

# New developments in HTA

Evolution not revolution in Health Technology Assessment



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### About this report

New developments in HTA: Evolution not revolution in Health Technology Assessment is a report by the Economist Intelligence Unit. The goal of the research is to identify and describe new and emerging developments in Health Technology Assessment (HTA) and describe the developments that will be seen in the near future. The research phase took place during the early stages of COVID-19, and while not a focus of the report, we have touched on the impact of the pandemic in relevant sections throughout the report.

We have used the definition of HTA provided by EUnetHTA—a collaborative network of European HTA agencies—as "a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner."<sup>1</sup> HTA is often used to inform decisions about the adoption of new health care interventions, including sometimes the financial reimbursement offered to the provider of the technology.<sup>2</sup>

There is a series of four associated animated infographics that summarise four of the five themes described in this report. These can be found at: <u>https://eiuperspectives.economist.com/healthcare/new-</u> <u>developments-hta-evolution-not-revolution-health-technology-assessment</u>

The report and infographics are sponsored by Roche. The views expressed are solely the responsibility of The Economist Intelligence Unit and do not necessarily reflect those of the sponsor. The report was authored by Leela Barham and Alan Lovell.

### Glossary

BWS	Best-worst scaling					
CADTH	Canadian Agency for Drugs and Technologies in Health					
CDF	Cancer Drugs Fund (England)					
CONITEC	The National Committee for Health Technology Incorporation (Brazil)					
DCE	Discrete choice experiment					
EUnetHTA	European Network for Health Technology Assessment					
HAS	National Authority for Health (France)					
HTA	Health Technology Assessment					
HTAi	Health Technology Assessment International					
ICER	Institute for Clinical Economic Review					
INAHTA	International Network of Agencies for Health Technology Assessment					
IQWiG	Institute for Quality and Efficiency in Health Care (Germany)					
ISPOR	International Society of Pharmacoeconomics and Outcomes Research					
MAA	Managed access agreement					
MEA	Managed entry agreement					
NASS	National Ankylosing Spondylitis Society					
NICE	The National Institute for Health and Care Excellence (England)					
OECD	Organisation for Economic Co-operation and Development					
PACE	Patient and Clinician Engagement (Scotland)					
PBAC	Australian Pharmaceutical Benefits Advisory Board					
pCODR	pan-Canadian Oncology Drug Review					
QALY	Quality Adjusted Life Year					
RCT	Randomised controlled trial					
RWD	Real-world data					
RWE	Real-world evidence					
SMC	Scottish Medicine Consortium					
TLV	Dental and Pharmaceutical Benefits Agency (Sweden)					
ZIN	The National Health Care Institute (Netherlands)					

### Introduction

#### A brief history of Health Technology Assessment

Health Technology Assessment (HTA) began in 1976, with the first report published by the US Office of Technology Assessment.<sup>3</sup> HTA is "a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner."<sup>1</sup> The findings from these processes are used to inform decisions about the adoption of new health care interventions, including sometimes the financial reimbursement offered to the provider of the technology.<sup>3</sup>

Despite its long history, HTA is not standing still. Even as recently as 2019 there has been an international effort to renew the definition of HTA itself,<sup>4</sup> and a new definition was published in May 2020.<sup>5, 6</sup> Practitioners recognise that HTA has to continue to innovate if it is to support changing health care environments. There are ongoing shifts in the typical pattern of doing HTA (sometimes also referred to as the paradigm of HTA).<sup>7</sup> We discuss here some of these shifts—through the adoption and refinements of new methods and processes—in the practice of HTA.

Practitioners see several challenges for HTA as it is practiced today. A survey of members of the International Network of Agencies for Health Technology Assessment (INAHTA)<sup>\*</sup>, conducted during November 2017, and published in December 2019, identified ten challenges for HTA:

- 1. Scarcity of human resources to conduct HTA
- 2. Need to design better approaches to involvement of stakeholders in HTA
- 3. Pressure to evolve existing HTA methods and processes
- 4. Inadequate data management and the declining quality and validity of evidence
- 5. Fragmented health systems and shifting political contexts
- 6. Enlarged scope of HTA and increased range of demands placed on HTA agencies
- 7. Increasing the impact and influence of HTA
- 8. Increasing demand for HTA and pressure for rapid assessments
- 9. Translating HTA into policy and practice
- 10. Insufficient financial resourcing of HTA

The list suggests that while practitioners are frustrated with a lack of resourcing including staffing, financing, and IT support they are ambitious about the future of HTA. Respondents talked of the need for HTAs to make a bigger impact in policy and practice, to bring in a wider range of voices and stakeholders, and help health systems to manage the sustainable introduction of innovative technologies. This illustrates that HTA is not a static endeavour, but one that must evolve if it is to overcome the challenges identified.

<sup>\*</sup> INAHTA is an international network of fifty publicly funded HTA agencies.

#### **Our approach**

The identification of new developments in HTA was approached through three routes. First, the websites of the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) and Health Technology Assessment International (HTAi) were reviewed. These organisations globally represent practitioners in HTA: they consist of members with a keen interest in identifying, understanding, and implementing innovations in doing HTA but whose membership is wider than just agencies performing HTA.

Each organisation has groups that are set up to research, discuss and guide members on contemporary issues. The new developments that HTA practitioners themselves think are most important were identified by looking at what newly set up groups are talking about. These include a new ISPOR task force on measuring patient preferences for decision making, as well as a patient and citizen involvement interest group at HTAi.

Second, we performed a rapid literature review for 'new developments in HTA/ Health Technology Assessment', 'innovation in HTA/Health Technology Assessment' (and related synonyms). Three papers were particularly helpful in shaping our thinking.<sup>7-9</sup> Third, we spoke to an international expert in HTA, that enabled us to prioritise the main trends recovered from the literature, including engagement, real-world data and evidence, as well as flexibility in HTA decision-making.

The five new developments we cover are:

- Industry engagement and involvement
- Real-world data/evidence
- · Patient, carer, and citizen involvement
- Incorporating patient and carer preferences and values
- Emerging elements of value

The themes are covered broadly in the order that they take place in the HTA process (Figure 1). Note that Figure 1 characterises when they generally occur and does not imply that these are the ideal places. Processes like patient, carer and citizen involvement and real-world data and evidence can happen over time (pre-during-post HTA) or more broadly outside of HTA (for example, to inform clinical trial design). We have used a stylised and generic approach, while recognising that HTA can be useful across the lifecycle of technologies.<sup>10, 11</sup>

### Figure 1: Where the five developments described in this report sit in a typical, stylised HTA process



Source: EIU research

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#### **Report objectives**

While we have drawn on recently published papers for each of the new developments covered, we do not in this report aim for comprehensiveness. This report should therefore be seen as a starting point to consider these new developments in HTA and not a systematic review.

The research for the report took place as the COVID-19 global pandemic started to unfold. The research is based on the literature and has necessarily drawn on already published papers, yet COVID-19 is leading to questions being asked about HTA. For example, the inconsistency in terms of the willingness to pay to save lives from COVID-19 that is vastly greater than the willingness to pay to save lives in 'normal' times in Australia. This has led to a call for a debate on the willingness to pay used by the Australian Pharmaceutical Benefits Advisory Board (PBAC).<sup>12</sup>

We also discuss the resonance of novel components of value with the COVID-19 situation in the fourth new trend, the emerging elements of value, later in this report. Some issues are not yet possible to comment upon; at time of writing no treatments or vaccines have been through an HTA process, with the exception of the US not-for-profit Institute for Clinical Economic Review (ICER) who looked at alternative pricing models for remdesivir as a treatment for COVID-19.<sup>13</sup>

It is also possible that appetite to accept uncertainty in the evidence base could change. We explore the potential impact of COVID-19 on the assessment of value in more detail at the end of the report.

On a practical level, COVID-19 has put HTA agencies under pressure, not only to support health care systems through new work (e.g. providing rapid guidance on treatment of patients with COVID-19)<sup>14</sup> but also because it has led to delays in their normal work.<sup>15</sup> This could distract HTA agencies from considering and implementing changes—alternatively, it could act as an impetus for change. While it is likely that COVID-19 will have an impact on the practice of HTA, the themes described in this report will remain central to the continuing development and relevance of HTA in the adoption of new technologies.

### Industry engagement and involvement



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#### Steps are being taken to enhance industry engagement and involvement to increase efficiency of HTA

Industry can be engaged and involved in HTA in a variety of ways.<sup>16</sup> This can range from broader policy discussions on the role and aim of HTA through to providing submissions that provide evidence on the clinical effectiveness, cost-effectiveness, and in many cases, the budget impact of a product.

Interest in industry engagement and involvement relates to wider pressures on HTA agencies. NICE, for example, has seen increasing demand for Single Technology Appraisals (STAs), equivalent to requiring 2.5 times their 2015 capacity by 2020.17 'Better' quality submissions from companies—in terms of submissions that meet the technical requirements from NICE—could therefore help the agency to meet demand by reducing the amount of time, and meetings required, to complete HTAs. For companies, it could also enable them to optimise their submission planning and delivery and achieve faster decisions. Where those decisions are positive, this can speed up patient access.

#### User groups can help HTA agencies to manage process and improve the quality of company submissions

Agencies including the SMC and NICE have user groups; these include companies that submit to the agencies. The SMC user group forum meets every quarter. The group discusses technical and process issues and helps facilitate industry representation on SMC committees.<sup>18</sup>

The user group at SMC has been a particularly useful forum to help take forward wider initiatives. In 2014, the group was tasked with ensuing good two-way communication on the development of new processes and methods that were recommended as part of a major review on access to new medicines in Scotland. The user group worked with the HTA agency on:

- A review of orphan and end of life medicines including the methods and processes used to conduct the review.
- The appropriate handling of confidentiality for public meetings held on specific products.
- Ensuring industry understanding of changes being made to the SMC process to support and maintain efficiency at the SMC, as well as improving the quality of submissions made by companies who infrequently make submissions to the SMC.<sup>19</sup>

The relationship between stakeholders and the SMC has been described as open and positive, and specifically with respect to manufacturers that there is a co-operative approach to data production.<sup>20</sup> It's not clear how this relates to the user group, but it would seem likely that this aids the relationship.

#### Company engagement during appraisals aims to increase efficiency for HTA agencies and companies

NICE introduced new consultation opportunities between companies and NICE staff, as well as a 'Technical Engagement' step before the first meeting of the NICE appraisal committee. This was one of the reforms consulted upon in 2017, with the aim of improving the efficiency of NICE.<sup>17</sup>

For companies, more opportunities for engagement during an appraisal by NICE should mean that they are made aware of any issues with their submission earlier. They can then respond and provide updated analysis and submissions before the first appraisal committee meeting. It could also potentially speed up the process at NICE, leading to faster recommendations.

The first drug to go through this new approach was durvalumab for lung cancer, in January 2019.<sup>21</sup> According to the final appraisal document—a document that is the last step before final guidance is published—five issues were resolved during technical engagement.<sup>22</sup> These included:

- Agreeing the appropriate comparator to be used in analysis.
- An acceptable way to extrapolate progression-free survival.
- A clinically plausible approach for extrapolating post-progression survival.
- That modelling should include age-related changes to utility.
- The appropriateness of modelling the distribution and costs of subsequent treatments in line with a trial.
- Agreeing that vial sharing was not realistic.

Despite these agreements, there remained issues outstanding after the technical engagement. NICE's final guidance was published on the 1 May 2020. It notes that the committee agreed with the conclusions reached during the technical engagement step.<sup>23</sup>

More experience has built over time; NICE board papers from May 2020 have highlighted that, in practice, the opportunities in the technical engagement step have not been taken up as much as expected.<sup>24</sup> Yet there has been an increase in the speed with which NICE can issue guidance: around 65 days faster with the technical engagement step compared to appraisals that did not include the technical engagement step.<sup>25</sup> Nevertheless, there have been questions raised about the degree to which more consultation and engagement can resolve questions that relate to the value of products.<sup>17</sup> Efforts to increase company engagement have been made by other HTA agencies. For example, since 2014, the SMC has invited pharmaceutical company representatives to the SMC meetings. Companies can respond to queries and provide clarification.<sup>26</sup> While in Australia, manufacturers have an opportunity to meet with representatives of the Department of Health to discuss elements of the submission prior to lodgement to the PBAC; this advice is non-binding. Manufacturer's may also request an opportunity to clarify any outstanding issues immediately prior to the PBAC deliberations on a submission, in the form of a verbal PBAC hearing.<sup>27</sup>

#### Evolution of opportunities for engagement before appraisals start to optimise evidence generation

The opportunity for technical engagement is relatively recent and complements wider activities. For example, NICE first offered companies the opportunity to get early scientific advice from the agency in 2009.<sup>28</sup> NICE suggests that typically the best time to seek advice is before beginning phase III trials.\*

NICE, PBAC and TLV were the first HTA agencies to offer such opportunities. Since then more agencies have followed suit.<sup>29</sup> Early engagement and dialogue continues to evolve. For example, in 2019, NICE and CADTH opened a parallel service, where companies can get advice from NICE and CADTH at the same time in a three-way engagement.<sup>30</sup> Early company feedback from Takeda has been positive, albeit this reflects promotion of the NICE early advice service.<sup>†</sup> Practical consequences include companies changing clinical trial design in light of the feedback that they receive from HTA agencies. They may also decide not to go ahead with some evidence generation if feedback suggests it will not be seen as all that useful or valuable by HTA agencies. It isn't clear, reflecting the confidentiality surrounding such engagements, what difference it makes to the decisions made by HTA agencies.<sup>29</sup>

#### Successful engagement and involvement have brought benefits to both companies and HTA agencies

There are examples of how successful engagement between HTA agencies and industry can bring benefits. In Brazil in the early 2010s there was no prior discussion with companies on the application and evidence submission from companies to CONITEC, the Brazilian HTA agency set up in 2011. This posed a challenge for CONITEC because many submissions were inadequate. In response, CONITEC introduced a period for discussion and consultation with companies before submissions. The result has been positive for both sides; the change was well received by industry and the number of inadequate submissions lowered.<sup>16</sup>

\* NICE. Scientific Advice: Pharmaceuticals. Available at: https://www.nice.org.uk/about/what-we-do/life-sciences/scientific-advice/pharmaceutical-products

<sup>†</sup> NICE. Scientific advice case studies. Available at: https://www.nice.org.uk/about/what-we-do/life-sciences/scientific-advice/case-studies

#### What next?

There is evidence that HTA agencies can benefit and improve their efficiency through improved submissions when they are proactive, engaged and involve companies, based on early experience at relatively young agencies such as Brazilian HTA agency CONITEC. Established agencies are also able to see the merits in engaging with industry, although it is not a panacea. This suggests that all HTA agencies should be similarly open and proactively work with companies. More efforts—including more research are needed on designing and incorporating new approaches to take not just the HTA agency perspective, but also the manufacturers. It is simply not enough to offer the opportunities, agencies also need to demonstrate the benefits to all, particularly in the case of paid-for services. Genuine two-way communication can provide context, clarification and interpretation which may save time and avoid unnecessary requests for data and/or reanalysis, and reduce inefficiencies in the longer term. While progress has been made to improve communication between HTA agencies and manufacturers, there remains a sense of frustration on both sides.

#### Areas of focus in... Industry engagement and involvement:

- Clear processes need to be in place to allow early, proactive engagement between HTA agencies and industry. Such engagement engenders a collaborative and solution-focused approach, plus it will save time and effort later in the process.
- There should be a shared clarity between HTA agencies and industry on evidence preferences and priorities. As well as improving submissions, clarity from agencies at the outset of the process will also increase efficiency. See the section on real-world data and evidence for more details.
- HTA agencies are encouraged to evaluate effectiveness of engagement efforts in order to create an evidence base of "what works".

- Industry needs to actively listen to the concerns and challenges of HTA agencies, and proactively deliver pragmatic solutions that have been informed by the advice of patients, clinicians, and other stakeholders.
- Both industry and HTA agencies should have a shared commitment to being open and transparent about limitations and work together to mitigate uncertainties.
- 6. Consideration should be given to when and how patients should be party to engagement too. Patients will have insights on what outcomes matter most to them and that could shape what is collected by companies in their evidence generation, and the weight that HTA agencies should give to it.

### **Real-world data and evidence**

## Real-world data and evidence complement trials

Most definitions for real-world data emphasise that such data is collected outside of a nonrandomized controlled trial setting.<sup>31</sup> It includes data from administrative data sets, case notes, surveys, registries, social media, electronic health records and many other sources. Real-world data can provide complementary data to that from randomised controlled trials (RCTs), helping to overcome limitations. For example, the effect of a treatment may not be replicated in the real-world versus the trial setting.<sup>32</sup> Real-world evidence can also validate outcomes in trials and provide evidence to support clinical decisions.<sup>33</sup>

The terms real-world data and real-world evidence are often used interchangeably. However, the distinction in terms relates to the need to analyse real-world data, in order to produce real-world evidence.<sup>34</sup> Realworld evidence can then be used to inform deliberations on the value of new health technologies, in addition to its use to help understand the natural history of a disease and in post-marketing surveillance by regulators.<sup>35</sup> Real-world evidence may be the only source of data when RCTs are not feasible, such as in the case of ultra-rare conditions.<sup>36</sup>

## Limited use of real-world data and evidence in HTA

HTA already uses some real-world data, and the evidence that can be generated from it, to some extent.<sup>35</sup> For example, a review of appraisals of melanoma drugs by HTA agencies in Europe published in 2018 found that real-world data was included in just over half the HTAs. Real-world use was primarily used to estimate the prevalence of melanoma and was far less often used to extrapolate long-term effectiveness or identify costs for drugs. ZIN and IQWiG primarily drew on real-world data for prevalence, whereas NICE, SMC and HAS drew on it for effectiveness as well as prevalence.<sup>37</sup>

A wider review, looking beyond melanoma drugs, and across HTA in seven markets (Germany, France, England, Scotland, Canada, Australia and South Korea) found use of real-world evidence varied from none to use in 9% of HTAs conducted between 2012-2017. It was used to provide insights across a number of areas, set out in Figure 2.<sup>38</sup> The review concluded that not only is real-world evidence infrequently used in HTA, it has been rarely influential in decision making.<sup>38</sup> This is consistent with IQVIA data too; their analysis of HTA recommendations with and without real-world evidence in Canada, Germany, France, England and Scotland did not find a direct translation between real-world evidence and the recommendation made (Figure 3).



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### Figure 2: Use of real-world evidence in HTAs conducted between 2012-2017

(% selected)



Source: Jao R et al. Value in Health. 2018.<sup>38</sup>

# Figure 3: Recommendations made by HTA agencies with and without real-world evidence (% selected)



Source: IQVIA HTA accelerator

Nevertheless, it should also be recognised that HTA can act as a driver for the generation of real-world evidence. Managed entry agreements (MEAs)-agreements that can address uncertainty in performance as well as other factors—can result from the HTA process. Note that MEAs is just one term, often used by academics, and many others are used—including managed access, value-based contracts, and others-and HTA agencies may have their preferred terminology. Performancebased MEAs can include coverage with evidence development, payment by results, and conditional treatment continuation.39 NICE similarly describe Managed Access Agreements (MAAs), where signatories typically include NICE, the manufacturer, healthcare professionals and/or patient groups.\* All of these have at their heart real-world evidence.

There is little public information on the outcomes of performance based MEAs, however. The barriers to greater transparency are significant; from changing the nature of agreements struck with pharmaceutical firms to potentially needing to change legislation.<sup>39</sup> Despite the lack of transparency on performance-based MEAs the OECD have identified four main themes for good practices:

- Using performance based MEAs only where the additional evidence generated outweighs the cost of negotiating and implementing the agreement
- Coverage decisions—often informed by HTA—should clearly identify the uncertainties to make sure performance-based MEAs can address the relevant uncertainties
- Governance frameworks should be implemented to ensure transparency of process

\* For example, see NICE's proposed Managed Access Agreement for Asfotase alfa for treating paediatric-onset hypophosphatasia. Available at: https://www.nice.org.uk/guidance/hst6/resources/managed-access-agreement-august-2017-pdf-4543781149

 A minimum level of transparency that limits confidentiality to those parts of the performance-based MEAs that are commercially sensitive (essentially prices)<sup>39</sup>

## Initiatives to increase the use of real-world data and evidence

Discussions amongst the HTA community at HTAi has identified several challenges for the use of real-world data in HTA. These include the quality and acceptability of real-world data, governance and accountability, transferability of the evidence, and how to use real-world evidence to inform decision making.<sup>35</sup> Resources exist to aid those involved in HTA to consider real-world data.<sup>40-43</sup>

Many in the HTA community see more scope for the use of real-world data and evidence in HTA.<sup>35</sup> There are ongoing efforts by HTA agencies to consider more systematically the scope for real-world data and evidence to be used as part of their work. For example, NICE consulted on the use of an expanded set of data sources in their work in June 2019. These included audits, registries, surveys and data on national trends such as how many people have a condition.<sup>44</sup> NICE followed up with a statement of intent in February 2020.<sup>45</sup> This sets out some areas when and why NICE would consider broader types of data, for example:

• To measure effectiveness, and costeffectiveness, in real-world settings. NICE suggests that qualitative data sources could provide useful contextual information, such as detail on challenges in delivering an intervention, or the experiences of patients.

- To demonstrate comparative effectiveness, for example, where the situation has changed since the relevant randomised clinical trials were conducted.
- To monitor and evaluate intermediate outcomes of interventions, such as quantifying rare but serious adverse events, or to validate modelling assumptions.

However, NICE's statement of intent is not prescriptive and does little to guide on exactly what real-world data and evidence NICE is open to.

CADTH, alongside others, has also been exploring how to define 'decision grade' realworld evidence. They held a sprint session-a type of time-boxed workshop including iterations of ideation and feedback-with regulators, public payers, clinicians/health care providers, academics, HTA agencies, patient group representatives and industry, in October 2018. The aim was to identify the value of realworld evidence to support both regulatory and reimbursement decision-making, as well as to identify the conditions where real-world evidence is of sufficient quality.<sup>46</sup> The workshop recommended that further work be continued. This has resulted in joint work on the use of realworld evidence across the product life cycle published in 2019. This includes key elements that should be considered with respect to protocol development, data quality, and prospective and retrospective data collection.47 As with NICE, this guidance is not prescriptive.

The wider HTA community has identified a number of actions that could advance the use of real-world data and evidence in HTA. These include developing good practice guidance as well as instructing those developing technologies on what data is needed.<sup>35</sup> Collaboration with companies is also seen as an enabler.<sup>32</sup>

Wider agencies also need to play a role. As an illustrative example, even though NICE has recommended use in the Cancer Drugs Fund (CDF)—a time limited fund where further data can be collected to support a later re-appraisal—there remain challenges with the datasets that generate real-world evidence to support the re-appraisal.<sup>48</sup> For example, existing datasets do not cover the clinical, economic and humanistic outcomes that are relevant, and even within the clinical dataset they may not include key outcomes such as overall survival.

#### What next?

Greater clarity may emerge from HTA agencies on the use of real-world data and evidence as agencies further refine and reflect on how it can add value to their decision making. Both at the time of taking an initial decision on a new intervention, but also as they review those decisions over time—for example, by allowing coverage but only with real-world evidence development over an agreed timescale. This needs to go beyond HTA agencies as it relies upon wider actors that influence what fit-for-purpose real-world data is collected.

There remains a need for HTA agencies to communicate with manufacturers and provide clarity on what and when real-world evidence might be acceptable to them—hitherto, real-world evidence has mostly been used to estimate prevalence/incidence and drugrelated costs; much less so for evidence of effectiveness.<sup>37</sup> Improved clarity would create a virtuous circle that would in time improve the real-world data and evidence that is available to inform HTA decisions. This will not only increase the likelihood that HTA agencies will receive the evidence that they find most useful, but also allow manufacturers to optimise their evidence generation.

There is also a need for lessons to be learned from MEAs that have included evidence generation; something that is sorely lacking. Again, this requires more than just HTA agency engagement as sharing may be limited by the agreements made with companies and legislation.

#### Areas of focus in... Real-world data and evidence:

- HTA agencies are encouraged to communicate with manufacturers and provide clarity on what and when realworld evidence might be acceptable to them—including when its use might elicit a negative response.
- Industry, payors, and providers need to work with HTA agencies to create an evidence-base on the effectiveness of managed entry agreements and similar initiatives—both in terms of financial and health outcomes.
- 3. Industry should mitigate uncertainties in the real-world evidence generated proactively as part of evidence packages and continue to validate the use and value of such evidence generated alongside RCTs to address payor and HTA concerns.

- HTA agencies may wish to work with one another to create shared learnings and good practice standards on the use of real-world evidence and data. This would help guide industry and improve the standard of submissions.
- 5. All parties need to look collectively at how real-world evidence may be generated proactively and systematically as part of centralised platforms and integrated registries, with a view to reducing fragmentation of data collection.
- 6. Patient perspective should be central throughout. Patients are the source of evidence and their views on the acceptability and engagement with real-world evidence generation is integral to its success.

### Patient, carer, and citizen involvement

## A desire to increase patient involvement

Patients need to be involved in the HTA process in two separate but complementary ways. They should participate in the process (the focus of this section) as well as being the focus of formal research into their experiences, preferences and perspectives (covered in the next section).<sup>49</sup> Patients can be involved too in the generation of evidence that is submitted to HTA agencies; for example, they can be involved in clinical trial design, including defining patientrelevant added value and outcomes.<sup>50</sup>

Patient, carer, and public involvement in the HTA process has many potential benefits. It improves wider understanding of the process, promotes accountability, transparency and a more comprehensive approach to assessing value, and may—it is hoped—result in better quality decisions.<sup>51, 52</sup> The contribution of carers provides both their perspective and the patient perspective when the patients themselves are unable to communicate.<sup>53</sup> There can also be 'spill over' health effects to caregivers, although currently these are generally not included in HTA.<sup>54</sup> Despite the general view among the HTA community that patient involvement is valuable, patients have not always been invited to take part in the processes used by HTA agencies for expert consultation in the past.<sup>55</sup> Even today, there is not a complete consensus on the role of the patient; for example, patients are not included in Japan's HTA framework.<sup>56</sup> Despite this lack of consensus, increased patient involvement has been identified as an important trend in HTA.<sup>7</sup> There are agencies that have taken recent action: for example, a patient involvement interest group was created at the 2017 Spanish Network of Agencies for Assessing National Health System Technologies and Performance (RedETS) annual conference. The aim of the group is to promote and facilitate patient involvement in HTA, including exchange between agencies on their experiences and to reach consensus on the main issues on patient involvement.<sup>57</sup> Patient involvement in HTA, according to a 2019 paper on RedETS, still needed to be expanded, as well as work to assess its results.58



## HTA agencies most commonly use forms to capture input

HTA agencies vary in terms of the opportunities throughout the HTA process. In an international comparison of HTA agencies approaches to patient input published in 2018, NICE and CADTH were highlighted as agencies that involve patients throughout the process. This includes scoping, evidence gathering, consultation, appeal/resolution, dissemination, and review. That contrasts with HTA agencies in Thailand and South Korea where patients can just comment on scope and assessment, respectively.<sup>56</sup>

The most common mechanism for patient involvement used by HTA agencies is a form (see Table 1).\* HTA agencies including NICE, CADTH and PBAC, describe how these written submissions are generally considered alongside other papers during a committee meeting.<sup>27, 59, 60</sup>

Form filling is not, however, the most active of activities. It has been suggested that patient submissions through this mechanism—at least in the context of the pan-Canadian Oncology Drug Review (pCODR), a review process conducted by the Canadian HTA agency, CADTH, specifically for oncology treatments-are fairly passive.<sup>51</sup> For example, the form requests information from patients on a range of topics, predetermined by the pCODR. Similarly, NICE are directive in terms of what to include as set out in their guide for patient organisations in completing an organisation submission.<sup>61</sup>

There are nuances in the approaches agencies take to written input. For example, the Common Drug Review (CDR) process at CADTH requests that patient input be through an organised patient group, if one exists, and using a template.<sup>†</sup> That contrasts with PBAC, who allows for an individual patient response, or an organisation, with comments provided via a web interface; if they are unable to access the website they are advised to write a letter using the same format as the website.<sup>‡</sup> In perhaps the most open of approaches, ICER posts a public call for evidence on their website which is distributed to anyone who signs up for their email alerts, and anyone-be that an individual patient or organisation-can respond with no predefined template.§

\* Agencies can use a variety of approaches, so this should not be taken to imply it is the only mechanism. For example, patients can also provide testimony at committee meetings.

<sup>†</sup> CADTH. CADTH common drug review patient input. Available at: https://www.cadth.ca/about-cadth/what-we-do/products-services/cdr/patient-input

\* PBAC. Consumer input. Available at: https://www.pbs.gov.au/pbs/industry/listing/procedure-guidance/6-consideration-submissions/6-7-consumer-input

<sup>5</sup> ICER. Patient, manufacturer, and other stakeholder engagement. Available at: https://icer-review.org/methodology/stakeholder-engagement/

	CADTH	HAS	ICER	NICE	PBAC	SMC	ZIN
Method of patient input	Form	Form	Form / conversation	Form	Form	Form	Verbal/ written

#### Table 1: The main mechanism of patient involvement in a selection of HTA agencies

Source: Extract from: Bond K. 2020 HTAi Global Policy Forum: Deliberative processes in Health Technology Assessment: Prospects, Problems, and Policy Proposals. [Internet.] HTAi; [cited 27 March 2020]. Available from:

https://htai.org/wp-content/uploads/2020/02/HTAi\_GPF-newOrleans\_program\_background-paper.pdf

Written submissions can be complemented with other mechanisms of engagement. Whilst now dated, experience as far back as 2013 illustrates that a number of approaches have been used to engage the public by HTA agencies, from opinion polls and surveys to town meetings with voting.<sup>62</sup> HTA agencies can also seek input from wider society. Agencies like NICE, for example, submit draft guidance for public consultation, providing the opportunity for citizens to contribute.<sup>63</sup>

Some organisations are experimenting with alternative approaches to patient input. An example is the Patient and Clinician Engagement (PACE) process, introduced in 2014 by the Scotland based HTA agency, the Scottish Medicines Consortium (SMC).<sup>64</sup> Where the SMC is minded not to recommend a medicine used at the end of life or used in treating rare conditions, at the manufacturers' request, they invite patient organisations and clinicians to do an additional submission and participate in a meeting with SMC staff. The meeting is held without other stakeholders.65 The meeting provides patient groups and clinicians an opportunity to describe the added benefits of the medicine that may not be captured during the usual HTA process: benefits such as the medicine's impact on the patient's ability to work or function, the convenience of treatment or the reduction in time needed for visits to healthcare professionals. The meeting results in a PACE statement that it then considered by the SMC Committee. Other agencies use similar approaches: for example, PBAC in Australia may sometimes request a meeting with a patient organisation in what is called a Consumer Hearings prior to deliberating on their recommendation for a medicine. Whilst practice by HTA agencies varies, based on a survey conducted in 2016, some agencies will also include members of the public or patients to participate in committees or working groups and they may also be involved in making recommendations.66

## Does patient involvement make a difference?

Efforts have been made to gather evidence on the impact of public and patient involvement. A case study can be found from NICE, where they used patient input in their appraisal of tumour necrosis factor (TNF)-alpha inhibitors for ankylosing spondylitis and axial spondyloarthritis. The patient view came from the National Ankylosing Spondylitis Society (NASS) who had conducted surveys every three years, and who take an average of 5,000 calls a year on their helpline, speak to members at an annual members day, and interact with them via social media. NASS surveys include statistics such as the number of patients currently on TNF therapy as well as open questions that can be analysed to provide an understanding of the advantages and disadvantages of treatment options. A further survey was run during the consultation phase of the NICE appraisal.

The patient input from NASS resulted in changed paragraphs in the final NICE guidance. For example, NICE guidance states: "There is also anecdotal evidence suggesting that a second or third TNF-alpha inhibitor can be clinically effective if the first has failed. [Infliximab] might benefit people with memory problems, learning disabilities, dexterity problems, or a fear of needles."<sup>67</sup> These were not represented as "a view from NASS" but rather formed part of the official guidance, and so may influence clinician behaviour when considering treatment options. Similar inputs have been seen elsewhere: for example, in the consideration of bevacizumab for glioblastoma by PBAC, where the large number of consumer comments was referenced in the public summary document.<sup>68</sup>

The impact of recent changes in process, such as the PACE programme of the SMC, is not clear. Analysis of SMC decisions for two years after the introduction of PACE in 2014 did not find any obvious relationship between the points covered in PACE discussions and funding decisions.<sup>64</sup> Patient advocates themselves have expressed the view that their involvement more generally can be 'tick box', although that view is not held by all. Impact, from the perspective of patient advocates, is perceived as mixed.<sup>69</sup> Some patient advocates have previously highlighted the lack of feedback from HTA agencies on their submissions, and that can make it hard to know the value of their suggestions.69

Despite the desire to increase involvement of patients, it must also be recognised that there may be times when involvement is unlikely to have an impact: for example, when the cost-effectiveness of a new intervention is far higher than is likely to be acceptable.<sup>49</sup> There is a paradox here though; in the case of orphan medicines that treat very rare diseases, it has been recognised that wider considerations from patients, and clinicians, can aid in understanding their value. Yet these are also the types of medicines that are likely to have very high cost-effectiveness ratios.<sup>70</sup>

Questions have been raised too about conflict of interest, given that many patient organisations receive funding from manufacturers with a vested interest in the decisions coming from agencies like NICE.71 Although research from Canada, looking at 372 submissions from 93 different patient groups up to July 2018, found that the views of patients groups were the same, whether or not they were funded by manufacturers.<sup>72</sup> A further challenge to patient participation is that it requires the time, effort and expertise of the patient groups involved: unless they are suitably funded, patient groups may not be able to participate effectively, even if they wish to do so.52

#### What next?

There is increasing acceptance that patients and carers need to be involved in the HTA process, and that this process needs to be both meaningful and impactful. However, there remain questions about the best ways to do this, when it is worthwhile, and what difference it can really make. While we can expect to see an increase in research and (hopefully) the emergence of best practices in involvement, in the short term there will continue to be a diversity of patient involvement approaches taken across HTAs.

What is desperately needed is an evidence base on what works and from whose perspective; it is insufficient to rely on the perspectives of agencies and what is arguably anecdotal case studies. The initiatives described in this section (and others) need to be collated, evaluated, and appraised, and agreed best practices developed.

#### Areas of focus in... Patient, carer, and citizen involvement:

- HTA agencies need to continue to move "beyond the form." While giving opportunities to offer feedback via online forms and similar are better than nothing, there is no substitute for genuine engagement with patient membership on panels and/or committees. There is a duty to seek input from the patient community as no decisions should be made for patients without the patient voice having a seat at the table—this applies to both industry and to HTA agencies.
- 2. All healthcare stakeholders should work to ensure that barriers to patient and public engagement are

identified and removed. It should not only be patient groups with extensive funding that are able to engage; individual patients and their caregivers should also be able to contribute.

- **3.** HTA agencies are encouraged—as in the case of industry engagement—to evaluate the effectiveness of public, patient and carer engagement efforts, and so create an evidence base of "what works".
- In order to ensure continuing and effective input from patients and patient representatives, all healthcare stakeholders need to contribute to an increase in wider health literacy.

### Incorporating patient and carer preferences

## Efforts to capture patient preferences quantitatively

There are two different but complementary ways that patients need to be involved in the HTA process. The previous section focussed on how patients and patient representative can be involved in the HTA process. We focus here on the second approach: the incorporation of formal research into patient experiences, preferences and perspectives.<sup>49</sup>

Patient preference studies are defined by NICE as studies that measure the preferences of patients in a standardised and quantitative way.<sup>63</sup> These studies include discrete choice experiments (DCEs) and best-worst scaling (BWS) where patients are asked a number of questions which, when analysed, can identify their preferences for certain attributes of medicines. For example, with respect to the risks of side effects and the way in which they take a medicine.

All else being equal, quantitative patient preferences can help to guide which therapy to recommend. Quantitative studies can also complement qualitative approaches to identifying patient preferences, which are typically generated from patient and carer involvement in HTA (see the section on Patient, carer, and citizen involvement).

## Limited use of quantitative patient preference studies in HTA

Evidence suggests that the benefits of bringing in patient preferences into HTA include improving uptake, adherence and patient satisfaction.<sup>73</sup> Despite these potential benefits of capturing patient preferences in a quantitative way, use of such studies is currently minimal in HTA.

There is a concern that HTA is not keeping pace with the progress being made by regulators in using patient preference studies. Possible reasons for this include:

- The dominance of cost-utility analysis. Whilst patient input is needed to derive utilities, no other quantitative patient preference data is required, so analysis can continue without it. It is argued that, given the focus on an acceptable risk-benefit in regulation, it is far clearer how DCEs and BWS can be used by regulators.
- HTA is often used in the context of publicly funded health care, so it follows that there is an argument that patient preferences are less relevant than that of those paying for health care (i.e. taxpayers).
- The focus by some HTA agencies on generic measures of heath related quality of life is to aid in comparability across diseases and health technologies. DCEs and BWS are, in contrast, disease specific, which may mean that they are less desirable by HTA agencies.

 Quantitative approaches to capturing patient preferences may not be seen as essential, given that qualitative approaches (as discussed in the section on Patient, carer and citizen involvement) are already used by some HTA agencies.<sup>74</sup>

#### Increasing openness to quantitative patient preference studies by HTA agencies

There are signs that HTA agencies are becoming more open to using quantitative patient preference studies. NICE, for example, in a paper published in April 2020, has recognised that patient preference studies could provide valuable insights for committees.<sup>63</sup> This paper built on work commissioned by a patient organisation, Myeloma UK, for NICE to look into how HTA agencies can use insights from patients in their decision-making.<sup>75</sup> This illustrates a proactive approach by a patient group and a desire to work collaboratively and directly with a HTA agency outside the 'usual' processes.

NICE notes that studies are not only more representative of patients beyond individual patient experts, but they also help reveal how patients view trade-offs between different treatment options where they differ in terms of administration, effectiveness, side effects and the risk of serious side effects.<sup>63</sup>

## The challenge of integrating patient preferences into decision making

There remains a debate within and between agencies of how best to capture and bring in patient preferences into HTA decision making. Stakeholders in Europe and the US have a number of concerns about incorporating patient preferences, according to research interviews conducted by an international group of researchers during April and August 2017. HTA agencies and payers, in particular, see a need for quality criteria to help them evaluate patient preference studies and how to weigh them in decision-making.<sup>76</sup> Yet this doesn't seem to accord with the fact that there are a number of good research practices available that predate that research.77-80 It's unclear if this is a question of awareness of these good research practices or whether it is driven by something else. It may be the challenge of how to weigh quantitative patient preferences is holding back use.

HTA agencies, including NICE, CADTH, HAS and ICER, have used discrete choice experiments as part of their decision-making, but in a limited way.<sup>81</sup> Although such techniques are well-established, given their limited use in HTAs it is arguably too soon to determine their impact on decisions made. Integrating patient and carer values to support decision-making within HTA is also part of a wider challenge for HTA agencies to bring in different values from other stakeholders at the same time.<sup>55</sup>

#### What next?

The use of quantitative approaches to identify patient preferences is becoming an area of interest for HTA agencies. Yet there remain challenges to their more widespread use, in part because HTA agencies need to be confident in the methods used and the conclusions drawn from such studies. It is unclear how far current guidance to support HTA agencies in evaluating patient preference studies meets their needs as guidance is available but concerns amongst the HTA community remain.

There is an emerging research agenda on the use of quantitative patient preference studies and future research could help to identify

the methods that will become acceptable to HTA agencies. Even with this, there remains a question about how HTA agencies will apply the results from quantitative patient preference studies and just how important they will be to the final decisions made.

The most significant barrier is in how HTAs draw upon such evidence and the weight it is given in decision making against the context of balancing patient preferences with 1) other stakeholders' preferences, and, in many countries, 2) the public nature of health care funding. This may yet stall a more whole-hearted adoption of quantitative patient preference studies to inform HTA.

#### Areas of focus in... Incorporating patient and carer preferences:

- The wider HTA community needs to work together to identify their concerns about patient preference studies, understand the barriers to their incorporation, and to then take a coordinated approach to incorporate these preferences. This process could provide clear guidance to researchers as to what evidence is needed and acceptable.
- Following the above step, agencies would be well placed to develop guidance on how patient and carer preference is weighed and incorporated into the wider evidence base.
- 3. Once the incorporation of patient and carer preference research is more commonplace in HTA decisions making, their impact into decision making needs to be evaluated: does patient preference data ever lead to a change in recommendation, for example?
- 4. HTA agencies may wish to work with one another to create shared learnings and good practice standards on the use of patient and carer preferences. This would help guide industry and improve the standard of this type of evidence.
- Patients who have contributed to quantitative patient preference studies should be given feedback on how they are being used.

### **Emerging elements of value**

## A narrow perspective on value has generated criticism of HTA agencies

Value is central to HTA. Many HTA agencies have traditionally focused on value in terms of cost per outcome, such as cost per Quality Adjusted Life Years (QALYs).<sup>82</sup> Such approaches assume that society wishes to maximise aggregate health.

In recent years there has been growing interest in re-defining value, and the potential for value to include a wider set of elements. In part, this reflects ongoing criticism of failing to account for broader societal preferences, for example, not giving favour in the past to treat more severe illness.<sup>83</sup> The latter was addressed with policies that allow for different treatment for end of life conditions by NICE, for example.

#### A wider perspective on value

The HTA community, via a special task force convened by ISPOR, has addressed the question of what elements warrant consideration in value assessments. The task force has specifically sought to broaden the definition of value and spur further research on how to incorporate a wider set of value elements into cost-effectiveness analysis.<sup>84</sup>

The task force published their report in 2018 and presented a value flower (figure 4). The flower outlines the traditional elements (QALYs and net costs) of HTA value assessment; elements of value that are common but inconsistently used (productivity and adherence improving factors), and finally those value elements that are novel (reduction in uncertainty, fear of contagion, insurance value, severity of disease, value of hope, real optionvalue, equity and scientific spill overs).<sup>84</sup>



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#### Figure 4: The ISPOR special task force's elements of value "flower"

The mid-blue circles are core elements of value. Light blue circles are common but inconsistently used elements of value. The dark blue circles are potential novel elements of value.



Source: Lakdawalla, D.N., Doshi, J.A., Garrison, L.P., et al. Defining elements of value in health care – A health economics approach: An ISPOR special task force report. Value in Health. 2018; 21(2) pp.131-139.

Recent research has been exploring whether it is feasible to adopt some of the novel elements of value. For example, considering "option value"—when extending life can offer the option for patients to enjoy the potential benefits of future advances in medicine—in the case of ipilimumab used in the treatment of metastatic melanoma increased both the QALYs gained and net costs; overall, it reduced the incremental cost effectiveness ratio.<sup>85</sup>

The analysis from the ISPOR task force also makes it clear that a societal perspectivewhere a study's point of view goes beyond just what those paying for health care would value-would capture all elements of value, whereas a health care perspective leaves out 7 of the 12 value elements: productivity, insurance value, severity of disease, value of hope, real option value, equity and scientific spill overs. There isn't, however, a consensus that the societal perspective is always preferred.<sup>86</sup> Aside from issues of whose preferences should matter, the collective versus individual patients, it's practically difficult to collect the data and deal with the uncertainty that taking a societal perspective implies.<sup>87</sup> Although just because something is difficult to measure, does not mean that it should be ignored.

## The fear of contagion: value in light of COVID-19

The ongoing COVID-19 global pandemic has been the backdrop against which this project has been conducted. Whilst it has undoubtedly affected all the areas we consider (not least, for example, the ability for HTA agencies to continue their work), it is perhaps arguably the most resonant with what is considered valuable within HTA. The ISPOR task force that produced the value flower did their work years before COVID-19. Yet their work highlighted that there are novel areas of value that perhaps should be considered, such as the fear and risk of contagion. The fear of contagion argument is that the sum of all benefits to vaccinated people is less than the sum of all societal benefitsi.e. many non-vaccinated people will benefit too, because of herd immunity. Not only that, but it is also important to capture the fear associated with the spread of a disease; particularly for diseases such as Ebola that are mostly dormant, but potentially deadly. Reducing the anxiety associated with the risk of outbreaks is valuable to a society; fear plagues everyone potentially exposed to the disease, not just those who are sick. The per-capita value of avoiding fear may therefore become quite significant in value assessments.84

In terms of the COVID-19 situation, it is clear, given the priority being placed on responding to COVID-19, that these are important motivators for government action, even before a vaccine is available for a more formal HTA. The immediate future of HTA could well be shaped by COVID-19 as it reveals the political—and perhaps the societal—views on what is valuable.

#### Adherence improving factors

COVID-19 is also of potential relevance regarding adherence improving factors. While a common but inconsistently used element in the value flower, HTAs have not historically placed much emphasis on the benefit of adherence to treatment based on a change in formulation or presentation.<sup>88,89</sup> For example, cost-effectiveness analyses often assume perfect adherence, even if the assumption

is unlikely to be correct.<sup>90</sup> Nevertheless, in the real world, therapies with improved convenience—and therefore higher chance of adherence-may help keep patients out of hospital and reduce exposure to infection: for example, therapies that are delivered orally or subcutaneously, instead of intravenously. While methods do exist for adjusting estimates of treatment effectiveness for nonadherence, most are not suitable for use in HTA.<sup>91</sup> We may see an increased focus on this area of research if such a change in presentation or formulation allows patients to be treated more effectively outside of hospital or other healthcare settings, which not only improves adherence but also reduces hospitalisation costs and often improves patient health outcomes.

## The value of insurance: bringing peace of mind

Another of the most impactful novel elements of value being discussed is insurance value.<sup>92</sup> There are two components to insurance value: physical risk protection and financial risk protection. To understand these two concepts, it is helpful to consider a condition such as Alzheimer's disease.

If an effective treatment were developed for Alzheimer's, we would all have less to fear from the disease, even though most of us will never develop it. Consequently, more people would be willing to pay for access to the treatment if ever needed—than those who would actually need it. This is the "physical risk protection" component of insurance value.<sup>93</sup> The "financial risk protection" component refers to how new technologies make health insurance policies more useful to a greater number of people. When you have health insurance, it often cannot stop you from getting sick; you can only insure yourself against having to spend money on medical care. When new technologies offer greater options for medical care, it expands the possibility of insuring against illness—making health insurance more useful, and therefore of greater value.<sup>84</sup>

#### Does broadening the assessment of value just mean everything will have to be reimbursed, or will it mean better investment decisions are made?

The argument for extending the assessment of value to bring in these novel elements is that HTAs can better estimate the relative value of new medicines; health systems will be more able to efficiently offer "reward-for-value", and thus incentivise more valuable innovations in the future.<sup>92</sup> However, the ISPOR Special Task Force still recommended that approvals should be made on cost-effectiveness principles (i.e. cost-per-QALY). They argue that it remains necessary to have a universal concept of value by which decision makers can compare technologies against a willingness to pay threshold. Rather than necessarily increase total spend, the broadening of value to create what the authors call an "augmented" costeffectiveness analysis, will help health systems spend their budget more wisely. In other words, choose between many things of value when we cannot afford to fund them all. 92

#### What next?

HTA agencies are evolving their approaches over time, including issues of value. For example, at the time of writing, NICE is undertaking a review of their methods for evaluating health technologies. This may provide an opportunity for the agency to re-consider value, particularly considering COVID-19. The results of that work are due out during 2020.

A broader debate is also already starting on what COVID-19 might mean for HTA: less about methods, and more about attitudes to risk as well as whether there will be enough money to go around. While HTA is not immune to COVID-19, it can and will adapt.<sup>94</sup>

#### Areas of focus in... Emerging elements of value:

- HTA agencies and other healthcare stakeholders should continue to discuss how best to augment costeffectiveness approaches with other elements of value, in order to better "reward-for-value".
- 2. HTA agencies need to work with payers and other stakeholders to understand when and/or in what circumstances they can shift to a societal perspective in their analyses. Taking a societal view brings in more elements of value and can help

ensure that health interventions are seen as an investment rather than a cost.

3. All healthcare stakeholders are encouraged to work together to consider how learnings from the COVID-19 pandemic have altered value priorities among healthcare stakeholders and the wider public. Are expectations going to change in the short to medium term, and how can HTA play a role in that to ensure appropriate investment decisions are made?

### What next for HTA?

We have focused on five new developments in HTA, informed by published papers from those practicing HTA. But we could have picked others. There is a healthy debate surrounding the practice of HTA, and a desire amongst practitioners to evolve the process to respond to the changing landscape of health and health care systems. Yet there is still a tension; for some, the speed at which HTA actually changes, versus the intensity of the debate, is too slow. This is the case with arguably the world's most influential HTA agency, NICE. HTA tends to avoid revolution and evolve in small steps over time.

That HTA will continue to evolve is clear. Across the five areas that we have looked at, common themes emerge: communication, collaboration, and the generation of an evidence base. HTA agencies must not only liaise with one another but with the stakeholders that are integral to their work. Be that in terms of the evidence that HTA agencies need or in making working with HTA agencies as easy and efficient as possible. This is perhaps needed now more than ever as COVID-19 puts pressure on health care system resilience and sustainability around the world.

We expect organisations to focus on processes, for example refining approaches to engagement and involvement of patients, carers and citizens and industry. These are areas where experience is building and where there is a growing consensus of the importance of engagement. There is a desire for agencies to learn from one another as well as evidence that it can benefit both HTA agencies and those who submit to them. Yet this evidence must come from those outside, as well as inside, HTA agencies for a holistic perspective.

It may be more difficult for agencies to make methodological changes, such as formally accepting a particular method to collect quantitative patient preferences and a method for their incorporation in decision making. It is often the case that the appropriate choice of method reflects the context of the healthcare intervention. We see this with respect to realworld data and evidence where HTA agencies like NICE have settled for general principles rather than more prescriptive approaches. Precedents may become, in absence of clearer guidance, the practical advice on what is acceptable or not to HTA agencies over time. This leaves the burden of investing in methods and experimenting with them on manufacturers who submit to HTA agencies. They are likely to learn through trial and error what is acceptable, rather than through a clear direction provided by HTA agencies.

#### The impact of COVID-19: a new normal for HTA agencies?

Like many industries, the pandemic has forced HTA agencies to work differently. For example, HTA committees are rapidly having to adjust to working remotely—with all the challenges this entails, particularly when the deliberation which is at its heart is a group activity. Many "nonessential" meetings have been cancelled or postponed. Even with these obstacles in place,

NICE have managed to create rapid guidance and evidence summaries.<sup>95</sup> They are also offering free scientific fast-track advice for companies responding to the pandemic.<sup>94</sup> Other NICE workstreams were deprioritised so that only therapeutically critical or COVID-19 related guidance and guidelines were published.<sup>96</sup> Other agencies—including CADTH and ICER—are also modifying processes or creating rapid content for COVID<sup>97,98</sup>: the pandemic is forcing innovation in what is often seen as a risk-averse environment.

When healthcare systems begin returning to the "new normal", will this innovative spirit remain? Certainly, well-functioning HTA systems will be even more critical than ever. NICE has already decided that appraisal committee meetings will be virtual from now on. However, HTA agencies might find themselves facing government-imposed budget constraints. They may therefore need to focus on "technology management" rather than "technology adoption"; on divesting in inefficient or low-value technologies rather than investing in new technologies.<sup>94</sup> For similar reasons, HTA recommendations may in the near future lean more heavily on risk sharing arrangements or managed access schemes, possibly accompanied by pricing innovations such as outcome-based payments.<sup>94</sup> Having less to work with is not always an obstacle when it comes to innovation: necessity is, after all, the mother of invention.

Issues relating to what is valuable and from whose perspective this value is perceived are likely to remain hotly debated; perhaps even more so in the light of COVID-19. The debate could be re-invigorated as we see the real trade-offs about care given to different types of patients. COVID-19 has made trade-offs clear in terms of which patients have been denied care during the pandemic in order to best cope with those with COVID-19.<sup>99</sup> Less clear are the trade-offs in terms of how much governments are willing to pay, with discussion ongoing on what the new cost per QALY thresholds actually are, and if they are only for COVID-19, or should be applied more generally.

In the near-term, HTAs will also be challenged with the arrival of much hoped for COVID treatments—be they repurposed or new—and a vaccine. Certainly, it is likely that the response to the pandemic will push up the agenda some of those issues described here, such as taking a societal view, the rapid collection and use of real-world data and engagement between stakeholders. As we have seen, while not new, their implementation has often been slow. "It's an ill wind that blows nobody any good". Maybe the realignment of healthcare and societal priorities post-COVID will create the impetus needed for the ongoing development and reform of HTA processes.

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