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DEFINING EARLY HEALTH TECHNOLOGY ASSESSMENT: BUILDING CONSENSUS USING DELPHI TECHNIQUE

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Running title

Consensus definition of early HTA

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Abstract

Although early health technology assessment (HTA) is increasingly being used to guide and inform decisions on product development, a consensus definition is currently lacking.

A working group under the Health Technology Assessment international society (HTAi) was established to develop a consensus-based definition of early HTA.

The working group developed a definition using an iterative process which comprised five stages of work and included a two round Delphi survey with 133 respondents in the first and 99 respondents in the second round of the survey, with various backgrounds and levels of expertise. Following this process, the working group reached the first-consensus based definition of early HTA, which is "a health technology assessment conducted to inform decisions about subsequent development, research and/or investment by explicitly evaluating the potential value of a conceptual or actual health technology." In total, eighty-six (87 percent) of the ninety-nine panellists who participated in the second round of the Delphi survey either strongly agreed or agreed with this definition.

This consensus definition represents an important milestone in early HTA. It will enhance uniformity of terminology increasing the visibility of research and policy in this field. We also hope that it will act as a catalyst, sparkling further research and developments in this discipline.

Keywords: Technology Assessment, Biomedical; Terminology as Topic; Value-Based Health Care; Decision Making; Translational Research, Biomedical

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Introduction

According to the HTA glossary definition (1), health technology assessment (HTA) is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The most familiar form of HTA is work conducted by HTA agencies, on behalf of healthcare systems or other payers, to inform reimbursement or adoption decisions (including price negotiations). HTA is often used to inform decisions about the adoption, use or pricing of pharmaceuticals, medical devices, and other technologies (defined widely in the HTA glossary definition) (2). However, HTA is also performed in earlier stages of development of a technology, to inform pre-market decisions (3). This has been named 'early HTA' or 'development-focused HTA' and encompasses a broad range of work and technologies (3-7). For example, early HTA could inform private or public innovators or investors during research into a new pharmaceutical, medical device or diagnostic; innovators looking to improve hospital processes; or potential users in the early stages of development, looking into the design or alternative adoption strategies of an innovative health technology (5, 8). Early HTA can be conducted within healthcare settings as part of broader hospital-based HTA (9), for example to help inform the in-house development of technologies, but is also performed within life science industries that supply technologies into the health system (10-13).

Early HTA is increasingly being used in all research and development phases, in different technology readiness levels. It has great potential to reduce research waste, ensuring that investment goes to technologies which are expected to create value, and are optimised to ensure they are fit for purpose (14-17). This focus on early assessment is in line with multiple policy initiatives from health systems and other payers set to provide information earlier in the lifecycle on the potential value of a new technology to guide investment and assessment prioritisation (18-21). Horizon scanning is the systematic identification of health technologies that are new, emerging or becoming obsolete and that have the potential to affect health, health services and/or society (22). Early HTA, on the other hand, refers to the assessment of these new and emerging technologies.

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Often stakeholders utilising early HTA do not explicitly state that they consider their activity to fall within this remit and use other terms to describe it. For example, pharmaceutical companies use a range of 'target assessment' frameworks in which important activities include the defining of unmet need and clinical differentiation (23). Both activities form part of early HTA, often as a first step. Much early HTA, particularly that undertaken primarily to inform innovators, remains unpublished as it may be commercially sensitive (24). Early HTA draws on a suite of complementary methods to assess the need for the innovation or develop target product profiles, such as interviews, expert (stakeholder) elicitation, and health economic modelling (3, 4, 7, 17, 25). These methods can be used to explore the potential value of a technology in development using scenarios based on real-world settings, for example, reflecting alternative positions in a clinical pathway a technology could be used, or considering alternative implementation contexts and the interoperability of a technology with existing health systems.

With increasing use of early HTA, there has been considerable debate over its precise definition, and if and how it differs from related concepts such as 'early awareness', 'early dialogue', 'early (scientific) advice' and 'development-focused HTA'. Considering the multiple policy initiatives emerging in different parts of the world (18-21) and the heterogeneity in the field, clear guidance on terminology, methods and reporting of early HTA would greatly assist practitioners, as well as journals seeking to ensure the quality of published work. The purpose of this study is to address the first of these issues and establish consistency in terminology. A working group under the Health Technology Assessment international society (HTAi) was initiated to establish consensus on the definition of early HTA. This paper reports the findings of this group and presents the first consensus-based definition of early HTA.

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Methods and Results

Our study used an iterative process comprising five stages of work undertaken by two bodies; the working group established under the auspices of HTAi and the panel who responded to the two stages of the consensus Delphi process. We chose to undertake a Delphi process as it is an appropriate method to reach consensus (26). With the Delphi process we wanted to reach as many people working in the field as possible. We report the methods and results of these stages chronologically, in line with the Guidance on Conducting and Reporting Delphi Studies (CREDES) (26) (see Figure 1). The working group was established from a group of individuals interested in early HTA who were brought together by the first authors (JG and JB) following a call across their networks and to attendees of the HTAi Annual Meeting in the Netherlands, in June 2022. Members of this wider group volunteered to join a terminology working group. Further members were added when it was formally accepted as a working group of HTAi in the summer of 2023. An advisory board was composed with five experts from different backgrounds. The total working group consisted of seventeen core working group members and five advisory board members. These twenty-two people are referred to as the working group. The panel for the Delphi survey comprised all those who responded to the first round of the survey. The characteristics of both the working group and the panellists can be found in the Supplementary Materials.

Stage one – development of definitions and supporting materials

Stage one started with a rapid review of reviews of early HTA, undertaken by JG in February 2023 based on an update of the search set out in Grutters et al, 2022 (4). Keywords were "('early health technology assessment' OR 'early evaluation' OR 'early assessment') AND 'methodology' AND 'review'." The search added eighty-five papers to the previous review of which two were considered relevant. Working group members were invited to add relevant review papers . Eleven papers were identified including nine separate definitions (3, 5, 6, 8, 24, 27-32). These were set out in the materials circulated in the first round of the Delphi survey (see Supplementary Materials). JG and JB developed

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an initial suggested definition based on the output from this review as well as the HTA glossary definition of HTA (1). These materials were then forwarded to the working group for their consideration. The working group decided to define the terms 'early HTA', 'development-focused HTA' and 'early dialogue'. Other terms were used in the papers reviewed, but the working group preferred early HTA due to its prominence in the literature and development-focused HTA as it captured the distinct nature of work undertaken to inform the development of health technologies. Early dialogue was included because when setting up the working group, there was much discussion about if and how early HTA was different from early dialogue. Often used terms such as early economic evaluation or early health economic modelling (28, 31, 32) were considered specific methods that could be used to inform early or development-focused HTA and were therefore not included in the scope of the study. The initial definition of early dialogue was taken from a recent publication by Blankart et al (33). To avoid bias, the first survey included a question asking panellists whether they agreed with the use of the terms we had suggested and asking for their own suggestions.

The first survey comprised background questions, definitions of 'early HTA', 'development-focused HTA' and 'early dialogue'; a table setting out a detailed definition of early HTA in stages; and a table reconciling the suggested definition of early HTA with the nine definitions found in the rapid review. The full text circulated was refined iteratively through consultation with the working group. The final draft of the survey was piloted with five colleagues who were not involved with this work and no changes to the context or structure were required. The survey, including the initial definitions is included in the Supplementary Materials. The Supplementary Materials also include the characteristics of the working group and panellists who responded to the survey Thirteen members of the working group were panellists in round one and two. Their characteristics are included in all relevant columns.

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Stage two – round one Delphi survey

A protocol for the Delphi study was developed by the working group (see Supplementary Materials). An ethical waiver was received from Radboud university medical center as no patients were included and participation in the study was not associated with any risks or harms. The first round of the Delphi survey was circulated on 26 October 2023 with responses required by 24 November 2023. The survey was accompanied by an information sheet for participants (see Supplementary Materials). The survey started with an explicit consent statement the respondents were asked to agree with. The purpose of the first round of the survey was to elicit qualitative comment rather than to seek consensus. We sought to reach a wide range of stakeholders with an interest in early HTA, including health policy makers and those in academia, HTA agencies, consultancy and industry. As early HTA is an emerging field we sought to be inclusive of all interested individuals regardless of their level of experience. We distributed the survey link through personal networks and social media and encouraged panellists to forward the survey link on to interested parties in their own networks. HTAi also distributed the invitation to all Interest Groups within their organisation and via their newsletter. Panellists in round one were asked to provide their email address if they wished to be included in round two.

We received 133 responses to round one of the survey, all of them gave informed consent. 119 (of 133) panellists included their email addresses in order to be invited to participate in round two and 114 panellists included free text comments for consideration.

In response to the question about whether panellists agreed with the use of the three terms we sought to define: ‘early HTA’, ‘development-focused HTA’ and ‘early dialogue’, many panellists found it difficult to distinguish between ‘early HTA’ and ‘development-focused HTA’. Panellists felt that the concept of development-focused HTA covered the earliest stages of early HTA and that – if included - then another complementary term covering the later stages of early HTA should also be included. There were contrasting views about the definition of ‘early dialogue’ and its fit with early HTA. Multiple panellists regarded early dialogue as a method of stakeholder involvement used for early

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HTA. If it was a specific type of stakeholder involvement, as the proposed definition suggested, panellists suggested changing the term accordingly, for example 'early regulatory dialogue'.

In response to our question about any other suggested terms, panellists proposed twenty-six alternative terms, with one term, 'developmental HTA', suggested twice.

Stage three – decision on scope and revision of definition

Stage three involved collaborative consideration by the working group of the feedback received from round one of the survey and amendment of the definition of early HTA. At this stage, we also discussed the characteristics of the panel and identified some additional questions regarding the panellists' characteristics which we wished to ask in round two. Given the responses on development-focused HTA being a subset of early HTA, the working group considered that introducing another complementary term covering the later stages of early HTA would create confusion. Hence, the working group decided to drop development-focused HTA and concentrate on the definition of early HTA, as the more comprehensive and recognised term. The working group also decided that, given the multiple policy initiatives in the area of early dialogue at present and the greater expertise elsewhere in HTAi on this topic, we would not seek to develop a consensus definition for this term. Regarding the alternative terms that were suggested by the panellists, many were suggested as mirror terms for development-focused HTA or in order to provide two terms to sub-divide early HTA. In view of the absence of a dominant alternative, the working group decided to focus only on the definition of the single term 'early HTA'

The working group reviewed the responses, and the main themes were discussed at length. An iterative amendment process was undertaken, comprising a meeting of the working group and subsequent group emails, until the working group were satisfied that the definition reflected their understanding of early HTA. At this stage, we also consulted a panellist and lexicographer who were involved in the HTA Glossary. Box 1 sets out the initial definition circulated with round one and the final definition arrived at by the working group. Based on the advice offered, 'health technology

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assessment' appears as the first phrase in the definition to link directly to the overall definition in the HTA glossary. Early HTA is a sub-set of health technology assessment, which means that concepts from the main definition such as 'in order to promote an equitable, efficient and high quality health system' are implied and therefore not required in our core definition. In the Supplementary Materials we explain the working group responses to feedback received in the first round and how that was taken into account in the different aspects of the definition.

Stage four – round two Delphi survey

In the second round of the survey, we asked participants to respond on a Likert scale to indicate whether they strongly agreed, agreed, were neutral, disagreed or strongly disagreed with the definition. They were asked to provide comments to support their responses. Participants who had provided their email addresses in round one were sent a personal link to complete round two. As pre-specified in the protocol, we considered consensus reached if seventy percent of panellists or more either strongly agreed or agreed with the definition. Panellists were asked to provide name and affiliation if they wished to be acknowledged in this paper. In addition, we asked them questions about their geographical background and follow-up questions about their expertise in (early) HTA.

Of the 119 panellists who provided their email addresses in the first round, 99 (83 percent) took part in the second round. Figure 2 shows the level of agreement reached in the second round. In total, eighty-six (87 percent) panellists either strongly agreed or agreed with the definition. This compared with a consensus threshold of seventy percent set in our protocol. Eight panellists (8 percent) neither agreed nor disagreed, and five (5 percent) disagreed. Of the thirteen members of the working group who were also panellists, five agreed and eight strongly agreed with the definition. Excluding these thirteen individuals results in a level of agreement of eighty-five percent with seventy-three panellists agreeing or strongly agreeing from a total of eighty-six. Excluding panellists with no experience of either early HTA or early dialogue, the level of consensus is eighty-eight percent.

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Stage five – decision on consensus

In the fifth and final stage of the study the working group considered the responses to the second round and decided whether any further amendment was required. The working group unanimously concluded that, given the strong level of agreement, the second definition, set out in Box 1, would be adopted as the consensus definition. Free text comments from the second round of the survey focused on three key areas: what early HTA can and cannot do; confusion with or between early dialogue/early awareness/early scientific advice and the timing of early HTA.

What early HTA can and cannot do

One panellist commented that early HTA cannot include early ethical, social, cultural, legal, organisational and environmental aspects. The working group felt that early HTA can consider these elements and that it was important to emphasise the relevance of exploring these aspects at an early stage of development to anticipate later issues, even though this is currently not often included in early HTA (34). Another panellist expressed concern that early HTA would be 'inaccurate' due to a lack of detail and fast-moving environment. The working group felt that this comment misunderstood the purpose of early HTA. Given the purpose of early HTA is to inform decisions about subsequent development, research and/or investment, an early HTA would highlight a fast-moving therapeutic or competitive environment and incorporate this uncertainty into analyses. Although it could be argued that all HTA is on some level imprecise, economic evaluation as part of early HTA does not typically give a definitive answer to a binary question about whether a health technology is or is not cost-effective. Rather it is intended to identify the key parameters which will influence cost-effectiveness and provide some guidance about threshold levels of performance which may be required in order for a technology to add value. Understanding the needs of stakeholders for a technology and the conditions under which it can provide value for money is particularly important in fast-moving therapeutic and competitive environments.

Confusion between early dialogue/early awareness/early scientific advice

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The responses highlighted some confusion on how early HTA relates to early dialogue, early awareness and early scientific advice. Possibly this is because early HTA undertaken within companies or on innovators' behalf by consultants and academics is largely unseen. Panellists from HTA agencies are aware that their own or associated agencies' horizon-scan for emerging technologies (early awareness) and engage with innovators to discuss process and evidence requirements (early scientific advice). They may be less aware of early HTA, which occurs at a much earlier stage of development than these activities and is not readily visible to them. Since early dialogue explicitly concerns the interaction between innovator and HTA agency and/or regulatory body, it is different from the method of stakeholder involvement that can be used as a qualitative method for performing an early HTA, which generally includes a broader set of stakeholders. Table 1 gives an illustration of the working group's view of how these activities relate to early HTA.

Timing of early HTA

Some panellists felt it was important to specify in the definition at what stage an HTA is 'early', in contrast to 'not early' HTA. The working group felt that the only clear distinction between early and other forms of HTA relates to the decision problems that the respective assessments are purposed to inform. The second definition (Box 1) is structured to place early HTA as a sub-set of HTA with a clear purpose that is different from, for example, HTA performed to inform reimbursement decisions. The further detail provided in Table 2 illustrates the typical timing of early HTA. Panellists felt it would be useful to be explicit about several aspects of early HTA such as: who requests, carries out and pays for the HTA; what the outputs are; whether the process is confidential; and the role of the HTA agency. The working group acknowledged the relevance of these questions, but noted that the answers will vary. For example, early HTA activities can be performed by a consultancy company to inform an innovator on the potential value for money of their technology or idea, in which case it will be paid for by the innovator and the process is probably confidential. However, early HTA could be facilitated by an academic expert, paid for by a public research funder, to inform decisions on funding a clinical

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study on a new technology. We added detail covering these points to Tables 1 and 2. Although the aim of the Delphi survey was to adopt a broad definition of technology and to make the definition of early HTA technology-agnostic, we acknowledge that some technologies, such as orphan drugs, digital health or service innovations may deviate from standard health technologies and our general descriptions may not capture every nuance.

Additional detail on stages of early HTA

In the first round of the survey, we included a detailed table which delineated early HTA into three stages shown alongside the phases of development of a technology (see Supplementary Materials). We amended the table in response to the feedback in round one (Table 2). Specific changes include a recognition that, as the development of the technology proceeds into what we have termed Stage 3 'Research and evidence generation', HTA can still be early, but it does not necessarily have to be, depending on the purpose of the assessment. If the purpose of HTA activities at this stage is to inform risk sharing and ongoing monitoring arrangements as part of reimbursement/adoption decisions rather than to directly inform decisions to adapt or develop the technology, it is no longer deemed early. We also added detail of typical methods at each stage of development, including some comments on how uncertainty may be explored, as this was a common request in the feedback to round one. It should be noted that these are examples only and not intended to be exhaustive or prescriptive. Table 2 should not be seen as part of the consensus definition as it was not included in the second round. However, we felt it addresses most of the comments that were made on the definition in round two of the Delphi process.

Discussion

We undertook a five stage process including a two round Delphi survey which produced consensus on a definition of early HTA. Based on this process, early HTA is defined as "a health technology assessment conducted to inform decisions about subsequent development, research and/or investment by explicitly evaluating the potential value of a conceptual or actual health technology".

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Eleven previous papers had suggested nine definitions for early HTA or related terms (see Supplementary Materials) (3, 5, 6, 8, 24, 27-32). Several of these definitions were limited to the health economic modelling component of early HTA (28, 31, 32) whereas our definition considers wider implications by incorporating the note from the HTA glossary definition of HTA on the dimensions of value, albeit slightly amended to include implications for the innovator. Pietzsch and Pate-Cornell (8) and Ijzerman and Steuten (6) both recognise that the purpose of early (health) technology assessment is to inform future development with the former explicitly recognising that investment and design decisions may be informed. Ijzerman et al (3) explicitly recognise that industry may be the primary audience defining early HTA as "all methods used to inform industry and other stakeholders about the potential value of new medical products in development". Fasterholdt et al (27) defined early assessment as "being performed when the initial selection of ideas or rough prototyping has taken place, but prior to large scale testing or traditional clinical research. Hence, early assessment is based on data from early phases, i.e. feasibility, pilot, or initial effect data". This focus on a specific stage in development or the un/availability of specific data is useful in the definition of early HTA and we have included both aspects in our detailed table (Table 2); however, the working group felt that the distinctive feature of early HTA is that it is intended to inform decisions around development, research and investment decisions. The availability or otherwise of data is not a defining characteristic of early HTA.

We present the first consensus-based definition of early HTA. Strengths of our approach are the extensive experience and different perspectives represented in our working group and by our Delphi panel members. We have representation from most geographic areas, although acknowledge that there is a preponderance of involvement from Europe and Australia. Although there is no recognised standard for conduct or reporting of consensus exercises such as ours, we have followed the CREDES best practice guidelines (26). We set out our methodology in our protocol, worked under the oversight of the Scientific Development and Capacity Building Committee of HTAi and have reported all aspects of our process transparently. Our study has a number of limitations. Both the working group and

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Delphi panel had a strong representation from Australia and Europe. Also, most working group members and panellists were from academia, and mostly had experience with quantitative methods. This is not surprising, given most early HTA activities focus on health economics, and are performed in Europe and Australia. Both the working group and panel were open to anyone interested, and we did not have a pre-defined threshold for representation of certain stakeholders, regions or experience. Our panel and working group thereby seem to be a good representation of the current interest in and use of early HTA.

The development of this consensus definition of early HTA is important because it provides clarity and raises the profile of the field. Although it fits within the umbrella definition of HTA developed by an international joint task group co-led by the International Network of Agencies for Health Technology Assessment (INAHTA) and HTAi (1) it does suggest an extension of the concept of 'value' in that definition to include wider implications for innovators. It also makes clear that early HTA is not restricted to the activities of HTA agencies but involves a wide range of actors from the very earliest stages and may precede the development of the technology itself, with much work remaining unpublished and potentially 'below the radar'. It clearly distinguishes early HTA from related but distinct activities of early awareness and early dialogue/early scientific advice. Developing a consensus definition of these terms was beyond the scope of this study, but would further clarify the differences between the activities. We urge authors to identify their papers as early HTA, where appropriate, and use our detailed table (Table 2) to report the stage of development of the technology and level of evidence available. We encourage journal editors to reinforce the use of this uniform terminology in order to improve visibility. Next steps for our group include the submission of the consensus definition to the HTA glossary and work on methods and reporting of early HTA. In developing methods, it will be useful to relate early HTA to other fields of research such as bioethics, philosophy of technology, responsible research and innovation, and decision making under deep uncertainty. In addition, we stress that like all definitions, this is a 'living' definition that may need to be updated in time to reflect the evolution continuously happening within the field of HTA.

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Early HTA is performed to inform decisions about development. It provides an opportunity to assess the potential value of innovation before significant funds are committed, thus guiding investment decisions. We also advocate the adoption of an early HTA approach in a proactive sense to identify and describe specific clinical needs, and the technology features required to meet them. Furthermore, early HTA provides the opportunity to ensure that technology is optimally designed and positioned to deliver the most value to a diverse range of stakeholders including the innovators themselves, whether they are working within the healthcare system or in industry. Early HTA, like HTA as a whole, seeks to promote an 'equitable, efficient and high-quality health system'.

Conclusion

In this paper we have reported a five-stage process, including a two-round Delphi survey that developed and reached consensus on a definition of early HTA, which is "a health technology assessment conducted to inform decisions about subsequent development, research and/or investment by explicitly evaluating the potential value of a conceptual or actual health technology." By providing a consensus-driven definition of early HTA, we hope to enhance uniformity and harmonisation of terminology. In addition, we hope to lay the foundation for more discussion, research and methods development in this important field.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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Box 1. Definition of early HTA included in the two rounds of the survey

Definition included in round one of the Delphi survey

Early HTA is a formal, systematic, transparent and multidisciplinary process that uses explicit methods, both quantitative and qualitative, to explore the potential and/or expected value of a health technology*, including the associated uncertainty, before or alongside the technology development process. Stages at which early HTA can be undertaken include the concept/discovery stage, prototype/proof of concept stage and research/evidence development stage. The stages impact upon the evidence/data available, the questions to be answered, methods to be used and the audience for the work. The purpose is to provide innovators with insight about the potential value** for the health system and commercial viability of a technology, and to inform decision-making about the (clinical) need, design of a technology, positioning of the technology in the care pathway, further research needed to prove value and potential for future market access and adoption, in order to promote a high-quality health system.

* A health technology is an intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organize healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, program, or system (definition from the HTA Glossary; http://htaglossary.net/health+technology).

**The dimensions of value for a health technology may be assessed by examining the potential intended and unintended consequences of using a health technology compared to existing alternatives. These dimensions often include clinical effectiveness, safety, costs and economic implications, ethical, social, cultural and legal issues, organizational and environmental aspects, as well as wider implications for the patient, relatives, caregivers, and the population. The overall value may vary depending on the perspective taken, the stakeholders involved, and the decision context

Accepted consensus definition

Early health technology assessment; early HTA

A health technology assessment conducted to inform decisions about subsequent development, research and/or investment by explicitly evaluating the potential value[1] of a conceptual or actual health technology[2].

[1]The dimensions of value for a health technology may be evaluated by examining the intended and unintended consequences of using a health technology compared to existing alternatives. These dimensions often include clinical effectiveness, safety, costs and economic implications, ethical, social, cultural and legal issues, organizational and environmental aspects, as well as wider implications, for example for the patient, relatives, caregivers, innovator and the population. The overall value may vary depending on the perspective taken, the stakeholders involved, and the decision context.

[2] An intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organize healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, program or system.

HTA, Health Technology Assessment

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Table 1. Relationship between early HTA, early awareness and early dialogue/scientific advice

	Early HTA	Early dialogue/ early scientific advice	Early awareness /horizon scanning
Stakeholders involved	Innovators Funders Healthcare providers Clinicians Patients and their advocate groups Technology transfer offices	Innovators Regulators HTA agencies	Regulators HTA agencies Healthcare providers
Purpose	To inform development of a technology, position in clinical pathway and value proposition	To ensure that innovators are aware of evidence requirements of regulators and HTA agencies (33)	To identify new and emerging technologies and assess their potential impact on health, health services and/or society (22)
Timing	TRL <8 Pre-concept stage to research and evidence generation stage	TRL 5-8 Prototype and proof of concept (small scale pilot testing) to research and evidence generation (large scale testing)	TRL 5-9 Prototype and proof of concept (small scale pilot testing) to adoption and implementation (market access adoption and post-market surveillance)
Conducted /commissioned by	Innovators Funders Healthcare providers	Innovators	Regulators and/or HTA agencies Healthcare providers

HTA, Health Technology Assessment; TRL, Technology Readiness Levels

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Table 2. Additional detail by stage of technology development

HTA terminology	Health Technology Assessment			
	Early HTA		Transitioning from Early HTA	
	Stage 1 – Concept and Discovery	**Stage 2 – Prototype and Proof of concept**	**Stage 3 – Research and Evidence Generation**	**Adoption and Implementation**
Technology-specific evidence	Bench, in silico and animal studies, formulation, pharmacokinetic absorption, distribution, metabolism and excretion (ADME) studies, establish safety, user studies of an early prototype. Often no efficacy or effectiveness evidence available.	Evidence of safety and efficacy from small sample Usability/patient acceptance studies Pre-clinical studies, including Good Laboratory Practice, animal safety and toxicity, Phase 1 and Phase 2a clinical trials conducted	Safety and clinical effectiveness study. May include randomised controlled trial or observational evidence depending on regulatory requirements. Phase 2b and Phase 3 clinical trials conducted.	Evidence of safety, clinical effectiveness, quality of life and cost implications is available but may be limited to certain settings, populations or jurisdictions. Post-market / Real-World studies
Typical project scenario	**Technology-driven** - either an emerging and generalised technology with broad application across several potential indications, or a technology with specific features requiring a target indication, setting and position in a pathway. **Needs-driven** - no technology yet specified, with emphasis on identifying and designing features required to realise a patient, payer or innovator improvement.	Potential indication and/or features have been narrowed down. Exploration of position in pathway and setting.	Technology and market development may be continuing.	Regulatory evidence base available. Indication is clear from regulation. Reimbursement application in process or completed.
Potential stakeholders	Innovators (industry/academic/health care professional) Funders (private or public entities; funding research, evidence generation and/or technology development) Health care providers Clinicians Patients and their advocate groups Technology transfer offices	Innovators (industry/academic/health care professional) Funders (private or public entities; funding research, evidence generation and/or technology development) Health care providers Clinicians Patients and their advocate groups Technology transfer offices	Innovators (industry/academic/health care professional) Funders (private or public entities; funding research, evidence generation and/or technology development) Health care providers Clinicians Patients and their advocate groups Technology transfer offices	Innovators (industry/academic/health care professional) Funders (private or public entities; funding research, evidence generation and/or technology development) Health care providers Clinicians Patients and their advocate groups Technology transfer offices

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			Regulators	Regulators
Example of appropriate methods (not comprehensive or prescriptive)	Qualitative methods: • Care pathway analysis • Stakeholder engagement (e.g. interviews/focus groups/surveys with range of stakeholders) Health economic modelling: • Using data from literature, pre-clinical data and assumptions • Simple exploratory models • Use of headroom and threshold estimates • Exploration of structural uncertainty using scenarios	Qualitative methods: • Care pathway analysis • Stakeholder engagement (e.g. interviews/focus groups/surveys with range of stakeholders) Health economic modelling: • Using early data from small studies, data from literature and assumptions • Simple exploratory models • Use of headroom and threshold estimates • Exploration of structural uncertainty using scenarios	Qualitative methods: • Care pathway analysis • Stakeholder engagement (e.g. interviews/focus groups/surveys with range of stakeholders) Health economic modelling: • Using early data from larger studies • Probabilistic models • Value of information analysis • Budget impact assessment	Qualitative methods: • Care pathway analysis • Stakeholder engagement (e.g. interviews/focus groups/surveys with range of stakeholders) Health economic modelling: • Prepared in accordance with context-specific requirement (E.g. NICE reference case
Key questions about development of the technology	What characteristics does the technology need to deliver on the proposed value proposition claims? What evidence needs be generated to meet future regulatory/HTA requirements? What is the feasibility of collecting evidence required to demonstrate value, assessment of epidemiology, natural history and burden of disease?	**Questions as per Stage 1 plus:** How usable is the technology? Would this be acceptable to intended users? Should we invest in preliminary data collection to inform safety and effectiveness? What are the barriers/facilitators to adoption and/or implementation?	**Questions as per Stage 2 plus:** What logistical considerations are required to provide timely access? What are the implementation considerations (health system readiness, work force planning and resource allocations)? What are the timeframes to meet to ensure timely access?	
Key questions about positioning of the technology	What is/are the current clinical pathway/s? How would the technology change the care pathway? What is the room for improvement? What is the targeted patient population?	**Questions as Stage 1**	**Questions as Stage 2**	

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Key questions about the value proposition of the technology	Who are main stakeholders for the future adoption of the technology? What is the potential impact on health, cost, resource availability, equity, accessibility, efficiency or sustainability? What is the minimum level of outcomes that is needed, given threshold costs? What is the maximum costs the expected outcomes could support, given threshold costs? What evidence is required to demonstrate that the technology is likely to deliver value as defined by the chosen decision-maker/s? How does the decision maker weight the different elements of impact/value? What other technologies are on the horizon, which may change the competitive or therapeutic environment? What is the market size?	**Questions as per Stage 1 plus:** At what price/performance characteristics is the technology likely to be cost-effective in selected jurisdictions? Are the expected revenues and commercial return on investment sufficient to develop the technology?	**Questions as per Stage 2 plus:** Does preliminary evidence on safety and effectiveness justify investment in large scale testing?	Is the technology likely to be cost-effective in the specific population, position in pathway and jurisdiction at set price? Should we fund/cover/adopt the new technology? Should conditions be placed on adoption for restricted coverage, risk-adjusted pricing, and further evidence generation? What are the financial implications and considerations to ensure continuing access?
Technology Readiness Levels (TRL) (35)	TRL<4 Review of scientific knowledge base, development of a technology's hypothesis, identification and characterization of candidate technologies, optimization and initial demonstration of safety and efficacy.	TRL 5-6 – Advanced characterization of technology and initiation of manufacturing and/or staff recruitment. Regulated production, regulatory submission and clinical data.	TRL 7-8 – Scale-up, initiation of good manufacturing practice process validation and Phase 2 clinical trials	TRL 9 – Market access, adoption and post –market surveillance

HTA, Health Technology Assessment; TRL, Technology Readiness Levels

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Figure 1. Stages of Delphi process

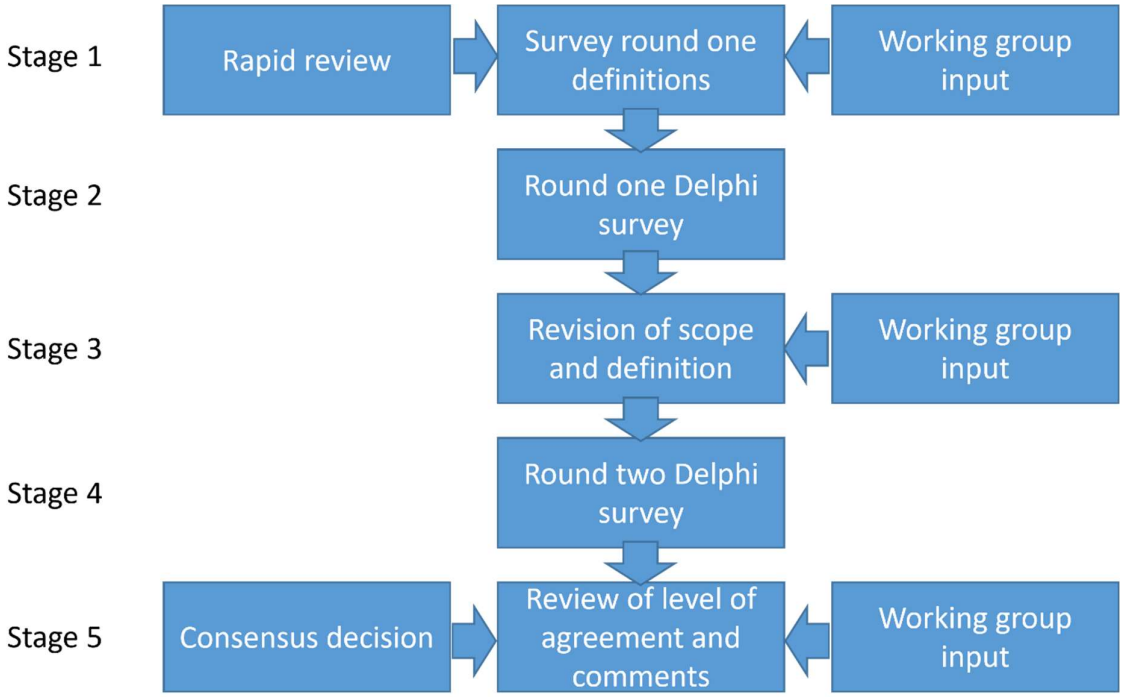

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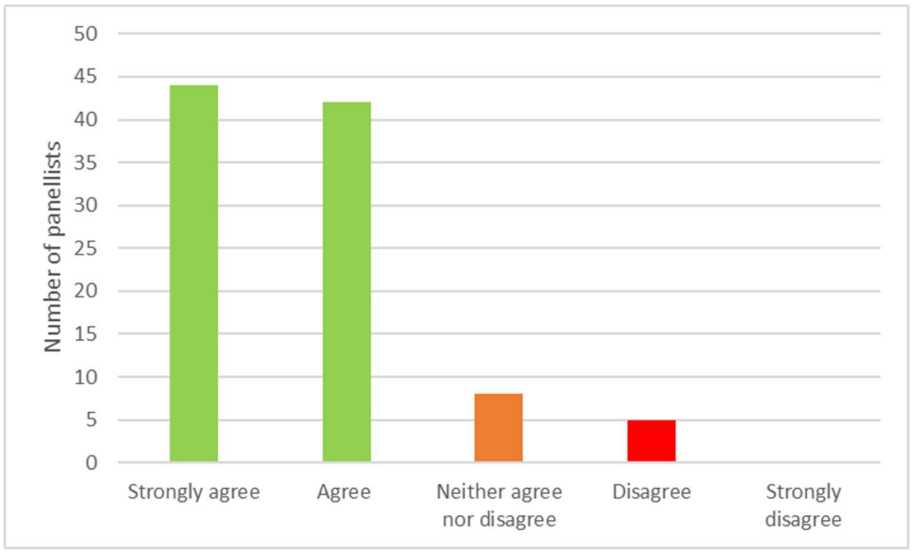
Figure 2. Level of consensus on provided definition of early HTA



HTA, Health Technology Assessment.

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