PHILIPPINE HTA METHODS GUIDE

CLINICAL EQUIPMENT AND DEVICES

Health Technology Assessment (HTA) Philippines
Department of Science and Technology
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Philippine HTA Methods Guide for Clinical Equipment and Devices (CED)

Contents

Chapter 1: Background

1.1. The differences between Health Technology Assessment (HTA) for Clinical Equipment and Devices (CED) and regular HTA

Health technology assessment (HTA) is defined under the *RA 11223 or the UHC Act* as a systematic evaluation of properties, effects, or impact of health-related technologies, devices, medicines, vaccines, procedures, and all other health-related systems developed to solve a health problem and improve the quality of life and health outcomes, utilizing a multidisciplinary process to evaluate the clinical, economic, organizational, social, and ethical issues of a health intervention or health technology.

HTA aims to provide evidence-based information to inform decision-making regarding the use, coverage, and reimbursement of health technologies, including clinical equipment and devices (CED) and drugs, within healthcare systems. While HTA for CEDs and drugs share common principles, there are some important differences in their evaluation processes due to the unique characteristics of each. The differences will be listed in chapter 2.2.

1.2. The general process of HTA in the Philippines

Figure 1 outlines the general process of conducting an HTA in the Philippines. The **Philippine HTA Methods Guide** (Philippine HTA Methods Guide | HTA. (2020). From https://hta.doh.gov.ph/philippine-hta-methods-guide/) is a vital document that aims to provide mandatory guidance to researchers in conducting HTA. Specifically, it endeavors to provide broad guidelines in the conduct of HTA and its domains in assessing the clinical, economic, ethical, legal, social and health systems implications of a specific health technology and, the production of standard HTA reports for healthcare decision makers and other target audiences in the health system.

Philippine HTA Methods Guide for Clinical Equipment and Devices (CED) complements the main methods guide, adjusting where appropriate when characteristics specific to CEDs entail changes in the HTA process.

Also available is the **Philippine HTA Process Guide** (Philippine HTA Process Guide | HTA. (2020). https://hta.doh.gov.ph/philippine-hta-process-guide/) which is a reference document detailing the general steps employed in HTA which aims to provide structure, transparency and clarity in the processes. It also serves as a guide for stakeholders in terms of their roles and participation in the processes.

*Figure SEQ Figure * ARABIC 1 General process of conducting HTA in the Philippines Note: Step "Protocol Development" and "Evidence appraisal and preliminary recommendation" are where main differences can be found in the process of conducting HTA for CEDs and for other health technologies.*

1.3. The purpose of this Guide

The HTA Methods Guide for CED aims to provide mandatory guidance to researchers (both internal and external assessors) in conducting HTA for CEDs based on the prioritized topics (mainly

Assessment stage as illustrated in the HTA process flow above) and producing a standardized HTA report that will be used to inform all public funding, coverage, and resource reallocation/optimization decisions made by the DOH and PhilHealth.

This methods guide is a complementary document to the Philippine HTA Methods Guide (also referred to as the main HTA methods guide) focusing on the steps where either methods or processes are different from the main HTA guidance. Users are encouraged to use both documents together as the HTA for CED guide will refer back to the main methods guide when appropriate.

There are four main laws and national policies that serve as the legal basis for using HTA as a tool for evidence-based decision making on the funding and use of health technologies in the Philippine healthcare system. [1] These are the following:

- National Health Insurance Act of 2013 (RA 10606);
- New Implementing Guidelines of the Philippine National Formulary System (Administrative Order 2016-0034);
- Framework for the Use of HTA to Guide Coverage Decisions in Support of UHC (Administrative Order 2018-0026); and
- Universal Health Care Act (RA 11223).[2]

1.4. The scope of this Guide

HTA aims to produce recommendations for healthcare decision makers on the use of CEDs. For the purpose of this document, CEDs include medical devices, radiation devices, and health-related devices, which are defined as follows in the Department of Health's Administrative Order No. 2020-0041:[3]

a. **Medical device** — refers to any instrument, apparatus, implement, machine, appliance, implant, in-vitro reagent or calibrator, software, material, or other similar or related article intended by the manufacturer to be used alone, or in combination, for human beings for one or more of specific purpose(s) of:
   - diagnosis, prevention, monitoring, treatment or alleviation of disease;
   - diagnosis, monitoring, treatment, alleviation of, or compensation for an injury;
   - investigation, replacement, modification, or support of the anatomy control of conception;
   - disinfection of medical devices; and
   - providing information for medical or diagnostic purposes by means of in-vitro examination of specimens derived from the human body.

[1] See Section 1.3 in the Philippine HTA Methods Guide for more details on the legal and policy framework of HTA in the Philippines.
[2] See Section 1.3 in the Philippine HTA Methods Guide for more details on the legal and policy framework of HTA in the Philippines.
[3] AO 2020-0041: The New Implementing Guidelines on Health Technology Assessment to Guide Funding Allocation and Coverage Decisions in support of Universal Health Care.

This device does not achieve its primary intended action in or on the human body by pharmacological, immunological, or metabolic means but which may be assisted in its intended function by such means.

b. **Radiation device** — refers to an electrical or electronic apparatus emitting any ionizing or non-ionizing electromagnetic or particulate radiation; or any sonic, infrasonic, or ultrasonic wave. It includes ionizing radiation emitting equipment which is not intentionally designed to produce radioactive materials.
c. **Health-related device** — refers to any device not used in health care but has been determined by the FDA to adversely affect the health of the people.

Currently, policy documents in the Philippines regarding medical devices with software do not specify machine learning (ML) technology or artificial intelligence (AI). The classification of a software with ML or AI technology as a CED should be based on its intended use aligning with the definition outlined in DOH AO No. 2020-0041 (definition above). Software that supports administrative work of a health care institution or intended for exercise, leisure activities do not qualify as CED. See Annex 1 for background on ML or AI-based medical devices, including examples of what would and would not classify as one.

Throughout this document, call out boxes such as this will provide additional information or guidance when evaluating this type of technology. See Section 1.7 on how this will be updated in later versions of the CED guide.

1.5. The target audience of this Guide

The target audience of this document are researchers aiming to produce an HTA report for CEDs, whether they are internal or external assessment groups. This also serves as a guide to the HTA Council and decision-makers on the methodological standards that are required in HTA for CEDs to inform their recommendations.

Nonetheless, since HTA implementation has to align itself with various processes involving existing policies and programs within the DOH and PhilHealth which covers, implements and monitors the delivery of various CEDs, the target audience of the HTA report itself would include not only the HTA Council, internal and external assessors, and major healthcare decision makers, but also the following key stakeholders:

- Department of Health (DOH) offices and national health programs
- Philippine Health Insurance Corporation (PhilHealth)
- Professional medical, paramedical, and scientific organizations
- Healthcare organizations/marketing authorization holders
- Government-recognized (with SEC registration) patient or civil society organizations (CSOs)
- Healthcare facilities and institutions
- Local Government Units (LGUs)

- Academic or research institutions
- Primary Health Care Units under the Universal Health Care Law

1.6. The process of development of this Guide

This document draws from the Philippine HTA Methods Guide (First Edition, 2020) that provides guidance on the conduct of HTA for medicines; vaccines; medical and surgical procedures; screening procedures; screening procedures and diagnostics; promotive and preventive health interventions; traditional and complementary medicines; and other health interventions and technologies. This document serves as a complementary document to the 2020 HTA Methods Guide, focusing on CEDs given the differences between CEDs and other health technologies, as laid out in Section 1.1.2.

The work proceeded as follows:

- Review of literature based on publicly available literature from publication databases and resources from major HTA agencies and HTA Networks that have additional guidance on CEDs (EUnetHTA, NICE, HAS, ACE, and MSAC);
- Review of local HTA and HTA-related reports on CEDs to identify methodological weaknesses or variations and address them in this document;
- Review of Philippine HTA Methods Guide to identify required updates given the characteristic differences between CEDs and other health technologies, particularly, pharmaceuticals;
- Consultation with fourteen Philippine-based experts from the industry and academia to review the draft outline of the document.

1.7. Updates to this Guide

This is the official first edition of the HTA methods guide for CEDs in the Philippines, to be used together with the main **Philippine HTA Methods Guide** (Philippine HTA Methods Guide | HTA. (2020). From https://hta.doh.gov.ph/philippine-hta-methods-guide/). A review of this document shall be done on a regular basis to draw on advances in HTA methodologies, specifically for CEDs, continuously improve based on past experience, and adapt to the dynamic nature of the Philippine healthcare context.

Updates should be considered as the global discussion around climate and health evolves and considerations surrounding green CEDs need to be accounted for in the HTA process. While Chapter 3 of this guide provides some soft guidance around assessing the environmental impact of a CED, set guidance on how to incorporate the environmental impact in HTA has not been widely established. Annex 2 provides additional details on some of the approaches taken by studies to account for the environmental aspects of health technologies.

Further, additional updates may be required as certain types of CEDs become more prevalent, particularly those that have advanced software technologies (e.g., utilizing artificial intelligence). Throughout this document, additional guidance is highlighted in boxes for medical devices that use

artificial intelligence. It will be valuable to have a separate complementary document to this CED guide that focuses on AI-based technology given its additional features when (1) local regulations in the Philippines evolve, including defining what would qualify as AI-based medical devices; and (2) the global discourse around guidance surrounding this type of technology nears consensus. See Annex 1 for additional background on this type of technology.

The review shall be rigorous, transparent, and consultative.

Chapter 2: Methodological Standards in Evaluation for CED

2.1. How other countries conduct HTA for CED

The practices for HTA of CEDs vary across countries. Each country incorporates specific entities, procedures, and evaluative criteria to assess the clinical effectiveness, safety, and cost-effectiveness of CEDs. This section summarizes the HTA practices from other countries with additional guidance on CEDs.

The European Network for Health Technology Assessment (EUnetHTA) was created in 2006 to support HTA in **Europe**. This collaborative network, comprising over 80 organizations from 31 European nations, facilitates policymaking and information exchange to optimize resource use (EUnetHTa, accessed 2023). A key output of EUnetHTA is the HTA Core Model, a comprehensive guide for evaluating health technologies encompassing domains like safety, clinical effectiveness, economic evaluation, ethical considerations, and legal aspects. The model, designed for use in full HTA, rapid assessments, and mini-HTA, includes several components such as an HTA Ontology, Methodological Guidance, a Common Reporting Structure, Synthesis Methods, and guidelines for Reporting and Interpreting (EUnetHTa, 2016). The EUnetHTA employs the Therapeutic Medical Device guideline alongside The HTA Core Model as a supplementary tool. The primary aim of this guideline is to acknowledge the unique difficulties that HTA methods encounter when evaluating therapeutic/medical devices and provide practical solutions to overcome these challenges (EUnetHTa, 2016).

The National Institute for Health and Care Excellence (NICE) operates the Medical Technologies Evaluation Programme (MTEP) in the **United Kingdom**. MTEP evaluates the clinical effectiveness, safety, and cost-effectiveness of medical devices (NICE, accessed 2023). The program subsequently generates the Medical Technologies Guidance to inform healthcare decisions from clinical practice to procurement. Key to these recommendations are extensive clinical and economic evidence evaluations, consultation with stakeholders, and a review by the National Health Service (NHS) and other funding bodies (NICE, 2017).

The National Authority for Health (HAS) coordinates the evaluation of health products in **France** (HAS, 2019a). One sub-entity involved is the Medical Device and Health Technology Evaluation Committee (CNEDiMTS). When evaluating a medical device, CNEDiMTS assesses its projected use, actual clinical benefit (ACB), and clinical added value (CAV) based on the application dossier submitted by the manufacturer or distributor (HAS, 2019b). The CAV is ranked from major (I) to absent (V) after comparing it with similar products, services, or procedures. If CNEDiMTS delivers a favorable opinion, the medical device's reimbursement tariff is negotiated between the Committee for the Pricing of Healthcare Products (CEPS) and the manufacturer or distributor. The Minister of Health then decides whether to include the device on the List of Products and Services Qualifying for Reimbursement (LPPR). The device's CAV level influences the tariff determination. Devices with CAV of I to III undergo a cost-benefit assessment by the Economic and Public Health Evaluation Committee (CEESP). However, low-cost procedures or public patents do not require an economic evaluation. When evaluating the device, CEESP considers therapeutic alternatives, cost-to-benefit ratios, and quality of life. CEESP ensures scientific validity, methodological integrity, and ethical quality of economic assessment and public health action evaluation (HAS, 2017).

Italy's Ministry of Health spearheaded the creation of the National Program for Health Technology Assessment of Medical Devices (PNHTADM), a program designed to centralize the HTA process for medical devices (Tarricone, et.al., 2021). The program's development involved extensive consultation with stakeholders, expert panels, literature reviews, and case studies. The process was underpinned by transparency, inclusiveness, and comprehensiveness, ensuring access to innovative technologies while accommodating Italy's decentralized healthcare system (Tarricone, et.al., 2021). Although the PNHTADM is still an orphan program, it stands out from other international HTA programs due to its unique characteristics. The methodology, governance, and entire process have been specially designed for medical devices without the involvement of pharmaceutical companies. The PNHTADM is based on a thorough examination of the latest methodological approaches developed by international organizations and consortia in the field of HTA for medical devices.

Australia requires the Medical Services Advisory Committee (MSAC) to evaluate new medical technologies/devices for inclusion in the Medicare Benefits Schedule (MBS) (Australian Government Department of Health and Aged Care, 2020). This entails the submission of comprehensive clinical and economic evidence. Co-dependent health technologies and hybrid technologies are collectively assessed by MSAC and either the Pharmaceutical Benefits Advisory Committee (PBAC) or the Prostheses List Advisory Committee. Applicants seeking co-dependent application approvals are advised to lodge their applications with both committees concurrently (Australian Government Department of Health and Aged Care, 2017).

South Korea's HTA system led to the formation of the National Evidence-based Healthcare Collaborating Agency (NECA) (NECA, accessed 2023). In association with the Health Insurance Review & Assessment Service (HIRA), NECA examines the cost-effectiveness and affordability of medical technologies (The International Network of Agencies for Health Technology Assessment, 2019). The New Health Technology Assessment (nHTA) determines whether a new medical procedure, excluding drugs, should be included in the service list (NECA, 2017). The Ministry of Health and Welfare (MoHW) oversees the nHTA system.

The Center for Drug Evaluation (CDE) in **Taiwan** conducts clinical and economic evaluations of new medical devices and drugs (CDE, accessed 2023a). These assessments aid the National Health Insurance Association make informed reimbursement and pricing decisions (CDE, accessed 2023b). Notably, the HTA process in Taiwan is not universally applicable to all Medical Devices and Diagnostics (MDD) (CDE, accessed 2023b). Instead, it is primarily required for new devices introducing novel functionalities or superior clinical effectiveness and those with a budget impact exceeding 30 million TWD[4] annually (CDE, accessed 2023a).

Singapore's Agency for Care Effectiveness (ACE) was established to assess clinical care effectiveness and cost-effectiveness (ACE, 2018). ACE undertakes HTAs to determine subsidies for two main technology areas: drugs and medical technologies/devices. ACE has distinct guidelines for drugs and medical technologies. ACE conducts full and expedited evaluations depending on the comparative outcomes and local economic studies (ACE, 2018).

[4] Approximately US$ 960,000 (based on 2023 exchange rate).

Overall, each country's approach to HTA for medical devices aims to ensure the delivery of safe, effective, and economically viable CED while managing resource allocation within healthcare systems.

Country	Evaluation Entity	Approach	Stakeholder Involvement	Patient Involvement in HTA process	Typical HTA Timeline	Key Characteristics
European network of countries[5]	EUnetHTA (HTA Core Model)	Comprehensive set of domains including safety, clinical effectiveness, economic evaluation, ethical analysis, legal aspects	Yes	Yes	Timelines are project-specific and can vary widely	• The information is standardized and shared across European countries to promote consistency and reduce duplication. • The HTA Core Model provides a detailed description of the technology and the comparator(s).
UK	Medical Technologies Evaluation Programme (MTEP) under the National Institute for Health and Care Excellence (NICE)	Clinical efficacy, safety, cost-effectiveness	Yes	Yes	38 weeks (about 8 and a half months) for the full MTEP	• The primary focus is on groundbreaking medical devices and diagnostic tools.
France	Medical Device and Health Technology Evaluation Committee	Medical and economic perspective, clinical benefits, added value	Yes	Yes	Approximately 30 weeks (about 7.5 months)	• There is an evaluation process for CE-marked devices to determine reimbursement.

[5] Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Spain, Sweden, Switzerland, Ukraine and United Kingdom

Country	Evaluation Entity	Approach	Stakeholder Involvement	Patient Involvement in HTA process	Typical HTA Timeline	Key Characteristics
	(CNEDiMTS) under the National Authority for Health (HAS)					
Italy	National Program for Health Technology Assessment of Medical Devices	Standardized proposal & review, clinical and cost-effectiveness, and social equity considerations	Yes	Yes	Timelines for different projects can vary.	• The design is tailored exclusively for medical devices without any involvement from pharmaceutical companies.
Australia	Medical Services Advisory Committee (MSAC)	Extensive clinical and economic evidence submission	Yes	Yes	MSAC process duration varies based on suitability and pathway used.	• The MSAC process considers co-dependent technologies, emphasizing situations where one health technology's efficacy is enhanced by another.
South Korea	National Evidence-based Healthcare Collaborating Agency (NECA); Health Insurance Review & Assessment Service (HIRA)	Clinical safety/ effectiveness evaluation, cost-effectiveness and affordability	Yes	Unclear	40 weeks (about 9 months) from the date of application receipt	• The "Parallel Program" for the medical approval process expedites new technology entry into clinical environments.

Country	Evaluation Entity	Approach	Stakeholder Involvement	Patient Involvement in HTA process	Typical HTA Timeline	Key Characteristics
Taiwan	Center for Drug Evaluation (CDE)	Clinical Effectiveness and economic assessment	Yes	Yes	The assessment report usually is completed within 42 days (about 1 and a half months) and submitted to the NIHA to aid in the NHI reimbursement decisions.	• HTA is only conducted for new devices that have a substantial impact on the budget.
Singapore	Agency for Care Effectiveness (ACE), Medical Technology Advisory Committee (MTAC)	Clinical Effectiveness, cost-effectiveness, organizational feasibility	Yes	Unclear	Full evaluations take 6-9 months, but expedited ones take 3-4 months	• Along with clinical and economic evidence, organizational feasibility is also taken into account. • Technologies with an estimated annual budget impact of less than $2 million receive expedited evaluations without the need for modeling.

2.2. Methodological differences in conducting HTA for CED

Conducting HTA for CEDs is challenging. This complexity arises from the distinct characteristics of clinical equipment and devices, which differ significantly from pharmaceuticals, coupled with the rapid pace of innovation within the medical device industry (EUnetHTA, 2015; Schnell-Inderst, et.al., 2015; Ming, et.al., 2022). While the standard HTA methodology can be applied to assess medical devices, it requires special considerations to accurately define, describe, and evaluate these interventions. The unique nature of medical devices, their life cycle, user dependency, and long-term effects and sustainability all contribute to the methodological differences in their HTA (EUnetHTA, 2015).

2.2.1 Complexity of the assessment

Medical devices are typically more complex than drugs. They can include a wide range of products such as diagnostic tools, surgical instruments, implantable devices, and medical equipment. Assessing the effectiveness, safety, and cost-effectiveness of medical devices often requires considering factors beyond clinical outcomes, such as the technical aspects of the device, operator expertise, training requirements, maintenance, and potential complications. For instance, CEDs undergo continuous improvement and incremental innovation, leading to various model specifications, requiring frequent updates to the assessment of its effectiveness. The operator's proficiency in using the device also impacts its effectiveness, a factor that is difficult to quantify. Finally, the use of CEDs is part of the clinical pathway in a patient's treatment and its direct impact on clinical outcomes are difficult to observe. This results not only in difficulty of quantifying clinical effectiveness but also in conducting economic evaluations.

2.2.2 Evidence requirements

The evidence needed to evaluate CEDs and drugs may differ. For drugs, randomized controlled trials (RCTs) are considered the gold standard for assessing efficacy and safety. However, RCTs may not always be feasible or appropriate for evaluating medical devices due to factors like the learning curve associated with device use[6], long-term effects, and small patient populations or a lack of an appropriate comparator. Other issues cited in studies conducting RCTs for CEDs include the difficulty in implementing double-blind procedures and the need for informed consent when the CED used involves an invasive procedure (e.g., implantable devices). Therefore, HTA for CEDs often relies on a broader range of evidence, including clinical studies, registries, real-world data, comparative studies, and expert opinions.

2.2.3 Regulatory pathways

The regulatory pathways for CEDs and drugs also differ. Drugs usually require approval from regulatory authorities, such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA), before they can be marketed. The approval process for CEDs may involve

[6] The learning curve refers to the period following the introduction or implementation of a CED where the healthcare professional receives training and acquires familiarity and proficiency with the CED. Over time, as the healthcare professional gains more experience, differences in how they handle the CED can affect the overall clinical benefits experienced by the patient.

conformity assessment procedures[7] that assess the safety and performance of the device (European Medicines Agency, accessed 2023). HTA for CEDs must consider the regulatory approval status as an additional factor in its evaluation. Please refer to the topic nomination and prioritization guidelines published by the HTA Philippines for the specifics on additional NRA requirements.

2.2.4 Market dynamics

CEDs and drugs operate in different market dynamics. The lifecycle of CEDs tends to be shorter than that of drugs, with frequent updates, modifications, and the introduction of new models or versions. This dynamic nature of medical devices requires HTA to consider the implications of rapid technological advancements and potential obsolescence. Because of these updates and modifications, pricing is typically also more dynamic than that of drugs, increasing the complexity of the economic evaluation (e.g., calculation of costs).

2.2.5. The life cycle, and rapid innovations

Medical devices exhibit a unique life cycle compared to pharmaceuticals (EUnetHTA, 2015; Schnell-Inderst, et.al., 2015; Ming, et.al., 2022). They are subject to rapid and iterative innovations, often evolving within 18 to 24 months. This fast pace of advancement leads to more incremental innovation rather than new breakthrough technologies. This rapid evolution presents a challenge for HTA, as the evidence base for a device can change significantly over a short period (EUnetHTA, 2015; Schnell-Inderst, et.al., 2015; Ming, et.al., 2022; Rummel, et.al., 2016). Patients may benefit over time from these changes, but these changes can also adversely affect efficacy and other endpoints, such as costs. Obtaining clinical evidence for medical devices can be difficult due to their short lifespan, usually shorter than the duration of clinical trials (Rummel, et.al., 2016). When conducting adaptive study designs, adjusting the sample size or randomization ratio is imperative as more data about the device's performance becomes available (EUnetHTA, 2015; Schnell, et.al., 2018). This can be accomplished using either frequentist or Bayesian approaches (EUnetHTA, 2015; Schnell, et.al.,2018). Bayesian methods are particularly crucial for analyzing MD trials, as they allow for considering prior information from earlier device versions (EUnetHTA, 2015).

2.2.6. User dependency

The operators' learning curve and incremental innovation often influence the effectiveness of medical devices (EUnetHTA, 2015; Schnell-Inderst, et.al., 2015; Ming, et.al., 2022; Rummel, et.al., 2016). The comparative efficacy between newly launched and traditional products is a function of the product and operators' proficiency, which is hard to quantify (EUnetHTA, 2015; Ming, et.al., 2022). The clinical adoption of medical devices may also be associated with a wider impact of organizational change (EUnetHTA, 2015; Rummel, et.al., 2016). For instance, there may be a need for additional training of physicians or other health professionals, or introducing a given device may

[7] The conformity assessment usually involves an audit of the manufacturer's quality system and, depending on the type of device, a review of technical documentation from the manufacturer on the safety and performance of the device.
https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices

require a hospital to reorganize services to accommodate the new technology (Rummel, et.al., 2016).

2.2.7 Reimbursement considerations

Reimbursement mechanisms for CEDs and drugs can vary. While drugs are typically included in pharmaceutical formularies or reimbursement lists, CEDs may have different reimbursement pathways. HTA for CEDs often evaluates the cost-effectiveness of the device in relation to its intended use and compares it with existing alternatives or standard care.[8] It may also assess the impact of the device on healthcare resource utilization and long-term costs.

2.2.8 Hospitalization phase

CED utilization may vary during pre- and post-operative care and potentially drive the used resources and incurred costs (Petcharapiruch, et.al., 2020). Assessing the value of CEDs should take into account these two phases to obtain comprehensive clinical and costs values. Additionally, clinical adoption may also impact organizational structures such as the need to conduct additional training for health professionals using the device, or reorganization of services to accommodate the new technology. These can lead to higher costs that should be accounted for in the economic evaluation of the HTA.

2.2.9. Long-term effects and sustainability

Long-term assessment of effectiveness and safety is another crucial aspect of evaluating medical devices (EUnetHTA, 2015; Rummel, et.al., 2016). Given the physical mode of action and the potential for long-lasting therapeutic effects, long-term registry data will often be needed (Schnell-Inderst, et.al., 2015). However, the availability of robust evidence, particularly from RCTs, may be limited at the early stages of technology assessment, leading to higher uncertainty for the decision maker (EUnetHTA, 2015; Schnell-Inderst, et.al., 2015; Ming, et.al., 2022; Rummel, et.al., 2016). Therefore, methods for integrating evidence of different designs, sources, and quality, such as cross-design meta-analysis with bias adjustment, are necessary (Schnell-Inderst, et.al., 2015). The long-term effects and sustainability of medical devices can be challenging to assess due to the scarcity of well-designed randomized controlled trials and the rapid innovation in the field. Real-world evidence (RWE) can provide insights into the long-term effects of medical devices in real-world settings, reflecting the actual impact of clinical interventions (see Box 1 for more on RWE) (Ming, et.al., 2022).

[8] Standard of care may frequently change for CEDs, particularly those with multiple specifications and models, due to rapid product iteration, making HTA more difficult. If no local specifications exist, regulatory specifications from World Health Organization, UNICEF, ISO, IEC or other reputable international institutions may serve as examples.

Box 1. Using real-world evidence for HTA

RWE is a vital component of healthcare data that originates from various sources, including electronic health records (EHR), electronic medical records (EMR), patient registries, hospital databases, and claims data. RWE is critical in post-marketing surveillance, enhancing outcome-based contracting, treatment compliance, and making coverage decisions more effective (Ming, et.al., 2022).

RWE is crucial in generating clinical effectiveness and safety data for medical devices. Given the scarcity of clinical research, RWE helps bridge the gap. Unlike RCTs, RWE studies are conducted in real-world clinical settings without pre-specified criteria to select patients. The patients enrolled in RWE studies represent various subgroups, making them more representative of the entire population (Ming, et.al., 2022). As such, RWE can provide more accurate results about the actual effects of clinical interventions. HTA based on RWE can offer insights that stem from real-world settings, making it an invaluable tool for healthcare decision-making.

2.3. Components of an HTA Report for CED

A standard HTA report for CED should consist of ten main sections:

I. Executive Summary
II. Health problem and clinical management options
III. Description, technical characteristics, and use of the health technologies
IV. Clinical effectiveness and safety
V. Economic evaluation
VI. Ethical analysis
VII. Legal aspects
VIII. Social aspects
IX. Health system impact
X. Relevant attachments (e.g. protocols, electronic copies)

Refer to the main HTA methods guide (section 2.2) for more details on each of the components of the HTA report. The project duration of assessment per stage is shown in Annex 3.

2.4. Defining the HTA Decision Problem for CED

Not all policy questions are answerable by HTA. **HTA questions, in our context, aim to respond to national-level service coverage or investment and optimization decisions** to ensure proper allocation of resources.

It attempts to answer the following questions:

- Does the technology work? Is it safe and effective for the clinical purpose or indication it is intended?
- Is there meaningful improvement in health status relative to its cost?
- Which patients or subgroups of the population benefit the most?
- Can the government through DOH and PhilHealth afford to pay for all people who might need the technology?

- What other considerations (e.g. ethical, legal, and social implications; environmental impact, health system impact) make this technology important in the local context?

Examples of policy questions answerable by HTA (CEDs):

Should the Department of Health use teleophthalmology-based diabetic retinopathy screening instead of human assessment in a national program?

Should PhilHealth cover the use of extracorporeal membrane oxygenation (ECMO) for patients with acute respiratory distress syndrome in COVID-19?

Examples of policy questions not directly answerable by HTA (CEDs):

What is the evidence related to the use of hearing aids for people with dementia?

Should DOH approve the conduct of a study to understand the role of heating technology in medical equipment?

After clarifying the policy questions, a focused HTA for CED research questions should be developed. This requires, at the minimum, specifying the target population (P), intervention (I), comparator (C), and relevant outcomes (O) to form the PICO question.

The research question should be delineated across four (4) elements (PICO):

P: Population of interest	The target population with a certain disease or health condition who may likely benefit from the introduction of the new technology. Note: ● Important characteristics, such as age, sex, ethnicity, disease severity, comorbidities, setting (I.e., in-patient or outpatient) should be included to the extent possible, to further specify the population.
I: Intervention/s	The CED considered for assessment Note: ● The proposed role of the *intervention/s* in the current clinical pathway should be defined. ● For all CEDs, the following must be defined where applicable: mode of use, setting (e.g. primary care, secondary or tertiary hospital, health center, home care, or remote monitoring); required co-interventions; duration and frequency of use. It

	should also be clarified if the CED is a replacement for, an adjunct to, or used in sequence with the current standard of care. ● Additional details for CED interventions device form, method of administration (e.g., invasive or non-invasive, implanted or externally used), degree of user interaction, and any necessary maintenance or servicing schedules.
C: Comparator	Current health technology/ technologies or standard/s of care or most prevalent practice used in the Philippines in the targeted population which may be replaced or whose administration may be affected/modified with the new intervention. A "do nothing" comparator should be explored if it is the current practice in the Philippines. Note: ● Substitute, adjunct, or adjuvant to existing CEDs o Comparators may not always be alternative CED but can be different methods of utilizing the same device, such as varied operating procedures or usage sequences. o Comparators may be medical devices currently in use, services presently offered by healthcare providers, treatment modalities recommended in clinical practice guidelines by professional societies, or widely accepted devices among clinicians.
O: Outcome	Defining the relevant outcome to measure to establish the effect of the intervention. Note: *Clinical outcomes* ● The clinical advantage of a CED should be evaluated using internationally recognized scales. Ideally, the trial outcome(s) should involve hard endpoints (e.g., survival rates, complication rates) and relevant outcomes to clinicians, patients, and policy-makers.

	• Specify primary, secondary and intermediate outcomes. • Intermediate outcomes and surrogate points are permissible, given that they are based on robust epidemiological evidence demonstrating a direct correlation with the primary outcome of interest. These intermediate outcomes should hold clinical significance as deemed by healthcare professionals. These intermediate outcomes must be validated through scientific literature and are verified through stakeholder consultations. *Economic outcomes* • Incremental cost-effectiveness ratio (ICER) and Cost-effectiveness acceptability curves (CEAC); Budget impact (to be discussed further in later chapters) *ELSI and Health System outcomes* • Relevant ethical, legal, social, and health system implications depending on the CED

Sample HTA policy question for a CED:

Should electrostimulation devices be used as an adjunct to usual care for the management of wounds?

Hao, Q, Horton, J, Hamson, A (2023). Electrostimulation Devices for Wounds, *Canadian Journal of Health Technologies,* Vol 3(7). Access here.

For example:

Sample CED HTA research questions

Clinical research question:

- What is the clinical effectiveness of automated external defibrillators (AEDs) (I) compared to status quo (C) in preventing mortality and improving survival rates due to sudden cardiac arrests? (O) of individuals in public spaces in the Philippines (P)?

Economic research question:

- Does the implementation of automated external defibrillators (AEDs) represent good value for money in the Philippines for preventing mortality and improving survival rates due to sudden cardiac arrests (O) in public spaces (P)?
- What are the budget and resource implications of introducing automated external defibrillators (AEDs) in public spaces in the Philippines?

Ethical, Legal, Social, and Organizational or Health System research question:

- What are the ethical, legal, social, and health systems implications of introducing automated external defibrillators (AEDs) in public spaces in the Philippines?

2.5. Scoping and Protocol Development

Scoping refers to the process of defining the overall scope or focus of the health technology assessment in terms of at least the following components:

1. population of patients who will benefit from the intervention
2. health technology or intervention of interest
3. appropriate comparators relevant to the local practice or context
4. clinically meaningful outcomes
5. timing and setting where the intervention will be used
6. any other consideration that will likely impact the results of the assessment such as appropriate perspective, equity issues, user context, skill, infrastructure, etc.

Refer to the main HTA methods guide (section 2.4) for details on how to go about scoping and protocol development for conducting HTA in the Philippines. Refer to Annex 4 (instead of Annex 3 in the main HTA methods guide) for guide questions in scoping the different components of the HTA report for CEDs.

Chapter 3: Health Technology Assessment for CED

Assessment refers to the application of formal scientific methods of evidence synthesis to evaluate the clinical, economic, health system, ethical, legal and social impact of covering or disinvesting a particular health technology in the local Philippine context.

- The general steps in the assessment stage include the review of clinical evidence which will then determine whether it will proceed to economic evaluation and the ethical, legal, social, and health system implications with the use of the health technology in the local Philippine context.
- **Members of the assessment team must meet the required criteria for authorship** (refer to the uniform requirements of authorship by the International Committee of Medical Journal Editors), depending on the expertise required by the type of the clinical assessment (i.e., rapid review, systematic review).

3.1. Clinical Assessment

The objective of the clinical assessment stage is to identify and synthesize all eligible clinical studies which report on the benefits and harms relevant to the PICO clinical research question. The report should clearly articulate the following:

- Whether the CED being evaluated is inferior, non-inferior, or superior to its comparator (i.e., the CED's clinical value) and report on the size of the relative treatment effects, the confidence intervals, and corresponding statistical p-values.
- The safety outcomes and risks relative to its comparator and if this impacts the clinical outcomes and/or have a cost implication in terms of, e.g., increasing or leading to additional health expenditure as a result of treating adverse effects. Any cost implications will have to be accounted for in the economic evaluation (see next subsection).

For the purposes of HTA, well-designed and well-conducted **systematic reviews** with or without meta-analysis **are considered the best source of evidence** due to the rigorous and comprehensive approach to search, appraise and synthesize all relevant studies and the larger statistical power resulting from the combination of several studies (if applicable), compared to single studies.[9]

3.1.1. Clinical assessment of diagnostic technologies

Devices for diagnostics vary significantly in their characteristics, particularly in terms of assessing their clinical effectiveness. A crucial distinction lies in the fact that the benefits of diagnostic tests are indirect; the impact on patients results from subsequent treatments rather than the diagnostic procedures or tests themselves. Moreover, these technologies might be utilized in conjunction with other tests or interventions, adding complexity to their evaluation. The primary outcome of a diagnostic test is information that can influence treatment, management decisions, and potential

[9] See next sections for additional guidance on the sources of evidence that can be considered given the limitations discussed around existing literature or studies for CEDs.

health outcomes. While there are benefits, there can also be harm, particularly with more invasive tests, a diagnostic odyssey, and anxiety stemming from the results.

Ideally, end-to-end studies that follow patients from testing through treatment to final outcomes are the preferred source of evidence for diagnostic technologies. Unfortunately, such comprehensive studies are seldom conducted and available. Hence, a linked evidence approach is typically employed, which consist of the following:

1. Evidence on diagnostic accuracy
2. Evidence on the impact of the diagnostics on management decision, and
3. Evidence on the effectiveness of treatment as a result of diagnostics

It is crucial to consider this linked evidence approach in the assessment of diagnostic technologies to ensure the acquisition of the highest quality evidence. For a detailed understanding of the methods for evidence review and economic modeling of diagnostics, the ACE technical team recommends consulting NICE (2011) part III: "Methods used for decision-making in Diagnostics Assessment Programme manual" available at www.nice.org.uk.

3.1.2. Location and Selection of Studies

To systematically locate relevant studies that should be included in the assessment, an extensive literature search should be conducted using relevant scientific databases. See the main HTA methods guide for more details on going about the location and selection of studies, including when to conduct a systematic review and when to do a rapid review. Evaluators may refer to Annex 5 (instead of Annex 4 in the main methods guide) in this complementary guide for the additional list of scientific databases that can be used in the study search.

The main HTA methods guide also elaborates on the conduct of both systematic and rapid reviews. Guidance on systematic reviews when conducting HTA for CEDs is updated in this guide. A rapid review is recommended when a systematic review is not appropriate due to the time it takes to conduct the study – for instance, during a public health emergency. Evaluators can refer to the main HTA methods guide for guidance on the conduct of rapid reviews for CEDs. Ultimately, HTAC will advise on the appropriate track for review.

Systematic Review

- A **systematic review (SR)** attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific, well-formulated research question. The research question should specify the types of population, intervention, and outcomes of interest (PICO). It uses explicit, systematic methods that are selected with a view to minimizing bias, thus, providing more reliable findings from which conclusions can be drawn and decisions may be made (Antman 1992; Oxman 1993 as cited in (Higgins et al., 2011).
- In appraising or conducting systematic reviews, appropriate study designs for different types of health technologies should be used in synthesizing the clinical evidence. While randomized controlled trials (RCTs) are considered the ‘gold standard’ in evaluating the efficacy of drugs and

other therapeutic interventions, these may not be feasible to conduct for many CEDs. Availability of robust evidence from RCTs may be limited at the early stages of technology assessment.

- While systematic reviews and RCTs are positioned on top of the hierarchy, other study designs, such as observational studies may offer the best source of objective evidence for some types of health interventions where randomization and/or blinding may not be feasible or where studies lack a control group. The quality of the evidence must be appraised to assess methodological rigor using validated appraisal tools (to be discussed in later sections). If designed and conducted properly, observational studies may be used to complement a poorly designed systematic review or RCT.
- Due to the key differences in characteristics of CEDs and pharmaceuticals outlined in earlier sections, screening for additional information is necessary. In some cases, a separate search may be necessary if the information is not reported in RCTs. Information on effect modifiers and critical factors for implementation will enhance the review of clinical effectiveness:
    - It is highly recommended to screen for studies that have investigated the association between user proficiency and treatment results. Individual expertise, learning effects or learning curves are potential modifying factors for the effectiveness of CEDs. Studies may use logistic regressions to quantify the learning curve effect. Subgroup analysis may also be done where existing studies are divided into different subgroups based on the level of operator efficiency. Statistical methods may then be used to estimate the difference in clinical outcomes between these subgroups and, as a result, quantify the impact of the learning curve.
    - Screen for studies that have analyzed device variations over time. Studies may use a Bayesian approach to account for the iterative nature of medical devices over time [Bonangelino, et al. 2011, United States FDA, 2020, Ming, et.al., 2022].
    - Screen for studies that have modeled outcomes in the context of operations research to show optimization, such as adaptive control algorithms, monitoring feedback, configuration, etc. which identify the chain processes that are critical in the use and operation of the device.
    - Screen for studies that investigate the context dependence of the CED, which not only looks at user characteristics but also associated therapies, institutional expertise, and healthcare settings (e.g. teaching or non-teaching hospitals).
    - Studies may use appropriate statistical methods to account for confounders or Bayesian approach to account for the iterative nature of medical devices over time.

When assessing a CED with ML or AI capabilities, evaluators should look for the following measures to validate the performance and clinical effectiveness of device: (1) sensitivity, (2) specificity, (3) positive predictive value, (4) negative predictive value, (5) receiver operating characteristic (ROC) curve, and (6) area under the curve or AUC. See Annex 1 for definitions of these metrics.

In addition, evaluators should account for cybersecurity requirements for devices that store and transmit medical information through networks by applying cloud-computing technology. Loss of medical information or possible modification of data during the transmission could impact the effectiveness of the device.

Just as for other CEDs, the performance of the human-AI team should be accounted for, meaning operator factor considerations and human interpretability of the model outputs are considered in the assessment of the device.

- Given the significant limitations of generating evidence through RCTs for CEDs, the search for CED-related literature should not be too restrictive. Additional study designs that generate non-randomized or even noncomparative evidence that explore effect modifiers should be considered. Evidence from trackers trials can also be considered. Tools such as the Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions can be used to assess the risk of bias in non-randomized controlled studies.

For ML- or AI-based technology, evaluators should be aware that most data on clinical AI performance originates from retrospective studies. Outcome modelling offers techniques to assess clinical impact with limited data like surrogate outcomes. The observational studies commonly utilized to assess its accuracy primarily focus on clinical validity measures like the algorithm's diagnostic sensitivity and specificity. When attempting to predict outcomes from these clinical validity data, researchers need to incorporate numerous additional assumptions into their models. These assumptions encompass aspects such as the response to new technology, the applicability of the intervention, and similar factors. Evaluators should check that the test data used should be independent of the data used in the product development process.

- Real-world evidence (RWE) can provide insights into the long-term effects of CEDs in real-world settings, reflecting the actual impact of clinical interventions. RWE is a vital component of healthcare data that originates from various sources, including electronic health records (EHR), electronic medical records (EMR), patient registries, hospital databases, and claims data. Unlike RCTs, RWE studies are conducted in real-world clinical settings without pre-specified criteria to select patients. The patients enrolled in RWE studies represent various subgroups, making them more representative of the entire population. As such, RWE can provide

more accurate results about the actual effects of clinical interventions. HTA based on RWE can offer insights that stem from real-world settings, making it an invaluable tool for healthcare decision-making.

- Expert evidence or expert opinion are valid and acceptable sources of information to complement published literature, or in cases when published research evidence is missing or inadequate. Experts may include clinicians, patients, or patient group representatives who may have contextual information, insights, values and preferences as well as experiences on the health condition or health technology of interest. It is important to obtain from the experts the evidence which forms the basis of their opinion, to document it through formal submission or transparent recording of the discussion, and to manage conflicts of interest, if any.
- The general steps of conducting an SR are outlined below. Additionally, Table 4 lists the minimum requirements in conducting a systematic review based on standard practices by Cochrane (Higgins and Green, 2011) and CRD (Center for Reviews and Dissemination, 2008).
    - **Scoping the literature**
    - **Forming a team, declaring, and managing conflicts of interest**
    - **Formulation of the research question and development of the protocol**
    - **Systematic search of the literature**
    - **Critical appraisal of included studies**
    - **Data extraction**
    - **Data synthesis**
    - **Interpretation and presentation of the results**
- When evaluators are able to find other HTA reports for the CED under evaluation, they may use the Speedy Sifting Section of the EUnetHTA Adaptation Toolkit[10] as a rapid screening tool to assess the adaptability of the report for the Philippine health care system.
- See Table 4 (Minimum Requirements for a Systematic Review of Clinical Evidence) in the main HTA methods guide (section 2.5.1.1 under *Location and selection of studies*) for details of the minimum requirements for the systematic review.
  For more guidance, resources are available online at:
    a. Cochrane: https://training.cochrane.org/handbook
    b. Centre for Reviews and Dissemination (CRD): https://www.york.ac.uk/media/crd/Systematic_Reviews.pdf.

3.1.3. Critical Appraisal of Clinical Evidence

Critical appraisal is the use of a systematic method to evaluate the methodological quality of studies assessing both their strengths and limitations, therefore, leading to the judgment on their internal validity and the reliability of the study's findings and conclusions. See the main methods guide for more.

Gathering information about health outcomes linked to AI presents difficulties. A challenge in producing evidence is the uncertainty surrounding the extent to which AI performance can be applied universally in diverse contexts. Evaluators should be mindful of "overfitting", which results from the technology being excessively tailored to a particular population, affecting the generalizability of the device.

[10] The toolkit can be accessed here:
https://www.eunethta.eu/wp-content/uploads/2011/01/EUnetHTA_adptation_toolkit_2011_version_5.pdf

3.1.4. Synthesis of Clinical Evidence

Please refer to the main methods guide for detailed guidance on synthesizing clinical evidence collected from the literature review. Evaluators should take extra caution in reporting the lack of effect of a health technology as this may simply be due to the lack of published good quality studies or the lack of statistical power to detect an effect. This is particularly relevant for CEDs if confounders are not controlled for in the assessment, if the evaluation is done in the early stages of the development of the CED, or if the sample size is too small.

Further, evaluators should not be too restrictive in terms of limiting the evidence review to just RCTs given its limitation of use for evaluating medical devices and the broad range of different CEDs. Evidence from non-randomized studies that have been thoroughly assessed, including for bias, should be included in the overall assessment. If, even when accounting for additional sources, availability of relevant and valid data is still limited, the HTAC shall be particularly cautious when reviewing the results and in drawing conclusions about the relative clinical effectiveness of the treatment options.

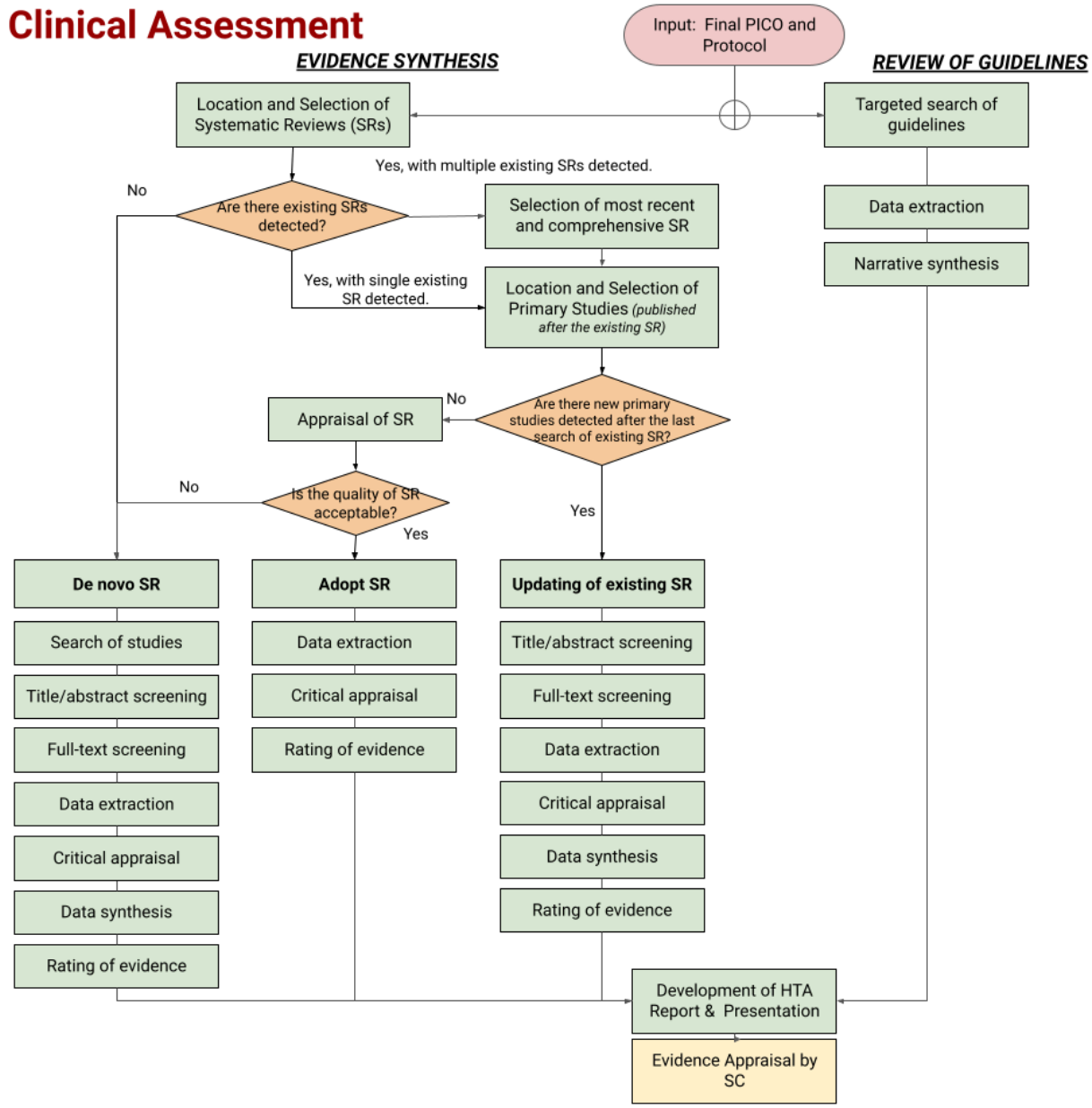
Review of Guidelines

In addition to the review of clinical evidence, scoping of available guidelines from country MoH and NRAs on the use of the proposed health technology is another requirement. For regular HTA, a minimum of 5 country and/or agency guidelines from global institutions, HICs, MICs and LMICs are required in this review process. Further, inclusion of countries and/or agencies in the review should be justified. Relevant information such as target population, approved/recommended indication/use case, dosing regimen/frequency, among others should be extracted and synthesized. Evaluators for CED should strive to adhere to the requirements for general HTA but this may not be feasible for HTA for CED for the reasons aforementioned, in which case a lower number of guidelines should suffice.

3.1.5. Algorithm of Clinical Assessment Stage

In summary, Figure 2 shows the overall framework in assessing clinical evidence. Conclusions on clinical evidence for the intervention of interest shall then be drawn from either the appraisal of an existing systematic review or the conducted SR or RR of the assessment team.

Figure 2 Clinical Assessment Process



3.2. Economic Assessment

An economic assessment in the context of HTA Council decision criteria in the Philippines includes the following components:

1. A health economic evaluation (EE) using Philippine-specific input parameters in terms of epidemiology, efficacy/effectiveness, expected health outcomes, and costs.
2. Budget impact analysis (BIA) to assess the affordability to DOH and PhilHealth, and aid decision makers on fiscal planning and implementation.
3. Household Financial Impact (HFI) analysis to assess the impact of the health technology on the out-of-pocket expenses of Filipino households.

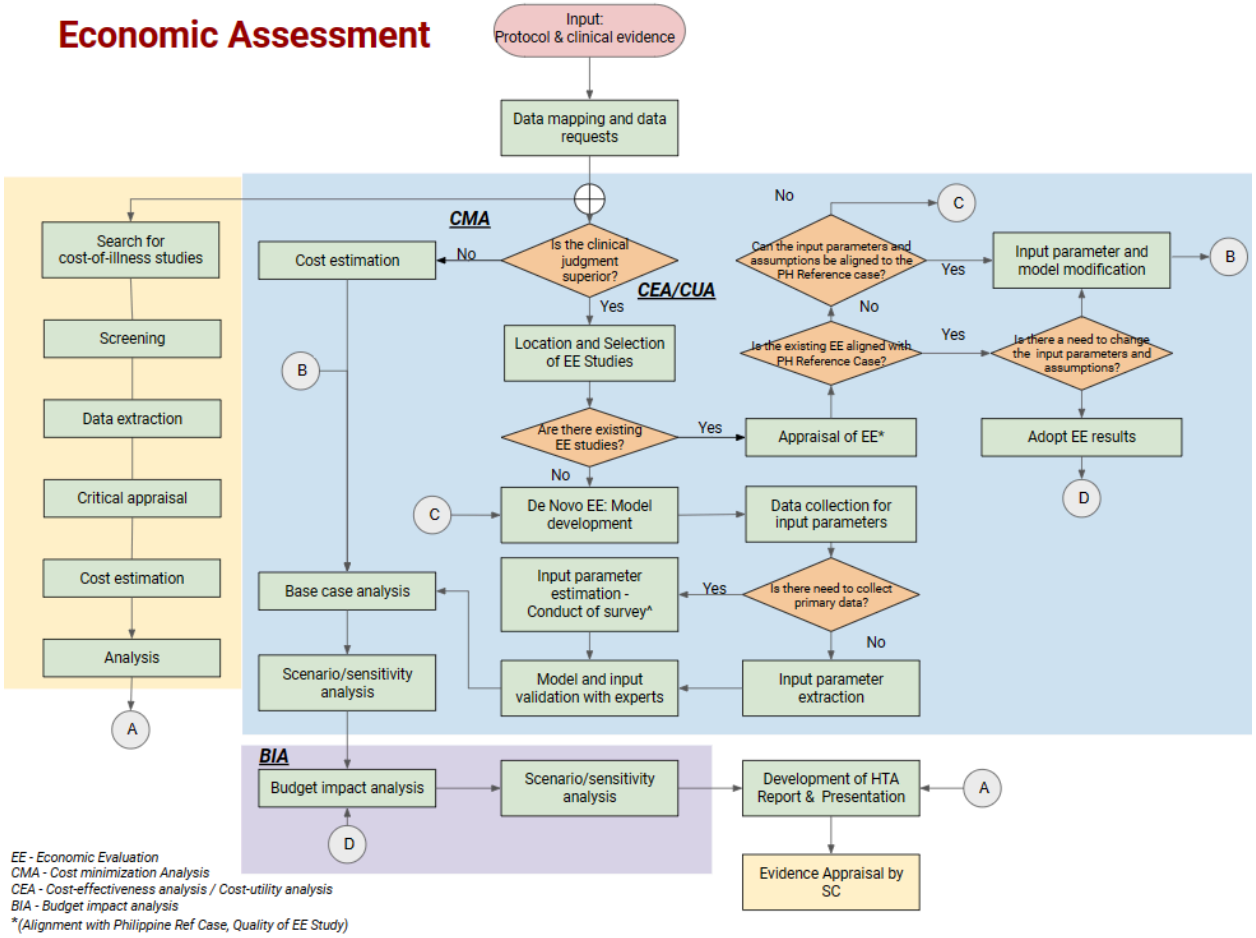
Economic assessment allows the determination of the relative costs and benefits of a health technology, the budgetary implications of its adoption to the national health system from the government's perspective, as well as the financial impact on the patients' households.

As new health technologies are introduced into the health system, the ability to pay for them is constrained by rapidly escalating healthcare costs, increasing public demands, and many competing health priorities.

With the goal of the DOH to maximize health outcomes across the population, an economic assessment is important to inform priority-setting and resource allocation decisions in healthcare. Economic evaluation provides information on the comparative costs and outcomes of various policy options most relevant to the Philippine context. The results of economic evaluations may also inform price negotiations of the government for innovative health technologies, such as drugs and medical devices. When conducted in a transparent, rigorous, and consistent manner, this can assist policy makers in dealing with complex decisions with greater objectivity and accountability to stakeholders.

Figure 2 shows the overall framework in assessing economic evidence which was elaborated in this section. The type of evidence needed for the cost-effectiveness criterion depends on the judgment on the clinical evidence. For non-inferior clinical evidence on the proposed health technology, cost-minimization analysis is sufficient. Otherwise, conclusions on cost-effectiveness criterion for the intervention of interest shall be drawn from either the appraisal or adaptation of an existing economic evaluation, or de novo economic evaluation of the assessment team. Subsequently, a budget impact analysis follows from the inputs on the economic evaluation model. In parallel, cost-of-illness studies are reviewed or performed to assess the household financial impact of the health technology.

Figure 3 Economic Assessment Process



3.2.1. Health Economic Evaluation

An **economic evaluation** is the comparative analysis of alternative courses of action in terms of both their costs (resource use) and consequences (outcomes and effects) (Drummond et al., 2015).

3.2.2. Selection of the Type of Economic Evaluation

The type of economic evaluation will depend on the decision problem as defined after the scoping and the availability of relevant data (e.g., QALY data). The preferred type of economic evaluation in the reference case is a **cost-utility analysis (CUA)** to meet the need of decision makers to compare the costs and outcomes of health interventions against the appropriate comparators. A **cost-effectiveness analysis (CEA)** reporting benefits in terms of natural health units should be reported alongside the CUA to further characterize the clinical benefit profile of the health technology although it does not allow for broad comparisons across diseases and interventions. **Cost minimization analysis (CMA)** may be sufficient where the intervention and the comparator have

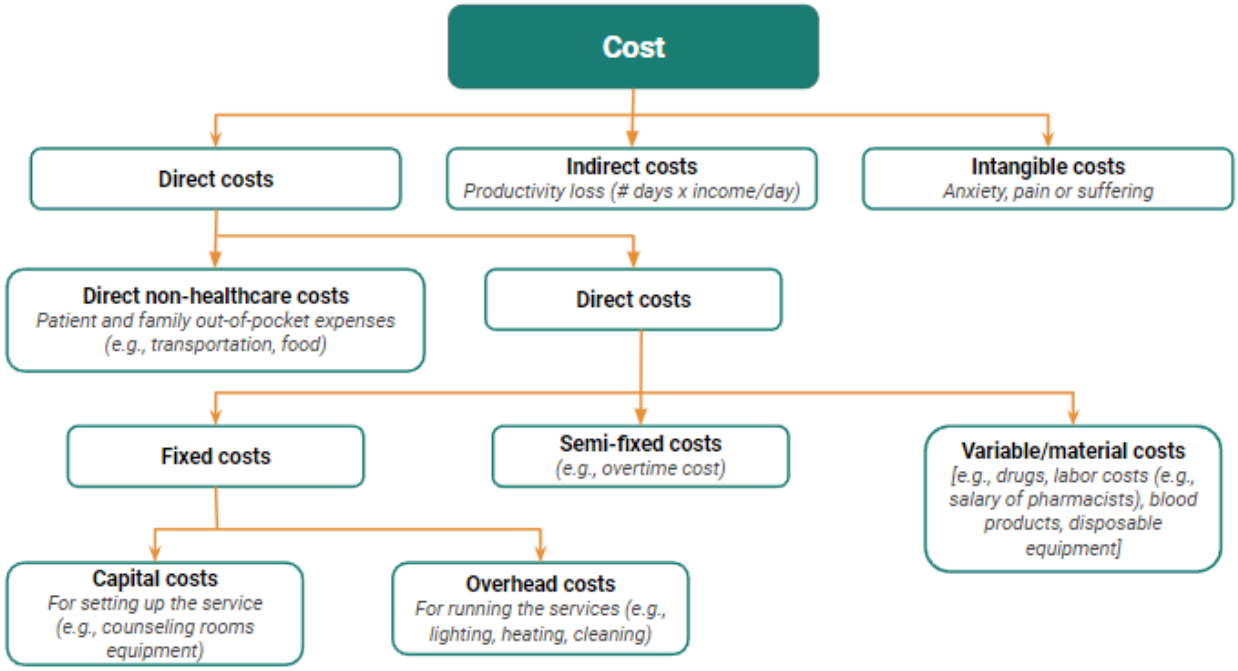
been shown to be equivalent or not significantly differently in terms of clinically relevant health outcomes. See section 2.5.2.4 in the main HTA methods guide for more details.

3.2.3. Cost Estimation

Costing, as defined by the *Global Health Costing Consortium* (Vassall et al., 2018), is the estimation of the cost of health interventions or services in a specific context (i.e., location, time period, population). There are different types of costs:

- **Direct costs** - the expenses incurred because of the illness (including medical care, travel costs, etc.)
    - o *Healthcare costs* - cost of all (medical) goods and services used for the provision of healthcare which are provided by the healthcare system, and further subdivided as *fixed* (covering capital, labor for installation and overhead costs), *semi-fixed* and *variable* costs (labor for use or operation of device). For CEDs in particular, additional semi-fixed costs that are typically not incurred for pharmaceuticals, need to be considered such as the cost of training health care professionals to operate/use the CED as well as maintenance costs. Other fixed costs such as any adjustments necessary to the physical infrastructure of the facility to ensure that the CED is operated and maintained effectively also need to be accounted for in the economic assessment.
    - o *Non-Healthcare costs* - cost of all goods and services used for the provision of healthcare which are not directly provided by the healthcare system.
- **Indirect cost** - the value of lost production because of reduced working time.
- **Intangible cost** - the cost of pain and suffering associated with the treatment.

Figure 4 Types of costs



The types of costs to be considered is defined by the perspective of the study (patient, provider, purchaser/healthcare payer, or societal perspective. The societal perspective includes all costs, regardless of who incurs them.

See Section 2.5.2.5 of the main HTA methods guide for more information on what to consider for the different types of costs that will input into the economic evaluation and the budget impact analysis.

Evaluators should ensure to report cost in real terms (e.g. deflate using the Consumer Price Index). This is especially relevant when prices or costs for the comparator intervention are taken from different years from the technology undergoing assessment.

When annualizing the cost of the CED (depreciation), there are a few methods to consider depending on what information is available.

- When salvage value (also known as scrap value or residual value) of the device is available, annualized cost can be calculated as follows:

$$Depreciated\ cost\ = \frac{P\,(n+1)+S(n-1)}{2n}$$

Where

P = purchase price of the device
S = salvage or scrap value of the device
n = useful life years of the device

- If the device's salvage value is zero, depreciation can be computed as follows:

$$Depreciated\ cost\ = \frac{Purchase\ price}{Useful\ life\ in\ years}$$

- When salvage value is unknown, there may be recommended depreciation rates for specific assets either established by literature or by government authorities (e.g. the IRS has suggested depreciation allowances for certain types of assets). The annual depreciated cost would then be:

$$Depreciated\ cost\ =\ Purchase\ price\ \times depreciation\ rate$$

When computing the present value of costs (discounting), the formula below can be used:

$$\sum_{t=1}^{n} \frac{C_t}{(1+i)^t}$$

Where

C_t = total cost incurred in year t

i = discount rate

Note that total cost includes yearly fixed costs (capital cost of which includes the annual depreciation computed using the methods above), semi-fixed costs, and variable costs.

In addition to the guidance for estimating direct healthcare costs provided in the main HTA methods guide, evaluators should also account for the following when doing the economic evaluation for CEDs:

- Ensure that associated procurement costs are incorporated into the purchase price of the device. These may be costs incurred by the payer directly or it may be marked up in the price set by manufacturers. Evaluators should note if there is a difference between procurement costs between the assessed device and the comparator device and if there is leeway to adjust the type of procurement and its associated costs.
- Maintenance costs (including preventive maintenance) for CEDs that are not single use should be added to the economic evaluation to account for the true cost of operating the CED during its life cycle.
- When estimating human resource costs, it should also include training time required to familiarize with the CED and any recurring trainings needed to keep health professional up to date on the operation or use of the CED.
- Capital costs that may occur if adjustments are needed to the facility's infrastructure should also be accounted for.
- Disposal costs of the CED after its useful life should be included in the economic analysis. This is relevant for devices with zero salvage value (used when computing annualized cost/depreciation) or if disposal costs are not accounted for when determining the salvage value of the device.
- Associated procurement costs should be accounted for. These may be costs incurred by the payer directly or it may be marked up in the price set by manufacturers. If the latter, this should be explicitly stated when requesting price quotations.

For ML- or AI-based technology, evaluators should account for additional costs that such devices may incur (aside from the aforementioned costs) including but not limited to:

Investment needs for AI implementation and upkeep.
Cost of integrating AI into electronic health records and workflows.
Cost of additional measures needed to be in place to ensure safe use of device and secure data management.
Performance monitoring and retraining of deployed models/devices.

See Annex 6 for a more detailed description of costs.

3.2.4. The Philippine Reference Case

The *'reference case'* specifies the methodological standards considered by the HTAC in making judgments on the value of health technologies to patients and the wider health system. By clarifying the methods that should be employed by the assessment team, transparency is expected to be provided to all stakeholders on all evidentiary requirements.

In making explicit the concept of the reference case, it is expected that consistency is achieved in HTA Report submissions and clear decision points are consistent with the methodological standards set out in this document.

While it is ideal to abide with the reference case analysis as much as possible, it is also recognized that some cases may necessitate divergence from the reference case (e.g., non-availability of data, emergency situations) and in which case, the use of methods that do not follow the reference case must be justified.

Please refer to the main HTA methods guide for methodological specifications for the Philippine reference case.

3.2.5. Economic Modelling

Refer to the main Methods Guide for a description of decision models that can be used to better understand the relationship between incremental costs and their consequences. The section also provides guidance on model development, input parameter estimation and model validation,

For model validation, extra caution must be taken if using predictive validation for CEDs given the factors that can affect their effectivity (i.e., learning curve effect has to be properly accounted for in both the model as well as in actual events to ensure comparability of results).

A summary of the decision analysis modeling process includes the following:

- Adaptation or construction of a model that depicts the relevant options and possible outcomes of these options, validated with a panel of experts;
- Estimation of probabilities;
- Estimation of costs and outcomes;
- Calculation of the expected value of costs and outcomes for all options;
- Identification of the option with the greatest expected value (most desirable option or alternative); and
- Sensitivity analyses to handle uncertainties.

The section also provides guidance on presenting the results of the evaluation. The result of the cost-effectiveness or cost-utility analysis should be presented in the form of an incremental cost-effectiveness ratio (ICER).

3.2.6. Criteria for Cost-effectiveness in the Philippines

There is **no explicit cost-effectiveness threshold** in the Philippines above or below which health interventions are considered cost-effective or not cost-effective. Traditional ICER thresholds set by the WHO (i.e., less than three times the GDP, or 1 GDP per capita per QALY/DALY) may be used as guides. However, other decision criteria like responsiveness to magnitude, severity, and equity; effectiveness and safety; household financial impact; and affordability and viability are also considered aside from cost-effectiveness in deciding possible coverage.

3.2.7. Appraisal of Economic Evaluations

Multiple tools may be used in the critical appraisal of existing EE if justifications and explanations in answering the tool are sufficiently provided. Meanwhile, for the review of preliminary economic assessment conducted by an external assessment group, the Drummond's tool shall be used by the evaluator to determine the quality of the assessment.

3.2.8. Budget Impact Analysis

The budget impact analysis (BIA) is a financial approach designed to estimate, over a defined time horizon, the financial consequences of adopting a health intervention. The objective of this analysis is to increase the awareness of DOH or PhilHealth policymakers of the financial impact of introducing a new technology, and to aid in budget or service planning of government and/or social insurance. Therefore, All BIAs shall use the public payer perspective which shall cover all costs borne by the government. This is required, along with the CEA or CUA.

See the main HTA methods guide for detailed guidance on performing a budget impact analysis. The budget impact analysis should clearly state the assumptions used as well as the parameters, its corresponding sources, and any formula used. Evaluators are to provide the computations in an attached costing template, using readily available software that will allow the budget holder to conduct their own analyses, adjusting for certain parameters and assumptions as deemed

necessary. The results of the computations for both the current and new health technology should be summarized as shown in Tables 1 and 2 below.

Table 1. Details of the CED under evaluation

Approved name of health technology		
Indications and any restriction(s) of use	Give the (anticipated) indication(s) in the Philippines.	
	Value	**Data Source**
Procurement cost of CED*		
Cost of disposable component of CED (if applicable)		
Anticipated frequency of use per course of treatment		
Average length of a course of treatment		
Anticipated number of repeat courses of treatments per year		
Maintenance costs		
Expected life years		
Total cost		
*When the marketing authorization or anticipated marketing authorization recommends the intervention in combination with other treatments, the list price of each intervention should be presented.		

Table 2. Details of the single-use CED under evaluation

Approved name of health technology		
Indications and any restriction(s) of use	Give the (anticipated) indication(s) in the Philippines.	
	Value	**Data Source**
Procurement cost of CED*		
Anticipated frequency of use per course of treatment		

Average length of a course of treatment		
Anticipated number of repeat courses of treatments per year		
Total cost		
*When the marketing authorization or anticipated marketing authorization recommends the intervention in combination with other treatments, the list price of each intervention should be presented.		

Table 3. Expected Budget Impact

	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Eligible population for intervention with **[new CED]**					
Population expected to receive intervention with **[new CED]**					
Total cost using intervention with comparator CED					
Total cost with intervention with **[new CED]**					
Net budget impact (difference in total costs)					
% changes in total cost					

3.2.9. Household financial impact

A Household financial impact (HFI) analysis is conducted to estimate the financial impact of the disease per capita which will reflect, or present cost covered by the government and those incurred out-of-pocket. This estimate can be done through cost of illness studies. A cost of illness analysis determines the estimated cost for the burden associated with certain illnesses represented in forms of economic and monetary values (Choi & Lee, 2019). Note that a HFI is complementary and will not affect the perspective of the economic evaluation. Refer to the main Methods Guide for more details.

3.3. Ethical, Legal, Social, and Health System Implications (ELSHI) Assessment

Along with the clinical and economic aspects of a health technology, HTA takes into account the Ethical, Legal, Social, and Health System Implications (ELSHI) associated with the use or non-use of a health technology. The consideration of such aspects aims to increase the relevance, applicability, and legitimacy of healthcare decisions. The main Methods Guide includes more information on each aspect and includes a general framework in assessing ELSHI evidence.

The relevance and adequacy of existing ELSHI evidence to the assessment may not always be sufficient to address the research questions. Subsequently, a qualitative systematic review (i.e., de novo/updating QSR, adopting QSR) or primary data collection may be performed as supplemental methods. Reviewers should keep in mind the additional factors that impact the effectiveness of a CED that have been laid out in the earlier sections (i.e, training, adjustment of infrastructure to best accommodate implementation of a new technology).

Conducting a de novo qualitative systematic review which may take up several months may not be always feasible especially in emergency situations where there is a need to balance rigor with practical considerations on the decision timelines of the policymakers.

Some of the legal and ethical factors that evaluators need to look out for when assessing ML- or AI-based technology include the following:

- A clear definition of whether the technology is used as a support tool vs. a decision-making tool.
- Outlining the legal implications of the technology's limitations.
- Determining responsibility for AI errors and patient harm.
- Managing clinician compliance with AI recommendations.
- Navigating complex consent and data usage issues.
- Protecting data origin, consent, ownership, and usage rights.

3.4. Assessment of Environmental Impact

When possible, evaluators should take into account the environmental impact associated with the use or non-use of the CED in question. The environmental dimension can be considered by means of a literature review. Evaluators should note if there is insufficient evidence in the literature to draw any conclusions on the environmental impact of the CED that is being assessed. If some information is available, qualitative methods may be used to synthesize the evidence. If sufficient information or data is available to conduct a quantitative assessment, see Annex 2 for additional guidance on potential approaches to use.

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Annexes

Annex 1 – Machine Learning or Artificial Intelligence-Based Medical Devices
Annex 2 – Approaches taken to assess environmental impact of a health technology
Annex 3 – HTA Scoping Tool
Annex 4 – Data Sources - Relevant Databases
Annex 5 - Description of cost items

Annex 1: Machine Learning or Artificial Intelligence- Based Medical Devices

Potential lies in the application of artificial intelligence (AI) and machine learning (ML) in healthcare, where they can revolutionize the sector by extracting valuable insights from the extensive data produced in daily healthcare operations. These technologies are being embraced by medical device manufacturers to enhance their products, aiding healthcare professionals and enhancing patient well-being. A major advantage of AI/ML in software is its capacity to learn from practical application and experience, resulting in continual performance enhancement. Prior to being incorporated into standard clinical practice, AI applications must traverse the AI chasm, which represents the disparity between the performance observed in controlled laboratory settings and the actual performance and consequences within the practical realm of healthcare delivery and services.

A systematic review of current clinical studies on AI-based medical devices foud that there are many challenges that need to be addressed in evaluating the value of AI-based medical devices and a standardized evaluations process and related criteria still need to be developed (Farah et al. 2023). The reviewers recommend the need for consensus on specific HTA criteria for AI-based MDs, the inclusion of transparency, interpretability, ethics, and organizational impact in the assessment process, and the reinforcement of requirements for data management and quality systems.

The U.S Food and Drug Administration, together with Canada and the United Kingdom, have identified 10 guiding principles that can inform the development of Good Machine Learning Practice which aims to help promote safe, effective, and high-quality medical devices that use artificial intelligence and machine learning.[11]

While the Philippines will have to clearly define what is and what is not classified as ML and AI-based medical devices, some examples outlined by South Korea in their guidance can be used in the interim (Table A1.1).

Table A1.1 Examples of software classification

Examples of software categorized as medical devices	Examples of software categorized as non-medical devices
● Software that diagnoses the presence or progress (stage) of lung cancer by analyzing lung computed tomography (CT) image	● Software that collects and processes data for insurance claims

[11] The guiding principles can be accessed through https://www.gov.uk/government/publications/good-machine-learning-practice-for-medical-device-development-guiding-principles/good-machine-learning-practice-for-medical-device-development-guiding-principles.

● Software that diagnoses or predicts cardiac arrhythmia using electrocardiography test	● Software that manages the medical care schedule of doctors, wards, and dosing time
● Software that calculates the probability of onset of a certain cancer based on medical information, including biopsy and electronic medical records (EMR)	● Software that supports medical bill claims and handles electronic procedures for patients in hospitals
● Software that diagnoses the presence of skin cancer by analyzing skin lesion images	● Software that encourages or promotes a healthy diet, exercise, weight loss, or a healthy lifestyle
● Software that predicts hypoglycemia by analyzing information, such as blood sugar data, food intake, and insulin injection	● Software intended only for research and education in universities and research institutions
● Software that predicts or provides warnings, including alarms for emergencies, such as shortness of breath, by analyzing vital signs measured and compiled in an emergency room	● Software that saves and manages EMR
● Screening software that detects and marks abnormal areas by analyzing stomach CT image	● Order communication system (OCS)
● Software that provides quantitative value for a particular characteristic of the blood vessel, such as blood flow velocity and blood vessel diameter, by analyzing medical images	● Software for clinical research that supports and manage records including patient treatment, examination, and Institutional Review Board (IRB) review.
● Software that establishes radiotherapy planning based on medical data	● Software that provides a tool for searching or organizing information, including literature information related to prescription and medical care, to medical professionals without replacing or modifying information, such as previously prescribed medicine or treatment
	● Software that helps medical professionals conveniently access medical information related to a patient's condition or treatment

Source: South Korea National Institute of Food and Drug Safety Evaluation, Ministry of Food and Drug Safety (2022)

Some of the metric for evaluators to consider when assessing the performance and clinical effectiveness of a device utilizing machine learning and artificial intelligence are summarized in Table A1.2.

Table A1.2 Metrics to assess device performance and clinical effectiveness

Metric	Description
Sensitivity	Probability to identify the population with the disease among the population with the disease
Specificity	Probability to identify those without the disease among the population without the disease
Positive predictive value	Proportion of patients truly diagnosed as positive to all those who had positive test results. It is the probability that subjects with a positive screening test truly have the disease.
Negative predictive value	Proportion of cases yielding negative test results who are already healthy. It is the probability that subjects with a negative screening test truly do not have the disease.
Receiver operating characteristic (ROC) curve	Graph drawn using sensitivity and false-positive rate (1-specificity) based on diagnostic test results. This curve can be used to assess the diagnostic performance on distinguishing positive or negative.
Area under the curve (AUC)	Refers to the area under the ROC curve indicating diagnostic accuracy. In a range of 0.5 to 1.0, the close the value to 1, the better the performance.
Accuracy	The proportion of the total number of predictions that were correct.
Precision	The proportion out of all positive predictions was correct.

Source: Adapted from South Korea National Institute of Food and Drug Safety Evaluation, Ministry of Food and Drug Safety (2022)

Annex 2: Assessing the environmental impact of a health technology

Integrating the assessment of the environmental impact of a health technology for health technology assessments has not yet been well established. A few studies that have attempted to include the environmental dimension have been mostly limited to high- income countries. Sweden and the United Kingdom are two of the countries where public health decision makers have started examining environmental impacts when assessing new technologies.

The main challenges in incorporating environmental impact into HTA include identifying key concepts, using adequate indicators for the assessment as well as having reliable and specific data to be able to perform the assessment. The methodologies and frameworks for integrating environmental impact into the economic evaluation are also not fully developed and/or agreed on.

Some of the approaches considered to incorporate environmental factors into HTA are summarized In Table A2.1 below. Evaluators need to take into account incorporating both the negative environmental impact (e.g., carbon emissions), the benefits, (e.g., health gains associated with improved environmental outcomes) and the economic costs.

Table A2.1 Methodological approaches and frameworks to incorporate environmental impacts into HTA

Approach	Description
Life Cycle Approach (LCA)	This approach considers the implications of resources throughout the technology's life cycle. This starts from the extraction of raw materials and its processing, the manufacturing of the technology, its usage, and disposal. This approach is considered the ideal approach for accounting for environmental impact evaluation of a health technology. However, a major limitation for this approach is the significant data requirements, with data collection necessary throughout a technology's life cycle. The mathematical models to estimate the environmental impact are also faced with its own limitations.
Environmentally extended input-output analysis or model (EEIOA)	This approach estimates the carbon emissions generated by each unit of output in a sector.
"Enriched" Cost-utility based frameworks	Two models using CUA frameworks have been explored in incorporating environmental impacts into the assessment. 1. Incorporating health gains associated with improved environmental outcomes into estimates of health-related quality of life (HRQOL). This involved translating

	environmental impacts into health impacts and using this metric in the CUA. 2. Reflecting the environmental impact associated with the life cycle of a health technology in the decision makers' willingness to pay for health gains.
Cost-benefit analysis	This approach converts all outcomes into monetary units making it possible to compare a wide range of social costs and benefits, including those brought about by the environmental impact of a technology. Evaluators may incorporate the social costs of carbon (SCC) into a CBA. However, SCC methods are still subject to significant uncertainty and debate due to the various factors that can impact the final estimate (discount rate, environmental impact included in analysis, nonmarket damages, risk factors, weights assignment to different geographic regions, and others). The monetary valuation of nonmarket goods such as health and environmental effects pose a main challenge in using this methodology.
Multicriteria decision analysis (MCDA)	This method is often used in environmental assessments. It elicits from decision makers how they trade off outcomes to determine the preferred treatment options. It includes steps such as defining the decision problem, identifying value criteria, weighting criteria, measuring the performance of alternatives against the criteria, aggregation into an overall estimate of value, and assessing the impact of uncertainty. There are various techniques used to conduct MCDA (analytic hierarchy process, analytic network process, multi-attribute utility theory, multi-attribute value theory, outranking, social multicriteria evaluation). While this method is seen to be a promising way of extending HTA to capture environmental impacts, it also faces some limitations. First, it faces the same valuation problem that a CBA faces. Additionally, unlike CUA and CBA, the application of MCDA in HTA face the challenge of it being in its infancy and being less familiar to health care decision makers.

Incorporating environmental evaluation into HTA is often limited to the overall estimations of the carbon footprint of healthcare institutions and their supply chain, or focusing on a particular service or intervention. However, the literature around this topic is expanding as additional methodological approaches are being developed to perform more accurate calculations. It is imperative for economists and environmental specialists to work closely together to choose the best approach and inputs required by the selected methodology that will facilitate decision making.

Annex 3: PICO Development Report Tool

In conducting an HTA for CED, there should be a defined scope of the content and focus of the report to provide a clear framework from the beginning on the relevant questions that needs to be addressed in assessing the overall value of a health technology to the Philippine health system.

In conducting an HTA, there should be a defined scope of the content and focus of the report to provide a clear framework from the beginning on the relevant questions that need to be addressed in assessing the overall value of a health technology to the Philippine health system.

This tool serves as a guide to assessment teams in developing the scope of the report through a review of both published and grey literature and consultation with relevant stakeholders such as potential users of the health technology, clinical experts, DOH program managers, industry representatives, patients, healthcare organizations, and other relevant health system partners. Please note that this does not reflect the totality of the items for deliberation during the stakeholder consultation and topic-specific questions must be included during the course of the discussion.

Area of focus	Guide questions	Comments/Responses
Population (P)	• Which patient population, health condition or disease is being addressed by the health technology in the Philippines? • What is the local incidence or prevalence of the condition being addressed by the health technology? What proportion of the target population is likely to use the health technology? • Who will likely use the health technology in terms of age, gender, ethnicity, level of risk/severity, place of residence or other determinants relevant to the health technology? • Is there a particular subgroup of the intended population likely to gain the most benefit from the health intervention/technology? • Is there a particular subgroup of the intended population likely to face harm or risks from using the health intervention/ technology?	

Area of focus	Guide questions	Comments/Responses
Intervention (I)	• What is the proposed indication of the health technology that is being applied for HTA? What are the FDA-authorized indications of the health technology? • Will the health technology be used for prevention, screening, diagnosis, treatment, monitoring of the progression of the disease, guidance in treatment selection, knowing the prognosis, rehabilitation or other purposes? • In what particular health setting or level of care will the health technology be likely used (e.g., home or community, primary care, general hospital, specialty hospital, inpatient/outpatient care, ambulatory care)? • What is the required expertise (e.g., nurse, general practitioner, primary care provider, specialist) to facilitate the use of the health technology? • What is the type/classification, indication, mechanism of action, mode of administration or delivery, dose/frequency/timing of use of the health technology? • What are the expected health benefits of the intervention to patients and healthcare providers? • What are the expected risks or harms that may arise from the use of the health technology? • What is the potential place of the intervention in the current clinical pathway in the Philippines? How might the intervention change the current treatment or management of the disease?	
Comparator (C)	• How is the disease currently being treated/managed in the Philippines? • Is there a local clinical guideline available which describes the current standard of	

Area of focus	Guide questions	Comments/Responses
	care or other alternative treatments available in the Philippines? ● Are there existing variations in how the disease/condition is being treated or managed in the local setting?	
Outcome (O)	Clinical Outcomes ● What are the measurable and clinically meaningful health outcomes that should be considered in assessing the health technology (e.g., morbidity, mortality, survival, patient admissions/readmissions, episodes of disease health-related quality of life, safety)? Economic Outcomes ● What are the costs related to treatment of the target health condition? ● What are the costs relevant to the use of the health technology for the targeted disease? ● What is the budget impact of implementing the health technology? ELSHI Outcomes ● Does the general population or specific subpopulations find the use of the health technology acceptable or controversial? ● Are there population factors that need to be considered in the assessment that may affect equity in distribution of health outcomes as a result of using the health technology? (refer to PROGRESS-Plus framework on p. 64 which includes determinants of health equity)	

Area of focus	Guide questions	Comments/Responses
Timeframe (T)	• When is the health technology used by or administered to patients in the disease trajectory or clinical pathway (i.e. emergency, recovery, early stage or late stage, acute or chronic stage)? • How long is the health technology used to produce clinically meaningful health outcomes?	
Sustainability	• Is this a single use to reusable healthcare device? • What is the life-cycle length of the device? • What materials have been used in the construction of the medical device, and have sustainable alternatives been considered? • Are there any certifications or standards the medical device meets in terms of environmental sustainability? • How does the medical device's energy consumption compare to similar devices on the market, and what steps have been taken to optimize its energy efficiency? • See Annex 1 on approaches taken to assess environmental impact of a health technology for more information.	

Annex 4: Data Sources - Relevant Databases

HTAs in Other Settings	**Clinical Evidence**
NICE (UK) CADTH (Canada) HITAP (Thailand) GEAR INAHTA Regulatory Agency Databases *Provides information on the approval status of medical devices, adverse event reports, and other regulatory information.* U.S. Food and Drug Administration The European Medicines Agency	PubMed/MEDLINE Cochrane Library EMBASE HERDIN **Clinical Trials Registries:** https://clinicaltrials.gov/ http://apps.who.int/trialsearch/ EU Clinical Trials Register **Unpublished local trials:** Coordinate with FDA or local manufacturers **Topic-specific databases:** • BIOSIS Previews (Biology and pharmacology) • AMED (Allied and Complementary Medicine) • CINAHL (Nursing and Allied Health) • PsycINFO (Psychology) • HuGE (Human Genome Epidemiology) • International Pharmaceutical Abstracts • Occupational Therapy Journal of Research Index • Applied Social Sciences Index and Abstracts

	Patient Registries and Databases and Healthcare Databases: *These include databases of electronic health records, insurance claims data, and other healthcare data that can provide real-world evidence about the use and outcome of medical devices.* Coordinate with PhilHealth, DOH, and local hospitals

Annex 5: Description of cost items

Below is a non-exhaustive list of different cost items to be considered in the economic evaluation with their corresponding description.

Cost item	Description
Device cost	Cost of the actual device.
Cost of the diagnostic or surgical procedure	Cost of the diagnostic or surgical procedure within which the device is used. For instance, it may include the cost of personnel used for the procedure (not just the operator of the device) and cost of other auxiliary equipment.
Trial cost	Cost of the trial before the device installation (if applicable).
Post-diagnostic or surgical procedure costs	Cost of the post-diagnostic or surgical procedure after the medical process within which the device is used. This is relevant when evaluating the device against comparators if post-use care will be different between the technology being evaluated and the comparator.
Cost of personnel skills adaptation	Cost of adaptation of personnel skills (e.g. training) as a consequence of the device introduction.
Cost of infrastructure adaptation	Cost of infrastructure adaptation following the device introduction.
Cost of engineering support	Cost of engineering support following the device introduction. Evaluators should ensure not to double count if this is accounted for in maintenance costs.
Reuse cost	Cost to reset the device for its reuse.
Cost of drugs	Cost of pharmaceuticals use in pre- and/or post-clinical process within which the device is used.
Depreciation rate unitary cost	Evaluates the medical device's economic flow, calculated as the annual depreciation rate on yearly performance.
Maintenance unitary cost	Indicates how much the maintenance cost is distributed for each service performed with the device.
Quality cost	Sum of the costs to prevent the occurrence of non-conformities of the diagnosis or treatment according to ISO standards.
Disposal costs	Cost of disposing or recycling the device at the end of its useful life.

Source: Adapted from Tallarico, et.al. (2021)