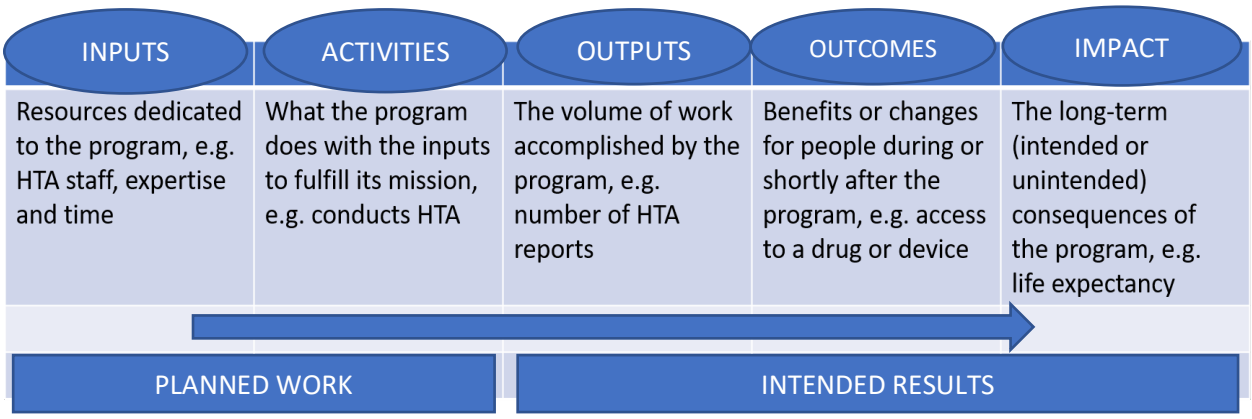
The main aim of the 2023 GPF will be to discuss, and explore, at a policy level, the development of a holistic approach to understanding, assessing, and communicating the current and projected future value and impact of HTA. To provide the most value from the GPF itself, it is hoped that clear next steps will be developed for HTA bodies, industry and other stakeholders regarding defining, measuring and enhancing the value and impact of HTA. The intention is that the focus of the GPF discussions remain policy-oriented, rather than at a detailed operational or methodological level. Outputs from the GPF will include a post-meeting report for GPF members, a freely available journal article, and a panel discussion at the 2023 HTAi Annual Meeting. Additional efforts may include creation of task forces or workgroups to take the topic and recommendations further.

Background

While the topic includes the terms "value" and "impact", these terms relate to both distinct and inter-related dimensions. For the purposes of our discussions, we ask readers to keep the following definitions (adapted from the Oxford English dictionary) in mind:

- *Value:* the perceived worth or benefit of HTA, which may vary according to stakeholder type, local setting, and other factors.
- *Impact:* qualitative and/or quantitative assessment or review of the effects of HTA, which may vary by perspective, setting, and other factors, and which may include *valuation* exercises (e.g., return of investment from implementation of HTA recommendations). Impact can be intended or unintended and considered as direct, indirect and intangible.

To help visualize the above definitions, below is a conceptual framework which represents the process of HTA and highlights how the terms will be defined in the discussions. This conceptual framework is based on a "logic model", defined as a graphic which represents the theory of how an intervention produces its output, outcomes, and impacts. The value of each of these elements can be defined and measured and may be expressed quantitatively or qualitatively. Knowing what a stakeholder considers valuable is critical when it comes to measuring the value of any initiative. Mark Taylor, head of impact at the National Institute for Health Research said that there are four broad reasons for measuring impact: advocacy; accountability; analysis and allocation.



Further to these definitions, this paper focuses on the application of HTA as a process, typically conducted by national HTA bodies in accordance with the updated definition of HTA (2). This is as opposed to the application of HTA-related concepts (such as comparative evidence considered in context with costs) by different health system stakeholders. It is recognized that HTA is not a homogenous process and that activities can include clinical assessment, economic assessment, and ethical, social, and organizational aspects. Where possible, these elements will be considered throughout the background paper and during the discussions. It is anticipated that key themes arising from the discussions could be extrapolated to a range of scenarios (for example, HTA conducted at a local, hospital-based level, or to the application of HTA principles by health system stakeholders).

In addition, these considerations need to be borne in mind alongside current and future developments in the field of medical technologies. Due to the recent and projected increasingly rapid influx of

innovative and potentially disruptive new approaches to diagnosis, prevention and treatment of disease, the health ecosystem is changing, from accelerated and flexible regulatory timeframes to new drivers of clinical practice, such as personalized medicines, treatment pathways and increased patient engagement in managing health (4). As noted, the pandemic has highlighted these issues, with a proliferation of information (including non-clinical trial data) and the emergency use of medicines and vaccine development (5). This is all coupled with increasing patient and other stakeholder demands on health systems that must operate within increasingly constrained budget environments(6).

The Value and Impact of HTA

The field of HTA was developed in a systematic way beginning in the U.S. Office of Technology Assessment (OTA), which published its first report on the subject in 1976. In 1987, Australian Minister of Parliament, Ben Humphreys, stated "*The Government has no objection to paying high process for new drugs that offer significant therapeutic advances over existing drugs or other forms of treatment. But it does not believe the taxpayer should foot the bill for very expensive drugs that offer only minimal advantages over much cheaper alternatives*".{MP, 1987 #1882}Many countries today use HTA as a policy tool to help health systems determine the best use of finite health resources, with HTA recommendations mandated within health systems and being used to facilitate pricing negotiations. There are jurisdictions where HTA is more advisory in nature and is hopes instead to prospectively shape healthcare (for example the Institute for Clinical and Economic Review, ICER in America). HTA can be considered as a tool that reflects a society's preferences for the choices to be made in healthcare, rather than just a tool to regulate access to healthcare within a given legal setting.

Considering whether the use of HTA itself represents value for money is also not new. In conducting the literature review for this paper, however, a marked increase in the number of articles published containing the words "value" or "impact" alongside "HTA" was noted from 2014 onwards, with an annual number exceeding 1,000 and a peak of 3,721 articles in 2021. While this was a basic search without filters applied, it provides an indication that the concepts of value within, and resulting from HTA more broadly, is of increasing global interest.

Factors Influencing the Value and Impact of HTA

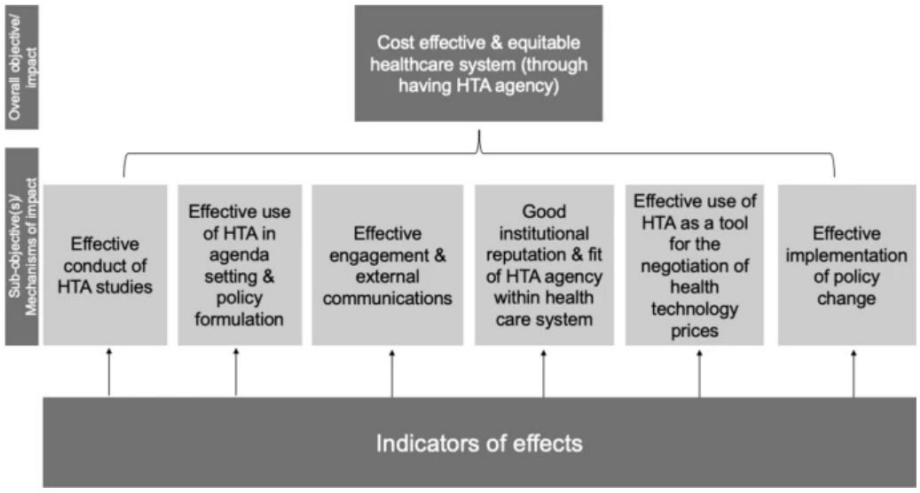
The value and impact of HTA is inextricably linked to the remit of a given HTA body and funding mechanisms employed within a health system. For example, value and impact may be more straightforward to measure when HTA guidance is binding, and less so when the output is advisory in nature only. Some HTA organizations are required to report on how recommendations are implemented in practice, increasing the likelihood that that some aspects of impact (for example changes in clinical practice) can be measured. Therefore, among the most important factors influencing the impact of HTA reports is arguably the directness of the relationship between an HTA program, policymaking bodies, and health care decisions (7). One of the potential reasons for this is the ability to ensure that the output of the HTA process is informing and answering the question the decision-maker is actually asking. For example, a decision maker may want to know about clinical effectiveness, pricing, and budget consequences; all of these questions require different outputs and so value and subsequent impact will be influenced by the perceived relevance (and therefore value) of the HTA outputs.

As the value and impact of HTA for payers is likely to be determined by a combination of policy and legislative or other mandates, administrative arrangements, and organizational structures, this may determine the scope of the outputs, including the types of technologies to be considered, the stage of the technology lifecycle, the stakeholders to include, and the opportunities to engage with them. Importantly, the role that a HTA body plays in informing, negotiating and setting/guiding prices of

technologies varies widely. The links with payer entities (i.e., those bodies with ultimate decision-making authority on funding) also vary, as do the policy tools that payers employ, such as ability to negotiate and publish prices and enter into managed entry agreements (MEAs).

Other factors influencing the impact of HTA include resourcing and staffing constraints in HTA bodies and manufacturer willingness/ability to engage in HTA processes (particularly so for small and medium biotech and device companies). A value tree developed by Millar et al.(8) summarizes some key indicators of effect that influence the impact of HTA:

Figure 1- Value tree reflecting impact mapping exercise structure taken from Millar et al (8)



Perspective Lens

The value of any activity depends on the lens through which it is evaluated. For example, a patient may place greater value on rapid access to innovative treatments without fully demonstrated clinical benefit, whereas a government, payer or even society as a whole, may place greater value on recommendations that will maximize population health more broadly, with some patients potentially disadvantaged as a result. Arguably, through an industry or commercial lens, outputs such as faster results and more positive reimbursement recommendations are the most valued metrics. Therefore, the value of HTA outputs using one lens may be at odds with that viewed through another lens. Determining the perspective through which value will be viewed is therefore a critical consideration when determining the value of the various outputs, outcomes and impacts of any program. Without doing so, the results of a value or impact evaluation could be inconsistent and even contradictory across perspectives.

One view that is particularly interesting when considering the value and impact of HTA is that of the citizens within a society; those who ultimately support the health system through tax contributions, and who may be eventually affected by HTA recommendations and subsequent decisions made by payers. While funding expensive treatments may be deemed a cost-effective use of resources, in an environment with budget constraints, such decisions may result in funds having to be diverted from other activities (for example hospital beds, nursing or palliative care). These inherent tensions within the health system that HTA bodies grapple with may not be transparent to external stakeholders and wider society. In a focus group study of demographic representatives of a Canadian province (9), results

suggested that the public were suspicious of the interests driving HTA, such as stakeholder biases and was an area that required improvement and greater transparency.

The interest in public involvement in HTA has been increasing in recent years. However, the terms patients, consumers, public, lay members, customers, users, citizens, and others have been variously used, sometimes interchangeably within the literature. In a paper by Stafinski et al (10) an operational definition for the public in the context of HTA was developed as: "a non-aligned community member with no commercial or professional interest in the HTA process who is not a patient or member of a stakeholder group". Street et al (11) conclude that the public should be explicitly included in ensuring democratic accountability of HTA processes but also to enable public values to be included in decision making. However, the goals of public engagement have not been well articulated in the past. Several methods such as focus groups, citizen juries and probability sample surveys were suggested as ways to increase public involvement to ascertain views and values. Challenges remain in involving the public in HTA, however; increased stakeholder engagement including public/citizen engagement was listed as one of the "Top 10" challenges for HTA agencies in an INAHTA survey of 30 HTA bodies (12). Initiatives that attempt to elicit societal perspectives on the value and impact of HTA, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) patient and community advisory group (13), the National Institute for Health and Care Excellence (NICE) program "NICE Listens" (14) and the Dutch Citizens Forum's consideration of the public reimbursement of healthcare (15) may help inform such measures and influence the policies and processes of HTA agencies.

Linked to the perspective lens, it is also important to consider the ultimate goal of value and impact assessments prior to undertaking them. As with any research activity, it is important to be clear why you are undertaking the work, primarily to ensure that the assessment itself is fit-for-purpose and proportionate. Value and impact assessment can be used to meet the requirements of a funding agency; for example, it may be necessary to meet defined performance indicators to ensure ongoing funding. It can be conducted for internal purposes to helpfully contribute to continual improvement practices and identify areas for development. Beyond this, it can be useful to measure and communicate the broader value and impact to a wider set of stakeholders; it was noted in expert interviews that it is important to have broad stakeholder understanding and buy-in (rather than technical capacity and feasibility alone) to ensure ongoing stability and security of funding (16).

Measuring the Value and Impact of HTA

Empirical evidence of the impact of HTA on either health outcomes or spending is relatively scarce. Critics argue that with the clear high upfront and ongoing costs to establish and conduct institutionalized HTA that vague measures of impact could potentially dissuade policymakers (17). Much of the existing literature has tended to focus on the outputs of HTA and the uptake of HTA recommendations by decision-makers. Some discussions around defining and measuring the value and impact of HTA within the literature are described in the section below.

'Traditional' Quantitative Metrics

Metrics to assess the value of HTA traditionally include capturing HTA outputs (i.e. positive and negative reimbursement decisions) as well as time-based measures such as the number of days between regulatory approval and an HTA decision or recommendation. The Centre for Innovation in Regulatory Science (CIRS) has developed the HTADock for benchmarking HTA agency performance (18) using such metrics compiled annually from 8 agencies. As noted, however, the value of these metrics may be most relevant for those with commercial interests in the outputs of HTA bodies.

A narrative systematic review in 2016 by Greenhalgh et al (19) identified a range of theoretical models and empirical approaches for measuring the impact of health research programs, arranged into a taxonomy. The payback framework (consisting of a logic model of the seven stages of research linked with five categories of [non-monetary] forms of payback, such as knowledge, benefits to research, policy and health) (20) was the most widely used approach and monetization of impact was an increasingly popular method applied to many approaches. The paper noted however that the most robust approaches are labor-intensive and not always feasible or affordable. The payback framework has also been used to assess the value of health research and HTA (21). This method was used for a 2016 review of returns on research funded under the National Institute for Health Research HTA program in the UK, (1) which concluded that if 12% of the potential net monetary benefit of implementing the findings of a sample of 10 HTA studies was realized, then the costs of the entire HTA program would be fully covered for a 20-year period.

Newer quantitative approaches to measuring the value of HTA conducted by HTA agencies include the Evaluating the Value of a Real-World HTA Agency (EVORA) project (22). EVORA is an Excel-based simulation workbook developed by the University of Strathclyde in collaboration with Thailand's Health Intervention and Technology Assessment Program (HITAP) that evaluates the impact of a threshold-based HTA to support decision making about reimbursement or implementation of health technologies. The performance of the HTA function is measured in terms of spending to implement health services "greenlit" by the HTA program/agency as well as health gains realized, compared to spending and gains in a hypothetical healthcare system which reimburses technologies on a random or first-come, first-served basis. The project was first made available in 2020{Barlow, 2022 #1881} and recently applied to activity by HITAP(23), with the hypothesis that, when applied to the Thai healthcare system, HTA can offer additional health and economic benefits by improving the efficiency of resource allocation decision-making as compared to the counterfactual. The net monetary benefit observed ranged from THB24,238 million (USD725 million) to THB759,328 million (USD22.7 billion) over a 5-year time horizon. In 2020, Grieve et al. outlined the development of a methodological framework that estimates the return of investment in HTA using net health benefit (NHB) as a measure of value – recognizing that the purpose of HTA is both to inform about health outcomes and efficiency (not necessarily about saving costs){Grieve, 2020 #1883}. A mixed approach using explanatory methods were used alongside quantitative methods to generate, test and refine explanations for a gap between potential and realized gains in population health. This was done to demonstrate the value of HTA (quantified in terms of NHB) and to progress knowledge as a theory or framework by which HTA impact might be optimized. A proof of concept to estimate the potential and realized population NHB and what can be attributed to the HTA process is currently being applied and further explored.

Considering lifecycle activities conducted by HTA bodies (and as discussed in the 2022 HTAi GPF), there seems to be particular value in early activities such as scientific dialog and early advice. Such activities have value in informing technology development plans and could potentially support priority setting for national health systems. In situations where early advice is provided and acted upon then theoretically access for patients (to the right technologies) may ultimately be quicker and delivered in a more effective and efficient manner. While scientific advice appears to be universally accepted as a valuable activity, the return-on-investment metrics applied to this activity lack clarity, primarily due to the confidential nature of the work. Efforts are underway through organizations such as CIRS and within industry organizations themselves to collect feedback and insights on the value and impact of early advice processes and outcomes. Challenges in the multiplicity of the various systems and the resource implications of changing trial plans based on scientific advice should be acknowledged. Industry

organizations have many steps of internal validation and approvals, and so conducting additional trials or changing trial plans can incur significant costs and can take many years.

Other quantitative measures can be considered when determining the added value of having a form of institutionalized HTA. For example, population health indicators (e.g., life expectancy, quality-adjusted life years and other morbidity indicators such as those used in the EVORA exercise) and patient reported outcomes and/or patient satisfaction can potentially be used as proxy measures for determining the benefits of HTA. Adopting a HTA approach to determining the value and impact of HTA itself using techniques such as cost-benefit analysis is potentially feasible, whereby the perspective through which the analysis can be specified and the costs and benefits can be estimated. Techniques such as this could be used to elicit an answer to the question as to whether HTA itself is a cost-effective use of health care resources: indeed what is the incremental cost effectiveness ratio (ICER) of an ICER, so to speak?

The audit of public spending against government policy to determine value for money is not a new concept. Audit institutions, also often referred to as National Audit Offices, are often essential players in countries' national accountability systems. These are oversight bodies that have the task of ensuring that, at a minimum, government transactions are tracked according to the required accounting standards, and that these (transactions) are in keeping with what is outlined in the approved budget. The main distinctive feature of these audit bodies is that they are autonomous with formal independence from the executive. Many audit bodies go beyond the scope of financial audits and conduct performance audits and evaluations of government activities, processes and services that can include integrity, effectiveness, quality, efficiency and value for money, and fairness (i.e. the impacts of policies or programs on different groups of society)(24). Internal and clinical audits and also external audits of hospital processes or finances are also not new concepts {Hut-Mossel, 2021 #1884}.

Other Impact Frameworks

The International Network of Agencies for HTA (INAHTA) has had a longstanding interest in exploring the impact of HTA reports, publishing a conceptual paper on the influence of HTA in 2014 (25) and developing an impact framework for agencies to complete (see Appendix). The impact framework is based on the six-stage model developed by Gerhardus et al (26). As noted during expert interviews, this six-stage model could be reasonably applied to most HTA settings, including HTA conducted in advisory and mandatory settings. The six-stage model is paraphrased below:

1. Awareness: the relevant stakeholder must know of the HTA report
2. Acceptance: the relevant stakeholder must see the HTA report as valid and a legitimate basis for action
3. Policy process: the policy process should explicitly utilize the HTA report
4. Policy decision: the policy decision should cite the HTA report
5. Practice: there should be "clear and measurable" changes in clinical practice in line with policy decision and thus the report
6. Outcome: health and economic outcomes should be realized on the basis of the changes in practice

INAHTA also issues an annual "David Hailey Award for Best Impact Story", and in 2020 published a mini-theme of impact stories (27). These resources highlight how a range of methods are used to measure the impact of HTA and the value that health systems derive from HTA reports. In one of the examples, the Health Policy Advisory Committee on Technology (HealthPACT) in Australia used horizon scanning to impact the development of a national clinical consent process that facilitated access to genomic

sequencing for clinical trials, led to the development of a national data management platform, and resulted in a new Commonwealth Government commitment of AUD 500 million over 10 years to support ongoing research into genomics sequencing. Other examples from Canada and Uruguay were presented that highlighted changes in government activities and priorities as a result of HTA efforts, development of national collaborations, and pricing negotiations with industry. The impact assessments were also used to improve HTA processes, including topic scoping, stakeholder engagement, and information gathering and sharing.

In a related field, the Research Excellence Framework (28) in the UK was first used in 2014 to assess the impact of research outside of academia during 2008-2013. The REF defined impact as 'an effect on, change or benefit to the economy, society, culture, public policy or services, health, the environment or quality of life, beyond academia'. Impact is assessed through university submitted impact case studies that are cited as providing a "unique and invaluable source of information on the impact of UK research." Analysis of the impact case studies found that the wider impacts and benefits often stemmed from multi-disciplinary work (i.e., from research teams formed across disciplines and countries, for example a study of same-day diagnostic tests for tuberculosis led to improvements in access to care and reductions in costs incurred by patients in Malawi, Nigeria, Yemen, Ethiopia, Nepal and elsewhere). An impact case study database has been developed which is a searchable tool and maps of impact case studies have been developed to indicate the local and global spread of research impact for UK universities. Critics of the REF however note that it has to measure impact across the full academic range (not just medical research) and so multiple perspectives must be considered. In addition, the REF specifies that case studies must have less than 1,000 words and be written in a way that anyone can understand; this can lead to 'gaming' with the way case studies are written or can miss important aspects of impact.

Contextual Factors and Other Metrics

There are other potential metrics that are more nuanced and/or harder to quantify. At a basic level, the ongoing commissioning and funding of HTA bodies as well as anecdotal, informal word-of-mouth feedback on activities are useful for many HTA bodies to at least signal presence of the immediate value they bring to a health system. Ongoing and increased integration into health systems and greater involvement in policies and processes throughout government departments were also highlighted in stakeholder interviews as proxy measures to demonstrate the perceived value of HTA. Even more indirectly, in some jurisdictions the value and impact of a HTA body could simply be the active and ongoing facilitation of conversations around patient access to effective technologies between payers, industry, and other key stakeholders. This may be particularly pertinent for more nascent HTA systems. Value and impact may be derived from promoting innovative, flexible or adaptive approaches, enabling effective health system responses to changing regulatory environments or emergency situations (such as the COVID-19 pandemic response). Stakeholder engagement and collaboration are also critical elements that can be attributed to HTA bodies. There is a growing body of literature looking at how these elements can be measured in practice through key performance indicators and with data collected digitally (29).

HTA may also bring value and have impact by changing mindsets rather than immediately determining policy actions and clinical decisions. For example, the introduction of institutionalized HTA clearly signals a departure from opaque and arbitrary pricing and reimbursement practices. It indicates a preference for evidence-based decisions, with independent expert input as well as inclusion of and dialogue with key stakeholders (30). The 2022 Inflation Reduction Act (IRA) in America may serve as a contemporary relevant example. The IRA will seek to lower the prescription drug costs by allowing Medicare to

negotiate prices with drug companies, put an inflation cap on drug prices, and lower out-of-pocket expenses for Medicare recipients. The role that HTA (and potentially HTA bodies such as ICER) may play in the implementation of the IRA will provide a demonstration of the perceived value and impact of HTA.

Increasing transparency in HTA reports (for example reduced redaction of clinical data) is another potential measure of additional value and impact, based on the ability to increase data sharing, promote collaboration, and enable a greater understanding of HTA decision making by external stakeholders. How HTA defines and implements its processes may also represent value to certain stakeholders; for example, public perceptions that HTA deliberations are impartial and transparent, and this includes reducing the judicialization of healthcare (i.e. lawsuits against healthcare providers or government agencies surrounding access to and/or provision of care) (31). Stakeholder satisfaction, for example measuring patient and clinician satisfaction with not only HTA outputs but also HTA processes, can also be a useful metric that can be easily implemented and repeated to determine trends and changes.

The predictability and transparency of HTA processes and timelines is a consistent theme of industry stakeholders, and may relate to activities such as early advice, topic scoping, or even descriptions of the methods employed. Sharing good practice and experience can help lead to a more efficient and equitable process, acknowledging that HTA is undertaken by humans and not machines. Considering the maturity of an HTA system is important; a positive correlation between the reimbursement of innovative treatments and maturity of HTA systems was observed by some interviewees. One further impact relevant to more mature HTA bodies is on the conduct of HTA in countries with nascent or no HTA operations; groups such as NICE International are active in adapting guidance to a local context, training and capacity building, and process development.

One of the core areas of potential value and impact of HTA is that of innovation; both how true innovation is fostered and also how expectations and system reactions (to developments that are not an efficient use of public resources) are managed (32). HTA is often viewed as a barrier to access or as a hurdle to innovation and can sometimes lack political backing in the face of pressures from manufacturers and patient groups who want access to new technologies quickly. Governments may also get involved, such as with initiatives to promote medical innovation as a means toward post-pandemic economic stimulation (33). In some jurisdictions, the separation between the value assessment and pricing processes is considered essential to avoid perceptions of bias in the decision-making process, and to ensure that it is evidence-based. In other jurisdictions, however, the HTA body has a direct role on pricing and negotiations. One recent example that will provide pertinent insights is the reorganization of the Italian Medicines Agency (AIFA). In December 2022, the Italian Parliament approved changes to the structure of AIFA that essentially merged two committees (the Technical-Scientific Commission, CTS and the Pricing and Reimbursement Committee, CPR) into one, smaller, single body (the Scientific and Economic Commission for Pharmaceuticals, CSE). Some argue this is evidence that HTA is not fully valued with a reduction in expertise, increased workloads and a reduced independence and greater political control, while others argue that it is a positive change to streamline processes, with potential efficiencies to be gained from a single committee charged with both evaluating the evidence on new drugs and negotiating pricing and reimbursement terms.

Assuming that the value of innovation is only realized when patients benefit from the advances in treatment, HTA bodies face the criticism that processes must be improved so that patient access to innovative drugs is not delayed or variable. (34) A review by the European Federation of Pharmaceutical

Industries and Associations (EFPIA) in 2021 (35) showed that the average time from market approval to reimbursement of innovative treatments ranged from 133 days to 899 days (average of 511 days). EFPIA conducted a root cause analysis on the access times (36) and suggested that late initiation of the HTA process, the speed of national HTA timelines and adherence, misalignment on evidence requirements, value and price were all factors leading to variable reimbursement timelines. However, the analysis also suggested that the speed of the regulatory process, accessibility of medicines, budget for implementing reimbursement decisions, availability of diagnostic and other supporting infrastructure also played significant roles in contributing to delays in patient access to innovative medicines. Further, there is a growing criticism of accelerated regulatory approval schemes, with a substantial proportion of drugs still having unknown benefits based on endpoints that may not matter to patients, and requiring confirmatory trials that often take many years to conduct (37).

One other major factor that is considered in the context of demonstrating the value and impact of HTA is around potential improvements in health equity. The concept of health inequalities has been described as “unfair, avoidable and systematic differences in health outcomes between groups which are determined by circumstances that are largely beyond an individual’s control” (38). While the reduction of health inequalities must be intersectoral and multidisciplinary,(39) HTA can provide a basis from which to incorporate equity considerations into decision making, and potentially reduce inequitable access to treatments under its remit (40). This was reflected in the updated definition of HTA(2), which many see as essential to achieve adequate universal health coverage (41). Incorporating HTA into health systems can ultimately help reduce health inequalities by ensuring that care is effective, consistent and makes efficient use of resources.

There are examples of HTA bodies that have the goal of reducing health inequalities as a core part of their work. For example NICE have adapted the Labonte model (42) as a simple but effective map of the causes of health inequalities to guide strategies to reduce them and explicitly guide their committees to take equality into account when making recommendations (43). The updated Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement now also includes specific reference to reporting the “key findings, limitations, ethical and equity considerations not captured and how these could affect patients, policy, or practice”(44). Work to more formally incorporate health equity considerations into existing methods, such as a distributional cost-effectiveness analysis or extended cost-effectiveness analysis is underway. These methods can identify whether an intervention provides value-for-money and whether the intervention enhances or reduces health equity so that the tradeoffs between efficiency and equity can directly be considered (45). However, evaluating the impact that HTA itself may have in reducing health inequalities is also important to demonstrate the effectiveness of any actions (46). Cookson and Mirelman (47) suggest that making equity a quantitative endpoint of HTA would help enable this, by expanding the well-known adage from “what is measured, gets done” to “what doesn’t get measured, gets marginalized”.

The table below summarizes some of the possible elements of value and potential impacts of HTA as described in the section above. The table includes short-term to long-term impacts and considers the individual patient level through system, macro-level, impacts. As noted, these outputs, outcomes and impacts may be valued differently according to stakeholder type, perspective lens and context.

Figure 2-Examples of metrics and indicators when considering the impact of HTA

Domain	Examples and possible metrics/indicators
Inputs: The contributions necessary to enable the program to be implemented	• Staff numbers (and skillsets) • Infrastructure • Funding (e.g. annual budget) • Relationship with key partners/position in health system
Outputs: The program's activities and outputs (direct products/deliverables of the activities).	• Number and type of HTA reports/products (e.g. technical reports to inform decision makers or mandatory guidance) • Time to produce reports/recommendations • Stakeholder satisfaction/engagement with the process • Price cuts/negotiations/MEAs (where relevant)
Outcomes: measure of effects/changes in the short- to medium-term	• Appropriate technology usage (investment/disinvestment, uptake) • Variation in health care (maps) • Improved health outcomes (behaviors/wellness and QoL measures) • Efficient allocation of system resources (funding/staffing) • Engagement and connectedness of system: inclusivity, transparency, trust (quality, quantity and timing of dialogues)
Health system and societal impacts: measure of long-term, distal effects	• Improved life expectancy / quality-adjusted survival • Reduced in health/education/social inequalities • Sustainable funding of health system(s) • Reduction in environmental effects of the medical technology industry • Use of evidence-based, transparent and fair decision-making (within health and beyond)

Challenges in Measuring Value and Impact

Assessing the value and impact of any program is time-consuming and costly. In 2020, INAHTA conducted a two-part study that first aimed to determine what impact assessment activities are currently being undertaken by INAHTA members(48), and then identified the factors that enable or inhibit impact assessment activities(49). The study found that just over half of HTA agencies conduct informal impact assessment, and around a third have formal strategies in place to assess the impact of HTA reports. Regarding barriers to impact assessment, a lack of qualified staff, standardized tools or methods, financial or organizational resources, staff motivation (for example wanting to move onto the next HTA, rather than review impacts of existing HTAs, particularly for organizations without dedicated implementation evaluation teams), and suboptimal integration of impact assessment were cited as major barriers.

Enablers of impact assessment included capacity (i.e. sufficient time, resources and expertise for impact assessment activities), but also the presence of a strong impact assessment culture, transparency and reliable data, appropriate timing of impact assessment, and clear strategies and conceptual models with good communication to mitigate the risk of bias and confounding. Further, there may be room to consider division of labor between all stakeholders, in particular an increase in the role and involvement

of industry(50). However, concerns around potential conflicts of interest would need to be carefully worked through to ensure there is benefit for all stakeholders.

Millar et al (8) describe the body of literature exploring the impact of HTA as heterogeneous, with the authors highlighting the following four sources of heterogeneity in how impact is determined in the literature: 1) variation in the purpose of the study; 2) differences in interpretation of HTA within studies (for example whether it is the impact of the HTA report and/or the resulting reimbursement recommendation that is being quantified, or even HTA as a process/discipline or institutionalized HTA bodies being evaluated); 3) differences in interpretation of impact; and 4) variability in scope and rigor of evaluation studies. By the nature of the question, contemporary and comparative data on what would happen within a health system setting with or without the presence of HTA is almost impossible to derive; comparable counterfactual states (where one health system has HTA and one does not) are problematic to identify. Further, heath systems are highly variable, each operating within different contexts, with differing roles of HTA bodies in decision-making, negotiation processes and coverage differing significantly across countries, making any comparisons challenging.

With any long-term impacts, disentangling what made the difference is challenging; HTA is a type of surrogate or intermediate outcome contributing to the complex context of patient outcomes within a healthcare system. Determining the explicit impact of funding (or not) of HTA recommendations is difficult. This is particularly true if HTA is well embedded into a health system, and tracking the flows of implementation funding within any health system is almost impossible. In addition, where HTA programs lead to price cuts or negotiated prices can also complicate the assessment of value and impact; this is especially so when many price cuts, rebates or MEAs are commercially sensitive and kept confidential.

As discussed in the expert interviews, one of the key challenges experienced in conducting value and impact assessment was obtaining the requisite buy-in from stakeholders to the assessment process. Stakeholders can be deterred from participating in such a process if they believe it to be a policing or superfluous exercise. Ensuring that the goals of value and impact assessment are clearly defined early, with studies and frameworks co-designed where possible can help increase engagement. A co-design process can also help stakeholders (particularly HTA bodies, committee members and researchers) to shift mindsets from a preference for attributing direct effects of actions using comparative, long-term datasets to more pragmatic measures that are readily attainable and proportionate to the aims of the assessment.

Efforts to reframe value and impact assessment are also underway in related fields, such as within medical research institutes. The Canadian Institute for Health Research (CIHR) have developed the Health System Impact (HIS) program. The HIS provides early career researchers, PhD trainees and postdoctoral researchers the opportunity to develop embedded research projects that address the most pressing problems faced by health system organizations to support evidence-informed decision-making (51). The HIS has trained researchers to enable them to straddle the research sector and the health system and enhanced research training and capacity to allow researchers to lead change and collaborate effectively with a culture of rapid learning and improvement. The CIHR also acknowledges that to advance embedded research and support evidence-informed healthcare system transformation that impact must be appropriately recognized and rewarded, and advocates from a move away from limited measures of impact, such as the number of peer-reviewed journal articles(52).

Communicating the Value and Impact of HTA

Beyond measuring and demonstrating HTA value, communicating this value and impact to external stakeholders is both a challenge and opportunity as identified through stakeholder interviews. The pandemic highlighted the critical role of transparency in scientific communication and how it can facilitate public engagement in healthcare. Where efforts have been made to improve the communication and dissemination of HTA recommendations themselves, communication of the value and impact of HTA is often lacking. While stakeholders involved in the HTA process (for example technology manufacturers, patients, clinicians and payers) may have some appreciation of the value and impact of HTA, any value and impact assessment that is conducted by HTA bodies is typically done for internal uses and is not often publicized. Without systematic, relatable and concise presentation and discussion of the tangible and intangible benefits of HTA, these are unlikely to be fully understood. Ensuring that the evidence and deliberative processes are democratized to be accessible, explaining the narrative about the difficult choices being made, and not being perceived as a "black box" are fundamental concepts.

These communication efforts undoubtedly require additional resources and potentially lending of expertise from other fields (such as knowledge translation, implementation science and communication science). The audience needs to include the funders (i.e. governments) and wider society and should ensure that the literacy and engagement of the end user is considered early in articulating the research question and developing the communication mechanism. Using plain language where possible and tools such as GRADE and other visual aids, such as "traffic light" depictions of the strength of evidence may help. However, it is acknowledged that there are specific skill sets required to do this well, and it can also be resource intensive.

The lack of a punchy "tagline" as to what HTA is and can do was noted as a barrier during many interviews. This was from both within HTA bodies but also industry, with some organizations noting that there are misinterpretations and negative connotations of HTA as a hurdle to patient access. Some companies noted that particularly for colleagues working in countries without institutionalized HTA (such as the USA), the value of HTA still requires acknowledgement and understanding. Communicating this value can be a challenge internally within some companies; greater interactions between HTA bodies and regulators is likely to result in positive trends in understanding the value and impact of HTA. There are examples of technology manufacturers who have publicly cited their belief in the value of HTA; for example, Roche has developed a position statement highlighting the importance of HTA as an evidence-based tool to inform reimbursement and other decisions (53). The statement outlines the value of early stakeholder involvement, holistic approaches to evidence (i.e., beyond cost-effectiveness alone), and being flexible and adaptable.

Current Value and Impact Assessment Activities

In developing the background paper, 11 HTA bodies were interviewed to gather data and insights on current and planned value and impact assessment activities. This was supplemented by website reviews where interviews were not possible. This section is not intended to present an exhaustive overview of plans and activities within each organization, but presents a brief overview with key examples of activities.

Agency for Care Effectiveness (ACE, Singapore)

ACE is an example of HTA body that regularly evaluates the impact of their work. The evaluation includes monitoring the adoption rate of recommendations, improvement of health literacy and real-world outcomes of patients. Working with clinical experts and patients and using an evaluation framework, various outcomes are measured through surveys, website analytics, indicator frameworks, administrative and utilization data, and real-world studies. These measures are regularly reported on the website in a transparent manner; key achievements between 2016 and 2021 listed on the ACE website(54) estimates that the agency has delivered $400 million in cost savings to the healthcare system, and improved access and affordability for selected medicines and medical technologies for over half a million patients during the first year of subsidy listing.

Canadian Agency for Drugs and Technologies in Health (CADTH, Canada)

Traditionally, CADTH have not adopted a formal approach to value and impact assessment, with data historically captured on more on the quantity, rather than quality, of outputs as per agreed metrics with the funding body. There is a growing conversation, however, on what future measures could be considered. Examples include measuring the effects of the CADTH "implementation panels" (which consider how a technology can be implemented in practice), stakeholder engagement, and post-market evaluation. These are areas in which CADTH is particularly active at present.

Health Improvement Scotland (HIS, Scotland)

While formal value and impact assessments have not been conducted recently at HIS, the INAHTA impact templates have been adapted and more informal, qualitative, self-assessments are undertaken for some products. While these are not made publicly available, they are used for internal improvement and will flow through into changes in the outputs of the organization. Determining the contribution HTA makes to the difference in long-term patient outcomes is noted as challenging due to multiple confounding factors, availability of routine data and a need to undertake an increasing amount of HTAs. The differences between the value and impact assessment for drugs and non-drug technologies was noted; as in other systems, recommendations on drugs often come with mandatory funding and have a potential for large scale budget impacts on the system. For non-drug topics, the implementation often involves multiple aspects of the health system, with new funding required alongside program and system level change.

Health Intervention and Technology Assessment Program (HITAP, Thailand)

In addition to the EVORA, as described above, two additional projects related to impact assessment have been undertaken by HITAP:

1. The cost-effectiveness threshold has increased twice in Thailand, starting at THB 100,000 (˜US$3,000) per QALY in 2008, increasing to THB 120,00 (˜US$3,600) per QALY and THB 160,000 (˜US$4,800) per QALY in 2010 and 2013 respectively. The impacts of this will be assessed by a government-funded study(55). The project will analyze the impact of increasing the threshold on drug prices submitted by companies to the Thai government as well as the probability of each drug being recommended for reimbursement and the overall budget impact.
2. In collaboration with the International Decision Support Initiative (iDSI) and the Indonesian government, HITAP's international consulting unit assessed the impact of building local HTA

> capacity to address non-communicable disease burden was assessed. By implementing all of the HTA Committee recommendations, it was estimated that the Indonesian government could generate potential annual savings of over USD$31million and "if reinvested into the health system, this could avert an estimated 44,787 [disability-adjusted life years] DALYs in the Indonesian population. Further policy discussions facilitated through the process also paved the way for drug registration and reimbursement processes to become more aligned (56).

Challenges in undertaking value and impact assessment activities were noted in terms of resource constraints (as previously identified for all HTA bodies), but also in terms of who can be sufficiently well-informed about the HTA body while remaining neutral, independent and unbiased. Consideration may be given to whether patient groups could represent a third-party evaluator. However, a lack of a standardized approach on how to conduct, analyze and interpret value and impact assessment was reiterated as a significant hurdle in this space.

Health Technology Wales (HTW, Wales)

HTW was established in 2017 with an explicit remit to monitor the adoption of its guidance. This was primarily to promote adoption of innovation and ensure that geographic differences in uptake were explored and reduced where possible. Utilizing existing committees and structures, a co-produced pilot audit process was undertaken to determine where recommendations had either been "adopted or justified". The pilot report has been recently published on the HTW website (HTW publishes pilot adoption audit report - Health Technology Wales) and suggested that in most cases guidance published by HTW is having an impact on decision-making, awareness of HTW guidance is high and HTW guidance is considered clear. Stakeholders were engaged and supportive of a lighter touch process that did not police activities but rather genuinely explored reasons for adoption or other decisions, or otherwise. Through this process trust has been further developed between stakeholders, and improvement actions were assigned to all key stakeholders involved. Ensuring that the audit was efficiently resourced and also proportionate was important. HTW developed a prospective evaluation framework at set up, utilizing a 'contribution analysis' approach. Case studies are developed asking the key questions: what did we do, who with, what were the reactions, what did people learn and what difference did this make? In addition, data are collected via the website, surveys and stakeholder engagements. The HTW Annual Report is then based on these case studies and data returns and an annual impact statement are published on the HTW website (https://healthtechnology.wales/impact/). Having staff with the appropriate qualitative skillset to analyze the softer aspects through case studies and other qualitative methods, and shifting mindsets when considering these data, is considered critical.

Institute for Quality and Efficiency in Health Care (IQWiG, Germany)

IQWiG does not conduct formal value or impact assessment; the work that they undertake is integrated into German law and as such the tasks and structures are clearly described. The HTA reports that they generate are requested by the decision makers and scoped in consultation with the end users to ensure their relevance. Outputs are measured (for example, the number of HTA reports generated and how these were used), noting that the HTA report recommendations are not mandatory but must be considered with reasoning provided if they are not followed.

Other elements of value that are implied through IQWiG's work are observed through the early advice provided from the Federal Joint Committee (G-BA) to drug and device manufacturers on appropriate

comparators, outcomes measures, and other study design considerations felt to be appropriate for the German context. Another element that alludes to impact and value is around the ability to request and commission new studies for devices if there is too much uncertainty in the data provided in the initial application (noting that for pharmaceuticals, access is provided when they receive regulatory approval with price negotiations occurring after a defined period). There are several pathways for additional evidence generation to occur for devices, through a coverage with evidence development approach, additional industry-funded trials, trials funded and set up the joint federal committee (called "testing trials", https://www.g-ba.de/studien/erprobung/) to be conducted by independent scientific bodies (e.g., universities or hospitals). The full impact of mechanisms such as these has yet to be formally assessed.

National Committee for Technology Incorporation (CONITEC, Brazil)

CONITEC is a governmental body that centralizes evidence-based recommendations on the incorporation and maintenance of technologies and on the approval of protocols in the public health system in Brazil. Established by law in 2011, the Committee was a result of an improvement to a previous HTA group, and its processes, deadlines, and competencies are well-defined in a legal framework. To improve budgetary management, internal areas of the MoH seek to plan their annual spending considering the potential incorporation of technologies that are under evaluation. No formal studies assessing the opportunity cost of incorporating new technologies have been conducted by CONITEC yet; while the Ministry of Health is interested in such an assessment, concerns regarding the complexity and cost of doing so were noted.

In December 2022, the configuration of CONITEC was changed from one committee that evaluated all types of technologies into three specialized subcommittees: drugs and vaccines; products and procedures, and; clinical guidelines. Members from the judiciary branch were included as observers, given the number of legal proceedings requesting access to drugs and other technologies in Brazil (estimated to have incurred BRL 2.5 billion a year in technology costs, and the cost of the legal proceedings has not been estimated), in which judges often issue decisions that counteract CONITEC's recommendations. Projects have been underway for several years to improve decisions of the Judiciary branch regarding the provision of technologies by providing adequate evidence, including collaboration with universities and the creation of technical support groups. More recently, a partnership was set between the MoH, the National Council of Justice, and universities to provide evidence on technologies and support judges' decision-making process. Public consultation is a mandatory step in the CONITEC process, and work is underway to amplify and diversify societal participation and to improve the transparency of CONITEC's work. Patients and clinicians are invited to present their experience with technology at CONITEC, and public health managers will soon be requested to speak as well - in addition to its representative entities, which are members of the Committee. Since 2019, the MoH conducts the HTA Forum, whose 4th edition is expected to happen in 2023, to gather together multiple relevant stakeholder groups to foster dialog and improve CONITEC's processes.

National Institute for Health and Care Excellence (NICE, England and Wales)

NICE has an established function which produces resources to help implement guidance in the system. This includes national implementation and support tools for priority topics, work with local and regional organizations to understand challenges and support implementation best practice, and support for safe and effective prescribing and medicines optimization within local health systems. Tools are also produced that review the resource impact of NICE guidance and support local areas in financial planning. NICE works with national partners to ensure that guidance is embedded in national policy, audits and quality frameworks. Innovation scorecards are prepared twice a year measuring the uptake of medicines and medical technologies in England, which have been positively appraised by NICE (and which are mandated for funding). Measuring uptake for guidance anticipated to have a high impact on the health and care system, will continue to be explored. This will be combined with intelligence from users on system priorities will create a more systematic approach to topic selection, product development and implementation optimization.

Promoting innovation within the system is also a priority of the current British government, and so exploring the impact of activities such as scientific advice on the research and development pipelines and trial development may become more important. The Innovative Licensing and Access Pathway (ILAP - as discussed at the 2022 HTAi GPF) and also the Accelerated Access Collaborative were highlighted as examples of a HTA body, in collaboration with many health system partners, having a positive impact on innovation through a more joined up, proactive, approach.

Norwegian Institute of Public Health (NIPH, Norway)

The Norwegian Institute of Public Health (NIPH) is a government agency under the Ministry of Health and Care Services. NIPH is the main investigative body for HTAs on medical devices, in-vitro diagnostics, procedures, and organisational aspects supporting decision making on what should be introduced or scaled down within the health services in Norway. NIPH continuously develops and adjusts methodology, templates, and its product portfolio to reflect stakeholder needs. They have begun to use machine learning in HTA work and are exploring the possibilities of including national clinical registry data more directly in HTA. NIPH are also involved in European efforts such as the implementation of the HTA regulation (HTAR), the HTA Coordination Group (HTACG) and Heads of Agencies (HAG), as well as the International Horizon Scanning Initiative (IHSI). While NIPH does not have any formal measures for value or impact assessment, they note that they are involved in aspects from market access to decision making on a national level, with HTA reports being the main source used for decisions and the broadly collaborative nature of their work (mainly clinicians and patient representatives, but sometimes also procurement services and others). Furthermore, the Norwegian Medicines Agency commission a dossier-based single technology assessment on every pharmaceutical with a new active substance or a new indication for use that gets marketing authorisation through EMA (European Medicines Agency) and those HTAs are always co-commissioned for price negotiations by the national procurement services.

Pharmaceutical Benefits Advisory Committee/Medical Services Advisory Committee (PBAC/MSAC, Australia)

In Australia at present, a strategic agreement between the Australian government and Medicines Australia (the pharmaceutical trade association) is in place. Under this strategic agreement, a HTA policy and methods review is being supported and resourced, with the stated goals of: "*reducing time to access to health technologies for Australian patients so that they can access new health technologies as early as possible, and; building on Australia's status as a world leader in providing patients access to affordable healthcare*". This review will consider the assessment processes to ensure that they keep pace with rapid advances in heath technology and that barriers to access are minimized. A HTA review reference committee has been established (with an independent chair) and the review will consider topics such as: selection of comparators; methods for evaluating rare diseases and new and emerging technologies and the suitability of existing funding pathways; use of real-world evidence; and managing uncertainty and the feasibility of international work-sharing for reimbursement submissions. In 2022, as part of the agreement, advice was sought from the PBAC on whether the base case discount rate aligns with international best practice. Following a review of international practices, the PBAC determined that there is no academic, professional or international consensus on what is a 'best practice' discount rate for the purposes of an economic evaluation in the HTA setting. The PBAC noted the impact that varying discount rates can have on a HTA and considered that the current base-case discount rate was reasonable and allows flexibility in the discounting methodology used where justified. The effect of the HTA review on the value and impact of HTA in Australia will be closely monitored by a number of interested stakeholders.

Zorginstituut Nederland (ZIN, The Netherlands)

The National Health Care Institute (Zorginstituut Nederland, ZIN) has a program for evaluating its impact. The impact is measured on various indicators of effect and can be illustrated by three examples. The first example is on the level of effective use of HTA as a tool for the negotiation of health technology prices. The HTA's performed by ZIN are used by the Ministry of Health for price negotiations. As these negotiations are confidential, the MoH reports on an annual basis the average savings based on the price negotiation. Independent research showed that the annual discount obtained in the period from 2015-2018 increased from 25% to 36%. The most recent letter from the MOH reports savings of more than 50% for 2020 for drugs for which ZIN advised a specific price (n=15). The second example is an annual monitor of the appropriate care program, which is a program in which ZIN assessed whether diagnostics and therapeutic interventions are being deployed in a patient-oriented, effective and cost-effective manner. The monitor measures the effective implementation of policy change recommendations. Tracking the implementation of policy change recommendations in 2022 shows that 3 years after publication of the recommendation (n=290), over 20% are fully implemented and around 50% are in progress. Finally, in 2022 a pilot was started to measure the reputation of the institute. The first results show that ZIN's reputation is considered to be stable and 'sufficient'.

The Response to the COVID-19 Pandemic

Variation in the global approaches taken to contain the COVID-19 pandemic were shaped by economic and political considerations, technical capacity, and assumptions about public behaviors (58). The role that HTA bodies played in the pandemic response also varied widely and exemplified the inherent

tension between evaluation and the imperative to urgently deploy solutions (59). Health systems struggled to cope with the population health impact of COVID-19, with healthcare facilities and critical care systems buckling under the extraordinary pressures (60). Extreme social distancing and shielding in place for vulnerable patients during the COVID-19 pandemic created both the challenge and the opportunity to provide care at a distance on a large scale (61).

The pandemic resulted in the emergency use of health resources, introduced using expedited regulatory pathways and implemented in health systems across the world in unprecedented fashion (62). Concerns were raised by some GPF members that the pandemic response may lead to future bypassing of HTA systems and processes in favor of expedited approvals, direct price negotiation and procurement in some jurisdictions. However, in other jurisdictions, HTA bodies played a key role in facilitating the healthcare system response to the pandemic. As noted, HTA can play a critical role in connecting science, innovation, technology, and health policy; for example the 'research to access' pathway for investigational drugs for COVID-19 (RAPID C-19), a multi-agency initiative facilitated by NICE in the UK. In particular, the multidisciplinary aspect of HTA and using a technology lifecycle and systems approach (as opposed to HTA for technology adoption or cost containment) was considered useful by many.

While sparse, specific examples of the value HTA played in the pandemic response are noted in the literature, included convening different skills to provide high-quality research information on the effectiveness, costs, and impact of biomarkers and vaccines. HTA methodology enabled rapid cost-effective implementation of diagnostic tests, allowing healthcare providers to make critical patient-management decisions (63). Another key area in the pandemic response played by HTA bodies was in the review, prioritization and implementation of COVID-19 vaccines. In an article by Refolo at al (64), the European Values in Doing Assessments of healthcare Technologies (VALIDATE) project was drawn upon to reframe the issues around prioritization of COVID-19 vaccines. The authors of this review stated that the European VALIDATE project was able to provide a useful approach to address policy-problem definitions, incorporate different perspectives, contextualize consideration and specification of moral principles in vaccination plan documents.

The HTAi 2021 Asia Policy Forum (65) considered the pandemic response by HTA bodies in the Asia region in detail. During this Forum, it was discussed that HTA bodies were able to clearly demonstrate their value in terms of priority-setting (particularly shifting the focus to prioritizing public health needs rather than technology-driven demand). The shift to new models of care (for example virtual care and the use of artificial intelligence) was supported by HTA bodies with an increased use of real-world evidence. The role of HTA bodies as a facilitator was particularly highlighted, with greater national regional and international collaboration observed within HTA bodies but also across health systems.

The role of HTA as facilitator was also noticeable elsewhere. Networks such as EUnetHTA prioritized work related to COVID-19 and introduced rolling collaborative reviews (RCRs) on relevant treatments and diagnostics. EUnetHTA acted as a central coordinating body for COVID-19 work, bringing partners, experts and relevant information together. The COVID-19 Evidence Network to support Decision-making (COVID-END) is another such example. This is a time-limited network that brought together more than 50 of the world's leading evidence synthesis, technology assessment, and guideline development groups. It aimed to support decision-making around COVID-19 using the best available evidence and by better coordinating the evidence synthesis, technology assessments and guidelines being produced. This network produced global spotlights that updated the 'best' living evidence

syntheses and horizon scan documents that include briefing notes about emerging and priority COVID-19 issues.

As summarized at the HTAi annual meeting in 2021 by Tracy Merlin (66), the pandemic accelerated collaboration and information gathering. In many countries, ultra-rapid HTA was the norm, but estimating the cost-effectiveness of interventions was often not attempted in the interest of timeliness. Additional longstanding challenges were exacerbated by the pandemic: the lack of capacity within HTA bodies and a general skills shortage was especially evident. There was a need to evaluate many COVID-19 related interventions with limited evidence in unprecedented short timeframes. These challenges were compounded by huge amount of information (and misinformation) on social media and the impact of societal expectations on speed, rigor, and equity of access. The combination of these two factors led to many HTA bodies (as well as many other organizations) to experience burn out of staff.

Enhancing the Future Value and Impact of HTA

A historical view on how the impact of HTA has been estimated and developing an understanding of which HTA efforts have resulted in the most value may help ensure that efforts can be directed to sustain the relevance of HTA in the future. This may include exploring whether particular activities result in greater value and impact than others (for example early scientific dialog and meaningful, ongoing stakeholder engagement and communication) or where resources are being used with a lower 'return on investment' (for example routine reassessments on lower-cost technologies). Prioritization of efforts by technology type or condition may also be possible; these issues were all raised at the 2022 HTAi Global Policy Forum(67).

Global initiatives such as Impact HTA (a Horizon 2020 project led by the London School of Economics) may also prove useful (68). Impact HTA is a project that is looking at new and improved methods, tools and guidance for decision-makers across 10 thematic areas (including methodological issues such as combining RCTs and real-world evidence and other methods to deal with non-randomized data, methods for calculating health care and social costs, conduct of hospital-based assessments, and how to measure fiscal impact and HTA implementation), with the aim of enhancing HTA. Another example is the HTx project, (69) also from Horizon 2020, that will facilitate the development of methodologies to deliver more customized information on the effectiveness of health technologies, methods to support personalized treatment advice, and implementation of a pilot of these methods in Europe. Examples such as these, and of course other effective collaborations across HTA agencies (i.e. the EU HTA Regulation, the AUS-CAN-UK collaboration) and with other key stakeholders such as regulators may also help in better coordinating and streamlining HTA activities. Measuring this will be a critical activity, one that must take all stakeholder perspectives into account.

Frameworks for Future HTA Value and Impact Assessment

Much of the literature around value and impact assessment and many academics and organizations involved in this space advocate for the development of a Theory of Change model to guide any value or impact assessment process. A theory of change model can explain how activities are understood to contribute to a series of results that produce the final intended impacts, and is even used as a platform for the development of HTA in low and middle income countries(70). Theory of change is a purpose driven, dynamic model that shows how a program (or any intervention) contributes to achieve the intended result through a chain of short-term, mid-term and long-term outcomes (71). Many not-for-profit organizations use theory of change models presented as a narrative statement or visual

illustration that connects the mission and strategy of the program to social change. During impact assessment, the existing theory of change should be reviewed and revised as needed; it is intended to be flexible without a particular format, and forms a blueprint for evaluation.

Another key concept in order to determine both value and impact of any activity is monitoring and evaluation (M&E), two distinct sets of organizational activities. Monitoring is the periodic assessment of activities to determine whether they are proceeding as planned. Evaluation involves the assessment of the program towards results and impact of the outcomes based on the use of performance indicators. M&E requires funds, trained personnel, tools, data collection and time. There are many frameworks and tools developed to facilitate and support M&E activities, and an increasing number of organizations that aim to support such activities.

Value and Impact Assessment in Related Fields

One sector that contains concepts that are aligned with HTA is that of philanthropy. In this field, there is a proliferation of organizations that support the assessment of value and impact of philanthropic activities. One such example is the recently established Centre for Strategic Philanthropy based at Cambridge University, UK, which noted that "*well over a trillion dollars of private philanthropic capital is now deployed every year, and there is evidence that…the world's emerging economies are becoming an increasingly powerful source of philanthropic capital and social innovation"*. In addition to a growing level of philanthropic funding there are additional efforts supporting philanthropic organizations (such as the Centre for Strategic Philanthropy and the New Philanthropy Capital) that aim to catalyze greater philanthropic impact by informing and cultivating strategic philanthropy and strengthening the broader philanthropic ecosystem through collaboration.

A key accelerant for these developments is the concept of "effective altruism"; coined about a decade ago, its focus is on using evidence and careful reasoning to take actions that help others as much as possible. Under effective altruism, action is prioritized to maximize impact of the limited time, energy and resources available. On a related note, the Mulago Foundation that suggests that the funders themselves should be accountable for impact; they argue that philanthropy and aid will never have more than a marginal difference if funders remain unaccountable. The argument is that impact is an observable and quantifiable change in terms of a specific outcome, with the outcome that matters most being the one central to the organization's mission. Another organization, GiveWell, explicitly uses cost-effectiveness analysis to assess the performance of their charitable investments and prioritize future areas for funding.

Finally, Social Return on Investment (SROI) is a systematic construct of incorporating social environmental, economic and other values into decision making processes and is used in health and non-health applications alike. SROI uses a weighting scheme to measure the economic value of social and environmental outcomes and creates a holistic perspective on whether a project or organization is beneficial and profitable placing the perspective of the stakeholder at the core. Advocates of the approach argue that SROI can be integrated into existing M&E approaches, rather than as an add-on activity. It has the capacity to create awareness of the needs and roles of stakeholders within a system, and can even lead to mind-shifts and realizations on the costs of activities. Critics however highlight that it takes a lot of work to find the financial value of each benefit, it needs whole-of-organization support – which takes a long time to build, and there is a degree of subjectivity as SROI analysts have to apply their own discretion when they measure and evaluate the effects.

Key Discussion Points

Below is a summary of the key discussion points contained within this document, arising from the literature review, stakeholder interviews and consultations:

- Can the HTAi GPF develop a tool, checklist and/or some principles around value and impact assessment conducted by HTA bodies globally?
- What are the most useful metrics for determining the value and impact of HTA? Can particular metrics be prioritized for recording and analysis? How does this vary by perspective taken?
- How can longer term impacts (such as shifts in population health, or infrastructure changes and development of training courses) best be captured?
- What metrics are overused and/or uninformative? Conversely, what measures are underappreciated or even missing?
- How can the holistic value and impact of HTA be best communicated to different audiences (for example, patients, the public, clinicians, policy makers, payers and the industry)? Can a 'punchy tagline' be developed that takes the perceived barriers and challenges associated with HTA into account?
- Are there differences in the value and impact of HTA according to:
    - technology type
    - condition
    - maturity and/or integration of HTA into the health system
    - in-country resources (e.g. LMIC compared to HIC)
- Are there different metrics that more usefully apply when considering different lifecycle activities or according to the definition of HTA applied (i.e. "full" HTA through to the application of the principles of HTA)?
- What are the main barriers and challenges in determining the value and impact of HTA?
- How can the impact (return on investment) of value and impact assessment activities be measured? How can value and impact assessment activities be undertaken in a pragmatic and proportionate way?
- How can resources, learnings and data best be shared (between agencies) to minimize the burden and resource implications of conducting value and impact assessments?
- What are the best approaches for engaging multiple stakeholders in determining the holistic value and impact of HTA? How can patients and other stakeholders be better trained to input, but without increasing perceptions of conflicts of interest and the burden?
- What role could and should external bodies (such as HTAi and INAHTA and others) play in determining and disseminating the value and impact of HTA?
- What approaches can be taken to enhance:
    - the measurement of the value and impact of HTA?
    - The demonstration of the value and impact of HTA
    - The future value and impact of HTA (taking into account the dynamic regulatory landscape and increase in innovative technologies); is the potential for HTA underestimated?
    - What are the key risks to the future value and impact of HTA?

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Appendix

INAHTA - Framework for reporting on impact of HTA reports

Before completing this form, please review the accompanying instructions (Appendix A).
To complete this form, tick boxes or add text where indicated.
Send completed form to the INAHTA Secretariat at INAHTA@ihe.ca

International Network of Agencies for Health Technology Assessment. INAHTA Framework for reporting on impact of HTA reports, Version 5 (2021). Available at: www.inahta.org

A. Agency	B. Name of Technology	B.1. Add any needed qualification – e.g., particular application
C. Date of this record:	D. Date of HTA report:	***The date of the record should be not less than 6 months after the publication date of the HTA report***
E. Origin of HTA request	[Give the name or type of organization that made the request. This might be government – related (e.g. health ministry) or non – government (e.g. professional body). If the report was not solicited from outside the agency, please indicate this]	
F. Purpose of HTA	F.1. [Tick one or more] ☐1 Coverage decisions ☐2 Capital funding decisions ☐3 Formulary decisions ☐4 Referral for treatment ☐5 Program operation ☐6 Guideline formulation ☐7 Influence on routine practice ☐8 Indications for further research ☐9 Other:	F.2. [Single sentence of explanation/qualification, if needed]
G. HTA conclusions	[1 or 2 sentences]	
H. Indications of impact	H.1. [Tick one or more] ☐1 HTA considered by decision-maker ☐2 HTA recommendations/conclusions accepted	H.2 [1 or 2 sentences to give further information]

	☐3 HTA demonstrated that technology met specific program requirements ☐4 HTA material incorporated into policy or administrative documents ☐5 HTA information used as reference material ☐6 HTA linked to changes in practice ☐7 HTA linked to changes in health status ☐8 No apparent impact ☐9 Other (specify):	
I. AGENCY'S opinion on level of impact	I.1. [Tick one] ☐1 No apparent influence ☐2 Some consideration of HTA by decision maker ☐3 Informed decisions ☐4 Major influence on decisions	I.2 [1 or 2 sentences indicating basis/ reasons for opinion] [indicate whether unintended influence led to a change in HTA procedure]
	I.3 Indicate any unintended influence the HTA had: Did the unintended influence lead to a change in HTA procedure? [Tick one] ☐1 Yes ☐2 No	
J. EXTERNAL opinion on level of impact of the HTA	Source of opinion: [Tick one] ☐1 No apparent influence: ☐2 Some consideration of HTA by decision maker: ☐3 Informed decisions: ☐4 Major influence on decisions:	

Appendix A.

INAHTA – Framework for reporting on impact of HTA reports

Instructions for use (3 pages)

Framework section	Action	Comments
A. Agency	Enter the acronym or name of your agency in this box	
B. Name of technology	Enter the name of the technology that was considered by the HTA	
	In box B.1 add any further explanation of the technology, for example a particular application that was considered	Entry of such information is optional
C. Date of this record	Enter the date that this record (the impact framework) was completed	As indications of impact may take some time to become apparent, the date of the record should be at least 6 months after the publication date of the HTA report. 6 months is the minimum period. The timing of the record of impact after 6 months is a matter for the agency to determine.
D. Date of HTA report	Enter the date of publication of the HTA report	
E. Origin of the HTA request	Enter the name or the type of organization that made the request for the HTA. If the HTA report was not requested from outside your agency, please indicate this.	Organizations might be government – related (e.g. health ministries) or non – government (e.g. professional bodies).
F. Purpose of the HTA	In box F.1 are eight types of decision that might have been informed by the HTA. Please mark one or more of these, as appropriate.	If there was some other type of decision that was informed by the HTA please mark " #9 Other" and briefly mention what it was
	In Box F.2 add any explanation regarding the type of decision that seems appropriate	This is optional. One or two sentences would be sufficient.
G. Conclusions reached by the HTA	Briefly outline the conclusions reached by the HTA.	One or two sentences would be sufficient. If appropriate, these might include major recommendations that were made.

Framework section	Action	Comments
H. **Indications of impact**	In Box H.1 are seven possible indications of the impact the HTA might have had . Please mark one or more of these. If there was some other type of impact of the HTA please mark "#8 Other" and briefly mention what it was.	1. HTA considered by decision - maker. [The HTA was considered but further impact was not obvious/ apparent.] 2. Acceptance of HTA recommendations/ conclusions [clear acceptance of HTA findings possibly, but not necessarily, linked to action by the decision maker.] 3. HTA demonstrated that a technology met specific program requirements [in circumstances where the HTA and its findings are linked to a program, for example where minimum standards must be met before some type of approval is given.] 4. HTA material is incorporated into policy or administrative documents [Material in an HTA is cited in subsequent documentation.] 5. HTA information used as reference material. [The HTA is used by decision makers as an ongoing source of information] 6. HTA linked to changes in practice [The HTA may be one of a number of factors influencing such change] 7. No apparent impact
	In Box H.2 provide further information, as appropriate.	One or two sentences should be sufficient
I. Agency's opinion on level of impact	In Box I.1. are four categories of influence of the HTA. Please mark one of these to indicate the opinion of your agency on the level of impact that was achieved.	
	In Box I.2 briefly indicate the basis for your agency's opinion	1 or 2 sentences should be sufficient Details might include reasons for the report having no apparent influence, or the way in which the agency's opinion had been formed (for example through a survey of stakeholders).
	If the HTA had an unintended influence, please note this in Box I.3	For example, the conclusions of the HTA might have been misunderstood by a decision maker and action taken that was contrary to the intent of the HTA.

Framework section	Action	Comments
	Also note if the unintended influence led to a change in HTA procedure at your agency	Reference could be made here to any significant media coverage that may have increased the impact of the HTA report.
J. External opinion on level of impact of the HTA	Please note the **source** of any external opinion on level of impact. Inclusion of this information is essential if this box is to be completed. Please mark one of the four possible categories of influence of the HTA. to indicate the opinion of other organizations on the level of impact that was achieved.	For example, feedback may have been obtained from the organization that requested the HTA. Organizations such as patients/consumer groups and professional bodies may also be sources of opinion on impact

References

1. Raftery J, Hanney S, Greenhalgh T, Glover M, Blatch-Jones A. Models and applications for measuring the impact of health research: update of a systematic review for the Health Technology Assessment programme. Health Technol Assess. 2016;20(76):1-254.
2. O'Rourke B, Oortwijn W, Schuller T. The new definition of health technology assessment: A milestone in international collaboration. Int J Technol Assess Health Care. 2020;36(3):187-90.
3. World Health Organization. Regional Office for E, European Observatory on Health S, Policies, Velasco Garrido M, Kristensen FB, Nielsen CP, et al. Health technology assessment and health policy-making in Europe: current status, challenges and potential. Copenhagen: World Health Organization. Regional Office for Europe; 2008 2008.
4. Eichler HG, Baird LG, Barker R, Bloechl-Daum B, Børlum-Kristensen F, Brown J, et al. From adaptive licensing to adaptive pathways: delivering a flexible life-span approach to bring new drugs to patients. Clin Pharmacol Ther. 2015;97(3):234-46.
5. Rome BN, Avorn J. Drug Evaluation during the Covid-19 Pandemic. New England Journal of Medicine. 2020;382(24):2282-4.
6. Pereno A, Eriksson D. A multi-stakeholder perspective on sustainable healthcare: From 2030 onwards. Futures. 2020;122:102605.
7. (NICHSR) NICoHSRaHCT. HTA 101: IX. MONITOR IMPACT OF HTA 2014 [Available from: https://www.nlm.nih.gov/nichsr/hta101/ta101011.html.
8. Millar R, Morton A, Bufali MV, Engels S, Dabak SV, Isaranuwatchai W, et al. Assessing the performance of health technology assessment (HTA) agencies: developing a multi-country, multi-stakeholder, and multi-dimensional framework to explore mechanisms of impact. Cost Eff Resour Alloc. 2021;19(1):37.
9. Lopes E, Street J, Carter D, Merlin T, Stafinski T. Understanding Canadian Health Technology Assessment through a systems lens. Health Policy. 2020;124.
10. Stafinski T, Street J, Menon D. OP114 The Public's Role In Understanding The Value Of Health Technologies. International Journal of Technology Assessment in Health Care. 2018;34:43-4.
11. Street J, Stafinski T, Lopes E, Menon D. Defining the role of the public in Health Technology Assessment (HTA) and HTA-informed decision-making processes. International Journal of Technology Assessment in Health Care. 2020;36:1-9.
12. O'Rourke B, Werkö SS, Merlin T, Huang LY, Schuller T. The 'Top 10' Challenges for Health Technology Assessment: INAHTA Viewpoint. International Journal of Technology Assessment in Health Care. 2020;36(1):1-4.
13. Berglas S, Vautour N, Bell D. Creating a patient and community advisory committee at the Canadian Agency for Drugs and Technologies in Health. Int J Technol Assess Health Care. 2021;37:e19.
14. (NICE) NIoHaCE. NICE Listens 2022 [Available from: https://www.nice.org.uk/get-involved/nice-listens.
15. Jansen M, Baltussen R, Bijlmakers L, Tummers M. The Dutch Citizen Forum on Public Reimbursement of Healthcare: A Qualitative Analysis of Opinion Change. Int J Health Policy Manag. 2022;11(2):118-27.
16. Tonkiss K, Skelcher C. Abolishing the Audit Commission: Framing, Discourse Coalitions and Administrative Reform. Local Government Studies. 2015;41(6):861-80.
17. Loblova O. What has health technology assessment ever done for us? Journal of Health Services Research & Policy. 2017;23:135581961772554.
18. Wang T, Lipska I, McAuslane N, Liberti L, Hövels A, Leufkens H. Benchmarking health technology assessment agencies—methodological challenges and recommendations. International Journal of Technology Assessment in Health Care. 2020;36(4):332-48.

19. Greenhalgh T, Raftery J, Hanney S, Glover M. Research impact: a narrative review. BMC Med. 2016;14:78.
20. Donovan C, Hanney S. The 'Payback Framework' explained. Research Evaluation. 2011;20:181-3.
21. Raftery J, Powell J. Health Technology Assessment in the UK. Lancet. 2013;382(9900):1278-85.
22. Morton AB, E. . EVORA (Evaluating the Value of a Real-world HTA agency) simulation spreadsheet 2020 [Available from: https://pureportal.strath.ac.uk/en/datasets/evora-evaluating-the-value-of-a-real-world-hta-agency-simulation-.
23. Kingkaew P, Budtarad N, Khuntha S, Barlow E, Morton A, Isaranuwatchai W, et al. A model-based study to estimate the health and economic impact of health technology assessment in Thailand. International Journal of Technology Assessment in Health Care. 2022;38(1).
24. Platform EI. Supreme Audit Institutions and Citizen Engagement 2014 [Available from: https://www.theicpa.org/files/OECDPolicy_brief_Supreme_Audit_Institutions_and_Citizen_Engagement.pdf.
25. Hailey DM, K. Aleman, A. Bakri, R. . The Influence of Health Technology Assessment: A Conceptual Paper 2014. Available from: https://www.inahta.org/wp-content/uploads/2014/03/INAHTA_Conceptual-Paper_Influence-of-HTA1.pdf.
26. Velasco Garrido M, Gerhardus A, Røttingen JA, Busse R. Developing Health Technology Assessment to address health care system needs. Health Policy. 2010;94(3):196-202.
27. Schuller T, Söderholm Werkö S. INSIGHTS FROM THE FRONT LINES: A COLLECTION OF STORIES OF HTA IMPACT FROM INAHTA MEMBER AGENCIES. International Journal of Technology Assessment in Health Care. 2017;33(4):409-10.
28. Sutton E. The increasing significance of impact within the Research Excellence Framework (REF). Radiography. 2020;26:S17-S9.
29. Choudhary S. Measuring Collaboration2021.
30. Löblová O, Trayanov T, Csanádi M, Ozierański P. The Emerging Social Science Literature on Health Technology Assessment: A Narrative Review. Value Health. 2020;23(1):3-9.
31. Daniels N, van der Wilt GJ. HEALTH TECHNOLOGY ASSESSMENT, DELIBERATIVE PROCESS, AND ETHICALLY CONTESTED ISSUES. Int J Technol Assess Health Care. 2016;32(1-2):10-5.
32. Goodman C. HTA AND INNOVATION OF VALUE: GETTING TO KNOW YOU. International Journal of Technology Assessment in Health Care. 2013;29(4):351-2.
33. Woolliscroft JO. Innovation in Response to the COVID-19 Pandemic Crisis. Acad Med. 2020;95(8):1140-2.
34. Leyens L, Brand A. Early Patient Access to Medicines: Health Technology Assessment Bodies Need to Catch Up with New Marketing Authorization Methods. Public health genomics. 2016;19:187-91.
35. IQVIA. EFPIA Patients W.A.I.T. Indicator 2021 Survey 2022. Available from: https://www.efpia.eu/media/676539/efpia-patient-wait-indicator_update-july-2022_final.pdf.
36. EFPIA. The root cause of unavailability and delay to innovative medicines: Reducing the time before patients have

access to innovative medicines2022. Available from: https://www.efpia.eu/media/636822/root-cause-unavailability-delays-cra-report-april-2022-final.pdf.
37. The Lancet H. Ensuring that accelerated approvals benefit patients. The Lancet Haematology. 2021;8(9):e613.
38. Cubi-Molla P. Economics OoH, editor2022. Available from: https://www.ohe.org/news/let%E2%80%99s-talk-about-health-inequalities.
39. Garzón-Orjuela N, Samacá-Samacá DF, Luque Angulo SC, Mendes Abdala CV, Reveiz L, Eslava-Schmalbach J. An overview of reviews on strategies to reduce health inequalities. International Journal for Equity in Health. 2020;19(1):192.

40. Santos M. Health Equity for HTA: A Conversation With Wanrudee Isaranuwatchai, PhD 2022 [
41. Organization WH. Health intervention and technology assessment in support of universal health coverage2014. Available from: https://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R23-en.pdf#:~:text=SIXTY-SEVENTH%20WORLD%20HEALTH%20ASSEMBLY%20WHA67.23%20Agenda%20item%2015.7,technology%20assessment%20in%20support%20of%20universal%20health%20coverage%3B1.
42. Labonté R. Health Promotion in an Age of Normative Equity and Rampant Inequality. Int J Health Policy Manag. 2016;5(12):675-82.
43. (NICE) NIoHaCE. NICE health technology evaluations: the manual2022. Available from: https://www.nice.org.uk/process/pmg36/chapter/committee-recommendations.
44. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value Health. 2022;25(1):3-9.
45. Cookson R, Mirelman AJ, Griffin S, Asaria M, Dawkins B, Norheim OF, et al. Using Cost-Effectiveness Analysis to Address Health Equity Concerns. Value Health. 2017;20(2):206-12.
46. Barsanti S, Nuti S. The equity lens in the health care performance evaluation system. The International Journal of Health Planning and Management. 2014;29(3):e233-e46.
47. Cookson R, Mirelman AJ. Equity in HTA: what doesn't get measured, gets marginalised. Isr J Health Policy Res. 2017;6:38.
48. Berndt NS, T. HTA Impact Assessment Study. Part I. Practices of HTA Impact Assessment in INAHTA Member Agencies 2020. Available from: file:///C:/Users/rebec/Downloads/Part%20I-HTA%20Impact%20Assessment%20Practices%20in%20INAHTA%20(3).pdf.
49. Berndt NS, T. HTA Impact Assessment Study. Part II: Factors that enable or inhibit HTA impact assessment activities in HTA agencies2020. Available from: file:///C:/Users/rebec/Downloads/Part%20II-Factors%20that%20Enable%20or%20Inhibit%20HTA%20Impact%20Assessment%20(2).pdf.
50. Valentim JS, V. . Unified Industry HTA position to partner with healthcare systems (HCSs) for HTA. HTAi Annual Meeting: Innovation through HTA Virtual 2021.
51. (CIHR) CIfHR. The Health System Impact Program 2022 [Available from: https://cihr-irsc.gc.ca/e/51211.html.
52. Meghan McMahon SBSJC-ADET, Adalsteinn B. How Do We Build the Human Capital for a True Learning Healthcare System? HealthcarePapers. 2022;20(3):44-52.
53. (Roche) HLR. Roche Position on Health Technology Assessment 2020. Available from: https://assets.cwp.roche.com/f/126832/18b080c040/roche-position-health-assessment-technology.pdf.
54. (ACE) AfCE. Key Achievements: 2016 - 2021 2021 [Available from: https://www.ace-hta.gov.sg/about-us/our-impact/key-achievements.
55. Isaranuwatchai W, Nakamura R, Wee H, Sarajan M, Wang Y, Soboon B, et al. What are the impacts of increasing cost-effectiveness Threshold? a protocol on an empirical study based on economic evaluations conducted in Thailand. PLOS ONE. 2022;17:e0274944.
56. Sharma M, Teerawattananon Y, Luz A, Li R, Rattanavipapong W, Dabak S. Institutionalizing Evidence-Informed Priority Setting for Universal Health Coverage: Lessons From Indonesia. Inquiry. 2020;57:46958020924920.
57. (HTW) HTW. HTW publishes pilot adoption audit report 2022 [Available from: https://healthtechnology.wales/htw-publishes-pilot-adoption-audit-report/#:~:text=Key%20findings%20from%20the%20audit%20included%20the%20following%3A,clarity%20of%20HTW%20guidance%20recommendations%20is%20considered%20good.
58. Ahmad R, Atun RA, Birgand G, Castro-Sánchez E, Charani E, Ferlie EB, et al. Macro level influences on strategic responses to the COVID-19 pandemic - an international survey and tool for national assessments. J Glob Health. 2021;11:05011.

59. Magrabi F, Ammenwerth E, Craven CK, Cresswell K, De Keizer NF, Medlock SK, et al. Managing Pandemic Responses with Health Informatics - Challenges for Assessing Digital Health Technologies. Yearb Med Inform. 2021;30(1):56-60.
60. Brambilla A, Sun TZ, Elshazly W, Ghazy A, Barach P, Lindahl G, et al. Flexibility during the COVID-19 Pandemic Response: Healthcare Facility Assessment Tools for Resilient Evaluation. Int J Environ Res Public Health. 2021;18(21).
61. Choudhary P, Bellido V, Graner M, Altpeter B, Cicchetti A, Durand-Zaleski I, et al. The Challenge of Sustainable Access to Telemonitoring Tools for People with Diabetes in Europe: Lessons from COVID-19 and Beyond. Diabetes Ther. 2021;12(9):2311-27.
62. Jit M, Ananthakrishnan A, McKee M, Wouters OJ, Beutels P, Teerawattananon Y. Multi-country collaboration in responding to global infectious disease threats: lessons for Europe from the COVID-19 pandemic. Lancet Reg Health Eur. 2021;9:100221.
63. Ferraro S, Biganzoli EM, Castaldi S, Plebani M. Health Technology Assessment to assess value of biomarkers in the decision-making process. Clin Chem Lab Med. 2022;60(5):647-54.
64. Refolo P, Bloemen B, Corsano B, Grin J, Gutierrez-Ibarluzea I, Hofmann B, et al. Prioritization of COVID-19 vaccination. The added value of the "VALIDATE" approach. Health Policy. 2022;126(8):770-6.
65. Mundy LK, B. . HTA in Asia Post COVID 2021 Available from: https://past.htai.org/wp-content/uploads/2021/12/2021-APF.pdf?_ga=2.221540254.720160264.1669356161-2036436427.1663739564&_gl=1*x0q8o9*_ga*MjAzNjQzNjQyNy4xNjYzNzM5NTY0*_ga_79CPBECN0V*MTY2OTQzODkzMy4xMi4wLjE2Njk0Mzg5MzMuMC4wLjA.
66. Merlin T, editor Evidence for HTA: Innovative Methods for Challenging Times HTAi Annual Meeting: Innovation through HTA 2021 Virtual
67. Trowman R, Ollendorf DA. HTA 2025 and Beyond: Lifecycle Approaches to Promote Engagement and Efficiency in Health Technology Assessment2022 August 2022.
68. HTA I. Improved methods and actionable tools for enhancing HTA 2021 [Available from: https://www.impact-hta.eu/.
69. 2020 EUH. Next Generation Health Technology Assessment 2020 [Available from: https://www.htx-h2020.eu/.
70. Rogers P. Theory of Change, Methodological Briefs: Impact Evaluation 22014.
71. Reinholz DL, Andrews TC. Change theory and theory of change: what's the difference anyway? International Journal of STEM Education. 2020;7(1):2.