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HEALTH TECHNOLOGY ASSESSMENT AS A MANAGERIAL TOOL FOR THE ADOPTION OF INNOVATIVE TECHNOLOGIES

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Introduction

Cardiovascular diseases are among the leading causes of morbidity and mortality, imposing a substantial clinical and financial burden on patients and society. In the Netherlands, it has been estimated that approximately 1.7 million people were affected by cardiovascular diseases in 2020, resulting in a total cardiovascular-related expenditure of 6.8 billion Euros, accounting for about 6% of the overall healthcare expenditure in Euros.[1] In Italy, direct healthcare costs associated with cardiovascular diseases have been estimated at approximately € 16 billion, alongside an additional € 5 billion spent on indirect costs calculated as productivity losses. Furthermore, in 2014, productivity loss due to premature mortality across six European countries amounted to € 19.6 billion (contributing to a total healthcare cost of € 81.1 billion).[2]

The advancement of novel diagnostic and treatment tools holds paramount significance in both preserving lives and conserving healthcare resources. For instance, the availability of more precise instruments for assessing aortic conditions assumes a life-saving role, given that the rupture of thoracic aortic aneurysms is linked with an overall mortality rate ranging from 97% to 100%. Another illustrative instance is the utilization of artificial intelligence in diagnostics, which has the potential to enhance accuracy and expedite the diagnostic process, as evidenced by Rueckel *et al.*[3]

An increasing array of healthcare technologies is emerging, and novel therapeutic avenues are being vigorously investigated within cardiovascular medicine research. These innovative interventions hold the promise of not only mitigating the prevalence of diseases but also imposing supplementary financial demands on healthcare systems that are already facing considerable strain.

In contrast to the process of innovation lies the reality that not all emerging technologies inherently represent advancements over existing technologies. Moreover, the efficacy of such technologies can exhibit variations contingent upon the specific patient cohort to which they are administered: while a certain patient subset may attain optimal outcomes, no demonstrable superiority over prevailing standard care might manifest within another subset. In a context where the population's healthcare needs exhibit incessant escalation, and the available healthcare resources remain inherently limited, the allocation of these resources becomes a matter of strategic significance. Discerning which technology is most likely to yield the maximal benefit (value) for patients, the healthcare infrastructure, and the larger society becomes an imperative for decision-makers. In essence, the act of investing in a particular technology signifies a corresponding divestment

in an alternative avenue. Furthermore, the cost of investment encompasses not only the acquisition expense of the chosen technology but also the foregone advantages resulting from the non-selection of the alternative option. Choices need to be made about "how to employ available resources optimally among innumerable possible or desirable actions to benefit the health of individuals and of populations."[4]

Questions arise as to whether a new technology is worth adopting, how to evaluate new programs or service delivery models, and how to determine whether the new technology gives value for money. Value for money is linked to the concept of accountability, *i.e.*, rendering a transparent account of resources. The concept aims to ensure that available resources are efficiently used to maximize desired health outcomes according to a health system's objectives. To answer these questions, health technologies should be evaluated for their ability to ensure an adequate level of appropriateness, efficacy, and cost-effectiveness.[5] Then, a decision-making process needs to be put in place that is informed, responsive to stakeholder demands, and capable of promoting both technological innovation and technology assessment.[6] Decision-makers should opt for healthcare technologies that appear promising based on decision-supporting tools that are efficient, transparent, and replicable.

Health technology assessment as a supporting tool to support decision-making on health innovation

Health technology assessment (HTA) is "an area of scientific research orientated toward clinical practice and designed to support decisions and their deployment about the adoption and use of healthcare technologies."[7,8] HTA thus forms a link between scientific evidence and organizational, political, and strategic decisions. HTA refers to a "multidisciplinary process that uses explicit methods to determine the value of health technology at different points in its life cycle. The purpose is to inform decision-making to promote an equitable, efficient, and high-quality health system."[9] The value of a technology is determined by assessing the direct and indirect consequences of clinical efficacy, costs, and economic, ethical, social, cultural, legal, and organizational implications "induced" by the technology compared to existing alternatives.

To gain a better understanding of what HTA is, we first need to define the concept of health technology. It is an umbrella category that comprises medical equipment and devices, drugs, diagnostic systems, medical and surgical procedures, care pathways, and structural, organizational, and managerial assets through which healthcare services are delivered. The World Health Organization (WHO) defines health technology as "health technology refers to the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives." In summary, health technology encompasses practical applications of knowledge employed to promote health and to prevent, diagnose, and cure disease.

HTA has garnered greater acceptance owing to its multidisciplinary basis. It can be applied to analyze healthcare complexity by combining clinical and socioeconomic variables to create a shared language that synthesizes the issues being investigated and the healthcare organization's actors or the institutions involved in the evaluation of alternative technologies.

Economic factors make up an integral part of the HTA model. According to Drummond *et al.*, economic evaluation in healthcare is "the comparative analysis of alternative courses of action in terms of both their costs and consequences."[10] Of note is that economic evaluation in HTA is not an accounting method or a means to cut costs but rather an analysis of technologies for their costs and benefit/utility from which information is

extrapolated to allocate resources efficiently. Economic analysis aims to provide information for making conscious choices so that resources can be allocated as efficiently and effectively as possible. This type of economic evaluation is a core component of HTA and should be viewed in connection with clinical and social variables.

Setting up a health technology assessment process

HTA can be illustrated as multiple steps of a process.

The first phase is *priority setting*, in which criteria are defined and applied to rationally orientate the selection of technologies to be evaluated, the chronological order, and the timeframe in which they should be evaluated.[11, 12] This step is particularly critical, given the huge pressure to conduct analysis in HTA and the diverse healthcare needs to be factored into the analysis. The HTA process is normally activated by clinicians' hospital managers or producers wanting to bring their products and services to market, for example, drug firms and medical device manufacturers. The success of an HTA depends on the selection of issues relevant for policymakers, managers, healthcare professionals, and – theoretically – all stakeholders involved (*e.g.*, manufacturers, scientific associations, researchers, patients, and their associations).[13, 14]

Assessment, the second step, refers to evaluation proper. It is conducted *via* the HTA methodology: a multidisciplinary and multidimensional evaluation of a technology. It is at this point in the process that HTA becomes a link between science and decision-making when the characteristics of health technology are examined, described, and evaluated for its safety, efficacy, social, economic, and ethical implications. The product is a report that relates the features of a technology that holds interest for decision-makers. The evidence produced during HTA is transmitted in the third step, *appraisal*, which may be defined as a deliberative process for formulating recommendations through the contextualization of the scientific evidence collected and analyzed during techno-scientific evaluation. Recommendations are derived from the information obtained during the assessment phase and are intended to determine whether a set of criteria has been met or not. The appraisal process provides decision-makers with a set of recommendations on whether to adopt the new technology.[14]

HTA domains

A HTA will comprise the fundamental aspects of a technology, a medical device, a drug, or a healthcare pathway. A healthcare team's task is to design an HTA using their skills and knowledge to conduct an epidemiological evaluation to determine the prevalence and spread of a disease; estimate the use of the technology and its cost to a health system; describe diagnostic-therapeutic-care pathways and strategies for patient management; evaluate the efficacy and safety of health technologies; conduct a cost-benefit analysis, a cost-utility analysis, and sustainability analysis within the budget; plan organizational changes to accommodate the technology and its implications for the organization/reorganization of services, access to care; funding and financing; as well as ethical, social, and legal aspects.[15]

Health problem and current use of technology

The first domain defines the health problem and the target population on which the appropriate use of the technology is to be evaluated. The health problem is framed as a qualitative description of the disease including its natural history (course), diagnostic methods, prognosis, epidemiology (incidence, prevalence), and risk

factors. The actual protocols for managing the disease are described, including the technology and its alternatives, and the policies recommended for determining the target population. When evaluating the effectiveness of new diagnostic tools or technologies for aortic pathologies, it is common to use existing standard diagnostic methods as comparators. These standard methods are well-established and widely accepted in the medical community, providing a baseline for comparison. The goal is to demonstrate that the new tool performs at least as well as, if not better than, the established methods.

In this phase, the comparators are described. For example, established imaging techniques like CT scans, MRIs, and echocardiography are often considered gold standards for diagnosing aortic pathologies. These methods have been extensively studied, and their accuracy and reliability are well-documented. The new diagnostic tool would need to demonstrate comparable or superior diagnostic accuracy.

The new technology and the current technologies are detailed and compared with what is done in other clinical settings, other regions, or other countries. For diagnostic tools can be interesting to estimate the burden of the miss diagnosis in its absence to measure hypothetical cost savings due to a new diagnostic tool introduction.[16] Since the analysis depicts a general scenario within which the new technology will be set, the technologies in use are accurately described because they may be selected for replacement or joined use.

Description and technical characteristics of the technology

The second domain describes the technology or a series of technologies and its characteristics: when it was developed and introduced, for which purposes and users, in which way, and under which conditions it is used. Included are the material requisites for the facility, the equipment, the personnel, the eventual need for training, and the norms regulating the use of the technology. The responses should be described in sufficient detail to enable distinguishing the technology from its comparator.

Indeed, the choice of comparators is important since HTA is a relative type of assessment in which a comparison is made between new and existing technologies in current use. The choice of one comparator over another can lead to diverse results. Comparators are normally chosen according to three criteria: current standard of care, *i.e.*, what the literature or expert opinion considers the standard most widely used in similar contexts; the most economical alternative; and the gold standard. In addition to defining a health technology, it is useful to define the stage of the technology's life cycle as this, too, may influence political or organizational decisions.

Safety

Safety refers to an undesired or harmful effect on the health of an individual caused using a health technology. The topics cover various safety aspects for the patient, the healthcare provider, and the environment where the device is used. An HTA report will include a safety assessment for the benefit of the patient and to inform decision-makers. This third domain influences all other domains. Decision makers need to consider not only a technology's effectiveness but also the potential undesirable effects its use may have in clinical practice and the direct and organizational costs such events will bear on from resources.

From a managerial point of view, this domain is also important. By quantifying the effects in economic terms of adverse events, it should be possible to map the process, measure the resources absorbed, and quantify them economically. For example, an adverse event can cause major use of hospitalization, specialist examinations, and drugs, as well as staff time. If the new technology can reduce adverse events, it also influences

the economic evaluation. Moreover, the organizational part is involved. Safety issues can be also indirect or not caused by the technology itself but rather by its incorrect use. For instance, damage resulting from lack of maintenance or lack of staff training on how to use the technology or the technology misapplied to a patient segment. In such cases, the HTA report will state the training needs and the management of the technology to render its use safer by modifying processes and protocols and raising staff knowledge and skills.

Clinical effectiveness

Effectiveness in healthcare refers to the ability of a health intervention to achieve a certain health outcome or endpoint.[10, 17, 18] It is necessary to keep in mind the distinction between theoretical efficacy and practical efficacy (effectiveness). Theoretical efficacy is the measure in which a technology/device/drug produces a desired effect in ideal circumstances (*e.g.*, as stated in the protocol of a randomized controlled trial [RCT]). Differently, practical effectiveness is a measure of whether a technology, medical device, or drug produces the expected effect in routine clinical practice (*e.g.*, as used by a physician in a hospital). Clinical trials, and RCTs in particular, are considered a primary source of information and the gold standard for obtaining scientific evidence of a causal relationship between an intervention and a health outcome. On the other hand, the fact that the sample population in an RCT is selected according to stringent inclusion criteria and that the trial is conducted in an ideal situation in which, for example, the patient undergoes 24-hour monitoring and the risk of non-compliance with treatment is minimized. Hence, RCTs do not represent the population that will receive the intervention.

Given that the objective of an HTA is to support decision-making on the use of technology in clinical practice and given that certain clinical studies are conducted in a protected environment, it is useful to integrate, the data from clinical trials with observational data from real-life contexts whenever possible. Thus, the second perspective evaluates the effectiveness of technology within normal circumstances of clinical practice (*e.g.*, a hospital ward) and includes real-world factors that consider the adoption of technology in the routine practice of healthcare providers.

Several metrics are available to assess the effectiveness of an intervention. Firstly, there are "physical" metrics that directly and with objective units of measure are linked to health improvements. For instance, these may comprise years of life gained thanks to the technology, years of disability avoided, quantified reductions in specific cases (such as occurrences of myocardial infarction), durations devoid of symptomatic manifestations, or even intermediary endpoints linked to subsequent enhancements in health status. These intermediary endpoints could encompass physiologically metabolic parameters such as LDL cholesterol levels, blood pressure readings, or measurements of bone mineral density. To exemplify, in the evaluation of a therapeutic regimen targeting hypertension, an intermediary endpoint could manifest as a discernible reduction in systemic blood pressure. Similarly, when scrutinizing diagnostic technologies effectiveness can refer to test accuracy (such as test specificity and sensitivity).

Secondly, there are the patient-reported outcome measures reported directly by the patient through the use of validated questionnaires. They seek to identify the health state of the patient. The following two types of instruments exist: disease-specific and generic health state.

Disease-specific PROMs are created to measure the health status of a specific pathology. Disease-specific scales exhibit an elevated sensitivity to variations in patients' conditions and can offer remarkable precision in assessing treatment-related improvements.[19] Examples of disease-specific scales are the following: the Kansas City Cardiomyopathy Questionnaire (KCCQ), the Seattle Angina Questionnaire (SAQ), the Toronto Aortic

Stenosis Quality of Life Questionnaire (TOQOL), The Minnesota Living with Heart Failure Questionnaire (MLHFQ). KCCQ is a disease-specific questionnaire designed to evaluate the health status of patients with heart failure. It assesses physical limitations, symptoms, social interactions, self-efficacy, and quality of life. This tool is especially relevant for assessing the impact of interventions on heart failure patients' quality of life.[20] SAQ is used to assess the impact of angina on patients' physical limitations, angina stability, and quality of life. It is particularly applicable for evaluating the effects of different interventions on patients with angina.[21] The TOQOL is a validated tool that focuses on evaluating the impact of aortic stenosis on various aspects of a patient's quality of life. It considers the physical, emotional, and social dimensions affected by the condition.[22] The MLHFQ is a widely used disease-specific questionnaire designed to evaluate the impact of heart failure on a patient's quality of life. It encompasses various dimensions of well-being, including physical limitations, symptoms, emotional distress, and social interactions.[23]

Conversely, generic measures of health status have a lower ability to detect minor health. They are less sensitive than disease-specific scales. However, these generic measures allow the analysis of outcomes beyond the confines of a specific disease context. This kind of scale help decision-makers to compare technologies in different clinical setting. In other words, it is complex to compare a 15% gain in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30, a widely used and validated questionnaire designed to assess the health-related quality of life in cancer patients) *versus* a 15% gain in TOQOL.

Generic scales are divided into preference-based and non-preference-based measures of health status.

The most used scale in non-preference-based measures of health status is Short Form Health Survey (SF-36).[24] It is a validated questionnaire that assesses health-related quality of life across multiple dimensions. While not specific to a specific pathology such as aortic pathologies, the SF-36 can provide valuable insights into how individuals perceive their overall health and well-being, which can be relevant in various medical contexts, including cardiovascular conditions.

The SF-36 consists of 36 questions that cover eight health-related domains:

- physical functioning;
- role limitations due to physical problems;
- bodily pain;
- general health perceptions;
- vitality;
- social functioning;
- role limitations due to emotional problems;
- mental health.

However, when aiming to capture the unique challenges and experiences associated with aortic pathologies, it is necessary to use SF-36 together with disease-specific questionnaires (like TOQOL) which might provide more targeted and accurate information.

The preference-based scales relate to economics research and are based on utility theory.[19] The same health status can be perceived in different ways by two different individuals. It depends on several factors such as age, sex, culture, and individual preference. For instance, individuals may exhibit a preference for immediate, or short-term, results over more enduring outcomes that might be postponed into the future. Consequently, the perspective of the decision-maker deems it advantageous to integrate both the qualitative and quantitative aspects of life, thus amalgamating individual preferences for specific health states. Among preference-based generic scales, the Quality-Adjusted Life Years (QALYs) metric is the most widely employed. Utilizing QALYs

to gauge health outcomes can encapsulate both the reduction in mortality (quantitative life gain) and the experiential aspect of the additional years of life (qualitative gain) within a singular measure. Central to the QALY framework is the assignment of weights, symbolizing utility values, to each health state. This utility value is inherently tied to the preferences associated with that health condition. Thus, the process involves two pivotal steps. Firstly, a validated instrument, typically in the form of a questionnaire, is employed to enumerate potential health states. Examples of these include the EuroQol-5 Dimension (EQ-5D) with both 5-level (5L) and 3-level (3L) versions, the Short Form 6D (SF-6D), and the Health Utilities Index (HUI).[25]

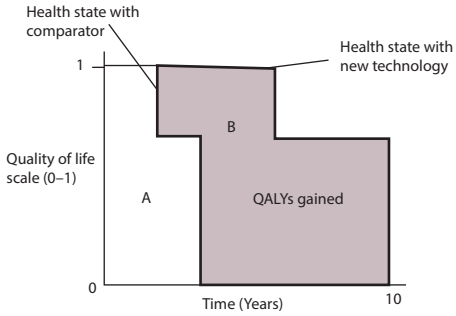

Figure 5.2.1 Representation of the impact of healthcare technology (concerning the comparator) measured using QALYs. QALYs: Quality-adjusted life years.

The subsequent step entails associating a utility value with each health state. This value is extrapolated through dedicated surveys conducted on a representative sample of the population, employing specialized techniques. Consequently, once the questionnaires are completed, the duration spent in each health state is coupled with the derived utility values, and these are aggregated over the specified time horizon. Utility values for health states can range between 0 (dead) and 1 (perfect health). In Figure 5.2.1, an illustrative depiction is presented, portraying the hypothetical impact of a healthcare intervention on both life expectancy (X axis) and quality of life (Y axis). The B region identifies the cumulative gain in terms of QALYs with the intervention (the use of new technology *versus* the comparator).

Cost and economic evaluation

The objectives of this domain are to determine the effectiveness of allocating financial resources, to inform decision-makers about the results of cost-effectiveness analysis or the cost-utility of technology, and to evaluate the sustainability of economic acceptability of an intervention based on budget impact analysis (BIA). Drummond states that economic evaluation entails the comparative analysis of alternative courses of treatment in terms of their cost and health consequences.[10] This domain aims to inform decision-makers about the cost-therapeutic effectiveness of technology and to summarize available economic evidence.

The main types of economic analysis in healthcare are cost minimization analysis; cost-efficacy analysis (CEA); cost-utility analysis (CUA); and cost-benefit analysis (CBA).[26] Cost minimization analysis is conducted only when treatments are equivalent; in other words, it has been statistically demonstrated that the treatments achieve the same outcome. In such cases, the costs are compared, and the least costly technology is chosen.

Differently, a CEA compares the costs with the outcome as measured in physical units (as mentioned in the previous domain): 1) life years gained (LYG); 2) days of disability prevented; number of events prevented; and 3) symptom-free days. CUA incorporates health outcomes in terms of utility, wherein utility is measured as quality-adjusted life years (QALYs). The results of a CUA are expressed as the cost per year of health or QALY gained due to the technology according to its comparators. These two types of analysis are widely used

in HTA.[27] In economic terms, they are considered constrained maximum problems. In other words, they consider a situation in which the aim is to optimize a set budget. Furthermore, it is as if it were taken for granted that one of the alternatives will be chosen. The assumption is that an action will be carried out anyway: the decision maker assigns value to resolve a health need, while the point is to find the technology that most efficiently reaches the objective.

A CBA asks whether it makes sense or not to increase the total budget. To answer the question, the analysis compares the costs and the health benefits in monetary terms. The result is a cost-benefit report or the sum (negative or positive) of benefits and costs that represents the net benefit (loss) of one program compared to another. Ideally, a CBA will provide an absolute value in addition to a relative value. If a program has a better ratio of benefits and costs, then it would make sense to deploy it. A CBA translates benefits into monetary terms and can be used in other areas besides healthcare, for example, for comparing investments in health technologies such as health education programs, transport, or the environment. CBA is seldom used in healthcare mainly because is complex to evaluate health outcomes in monetary terms.[28, 29]

Modelling a health economic evaluation

State the research question

In decision modeling for health economic evaluation, a series of steps to create the model need to be determined as they will influence the nature of the assessment. For example, what is the target population of the analysis? Which technologies will be compared? How far does the temporal horizon extend? From which perspective will the costs and benefits be reported that of the health system, the hospital, or the societal impact?

When building a decisional model, analysts choose the structure adequate for analyzing the health problem and they then identify the data to fill it. To do this, the problem needs to be described in detail. As mentioned above, the health problem and the objective of the evaluation need to be identified, the population or the subpopulation defined, and then the choice between alternative actions, *i.e.*, the technologies to be compared. Defining the temporal horizon and the study perspective is of foremost importance.[30]

For example, the use of 3D in surgical practice is now widely acknowledged. Its utility spans a spectrum of applications, ranging from the creation of anatomical models primarily aimed, at facilitating surgical planning to the production of surgical guides, at implants until patient engagement.[31, 32] It is imperative to delimit the scope of the application of the technology to a specific realm of intervention.

Define the target population and subgroup analysis

Also important for conducting an analysis is to define the target population and the subpopulations. The target population should be defined in terms of characteristics relevant to the final decision. For instance, geographic area and patient characteristics, type of comorbidity, disease severity, disease prevalence, and stage. The target population is composed of patients who have or may develop a disease chosen for analysis. To render the model more specific, the focus should be directed to the level or the stage of disease. Thus focused, the model will be closer to the real world and able to consider the costs and benefits specific to the situation under study.

Another step is to divide the population into subgroups[33] by characteristics that may influence the course of the disease the effectiveness of interventions, or the costs in the model. Subgroups can be categorized by age (*e.g.*, under or over age 65 years), course of the disease (*e.g.*, onset or not of complications), lifestyle (*e.g.*,

smoker or non-smoker), and comorbidity (*e.g.*, diabetes). All these factors can influence the impact of the technology on the expected health outcome.

For example, in deciding on an abdominal aortic aneurysm (AAA) screening program it can be useful to differentiate in economic analysis between women and men. The reason is the lower prevalence of AAA in women and its development later in life. However, some aspects of the disease, like a higher chance of the AAA rupturing, suggest that AAA might be more serious in women than in men.[34] Therefore, the decision model needs to account for these kinds of differences finding different thresholds of cost-effectiveness interventions according to a subset of populations (*i.e.*, age, sex, or comorbidities).

Moreover, socioeconomic and cultural differences also need to be taken into account. For example, screening for a certain aortic pathology type may differ in effectiveness and cost depending on the country or the target population. This is why it is important to define both the population and the geographical/administrative setting, hospital organization, local health board, and regional or national health system and to describe in detail the models and types of procedures. Readers will be able to compare the differences between their situation with the study setting and make changes as necessary. Target population and subgroups should be defined before the start of a study, although sometimes differences begin to appear only after a study has begun.[35]

Define the alternative technologies to be evaluated

The choice of technology holds importance because economic evaluation is comparative. The cost-effectiveness ratio of a certain technology, program, or intervention can be obtained only by comparing it with the alternatives potentially used in practice. Theoretically, all the technologies for treating a disease in a target population should be included in the research. In other words, the comparison should include all interventions relevant to the health problem.[30]

In practice, the comparison is performed *versus* a standard of care that the technology is planned to replace. If there is no standard of care, then a comparison is conducted *versus* the interventions most commonly performed in clinical practice. If a comparator that is not a standard of care is chosen, then the economic evaluation cannot be generalized beyond the comparison at hand. Indeed, a standard of care can differ between settings, countries, and facilities. The choice of the standard of care will also depend on the perspective and the objective of the evaluation. Non-intervention or natural course of a disease may be considered comparators when deemed clinically reasonable.[10]

Define the time horizon

The temporal horizon and its justification should be explicitly stated in the presentation of the model. The temporal horizon should be long enough to capture relevant differences in the costs and the effects of the strategies under comparison. If an intervention has life-long repercussions, then a life horizon should be set.[36] In general, a horizon that comprises the entire life of a patient is to be used for interventions that may have effects on mortality, for example, organ transplantation. It is not unusual that the new technology has a higher cost in the first period to see a decrease in cost during a longer time horizon (see for example Russo *et al.*[37] where the new technology had higher costs in the first weeks, but it started to generate savings after 8 weeks).

A seminal work that compares two alternative programs for myocardial infarction coronary artery bypass grafting (CABG) surgery and percutaneous transluminal coronary angioplasty (PTCA) is reported as an example.[38] The CABG procedure entails significantly higher costs when considering expenses solely up until the

point of hospital discharge. Nevertheless, it is plausible that patients undergoing PTCA may subsequently require additional interventions, including CABG. In Henderson's study, findings show that at discharge the cost was $ 22,711 *versus* $ 9138 in favor of PTCA, but at 2 years the difference was smaller, and at 6 years there was no difference. In the examples above the choice of the time horizon is not neutral, it can change the final decision.

A cost-effectiveness report should be calculated for different temporal horizons (*e.g.*, 2, 5, 10 years, or according to the disease) to create a trend for costs and benefits over time. If the temporal horizon for deciding on a technology is beyond the available clinical data (RCTs and observational studies), information needs to be extrapolated from other sources (published literature, historical series, clinical experience) to extend the economic model. This is an advantageous feature of decisional analytical models since they allow for entering data from diverse sources to make projections or simulations on horizons longer than those of a clinical study. Such models project the results for a longer period than the data from clinical studies using scenarios for the development of a disease and by calculating the costs and effects that could probably occur if the study period were prolonged.[39] When scenarios not based on direct evidence are created, the assumptions and the relative uncertainties entered into the model to make the projections should be described and justified.[35] The results should be distinguished between short-term effects, for which direct evidence is available, and long-term effects based on assumptions and extrapolations gleaned from other sources.

Moreover, the models can be used for sensitivity analysis of various parameters for which uncertainty exists. Sensitivity analysis is conducted by examining the upper and lower bound cases of the hypothesis (discussed in the section on decisions). Sensitivity analysis should be conducted for each estimated parameter which, if there is variation, may influence the final decision. The definition of the temporal horizon will include temporal preferences and the use of discount rates. How then to evaluate the costs that will occur three years from the present? They cannot be evaluated in the same way as the costs sustained in the present. In other words, having a perfect state of health next year is less valuable than the current state of health because being healthy today means being able to enjoy other aspects of life till next year.

This aspect needs to be taken into consideration when the economic evaluation is projected over a long period, and particularly when the costs and the benefits are apt to change in the long term. For example, the major costs of screening programs are incurred in the present, while the no-screening comparator incurs costs in the future. If the temporal horizon of the screening program is cut too soon, the program may not be cost-effective. Therefore, the choice of a clinically sensible temporal horizon holds fundamental importance. Finally, the economic evaluation actualizes future costs and benefits using the discount rate (r), which varies with time depending on the choices of the decision makers.[27]

Decide the study's perspective

The choice of perspective is important because it can influence further decisions about the nature of economic valuation, the nature of costs and benefits, and the method for calculating them. The perspective should be made explicit because a program might appear beneficial from one perspective but not from another. The analysis distinguishes the perspective of a health care organization (*e.g.*, local health department, county, hospital) from that of a third party (*e.g.*, national health care system, regional health care system, insurance company), that of the citizen (*i.e.*, patient, family member, caregiver), and finally that of society at large, which includes all of the above perspectives.

Criteria supporting a decision

The general rule for evaluating one or more alternative programs is to compare the difference in costs and the difference in outcomes, measured in natural units of program effectiveness or benefit, according to incremental analysis. The incremental cost-effectiveness ratio (ICER) refers to the relationship between the difference in cost of a new technology compared to an existing alternative and the difference in effectiveness of a new technology program compared to an alternative. In short, the ICER expresses the incremental cost of obtaining an additional unit of effectiveness (*e.g.*, an additional year of life or 1 QALY or an additional year of good health) (Equation 1).

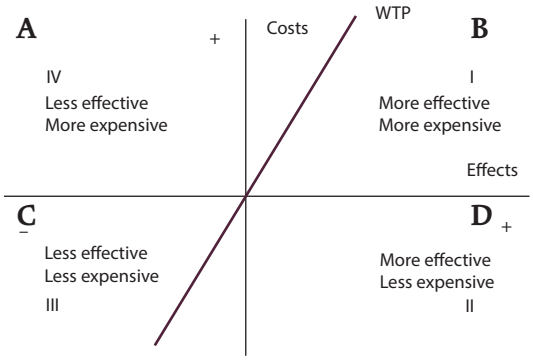

Figure 5.2.2 A-D) The cost-effectiveness plane. Modificata da: Landi *et al.*[40].

$$\text{ICER} = \frac{\text{Total cost}_{\textit{new therapy}} - \text{Total cost}_{\textit{alternative therapy}}}{\text{Outcome}_{\textit{new therapy}} - \text{Outcome}_{\textit{alternative therapy}}} \quad (1)$$

Three categories of possible outcomes of economic evaluation are distinguished:

The dominant solution in which the new technology leads to an improvement in health along with cost savings (or at equal cost) (Figure 5.2.2D).[40] In such cases, the analysis suggests that the new technology can be adopted into clinical practice as a cost-saving opportunity.

Dominated solution in which the new technology leads to a decrease in the level of health and/or an increase in costs (or at equal cost) (Figure 5.2.2A).[40] The analysis suggests that the new device not be adopted into clinical practice.

In the latter case (Figure 5.2.2B, C)[40] the new technology leads to an improvement in health but also an increase in costs.

Then, the cost-effectiveness assessment will involve an external parameter. In the situation shown in the upper right quadrant, the new technology is more costly than the alternative, therefore a judgment must be made whether the decision maker is willing to pay for an additional unit of effectiveness. The parameter is reported in the literature as willingness to pay (WTP) by society to resolve a specific health problem. By incorporating an external judgment, which can differ by setting (*e.g.*, country, region, facility) or by disease (chronic, cancer, acute). For example, the NICE has a £ 30,000 threshold and Italy has around € 30,000. Debate surrounds the correct threshold values and how and whether to differentiate by type of disease.[10, 27]

Ethical, organizational, social, and legal aspects

The five main domains of the HTA Report were described in the preceding paragraphs. The following paragraphs describe the four remaining domains of the full report: 1) ethical analysis; 2) organizational aspects; 3) patient and social aspects; and 4) legal aspects.

Ethical analysis

The term "ethical" is often used to describe activities for understanding and exploring the "moral life." The term "moral" refers to beliefs, norms of behavior, principles, and rules that guide personal, professional, and institutional behavior. Ethical analysis provides detailed knowledge of the norms and values that must be considered when preparing the HTA report and making decisions. Moral values and norms form the basis of social life and, as such, play a fundamental role in shaping the environment in which health technologies are used. Ethical analysis also reflects the fact that HTA is a complex process. The evaluation of devices and technologies should not be viewed as a purely technical process that focuses on maximizing benefits and minimizing costs. Instead, an HTA should also consider the person receiving the treatment and equity of access to innovative therapies.

Organizational aspects

This domain is about how different types of resources (*e.g.*, material, skills and knowledge, financial resources) need to be activated and organized where technology will be used, as well as the consequences that such use may have for the organization and the health system in general. Organizational aspects include work processes and patient flows, quality and sustainability, centralization, communication and cooperation, management structure, and acceptance. These aspects become important and necessary when the perspective of the assessment is that of the healthcare organization owing to the demand for internal efficiency and the guarantee of an adequate level of services.

For example, 3D printing will advance medical training for students, residents, and cardiologists by deepening their understanding of complex anatomy. Anatomical models are valuable for medical education, and integrating 3D models is expected to reshape how medical students learn. These models can also help less experienced trainees in procedures like endovascular repair for abdominal aortic aneurysms. The direct visual and tactile interaction enhance understanding and allows hands-on practice, filling a gap left by virtual reality simulations for real-world experimentation with devices like valves. Reducing or improving the learning curve of cardiologists can have organizational impacts.[41]

Another instance that can change the organizational flow involves the application of artificial intelligence (AI) in monitoring aortic aneurysms using computed tomography (CT). AI-supported radiology is reporting potential time efficiencies. With AI assistance, the average reporting time decreased by 63%, going from 13 minutes to 4 minutes and 46 seconds, even accounting for manual adjustments to AI measurements.[3] The results can lead both to economic savings and organizational change. Either aspect needs to be evaluated.

Patient and social aspects

This domain sets the patient or the person at its center. The implications for patients may also extend well beyond the initial adoption of a technology. Perceptions are related to feelings of hope, fear, and uncertainty. Analysis of the social aspects of health technology may address two questions: 1) the resources (healthcare providers, equipment, financial resources) that need to be activated before, during, and after a technology is adopted; and 2) the experience, actions, and reactions of patients toward the disease and its treatment in a work context, social relations, or attitude toward the person using the technology.

For example, cardiovascular 3D printing is set to revolutionize patient education, decision-making, and consent processes. For instance, using 3D models of heart conditions improves patient engagement and communication among doctors, parents, and patients.[41] These factors need to be valued and assessed.

Legal aspects

This domain concerns the rules and regulations in place to protect patient rights and the interests of society. These aspects are part of the legislation governing patient rights, data protection, healthcare workers, and their rights and duties. The domain may also include preventive approval processes by competent agencies.

Conclusions

introduction of new technologies into the national health system has attracted greater regulatory and managerial scrutiny. Economic sustainability is not solely a question of more than mere resource optimization and cost management. A healthcare system unable to take up new technologies that advance scientific development will not be able to meet the health needs of its users nor enable healthcare providers to apply their expertise effectively.

References

1. Rijksinstituut voor Volksgezondheid en Milieu (RIVM). Hart- en vaatziekten [Heart and vascular disease]; 2022 [Internet]. Available from: https://www.vzinfo.nl/hart-en-vaatziekten [cited 2023, Nov 17] [German].
2. Bernick S, Davis C. The economic cost of cardiovascular disease from 2014-2020 in six European economies. London: Centre for Economics and Business Research; 2014.
3. Rueckel J, Reidler P, Fink N, *et al.* Artificial intelligence assistance improves reporting efficiency of thoracic aortic aneurysm CT follow-up. Eur J Radiol 2021;134:109424.
4. Roemer MI. National health systems of the world. Oxford: Oxford University Press; 1993.
5. Garrido MV, Kristensen FB, Busse R, *et al.* Health technology assessment and health policy-making in Europe: Current status, challenges, and potential. Copenhagen: World Health Organization; 2008.
6. Cicchetti A, Iacopino V, Coretti S, *et al.* Toward a contingency model for hospital-based health technology assessment: evidence from ADHOPHTA project. Int J Technol Assess Health Care 2018;34:205–11.
7. Lega F. Management e leadership dell'azienda sanitaria. Conoscere il settore e il sistema, organizzare i servizi, dirigere i professionisti. Alba, Cuneo: EGEA; 2016.
8. Landi S. Health Technology Assessment (HTA). Turin: G. Giappichelli Editore; 2021.
9. O'Rourke B, Oortwijn W, Schuller T; International Joint Task Group. The new definition of health technology assessment: A milestone in international collaboration. Int J Technol Assess Health Care 2020;36:187–90.
10. Drummond MF, Sculpher MJ, Claxton K, *et al.* Methods for the economic evaluation of health care programs. Oxford: Oxford University Press; 2015.
11. Robinson S, Williams I, Dickinson H, *et al.* Priority-setting and rationing in healthcare: evidence from the English experience. Soc Sci Med 2012;75:2386–93.
12. Noorani HZ, Husereau DR, Boudreau R, *et al.* Priority setting for health technology assessments: a systematic review of current practical approaches. Int J Technol Assess Health Care 2017;23:310–5.
13. Facey K, Boivin A, Gracia J, *et al.* Patients' perspectives in health technology assessment: a route to robust evidence and fair deliberation. Int J Technol Assess Health Care 2010;26:334–40.

14. Tarricone R, Amatucci F, Armeni P, *et al.* Establishing a national HTA program for medical devices in Italy: Overhauling a fragmented system to ensure value and equal access to new medical technologies. Health Policy 2021;125:602–8.
15. EUnetHTA Joint Action 2, Work Package 8. HTA Core Model ® version 3.0 (Pdf); 2016. Available from: www.htacoremodel.info/BrowseModel.aspx [cited 2023, Nov 17].
16. Tinazzi M, Gandolfi M, Landi S, *et al.* Economic costs of delayed diagnosis of functional motor disorders: preliminary results from a cohort of patients of a specialized clinic. Front Neurol 2021;12:786126.
17. Epstein RS, Sherwood LM. From outcomes research to disease management: a guide for the perplexed. Ann Intern Med 1996;124:832–7.
18. McLeod C, Norman R, Litton E, *et al.* Choosing primary endpoints for clinical trials of health care interventions. Contemporary Clinical Trials Communications, 2019;16:100486.
19. Gray AM, Clarke PM, Wolstenholme JL, *et al.* Applied methods of cost-effectiveness analysis in healthcare. Oxford: Oxford University Press; 2011.
20. Green CP, Porter CB, Bresnahan DR, *et al.* Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. J Am Coll Cardiol 2000;35:1245–55.
21. Spertus JA, Winder JA, Dewhurst TA, *et al.* Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. J Am Coll Cardiol 1995;25:333–41.
22. Styra R, Dimas M, Svitak K, *et al.* Toronto aortic stenosis quality of life questionnaire (TASQ): validation in TAVI patients. BMC Cardiovasc Disord 2020;20:209.
23. Kularatna S, Senanayake S, Chen G, *et al.* Mapping the Minnesota living with heart failure questionnaire (MLHFQ) to EQ-5D-5L in patients with heart failure. Health Qual Life Outcomes 2020;18:115.
24. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–83.
25. Stamuli E. Health outcomes in economic evaluation: who should value health? Br Med Bull 2011;97:197–210.
26. Brazier J, Ratcliffe J, Tsuchiya A, *et al.* Measuring and Valuing health benefits for economic evaluation. Oxford: Oxford University Press; 2007.
27. Briggs AH, Weinstein MC, Fenwick EA, *et al.*; ISPOR-SMDM Modeling Good Research Practices Task Force. Model parameter estimation and uncertainty analysis: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force Working Group-6. Med Decis Making 2012;32:722–32.
28. Fattore G. Measuring Public Value: A Cost-benefit Analysis of In-vitro-fertilisation in Italy. Alba, Cuneo: EGEA; 2011.
29. Pavel MS, Chakrabarty S, Gow J. Assessing willingness to pay for health care quality improvements. BMC Health Serv Res 2015;15:43.
30. Caro JJ, Briggs AH, Siebert U, *et al.*; ISPOR-SMDM Modeling Good Research Practices Task Force. Modeling good research practices--overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-1. Med Decis Making 2012;32:667–77.
31. Tack P, Victor J, Gemmel P, *et al.* 3D-printing techniques in a medical setting: a systematic literature review. Biomed Eng Online 2016;15:115.
32. Magagna P, Gallo M, Salvador L. Aortic Arch Repair in Chronic Dissection using 3D-Printing Planning. Ann 3D Print Med 2023;11:100116.
33. Sculpher M. Subgroups and heterogeneity in cost-effectiveness analysis. Pharmacoeconomics 2008;26:799–806.
34. Wanhainen A, Lundkvist J, Bergqvist D, *et al.* Cost-effectiveness of screening women for abdominal aortic aneurysm. J Vasc Surg 2006;43:908–14.
35. Ramsey SD, Willke RJ, Glick H, *et al.* Cost-effectiveness analysis alongside clinical trials II—an ISPOR Good Research Practices Task Force report. Value Health 2015;18:161–72.
36. Hay JW, Smeeding J, Carroll NV, *et al.* Good research practices for measuring drug costs in cost effectiveness analyses: issues and recommendations: the ISPOR Drug Cost Task Force report--Part I. Value Health 2010;13:3–7.

37. Russo S, Landi S, Courric S. Cost-Effectiveness Analysis for the Treatment of Diabetic Foot Ulcer in France: Platelet-Rich Plasma vs Standard of Care. Clinicoecon Outcomes Res 2022;14:1–10.

38. Henderson RA, Pocock SJ, Sharp SJ, *et al.* Long-term results of RITA-1 trial: clinical and cost comparisons of coronary angioplasty and coronary-artery bypass grafting. Randomised Intervention Treatment of Angina. Lancet 1998;352:1419–25.

39. Eddy DM, Hollingworth W, Caro JJ, *et al.*; ISPOR–SMDM Modeling Good Research Practices Task Force. Model transparency and validation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force--7. Value Health 2012;15:843–50.

40. Landi S, Russo S, Landa P. Knee OA management: a cost-effectiveness analysis of platelet-rich-plasma versus hyaluronic acid for the intra-articular treatment of knee OA in France. Int J Clin Rheumatol 2018;13:307–18.

41. Giannopoulos AA, Mitsouras D, Yoo SJ, *et al.* Applications of 3D printing in cardiovascular diseases. Nat Rev Cardiol 2016;13:701–18.