Course Book

HEALTH TECHNOLOGY ASSESSMENT

DLMIHMHTA01

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LEARNING OBJECTIVES

Health Technology Assessment (HTA) aims to improve the performance of health systems, contribute to informed policy decision-making in healthcare related to the use of healthcare technologies, and to contribute to health equity. The assessment and appraisal functions of an HTA are two separate parts of the evaluation of health technologies.

The assessment aspect of HTA focuses on reviewing clinical and economic evidence, whereas the appraisal is usually designed as a deliberative process that evaluates the assessment, taking into account legal and ethical considerations, health system-specific aspects, and potential peculiarities of local context. HTA forms the basis of evidence-based advice to relevant authorities and agencies. Specific recommendations can result in outcomes such as financing a particular product or the support or rejection of the implementation of a particular healthcare program or intervention. Healthcare innovation and the development of advanced therapies have led to improved treatment options and patient recovery rates while exerting a burden on healthcare expenditures. Developing oversight strategies for price monitoring of healthcare products is the responsibility of governments, irrespective of a country's level of economic development. HTA has become a gamechanger in priority setting and price negotiations for national and institutional agencies in healthcare. Clinical practice guidelines (CPGs) are formulated based on the data acquired by systematic reviews of evidence and the evaluation of therapeutic treatment options. Horizon scanning is referred to as a systematic examination of information to identify potential threats, risks, emerging issues, and opportunities. Approaches like Multicriteria Decision Analysis (MCDA) allow evaluations based on multiple factors that can influence decisions.

One of the key objectives of HTA is to provide a scientific basis for priority setting and efficient resource allocation. Thus, many countries, including an increasing number of low- and middle-income countries (LMICs), have identified HTA as an efficient policy tool. There is considerable demand for evidence to recommend and shape policies toward universal health coverage (UHC), such as benefit package design, strategies for upgrading standards, and overall quality to advance access to health services. Politics, ethics, and rights are core to designing health benefit packages for UHC.

UNIT 1

DEFINING HEALTH TECHNOLOGY ASSESSMENT

STUDY GOALS

On completion of this unit, you will be able to …

- define health technology assessment (HTA).
- understand the context, extent, and interventions of HTA.
- identify the purpose and tools of HTA.

1. DEFINING HEALTH TECHNOLOGY ASSESSMENT

Introduction

Health technology assessment ~~(HTA)~~ is defined as a bridge between "evidence" and "policy" in healthcare (Velasco-Garrido & Busse, 2005). It is a multidisciplinary process that uses specific methods to determine the value of health technologies at different stages of their developmental cycle (O'Rourke et al., 2020). Its purpose is to guide governance and policymaking to promote an effective, unbiased, well-structured, and optimal health system (O'Rourke et al., 2020). HTA involves structured assessment of the characteristics, effects, and impacts of healthcare technology. There are different forms of policy research and analysis on health and resource use, such as foresight, economic analysis, systems analysis, and strategic analysis. HTA investigates the short- and long-term medical, societal, organizational, and economic impacts of health and resource use, as well as the application of health technology (Velasco-Garrido & Busse, 2005).

1.1 HTA Context

The context in which HTA research is conducted influences the assessment strategies applied and the degree, scope, and magnitude of the evaluation. The sphere and scale of the assessment differs based on the entity commissioning the study and the purpose of the assessment. It is important to evaluate various aspects of technological or therapeutic intervention, such as the type of interventions within health systems and the interventions on health policy economics, health infrastructure financing, and running healthcare facilities (O'Rourke et al., 2020).

Historical Context of HTA

Distinctions in country-specific health systems globally reflect the diverse social and political complexities of each country. In 1965, the Committee on Science and Astronautics of the U.S. House of Representatives reiterated the necessity for policy makers to have the knowledge required to enable an assessment of the overall impact of health technology (Goodman, 2014). This led to the formation of the Office of Technology Assessment (OTA), an organization for unbiased evaluation of various technologies including medicine and healthcare (O'Donnell et al., 2009). The OTA framework was adopted by several European countries, including Austria, Denmark, France, Germany, the United Kingdom, the Netherlands, Sweden, and the European Community.

The earliest version of something resembling the HTA model, known as the Swedish Council for Health Technology Assessment and Assessment for Social Services (SBU), was established in Sweden in 1987, focusing exclusively on healthcare interventions for healthcare policy makers and patients (Hailey, 2009). The purpose of the SBU was to guide

healthcare policy decisions focused on the effective use of available resources. In Australia, the Australian Pharmaceutical Benefits Advisory Committee (PBAC) was assigned a similar role. In Canada, the *Conseil d'Évaluation des Technologies de la Santé* (CETS) was formed at the provincial level in Quebec, which was later renamed the *Agence d'Évaluation des Technologies et des Modes d'Intervention en Santé* (AETMIS). At the national level, the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) was established in 1989. CCOHTA was reorganized as the Canadian Agency for Drugs and Technologies in Health (CADTH) and was responsible for reviewing drugs and recommendations (O'Donnell et al., 2009). Later, the UK established the National Institute for Clinical Excellence (NICE) in 1999 to steer and guide technological progress and advance therapeutic treatment (Charlton, 2020).

After the OTA was eliminated, the U.S. has adopted different versions of HTA since the 1990s (Mulligan et al., 2020). Several HTA-like associations and third-party organizations, such as the Blue Cross Blue Shield Association Technology Evaluation Center (BCBS TEC) and the Emergency Care Research Institute (ECRI), have guided decision-making by providing healthcare assessments. The Drug Effectiveness Review Project (DERP) focused on randomized clinical trials and health policy-based decision-making. In addition to DERP, BCBS TEC, and ECRI, dossiers recommended by the Academy of Managed Care Pharmacy have been adapted by many public and private healthcare bodies. This provides access to standardized clinical and economic information necessary for decision-making. In 2006, the Institute for Clinical and Economic Review (ICER) was established. The U.S. is still awaiting the creation of an official HTA institution. Such an organization should first focus on clinical impact and gradually include economic assessment and evaluation of healthcare technologies. If a national organization for HTA is established, collective efforts will be needed to engage public and private healthcare institutions and stakeholders to work together. Similarly, in countries such as Brunei, Malaysia, Singapore, and Thailand, universal health coverage (UHC) is provided to citizens, together with a developed HTA model (Van Minh et al., 2014). The Association of Southeast Asian Nations (ASEAN) of Indonesia, the Philippines, and Vietnam have taken steps toward UHC, but the HTA model remains to be implemented (Chongsuvivatwong et al., 2011). Cambodia, Lao People's Democratic Republic (PDR), and Myanmar conduct periodic HTA assessments.

Contextual Aspects of Policy Questions

HTA is significant, as it assesses the medical, ethical, and socioeconomic impact of adapting modern technologies or changes to existing technologies and implementing structural or organizational changes. It is necessary to address safety, economic, and ethical concerns for any urgent healthcare technology, practice, or policy-related issue.

HTA is policy-oriented and supports evidence-based decision-making related to resource allocation, market investment, drug licensing, health-benefit coverage, insurance, reimbursement, and future research funding. Various contextual factors influence HTA reports, further impacting health systems, including health policy and decision-makers, regulatory authorities, third-party agencies, pharmaceutical companies, healthcare facility managers, and civil servants (Velasco-Garrido & Busse, 2005).

As described, the context in which HTA is performed defines the strategy to be employed, as well as the degree and scale of the assessment. For instance, a recommendation regarding the purchase of advanced medical equipment necessary for a hospital to enter a new clinical research arena requires thorough evaluation.

1.2 HTA Objectives

The primary aims of HTA are to improve the performance of health systems for health gains, enhance informed policy decision-making in healthcare for improving uptake, promote the use of new cost-effective healthcare technologies, achieve the efficient use of healthcare resources, and create healthcare equity. HTA reports can impact regulatory guidelines with respect to market access, third-party coverage for reimbursements, health coverage, the speed with which modern technology is employed, healthcare guidelines, patient and clinical awareness, technology implementation by users, research priorities, data collection, technology marketing, and resource allocation (Goodman, 2014).

The six-stage model illustrating HTA impact from study to health and economic outcomes includes the following (Millar et al., 2021, Goodman, 2014):

1. Awareness from relevant stakeholders
2. Acceptance of a justified basis for action
3. Policy processes that use HTA reports
4. Policy decisions that refer to HTA reports
5. Practice defined as precise action in accordance with policy decisions
6. Outcomes defined as health and economic results based on policy reform

Figure 1: The Six-Stage Model for HTA Impact

Source: Swati Sharma (2022), based on Millar et al. (2021).

HTA Goals

HTA intends to guide and propose safe, efficient, and patient-friendly healthcare policies and ensure the best outcomes and decisions for stakeholders (Health Equality Europe, 2008). The role of HTA is significant for determining and impacting the following health-care aspects.

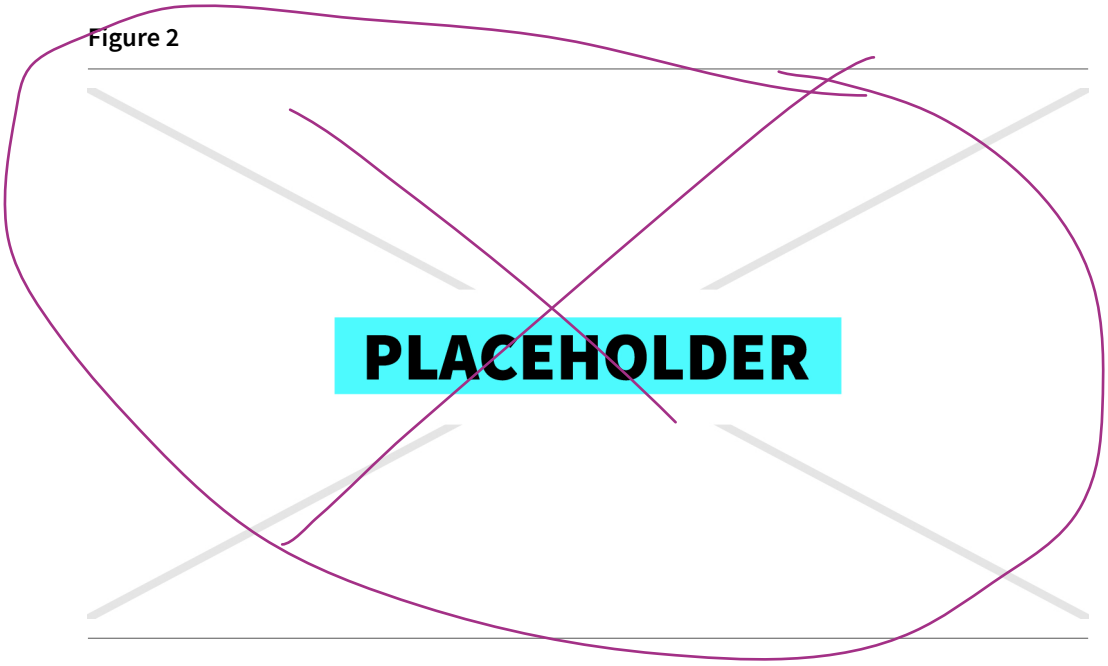
Patient treatment and reimbursement policy

Decisions by HTA will determine whether patients should receive reimbursement for specific treatments like operative surgery or chemotherapy, which subgroup of patients should receive treatment and when, the patient shortlisting criteria that will be followed for reimbursement, and the treatment duration covered by reimbursement.

Impact of the pharmaceutical industry

HTA guidelines play a significant role in aiding recommendations for the use of pharmaceuticals. Both HTA agencies and pharmaceutical companies need to work together to overcome the existing challenges. The economic impact and cost-effectiveness are assessed for market approval. Clinical trials are planned to evaluate the economic and patient benefits, as well as relevant clinical endpoints. The pharmaceutical industry pursues harmonization of international guidelines for economic evaluation.

Figure 2



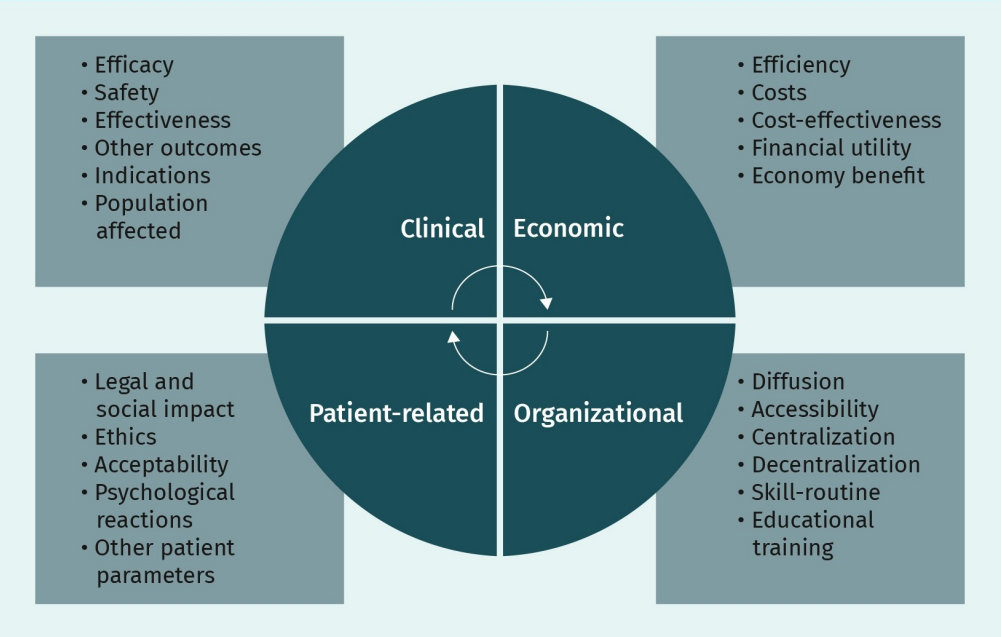
Impact of technology on healthcare

One of the key goals of HTA is to assess the impact of technology on healthcare services. Technology has a key role in reviewing proof or evidence from existing users. Clinical trial reviews, financial assessment, and impact on healthcare services can be efficiently assessed by HTA. Law and ethics in public health reflect societal values in the context of social, economic, demographic, epidemiologic, and political changes specific to each country. As technology and societies continue to evolve, new health challenges arise (Tulchinsky & Varavikova, 2014). The impact of technology from a legal perspective is highly relevant, e.g., the use of the abortion pill or certain “lifestyle” drugs. These are not mere ethical debates but involve country-specific legislation and expertise.

Priority setting

Setting the right priorities is significant for appropriate resource allocation of public funds, for example, in the case of whether public money should be spent on establishing a palliative care facility, a cancer research department, or a psychiatric clinic. When selecting patient-specific treatment regimes, some patients may be responsive to certain therapies while others may not respond. Healthcare organizations must prioritize decisions on implementing modern technologies.

Figure 3: Impact of HTA



Source: Swati Sharma (2022), based on Bowen et al. (2009).

Key elements in a health technology assessment are as follows:

- unmet medical requirements
- clinical treatment or healthcare technology that addresses needs
- evidence or technology review from current users
- economic viability and value of technology

The review of existing evidence will reveal if the technology is effective, relevant, and applicable in the current country-specific healthcare setting or whether it has become obsolete and needs to be replaced. If the technology is still functional, how does it support the stakeholders and who is directly affected? What are the costs to healthcare service providers and patients? Are the priorities right, and have alternate opportunities been explored?

Impact Mapping of Cost-Effective and Equitable Healthcare Systems

Impact mapping is performed to model and analyze the impact of HTA institutions. General outcomes and consequences are profiled using a reverse mapping strategy to determine how individual steps influence the impact of HTA (Millar et al., 2021). HTA's impact can be assessed using the following criteria:

1. Efficient management of HTA studies
2. Optimum application of HTA for schedule and goal setting, as well as policy conceptualization and formation
3. Successful engagement and exterior conversation

4. Excellent organizational influence and involvement of HTA institutions in healthcare structures and systems
5. Efficient application of HTA as a strategy for the health technology price deal
6. Effective administration and application of policy reforms

1.3 HTA Instruments

The assessment and appraisal functions of an HTA make up two separate packages in the evaluation of health technologies. The assessment function may be conducted by one entity whose role is to critically review the evidence, while a separate entity may carry out the appraisal function, the objective of which is to review the existing evidence, considering broader aspects. Accordingly, advice or suggestions are provided based on the assessment and appraisal (Health Equality Europe, 2008).

Assessment

Assessment
This is the procedure by which the health technology institution assesses the existing evidence to reach a valid outcome regarding the technology being assessed.

Cost-effectiveness
This is the ratio that commonly measures the costs associated with a unit of benefit, or the benefit produced with a unit of costs.

The **assessment** process varies for each country, depending on country-specific needs and requirements (Velasco-Garrido & Busse, 2005). It also varies with the assessment purpose. HTA assessments related to medicines are initiated by the company with dossier submission to the relevant healthcare agency. In the case of non-drug-related interventions, a systematic review of existing publications is performed. The dossier contains comprehensive evidence regarding the efficiency of modern technology and a comparison of existing technologies. The economic impact of recent technology on a health system's finances or its **cost-effectiveness** is also assessed by the HTA.

Furthermore, a comparative cost-effectiveness evaluation – an additional clinical benefit – is measured. The assessment tends to include more quantitative elements, while the appraisal incorporates more qualitative elements, such as legal and ethical aspects. Elements include the following:

- **patient pool:** This is the subpopulation to be included in the HTA study.
- **disease impact:** This is the qualitative analysis of untreated patients, including additional costs to the public exchequer.
- **intervention:** This is how an administered drug acts on patients when delivered, for example, by intravenous injection or oral tablet.
- **efficacy and effectiveness of therapeutic intervention:** Efficacy trials, referred to as explanatory trials, indicate whether an intervention leads to the expected outcome. Effectiveness trials, referred to as pragmatic trials, assess the scale of the advantageous effect in clinical situations. Study designs detailing the effectiveness trials are created depending on situations of everyday clinical practice and the results necessary for clinical research and everyday decision-making (Gartlehner et al., 2006).
- **cost-effectiveness:** Cost-effectiveness is calculated by analyzing the same outcome from distinct treatments and interventions, such as the number of cardiac arrests and mortalities prevented. Cost efficacy is one of the decisive criteria deciding whether additional interventions should be prioritized.

- **monetary impact:** It is important to analyze the economic impact of HTA with regard to implementation costs. Some of the HTA-sponsored studies do not cover the total cost of putting new treatments into practice, such as training requirements. These can prevent new treatments from being taken up and should be considered in the economic analysis (Guthrie et al., 2015).
- **innovation:** Innovations in healthcare, such as precision-medicine interventions, are expected to boom in the coming years. Innovation will transform the way the healthcare industry functions, encompassing various aspects from patient care to healthcare management and assessment. For instance, complexity and unpredictability regarding delivery of therapies employing biomarker data and applying advanced AI-based technologies will be challenging. However, global healthcare systems will have to reassess their strategies and assessment systems to implement changes and upgrade redundant systems, continually evaluating the monetary value of new treatments and services (Love-Koh et al., 2018).
- **availability of therapeutic alternatives:** Alternate therapeutic interventions to replace traditional therapies and treatment strategies need to be discussed.
- **health equity:** The evaluation of how novel therapeutic treatments may influence uniform access to healthcare resources, for example, if people with a low socioeconomic level should be prioritized for treatment.
- **public health impact:** This is the assessment of how change in treatment may generally affect public health; for example, advanced therapy to treat cancer may reduce the mortality rate of cancer patients.

HTA institutions in each country have adapted guidelines to make decision-making more uniform and justified for HTA agencies in various countries.

Appraisal

HTA aids decision-making at the policy, clinical, and management levels. Reimbursement discussions among healthcare providers concerning novel health technology can be complex; thus, HTA influences these negotiations and decisions. The analysis of evidence should be separate from **appraisal** and decision-making (Hettle et al., 2017). Entities such as regulatory agencies, public sector HTA agencies, government-sponsored institutions, and organizations performing appraisals will make suggestions depending on the results of evidence assessment, in addition to cues from regional healthcare policies and impact and stakeholder declarations. Based on HTA procedures, the outcome is either to include or exclude the new therapy or technology for or from reimbursement, respectively, in health insurance agencies. Available evidence regarding an intervention may not always constitute full proof. Thus, multiple strategies, including published scientific literature or clinical trial-based evidence, should be used for making valid conclusions. A group is assigned the task of appraisal procedures to make recommendations. Economic impact is one important consideration by HTA agencies when deciding whether a new therapy is recommended for market launch. In the case of national emergencies, how can economic impact be managed by HTA agencies and a wider group of stakeholders?

Appraisal
This is the procedure of employing the assessment evidence to provide suggestions regarding application of technology. It may be country-specific, keeping in mind the value of this technology in relation to their own national interests.

For example, the UK's National Institute for Health and Care Excellence (NICE) is responsible for conducting HTA on behalf of the National Health Service (NHS). NICE invites citizens to support the decision-making process in the form of a citizens' jury model. Such a

jury informs and aids NICE appraisal committees with their functions (Charlton, 2020). To justify its recommendations to the NHS about which technologies to fund, NICE has adopted two complementary ethical frameworks: a procedural framework – accountability for reasonableness (AfR); and a substantive framework – and ethics of opportunity costs (EOC) that is based on the concept of allocative efficiency. Findings from a study that empirically investigates the normative changes to NICE's approach analyze whether these enhance or diminish the fairness of its decision-making, as judged against these frameworks. Accelerating the characterization and rationale of NICE's strategy and undermining the strain of evidence that emphasizes technologies downplay its association with EOC. This indicates a reduction in allocative efficiency and a switch in the manner that NHS delivers to various users, accommodating those who benefit directly from NICE's guidance. These modifications diminish NICE's commitment to AfR by reducing the transparency of its decision-making and by supporting the implementation of concepts that cannot be demonstrated to meet the associated circumstances. This indicates a requirement for the meaningful upgrading of NICE's approach, or the adequate communication of the ethical reasoning on which it relies. These reports highlight the necessity for empirical work to assess the impact of these policy reforms on NICE's implementation of HTA.

NICE Citizens Council Reports have often contributed to the improvement of processes. Some examples of such changes in process within the assessment and appraisal phases have been documented by NICE and discussed in the literature (e.g., Goobermann-Hill et al., 2008).

Assessment process examples

The following two phases are examples of assessment processes:

- Members of the public and patients can suggest topics of interest through an online form, which the NICE appraisal committee can consider.
- Technology that is used by the patients is compared with alternate medication or therapy.

Appraisal process examples

The appraisal process proceeds as follows:

- The appraisal starts with consultation of the appraisal committee with groups of stakeholders, such as patients or caregivers, hospitals, public, technology producers, and clinicians, who are applying this technology in healthcare settings.
- After data collection, an assessment report on clinical efficiency and economic efficiency of the technology is generated.
- The appraisal committee critically reviews the report.
- Evidence and suggestions from clinicians and other stakeholders are invited.
- The appraisal committee provides provisional or arbitrary reports regarding technology. Suggestions and comments from stakeholders are invited.
- All comments and suggestions are considered in discussion, after which recommendations are made to NICE.

- The final report is published by NICE for use by government agencies, such as the NHS, and stakeholders who directly intend to use the technology.

SUMMARY

HTA is a diverse and multi-disciplinary process. It aims to regulate governance in healthcare. HTA involves structured assessment of characteristics and impacts of healthcare technology. There are various types of policy research and analysis on health and resource use, such as foresight, economic analysis, systems analysis, and strategic analysis. Historically, country-specific HTA guidelines consider distinct socio-political complexities prevalent in each country. The HTA review influences health-policy-based decision-making. The overall purpose of HTA is to impact patient treatment and insurance reimbursement policies and market drug approval policy and assess the impact of technology, priority setting, and impact mapping. Two key instruments of HTA are assessment and appraisal, which can be conducted by one or more institutional agencies. Assessment focuses on the critical review of the evidence and appraisal focuses on the review of existing evidence. Based on assessment and appraisal, new suggestions and policy changes are recommended by institutional agencies.

UNIT 2

BASIC PRINCIPLES OF EVIDENCE-BASED MEDICINE (EBM)

STUDY GOALS

On completion of this unit, you will be able to …

- learn the basic principles of evidence-based medicine.
- understand the three theories of causation.
- learn how to search for medical literature and design a research study.

2. BASIC PRINCIPLES OF EVIDENCE-BASED MEDICINE (EBM)

Introduction

Health technology assessment (HTA) serves as a bridge that links research and decision-making. It provides the knowledge developed in scientific research for making decisions. HTA collects and analyzes data from research and uses them for making recommendations. It shares fundamental principles with evidence-based medicine (EBM) and clinical practice guidelines and develops best practice initiatives (Perleth et al., 2001). HTA is policy-oriented, while EBM focuses on supporting decision-making at the clinical and patient level.

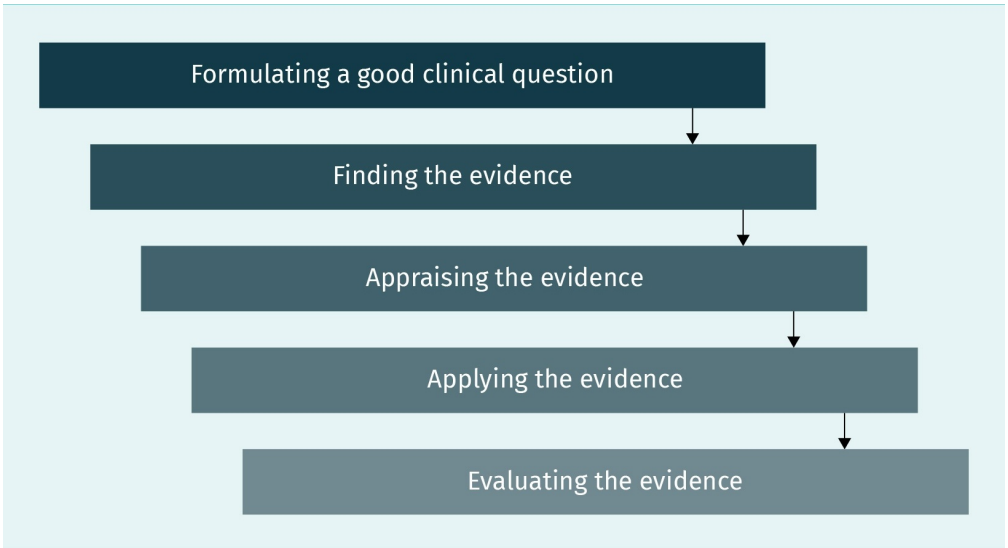
2.1 What is Evidence-Based Medicine?

The concept of EBM, introduced in the 1980s, has great clinical relevance (Pannucci & Wilkins, 2010). It is defined as a combination of clinical proficiency, patient principles, and best available information in the decision-making process related to patient healthcare (Masic et al., 2008). EBM promotes scientific data-driven and research-based decision-making by clinicians. Randomized control clinical trials provide valid scientific proof of the benefits and harmful effects of new and existing drugs. It is significant for predicting accurate diagnoses, making precise prognoses, and devising effective therapeutic treatment plans (Akobeng, 2005). EBM refers to the use of best evidence in decision-making about individual patients. Decision-makers need information about available options and potential consequences. Some interventions thought to be beneficial, after careful evaluation, turn out to be harmful or of no benefit. This has led to the emergence of EBM (Akobeng, 2005).

The Five-Step EBM Model

The practice of EBM involves five key steps: transforming information needs into answerable questions, identifying best evidence to respond to questions, critical review of the evidence for its validity and usefulness, applying the results of the appraisal into clinical practice, and evaluating performance (Sackett et al., 2000).

Figure 4: Five-Step Model for Evidence-Based Medicine



Source: Swati Sharma (2022).

Formulating a good clinical question

The first step is to formulate a good clinical question. “Background questions,” referred to as “general questions,” and “foreground questions,” referred to as “patient-oriented questions,” are important for the clinicians to formulate good research questions (Aslam & Emmanuel, 2010). For instance, if a child is suffering from a hereditary disorder, inherited from the mother, and the mother is expecting another baby, how could the probability of transmitting the hereditary disease be eliminated?

Good clinical questions should be framed in PICO (patient or problem, intervention, comparison, outcome) format (Akobeng, 2005). “Patient or problem” refers to a particular subpopulation, features, and sociodemographic profile regarding the specific age range, biological sex, and case history. “Intervention or treatment of interest” refers to therapeutic treatments, procedures, diagnostic tests, risk of predictive factors, and corrective treatment or surgical procedure. “Comparator or control” is used to compare an advanced treatment or therapy to an existing therapy. “Outcome” refers to the result of the intervention, which should be measured quantitatively and accurately, and be reproducible (Aslam & Emmanuel, 2010). See, for example, the following question: “Is adherence to daily exercise associated with reduced risk of obesity?” In this case, the population refers to the adult population with a history of obesity, the intervention is the daily exercise, the control is no exercise, and the outcome is reduction in obesity.

In addition to PICO, FINER (feasible, interesting, novel, ethical, and relevant) criteria should be followed in framing research questions (Hulley et al., 2007). “Feasible” refers to sufficient time, staff, and funding resources by following a well-designed study design of a research question with a defined scope, sufficient sample size, and trained research staff. Research questions should be made “interesting” to scientists, healthcare professionals, researchers, and principal investigators. The “novel” criterion suggests that the research

should result in new publications and literature search findings, with expert supervision from senior investigators and research experts. “Ethical” guidelines are expected to be followed by complying with the regulatory requirements that entail approval from the Institutional Review Board. The research must have “relevant” impact on clinical practice guiding research and health policy. According to the FINER criteria, feasibility is assessed by conducting a proof-of-concept study. Cost-effectiveness is maintained by hiring a statistician and bioinformatician, selecting a cheaper design and outcomes, and assessing the cost of each component of the study, staff members, and other infrastructural resources. In case a sufficient number of patients is not reached from the target population, inclusion and exclusion criteria can be modified accordingly.

Finding the evidence

After a good clinical question has been formulated, the second step is to search for relevant evidence that will provide the answer to the clinical question. Evidence can be sourced from medical journals and electronic databases, which treat specific problems and diseases. These sources are expected to be valid, clinically relevant, accessible, comprehensive, and user friendly (Masic et al., 2008).

Appraising the evidence

It is important to assess the validity and significance of published information and evidence. The articles must be critically assessed by careful evaluation and analysis of methodology, contents, and conclusions. The appraisal of evidence should be conducted with an objective of evaluating and judging the validity of the methodology and whether an identical strategy should be adapted? Thus, skills to critically evaluate the evidence should be acquired, similar to other clinical skills.

Applying the evidence

The fourth crucial step deals with the application of evidence in the process of EBM. Decisions are required about how to apply acquired information and knowledge to situations concerning each patient. It is important to answer several questions before applying the decisions to the results of the study. Are the patients in the study identical to the patient cohort in the study in question? Is the healthcare system ready to treat the patients and are facilities up to standards? What alternative options are available? Do the side effects of the drug or procedure exceed the benefits of the treatment? Are the results adequate for the patients, and do they align with patient values? It is important to take necessary steps in consultation with the patients if there are any chances of harm to the patient.

Evaluating the evidence

The final step is the evaluation of the evidence-based approach and the efficiency of its application in a clinical setting to patients. It is important to evaluate whether specific evidence applied to patients will be beneficial and to what extent the results can be replicated by research. If there are any discrepancies, it will be imperative to answer why some patients do not respond in the expected way to the modifications introduced and how that can be modified.

2.2 Causation

Causation can have different meanings when elucidated and understood from different perspectives (Kerry et al., 2012). The three general distinct theories of causation are interventionism, counterfactual dependency, and regularity.

Causation
This term refers to the relationship between cause and effect.

Interventionism or Interventionist Theory of Causation

The interventionist theory of causation suggests that causal relations can be analyzed by systematic interventions (De Grefte & Gebharter, 2021). Over the years, different definitions of interventionism have been introduced. It was originally more about the causal connections between random variables (e.g., alcohol drinking habit is causally relevant for whether liver cancer occurs) than about the causal relations in peculiar events (Satish drank each day from 1995 to 2010, resulting in liver cancer in 2013). Interventionism refers to the addition of an intervention to the existing scenario (Kerry et al., 2012), for instance, the impact of introducing modern technology or a drug medication to a particular population. Why do we conduct Randomized Control Trials (RCTs) and observational studies? How do strategies employed at one end connect with, e.g., case studies and research reports? Causation can be deduced from interventionism exclusively. Thus, it is important to include dominant research methods, which are fundamental to evidential frameworks.

Counterfactual Dependency

Counterfactual refers to the control or reference group. Kerry et al. (2012) consider a counterfactual as the truth maker of causation. Events occur consecutively, one after the other, but causation is observed if similar regularity is missing in the second situation. Thus, in healthcare, causation is counterfactually dependent. The accounting issue still exists for causal claims depending on observational studies. For instance, drinking alcohol leads to cancer. It could comply with the **GRADE** statement, which entails the grading of recommendation, assessment, development, and evaluation. According to the Scottish philosopher and economist David Hume (1711–1776), this is considered a counterfactual condition, and causation can be completely depicted by complying with the three criteria: temporal priority, contiguity, and constant conjunction (Hume, 1739; Kerry et al., 2012).

GRADE
The GRADE statement refers to grading of recommendations, assessment, development, and evaluation.

Regularity

Regularity refers to the perspective of causation that provides theoretical and logical views for aiding in causal claims from observational studies. Continuous regularity of one event after the other is observable. As per Hume (1739), medical science has no difficulty in interpreting any causes besides regularity. Thus, causation is said to be one event followed by another event.

Dispositional Account of Causation

Dispositional account of causation refers to an account that offers an appropriate solution to the identified problem. Based on evidential frameworks, it is demonstrated that causation can be better investigated and understood using established methods and causal

accounts. A dispositional account highlights the significance of background situations in understanding causes. The association of causes to specific case-by-case situations in an evidence-based practice framework is elaborated (Kerry et al., 2012). Dispositionalism considers causation to be primitive, such that causation cannot be reduced to noncausal effects (like regularity or counterfactual dependence). Research strategies, such as RCTs, make causal claims; however, they rely on a Humean view, which considers causation as an observed series of events with and without counterfactual support. It leads to interventionism defined as anything in a new situation that may causally influence the situation.

Dispositionalism is associated with counterfactuals, in the sense that counterfactual truths have dispositions as their truth makers. Counterfactually deduced results are considered clinically valuable, like outcomes from RCTs. Counterfactual dependency suggests that previous records of results or outcomes will be a cause of this; in contrast, a dispositional account only counts those factors as causes, which favor the outcome. For instance, consider the case of two alcoholics; the probability of them receiving a cancer diagnosis will be distinct. A person who drinks alcohol and is genetically prone to suffer from cancer is more likely to have cancer compared with someone with no family history of cancer. Causation is associated with the habit of drinking alcohol, and it is linked with different physiological responses, rather than statistical outcomes.

Dispositionalism connects to regularities, as there is a force that inclines toward the effect (Copley, 2018). This suggests that there is a regularity from cause to effect, like drinking alcohol or smoking leading to cancer. But not all those who smoke or drink have cancer. Thus, the presence of a tendency is not sufficient to generate an effect. If an effect does not occur due to a cause, this may be a counter-example of dispositionalist causation. Identical causes in distinct scenarios may lead to generating distinct results and conclusions. For instance, if two medications are administered separately, they may lead to different outcomes; alternatively, when two medicines are taken together, the outcome might be completely different.

Factors Supporting Causal Relationships

A causal factor can be defined as an unplanned, unexpected cause of an event. Therefore, the elimination of the factor will prevent the event from occurring or will decelerate the intensity of the event. According to the U.S. Federal Drug Agency in an individual case report, it is almost impossible to know accurately whether a specific event was caused by a particular product. There are no international standards or criteria for evaluating causality in specific or individual cases. For instance, in cases like brain stroke or cardiac arrests, it is difficult to establish causality. Thus, rigorous case control and long-term cohort studies will be required, which can be monitored for a longer period. It may be difficult to identify causality in cases of polypharmacy, that is, where patients are taking multiple drugs; of heterogeneity in clinical response; or in cases of disease history.

The following factors support causal relationships, including strength of the association between factors, consistency of the association, biological plausibility (in clinical studies), and the dose-response relationship in cases of drug approvals (Kerry et al., 2012).

2.3 Searching the Medical Literature

Literature searches are conducted for compiling and writing the introductory section of all quantitative and qualitative journal articles (including review articles) (Siddaway et al., 2019). Before searching the literature, the research question is assessed in the context of the study design, required sources are determined, it is verified that it is interesting and significant, the literature review is conducted, the data are analyzed, and the research outcome is summarized (Cooper et al., 2018).

Research Question Identification

Identifying a research question based on the PICO model is the first step. This helps researchers generate keywords that can be used for a database search at a later stage. With the PICO model, the question is divided into subquestions and concepts, which can lead to an either a wider or more in-depth search. A preliminary exploratory search is performed with databases like PubMed Clinical queries, Google, Books, DynaMed, and UpToDate. It should be confirmed whether the question or part of the question has not been previously investigated by any researcher. The research question should be confirmed based on a preliminary investigation.

Planning the Literature Search

Generally, the available literature on any topic is enormous; therefore, careful planning is necessary to search for the most relevant and useful publications and references during a literature search. Past literature not only provides information on a particular topic but also provides insights into the types of areas and approaches to the topic taken by previous researchers. What are the overstudied and understudied research questions? What was the rationale for the study? Which methodology proved to be useful? What were the drawbacks of the previous methodologies? What were the findings applied and were those strategies beneficial or not? All these questions can be efficiently answered by planning an effective literature search, which saves plenty of time and resources. It helps to interpret ideas and identify drawbacks and opportunities. A systematic and well-structured review of previous research studies may aid in designing a good research question (Grewal et al., 2016).

A literature search can be planned by employing the following available research methods, which can be used efficiently by the database selection. Databases such as Medline, Embase, Scopus, and Web of Science are used to conduct literature searches. The search strategy is defined with keywords and index terms. High-impact references are identified by finding those references that are most cited on the topic. Articles may be either research or review articles. Initiating the search with a high-impact reference will be useful in identifying and shortlisting the most cited and relevant publications on the topic. It is important to select keywords together with subject headings, as this may lead us to novel concepts on the topic. Symbols like asterisks (*) are used with search terms to provide additional combinations of the root term. Instead of abbreviated words, full forms should be used to achieve the best search outcome. Subheadings are used to describe vocabulary terms within the database. Headings and subheadings indicate the most significant infor-

mation from an article. Medical Subject Headings (MeSH) used in PubMed provide a database of such terminology, known as MeSH terms. Boolean language terms like AND, OR, and NOT can be used to include, exclude, or add a few terms. Clear inclusion and exclusion criteria are specified. Any peculiar features of the articles that we expect to be included in the literature search should be specified. Criteria such as date of publication, article type, language, and study type can also be included.

Conducting the Literature Search

The literature search should be conducted by customizing the search based on the particular database. Databases retain a record or history of search strategies employed during literature searches and a record is maintained on the search portals. Citation mining should be applied to search for additional literature, which may have been overlooked during the primary search. This involves further searching for the key citations to mine relevant references. The Web of Science, Google Scholar, or Scopus can be used to search these references.

Saving and Sharing

Most databases like PubMed offer the opportunity to save, store, and share the searched literature. It is possible to save several search iterations of the selected strategy. Similarly, references can be saved for organizing, storing, and sharing using the reference managers. Reference managers can store references in searchable databases, attach PDFs, auto-generate citations, and create references in a selected formatting style in manuscripts. There is also the possibility to share references with other users, in addition to synchronizing them with other electronic devices. Most of the newer reference managers focus on the aspects of collecting and storing references and writing manuscripts. A number of these newer tools are web-based in order to facilitate and accelerate the process. Many reference managers now have integrated PDF viewers for research articles. Reference managers are also being upgraded to handle other types of literature and scholarly content, ranging from presentation slides to blog posts and web links. Open-source software and open standards play a key part in reference management.

Tools like Citavi, EndNote, JabRef, Mendeley, RefWorks, and Zotero are commonly used by researchers to manage databases of academic references. JabRef and Zotero are free, open-source products.

Staying Updated

Databases are constantly being updated with the most current information and the most recently published literature. Email alerts for new publications can be set up from a specific database. Similarly, social media and journal subscriptions are other means of staying updated regarding any recent publications in the field. Various stages involved in literature searches are included in the flowchart below.

Figure 5: Flowchart Depicting Various Stages Involved in Literature Search

Source: Swati Sharma (2022), based on Cooper et al. (2018).

Tools and Resources

Medical literature can be categorized as primary, secondary, and tertiary literature (Maggio et al., 2013). Primary literature includes original research data and peer-reviewed research articles published in journals, conference proceedings, dissertations, and correspondence.

Secondary literature includes evaluations from primary source articles, such as abstracting and indexing services, review articles, meta-analyses, and practice guidelines.

Tertiary literature includes summarized collections of primary and secondary literature, sources such as reference textbooks, encyclopedias, and handbooks.

2.4 Study Design and Strength of Evidence

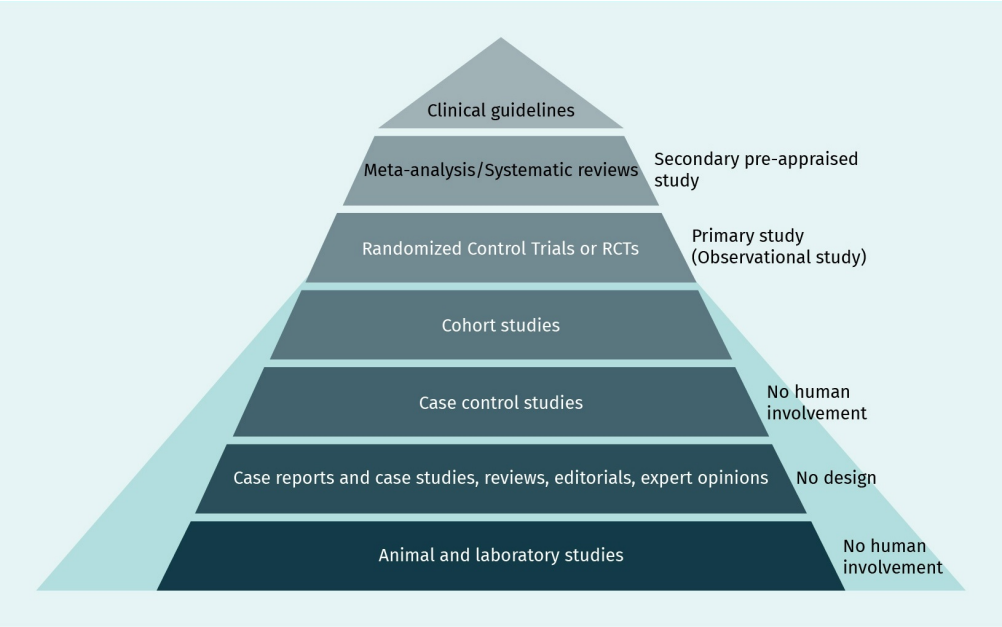
The evidence is drawn from research; thus, it is important to consider the hierarchy of research design and the quality of research execution. However, there is no universal hierarchy and study designs can be ranked in any order (Velasco-Garrido & Busse, 2005). The hierarchy of studies for obtaining evidence is as follows: systematic reviews of randomized control trials (RCTs); controlled observational studies; and uncontrolled studies, such as case reports. The hierarchy is dependent on the issue being investigated. The Centre for Evidence-Based Medicine (CEBM) has outlined different levels of evidence for clinical research questions dealing with diagnosis, prognosis, therapy, and treatment benefits.

For instance, cohort studies involving a group of people are rated higher than individual case studies, as they are followed over many years to ascertain how specific variables, such as smoking habits, exercise, occupation, and geography, may affect the outcome. In contrast, individual case control studies (for rare diseases, for example) may not have a large enough study group to collect sufficient evidence and data.

Levels of Evidence

The Evidence-Based Medicine Pyramid is an illustration used to facilitate comprehension of how the various levels of evidence are weighed for healthcare-related decision-making.

Figure 6: Evidence-Based Medicine Pyramid (EBM)



Source: Swati Sharma (2022).

Each study design is reviewed and analyzed based on the relative strengths and shortfalls of each design. Each level of the pyramid represents a distinct type of study design. As we move through the different study designs, we become more confident that results are correct, that statistical error has been minimized, and that there is a reduced bias from confounding variables that could have influenced the results.

Distinct levels of evidence include systematic review or meta-analysis, evidence from RCTs, evidence from well-designed control trials without randomization, case control or cohort studies, systematic reviews, single descriptive or qualitative studies, and expert committees (Burns et al., 2011; Murad et al., 2016).

The grading of recommendations, assessment, development, and evaluation (GRADE) approach is a system for grading the quality of evidence and strength of recommendations that is clear, comprehensive, valid, and pragmatic; it is increasingly being adopted by organizations around the world.

Table 1: GRADE Recommendations and Evidence Levels

Grade of Recommendation	Evidence Level	Type of Study
A	1a	Systematic review of (homogeneous) randomized controlled trials (RCTs)
A	1b	Individual RCTs (with narrow confidence intervals)
B	2a	Systematic review of (homogeneous) cohort studies of "exposed" and "unexposed" subjects
B	2b	Individual cohort study/low-quality RCTs
B	3a	Systematic review of (homogeneous) case-control studies
B	3b	Individual case-control studies
C	4	Case series, low-quality cohort, or case-control studies
D	5	Expert opinions based on nonsystematic reviews of results or mechanistic studies

Source: Swati Sharma (2022).

Systematic Summaries of High-Quality Study Results

A systematic review is a comprehensive, structured, systematic, and transparent means of collecting, appraising, and processing evidence to answer a well-defined question. In contrast, a meta-analysis is a statistical procedure for combining numerical data from multiple studies. A meta-analysis aims to reduce bias at all stages of the review process.

Systematic review involves the systematic search of literature (Cooper et al., 2018). It is a multistage process initiated by the person who is assigned or eligible to conduct a literature search. A literature search comprises various stages, including establishing the objec-

tives of the literature search, defining a search strategy, searching bibliographic databases, arranging references, and reporting the search process. A systematic review focuses on reviewing the literature and medical evidence available to answer clinical questions (Charrois, 2015).

Meta-analysis entails reviewing literature using statistical tools to analyze and interpret numerical data from research studies. All systematic reviews cannot represent the analyzed/reviewed numerical data, thus a meta-analysis is needed (Charrois, 2015). From 1991 to 2014, a sharp increase of 2,700 percent was recorded in the total number of published systematic reviews and meta-analyses (Niforatos et al., 2019).

When a systematic literature review or meta-analysis is conducted, in case the quality of studies is not properly assessed or if a strategy or methodology is not correctly implemented, the outcome may be biased and inaccurate. Moreover, when systematic reviews and meta-analyses are properly implemented, the results may be on par with large-scale RCTs, which are unexpected in individual or case-control studies.

Randomized Control Trials

RCTs are well planned and have a specific purpose to prevent selection bias by the random scatter of patient characteristics (e.g., age, biological sex, and diagnosis history), which may affect results (Akobeng, 2005). Inclusion and exclusion criteria are established for the patients (Charrois, 2015). RCTs provide substantial proof of the efficiency of interventions because the procedures employed minimize the risk of confounding variables which may distort the results (Akobeng, 2005). The scientific evidence of RCTs is considered the most reliable for concluding the effectiveness of a new intervention or treatment. Not all clinical studies will require RCTs; thus, alternate observational study designs might be required. Randomization refers to assigning study participants to experimental or control groups at random. Appraising an RCT is a process that determines how robust and effective the trial procedure is, the scale and efficacy of the treatment outcome, and the practical usefulness of the result to patients or the population.

Cohort Studies

Cohort studies follow a group of people over an extended period to monitor the impact of drug exposure on their health outcomes. Such studies can be used to detect the long-term impact of a daily dietary habit, for instance, that long-term alcohol drinking habits lead to cancer diagnosis. An additional intervention group is included as a reference control for comparison. It may be challenging to have cohort studies as blinded studies.

Case-Control Studies, Case Reports, and Case Series

Case series reports include very few participants who are administered similar treatment and receive follow-up treatment. Case-control studies analyze retrospective data and compare them to a control group that has received no treatment. A small number of participants is a challenge for analysis (Cooper et al., 2018).

2.5 Sources of Bias

Bias is the tendency to diverge or differ from accuracy in data collection, data analysis, interpretation, and publication, which can cause flawed data interpretation and outcomes. Bias can take place either deliberately or unintentionally (Šimundić, 2013). It is considered the structured likelihood of elements involved with a plan and actions.

The following precautions should be taken to avoid research bias (Pannucci & Wilkins, 2010):

- **bias:** Bias during trials can occur at either pre- or post-trial stages due to failures at multiple levels. These may include a lack of clinical significance of the study question, missing data, poorly identified criteria and outcomes (such as sub-standard diagnostic measures and parameters), selectively reported results, flawed interpretation, and duplicity of results.
- **pre-trial bias:** This may involve a flawed study design, selection bias, or channeling bias. Bias in the study design can be prevented by outlining the risks and expected results, keeping in view the purpose of the study, and following an established, standardized methodology. To avoid bias, data collection should be blinded. Bias during selection can be avoided by following strict inclusion and exclusion criteria for patients and preventing skewed outcomes. Channeling bias can be avoided by structuring cohorts using rigorous selection criteria.
- **bias during study trial:** Interviewer bias can be minimized by following standardized interview procedures and blinding interviewees to exposure status. Chronology bias in research or clinical trial studies can be controlled by excluding traditionally used reference controls. Recall bias is avoided by using objective and subjective data sources in specific circumstances. Objective data sources can be used anytime; in contrast, subjective data references should be cross-checked and tallied with research and clinical data. Transfer bias can occur when patients relocate; a study plan is designed to ensure the number of patients in the cohort. Exposure description requires that drug treatments be predescribed together with the dose regimen. Valid results are considered the valid outcomes and findings from the study. Finally, to avoid performance bias during operative procedures, the study population needs to be stratified.
- **bias after trial:** Citation bias can be prevented by registering for a trial in a clinical trial registry. Confounding bias can be avoided with a study design or during analysis.
- **bias in data collection:** Research studies focus on investigating an event or occurrence of an event of interest. Thus, a limited number of samples are studied to investigate specific treatment groups or a population of interest. Data collection is performed without selection bias. Selection bias is avoided by adhering to rigorous exclusion and inclusion criteria during this data collection (Šimundić, 2013). While collecting data for research, there are numerous ways by which researchers can introduce bias in the study. If, for example, during patient recruitment, some patients are more or less likely to enter the study than others, such a sample would not be representative of the population in which this research is conducted.
- **bias in data analysis:** Data can be analyzed with a bias toward a preferred conclusion to support a particular research hypothesis. Bias can occur through the misappropriation of results, fabricating false data, or by removing or excluding results, all of which produce negative results that contradict the hypothesis. Bias can be created by opting

for weak statistical tests for the sake of showing statistical significance. For instance, perhaps a study aims to demonstrate that one biomarker is associated with another in a cohort of patients, but this connection is not significant in a complete cohort. In this case, researchers may try to divide the patients into various subgroups until they achieve statistically significant differences. If this patient subgroup is not included or mentioned in the original research hypothesis, this type of data analysis would be considered unethical and not generalizable to the whole population.

- **bias in data interpretation:** To avoid bias in interpreting data, appropriate statistical tests are employed for data analysis. Results are reported as the statistical significance of observed relationships (Šimundić, 2013), for example, a discussion of observed differences and associations despite being nonsignificant, a debate on the basis of statistical significance overlooking clinical significance, deriving interpretations on causality, or extrapolation of results to the general population.
- **publication bias:** There is a tendency among journals to publish research studies with positive findings and outcomes compared with negative results. However, publishing negative results is useful for the scientific community, as scientists will avoid repeating similar experiments and save research time and resources (Šimundić, 2013; Tenny & Varacallo, 2018). The medical literature, especially the results of cohort studies, provides evidence of publication bias. A systematic review of 20 cohort studies using RCTs indicates that studies with statistically significant results have a higher chance of being published than those with nonsignificant outcomes. Similarly, another systematic review by Schmucker et al. (2014) examined the results from 23 cohort studies and reported that studies with statistically significant outcomes have higher chances of being published than others (DeVito and Goldacre, 2018).

2.6 Meta-Analysis and Systematic Reviews

A literature review is different from reviewing literature. It provides a detailed, in-depth understanding of the existing evidence to enable the authors and readers to make valid inferences (Siddaway, et al. 2019). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement is designed to guide reviewers to report their objectives, methodology, and findings in an unbiased manner. The updated PRISMA 2020 guidelines propose new reporting guidance that indicates advances in methodology to identify, select, appraise, and synthesize studies. The PRISMA checklist provides a transparent reporting system for compiling systematic reviews and meta-analyses (Page et al., 2021). Salient features of the 27-point PRISMA checklist are outlined below.

PRISMA Checklist

Title

The title should identify the report as a systematic review.

Abstract

The abstract should have the following characteristics:

- The title should identify the article as a systematic review.
- The background (objectives) should provide an explicit statement of the main objective(s) of the review or the question(s) the review addresses.
- Methods should specify the inclusion and exclusion eligibility criteria for the review. Information sources specify the databases and registers used to identify studies and the date when each was last searched. Risk of bias specifies the methods used to assess risk of bias in the included studies. Synthesis of results specifies the methods used to present and synthesize results.
- Results provide the total number of included studies and participants and summarize the relevant characteristics of the studies. Present the results for the main outcomes, preferably indicating the number of included studies and participants for each. If a meta-analysis was performed, provide a report of the summary estimate and confidence/credible intervals. If comparing groups, indicate the direction of the effect (i.e., which group is favored).
- In the discussion, provide a brief summary of the limitations of the evidence included in the review (e.g., study risk of bias, inconsistency, and imprecision); a general interpretation of the results; and the important implications.
- For additional information, mention the funding sources and registration details including name and number.

Introduction

In the introduction, the following two steps must be taken:

- Describe the rationale for the review in the context of existing knowledge.
- Provide an explicit statement of the objective(s) of the review or the question(s) the review addresses.

Methods

The methods section includes the following steps:

- **eligibility criteria:** Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.
- **information sources:** Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify the selected studies. Specify the date when each source was last searched or consulted.
- **search strategy:** Present the full search strategy for all databases, registers, and websites, including any filters and limits used.
- **selection process:** Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved; whether they worked independently; and, if applicable, details of the automation tools used in the process.

- **data collection process:** Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and, if applicable, details of the automation tools used in the process.
- **data items:** List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, and analyses), and if not, the methods used to decide which results to collect. List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.
- **risk of bias assessment:** Specify the methods used to assess the risk of bias in the included studies, including details of the tool(s) used; how many reviewers assessed each study and whether they worked independently; and, if applicable, details of automation tools used in the process.
- **effect measures:** Specify effect measure(s) for each outcome (e.g., risk ratio, and mean difference) used in the synthesis or presentation of results.
- **synthesis methods:** Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis). Describe any methods required to prepare the data for presentation or synthesis, such as handling missing summary statistics or data conversions. Describe any methods used to tabulate or visually display the results of individual studies and syntheses. Describe any methods used to synthesize results and provide a rationale for the choice(s). If a meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.
- **reporting bias assessment:** Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).
- **certainty assessment:** Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.

Results

In the results section, the following steps are involved:

- **study selection:** Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review. Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.
- **study characteristics:** Cite each included study and present its characteristics.
- **risk of bias in studies:** Present assessments of risk of bias for each included study.
- **results of individual studies:** For all outcomes, present for each study, the summary statistics for each group (where appropriate) and an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots.
- **results of syntheses:** For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies. Present results of all statistical syntheses conducted. If a meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If

comparing groups, describe the direction of the effect. Present the results of all investigations of possible causes of heterogeneity among study results. Present the results of all sensitivity analyses conducted to assess the robustness of the synthesized results.
- **reporting bias:** Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.
- **certainty of evidence:** Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.

Discussion

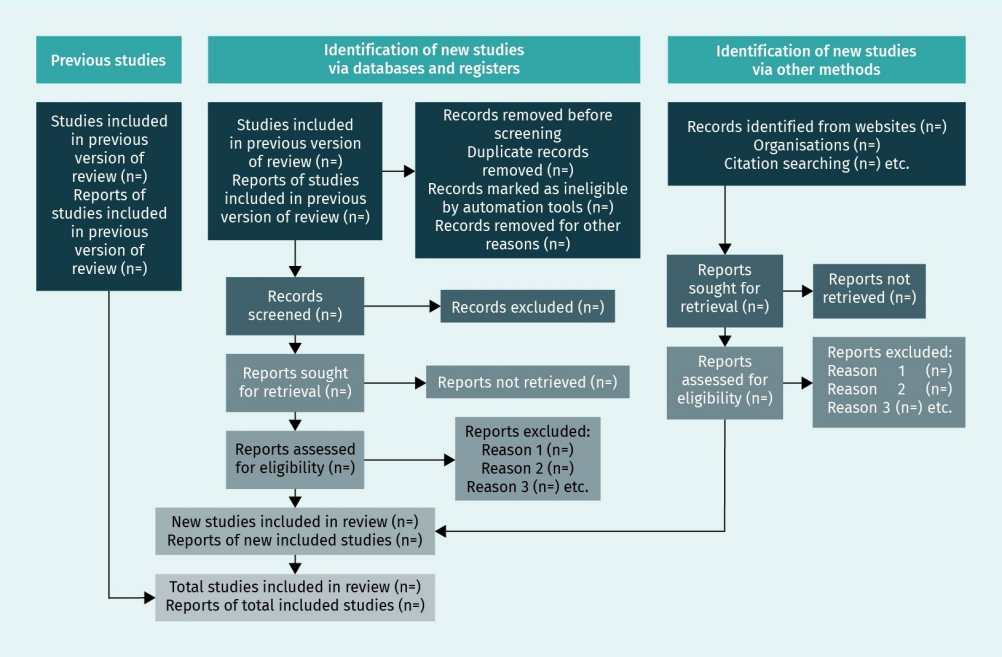
Provide a general interpretation of the results in the context of other evidence. Discuss any limitations of the evidence included in the review. Discuss any limitations of the review processes used. Discuss implications of the results for practice, policy, and future research.

Additional information

Steps for providing additional information are as follows:

- **registration and protocol:** Provide registration information of the review, including the registration name and number, or state that the review was not registered. Indicate where the review protocol can be accessed, or state that a protocol was not prepared. Describe and explain any amendments to information provided at registration or in the protocol.
- **support:** Describe sources of financial or nonfinancial support for the review and the role of the funders or sponsors.
- **competing interests:** Declare any competing interests of the review authors.
- **availability of data, code, and other materials:** Report which of the following are publicly available and where they can be found: template data collection forms, data extracted from included studies, data used for all analyses, analytic code, and any other materials used in the review.

Figure 7: PRISMA 2020 Flow Diagram Format for Systematic Reviews



Source: Swati Sharma (2022), based on Page et al. (2021).

It is believed that implementing PRISMA 2020 will enable readers of the review to accurately evaluate the applicability and validity of the findings. The implications of the review report will aid policy makers, healthcare providers, and decision-makers to develop efficient recommendations for policy preparation and application.

The differences between systematic reviews and meta-analyses are outlined below: A systematic review involves the systematic searching of the literature (Cooper et al., 2018). It is a multi-stage process initiated by the person assigned or eligible to conduct the literature search. Various stages of literature search involve establishing the objectives of literature search, defining a search strategy, searching bibliographic databases and supplementary literature, arranging or sorting references, and reporting the search process. A systematic review focuses on reviewing the literature and medical evidence available to answer clinical questions (Charrois, 2015). In contrast, a meta-analysis deals with reviewing the literature using statistical tools to analyze and interpret numerical data from published research studies. All systematic reviews cannot represent the analyzed/reviewed numerical data; thus, meta-analysis is needed (Charrois, 2015). Systematic reviews should be able to meet the following objectives (Baumeister et al., 2013):

- Make unbiased and valid inferences from a specific research study or data.
- Review literature critically and in an unbiased manner.
- Develop hypotheses and analyze theories to accurately interpret data and identify how separate or independent studies could be interlinked.
- Critically discuss the effect and impact of existing policies and how future studies can provide new research directions.

Reasons for Systematic Literature Review

Systematic reviews provide a balanced summary of the detailed results of individual studies. They thus show whether individual study results fit meaningfully into the overall picture or whether they are outliers. In contrast to individual studies, they are therefore more reliable and leave less room for bias. They tend to be more amenable to publication in higher impact journals. Even if they "recycle" findings, they are considered to often bring a novel and significant perspective. The inclusion and exclusion criteria in a review are very clearly stated. Inferences and conclusions can be linked to the available evidence. It is easy to conduct and compile a systematic review in a structured manner compared with other kinds of review articles. A series of sections and subsections are included to give a coherent flow to the whole review. (Baumeister et al., 2013). Systematic review articles may also highlight if a replication crisis exists in science, and if it can be resolved (Nelson et al., 2018).

Steps in a Systematic Review

Scoping is carried out to determine the scope of the review article. A research question or topic is defined for reviewing. The research question is described and the subtopics to be covered within the scope of the research question are listed and shortlisted. The novelty of the research topic is discussed, and whether similar questions have been answered earlier is established. After the research question has been finalized, the existing literature on the topic is reviewed. It is determined if the systematic review will be an upgrade of an existing review article or if a new review article should be conducted on a novel research theme and topic. The next steps for compiling the systematic review are planned. Keywords for the literature search are identified, and the terminology is searched with alternate terms. The selection criteria are established, the inclusion and exclusion criteria are further refined, and the validity of the criteria is verified. Criteria may include research questions, concepts, variables, research designs for quantitative or qualitative studies, participants, time frame, and data. Data are organized and arranged systematically. The literature search is performed in two distinct electronic databases, such as Medline, EMBASE, and ISI. The outcome of the literature search result is investigated and analyzed; if necessary, additional literature is searched for any relevant publications. After the literature search and screening, references are exported to a citation manager. Identified publications are read and inclusion criteria are rechecked for eligibility to be included in the study. All the significant and relevant information is used in the review. To evaluate the quality of the study, different tools are used.

Reasons for Conducting Meta-Analyses

A meta-analysis is used to conduct a quantitative review and analyze data from different publications that examined and investigated similar hypotheses. A meta-analysis analyzes quantitative data from a group of studies, usually in addition to performing a qualitative analysis (Siddaway et al., 2019). These identical research studies investigate similar data extracted from comparable research designs. A meta-analysis analyzes effect sizes and quantifies uncertainty using confidence intervals. Traditionally, some amount of uniformity or heterogeneity is achieved in study outcomes, as effect sizes can be impacted by varying characteristics. Diverse sources may result in heterogeneity of the studies enrolled

in the meta-analysis. Heterogeneity caused by sampling inaccuracy also exists, as each study employs an independent sample. Other variables,such as the number of participants, exposure or treatment regime, and study design, can lead to population effect size.

Forest plots are used to represent the study effect size and associated confidence intervals; thus, the distribution can be estimated. Meta-analysis data from all the studies can be analyzed to assess the effect on the population.

SUMMARY

EBM emerged as a concept in healthcare three decades ago. It involves the use of the best available evidence for making informed decisions about individual patients. It underscores the significance of scientific data-driven and research literature-based decision-making by clinicians. EBM includes formulating good clinical questions based on PICO and FINER models. Literature searches are performed with respect to the study design, required sources are determined, data are analyzed, and research outcomes are summarized. The theories of causation include the interventionist theory of causation, counterfactual dependency, and regularity. The factors that support causal relationships include strength of the association between factors, consistency of the association, biological plausibility (in clinical studies), and the dose-response relationship (in drug approvals). Precautions should be taken to prevent research bias at various stages, including pre-trial bias, bias during trials, bias after trial, bias during data collection, bias in data interpretation, and publication bias. The literature review provides a detailed, in-depth understanding of existing evidence to enable authors and readers to make valid inferences.

UNIT 3

FUNCTIONS OF HEALTH TECHNOLOGY ASSESSMENT

STUDY GOALS

On completion of this unit, you will be able to …

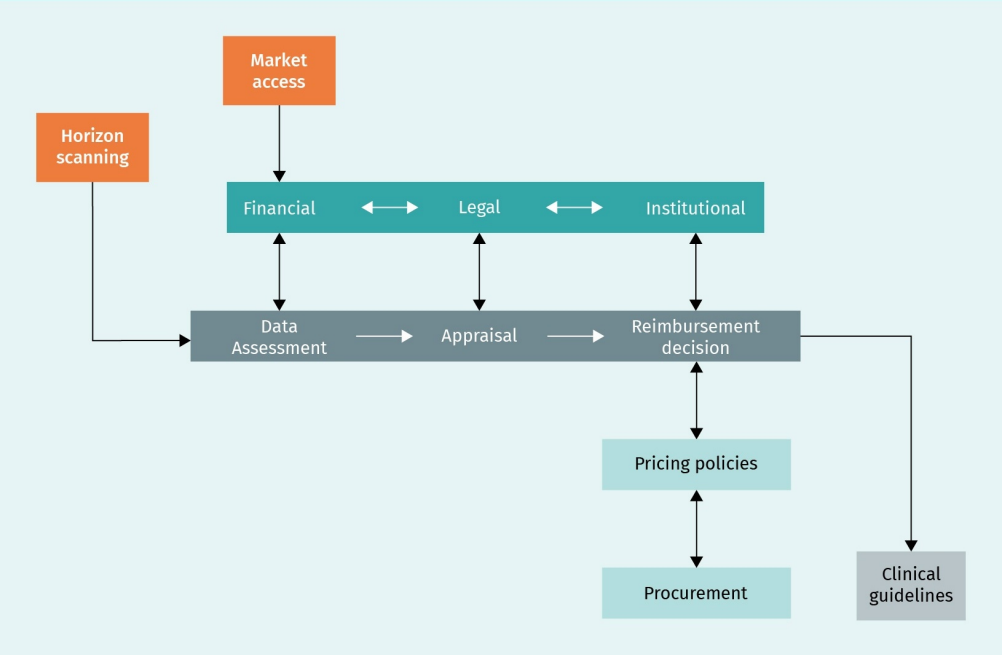
- understand the functions of health technology assessment (HTA).
- understand market access, HTA, and approval.
- evaluate price policies and clinical guidelines.

3. FUNCTIONS OF HEALTH TECHNOLOGY ASSESSMENT

Introduction

The function of health technology assessment (HTA) includes the assessment of clinical evidence and economic analysis necessary for decision-making and the appraisal process that involves strategy, ability, and potential (Bertram et al., 2021). Based on the assessment, the role of HTA is to provide advice to relevant authorities and review and make appropriate recommendations to federal and institutional agencies (Scaletti, 2014). The HTA mechanism encompasses various significant functions, including legal arrangements and institutional systems as outlined in the figure below.

Figure 8: Overall Functions of HTA



Source: Swati Sharma (2022), based on Bertram et al. (2021).

3.1 Market Access

Market access to healthcare technologies requires diligent evaluation, considering stakeholder interests and viewpoints (Ducournau et al., 2019). Different stakeholders, including patients, pharmaceutical companies, manufacturers, hospitals, health insurance companies, government health agencies, and public funding institutions, have diverse perspectives on market access to novel healthcare technologies and products. A process is estab-

lished to ensure all appropriate stakeholders, especially patients, who would benefit from these advanced healthcare technologies have rapid and equal access at an appropriate price. At the same time, patients ought to benefit from timely access to therapeutic interventions that offer clinical and economic value.

Market Authorization Process

Market access is initiated by national registration and approval for market authorization. Regulatory agencies require clinical proof from **sponsors** for safe use and optimum quality and standards. Due to the absence of any binding compliance and requirements for proof of clinical effectiveness, information about market registration is insufficient for decisions regarding market access. Therefore, additional clinical proof is required from the sponsor. Steps are being initiated to acquire more substantial clinical evidence to support decisions regarding market access. Market authorization is initiated by an independent organization with no influence over HTA agencies in the decision-making process. Market authorization occurs prior to HTA assessment; thus, the two institutions must establish a healthy working arrangement (Bertram et al., 2021).

Sponsor
A sponsor is an agency, company, or individual that initiates, manages, and finances clinical trial operations.

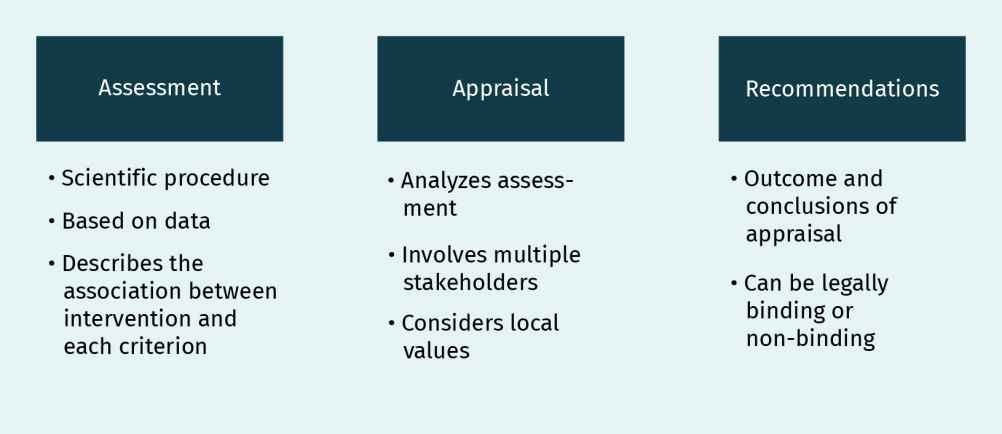
Significance of Regulatory Evidence and Access Evidence in Market Access

Market authorization is provided based primarily on the quality, safety, and efficacy of the technology referred to as "regulatory evidence." Recommendations regarding medical coverage and reimbursement procedures are made by determining the value of the relevant health technology, which is referred to as "access evidence" (Lakdawalla et al., 2018). Access evidence indicates the value of technology to patients, healthcare providers, and healthcare payers by analyzing the advantages of novel technology compared with routine clinical interventions, for instance, achieving better clinical outcomes and improved quality of life (Akehurst et al., 2017). The clinical effects and benefits of health technology to patients are assessed by pharmaceutical companies or technology manufacturers and reviewed in the HTA. This allows HTA agencies to recommend guidelines relevant to medical coverage and reimbursement decisions (Ducournau et al., 2019). The particular characteristics and disparities in different national jurisdictions can create bottlenecks, although efforts are being made to harmonize the process.

3.2 HTA Assessment and Appraisal

Within an HTA, assessment refers to assessing clinical evidence and economic analysis or the cost-effectiveness of particular health technology. Appraisal refers to a type of suggestion or advice regarding the application of technology (Sandman & Heintz, 2014). As outlined in the figure below, the assessment, appraisal, and recommendations are interrelated.

Figure 9: Association Between Assessment, Appraisal, and Recommendations



Source: Swati Sharma (2022), based on Bertram et al. (2021).

Different HTA institutional agencies have specific roles in the assessment and appraisal of health technology (Sandman & Heintz, 2014). This distinction in functional roles is clearly demarcated in countries such as the United Kingdom, where the National Institute for Health and Care Excellence (NICE) conducts the appraisal and recommends new technologies to the National Health Service (NHS).

Similarly, in Sweden, the Swedish Council for Health Technology Assessment (SBU) is the only institution that performs technology assessments, while the county council undertakes the appraisal role. This prevents political intervention and vested interests from influencing an impartial evaluation and assessment of health technology (Banta & Jonsson, 2009).

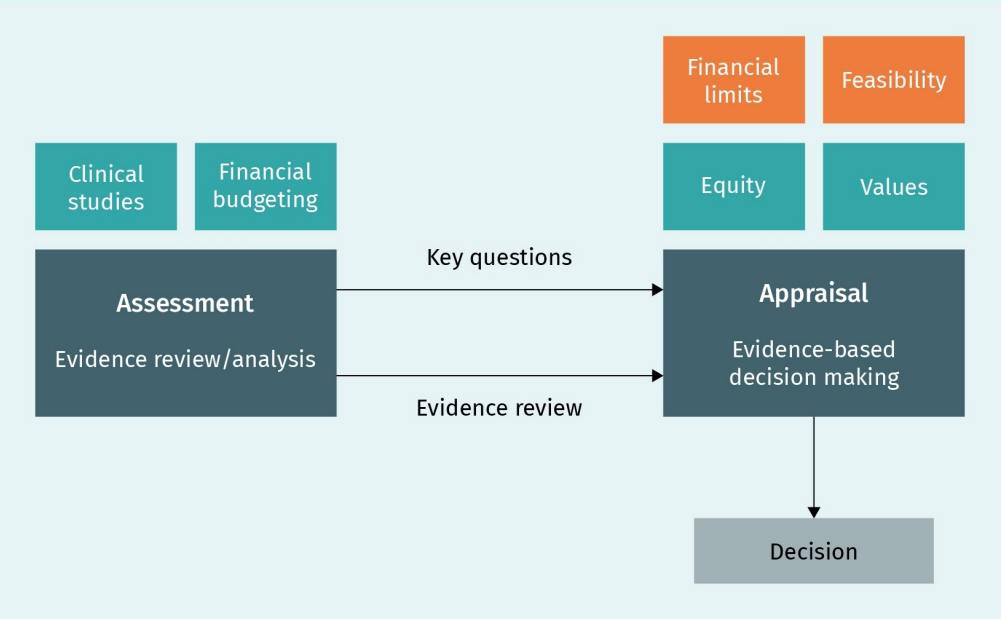
Value Assessment and Appraisal Model

Several studies have employed the Multi-Criteria Decision Analytic (MCDA) model in the assessment and appraisal of pharmaceutical drugs used as therapeutic agents. In an MCDA study, stakeholders assess and appraise technologies using the value measurement concept. Ratings are prediscussed, and scores lead to realistic assessment and appraisal scenarios. The assessment and appraisal of **orphan drugs**, and pharmaceutical agents to treat rare medical conditions offer particularly interesting case studies in this context (Baran-Kooiker et al., 2018).

Orphan drug
This is a pharmaceutical product expected to be used for detection, prognosis, treatment, or safeguarding from life-threatening ailments and rare disorders.

Cohorts of public health stakeholders comprising clinicians and healthcare professionals, chairs or representatives of specific patient groups, officials from health agencies, and pharmaceutical industry executives were included in a 307-participant study in Bulgaria. Participants participated in decision-making on drug reimbursement. A heterogeneous mix of stakeholders in terms of age, biological sex, geography, and pathology, among others, were selected to avoid any bias. Stringent threshold criteria confirm that only therapies used to treat medical conditions with value and monetary incentives were reimbursed with public funds (Iskrov et al., 2016).

Figure 10: HTA Components Assessment and Appraisal



Source: Swati Sharma, based on Teutsch & Berger (2005).

Ethical View on Appraisal

Diverse types of ethical appraisal lead to various outcomes. An appraisal can have different implications based on regulatory or organizational context (Sandman & Heintz, 2014). An appraisal with a positive outcome leads to the implementation of technology or financial allocation for enabling technology access for patient use. A neutral appraisal would lead to a nondecisive outcome on the technology, while a negative appraisal leads to barring the application of the technology (Blank, 2010). In addition, incentives such as funding allocations are often based on appraisal decisions. Ethical decisions have different implications. If a clinical **intervention** is ethically necessary, a possible outcome will be the influence of financial incentives, compulsory implementation, and supporting application in the healthcare system. If an intervention is not apt to be implemented for ethical considerations, its use should be prohibited. Various ethical reasons prevent the application and use of an intervention, and in those scenarios, a convincing argument barring an intervention should be presented. In contrast, if there are strong ethical reasons supporting the implementation of an intervention, funding or the use of an application should be supported. The ethical assessment of HTA is distinct from the assessment of other features such as effectiveness, cost-effectiveness, and social consequences. Ethical analysis directs actions and results in a conclusion, which can be referred to as an appraisal.

Intervention
This is an action performed to evaluate, improve, upgrade, or maintain a person's health.

3.3 Price Policies and Procurement

Innovation in healthcare and the development of advanced therapies has led to improved health treatment and patient recovery rates, despite exerting a burden on healthcare expenditures (Callea et al., 2017). Developing oversight strategies for price monitoring of pharmaceutical products is the responsibility of governments, irrespective of the country's level of economic development or gross domestic product (GDP) (Vogler et al., 2019). HTA is turning into a major gamechanger in priority setting and price negotiations for national and institutional agencies in healthcare. Relevant policy changes and amendments are introduced by national governments to attain universal health coverage (UHC) by providing safe, efficient, and affordable medicines and vaccines, which is one of the Sustainable Development Goals (SDGs) recommended by the United Nations (Glassman et al., 2017). UHC entails providing comprehensive health services, including prevention, treatment, and post-treatment care to the world's population, regardless of people's region, religion, or financial status. Nevertheless, the quest to achieve affordable and homogenous access to healthcare should not weaken or puncture the financial dynamics of the healthcare industry and system.

Different financing and policy pricing criteria are used to establish prices for pharmaceutical and healthcare products (Vogler et al., 2019). "External price referencing" allows price setting in other countries, "internal price setting" establishes prices in a particular country, "value-based pricing" determines prices by including additional therapeutic value to the products, "conditional pricing" offers pricing based on specific conditions such as health outcomes or procurement orders, "tendering" refers to the best offer based on pricing and in reference to other bids, and "cost-plus pricing" deals with production and research and development (R&D) costs.

Buyer-side traders are the investing institutions in financial markets whose trading strategies are important regarding access to pharmaceuticals in low- and middle-income countries (LMICs) (Borges dos Santos et. al, 2019). According to World Bank criteria, fifty-five countries fall into the LMIC category, 20 of which are considered low-income with per capita gross national income (GNI) of less than USD 1,000 and are eligible to seek vaccination support through the Global Alliance for Vaccines and Immunization (GAVI) partnership (World Health Organization, 2020).

Several aspects are impacted by pricing policy, including homogenization of prices, establishing fair procurement policies, and cost-plus pricing across countries. It is imperative to establish criteria for setting prices of each new product, to ensure a fair margin with equitable profit sharing and the acquisition of Intellectual Property Rights (IPR) and healthcare technology rights by governmental agencies in the broader public interest.

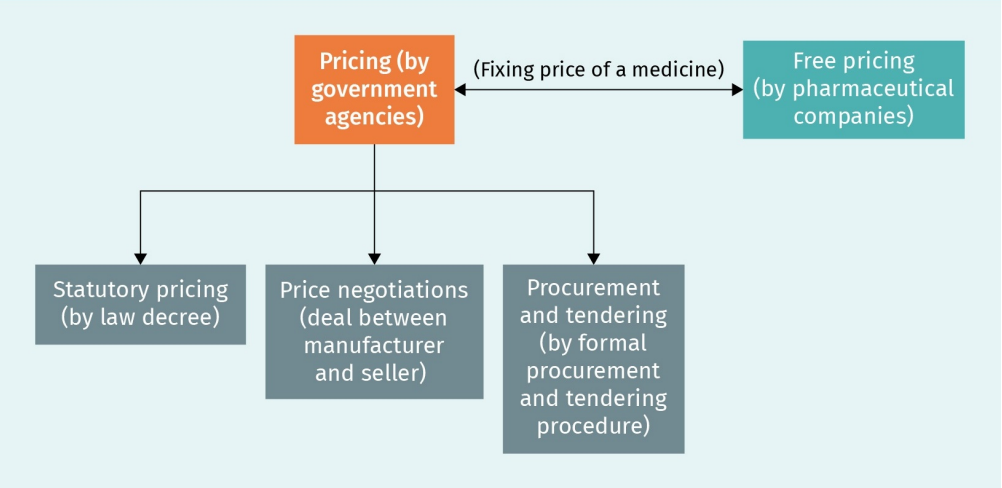
Table 2: Description of Pricing Policy Impact and Limitations

Pricing policy	Impact	Limitations
External pricing policy	Tends to result in low drug prices and can lead to lower public health expenditure	Not easily accessible, nontransparent, expertise needed, and volatile

Internal reference pricing	Reimbursement policy with identical medication clustered, public funding, promotes use of generic medicine, patient pays difference in price	May vary across countries
Value-based pricing	Authorities set pricing, payment of pharmaceutical drugs connected to evidence-based value assessments, assess through HTA	No incentives for manufacturers, enhanced capacity required, nation-specific value assessment
Procurement	Strategic purchasing by stakeholders and effective procurement process	Not done centrally, widely performed in low-income countries
Pricing negotiations	Mutual strategic agreement on medicine prices, price kept confidential	-

Source: Swati Sharma (2022).

Figure 11: Overview of Pricing Policies



Source: Swati Sharma (2022).

World Health Organization (WHO) guidelines are based on the following key principles for establishing country-specific pricing policies, which need to be implemented (World Health Organization, 2020).

- The combination of diverse drug pricing policies fulfills supply and demand.
- Transparency allows clarity in forming transparent policies and decisions.
- Legal guidelines allow an adequate legislative framework. If regulation is introduced, an efficient implementation will be required to ensure compliance (e.g., incentives, enforcement, price monitoring system, and fines).
- The use of optimum quality generic medicine is encouraged by implementing schemes to promote the application and usage of such medication to enable health equity for all.

- Association with other countries is carried out to encourage knowledge exchange regarding pricing policies and their effects.

3.4 Clinical Guidelines

Clinical practice guidelines (CPGs) are developed recommendations to assist clinical practitioners in making patient decisions to optimize patient care for clinical pathologies and treatment (Graham et al., 2011). These guidelines ought to be formulated based on the data acquired by a systematic review of evidence and an evaluation of the pros and cons of alternative therapeutic treatment options. These guidelines draw inferences from the research quality of associated scientific publications and an evaluation of the strengths and weaknesses of specific therapy and intervention. CPG guidelines should be formulated by a group of experts; such panels should represent affected cohorts, patient groups, and subgroups and prioritize accordingly. These guidelines should depend on standard procedures to avoid any bias, distortions, and conflicts of interest. Obsolete and outdated guidelines should be updated as soon as new evidence is available.

According to the CPG manual of the U.S. Institute of Medicine (IOM), practice guidelines are formulated using stringent proof-based strategies with the strength of evidence for each one clearly expressed as follows (Graham et al., 2011):

- These guidelines should be realistic, practical, and quantifiable.
- Clinical actions and measures evolve from clinical practice guidelines and are applied to improve standards.
- These actionable measures are implemented into public descriptions; liability, the strength of evidence, and the degree of interest should be appropriate to explain the charge of execution and accomplishment.
- Application of CPG remains a prime preference of those with the most compelling evidence.
- Those with the most compelling proof and the greatest influence and effect on population are morbidity and mortality.
- Research should be conducted on investigating the strategies to efficiently apply clinical practice guidelines and the effect of their use as standard counts.
- Different agencies recommend specific guidelines based on national and institutional interests.

Generating Evidence-Based Clinical Practice Guidelines (CPGs)

CPGs include suggestions to harmonize patient care that are guided by evidence and data from systematic reviews. These reviews provide a comprehensive view of the pros and cons of alternative therapy and treatment care options. This includes an assessment of the research literature and a fair review of the strengths and weaknesses of specific therapies. Reviewing the literature allows healthcare workers to choose the most suitable and preferred treatment option. Depending on country-specific local jurisdictions, the formu-

lation of CPG guidelines may vary. In some countries, a commission on public health and/or science, together with the board of directors, may oversee the formulation and agreement on CPG guidelines (Graham et al., 2011).

Eight-Point Criteria for CPG Development

The principal standard features for establishing effective CPG guidelines include establishing clarity, ensuring there is no conflict of interest, developing categories of people that focus on guideline development and CPG guideline systematic reviews, ensuring the strength of evidence, suggesting recommendations, conducting external reviews, and upgrading (Reames et al., 2013).

Standard Guidelines

Patient-focused CPG development occurs in collaboration with external organizations such as medical organizations and societies. A clinical subject for CPG is recommended, keeping in mind the following criteria: a lack of evidence-based guidelines on the specific clinical topic, which should comply with the strategic objectives and strategies. The clinical guidelines of the British HTA agency NICE make evidence-based recommendations on the prevention and management of specific diseases to strategically plan a wide range of healthcare services and interventions to upgrade public healthcare services and overall citizen health. (Kredo et al., 2016)

A systematic evidence report on the topic is provided with the availability of a funding source.

Conflict of Interest (COI)

To avoid conflict of interest (COI) and bias in CPG development, certain criteria should be considered (Norris et al., 2012). Members, chairs, co-chairs, collaborators, and sponsors should have no COI in guideline development.

Any **financial** or **intellectual COIs**, involvement, or activities falling under the ambit or scope of CPG should be declared by members through a written declaration prior to their involvement in CPG development. Professional involvement in clinical guideline development, which could amount to a COI, or official involvement by oneself or a close family member (i.e., spouse, siblings, or children) in similar activities within the past three years should be declared prior to official engagement in the guideline development activities. Disclosures and COI declarations are then reviewed by staff prior to recruitment to the CPG development panel.

Financial COI
This is a material interest that could influence, or be perceived as influencing, an individual's point of view.

Intellectual COI
These are actions establishing the scope of an attachment with a specific perspective that may influence a subject regarding a particular aspect of CPG. recommendations.

If required, members can divest themselves of related financial, marketing, or advisory responsibilities from boards of specific organizations whose interests are being influenced by the CPG recommendations. In necessary scenarios, relevant clinical specialists drawing salaries or remuneration may have to withdraw from the services in the case of a COI.

Constitution of CPG Panel

A mutually agreed timeline is proposed to fulfill the CPG development task in the specific time period. A document with specific activities and a list of actions is maintained and updated during the process. Members may be requested to volunteer and participate in specific tasks such as compiling assignments to develop suggestions and providing supporting evidence. An outline is developed with an overview of the significant questions for recommendations and evidence sharing. Members will communicate via different modes, such as conference calls, electronic communication, and publications, and engage in active dissemination via press articles, editorials, and conducting literature reviews (Kredo et al., 2016).

Framing Guidelines

The identification of the scope of the guidelines is the first step. The methodology must be mentioned, such as a summary of the literature search, use of evidence reports, search terms, dates, outcomes assessed, and important questions. Recommendations are based on the evidence from the linked articles. The grading of the strength of evidence and recommendations is performed. Panel writing assignments are assigned to those members of the panel involved, and the draft is compiled with the appropriate recommendations.

3.5 Horizon Scanning

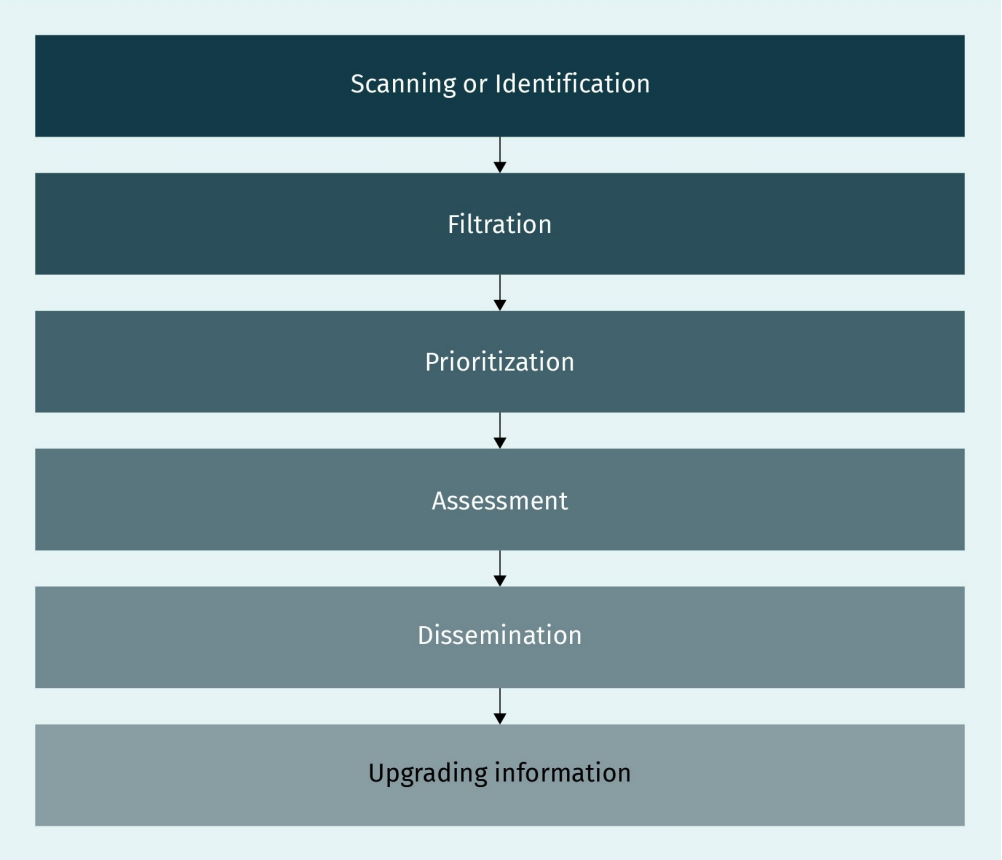
Horizon scanning refers to a structured assessment of available data and knowledge to recognize viable challenges, dangers, upcoming problems, and chances. Horizon scanning is like a ductile tool with various robust and reliable strategies (Hines et al., 2019). It can impact decision-making by recognizing the pros and cons, possibilities, and drawbacks ranging from the institutional to the global levels. Additional research is required to earmark the most efficient strategies that will include substance to this scenario and predict innovations and progress. The European Medicines Agency (EMA) is proposing to look at the accessibility of innovative medicines by employing horizon scanning. Based on horizon scanning, the outcome will be further shared with the Regulatory Science Strategy and the European medicines regulatory network strategy of the EMA (Bujar & Liberti, 2017; O'Dwyer et al., 2017). Horizon scanning was previously employed as a foresight strategy by Japan in the 1970s and has since been applied in diverse sectors for policy and strategy planning (Plüddemann et al., 2010).

Methodology for Horizon Scanning

A systematic review is conducted to map the horizon scanning activity. The review usually follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). As illustrated in the flowchart below, the literature is screened and filtered using inclusion and exclusion criteria, the data are extracted and analyzed, and the scanning strategy is mapped. The search strategy is applied by screening databases such as Medline and the Embase bibliographic databases (Hines et al., 2019). Inclusion and exclusion criteria are applied by screening a match of keywords in

abstracts or titles with the methodology in the specific field or across different fields. Full texts of the articles are screened in the following round, with a detailed foresight methodology or horizon scan. Priority areas include science and technology. A collaborative or integrated strategy is applied to perform horizon scanning across a period of 10 to 15 years.

Figure 12: Steps involved in Horizon Scanning



Source: Swati Sharma (2022), adapted from Grossman et al. (2019).

Information is sourced through diverse sources for signal identification, including scientific and biomedical literature reviews, patents, inputs from industry and industry associations, media, institutional agencies, expert committees, federal government bodies, international conferences, and meetings.

Table 3: Criteria for Horizon Scanning

Filtration	Viable effect, magnitude of impacted people, originality, degree of change or transformation, proof, departmental influence, validity, stakeholder interest, strategy preference, evolution step, moral compliance, and predetermined time
Prioritization	Potential impact on outcomes, population size, variable impact, time period, evidence of effectiveness, relevance to strategic priorities, novelty, and expertise availability

Signal assessment	Impact, level of innovation, risk assessment, legal and ethical issues, market barrier, stakeholder perception, required actions, and impact time
Dissemination	Format, methods, audience, frequency, and upgrading
Evaluation	Short, medium, long term, process and output audit, validation, focus groups, metrics, and database access

Source: Swati Sharma (2022), adapted from Hines et al. (2019).

Table 4: Methods Employed in Horizon Scanning

Filtration	Classification criteria, automated text-mining strategies, individual and group filtration, peer review, and expert involvement
Prioritization	Qualitative, quantitative, and semi-quantitative approaches, grading, risk analysis, signal homogenization, expertise, and public consultation
Assessment	Expert lens; driver analysis; scenario planning, peer review; and expert, user, and policy maker participation

Source: Swati Sharma (2022), adapted from Hines et al. (2019).

Horizon scanning as a strategy is being used globally and is now combined with artificial intelligence to self-evaluate its signal regulation. Further research needs to be conducted to evaluate and implement more effective methods that are beneficial for diverse groups of stakeholders.

SUMMARY

Clinical efficacy and cost-effectiveness of health technologies constitute the key considerations within the “assessment” in HTA mechanisms. Based on the assessment, an HTA agency provides guidance and recommendations to federal and responsible health agencies, such as the National Health Service (NHS) in the United Kingdom. Healthcare technologies need rigorous assessment based on the interests and needs of various stakeholders, including patients. A systematic mechanism is incorporated to ensure health equity among all stakeholders. HTA assessments and appraisals can lead to recommendations and the establishment of criteria for relevant decision-making. HTA plays a key role in priority setting and price negotiations for national and institutional agencies in healthcare. Necessary amendments and modifications in policy are introduced by national governments to attain universal health coverage (UHC) by providing safe, efficient, and affordable medicines and vaccines as one of the Sustainable Development Goals (SDG). A structured assessment to investigate challenges, risks, issues, and opportunities referred to as horizon scanning is being implemented

in various sectors. Horizon scanning can influence decision-making by identifying opportunities and challenges at the regional, national, and international levels.

UNIT 4

REIMBURSEMENT OF MEDICINES AND HTA

STUDY GOALS

On completion of this unit, you will be able to …

- understand health technology assessment (HTA) decision analytics.
- recognize health-related quality of life.
- interpret real-world data.

4. REIMBURSEMENT OF MEDICINES AND HTA

Introduction

This unit will introduce methods relevant for decision-making in healthcare systems, including the Evidence and Value: Impact on Decision-Making (EVIDEM) framework. Effectiveness and efficacy will be introduced and compared in the context of health technology assessment (HTA), and relevant examples given to deepen understanding. The background of health-related quality of life (HRQoL) is explained, as well as its importance in measuring health status and the relevant models for understanding and applying this knowledge. Finally, real-world data (RWD) are introduced and their significance in the scope of HTA explained.

4.1 Decision-Analytic Models

Healthcare decision-making is based on value-based and science-based needs and frameworks. Distinct factors and complex steps involved in healthcare systems at various stages from diagnosis to treatment require the analysis of systematic strategies and methods based on the existing evidence (Baltussen et al., 2007). Inferences drawn from diverse sources, such as scientific research-based evidence; medical need; financial burden; and societal, ethical, and legal perspectives, lead to crucial decision-analytic models (Goetghebeur et al., 2012). To improve decision-making models in healthcare, several governments and institutional HTA agencies are taking steps to achieve greater clarity within their health systems by enhancing accountability and responsibility in this direction.

Decision-Making Tools and Frameworks

During the process of decision-making, each therapeutic intervention is scored based on a set of criteria, considering the associated benefits and drawbacks (Goetghebeur et al., 2012).

EVIDEM framework

An exemplary framework linking health technology assessment (HTA) and multicriteria decision analysis (MCDA) is the Evidence and Value: Impact on Decision-Making (EVIDEM) framework. The purpose of developing EVIDEM was to generate a core MCDA model that can be applied by decision-makers as an associated tool and that supports the deliberative process (Goetghebeur et al., 2008, 2012). The EVIDEM framework is accessible worldwide via the EVIDEM Collaboration. It consists of an MCDA and an HTA module (Goetghebeur et al., 2012). The EVIDEM framework was based on the decision criteria that resulted from a comprehensive analysis of more than 20 jurisdictions around the world. The MCDA

approach integrates those 15 decision and scoring criteria. EVIDEM provides a framework for building upon a finer model for advising on healthcare interventions, policy foresight, and strategies.

Decision criteria

Multicriteria decision analysis (MCDA) allows evaluations based on the criteria listed in the table below that influence decisions (Baltussen et al., 2007, 2010). By employing MCDA criteria, the decision problem statement is identified, specifying all the necessary elements that influence a decision, and establishing the relevant criteria for decision-making.

Table 5: Elements of the MCDA Model Decision Criteria

Disease impact	Severity and population size (mild-moderate-severe)
Intervention context	Clinical guidelines and comparator intervention limitations (no-minor-major limitations)
Intervention outcomes	Effectiveness, improvement of safety and tolerability, and improvement of patient-reported outcomes (PRO) (low-minor-major improvement)
Type of benefit	Public health interests and type of medical service (no-minor-major risk)
Economics	Budget impact, cost-effectiveness, and impact on other spending (substantial expenses-no expenses-cost effective)
Quality of evidence	Adherence to decision-making institutions, accuracy in evidence reporting, and relevance and validity of evidence (low-high adherence-inconsistent-consistent-low-high relevance)

Source: Swati Sharma (2022).

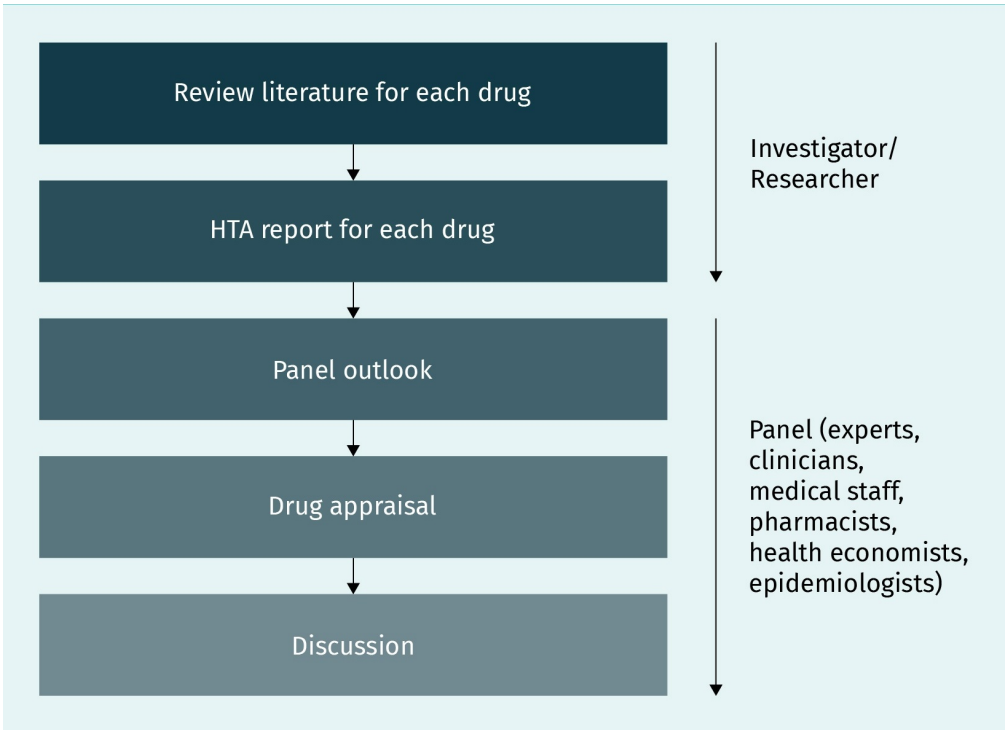
Decision framework

The decision framework comprises comprehensive protocols for the collection, analysis, assessment, interpretation, and presentation of evidence for each decision criterion (HTA module) to produce HTA reports that are connected to the multicriteria decision analytics (MCDA) model (Goetghebeur et al., 2012). This model allows for testing of the feasibility and utility of interventions, enabling knowledge exchange and the appraisal of healthcare interventions (Goetghebeur et al., 2012).

Example depicting multi-step decision-analytic modeling criteria

A two-criteria HTA report is developed by investigators based on an extensive analysis of 15-point decision criteria. The appraisal group conducts an appraisal of the significance of each of the criteria and then appraises the drug by grading the criteria. A discussion is conducted to collect feedback from all participants. The flowchart below depicts the complete drug appraisal process.

Figure 13: Flowchart Depicting Multistep Decision Analytic Modelling Criteria



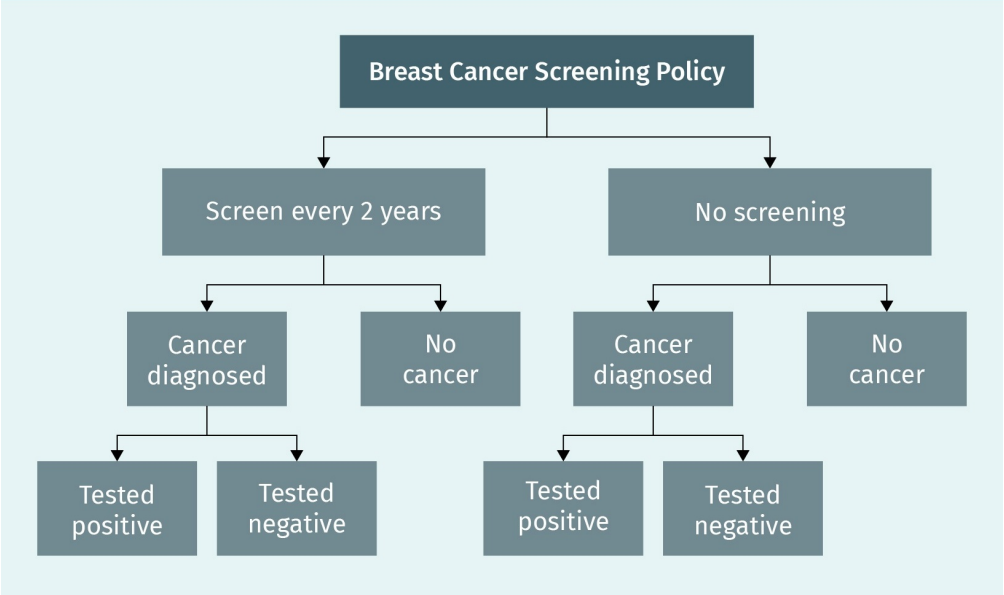
Source: Swati Sharma (2022), based on Goetghebeur et al. (2012).

Structure of Breast Cancer Screening Model Using Decision-Analytic Modeling Approach

Here, we describe an example depicting decision analytics for breast cancer screening options from a national mammography screening program for Vietnamese women reported by a recent study (Nguyen & Adang, 2018). The total expenditure and implications of implementing the breast cancer screening initiative for specific age groups of women were assessed compared with a lack of screening in the existing scenario. While breast cancer occurrence rates are steadily increasing in Vietnam, poor prognosis has resulted in high mortality rates. With a regular screening policy, the probability of detecting cancer early would be significantly higher and would result in better survival rates. If breast cancer screening is performed every two years or not, cancer may or may not be diagnosed. If a cancer diagnosis is made, patients may be diagnosed as positive or negative in both scenarios. According to the screening strategy being assessed, females older than 45 years of age were screened by mammography and categorized into four groups based on their age range: 45–49 years, 50–54 years, 55–59 years, and 60–64 years. The entire population (100%) was expected to participate in the screening program. Based on the data from the national breast cancer screening initiative, the effect of participation on the cost-effectiveness of mammography screening was assessed in the range of 23.6%–100%. The expenditures and results of breast cancer screening were analyzed and compared with three scenarios: no screening, combining five percent mammography screening at a private hospital with no screening for the remaining population, and combining ten percent mammography screening with no screening for the rest of the population. A

decision-analytic modeling strategy was employed to diagnose breast cancer patients, as illustrated in the figure below. Patients for whom breast cancer had been detected were further examined to confirm the diagnosis and disease stage (Stage 1, 2, 3, 4, or metastatic cancer). A Markov chain analysis was applied to evaluate the expenditure and increased survival time based on timely detection. The different stages considered in the Markov model are relapse post-therapy, localized relapse, relapse in other body organs, mortality due to relapse, and mortality due to other comorbidities. Patients with local relapse may stay stable, suffer a relapse in other body organs, or die due to breast cancer or other diseases. Patients with a Stage 4 diagnosis may stay stable or die due to another sickness. This model covers assumptions encompassing the entire lifespan of the patient.

Figure 14: Decision Tree for Breast Cancer Screening Options



Source: Swati Sharma (2022), based on Petrou & Gray (2011).

4.2 Effectiveness Versus Efficacy

Approval of a pharmaceutical drug for use is provided based on evidence of a positive efficacy-safety index, which refers to the degree to which the drug causes more harm than benefit (Nordon et al., 2016). The efficacy-safety index is measured by employing randomized controlled trials (RCTs). The efficacy-effectiveness gap (EEG) refers to the existing pitfalls and supportive supplementary scientific evidence on **efficacy** and **effectiveness**. It is important to understand how this concept influences clinical and policy decisions.

Efficacy
This refers to the outcome of a therapeutic treatment under preferred and regulated conditions.

Effectiveness
This measure evaluates whether an intervention causes more benefits than harm when administered according to usual healthcare practices.

Tenets of Efficacy-Effectiveness Gap

Different ways to understand the efficacy-effectiveness gap (EEG) have been suggested. EEG has been classified into three different categories: the effect of healthcare settings, strategies to measure the effect of drugs, and the interplay between drugs and dependent aspects.

According to the first principle of EEG, discrepancies in the healthcare system in real life may explain why effectiveness results cause concern compared with efficacy results. Therefore, all features of healthcare in real life should meet the benchmark of experimental conditions with different grades of intervention, such as medical regulations, knowledge transfer, and approaches for increasing patient adherence, among others. The real impact of these laudable interventions is difficult to evaluate. This principle does not consider effectiveness to be superior to efficacy. The patient-doctor network is key to patient compliance and leads to better results. Doctors should select the best treatment strategies for each patient to enhance the probability of having a favorable outcome. The second principle of EEG states that the strategy employed to assess the impact of a drug influences the outcome of drug use; thus, there is an EEG. Both efficacy and effectiveness investigations provide answers to complementary questions. According to the third principle, advocating for the therapeutic impact of a drug is the outcome of the interplay between biological and dependent aspects, such as patient or healthcare-related issues. Irrespective of the study design, the impact of a drug in different conditions, such as routine clinical trials or in real life, may vary, leading to inconsistent results (Nordon et al., 2016).

Example of Efficacy and Effectiveness

The terms efficacy and effectiveness can be further explained with examples from the literature. The efficacy and effectiveness of the impact of COVID-19 vaccines were evaluated in a systematic review (Mohammed et al., 2022): To compare the efficacy and effectiveness of seven COVID-19 vaccines, a comprehensive systematic literature review was conducted covering different databases to identify studies reporting vaccine effectiveness or efficacy. Based on the inclusion criteria, 42 reports were included indicating that COVID-19 vaccines resulted in decreased infection rates, milder symptoms, reduced hospital stays, and lower death rates. Specific vaccines were found to be more effective against different variants, e.g., the product by Pfizer-BioNTech came out to be more effective against B1.1.7 and B1.1.8 variants. Irrespective of the effectiveness of a vaccine, it will be necessary to check its effectiveness against any new strain.

A wider contrasting view on efficacy and effectiveness influences research, policy, and policy-based decisions for policy approval for added patient value; regulating pricing; and maintaining cost-effectiveness, public financing, and sponsoring of healthcare expenditures (Romero et al., 2013).

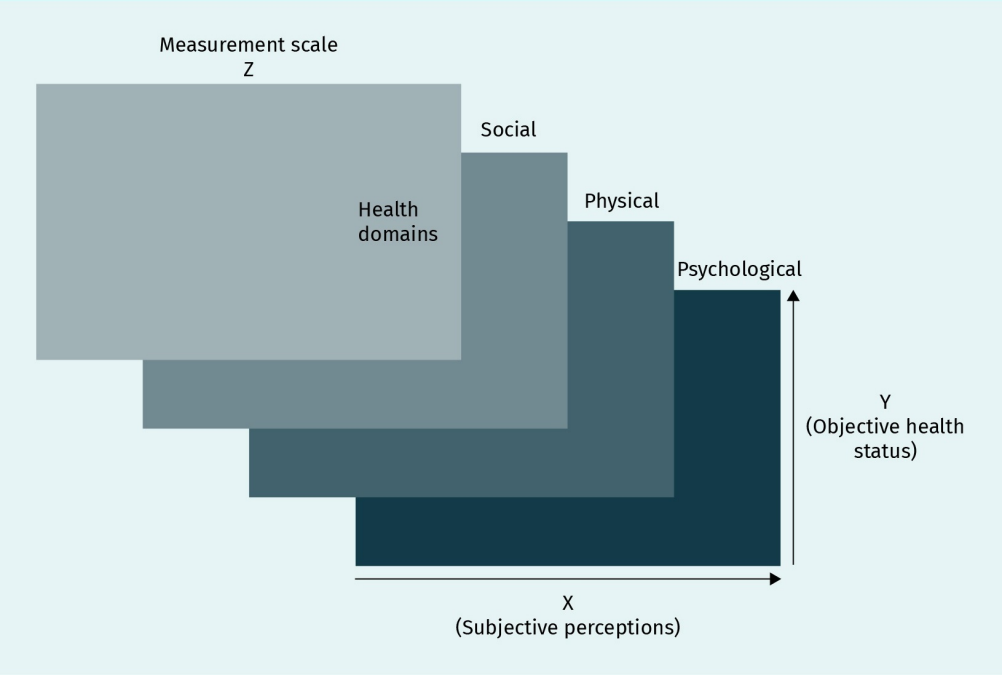
4.3 Health-Related Quality of Life

The terms “health” and “quality of life” (QoL) existed far before the term “health-related quality of life” (HRQoL) became popular (Karimi & Brazier, 2016). The World Health Organization (WHO) defined health as a “state of complete physical, mental and social well-being” (World Health Organization, 2014). This conceptualization shaped the development of the Medical Outcomes Study Short Form Family of Measures, SF-36, and EQ-5D, also known as measures of HRQoL. Although the HRQoL concept has existed since the 1940s, its current form was proposed in the 1990s (Testa & Simonson, 1996). Conceptually, HRQoL encompasses the physical, social, and psychological spheres. Each sphere can be quantified subjectively (using patient reports and perception) or objectively (using clinical diagnostic data). Measuring and assessing the quality of life was significant for evaluating health-related consequences beyond mortality and natural activity (Karimi & Brazier, 2016).

Measures of Health Status

HRQoL is measured to assess the effectiveness of an intervention (Fryback, 2010). It is imperative to measure HRQoL because of its implications for both clinical and policy issues. From a clinical perspective, measuring HRQoL permits an assessment of the effect of care on a patient and the status of patient health. HRQoL measures are used to determine the change in the health of patients prior to, during, and after treatment or an intervention such as surgery. We know that health status can be measured on a generic or disease-specific basis. The physical, psychological, and social domains of health are measured on a general basis. How healthy do we feel? That is a general health condition. In contrast, if we compare the conditions within a particular disease, the HRQoL scales and measures will be different. We must be inquisitive about the severity or mildness of the disease, symptoms, or behavior of the patient. HRQoL questionnaires report on health by measures of functioning (capacity to perform activities) and well-being (physical, mental, and social). The models and measurement scales of HRQoL frameworks are presented below. They span the X, Y, and Z planes, going beyond subjective and objective conditions, and they span the social, physical, and psychological spheres across health domains. This model represents broadly-applied tools to capture HRQoL, such as SF-6D and EQ-5D.

Figure 15: HRQoL Conceptual Framework

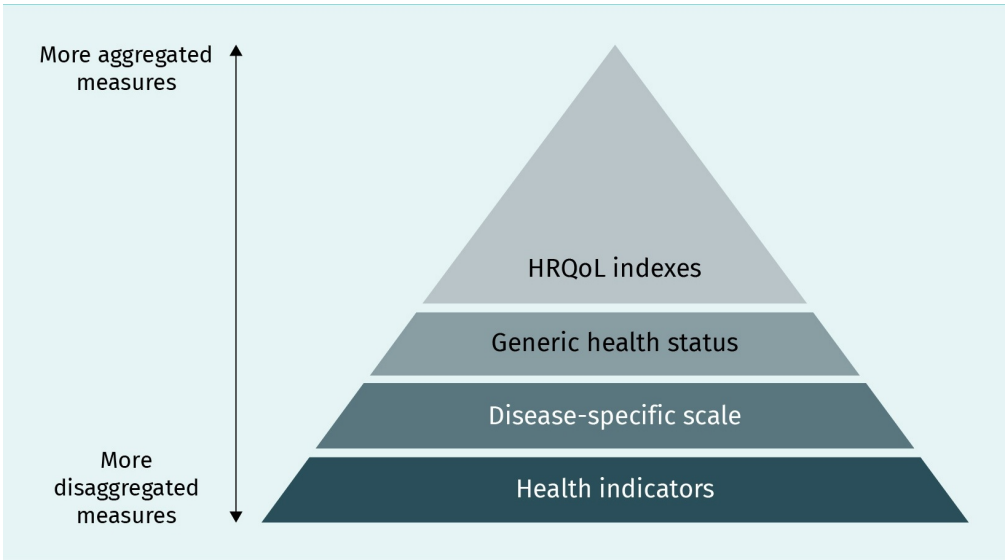


Source: Swati Sharma (2022).

HRQoL Data Pyramid

As illustrated in the HRQoL data pyramid, generic, disease-specific, and health-related indicators are represented. HRQoL indexes are preference-weighted aggregate scores that summarize overall health. Generic health status profiles are vectors of health status domain scales. Disease-specific domains, as the name suggests, do not cover all health domains (Romero et al., 2013). Multi-attribute classification systems, such as SF-36 and EQ-5D, are considered the measures of health status, HRQoL or QoL, and can develop both health profiles and index values. SF-36 includes physical functioning, role limitations, social functioning, pain, psychological health, and vitality, while EQ-5D comprises mobility, daily actions, self-care, pain, discomfort, and anxiety (Karimi & Brazier, 2016).

Figure 16: HRQoL Data Pyramid for Population Health

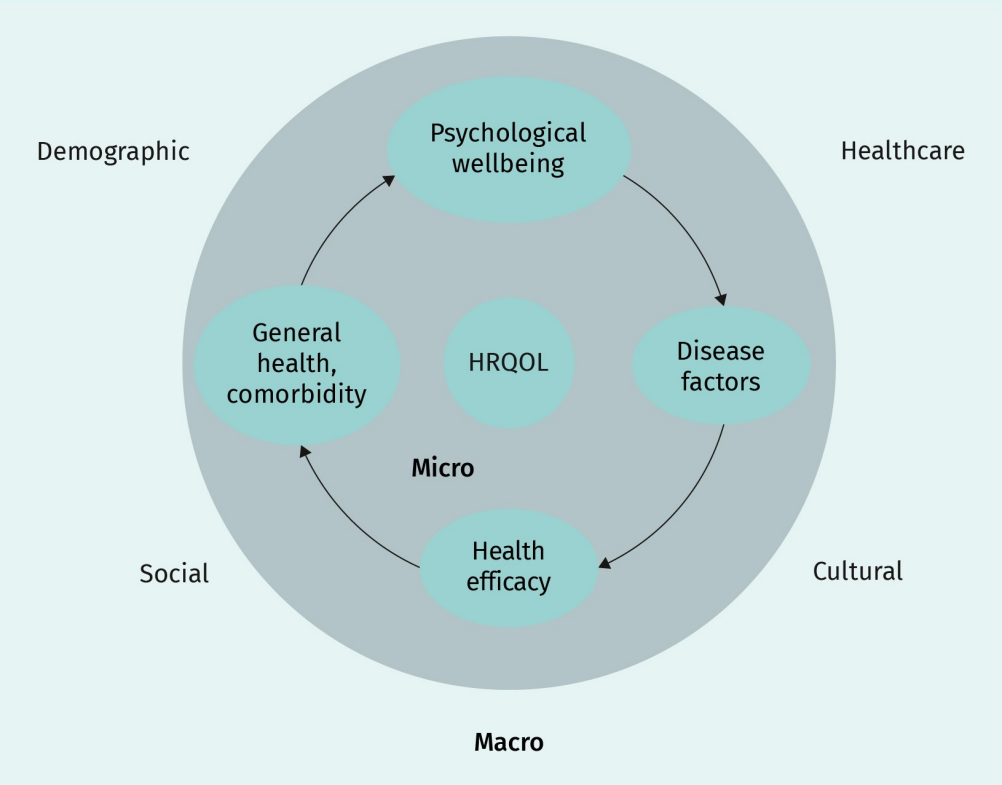


Source: Swati Sharma (2022), based on Fryback (2010).

Contextual Model of HRQoL

Numerous research studies have investigated HRQoL indexes and contextual factors impacting HRQoL in different cohorts of healthy and diseased populations. For instance, a recent study investigates HRQoL predictors and factors impacting COVID-19 patients (Chen et al., 2020). As illustrated in the figure below, the contextual model of HRQOL includes social, cultural, demographic, and healthcare-related aspects. This model amalgamates the conventional HRQoL model, social setup, qualitative and quantitative research studies, and cultural literature (Ashing-Giwa, 2005). The socioecological aspect is frequently excluded in HRQoL studies. The contextual model of HRQoL is appraised by the conventional HRQoL model, the biopsychosocial model, quantitative and qualitative studies with survivors, the oncology literature, and the multicultural and psychological literature. Various HRQoL dimensions differ across ethnic groups. The socioecological aspect will include dimensions such as socioeconomic status, life burden, and social support. The socioeconomic state encompasses income, education, employment status, and ethnicity. For instance, a lower socioeconomic state indicates a poorer chance of survival, leading to poor HRQoL. The cultural aspect includes dimensions such as ethnicity, spirituality, global view, interconnectedness, acculturation, and beliefs. For example, different ethnic minorities suffer challenges and disparities in healthcare access, leading to varying HRQoL outcomes. Survivors draw strength from spirituality, faith, and cultural belief systems. Demographic factors, such as age and gender, affect HRQoL outcomes and survivorship. Healthcare systemic factors, including specific treatment and follow-up checkups, as well as other variables such as general health and comorbidities, may also influence HRQoL (Ashing-Giwa, 2005).

Figure 17: Contextual Model of HROoL



Source: Swati Sharma (2022), based on Ashing-Giwa (2005).

4.4 Real-World Data

Real-world data (RWD) are derived from a wide variety of sources that contain patient data. These include electronic health records, patient registries, pharmacy and health insurance databases, clinical records, data from social media and health apps, and other patient-reported data. Different pharmaceutical and health agencies define RWD as data collected by any noninterventional methodology and nontraditional strategy. Various stakeholders, such as regulatory agencies, HTA institutions, and pharmaceutical industries, are exploring the possibility of using RWD data for various purposes. Regulatory agencies encounter challenges in decision-making based on the available conventional data from randomized controlled trials, which is considered unpredictable to rely on in terms of real-world effectiveness. Thus, RWD complements the evidence from RCTs, aids in making valid decisions, and provide opportunities for improving HTA (Makady et al., 2017).

Significance of RWD

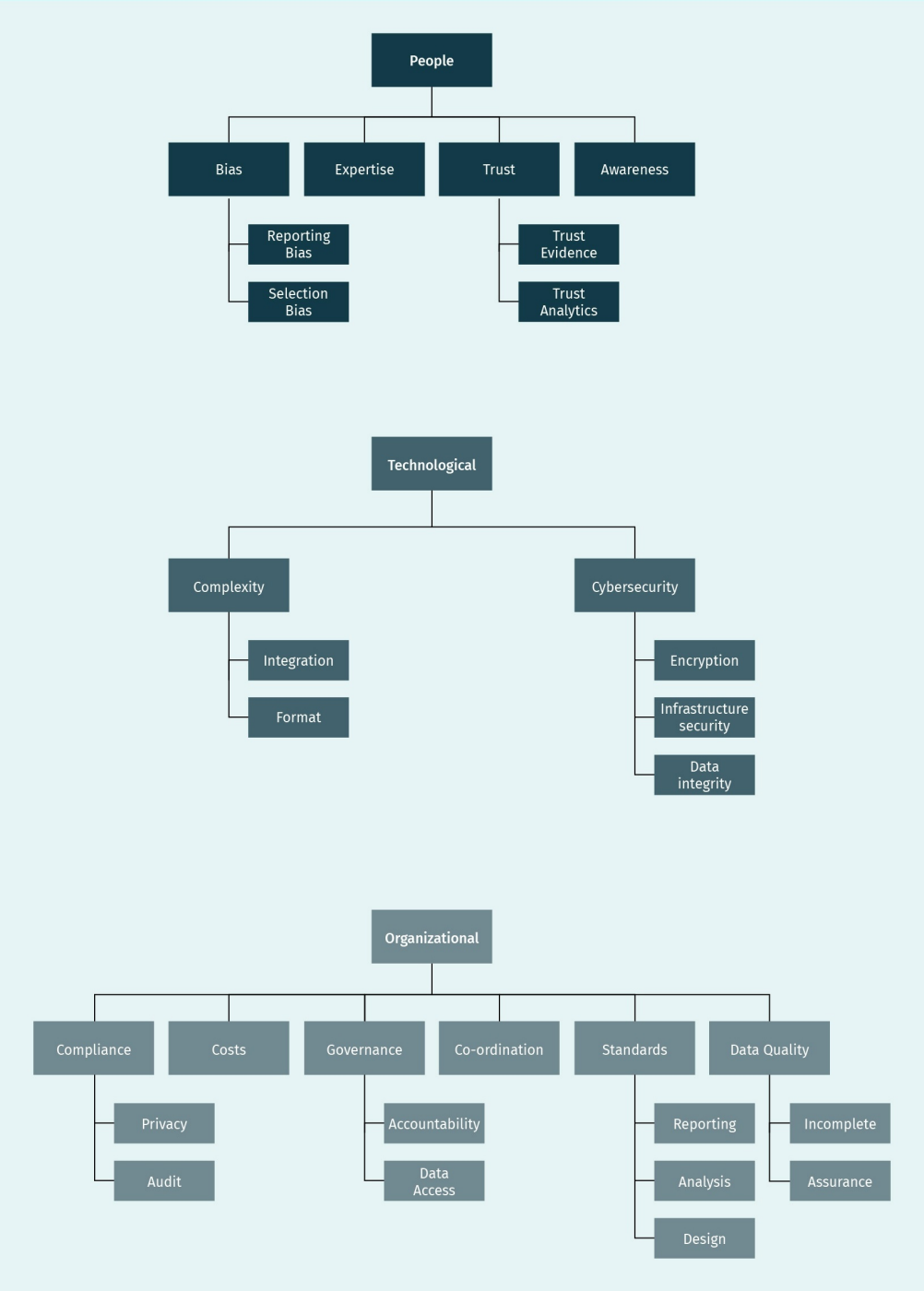
With the global digital revolution, an enormous amount of healthcare and patient data are accessible to various stakeholders. RWD provides opportunities to use these data as clinical evidence concerning the therapeutic effect, treatment benefits, and potential side effects of pharmaceutical drugs and therapies. The pharmaceutical and medical industries are complementing and combining these data into their regulatory and experimental systems. RWD can transform future clinical research by coordinating with healthcare providers, pharmaceutical companies, and claim payers or sponsors. Healthcare providers should make evidence-based decisions, remove gaps in healthcare, and allow easier patient enrollment in clinical studies. Pharmaceutical companies can plan for better trial design, patient recruitment strategies, proof of treatment efficacy, and more efficient clinical engagement (Grimberg et al., 2021).

With RCTs, data extrapolation to real-world clinical scenarios is difficult. Therefore, HTA authorities are investigating the possibility of using RWD to increase the efficacy of relative effectiveness assessments (REAs). REAs are the degree to which treatment or therapy benefits the patient, in contrast to the situation in which multiple therapies are administered to the patient under clinical supervision. With increasing healthcare costs, the emergence of modern healthcare technologies, and advanced healthcare and pharmaceutical products, country-specific HTA authorities are looking for efficient procedures for relative effectiveness assessments (REAs) of commonly used drugs (Makady et al., 2017).

Challenges Associated with RWD

RWD may have their own challenges and risks for different stakeholders and institutions with respect to their application. Challenges have been identified at the people, technological, and organizational levels as illustrated in the figure below (Grimberg et al., 2021).

Figure 18: RWD Challenges



Source: Swati Sharma (2022), based on Grimberg et al. (2021).

People dimension

From the people's perspective, poor perception and knowledge of the application of RWD prevents their use. It is important to create public awareness regarding the advantages of RWD and the importance of data privacy and protection. At the same time, it is imperative to educate healthcare regulators and professionals regarding the clinical significance of RWD. It is necessary to determine the pros and cons of RWD during application, as they can be either advantageous or disadvantageous (Grimberg et al., 2021). Regulatory institutions such as the U.S. Food and Drug Administration (FDA) have suggested recommendations on the use of RWD data in clinical studies and risk-reduction strategies to ensure that RWD is trustworthy and reliable (Food and Drug Administration, 2018). Knowledge is required to develop an in-depth understanding of RWD, to have the expertise to analyze them, and make valuable interpretations useful for decision-making.

Technological dimension

Technology plays a key role in RWD generation with the digital revolution and easy access to technology by everyone (Grimberg et al., 2021). However, diverse country-specific data formats and cybersecurity risks are obstacles that prevent RWD applications globally. Unified RWD formats and data models, such as the Observational Medical Outcomes Partnership, are being developed as an independent database for rigorous analysis (Observational Health Data Sciences and Informatics, 2019). Necessary steps should be taken to avoid cybersecurity risks, including illegal access to and use of RWD, and prevention of cyberattacks, such as the ''WannaCry'' attack reported in 2017 (Armis, 2019).

Organizational dimension

The transformation of real-world data (RWD) into real-world evidence (RWE) for regulatory applications should be arranged in an organizational system. Certain risks should be prevented to have a robust organizational structure. Assurance of optimum data quality is vital for good RWE. Partial or substandard data from poor-quality patient registries and observational studies affect the quality of RWD. Data standardization is another important parameter, as gaps in data collection, processing, and reporting may influence data quality. Thus, regulatory institutions are making attempts to recommend implementation of uniform data standards (Food and Drug Administration, 2018). The absence of coordination between distinct institutions at the regional and global levels is a major hindrance to deriving substantial RWE from RWD. Robust governance structures are key to enabling stakeholders and organizations to have timely access to RWD. Legal compliance and stricter ethical regulations might threaten the use of RWD; thus, legal frameworks must protect the use of RWD. Cost benefit analysis is recommended to assess RWD costs and expected benefits (Grimberg et al., 2021).

RWD opens new opportunities for various stakeholders, especially the pharmaceutical industry, for access to clinical data. Evidence from RWD will be crucial for the development and approval of new drugs, therapies, and products, if the different challenges discussed above can be addressed adequately (Grimberg et al., 2021).

SUMMARY

Decision analytics in healthcare depend on value- and science-based requirements and fundamentals. Methodological approaches, such as multicriteria decision analysis (MCDA), enable assessment based upon various factors and criteria that can impact decisions. By implementing MCDA criteria, decision-based problem statements are structured to identify required elements that can impact decisions and establish useful guidelines for making decisions.

Approval for the use of a pharmaceutical drug is granted based on proof of the efficacy-safety index, which is derived from the data generated in clinical studies that often employ RCTs. RCTs provide insights into the efficacy of drugs prior to market launch.

The notion of the “efficacy-effectiveness gap” (EEG) refers to the existing pitfalls and supportive supplementary scientific evidence on efficacy and effectiveness. It is important to understand how this concept influences clinical and policy decisions.

Conceptually, HRQoL encompasses physical, social, and psychological spheres. Each sphere can be quantified subjectively using patient reports and perceptions or objectively using clinical diagnostic data. HRQoL is measured to assess the effectiveness of an intervention. It is necessary to measure HRQoL in order to address clinical and policy issues. From a clinical perspective, it is vital to evaluate the impact of care on the patient and the status of patient health. HRQoL measures are used to oversee the changes in the health of patients prior to, during, and after treatment or intervention such as surgery.

UNIT 5

HTA IN BENEFIT PACKAGE DESIGN

STUDY GOALS

On completion of this unit, you will be able to …

- understand the role of health technology assessment (HTA) in health benefit package design.
- define evidence-based priority setting.
- comprehend ethics, rights, and the political economy.

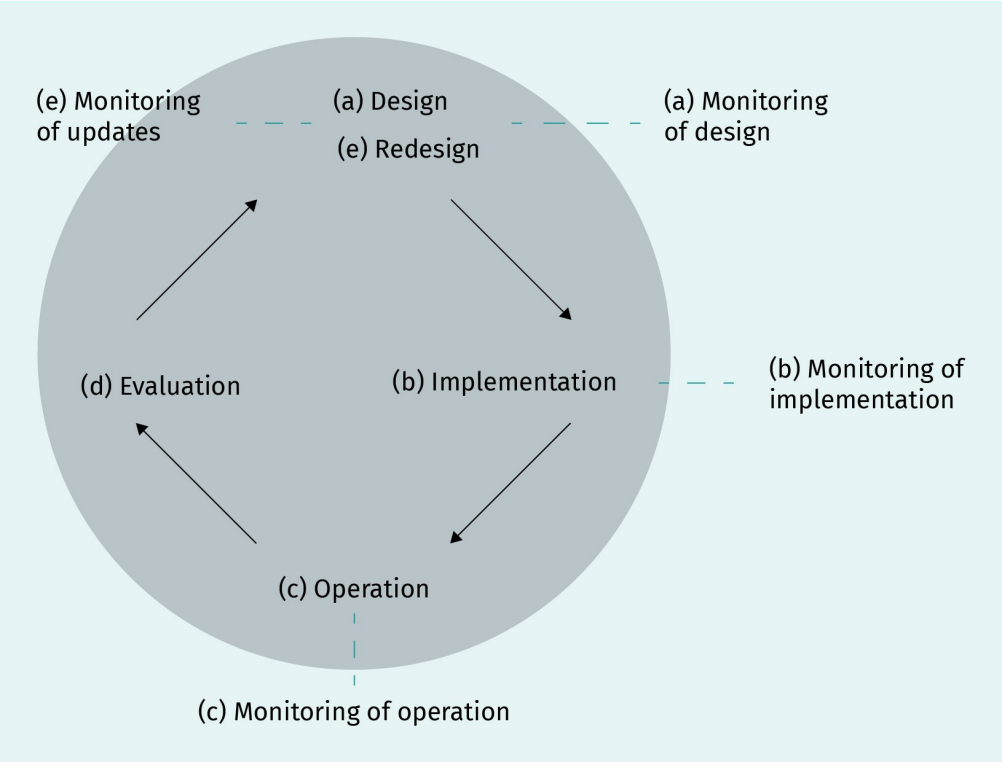
5. HTA IN BENEFIT PACKAGE DESIGN

Introduction

One of the key objectives of health technology assessment (HTA) is policy research that focuses on priority setting and efficient resource allocation. Thus, low- and middle-income countries (LMICs) identify HTA as an efficient policy apparatus. There is considerable demand for evidence to recommend and shape Universal Health Coverage policies, including benefit coverage, strategies for upgrading standards, and overall quality level to advance healthcare access and services (Tantivess et al., 2017).

Monitoring and evaluation of health benefit package design can be performed by following the cyclic steps illustrated below.

Figure 19: Monitoring and Evaluation of Health Benefit Package Design



Source: Swati Sharma (2022), based on Bitrán (2017).

5.1 Evidence-Based Priority Setting

HTA institutional mechanisms function efficiently in high-income countries such as Australia, European countries, and Canada. Most LMICs, however, do not have such institutional HTA systems in place, with gaps in the connection between evidence and policy. In the pursuit of **universal health coverage (UHC)**, the quest holds numerous challenges when it comes to the fair, efficient, and sustainable financing of health services that are considered essential. Regional research infrastructure and facilities are insufficient to provide evidence for HTA-related decision-making. Factors including poor know-how, expertise, and skill gaps between responsible authorities, policy legislators, and HTA-related staff influence evidence-dependent verdict. International agencies have started special local and global HTA initiatives, including conferences, workshops, and trainings for skill development. The Asian regional initiative HTAsiaLink, the Latin American association RedETSA, and international organizations Pan American Health Organization (PAHO) and the Inter-American Development Bank (IDB) work in close cooperation with each other (Tantivess et al., 2017).

universal health coverage
UHC signifies access to equitable health services by all citizens worldwide, without experiencing any financial hardship.

Priority Setting by HITAP and NICE

To enhance **priority setting** in LMICs, NICE International and Thailand's HTA program Health Intervention and Technology Assessment Program (HITAP) and their associate institutions forged collaborations approximately 15 years ago. The lessons learned from the work of NICE and HITAP will aid in implementing HTA at national levels and providing supporting evidence for the generation and application of research in decision-making in LMICs (Tantivess et al., 2017).

Priority setting
This refers to the decision-making procedure regarding the efficient allocation of available resources to safeguard public health.

Institutionalizing HTA in Vietnam

NICE International collaborated with Vietnam's Ministry of Health to upgrade service quality and healthcare standards, focusing on grade and performance based on certain factors. Vietnamese doctors initiated a process in close cooperation with NICE and NHS associates to aid in applying and learning from the evidence available globally at the national level. They implemented institutional steps by establishing stroke units and increasing patient awareness. Hospitals in Hanoi are adapting these practices to improve care standards, and further implement these services in different hospitals throughout the country. There was limited financial evaluation and a lack of research on cost effectiveness in Vietnam until efforts were initiated to institutionalize HTA. Thus, NICE and HITAP started a scheme for HTA institutionalization for priority setting in Vietnam, with the health department's vision of implementing UHC. An evaluation was performed to acquire knowledge regarding the practices used in resource allotment, HTA requirements, practical potential, and the political will to interlink research and policy. The initial steps included measures to increase stakeholder understanding of HTA as an instrument for priority setting. The Vietnamese health department established the Vietnamese Health Strategy and Policy Institute (HSPI) to perform HTA-related tasks in association with stakeholders and to develop new actions, a strategic vision, and an HTA institutional framework.

HITAP was approached in 2016 to guide the development of a Vietnamese Benefit Package resulting in a review of the benefits for expensive pharmaceutical medicines and health technologies within the ambit of the Vietnamese social security scheme (VSS). This resulting potential reduction in healthcare expenditure was estimated at 147 million USD without compromising on healthcare services and quality (Tantivess et al., 2017)

Despite the disparities in the Vietnamese social, political and regional setup compared with Thailand and the United Kingdom, the lessons from the HTA models were instrumental in institutionalizing the HTA system in Vietnam. Vietnamese stakeholders were strengthened with the institutionalization of HTA, while certain aspects from other HTA systems were replicated, including the fundamentals of clarity, technical competence, public accountability, the importance of policy in developing HTA agencies, managing research, and social and public outreach for transforming evidence into policy. These steps were significant in encouraging leadership and boosting regional institutional initiatives by stakeholders. HTA-related capacity development in Vietnam is necessary to boost decision-making in healthcare, improve healthcare services, promote health equity, and expand UHC throughout the country (Tantivess et al., 2017).

5.2 Ethics, Rights, and the Political Economy

Politics, ethics, and rights are core to designing a health benefit package for universal health coverage. Policy makers often make decisions that have enormous impacts on entire populations, budget expenditures, funding sources, and modes of expenditure by allocating different resources for specific purposes. Based on the political will of the people, options and choices made have both moral and ethical implications. Due to funding shortages, any decisions exclusively focusing on specific disease etiologies may lead to objections and even outrage. Any problems related to healthcare ethics, rights, or political matters may be solved by establishing a robust governance model with fixed accountability. For instance, a clear and transparent strategy helps to inform stakeholders, maintain communications, and network with the public, allowing for better public outreach and avoiding conflicts of interest. Any strategy adapted to perform cost-benefit analysis can solve ethical, social, and rights issues. Cost-effective plans demonstrate how distinct strategies influence outcomes, aiding decision-makers in adhering to the standards of evidence or spectrum of results. Patient age may be a variable factor that influences drug choice with reduced or minimal side effects. Political, ethical, and rights issues need to be prioritized, irrespective of governance and strategy choice (Glassman et al., 2017).

Politics and Priority Setting

Designing health benefit packages is complex and may present political and economic challenges. For example, the types of services to be provided, under what circumstances, and the monetary expenditure incurred are all open questions. Decision-making is becoming increasingly crucial as countries are adopting UHC, low-income countries are transitioning to middle-income countries, and the global population's life expectancy increases.

In the case of LMICs, global agencies have recommended various priority-setting strategies, including financial analysis, disease impact, and monetary budgets to aid the decision-making method for determining the interventions for health benefit packages. Priority-setting in this sector focuses on technical aspects such as analyzing disease load and training staff to implement cost-effective plans. Less focus has been given to the politics and economics surrounding health benefit packages, particularly the different spheres of political interest that shape decisions about funding accounts, the range of health services, and the level of health expenditure. Understanding the political economy of priority setting can aid in arranging more efficient resource allotment, methods, and decisions by identifying and regulating instead of overlooking any potential conflicting interests (Glassman et al., 2017).

Several examples illustrate the complexity of how political and economic considerations affect healthcare policies. For example, Costa Rica adopted the pneumococcal vaccine despite opposition from the country's top technical organization. The only supporting evidence was provided by a research student who was sponsored by the pharmaceutical company that produced the vaccine. The insurance programs in Ghana and Mexico are facing economic challenges, but they still cover the high healthcare costs of the privileged subpopulations in these countries (Agyepong & Sam, 2008). The United Kingdom has mechanisms for ensuring cost-effectiveness in treatment provided by the National Health Services (NHS); nevertheless, a Cancer Drugs Fund was specially developed to override the cost-effective requirements (Duerden, 2010). All these examples demonstrate how politically-motivated decisions can subvert the integrity of health benefit coverage and programs in different countries.

Comprehending the scope of political economy-related challenges to healthcare programs is itself a challenge for policy makers. Politics and economics are significant for evaluating the procedures that govern priority-setting in health among competing interests. These are key areas for three reasons: limited resources and unlimited demands for health services, health policy-making is divided, scattered, and impacted by market failures, and the implementation of national policies is mandatory, which creates competition between different stakeholders and parties involved due to conflicting interests (Glassman et al., 2017).

The political economy of health benefit packages involves a diagnostic and illustrative framework and four stages of the political cycle as outlined below:

- **agenda setting:** This is the procedure through which the requirement for a health benefit package generates interest, expenditure, and health equity objectives.
- **formulation and adoption:** Decision-makers and concerned authorities decide on how to direct the issue via the health benefit package.
- **implementation:** This is the implementation of the policy into action by applying a health benefit package policy.
- **evaluation:** This is the evaluation of impact through assessing the effects of a health benefit package policy.

Understanding the policy cycle provides insight into how decisions aid in shaping the response of different players and stakeholders throughout the design and policy-making process of health benefit packages.

Ethics and Priority Setting

During the designing of health benefit packages, policy makers face a series of difficult decisions and questions about the kinds of services, products, and processes to be included; the population to be covered; which agencies will cover the expenditure and healthcare costs; and budget sources. All these challenges have ethical implications. Specific decisions lead to conflicts regarding selective bias for a specific group of people or bias toward overlooking the interests of a particular disease group. Cultural factors, rights of patients, stakeholder engagement, and lack of clarity regarding moral compliance may give rise to ethical issues. Thus, the implications of any procedures and results must be evaluated and analyzed based on ethically significant moral and fundamental values. An ethical evaluation is important for policy makers, as it provides significant strategies and foresight for improved decision-making. Over the years, there has been growing demand that issues of equity be taken into consideration in the implementation of health benefit packages. Such recommendations have also been made by the World Health Organization Committee on Equity and UHC.

Role of ethics and equity in policymaking

Policy makers face a challenge in providing health benefit package policies that address health equity, provide necessary health services, and prevent the public from unnecessary treatment expenditures. A major purpose of undertaking an ethical evaluation while designing health benefit packages is to acquire comprehensive knowledge about its objectives. A strong set of objectives provides a solid foundation for policy-based decision-making in healthcare. Thus, core ethical elements of a health benefit package may include setting goals and criteria; implementing general criteria and defining methods for the appraisal; choosing the shape of the health benefit package and selecting areas for further evaluation; collating existing evidence and collecting new evidence; undertaking appraisals and budget impact evaluation; deliberating on appraisals and evidence; making recommendations and decisions; transforming decisions into resource allotment and use; managing and applying health benefit packages; and reviewing, learning and revising. While some countries may design a health benefit package considering that health equity is identical to providing human rights, other countries may prefer providing priority treatment based on specific diseases or patient populations. A primary goal of policy-making is to cover health costs and prevent healthcare-related expenditures. A health benefit package is considered an instrument to upgrade healthcare infrastructure and facilities and frame better policies for financial security and a transparent, sustainable strategy. Thus, it is important to implement fair processes in health benefit packages, and have equitable participation, equal representation, and inclusion addressing the needs of all patient populations.

Rights in Priority Setting

Decision-makers have a tough task in making health packages transparent, fair, equitable, and cost effective, as well as in taking care of the needs and demands of the various stakeholders and patient groups. It is important for policy makers to determine whether implementing or removing a certain policy may impact or conflict with a patient's right to health. Such conflicts commonly emerge in situations when patients do not have the right to access certain therapies, medicines, treatments, or healthcare benefits, which is a fundamental component of UHC. Patients have the right to take legal action, seek legal assistance from a court of law, and contest treatment rulings to receive the right to health via the law (Glassman et al., 2017).

The right to health is not generally embedded in regional or national constitutions, with a few exceptions (e.g., Brazil, Colombia, Latvia, Kenya, and South Africa). However, the right to health is embodied in international law as outlined below:

- Universal Declaration of Human Rights states all people have the right to a standard of living adequate for their health and well-being and that of their families, including medical care and necessary social services (United Nations, 1948, art. 25).
- The International Covenant on Economic, Social and Cultural Rights recognizes the right of everyone to enjoy the highest attainable standard of physical and mental health (United Nations General Assembly, 1966, art. 12).
- The International Covenant on Economic, Social and Cultural Rights explains the three right-to-health obligations of states: to respect, protect, and fulfill (United Nations General Assembly, 1966, general comment 14).
- World Health Organization Constitution Preamble states the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being (World Health Organization, 1946).

It is important for policy makers to involve the judiciary and international organizations, such as the WHO, to create public awareness regarding rights-based priority setting and to create a balanced health benefit package by prioritizing the interests of all stakeholders.

SUMMARY

The primary goals of HTA are priority-setting, evidence-based guidance for safe and effective policy-based decision-making, and to achieve Universal Health Coverage (UHC) and health equity. Effective HTA is also an aspiration of health policy in many LMICs in order to better manage resource allocation in healthcare. The availability of evidence is essential to guide UHC policies. These policies encompass the efficient and equitable design of benefit packages. Ethics, rights, and politics are fundamental to shaping a well-balanced health benefit package for UHC. Policy decisions affect the whole population. Smart analytical toolkits support decision-making processes.

The exclusion of specific categories of diseases from healthcare benefits may lead to ethical conflicts. Thus, it is important to address any emerging issues with an equitable governance model that benefits all population groups by maintaining communication with all stakeholders. Different assumptions may lead to distinct outcomes. A fair health benefit package that complies with ethical and moral values ought to be free of political maneuvering, and respects the individual right to health and healthcare.

UNIT 6

INSTITUTIONALIZING HTA MECHANISMS

STUDY GOALS

On completion of this unit, you will be able to …

- identify institutional health technology assessment (HTA) mechanisms.
- design institutional and governance arrangements.
- understand the international initiatives National Institute for Health and Clinical Excellence (NICE), the German Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG), the European Network for Health Technology Assessment (EUnetHTA), and the International Network of Agencies for Health Technology Assessment (INAHTA).

6. INSTITUTIONALIZING HTA MECHANISMS

Introduction

In order to institutionalize health technology assessment (HTA) mechanisms, it is important to design an institutional arrangement, build institutional capacity, evaluate the risks involved, and create a governance and operational structure. To design an institutional system, different HTA systems should be assessed, and the most appropriate system should be adopted based on country-specific demands and needs. A suitable location is chosen, and the right public authority is nominated to make reimbursement decisions. All key stakeholders are identified. The institutional system is developed by assessing existing bottlenecks, and competences needed. An action plan is created to learn about assessment models and exercises, the state of the appraisal agency, the resolution of any conflicts during assessment and appraisal, regional law, legal compliances, and responsibilities. Risk assessment is conducted by recognizing institutional bottlenecks such as data quality and access, resource supply, and aid. A program should be drafted to overcome and quell any risks. An institutional structure needs to be created that encompasses all aspects (Bertram et al., 2021).

6.1 Institutional and Governance Arrangements

Governance
This is an institutional arrangement that oversees the operational control of the health system.

Institutional and legal frameworks are necessary for implementing and maintaining viable HTA mechanisms and systems. **Governance** structures establish institutional rules and regulations, which should be acknowledged and practiced. Governance is the set of procedures and structures that manage HTA mechanisms. The foundation of good governance is based on statutes of clarity, involvement of stakeholders and partners, logical and rational decision-making, accountability, and a steady equilibrium (Bertram et al., 2021).

Benefits of Good Governance

Effective governance has both intrinsic and extrinsic benefits. Intrinsic benefits for all stakeholders include the participation of stakeholders in governance structures, a significant role in decision-making, and questioning the rationale and relevance of specific policies. Extrinsically, a robust governance mechanism allows for a healthy dialog and exchange of views between all stakeholders on different structures of governing principles.

Designing an Institutional Arrangement

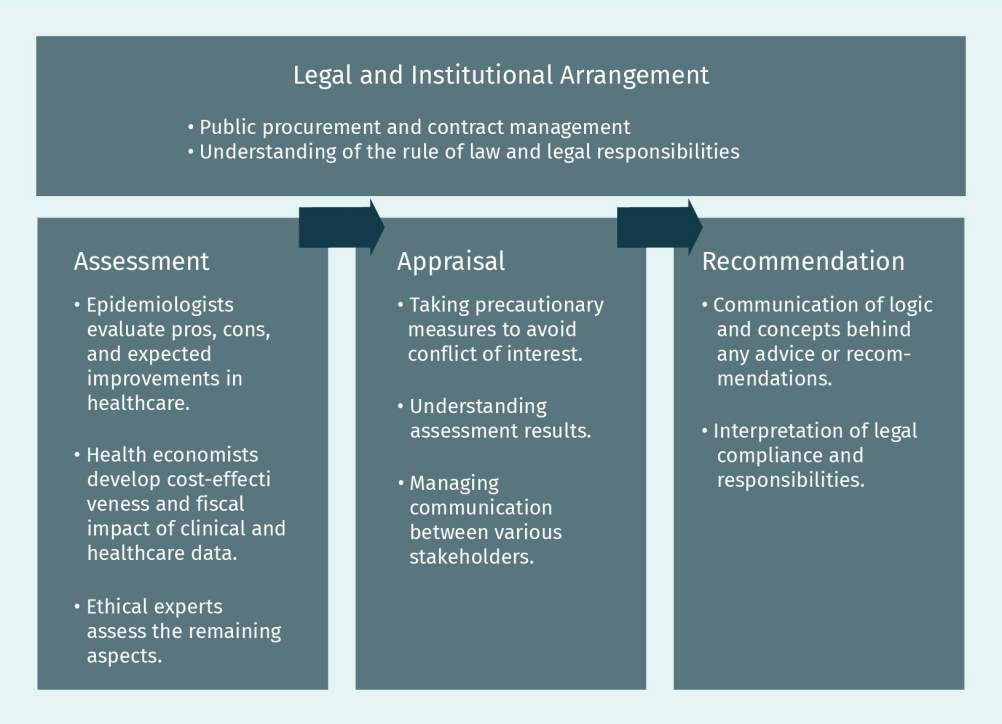
Different countries have distinct HTA models to fulfill their needs and adapt to country-specific institutional arrangements. Institutional arrangements are designed based on three key points: (1) the execution of the appraisal process; (2) if the assessment process is

to be performed internally or by an external agency; and (3) the scale of the HTA function to be determined when developing the structure of the model, complying with the legal jurisdiction. Most HTA entities are multidisciplinary, involving stakeholder groups, including representatives of the pharmaceutical industry and patients. Some agencies manage both the assessment and the appraisal functions, such as National Institute for Health and Clinical Excellence (NICE) in the United Kingdom, which directs other agencies for assessments and that also perform appraisals themselves. An HTA agency can review assessments and international regulations and provide customized guidance for their use. Thus, HTA institutions could think about taking up the role of appraisal instead of performing assessments. In such a scenario, assessments can be partly or exclusively conducted by external agencies. Assigning assessments to external or contractual staff may facilitate the efficient and timely completion of the task. Different considerations should be taken into account, such as budget and staff availability and appraisal of country-specific HTA functions. If there is an intention to establish an HTA institution, the right organization should be involved, and an analysis should be conducted to identify the existing HTA mechanisms and the appropriate expertise. Public funding sources should be determined and the authorities that should provide reimbursements should be identified in compliance with the national legal jurisdiction. Any necessary legal processes should be initiated and the concerned authorities and stakeholders should be contacted to involve them in the process of designing the HTA institutional framework (Bertram et al., 2021).

Developing Institutional Capacity

HTA institutional capacity can be developed by acquiring the necessary skills for assessment and appraisal and by identifying the right skillset and competent expertise, which are already available. Public authorities, social nongovernmental organizations, and healthcare providers should be consulted to identify the existing HTA-related mechanisms and resources that can be used to build up institutional capacity. In local contexts, it is important to know how and where health data can be accessed, which public authority should be approached, and where the demographic, epidemiological, and relevant cost information in local markets is accessible. Human resources and staff with different skills and expertise are required to be included in the HTA process. Physicians, nurses, biomedical engineers, pharmacists, health facility managers, epidemiologists, health economists, legal experts, ethicists, patients, civil society organizations, and communication officers are involved in the HTA process. HTA mechanisms and capacity development are performed as outlined and illustrated in the figure below.

Figure 20: Development of HTA Mechanisms During Institutional Reimbursement



Source: Swati Sharma (2022), based on Bertram et al. (2021).

Conducting Risk Assessment

The challenges involved with the specific drivers of or hindrances to the development of HTA mechanisms within a national HTA system should be addressed.

Drivers and associated risks are as follows:

- **data availability and quality:** Substandard assessment outcomes result in bad decision-making and disregard the impact of HTA.
- **cultural scenario:** Stakeholders are unwilling to accept transformation in decision-making and HTA-related concepts such as the use of HTA for budget management.
- **monetary support:** Lack of monetary support and substandard work disregard faith in and sanctity of the HTA system.
- **healthcare infrastructure:** Challenges arise in providing and extrapolating substantial proof from global to local scenarios. Application of HTA guidelines in different aspects of the healthcare system may be deemed risky and difficult. Buying technology may be challenging, as sellers may or may not follow HTA recommendations. Adaptation of institutional mechanisms to a wider regional, national scale may be another challenge.
- **political assistance:** Lack of political will to provide support via federal funding may create a new series of challenges.
- **knowledge of stakeholders and their interests:** Stakeholders may try to dissuade and hinder the implementation of HTA recommendations.

- **communication:** Communication and networking among the HTA players may help to overcome any challenges.
- **other challenges:** Changing priorities, overly ambitious plans, and management of conflicts of interest (COIs) are other challenges.

A risk mitigation plan should be carried out to avoid these challenges. A well-planned communication mechanism should be developed to counter these risks, and staff should be appointed to deal with various associated aspects.

Establishing Operational Systems

After evaluating the system and mapping the available institutional capacity, it is important to determine and allocate the necessary human resources and financial support required for establishing and executing the institutional operations. The table below reports the operational structures implemented in different countries.

Table 6: HTA Structure, Budget, and Expenditures in Specific Countries

Country	Purpose	Members and staff	Time required	Cost per HTA (USD)	Budget
Australia	Pharma Advisory Council	18 members, > 40 staff, 5 external	8–9 weeks	60,000	15 million
Brazil	Science & Technology Department	30	3 months–2 years	15,000-150,000	-
Germany	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen	122	3–18 months	65,000-650,000	19 million
Poland	Agency for Health Technology Assessment in Poland	55	2–3 months	28,000-43,000	3.8 million
Thailand	Health Intervention and Technology Assessment program	50	9–12 months	17,000	1 million
United Kingdom	NICE	500	7–14 months	Up to 400,000	90 million

Source: Swati Sharma (2022).

Uninterrupted monetary support is important for the smooth functioning of HTA systems. Participating industries and companies can be charged a specific amount for each dossier submission. Depending on the adapted assessment system, various countries may have

different financial and staff necessities. In the case of limited financial support, systems that are prevalent in countries such as Romania can be adapted. The Romanian assessment model and criteria accept HTA decisions from France, Germany, and the United Kingdom and a reimbursement model from other European Union countries. This enables them to examine more medicines and technologies than other governments with limited budgets (Bertram et al., 2021).

6.2 Country Case Studies and International Initiatives (NICE, IQWiG, EUnetHTA, and INAHTA)

Country case studies focusing on the characteristics of particular schemes and various grades of priority setting are elaborated on below.

Development of Mother and Child Health Development Program in Myanmar

In 2012, the government of Myanmar initiated a voucher program to upgrade mother and child health standards that was supported by Gavi, the Vaccine Alliance. Thailand's HTA agency, health intervention and technology assessment program (HITAP), was approached by WHO to provide assistance in guiding financial planning and the budgeting strategy for priority setting of health issues. The voucher scheme was introduced to enable mother and child health-related treatment and service access. It was piloted in a small region of the country. Various aspects, such as a financing strategy, voucher benefits, voucher distribution, funding mechanisms, and the population intended to benefit, were discussed and mutually agreed upon by the agencies and establishments involved. A cost benefit evaluation revealed the advantages of implementing this scheme and the benefits of reducing mother-child mortality rates.

The objective of the initiative was to improve evidence-based decision- and policy-making in Myanmar with the assistance of HITAP, the HTA agency from neighboring Thailand, rather than institutionalizing HTA in Myanmar itself. This was expected to strengthen the country's evidence-based policy-framing capacity with the aid of external partners (Millar et al., 2019).

Institutionalizing HTA in Colombia

With financial seed funding from the WHO, through a five-year program (2008–2013) funded by the Inter-American Development Bank (IADB) and supported by NICE International, the Colombian Ministry of Health and academic and research institutions collaborated to institutionalize and develop a basic system with a focus on technology assessment. This initiative was spearheaded by court directions to the political authorities to integrate two benefit packages – one that was more generous and one that was less subsidized. The technical challenges and strategies in merging the two systems were major challenges to overcome through this collaboration. The consortium coordinated its action

plan through knowledge exchange and meetings between different international partners and research organizations, including the Argentinian Institute for Clinical Effectiveness and Health Policy (IECS) and NICE International. The consortium supported the development of an institutional framework and an executable action plan, which led to the enactment of legal regulations and the establishment of the Institute for Health Technology Evaluation (IETS), now the main HTA agency in Colombia. A comprehensive assessment and evaluation of the Latin American and Western HTA systems were performed and price lists were established by the judicial system.

Local capacity development and skill training were carried out in close cooperation with academic institutions and universities and through international secondment options for Colombian experts. Since its inception, IETS has been facing several challenges, including financial sustainability and court rulings that have superseded and undermined policy decisions (Castro, 2017).

International Initiatives

International initiatives including NICE, IQWiG, EUnetHTA, and INAHTA are shaping policy-making and influencing healthcare-related decision-making globally. Features of some of these initiatives are described below.

NICE

NICE performs HTA for the NHS in the United Kingdom. NICE is responsible for recommending specific technologies to be funded by the NHS (Charlton, 2020).

Purpose and development of NICE

In 1997, the British government realized that patients being treated at the NHS did not have easy access to expensive medicines, which were allocated based on a postal code lottery system. Limited financial support was granted by the central government to the NHS. Therefore, the government created NICE in 1999, which was commissioned to guide the NHS in the application of a single or a set of identical therapeutic medicines, products, and systems (technology appraisal), and to prepare guidelines for clinical care by healthcare workers to improve the NHS standard of care. Its purpose was to improve the clinical efficacy and cost effectiveness of new health technology (Bertram et al., 2021). The development of NICE was based on certain fundamentals, including involvement of multiple stakeholders, clarity, no overlapping interests, and open debate. NICE has since expanded its scope by making decisions on advanced and the latest drugs and technologies implemented by the NHS and recommending benchmark guidelines for various aspects of clinical and public healthcare. NICE played a key role in transforming scientific and clinical evidence into policy in the context of healthcare (Tantivess et al., 2017).

NICE International

Due to the increasing prominence of NICE, international HTA agencies approached the institute for support in improving and upgrading their own HTA systems and help in decision-making and effective resource allocation. To support the international HTA commun-

ity, NICE established NICE International in 2008 to provide guidance on capacity development for assessment and to transform evidence into policy. NICE International currently serves in seven countries across Asia, Africa, Latin America, and Europe (Tantivess et al., 2017).

IQWiG

The German Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG) is a technically independent research institute with legal capacity within the German **statutory health insurance (SHI)**. The bulk of the SHI expenditure is on curative services, not only on chronic diseases. This includes inpatient services (about a third of total expenditure) and prescription medicines. As an HTA institute, it provides evidence to the Federal Joint Committee (G-BA), the main decision-making body within the system. IQWiG conducts autonomous proof-based reviews of pharmaceutical drugs, medical interventions, and clinical examinations. The IQWiG has a key role in the early benefit assessment of innovative medicines and conducts health economic evaluations. IQWiG is funded by grants and allowances from statutory health insurance and receives some financial support from the Federal Ministry of Health (International Network of Agencies for Health Technology Assessment, n.d.).

Statutory Health Insurance (SHI)
German statutory health insurance (SHI) covers healthcare of all beneficiaries and provides comprehensive coverage that comprises treatment at the hospital, consultation with general practitioners and clinicians, rehabilitation, physiotherapy, health examinations, oncological screening and scanning, medicines, therapies, hearing aids or wheelchairs, dental checkups and orthodontic treatment up to 18 years of age.

Purpose of IQWiG

IQWiG has played an important role in the German health system since its inception in 2004. The purpose of IQWiG is to participate in advancing and improving healthcare services in Germany. IQWiG performs and publishes evaluations relating to the effectiveness, standards, and competence of health services. It also executes assessments of the benefits of drug and nondrug treatments and therapies, conducts assessments of clinical evidence-based regulations for the epidemiology of a disease, and provides knowledge to the public regarding standards and efficiency of healthcare. Two new reforms in 2007 and 2010 were implemented to broaden the scope of IQWiG. Through the 2007 reform, known as the Act to Promote Competition of SHI (GKV-Wettbewerbsstärkungsgesetz, 2007), IQWiG is authorized to compare the cost-effectiveness of drug interventions with earlier treatment options. The 2010 reform created the Law on the Reorganization of the Pharmaceutical Market (Arzneimittelmarktneuordnungsgesetz AMNOG, 2011), which establishes the liability of the (G-BA) to evaluate the benefits of recently authorized drugs. The evaluation is conducted on the basis of “value dossiers” provided by the manufacturers to the Federal Joint Committee (G-BA), which then instructs the IQWiG with dossier evaluations. If additional benefits are established, the reimbursement price of the new drug will be determined following a process that involves the Federal Association of the Health Insurance Funds and the (industry) stakeholders.

Functioning of IQWiG

IQWiG compiles reports on subjects commissioned by the G-BA or the Federal Ministry of Health or on matters determined by the IQWiG itself. All the reports are developed employing a defined set of methods. Stakeholder organizations are regularly requested to participate in IQWIG’s processes in different capacities. Reports compiled by IQWiG are publicly available online.

EUnetHTA

To establish a robust and balanced HTA system, the HTA Core Model was established by the European Network for Health Technology Assessment (EUnetHTA; Kristensen et al., 2017). The task of Work Package 4 (WP4) of the EUnetHTA project was to produce a common multidisciplinary core of HTA evidence (EUnetHTA, 2008).

Purpose of EUnetHTA

The strategic aim of the EUnetHTA was to eliminate any overlap or duplication of work and use available resources efficiently, enhance HTA to recommend or impact decisions in associated member states within the EU, focus on the association between HTA and healthcare policy-making within the EU, and guide countries with limited knowledge and HTA experience. The two key issues of the existing HTA system were differences in the degree and scope of analysis, and variability in describing outcomes.

Purpose of the HTA Core Model

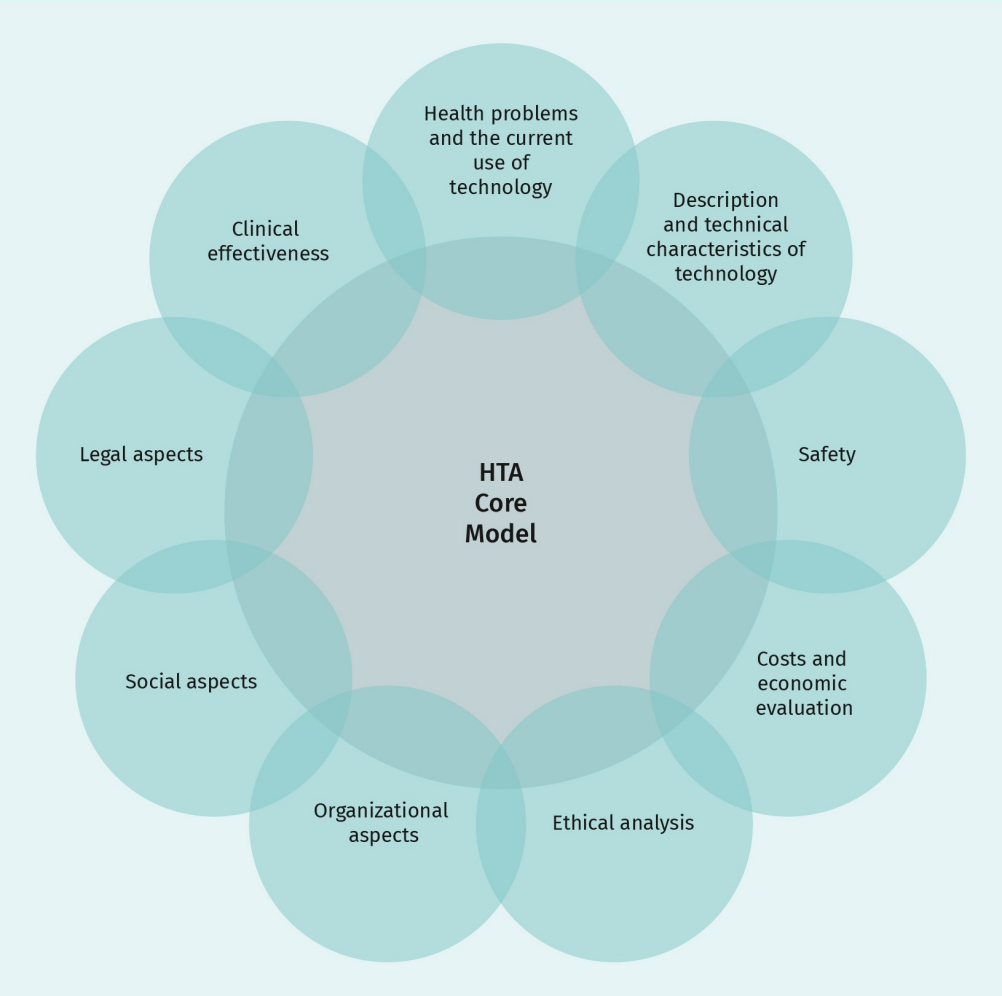
The purpose of the HTA Core Model was to develop a framework that allows useful association and knowledge exchange to avoid and overcome the aforementioned issues. This will increase the global acceptance, relevance, and usefulness of international, national, or regional HTA reports (Lampe et al., 2009). The HTA Core Model was developed based on views of members from 24 institutions in 17 different countries. This model evaluates medical and surgical interventions and assesses diagnostic technologies. These assessments formed the basis of the Core HTAs (Lampe et al., 2009), which were developed together with the medical and diagnostic assessments to improve the HTA model based on assessment feedback.

The validation of the HTA Core Model and pilot assessments allowed each domain participant to implement modifications to the model. The validation was performed by EUnetHTA and INAHTA members via an online questionnaire. Participants were asked to respond to the questionnaire encompassing three domains they had not worked on earlier and to compare the model with an existing model or with a completed HTA. Percentages were evaluated based on the questionnaire, and ideas from these comments were taken. Public feedback was collected using a standard protocol and the pros and cons of developing the HTA Core Model were outlined (Lampe et al., 2008, 2009).

Elements and domains of the HTA Core Model

Elements of the HTA Core Model include “ontology,” which refers to the problems and questions to be answered by an HTA; “methodological guidance,” which includes how to answer questions; and “reporting structure,” which refers to how the problem should be addressed (Lampe et al., 2009). The HTA Core Model encompasses nine HTA domains, as illustrated below.

Figure 21: Health Technology Assessment Core Model



Source: Swati Sharma (2022), based on Lampe et al. (2009).

The four domains of the HTA Core Model, including the health problem and current use of technology, description and technical characteristics of technology, safety, and clinical effectiveness, influenced the generation of access evidence tools (EUnetHTA, 2008). The primary objective of evidence generation included the following: scoping the disease and indication-specific evidence required for HTA agencies and patients, assessing the existing evidence creation plan, identifying gaps that may lead to threats in market access, assessing diverse options regarding evidence gaps, providing supplementary evidence, and summarizing access evidence for application in HTA guidelines. Exclusive access evidence tools were developed to address each of the objectives.

The EUnetHTA WP4 project was led by the Finnish Office of Health Technology Assessment. Germany and Belgium shared the Quality Management (QM) responsibility, while the HTA Core model fell under the responsibility of the Belgian Activity Center B under QM Scientific Guidance and Tools (EUnetHTA, 2008). A handbook has been developed for

online users detailing the basic principles of the HTA Core Model, practical guidelines on applying the model, and methodological instructions for identifying answers to research questions of the core HTA (Lampe et al., 2009).

INAHTA

INAHTA stands for the International Network of Agencies for Health Technology Assessment.

Purpose

The key objective of the INAHTA is to allow mutual coordination and sharing of knowledge across various HTA sources and to decrease the burden on various national and international agencies working on identical topics (Hailey, 2009).

Structure and Function

INAHTA was formed by 13 founding organizations from Australia, Canada, France, the Netherlands, Spain, Sweden, Switzerland, the United Kingdom, and the United States and currently involves approximately 50 agencies that impact the health of people in 31 nations. The functions and tasks of INAHTA were structured and defined in 1994. Institutions eligible for INAHTA membership are involved in the HTA initiative, provide consultations to governments, compile HTA records, and accept half of the allowances from the public. All members contribute to the incorporation of a council and a three-member committee at the Canadian HTA office (Hailey, 2009).

Development

INAHTA has included members on a yearly basis. Some of the members opted out of the network due to changes in their scope and objectives or due to a sponsorship crunch. The INAHTA secretariat relocated to the Swedish Council for Technology Assessment in Health Care (SBU) Sweden in 1996, and the executive council was expanded to facilitate the smooth functioning of the network. A website was incorporated as a platform for knowledge exchange for all members of the network. The network has been actively working to develop HTA reports, guidelines, abstracts, and frameworks, and the members collaborate on projects. Even with a limited financial budget, INAHTA has been a success in establishing communication between different institutions. INAHTA is continuously attracting members from different parts of the world and is actively working on HTA-related projects.

SUMMARY

To institutionalize HTA mechanisms, it is important to design an institutional arrangement, build institutional capacity, evaluate the risks involved, and create a governance and operational structure. To design an institutional system, different HTA systems should be assessed, and the most appropriate system should be adapted based on country-spe-

cific demands and needs. A suitable location is chosen, and the right public authority is nominated to make reimbursement decisions. All the key stakeholders are identified. The institutional system is developed by assessing the existing bottlenecks and competences needed. An action plan is created to learn about assessment models and exercises, the state of the appraisal agency, the resolution of any conflicts during assessment and appraisal, regional law, legal compliances, and responsibilities. Risk assessment is conducted by recognizing institutional bottlenecks, such as data quality and access, resource supply and aid. A program should be drafted to overcome and quell any risks. An institutional structure needs to be created that encompasses all healthcare-related aspects of the country. Several international agencies and initiatives, among them NICE, IQWiG, EUnetHTA, and INAHTA, are influencing the development of HTA-related institutional mechanisms and policy-making in low- and middle-income countries.