HTA 101: Essential Information for Newcomers

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Health technology

A health technology is defined as an intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organize healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, program or system [http://htaglossary.net/health-technology].

Health technologies can be described in terms of their physical nature, clinical purpose, stage of development or diffusion.

Physical nature:
- Drugs: e.g., aspirin, antibiotics, cancer chemotherapy
- Biologics: e.g., vaccines, blood products, biotechnology-derived substances
- Devices, equipment, supplies: e.g., cardiac pacemaker, MRI scanner, mosquito netting
- Medical and surgical procedures: e.g., acupuncture, bariatric surgery, cesarean section
- Public health programs: e.g., water purification system, vaccination program, smoking prevention program
- Support systems: e.g., clinical laboratory, drug formulary, electronic health record system
- Organizational, delivery, managerial systems: e.g., primary care network, health care payment system

Clinical purpose:
- Prevention
- Screening
- Diagnosis
- Treatment
- Rehabilitation
- Palliation

Stage of development or diffusion:
- Future
- Experimental (laboratory or animal testing)
- Investigational (clinical studies, i.e., in people)
- Established (standard approach)
- Obsolete

Health Technology Assessment and its Role in Health Care

Origins of Technology Assessment

Technology assessment (TA) arose in the mid-1960s from an appreciation of the critical role of technology in modern society and its potential for unintended, and sometimes harmful, consequences. The term "technology assessment" was introduced in 1965 in the US House of Representatives, with the primary purpose of serving policymaking. Examples of early assessment topics were offshore oil drilling, pesticides, automobile pollution, nuclear power plants, supersonic airplanes, and the artificial heart.

Development of TA in 1960s and 1970s coincided with the introduction of health technologies that prompted widespread interest in matters that transcended their intended health effects. Examples of topics of early HTAs include: multiphasic health screening; in vitro fertilization; predetermination of the sex of children; slowing of aging; modifying human behavior by neurosurgical, electrical or pharmaceutical means; and drug bioequivalence.

Health Technology Assessment

HTA can be defined as follows:
- HTA is the systematic evaluation of properties, effects, or other impacts of health care technology.
- The main purpose of HTA is to inform policy making for technology in health care.
- HTA may address the direct and intended consequences of technologies, as well as the indirect and unintended consequences of technologies.
- HTA is conducted by interdisciplinary groups.
- HTA uses explicit analytical frameworks and a variety of methods.

In 2020, a joint task force of INAHTA and HTAi developed a definition of HTA as follows:

"HTA is a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system.[1]" (O'Rourke et al. 2020)

HTA is used to inform various functions. It is essential to understand that HTA usually does not generate a policy or decision; instead, it informs policies or decisions made by others. In particular, HTA is used to:

- Advise payers (health authorities, health plans, etc.) about technology reimbursement: coverage, coding, and payment amounts
- Advise/guide clinicians and patients about technology use (e.g., with evidence-based clinical practice guidelines)
- Help managers of hospitals, health care networks, other provider institutions/organizations to make decisions about acquiring or investing in technology
- Support decisions by national and regional public health authorities about conducting population health programs

Also, HTA can be used to:

- Support decisions by health technology companies about technology development and marketing
- Support decisions by investors in the health care sector
- Inform research agencies about evidence gaps, unmet needs

Related Concepts

There is a variety of methods, sources of evidence, and concepts that can be related to HTA or interact with HTA. Among these are:

- Outcomes research
- Patient-centered outcomes research
- Real-world evidence
- Comparative effectiveness research
- Systematic review
- Meta-analysis
- Pharmacoeconomics

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1 http://htaglossary.net/health-technology-assessment

- Coverage with evidence development
- Clinical practice guidelines
- Evidence-based medicine

Demand for HTA

Multiple factors contribute to the demand for HTA. Among these are:

- Aging populations
- Increases in chronic disease
- Growth of the middle class in developing nations
- Growth in patient/consumer demand for health information
- Ongoing development and marketing of new drugs, biologics, diagnostics, devices, other technology
- Public attention to high-priced technologies (e.g., for cancer care, rare diseases)
- Large variations in health care practice
- Inappropriate use of health care technologies, including over-use, under-use, and improper use
- "Off-label" uses (i.e., not approved by regulatory agency) of drugs, biologics, devices
- Rising health care costs (constraining resources for other important needs)
- Major reforms of national and regional health care systems
- Concerns about social, ethical, legal impacts of health technology

Unintended and Intended Consequences

Consistent with the origins of TA, health technologies can have unintended consequences/effects as well as their intended ones. Unintended consequences can be beneficial or harmful. HTA seeks to anticipate and examine their implications. Some examples of technologies with unintended consequences in some patients are:

- Aspirin: anticoagulation
- Bariatric surgery: cure for diabetes
- Antibiotics: overuse and improper use resulting in multi-drug resistant bacterial strains
- Highly active anti-retroviral therapy (HAART) for HIV/AIDS: increase in high-risk behaviors
- Medical ultrasound: fetal sex selection
- Prostate-specific antigen (PSA) testing: unnecessary invasive testing, therapies, and adverse effects for some men

Inappropriate Use

Inappropriate use of technology can call attention to the need for HTA. It can occur in different ways, including:

- Over-use: used in patients who are not indicated (i.e., for whom there is no evidence of benefit), or used too frequently in those patients
- Under-use: not used in patients who are indicated, or used too infrequently in those patients
- Improper use: although used in patients who are indicated, used incorrectly (e.g., incorrect surgical technique, incorrect drug dosing, incorrect radiation exposure)

Diffusion of Ineffective or Harmful Technologies

The history of health care technology includes many instances in which technologies became widely used with inadequate or even falsified evidence, only to be discovered later to have serious adverse health effects in at least some patients. Among the many examples are:

- Autologous bone marrow transplantation with high-dose chemotherapy for breast cancer
- Antiarrhythmic drugs
- COX-2 (cycloogygenase-2) inhibitors for patients at risk for heart disease, stroke, and certain other conditions
- Hormone replacement therapy for healthy menopausal women
- Intermittent positive pressure breathing
- Magnetic resonance imaging (MRI) for low back pain in first 6 weeks
- Oxygen supplementation for premature infants
- Prefrontal lobotomy for mental disturbances
- Prostate specific antigen (PSA) screening for prostate cancer
- Radiation therapy for acne
- Thalidomide for sedation in pregnant women

These and other examples of technologies, including some in current use, call attention to the need to conduct methodologically rigorous HTA in a timely manner.

Properties and Impacts Assessed

What does HTA assess? The main properties and impacts assessed include:

- Technical: conformity with design, performance characteristics, e.g., pharmacodynamics, diagnostic test accuracy

- Safety: judgment of the acceptability of risk (probability and severity of an adverse outcome) associated with using a technology in a given situation
- Efficacy and effectiveness: how well a technology achieves its intended purpose, especially in health outcomes
- Cost and other economic: microeconomic, e.g., cost-effectiveness of particular technologies, cost burden on patients; macroeconomic, e.g., impact on national health care costs, gross domestic product, employment, resource allocation across health care and other industrial sectors
- Ethical, legal, patient and citizen, and political: impacts on or challenges to normative concepts (e.g., valuation of human life, equity); choices about how and when to use technologies; research and the advancement of knowledge; resource allocation

Efficacy vs. Effectiveness
HTA makes an essential distinction between these terms:
- Efficacy: benefit of using a technology for a particular health problem in ideal conditions of use, for example, in a strict protocol of a randomized controlled trial or at a "center of excellence."
- Effectiveness: Benefit of using a technology for a particular health problem in general or routine conditions of use, for example, in a community hospital.
- Among the main categories of health outcomes that are used to assess efficacy and effectiveness are:
- Mortality (death rate)
- Morbidity (disease rate)
- Adverse health events (e.g., harmful side effects)
- Quality of life
- Functional status
- Patient satisfaction

Biomarkers and Surrogate Endpoints:
A biomarker (or biological marker) is an objectively measured characteristic (such as from a laboratory test or radiological image) that is used as an indicator of normal biological processes, natural history of disease, or effect of a therapy. Examples:
- Blood pressure
- EKG (electrocardiogram)
- Bone density
- Hemoglobin A1c

Biomarkers are not health outcomes (or endpoints). However, when a biomarker is closely associated with a health outcome (or clinical endpoint), and particularly when it is predictive of a health outcome, it can be a surrogate endpoint. Example:

- Decreased blood pressure for decreased risk of stroke
- White spots on an MRI scan for multiple sclerosis lesions

Patient-Centered Outcomes

Patient-centered outcomes and patient-reported outcomes are increasingly important in contributing to evidence that informs care decisions by clinicians and patients, and coverage policies of payers.

Patient-centered outcomes are those that patients experience in real-world settings, including: survival, functional status, quality of life, quality of death, symptoms, pain, nausea, psychosocial well-being, health utility (patient-perceived value of particular states of health), and patient satisfaction. Can be assessed at a generic level or a disease/condition-specific level.

Patient-reported outcomes are those that are self-reported by patients or obtained from patients (or reported on their behalf by their caregivers or surrogates) by an interviewer without interpretation or modification of the patient's response by other people, including clinicians.

Examples of generic patient-centered outcomes include the following (of which there are multiple versions):

- EuroQol (EQ-5D)
- Health Utilities Index
- Nottingham Health Profile
- Quality of Well-Being Scale
- Short Form (12) Health Survey (SF-12), Short Form (36) Health Survey (SF-36)
- Sickness Impact Profile

Examples of disease-specific patient centered outcomes in multiple sclerosis:

- Multiple Sclerosis Quality of Life Inventory (MSQLI)
- Multiple Sclerosis Quality of Life-54 scale (MSQoL-54)
- Functional Assessment of Multiple Sclerosis (FAMS)
- Multiple Sclerosis Impact Scale (MSIS-29)
- Leeds Multiple Sclerosis Quality of Life scale (LMSQoL).

Hybrid or Combination Outcomes

Another category of health outcomes used in HTA is aggregated outcome measure. These are measures of health improvement (or loss) that combine survival and morbidity (including mortality/survival, quality of life, or functional status) into a single unit:

- QALYs: quality-adjusted life years
- DALYs: disability-adjusted life years
- HYEs: healthy-years equivalents

A strength of these outcomes is that they enable comparisons of the impact of health care or other changes (e.g., environmental or economic) where the outcomes (other than survival) are not the same, e.g., incidence of diabetes, reduction in heart attacks, or prevalence of tobacco use.They are based on somewhat different assumptions and methods (e.g., for determining quality of life and disability).

QALYs are used more often in cost utility analyses to determine ratio of change in cost to QALYs gained from using a particular health care technology. DALYs are used more often in public health to measure population disease burden and impact of health programs on population health.

Some basic principles of QALYs are:

- It is widely accepted that one year of life spent in a good state of health (or function of quality of life) is preferred to one year spent in a poor state of health.
- "Utility" refers to the relative preference (value) that an individual (or society) has for a particular state of health.
- Utility weights are determined using direct methods, e.g., time trade-off or standard gamble, or indirect methods, e.g., SF-36, EQ-5D, Health Utility Index, Quality of Well-Being Scale.*
- The QALY is a unit for measuring outcomes of health care (or other interventions). QALYs combine length of life with quality of life. That is, years of life are adjusted (weighted) by patient/user utility for the quality of life experienced during those years.
- The QALY may be used as the unit of patient/user outcomes in a cost-utility analysis.

QALY = Length of Life X Quality Weight

Survival and QoL with:
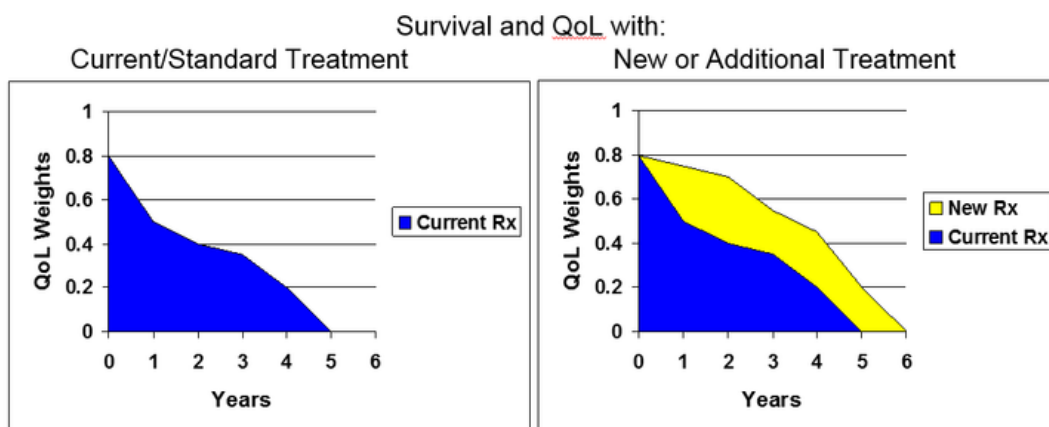
Using QALYs to capture changes in length of life (survival) and quality of life (e.g., utility for state of health) resulting from new or additional treatment

HTA Methods

Three main categories of methods used in HTA are: primary data collection, secondary (integrative) methods, and economic analyses:

- Primary data methods involve collection of original data, for example, using experimental designs (e.g., randomized clinical trials) or non-experimental designs such as observational studies (prospective or retrospective). Most HTAs do not involve conducting primary data collection, but they use evidence from available primary data studies.
- Secondary / integrative analyses combine data from existing sources, e.g., systematic reviews, meta-analyses. Combine data from existing sources, e.g., systematic reviews, meta-analyses, modeling. Most HTAs involve conducting one or more of these methods; some HTAs also involve using evidence from available integrative studies.
- Economic analyses involve various techniques of weighing costs and benefits (outcomes or other results). Many HTAs involve one or more of these analyses.

Primary Data Methods

When HTAs examine evidence from primary data studies, they consider attributes associated with stronger or weaker evidence for determining the causal effect of a technology on outcomes (e.g., efficacy or effectiveness and safety). In general:

- Prospective studies > retrospective studies
- Interventional studies > observational studies
- Controlled studies > uncontrolled studies

- Studies with contemporaneous control groups > studies with historical control groups
- Studies with randomized assignment of patients to treatment and control groups > studies with non-random assignment.
- Large studies (with enough patients to detect true treatment effects) > small studies
- Blinded studies (patients, providers do not know which intervention is being used) > unblinded studies

Primary data methods include experimental and non-experimental designs. Main types of experimental designs include:
- Randomized controlled trial (RCT)
- Randomized cross-over trial
- N-of-1-trial
- Group randomized trial
- Non-randomized controlled trial*
- Pragmatic trials (randomized or non-randomized)

*A controlled trial in which participants are assigned to treatment and control groups using a method other than randomization, yet intended to form similar groups. Sometimes known as a "quasi-experimental" design.
The diverse types of non-experimental designs include:
- Prospective cohort
- Retrospective cohort
- Case-control
- Cross-sectional
- Interrupted time series with comparison
- Non-concurrent cohort
- Interrupted time series without comparison
- Before-and-after
- Time series
- Case Series
- Case study

Evidence Hierarchies

HTA organizations (and others) use various evidence hierarchies or frameworks to rate the quality of individual studies and bodies of evidence (groups of studies). Most of these are based on, or start with, principles of stronger vs. weaker evidence for establishing causal effects of a technology, as noted above. Different types of evidence questions call for different evidence hierarchies. For example, evidence hierarchies for questions about disease prevalence, diagnostic accuracy, or detecting rare adverse events will differ from evidence hierarchies for efficacy/effectiveness of treatments. A basic example of an evidence hierarchy for therapies is:

- Systematic reviews and meta-analyses of RCTs
- Randomized controlled trials (RCTs)
- Non-randomized controlled trials
- Prospective observational studies
- Retrospective observational studies
- Expert opinion

There are many versions of such hierarchies, including some with more extensive levels/breakdowns.

A weakness of such hierarchies is that, while they tend to reflect internal validity of a cause-and-effect relationship between a technology and one or more outcomes (e.g., mortality, morbidity), they do not generally reflect external validity(generalizability) of the evidence to more diverse patients and care settings.

Secondary or Integrative Methods

The main categories of secondary methods, which combine or integrate data from primary data studies, include:

- Systematic literature review
- Meta-analysis
- Modeling (e.g., decision trees, Markov models)
- Group judgment ("consensus development")
- Unstructured literature review
- Expert opinion

The set of methods shown above is not arranged in a hierarchy. However, the general trend in HTA is to rely on systematic reviews, meta-analyses, and modeling. Unstructured literature reviews are not considered good practice in HTA, because they are especially subject to biases that can diminish the credibility of HTA findings. Although expert perspectives are an important part of certain aspects of HTA, the use of expert opinion as the main method for conducting HTA is not considered good practice in HTA.

Systematic Literature Review

A systematic literature review (or systematic review) is a form of structured literature review that addresses one or more evidence questions that are formulated to be answered by analysis of evidence. Systematic reviews involve:

- development of evidence questions (or "key questions") that are intended to capture the body of evidence to be assessed
- an objective means of searching the literature, typically using prospectively designed automated searches of bibliographic databases (usually peer-reviewed literature and selected other sources, including "grey literature" as appropriate for an assessment topic)
- applying predetermined inclusion and exclusion criteria to this literature derived from the search
- critically appraising the relevant included literature
- extraction and synthesis of data and information from relevant body of evidence base to formulate answers to the evidence questions
- A systematic review may include one or more meta-analyses.

Systematic reviews differ from unstructured literature reviews in multiple ways. Most systematic reviews start with focused evidence questions, have predefined literature search and inclusion/exclusion criteria to identify relevant evidence, include a detailed description of the methods used, are quantitative (accounting for the numbers of articles retrieved from the initial searches and numbers of articles excluded consistent with predefined criteria), and are reproducible. In contrast, a traditional or unstructured literature review may have broad or poorly defined methods section, be less likely to be quantitative, and not be reproducible.

Most systematic reviews use a format for defining a set of evidence questions and related parameters that define the evidence base for the HTA. A commonly used approach is:

PICOTS
- P: Patient, population, or problem of interest
- I: Intervention or exposure
- C: Comparator (basis of comparison, e.g., standard of care, control group)
- O: Outcomes (primary or secondary endpoints, e.g., mortality, morbidity, quality of life)
- T: Timing (duration of intervention or follow-up period of data collection, if applicable)
- S: Setting (location of delivery of intervention, e.g., inpatient, outpatient, home)

For example, an evidence question about treatment for hypertension could be expressed in the following PICOTS format:
- Population: males and females age 55-75 years with mild hypertension
  - diastolic blood pressure 85-99 mm Hg
  - systolic blood pressure 130-159 mm Hg
  - no other serious health problems
- Intervention: standardized, moderate exercise program
- Comparator: usual physical routine and diet
- Outcomes: changes in:
- general and abdominal obesity
- systolic blood pressure
- diastolic blood pressure
- aerobic fitness
- Timing: 6-24 months follow-up
- Setting: outpatient (clinics, physician offices)

Meta-Analysis

Meta-analysis refers to statistical procedures for combining results from different studies. This combination may produce a stronger conclusion than can be provided by any single study. Meta-analysis is generally most appropriate when there are not definitive studies on a topic (e.g., when their sample sizes are too small) and non-definitive studies are in some disagreement (e.g., when their treatment effects are contradictory or show large variance). The purposes of meta-analysis include:

- Encourage systematic organization of evidence
- Increase statistical power for primary end points and general applicability of findings
- Resolve uncertainty when reports disagree
- Provide quantitative estimate of effect (e.g., effect size or odds ratio)
- Answer questions not posed at the start of individual trials
- Identify needs and planning for major trials

Certainly, meta-analyses can be very useful in synthesizing evidence from multiple sources. However, like other forms of analysis, they can have weaknesses. These may include: publication bias of the primary studies comprising the meta-analysis, biased selection of available relevant studies, poor quality of the primary studies, unexplainable heterogeneity across the studies (differences in, e.g., study populations, delivery/dosage of the interventions or comparators, or how outcomes were measured), and biased interpretation of findings by the authors.

In recent years, there has been increased interest in applying meta-analysis in circumstances in which there are insufficient direct ("head-to-head") comparisons of technologies. Network meta-analysis is a type of meta-analysis in which multiple (three or more) alternative technologies are compared when there are limited or no available "head-to-head" trials of those technologies. This enables integration of data from available direct trials and from indirect comparisons across trials based on a common comparator, which could be a placebo or standard care. Network meta-analysis is also known as "multiple-treatment" or "mixed-treatment comparisons meta-analysis."
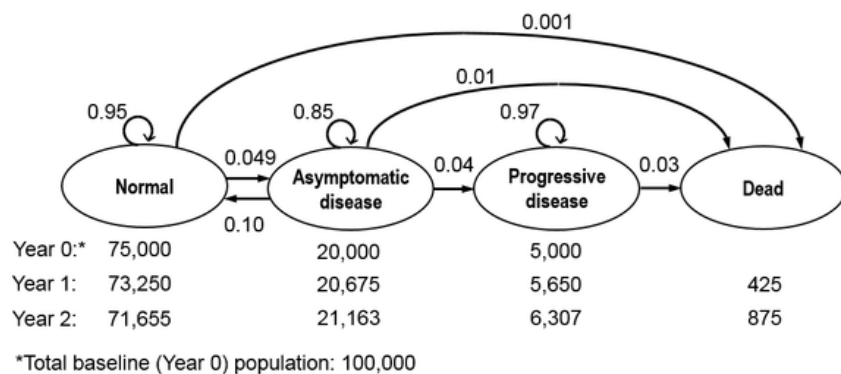
Modeling

In HTA, modeling refers to analytical techniques for simulating (representing) real processes involving decisions and their outcomes. For example, in determining which technology or regimen option is more effective or cost-effective for a particular patient population, modeling can account for the uncertainties (probabilities) that each option or decision will result in particular outcomes (e.g., health states), and/or the value (e.g., patient utility, cost-effectiveness) associated with each outcome.

Among the main types of modeling used in HTA are: Markov modeling; decision tree; multi-criteria decision analysis; Monte Carlo simulation; and various simulations of disease processes, health care interventions, and health care systems. For example, Markov modeling represents changes from one state of health to another, such as different stages of disease and death. This type of modeling is useful for representing patient or population experience when: health states change over time, some or all of the health states may recur, and there are known probabilities of transition across health states. Markov modeling assumes that each patient is in one of a set of mutually exclusive and exhaustive health states for a given period of time, there is a set of allowable (i.e., non-zero) probabilities of moving from one health state to another (including remaining in the same state from one period to another), and patient utilities and costs can be assigned to each health state.

Shown below is a general hypothetical example of a Markov modeling in which there are four possible health states: normal, asymptomatic disease, progressive disease, and death. Transition probabilities are shown for one-year periods. In this example, a baseline population of 100,000 is followed for two years (i.e., year 0 to year 2) as is progresses through the transition probabilities. A model such as this could be made more complex, such as if the transition probabilities were to differ for patient subgroups (e.g., by age, sex, or comorbidities).

Markov Modeling Disease States and Transition Probabilities (Annual, Year 0 to Year 2)

	Normal	Asymptomatic disease	Progressive disease	Dead
Year 0:*	75,000	20,000	5,000	
Year 1:	73,250	20,675	5,650	425
Year 2:	71,655	21,163	6,307	875

*Total baseline (Year 0) population: 100,000

Economic Analyses

HTA can use various types of economic analyses. Each of these has different purposes. Any particular HTA may include one or more of these. The main types include:

- Cost effectiveness analysis (CEA): costs weighed against outcomes focused on a single natural unit, e.g., deaths, heart attacks, lung cancer cases
- Cost utility analysis (CUA): form of CEA, outcomes aggregated into a unit of utility, e.g., quality-adjusted life-years (QALYs)
- Cost benefit analysis (CBA): costs weighed against outcomes aggregated into monetary units. Cost benefit analysis depends on assigning monetary values to the costs of interventions as well as the outcomes.

A basic example of a cost effectiveness calculation, to yield an ICER in the form of a cost per life-saved, is shown below.

$$\text{CE Ratio} = \frac{\$Cost_B - \$Cost_A}{Effect_B - Effect_A}$$

A: Comparator
B: Intervention

For example:

	Total $ per 100 pts	Lives saved (LS) per 100 pts	Average CE Ratio	Incremental CE Ratio (ICER)
Drug A	1,000	8	$125/LS	–
Drug B	1,000,000	10	$100,000/LS	$499,500/LS

A basic cost utility analysis, which is a form of cost effectiveness analysis that uses a measure of patient utility such as a quality-adjusted life-year (QALY) is shown below.

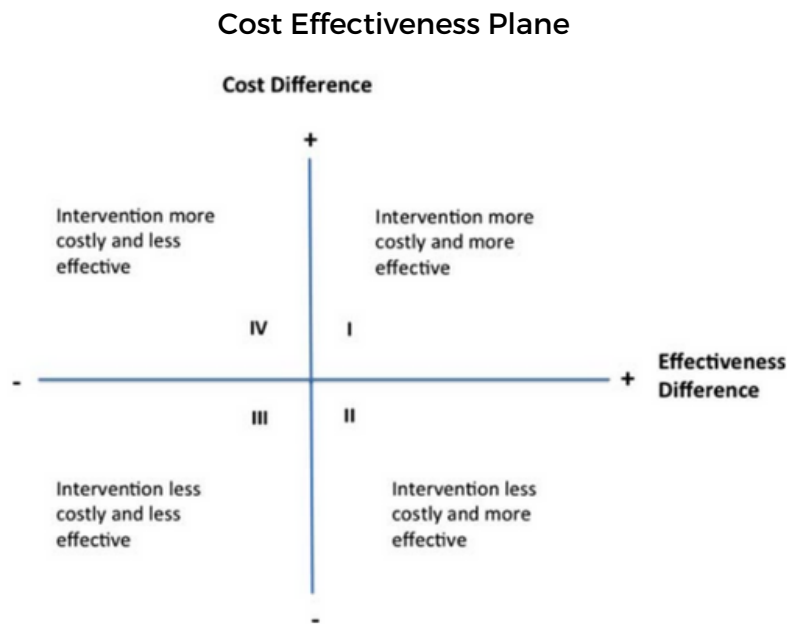$$\text{CU Ratio} = \frac{\$Cost_Y - \$Cost_X}{QALY_Y - QALY_X}$$

X: Comparator
Y: Intervention

For example:

	Total $ per patient	Life years per patient	Utility*	QALYs	Cost/QALY gained
Drug X	5,000	5.0	0.5	2.5	–
Drug Y	250,000	6.0	0.8	4.8	$107,000

*Patient utility for remaining life years, ranging from 0=death to 1.0=perfect health

A useful concept for understanding the concept of cost-effectiveness is the cost effectiveness plane. This can be understood in four quadrants, which depend on the differences in costs and the differences in outcomes between a technology and its comparator, as shown below. The CEP plane demonstrates that any interventions that fall in either quadrant II or IV do not need ICERs to be calculated as they are either more effective and less costly (II), or more expensive and less effective (IV). Interventions falling in quadrant II are typically accepted, while those falling in quadrant IV are typically rejected. Since interventions in quadrant I are more effective but more costly, and those in quadrant III are less effective but less costly, ICERs need to be calculated and compared.

Cost Effectiveness Plane

Cost Difference

+

| Intervention more costly and less effective | Intervention more costly and more effective |

IV   I

- — — — — — — — — — — — — — — + **Effectiveness Difference**

III   II

| Intervention less costly and less effective | Intervention less costly and more effective |

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HTA has increasingly included budget impact analysis in recent years, particularly to provide a distinctive perspective of "affordability" to complement cost effectiveness analysis in support of decision making. Indeed, allocating resources efficiently (e.g., maximizing cost-effectiveness) may not be consistent with affordability, i.e., remaining within a particular budget.

Cost Measurement
When conducting a cost measurement or reviewing the quality of cost measurement and analyses, it is helpful to examine particular attributes of those studies.There are many excellent resources for assessing the quality of cost analyses. (See, e.g., Neumann PJ et al. Cost-Effectiveness in Health and Medicine. Second Edition. New York: Oxford University Press, 2017; and Drummond MF et al. Methods for the Economic Evaluation of Health Care Programmes. Fourth Edition. New York: Oxford University Press, 2015.)

Some key attributes to examine quality of cost measurement are: perspective for measuring cost; direct costs (health care and non-health care); indirect costs (e.g., loss of productivity); data capture method; time horizon of analysis; discounting of costs and outcomes over time.Cost Utility Analysis Using Cost per QALY

QALYs are often used in cost-utility analysis for the purposes of optimizing allocation of health care spending to maximize QALYs gained, and thereby maximize social welfare. Cost per QALY gained, i.e., the marginal (additional or incremental) cost required to gain 1.0 QALY by using a technology (a type of ICER), is one way to quantify the value to society of using that technology instead of the standard of care or other alternative. Because the QALY incorporates length of life and quality of life but is not specific to any particular disease state or condition, it enables cost-utility comparisons across a wide spectrum of health care interventions.

Certain cost-per-QALY-gained levels have been cited as formal or informal decision "thresholds" for coverage of new interventions (e.g., the equivalent of approximately US$50,000, or US$100,000, or US$150,000 per QALY in the wealthy nations). There is increasing interest in using such thresholds in low- and middle-income countries, where the thresholds are adjusted downward for national wealth, sometimes as a function of gross domestic product (GDP) per capita. Comparisons of the cost per QALY gained from various health care interventions in widespread use can be revealing about how efficient health care systems are in allocating their resources.

Evidence Sources for HTA
The field of HTA has made great advances in methods for systematically searching literature to assemble the evidence base for conducing HTA. In planning for what types of literature should be searched, some considerations might be whether the following should be included any particular languages; grey literature; and data sets, registries, or information about ongoing clinical trials.

Depending on the purpose, scope, and target audience of an HTA, the potential sources of evidence and related information for an HTA could include any of: Bibliographic databases, study registries, scanning reference lists, queries to authors, searching for grey literature and so on. Among the bibliographic databases used most often in HTA are:
- PubMed (including MEDLINE)
- EmBase

- Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials
- INAHTA Health Technology Assessment Database
- CINAHL
- PsycINFO

Horizon Scanning

In HTA, horizon scanning refers to ongoing tracking of multiple information sources to identify potential topics for HTA and provide input for setting priorities. Horizon scanning reports can provide rapidly completed, brief descriptions of new/emerging technologies and their potential impacts. While horizon scanning usually is used to identify new technologies that eventually may be topics for assessment, it can also involve identifying technologies that may be outmoded or superseded by newer ones. Horizon scanning can be used to:

- Identify technologies that have potentially major implications for health care
- Manage adoption and use of new technologies
- Identify areas of technological change
- Identify inappropriately used (including under- and over-used) technologies
- Enable health care providers, payers to plan for, adapt to technological change
- Plan data collection to monitor adoption, use, and impacts

Priority setting in HTA

Given the many technologies that could be assessed in HTA, it is necessary to set priorities. Horizon scanning can help to identify candidate technologies for assessment. Most HTA programs establish criteria and processes for selecting technologies for assessment. Examples of such criteria include:

- High individual burden of morbidity/mortality
- Large number of patients affected
- High individual or population cost of disease
- High unit or aggregate cost of technology
- Substantial variations in practice
- Unexpected adverse event reports
- Available findings not well disseminated or adopted by practitioners
- Sufficient research findings available upon which to base assessment
- Recent or impending regulatory approval
- HTA findings likely to have impact on clinical practice or coverage policy
- Public or political interest/pressure

Bibliographic sources and suggested readings

Goodman CS. HTA 101: Introduction to Health Technology Assessment. Bethesda, MD: National Library of Medicine (US); 2014. https://www.nlm.nih.gov/nichsr/hta101/ta10103.html.

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