Norwegian Institute of Public Health

Technical guidance for Health Technology Assessment in low-and middle-income countries

Developed by the Global Health Cluster for use in international projects and collaboration

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I Contents

II About this Guidance

Purpose

This document has been developed by the Norwegian Institute of Public Health Global Health cluster (NIPH-GH) for the programme of work "*Support evidence to decision through HTA in low- and middle-income countries"* (LMIC). The purposes of the document are:

- To outline NIPH's approach and understanding of Health Technology Assessment (HTA) processes
- To support harmonization and consistency in NIPH-GH's support and collaboration with bilateral and global partners
- To describe the aspects of HTA that NIPH-GH emphasises, considering the wide variations in HTA practices globally and the unique settings of our collaborators
- To describe the aspects of a thorough HTA process that are relevant to making HTA part of health systems and decision-making practices.

In this document, we outline NIPH-GH's interpretation of thorough HTA practice, including definitions of concepts, and widely used methods. The document highlights key considerations for the development, production, reporting, and use of HTA in a LMIC setting. We use understandable terminology for the concepts, noting that the type of product produced for an HTA depends on its context, its methodology, and the resources available to complete and implement it. This document is not meant to be an exhaustive approach to conducting HTAs, but instead aims to provide an extensive overview of HTA.

See Table 4 for links to guides and templates to support the production of HTA products.

Norwegian Institute of Public Health

The Norwegian Institute of Public Health (NIPH) is the national HTA agency[1] and is responsible for producing HTAs to support policy and decision making for the Norwegian specialist (hospital level) health care service. We have practical insight and competences in conducting HTAs nationally and internationally. We have experience in collaborating on the development of HTA processes and methodology, and extensive experience in training in clinical evidence synthesis.

NIPH has been actively contributing to the European Network for HTA (EUnetHTA) Joint Actions, and we are currently providing input to EUnetHTA 21 that builds on achievements from earlier EUnetHTA Joint Actions and supports the preparation of a permanent HTA collaboration under the European HTA Regulation.[2] NIPH is also a member of Health Technology Assessment international (HTAi) and the International Network of Agencies for Health Technology Assessment (INAHTA) and contributes to those organisations' task forces and learning groups therein.

[1] The Norwegian Medicines Agency is commissioned to produce Single Technology Assessments of pharmaceuticals.

[2] Regulation 2021/2282 of the European Parliament and Council, 15 December 2021, on health technology assessment and amending Directive: 2011/24/EU. Accessible: http://data.europa.eu/eli/reg/2021/2282/oj

The NIPH-GH's *"Support evidence to decision through HTA in LMICs"* programme is built on the competence of experts employed at NIPH. Initially funded by the Norwegian Agency for Development Cooperation (Norad).

III Overview of HTA

Definition of HTA

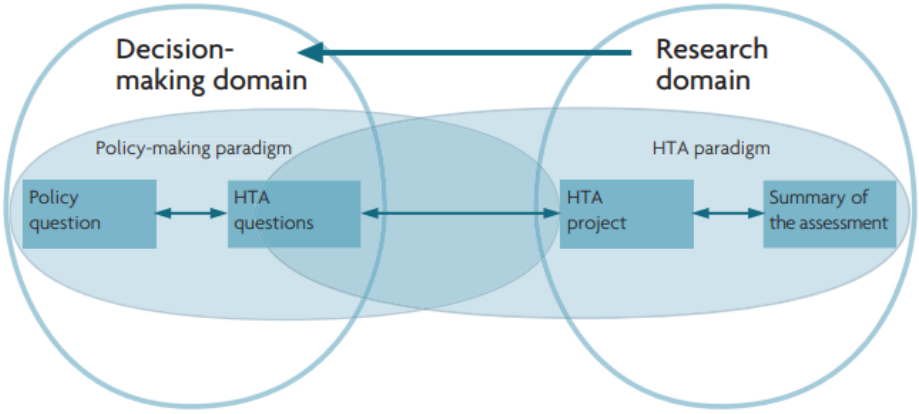
The definition of HTA for this document is that HTA is *"*a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system" (1). In HTA 'health technologies' are broadly defined as "an intervention developed to prevent, diagnose, or treat medical conditions; promote health; provide rehabilitation; or organise healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, programme or system" (2).

What can HTA be used for?

An effective and relevant HTA process finds, selects, synthesizes, and evaluates evidence. This evidence is then used to support transparent and evidence-informed decision-making ensuring that policymakers have access to the most relevant, accurate and up-to-date scientific evidence on a specific topic.

An example of a question currently relevant to policymakers relates to the benefits and harms of e-cigarettes. To decide on whether and how e-cigarettes should be sold, policymakers may need evidence on whether, for example, e-cigarettes could be a healthier alternative to smoking and potentially help people to give up cigarettes (3) . However, policymakers may also want information on the long-term health effects of e-cigarettes (4) to inform their decision.

Figure 1: Bridging between the decision-making and research domains



From Kristensen and Sigmund (2007) (5)

Figure 1 illustrates how policymakers' decision-making domain overlaps with the research domain. For the e-cigarette example, the HTA question would be developed from the policy question. In contrast, the HTA project itself, answering the HTA question, is embedded in the research domain,

seeking and synthesising research evidence. The HTA handbook from the former Danish Centre for HTA describes the process of bridging the decision-making and research domains (5).

Organisation of the HTA process

How the HTA process is organised varies by country, depending on how they organise and resource their health care decision-making processes (6). A country's HTA system can be facilitated by a single entity or body (e.g., a unit in the Ministry of Health) or by several institutions and stakeholders working together to support decision-making.

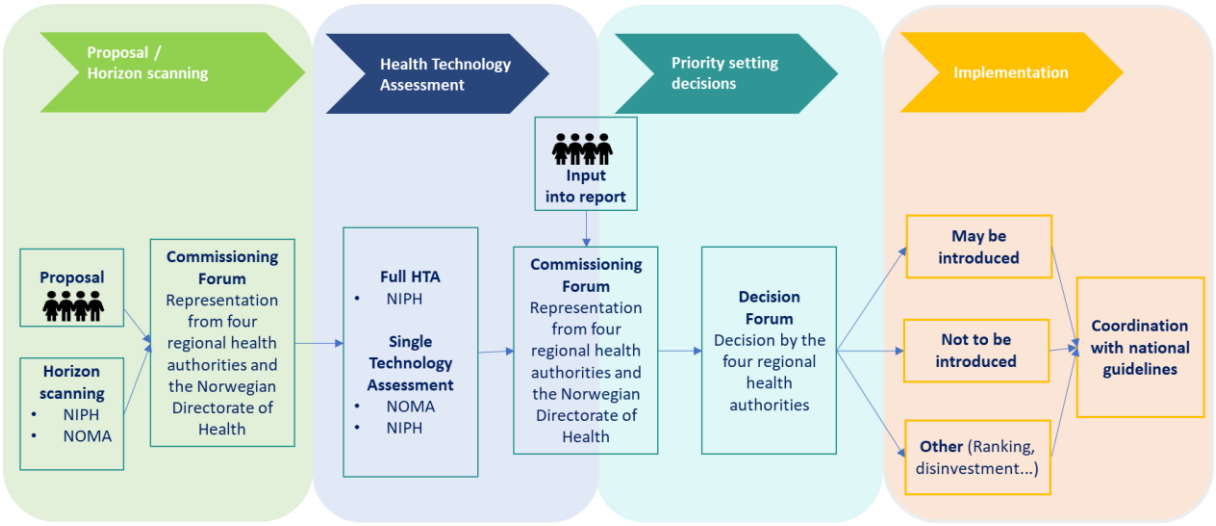
Typically, the HTA process follows a series of steps starting with topic identification. As only a limited amount of HTAs can be conducted at the same time, a selection and prioritisation from the list of identified topics is made and an HTA will be commissioned. These first steps, referred to as Topic Identification Selection and Prioritisation (TISP), are followed by conducting the HTA. The completed HTA is presented to policymakers to facilitate appraisal, decision-making, and implementation (7). Below figure 3, each step from the HTA process will be described in more detail.

NIPH's approach to HTA

In the Norwegian HTA system, the NIPH Department for Reviews and Health Technology Assessment and the Norwegian Medicines Agency (NOMA) conduct HTAs. Figure 2 shows the Norwegian system for introducing health technologies into Specialist Health Care Services (including hospitals). In this process health technologies are proposed for assessment, selected by a Commissioning Forum, who then forwards to either NIPH or NOMA for the creation of the evidence synthesis (with or without economic evaluation). The evidence synthesis is appraised and submitted to a Decision Forum, comprised of the four Norwegian regional health authorities for final decision making.

More information on the national Norwegian System for Managed Introduction of New Health Technologies within the Specialist Health Service can be found on the website [nyemetoder.no/en].

Figure 2: The Norwegian System for Managed Introduction of New Health Technologies



NIPH: Norwegian Institute of Public Health; NOMA: Norwegian Medicines Agency; HTA: Health Technology Assessment

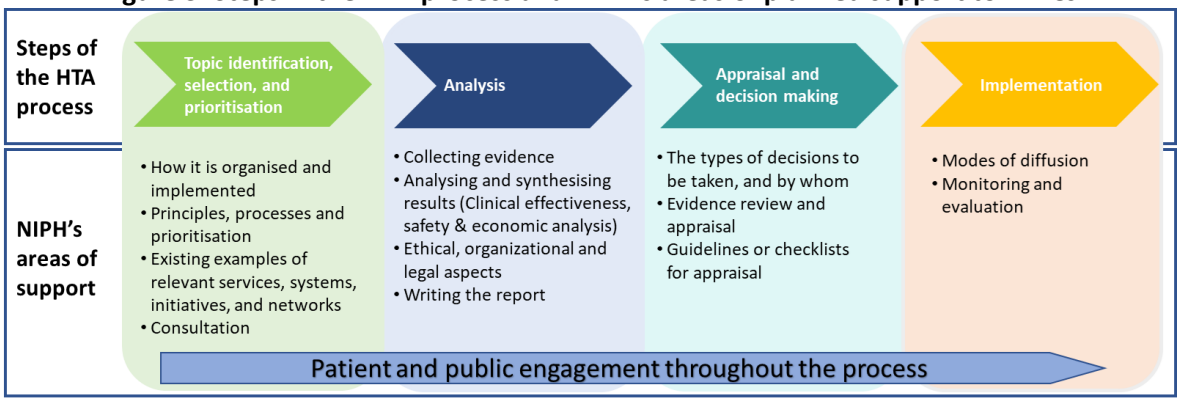
NIPH Global Health's approach to HTA

The NIPH-GH HTA process has four steps, as shown in Figure 3. These four steps are:

1. **TISP** defines the decision space by specifying how the topic identification-selection- and prioritisation is organised and implemented, and what principles, initiatives and networks are used in the process to select a topic for an HTA.
2. **Analysis** includes activities such as developing assessment plans, collecting evidence with input from stakeholders where relevant or necessary, analysing, and synthesising results, and discussing possible consequences for practice, and may include recommendations
3. **Appraisal** and **decision making** refers to the types of decisions to be taken and by whom, and the which guidelines or checklists are used for appraisal.
4. **Implementation** of decisions that have been informed by an HTA, considering modes of dissemination, policy or procurement changes, monitoring, and evaluation.

The number of steps in any given HTA process may vary. It may be more suitable for some countries to choose a different division of steps, for example, by separating out appraisal (i.e., confirming the product is appropriate and of good quality) from decision-making (8).

Figure 3: Steps in the HTA process and NIPH's areas of planned support to LMICs



The HTA processes can be referred to by different names such as an HTA informed deliberative decision process (8), an HTA system, or an HTA framework (9). The **process of decision-making** is a key aspect of an HTA system, demonstrating that the decision-making process is fair and transparent.

One example of an HTA process that is promoted widely in the literature, and could be relevant to countries with emerging HTA systems, is referred to as *evidence-informed deliberative processes* (8). This is a stepwise approach that HTA bodies can follow, to maximise the legitimacy of the HTA system and its related decisions. The evidence-informed deliberative process highlights the value of including a broad range of stakeholders in all of the steps (10), offering mechanisms to collect a broader set of social values, and thus a very important feature when producing HTAs (11, 12). This approach may not be appropriate to all contexts.

Patients and members of the public form a group of stakeholders whose engagement is an important component of a transparent and inclusive HTA process. Their engagement should result in the incorporation of the views and perspectives of those affected both directly and indirectly by health technology into the HTA process. By including the perspectives of stakeholders, decision-makers seek to support a fairer and more legitimate process. Hence, ideally stakeholders should be included at every step of the HTA process.

Before the HTA process begins, all stakeholders contributing to it should declare any interests that they have, and conflicts of interests should be managed accordingly to the policies of the institutions organising the process. Stakeholders should declare conflicts that relate to all domains of the HTA product, and conflicts are not limited only to the health problem and the current technology.

The *HTA 101: Introduction to HTA document* introduces fundamental aspects and issues related to HTA and is a useful reference document for those new to HTA (available online) (13).

Institutionalised or formalized HTA

An effective HTA system ideally needs to be mandated by the government. An institutionalised or formalized HTA system is authorised through statutory law and regulatory law (14). Statutory support for HTA is intended to promote fairness and transparency. To ensure that the process is run in a fair way, the regulations that provide oversight for the HTA process should clarify how HTA topics are selected, the decision-making process, and how decisions should be implemented. The types of statutory rules that are implemented will depend on a country's government (e.g., parliamentary, federal, presidential), and differences between national or sub-national technology procurement. Statutory rules should include how to clarify the selection criteria, its mandate, principles, responsibilities, implementation considerations, and the financial consequences of HTA decisions (14). WHO has published in-depth guidance to support decision-makers to consider the institutionalisation of HTA in their own context, see: *Institutionalizing health technology assessment mechanisms: a how to guide* (2021) (14).

IV Step 1: Topic identification, selection, and prioritisation (TISP)

In the following sections (IV – VII), we will describe each of the steps of a typical HTA process and domains in an HTA report.

The first step of the HTA process is to select the priority topic for an HTA, given all the competing alternative priorities. Topic selection is informed by the need of the health care system, and the scope and capacity of the HTA system. This step is also referred to as "framing the decision space" (15), "nomination of topics" (14), or simply "selection or prioritisation of topics". Table 1 outlines the purpose of TISP.

Topic **identification** can be divided in three broad categories:

- **Reactive**: awaiting input from someone e.g., a policymaker, clinical expert, technology developer, such as a pharmaceutical company.
- **Proactive:** actively searching for topics as part of the HTA system's mandate or work programme, e.g., horizon scanning.
- **Hybrid:** a mixture of both approaches.

Table 1: Why is TISP undertaken, how is it undertaken, by whom, and what are its outputs?

Topic	Why?	How can it be done?	Who are possible stakeholders?	What is the output?
Identification	To identify topics that are likely to be within the scope of the HTA system	• Reactive • Proactive • Hybrid mixes of both approaches	• Clinicians • Patients • Patient representatives • Policymakers • Industry committees • A horizon scanning service	• Information to allow selection • A specification of the topic which is detailed enough to help with selection and prioritisation processes
Selection *(also known as filtration)*	Verify that topics are within the HTA system's scope	Follow pre-defined criteria	• HTA steering group or secretariat members • An horizon scanning service	• Factors relevant for the prioritisation in the setting e.g., contextual information, feasibility of implementation, current use (if relevant).
Prioritisation	A decision is made to either initiate, reject or postpone the assessment	Follow pre-defined criteria	• Policymakers • Specialised committees or forums • The HTA agency	• A prioritised list of topics for HTA

Adapted from Lauvrak et al. (2021) (16)

Topic **selection** refers to whether the identified topics align with the scope of the HTA system. These selection processes are usually based on predefined criteria, and the decision-making process may include advice from clinical experts and/or industry representatives (17, 18).

Topic **prioritisation** is when a decision is made to initiate, reject, or postpone an assessment (19). While topic selection ensures that identified topics are aligned with the aims of the HTA system, prioritisation can help when resources are limited, to determine which topics are assessed at which level of detail. Typically, it is not possible to assess all identified or selected topics to the same depth. Ideally, the purpose of prioritisation is to ensure that topics that meet the national priority criteria (e.g., of greatest value or benefit to the country's health system), are adequately assessed as quickly as possible. Prioritisation may use an explicit or implicit ranking process (16, 18).

The organisation of TISP depends on the context where it is performed and resource availability. Who to involve, what criteria to apply, and what dissemination strategies to use need to be agreed upon in advance. Best practice would be to promote a transparent and inclusive process, led for example, by a government mandated steering committee with representation from across different areas of the health sector, as well as patient representatives and members of the public. The

outcomes of the identification and selection processes are used to inform topic prioritisation, which should then be disseminated publicly to promote transparency. The dissemination products of TISP may include lists of topics, short alerts, or vignettes, or early assessment reports.

The costs, time, and other resources allocations necessary to set up a proactive TISP process may be difficult to determine, even though benefits may be far reaching. Countries with emerging HTA systems could consider joint horizon scanning activities and collaboration in global or regional networks. The International Horizon Scanning Initiative (IHSI) is an example of a joint horizon scanning system involving eight European countries, see Table 4 for further information. One practical option to consider when establishing an HTA system is to use a strict reactive process which simply responds to requests from policymakers, health care workers or other stakeholders.

V Step 2: Analysis

The aim of the analysis step of an HTA is to deliver adequate information on the value of the health technology to inform evidence-based decisions. In line with the definition of HTA, the overall attributed value of a new technology may vary depending on the perspective taken, the stakeholders involved, and the decision context. The key product of an HTA system is the HTA report, therefore, some countries would begin the implementation of HTA by piloting one HTA and developing a report.

Analysis results are typically presented in reports, whose content may differ depending on the setting and technology type (Table 3). Many HTAs include evidence syntheses, such as systematic reviews[3], or a meta-analysis.[4] A **full HTA report** (henceforth referred to as an 'HTA report') is the most comprehensive format and it includes sections (or 'domains') on the characteristics of the health technology, its safety and clinical effectiveness, its cost effectiveness, and its budget impact. It may also include information on organisational, social or patient, ethical, and legal aspects (20) of introducing the new technology. An example of what might be included in an HTA report is provided in the section Writing the HTA report. The choice of which domains to include in an HTA depends on the health technology being assessed and the specific request received from the HTA commissioner. The question agreed with the commissioner, but also the time decided to be allocated to the assessment (if urgent for example) and the type of decision (e.g., coverage, guideline, procurement) will influence whether you undertake a rapid HTA or develop a full detailed HTA. Some HTA products, for example rapid or mini HTAs, may only include one or a selection of the domains.

The availability of methodological guidance on the conduct of each domain section of an HTA varies. For example, well-developed guidance is available on how to conduct the clinical effectiveness domains. Guidance on the organisational, patient, ethical, and legal domains, and the aspects of public involvement have also been developed. Figure 4, adapted from the EUnetHTA Core Model®(21), outlines the main considerations for the analysis process.

[3] A synthesis that collates all empirical evidence fitting pre-specified eligibility criteria to answer a specific research question (http://htaglossary.net/systematic-review)
[4] Statistical combination of results from multiple studies to obtain a single estimate of effect of a particular intervention or variable (http://htaglossary.net/meta-analysis)

Figure 4: Main considerations for analysis within an HTA

Adapted from the EUnetHTA Core Model® (21)

The assessment of a technology's clinical effectiveness should follow internationally accepted guidance for the conduct of systematic reviews on the effectiveness of interventions or diagnostics. Table 4 shows some examples, but the guidance may need to be adapted for specific contexts and purposes. In terms of HTA approaches to analysis, the Cochrane Handbook [https://training.cochrane.org/cochrane-handbook-systematic-reviews-interventions], and the EUnetHTA tools [https://eunethta.eu/tools/] are highly relevant comprehensive resources.

Protocol development and project planning

HTA is characterised by a systematic and structured way of answering questions by identifying, evaluating, and synthesizing available evidence.

After an HTA has been commissioned, the first step is planning the HTA. This includes translating the policy question into a research question if it has not been clearly formulated during the TISP process. This will determine how comprehensive the assessment should be and to what extent the value of a new health technology should be assessed. In other words, here it should be decided which domains to include in the HTA and what perspective to use in an economic evaluation.

For clinical question generation, the PICO framework (Population, Intervention, Comparators and Outcomes) helps formulate the question (22). The PICO defines the inclusion and exclusion criteria that research must meet to be considered eligible for inclusion in an evidence synthesis considering effects and safety. The choice of comparator(s) and outcomes often depends on local context (what comparators are approved already) and the purpose of the HTA product. Other question definition frameworks are available for non-effectiveness questions.

When planning an HTA, the research question, the eligibility criteria for inclusion of literature or empirical data, the HTA methodology, quality assurance and quality assessment methods, timelines,

planned products, and resource requirements as well as project team details should be prespecified in a protocol. The protocol should be made publicly available.

If the HTA includes a systematic review of interventions with health-related outcomes, the protocol should be registered in the PROSPERO database, an international database of prospectively registered systematic reviews addressing health-related outcomes (23). When reporting the systematic or scoping review within an HTA report, the Preferred Reporting Items for Systematic/Scoping Reviews and Meta-analysis (PRISMA) statement should be used (24) to ensure all essential information about the methods are reported. Deviations from the PRISMA statement may be required for reviews of non-effectiveness questions or for other HTA products. For example, a diagnostic test evaluation would use the STARD (25) reporting guidelines, and there are other checklists for other HTA question. The methods used to prepare an HTA should always be transparent.

Identifying the evidence

Evidence for the analysis should be collected in a systematic way. It is necessary to develop a clear search strategy based on the PICO and complete a thorough, objective and reproducible search of a range of information sources to identify as many eligible studies as possible (26). To support this, an experienced healthcare librarian or information specialist should be engaged in every step of the process, including the drafting of the protocol. The aim is to develop a systematic and comprehensive approach to identifying studies that meet the eligibility criteria for the review within the HTA (see Table 4 for relevant guidance). Each domain may require adaptations to the information collection process. For a rapid review, or other rapid HTA methods, the approach may be less extensive (e.g., fewer databases searched).

Health problem and current use of technology

Understanding **the health problem and current use of technology** may be presented as a standalone report, a scientific publication, a chapter within an HTA product, or covered in a background chapter or the introduction of an HTA product. The information collected and assessed for this section covers the target conditions, target groups, epidemiology of the conditions and the availability and patterns of use the current technologies in use in the healthcare system of interest. This domain also addresses the burden experienced by individuals and society as result of the target condition, and the current technologies being investigated. Health care providers, the industry, and patients can provide useful information for this domain.

The **technical characteristics** of the technology (or sequence of technologies) under assessment may include information on any requirements for the premises, equipment, staffing, training, and other aspects that support the operationalisation of the technology. The regulatory status of the technology should be listed, where applicable. The characteristics of the technology need to be described in enough detail to differentiate the technology of interest from its comparators. Important terms should be defined, and a glossary or a list of product names may be provided. The domain may include pictures, diagrams, videos, or other visual material, to help non-experts understand the technology and its use.

The length of the text and the level of detail required in for this domain depends on the context, the HTA product to be produced, available resource availability and any time constraints.

Synthesis of clinical effectiveness & safety

Research evidence shows how well a health treatment, intervention, or technology works. In this domain of the HTA, the report should describe the current knowledge on effectiveness and safety of a health technology.

Commonly, the focus of the evaluation of clinical effectiveness is to determine the net benefits (benefits minus harms) achieved by a technology (28). While clinical efficacy indicates whether a technology *can* work (as compared with placebo or standard care), clinical effectiveness research compares a technology with another technology, which is usually is the current practice or standard of care. When assessing health benefits, HTAs often primarily consider patient-relevant outcomes such as mortality, morbidity, and quality of life. Additional outcomes which can help with analysis of other domains in the HTA, such as costs for cost-effectiveness analysis, are also identified. The selected outcomes are likely to be context specific. HTA encourages the incorporation of patients' views via patient input, involvement, or engagement.

Addressing **safety or adverse events** is a mandatory topic in any HTA to ensure information about the possible harms of a technology are made clear to patients and informs the decisions of policymakers. Safety is an umbrella term for any unwanted or harmful effects caused by a technology. Safety information, combined with effectiveness data, inform other assessments of the impact of a new technology including its cost effectiveness and any organisational changes required to implement it.

Various types of study design are used to assess clinical effectiveness and safety. Data from high quality randomized controlled studies (RCTs) are considered more reliable, i.e., with less risks of biases (due to systematic errors) than studies without a control group or studies where participants are not randomized. Checklists for assessing risk of bias (RoB) for various types of studies are available (22). Determining the certainty (or quality) of the evidence (or grading the evidence) is usually done by using the Grading of Recommendations Assessment, Development and Evaluation, GRADE tool (27), which considers the RoB studies included in the assessment, as well as other parameters related to directness or transferability, consistency, precision, reporting, and dose-response effects (27). The level of certainty or quality of the evidence following quality assessments determines the extent to which the reader believes that estimates of effectiveness are correct (28, 29).

Preferably, the evidence on efficacy, clinical effectiveness, and safety is gathered by conducting a systematic review, and, if feasible, a meta-analysis. Other methods for analysing these outcomes can include, literature reviews, synthesis of best evidence, and rapid reviews.

Economic analysis

Economic evidence shows how well the technology works in relation to how much it costs for the health system. Using societal and health care system perspectives, the analysis relevant to this domain seeks to answer the question, does the technology represent value for money?

The economics analysis domain aims to provide insight on how to balance unlimited wants within context of scarce resources, since resources can only be used or spent once. Economic evaluations can help to demonstrate the value of forgone benefits or the consequences that arise when a technology is given up when another technology is chosen (the **opportunity cost** of a technology)

(30). In economic evaluations, a certain health technology of interest for example a new hypertension medicine, is compared to relevant alternatives, such as currently prescribed hypertension medicines, to assess the difference in costs and consequences of selecting the new hypertension medicine. In some cases, not providing any treatment, "do nothing", can also be an important comparison.

The results of an economic evaluation inform judgements about the health technology's value for money, aid in priority setting, and optimise the use of existing available resources. In general, there are three different ways to collect economic evidence relevant to the technology being assessed:

- A (systematic) review of published economic evidence
- A critical review of an existing economic evaluation (e.g., evaluations submitted to relevant organisations to achieve market authorization for new technology) and where necessary an adaptation it to the local-setting, or
- Develop a new (*de novo*) economic evaluation (21).

Many checklists are available to assess the quality of economic studies when undertaking a review the quality of economic evidence (31). For modelling-based economic evaluations, checklists by Philips or Caro et al. are appropriate, and for trial-based economic evaluations BMJ Guidelines for economic submissions or the CHEC-extended tool could be considered (32, 33). The Welte checklist (34) is relevant when an economic evaluation is reviewed with the aim to transfer it to another setting (see Table 4 for references to these checklists).

De novo development of an economic evaluation may involve one of the following methods: cost effectiveness analysis, cost-minimization analysis, cost-effectiveness analysis, or cost-utility analysis. The difference between these types of evaluations is how the consequences of a technology are measured. In some circumstances a budget impact analysis (BIA) may be most appropriate. A BIA differs from an economic evaluation as it only compares the financial impact of a (new) health technology to relevant alternatives, and health consequences are not considered. BIA estimates the financial cost-consequences from the perspective of the payer and for a short timeline which is relevant to the payer, but often does not consider the technology's benefits to the patient.

Ethical, Organisational and Legal aspects

Ethical analysis

Ethical analysis aims to provide an understanding of norms and values for consideration in the HTA and in the decision-making process. Ethical analysis involves an understanding of the consequences of implementing or not implementing a health technology. The analysis considers the norms and societal values when the technology is put into use. The most cited values in HTA are fairness and equity. However gaps have been identified in the implementation of ethical analysis, such as the lack of shared standard models for ethical analysis and obstacles to its integration into the HTA process (35).

The EUnetHTA Core Model® provides guidance on when to consider integrating ethical analysis into an HTA (36, 37). Ethical considerations may be reflected in other domains of an HTA, during the planning of the HTA and in the deliberation stage of the HTA process. If the ethical analysis is informed by newly commissioned research, that research should follow a protocol ensuring the use of predefined approaches which are relevant to the technology being assessed and informed by the

needs of the HTA decision maker and the public. If *de novo* research is required, experts and stakeholders should be consulted or involved in choosing the methodology, conducting the research, and reviewing the research.

Organisational Aspects

Organisational analysis includes assessing the ways in which different kinds of resources need to be mobilised and organised when implementing a technology, and the consequences of implementing that technology, for example, to an organisation or the health care system. Relevant issues include the impact of a new technology on work processes and patient/participant flow, quality of service delivery, and sustainability within the specific setting, considerations of centralised services, how the technology will be disseminated, any changes to managerial structures, and how staff and patient acceptance of a technology will be achieved. Organisational consequences may be reflected in other domains of the HTA and the discussion section of the final HTA product. Relevant questions for consideration are listed in the EUnetHTA Core model® (21). The choice of methods to use to answer the questions that arise for this domain will be informed by the information needs of HTA decision makers and policymakers. As with ethical analysis, experts and stakeholders should be consulted or involved in choosing the methodology, conducting the research, and reviewing the research.

Legal aspects

In many jurisdictions, rules, and regulations have been established to protect the patients' rights and society's interests. These rules and regulations may form part of patients' rights legislation, data protection legislation, health care personnel's provisions, or the general rights and duties of citizens. Market access authorisation for new health care technologies or technology regulation processes may also influence the HTA process. The EUnetHTA Core Model® provides some relevant questions around legal aspects to consider when planning an HTA (21). When extensive analysis of legal aspects is requested by the HTA decision makers and policymakers, legal expertise will be required. Initial guidance can be found in WHO's *How to guide on Institutionalising HTA mechanisms* (14).

Patient and Public Engagement in HTA

The field of public and patient engagement in health care research and policymaking has grown in the last decades. Its roots can be traced back much further, and to numerous contributing disciplines and fields, but over the last decade it has witnessed unprecedented attention as societies seek a more transformative role for patients in health research and health systems and policy decision making (38). Best practice for HTA is to include mechanisms for public and patient engagement throughout the whole HTA process.

"Public and patient engagement" in HTA can be understood as:

- The incorporation of the views and perspectives of those who use or are affected by technologies into the assessment of those technologies. In HTA, public and patient engagement can take many forms, including inviting patients to join expert panels, to provide evidence mediated by an interviewer or survey, or to provide written submissions about the technology or condition being considered (39).
- Incorporating patients' perspectives within the HTA by conducting syntheses of literature on patients' experiences, opinions, and beliefs.

How to include patients and the public in the HTA process has been much debated. An article by Thompson et al (40) suggest five distinct levels of patient involvement in consultations (see Table 2). These five levels progress from simple requests for patients and the public to have more information to patients and the public having the ability to share or control decisions about health care, whilst acknowledging that some patients in some contexts would prefer not to be involved at all.

Table 2: Thompson's levels of patient involvement (40)

Patient-Desired level	Patient-determined	Patient and professional co-determination (Participation)	Professional-Determined
4	Autonomous decision-making		Decision-making informed by patient input
3		Shared decision-making	Professional-as-agent
2	Information-giving	Dialogue	Consultation
1	Information-seeking/ receiving relevant information		Information-giving
0	Non-involved		Exclusion (acting without patient input)

Colour added by authors to denote where the ideal level of engagement should occur.

It is important to consider carefully how to 'meaningfully' engage patients and to ensure that the approaches used will add value to the HTA process and to the stakeholders. Planning patient and public engagement in the HTA process can be informed by a growing number of systematic reviews, conceptual frameworks, surveys of the field, stakeholders' perspectives, and case studies (41-44). For a list of resources for patient and public engagement, see Table 4.

Writing the HTA report

The structure of the HTA report should be based on the structure to reflect the protocol used to initiate the Analysis (see Protocol development and project planning). The results of an HTA analysis can be presented and packaged in several ways, and the chosen structure will depend on what aspects the HTA commissioners have requested. Important considerations which will influence the type and name of the HTA end-product are:

- How many technologies were included for assessment?
    - Single technology assessment
    - Multiple technology assessment
- What domains of the HTA were included?
    - Clinical effectiveness and safety, health economics, patients, and public involvement, ethical, organisational, or Legal.
- How much time was allocated to the assessment?

The name and structure of the final HTA product will depend on the factors outlined above. In Table 3 we have described commonly used or referred to HTA end products. However, HTA products name and structure can vary according to HTA agencies organisation, culture, and mandate. In this guidance document we have used common terms known across several HTA bodies.

Table 3: Types of HTA products

Type	Definition
Full HTA Report	The most comprehensive format and it includes some or all the following domains on the current use of the health technology, its characteristics, its safety and clinical effectiveness, its cost effectiveness, and budget impact. It always uses a comprehensive and systematic search of the literature and appraises quality of the evidence. It may also include information on organisational, social, or patient, ethical, and legal domains.
Rapid review	A report that usually includes a review of the highest level of evidence on effectiveness and safety or of recent evidence and that may restrict the literature to one or two databases (http://htaglossary.net/rapid-review). Optionally it appraises quality of evidence and provides information on cost.
Rapid Relative Effectiveness Assessments (REA)	Product from EUnetHTA core model, includes domains on current use of the health technology, its characteristics, its safety, and clinical effectiveness. It may use a rapid review (see above) or more comprehensive searches.
National Appraisal	Produced from EUnetHTA core model, includes domains on cost effectiveness, budget impact, organisational, social, or patient, ethical, and legal domains.
Mini-HTA or hospital-based HTA	Mini-HTA includes a rapid review (see above) with an appraisal of the quality of the evidence and provides information on cost. It may include organisational issues.

Information in table 3 adapted from INAHTA Product Type Classification (here) and EUnetHTA Core Model (here)

Adaptation of published HTAs

Producing HTAs requires time and resources, scientific expertise, and political commitment, however, but these are not always available in all settings. Additionally, there is an opportunity cost associated with conducting HTAs, especially in countries where HTA processes may be less institutionalised and resources for HTA are limited. Transferring and adapting published HTAs from one setting to another could enable more efficient production of HTAs in the countries with limited resources, while also reducing duplication of efforts.

Most HTA transfer approaches reflect the traditional HTA process but include some additional steps. For example, after selecting a "to-be-transferred" HTA, its applicability to the new decision context should be checked, using guidance such as Grutters checklist (45). If the technology is not applicable, to the new context, a transfer process is irrelevant and a de novo HTA process should be initiated. Other additional steps involve assessing the quality and transferability of the selected HTA(s), as well as steps to identify factors affecting transferability and replacing identified important contextual issues, where possible, with information relevant to the new decision context. Currently there is no checklist that covers all HTA domains, but the most comprehensive checklist available is the EUnetHTA Adaptation toolkit (Table 4).

Although these adaptive HTA approaches might seem simpler, the effort required to achieve them should not be discounted. A transparent process should still be followed, and it requires critical appraisal skills to assess quality, bias, and transferability of various types of evidence, as well to as to understand and be able to explain any new uncertainties identified during the process (31). Relevant tools for adapting HTAs are listed in Table 4.

VI Step 3: Appraisal and decision-making

The purpose of HTA is to inform decision-making, therefore the decision-making process should be integrated into the whole HTA process. This should include the initial decision about the topic of the HTA, the scope of the HTA question and then how the HTA will be appraised and inform decision making. It is important that there is a clear linkage between the final HTA product and the decision-making process, and a range of tools are available to support this. This stage of the process may be organised in different ways in different countries

There are several tools that can help this process (see Table 4 for a reference to a range of tools). The Evidence to Decision (EtD) framework appraises all the evidence in a structured and transparent way to inform decision in many different contexts (44). The GRADE interactive Evidence to Decision (iEtD) tool, co-created by NIPH with international partners, is also used worldwide.

Another relevant tool is INTEGRATE-HTA although its implementation in LMICs may need to be considered on an case by case basis as some of its conditions for HTA are not always fulfilled in LMICs (46). Oortwijn et al. have described the use of the INTEGRATE-HTA model. INTEGRATE-HTA is used to collect different types of evidence and engagement with various stakeholders who might be affected by the decisions (47). The steps include:

1. Involving stakeholders to elicit needs, topics, and outcomes
2. Gathering patients' preferences, and characteristics, and implementation issues, and taking context into account
3. Assessing the evidence available for the key domains (effectiveness, economic, ethical, sociocultural, and legal)
4. Integrating the evidence in a structured way to reflect the needs of the stakeholders
5. Feeding the evidence into the decision-making process to support the decision makers, by selecting an EtD tool to structure the decision makers' deliberations (in cooperation with the decision/appraisal committee).

VII Step 4: Policy Implementation

The implementation of a health policy (informed by the findings of an HTA) includes a series of activities and processes when governments and other actors attempt to translate the intention of the policy into concrete action and outcomes. Such outcomes can include designing and launching procedures, guidance on the procedures, and then transferring human and financial resources to enable the implementation of the new technology. In the case of HTA, it would usually mean acting on the recommendation or decision from an HTA committee, for example, to introduce of a new medicine, or new public health programme. For an HTA system, the methods of implementation are context-specific, and may vary substantially depending on the structure and role of HTA committee(s), the mandate of such committees, and the organisation of the decision-making processes. Usually there will be an executive role, mandated to act on the recommendation. To implement the decision, statutory or regulatory requirements can often be necessary. These could include setting up administrative, regulatory, and other supportive structures (48-50).

The tools that support with decision-making processes also enable implementation. The GRADE interactive Evidence to Decision Framework is also relevant here. For example, in addition to

supporting decision-making, the framework is also relevant for policy implementation, such as coverage decisions, or health system or public health recommendations and decisions (51).

Ideally, it is best practice to evaluate new technologies following their implementation. The Context Implementation of Complex Interventions (CICI) framework one tool that decision makers could use to evaluate the implementation of a new technology (52).

VIII Resources

Table 4: List of selected relevant resources

This table provides a quick reference to selected resources when considering each stage of the HTA process. The list is based on tools used by the NIPH-GH members, as well as other useful tools known to the NIPH-GH. No systematic searches were conducted to do make this list. This is not an exhaustive list.

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implementation	Adaptation
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
Assasi N, Tarride J-E, O'Reilly D, Schwartz L.	2016	Steps toward improving ethical evaluation in health technology assessment: A proposed framework.				*					
Canada's Drug and Health Technology Assessment Agency (CADTH)	2022	CADTH Framework for Patient Engagement in Health Technology Assessment https://www.cadth.ca/cadth-framework-patient-engagement-health-technology-assessment					*				
Caro JJ, Eddy DM, Kan H, Kaltz C, Patel B, Eldessouki R, et al.	2014	Questionnaire to assess relevance and credibility of modelling studies for informing health care decision making: an ISPOR-AMCP-NPC Good Practice Task Force report.			*						

[5] PPE: Patient and Public Engagement

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implementation	Adaptation
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
		https://doi.org/10.1016/j.jval.2014.01.003									
Cochrane	2022	Cochrane Handbook https://training.cochrane.org/handbook		*	*	*	*	*	*		
COMET	2022	Core Outcome Measures in effectiveness trials https://www.comet-initiative.org/		*			*				
CONSORT PRO		http://www.consort-statement.org/extensions?ContentWidgetId=560		*	*						
Danish National Board of Health	2007	Health Technology Assessment Handbook https://www.sst.dk/~/media/ECAAC5AA1D6943BEAC96907E03023E22.ashx		*	*	*	*	*			
Dimairo, M., Pallmann, P., Wason, J. et al.	2020	The adaptive designs CONSORT extension (ACE) statement: a checklist/guideline for reporting randomised trials with adaptive design. https://doi.org/10.1186/s13063-020-04334-x		*				*			*

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implementation	Adaptation
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
Drummond MF, Jefferson T	1996	Guidelines for authors and peer reviewers of economic submissions to the BMJ. https://www.jstor.org/stable/29732468			*						
European network of health technology assessment (EUnetHTA)	Varies by year	EUnetHTA tools https://eunethta.eu/tools/		*	*	*	*				*
EUnetHTA	2016	The EUnetHTA Core Model® https://www.eunethta.eu/wp-content/uploads/2018/01/HTACoreModel3.0.pdf?x50316		*	*	*	*	*			
EUnetHTA Guegan, Milne, Pordage, et al.	2011	EUnetHTA Adaptation Toolkit https://www.eunethta.eu/wp-content/uploads/2011/01/EUnetHTA_adptation_toolkit_2011_version_5.pdf									*
Evers, Goossens, De Vet, Van Tulder, Ament.	2005	Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. https://research.vumc.nl/en/publications/criteria-list-for-			*						

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implement ation	Adaptat ion
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
		assessment-of-methodological-quality-of-economi									
Thielen, Van Mastrigt, Burgers, et al.	2016	How to prepare a systematic review of economic evaluations for informing evidence-based healthcare decisions: data extraction, risk of bias, and transferability - Focus on searches (part 2/3). https://www.tandfonline.com/doi/full/10.1080/14737167.2016.1246961?src=recsys		*	*						
GRADE	2000	GRADE: Grading of Recommendations, Assessment, Development and Evaluations https://www.gradeworkinggroup.org/		*							
GRADE	2022	Interactive Evidence to Decision framework (iEtD) tool https://ietd.epistemonikos.org/	*					*	*	*	
Heupink LF, Peacocke EF, Sæterdal I, Chola L and Frønsdal K.	2022	Considerations for transferability of health technology assessments: a scoping review of tools, methods, and practices.									*

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implement ation	Adaptat ion
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
		doi:10.1017/S02664623220032 1X									
James Lind Alliance	2022	James Lind Alliance https://www.jla.nihr.ac.uk		*							
ISPOR	2013	Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement, BMJ, 2013 https://doi.org/10.1136/bmj.f1 049			*						
ISPOR	2007	Principles of Good Practice for Budget Impact Analysis I https://www.ispor.org/heor-resources/good-practices/article/principles-of-good-practice-for-budget-impact-analysis			*						
ISPOR	2022	Published Pharmacoeconomic (PE) Recommendations, PE Guidelines, and Submission Guidelines from countries across the globe https://www.ispor.org/heor-resources/more-heor-resources/pharmacoeconomic-guidelines			*						*

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implement ation	Adaptat ion
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
Mauskopf JA, Sullivan SD, Annemans L, et al.	2007	Principles of good practice for budget impact analysis: report of the ISPOR Task Force on Good Research Practices—Budget Impact Analysis. https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1524-4733.2007.00187.x			* **Budget Impact Analysis**						
Munthe-Kaas, H., Nøkleby, H., Lewin, S. et al.	2020	The TRANSFER Approach for assessing the transferability of systematic review findings. https://doi.org/10.1186/s12874-019-0834-5		*							*
NICE Public Involvement	2022	https://www.nice.org.uk/about/nice-communities/nice-and-the-public/public-involvement					*				
Norwegian Institute of Public Health		Template for prioritisation from the Norwegian Early Awareness alerts can be found here: https://nyemetoder.no/en	*								
Norwegian Medicines Agency (NoMA) [Statens legemiddel-verk]	2018	Guidelines for the submission of documentation for single technology assessment (STA) of pharmaceuticals https://legemiddelverket.no/Documents/English/Public%20funding%20and%20pricing/Docum			*						

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implementation	Adaptation
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
		entation%20for%20STA/Guidelines%2020.05.2020.pdf									
Oortwijn W, Jansen M, & Baltussen R.	2021	Evidence-informed deliberative Processes: A practical guide for HTA bodies for legitimate benefit package design	*						*	*	
Philips Z, Bojke L, Sculpher M, Claxton K, Golder S.	2006	Good practice guidelines for decision-analytic modelling in health technology assessment. https://link.springer.com/article/10.2165/00019053-200624040-00006			*						
Rehfuess EA, Stratil JM, Scheel IB, Portela A, Norris SL, Baltussen R	2019	The WHO-INTEGRATE evidence to decision framework version 1.0: integrating WHO norms and values and a complexity perspective							*		
Sullivan SD, Mauskopf JA, Augustovski F, et al.	2014	Principles of good practice for budget impact analysis II: report of the ISPOR Task Force on Good Research Practices – Budget Impact Analysis. https://www.sciencedirect.com/science/article/pii/S1098301513042356			* **Budget Impact Analysis**						

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implement ation	Adaptat ion
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
SuRe Info		Summarized Research in Information Retrieval for HTA (SuRe Info) https://sites.google.com/york.ac.uk/sureinfo/home		*	*	*					
Swedish HTA agency		Assessment of Methods in Health Care: A Handbook https://www.sbu.se/contentassets/76adf07e270c48efaf67e3b560b7c59c/eng_metodboken.pdf		*	*	*	*	*	*		
Welte R, Feenstra T, Jager H, Leidl R.	2004	A decision chart for assessing and improving the transferability of economic evaluation results between countries.			*						
WHO	2014	Compendium of innovative health technologies for low-resource settings: assistive devices, eHealth solutions, medical devices https://apps.who.int/iris/handle/10665/108781	*								
WHO	2021	WHO lists of essential health technologies is a continuously revised and updated list of essential and prequalified health technologies	*								

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implement ation	Adaptat ion
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
		https://www.who.int/teams/health-product-policy-and-standards/assistive-and-medical-technology									
WHO	2021	Institutionalizing health technology assessment mechanisms: a how to guide https://apps.who.int/iris/handle/10665/340722								*	
WHO	2022	Health Systems Governance and Financing group of WHO, publishes relevant tools and guidance for HTA (especially economic evaluation), such as WHO Choice, OneHealth tool, etc. https://www.who.int/teams/health-systems-governance-and-financing/economic-analysis			*				*	*	
Wijnen B, Van Mastrigt G, Redekop W, Majoie H, et al.	2016	How to prepare a systematic review of economic evaluations for informing evidence-based healthcare decisions: data extraction, risk of bias, and transferability - Focus on transferability (part			*						*

Author	Year	Title, Link	TISP	HTA analysis					Appraisal & decision making	Implementation	Adaptation
				CE & safety	Economic analysis	Ethical, legal, organisational	PPE[5]	Writing the report			
		3/3). https://www.tandfonline.com/doi/pdf/10.1080/14737167.2016.1246961									

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