## **Glossary of Terms for Health Economics and Systematic Review**

Adapted from Chapter 12 of the book Evidence Based Health Economics: From Effectiveness to Efficiency in Systematic Review (Evidence-Based Medicine) (Currie, 2002) and Chapter 16 of ABDELHAMID, A. & SHEMILT, I. 2010. Glossary of terms. Evidence-Based Decisions and Economics Health Care, Social Welfare, Education and Criminal Justice. 2nd ed. Oxford: Wiley-Blackwell, 186-197.

Administrative data consists of data sets collected for any administrative purpose that can be used to assess the 'real world' prevalence and incidence of disease or condition and/or use of health care resources. This includes drug use data contained in prescription databases, hospitalisation data contained in hospital databases and GP practice databases.

Allocation concealment refers to the process used to prevent prior knowledge of which comparison group an individual will randomly be assigned to in a **randomised controlled trial** or **randomised trial**. Inadequate concealment of allocation may lead to selection bias.

Allocative efficiency refers to decisions about the distribution of resources across a range of interventions within a given system; interventions compete with each other for implementation. Within the healthcare system, allocative efficiency involves the distribution of health care resources across health care programmes and interventions, that is how much, or whether, to invest resources in a particular health care programme versus another. Allocative efficiency in health care occurs when the health benefits or outcomes achieved with the available resources match the priorities of the health system (Shiell et al., 2002), this is where the ratio of marginal benefits to marginal costs is equal across all healthcare interventions. At this point, it is impossible to increase overall health benefits produced by the health system by reallocating resources between interventions (i.e. all opportunity costs of intervention are considered).

Attrition bias is a systematic error that occurs due to unequal loss of patients/participants from a **randomized controlled trial**. In clinical trials, patients might withdraw due to unsatisfactory treatment efficacy, intolerable adverse events, or even death.

**Baseline characteristics** refers to the values of demographic, clinical and other variables that are collected for each patient or participant at the beginning of a trial or intervention, before the drug or intervention is given.

**Benefits:** benefits of a health care intervention include health outcomes and effects on well-being not related to the health impact per se (for example, information or reassurance), Offsetting these positive impacts on the benefit side are negative impacts such as health deterioration (due to side effects) and effects on well-being not related to the health impact (such as anxiety).

**Bias** refers to a systematic error in the design or conduct of a research study that results in a distortion of the inferences made from the data. It may be intentional or accidental.

**Capitation** is a method of remuneration in which service providers are given a fixed payment based on the number of patients under their care; payments are not made based on the on the amount of medical treatments or services provided.

**Case-mix** is a system that classifies patients or service users into groups that are homogenous in terms of their use of resources within a specific jurisdiction over a specified period. An example in healthcare is a mix of clinically homogenous patient groups, based on the collection of both clinical and administrative data on treatment and associated costs.

**Checklists** are a means of assessing the quality of a completed study, which incorporates the extent to which existing **guidelines** are followed, whereby a set of criteria used to assess the quality of a study are listed and possibly prioritized. For example, the CHEERS (Husereau et al., 2013) checklist is used to describe the methodological quality of **economic evaluation** studies.

**Choice** in economics refers to the decisions made by individuals, firms and governments on what needs and wants to satisfy and what products and services to produce or provide. Choices are inevitable due to **scarcity** of resources.

**Cohort models** consider and characterises the 'average' but not the individual patient experiences from a population that shares the same characteristics (Briggs et al., 2006). **Decision tree** and **Markov** models are the two most common cohort models.

**Comparator** refers to the alternative course of action that the **intervention** under investigation is compared with. For example, in a **randomised controlled trial**, the intervention under investigation (i.e. the experimental intervention) is compared to one or more comparators, where the alternative course of action (s) may be another intervention (this is usually current/ standard practice in the study setting, a placebo or no intervention (i.e. a 'do nothing' alternative).

**Confounding** occurs when there is a variable that affects the outcome of interest, which is associated with one or more of the factors being investigated. If it cannot be adjusted for, the effect of the confounding variables may not be distinguished from the factors being studied, making it impossible to draw conclusions about the causal relationship of the factors under investigation on the outcome of interest.

**Conjoint analysis** (a common form is known as **discrete choice experiment**) is a method for eliciting stated preferences(Ryan et al., 2007). The technique involves valuing the benefits of health services by asking respondents to make discrete choices between alternate bundles of attributes, which make up that health service. If the cost of the service is one of the included attributes, this technique allows one to determine **willingness to pay** indirectly.

**Contingent valuation method (CVM)** is a method for eliciting **stated preferences**. This involves valuing the benefits of health services by determining an individual's maximum **willingness to pay** for the health service or intervention to be provided or the minimum amount the individual would accept as compensation (i.e. **willingness to accept**) for not having that service/ intervention.

**Cost**(s) refer to value of any resources which have an **opportunity cost** as a result of being used in that health care service or intervention, in the context of an economic evaluation of a health care service or intervention.

**Cost benefit analysis (CBA)** is a form of economic evaluation whereby both costs and benefits of an intervention are measured in commensurate, normally monetary units to assess whether an intervention is worthwhile. A full or an ideal CBA (where all the benefits can be valued in monetary units and all alternative uses, **opportunity costs**, are incorporated) can be used to address the question of **allocative efficiency**. Benefits in a CBA are valued in monetary units usually by using stated preference (see **willingness to pay, contingent valuation, discrete choice experiment or conjoint analysis)** or revealed preference (see **hedonic models/pricing, travel cost models, defensive behaviour** and **damage cost methods**) approaches.

**Cost consequence analysis (CCA)** is an economic evaluation whereby an array of health and potentially other outcome measures are enumerated alongside costs. This is distinct from **cost-effectiveness analysis** where there is a single summary (health) outcome measure. In cost consequence analysis, an overall valuation of the bundle of outcome measures is not attempted but rather left to the decision-maker to choose which outcome measure suits the decision-making context.

**Cost-effective:** An intervention is cost effective if it yields the highest value for money. The cheapest alternative in terms of cost will only be the most cost effective if it also yields the highest health outcomes. If it happens that the cheapest alternative does not yield the highest outcome then the most cost effective alternative is the one with the lowest **incremental cost effectiveness ratio.** 

**Cost effectiveness acceptability curve (CEAC)** is a graphical representation of the uncertainty associated with the results of an economic evaluation.(Drummond et al., 2015) It plots for a range of **cost effectiveness thresholds** against the probability that the new technology /intervention will be **cost effective** at that **threshold**. This helps decision-makers understand the uncertainty surrounding the optimal treatment strategy.

**Cost effectiveness analysis (CEA)** is a form of economic evaluation that is best suited to addressing questions of **technical efficiency**. Comparisons are limited to services or treatment options that produce the same type of benefit, which is valued strictly in one-dimensional, natural units.

**Cost-effectiveness ratio** (**CER**) refers to the ratio of the difference between two programmes' mean costs to the difference between two programmes' mean effects.

**Cost-effectiveness thresholds** help a decision-maker make judgement about the **opportunity costs** of an intervention. If an intervention has an incremental cost effectiveness ratio below a given threshold it is assumed that resources can be reallocated from interventions who have an incremental cost effectiveness ratio above that threshold.

**Cost minimization analysis (CMA)** is a special type of **cost-effectiveness analysis**, which is possible only if it has been determined (or more often assumed) that there are no differences in benefits between the alternate interventions compared and thus the evaluation is based on only the costs of the interventions.

**Cost of illness (COI) studies** aim to identify and measure the total costs attributable to a particular disease. These are not a type of **economic evaluation**, as they are not used to assess

the **costs** and **benefits** of alternate courses of action. They may provide useful information, which can be used in the context of an economic evaluation of interventions related to the disease category, although care must be taken as not all costs included in a cost of illness study represent resource costs.

**Cost per QALY** is a way of expressing the results of a **cost-utility analysis**, in terms of a cost per unit of benefit attained measured in **quality adjusted life years (QALYs)**.

**Cost utility analysis (CUA)** is a variant of **cost effectiveness analysis** where the health outcome measure of interest is usually expressed as a **quality adjusted life year**, a single index that combines length of life and a quality adjustment for less than perfect health (i.e. the **utility** score).

**Covariate** is an independent variable that may affect or predict the outcome(s) under investigation.

**Disability adjusted life year (DALY)** is a **generic measure** of health outcome that can be used in **cost utility analysis**. DALYs are a measure of overall disease burden, expressed as the number of years lost due to ill health, disability or mortality.

**Decision analysis** is a systematic approach to decision making under conditions of uncertainty. It is used to determine the **costs** and benefits (usually health outcomes) for a hypothetical patient cohort with the disease of interest when they are treated with different clinical strategies. The analysis may incorporate information derived from observational datasets that provide information on prevalence, average mortality rates, and costs, or from clinical trials, which examine the effectiveness of a therapy.

**Decision tree** is an analytical model in which distinct branches are used to represent a potential set of outcomes for a patient cohort. A decision tree consists of a series of 'nodes' where branches meet: each node may take the form of a 'choice' (a decision about which alternative intervention to use) or a 'probability' or chance node (an event occurring or not occurring, governed by chance). Probabilities at each decision node must always add up to one.

**Defensive behaviour** and **damage cost methods** (see **revealed preference approach**): defensive behaviour method estimates the expenditure that individuals make or cost incurred to prevent or reduce the effects of negative **externality** (e.g. the effects of environmental pollution on health) while damage cost method estimates the cost and resource cost associated with the effects of a negative externality. The two methods are typically applied in valuing the health effects of pollution, where the damage cost maybe referred to as the **cost of illness.** 

A **Delphi panel** is a structured group communication method designed to reach consensus, if possible, on particular issues. Thus, it provides a means of synthesizing information from a wide range of sources particularly from unpublished material via experts.

The **determinants of health** refer to the various inputs to the production of health in a population including medical care, socio-economic factors, environment, genetics, and individual behaviour.

**Deterministic sensitivity analysis**: Uncertainty in the cost-effectiveness of interventions is explored as either a series of one way (only one parameter is varied) or a multiway (multiple parameters are varied simultaneously) **sensitivity analysis**.

**Dichotomous-choice questions** also known as closed ended or discrete question(s) are **contingent valuation methods**. The questions are structured with a Yes/No response from participants who are presented with a' bid value' or an amount and asked if they are willing to pay the amount. The values are altered across the sample to be able to estimate the percentage of respondents who are willing to pay as a function of the 'bid' (Frew, 2010).

**Direct costs** refers to the use of resources for the treatment and health care process. These include cost of drugs, equipment and material used in providing the services, medical and other staff involved in the delivery of the care and administration procedures and cost to patients (time costs, transport cost and out of pocket expenses).

**Discounting** is the process of converting **costs** or **benefits** to be incurred or received at different points in the future to a present value so that they can be compared in commensurate units as if they all occurred at the same point in time. Discounting is used in economic evaluations to adjust for the social or individual preference for the timing of costs and outcomes.

**Discrete choice experiment (DCE)** is an attribute based hypothetical survey measure of benefit (Ryan et al., 2007). Respondents are presented with a sequence of hypothetical scenarios and choices composed of two or more competing alternatives that vary by attributes. If the cost of the service is one of the included attributes, this technique allows one to determine **willingness to pay** indirectly.

**Discrete event simulation models** (see **modelling and decision analysis**) structures the 'events' ('clinically relevant occurrences) that occur to the patient and the consequences of these events are tracked and followed (Karnon et al., 2012). In a discrete event simulation, the movements between or among patients' health states are usually driven by events, which may occur at varying times rather than during cycles of fixed length as they would be in **state transition models**(see **Markov and micro-simulation models**), time-to-event distributions are required for each event.

**Dominant** is a term used in full economic evaluations (a dominant strategy) to describe an intervention that is both more effective and costs less than one or more specified **comparators**. A **dominated strategy on the other hand** refers to an intervention that is both less effective and costs more than one or more of the specified comparators.

**Ecological fallacy** refers to the potential to draw incorrect inferences on individual level associations based on aggregate level associations. For example, aggregate data may indicate an association between fee-for-service payment and use of laboratory tests although there is no effect of payment system on the likelihood of ordering tests at an individual consultation.

**Economic evidence** is a broad term used to describe the full range of types of evidence that may be used to inform an economic analysis, including, among other things, evidence on

beneficial and adverse effects, baseline risks of events, resource use, unit costs, utilities or other measures of outcomes, etc.

**Economic Evaluation** is the application of analytical methods to identify measure and value both the **costs** and **benefits** of alternative interventions in order to provide evidence regarding **technical** or **allocative efficiency** and aid decision making for resource allocation.

**Effect size** is a measure of the difference in effect (relative or absolute) between intervention and control group/treatment in an experimental study. This may measure the absolute difference in the means or proportions, or may be a standardised measure taking account of variance of the mean and size of sample.

**Effectiveness** refers to the extent to which a given intervention or service produces health outcomes in individuals who are offered that intervention or service. This will be dependent on both the **efficacy** of the treatment, but also the acceptance and compliance with the treatment in 'real world' environments.

**Efficacy** refers to the extent to which a given intervention or service produces a particular health outcome in individuals who fully comply with the recommended treatment under ideal clinical settings. This is in contrast to **effectiveness**.

**Efficiency** refers to the optimal allocation and use of scarce resources. Two common and related types of efficiency are **technical** and **allocative** efficiency.

**Elasticity** is the measure of the responsiveness of a dependent variable to an associated explanatory variable; it is the percentage change in the dependent variable in response to a 1% change in the independent variable.

**Epidemiology** is a field of study that examines the statistical frequency, distribution and determinants of disease in a population and evaluates the clinical effectiveness of different forms of care. The latter is sometimes referred to as Health Services Research. This field is important for economic evaluation because it provides information on disease prevalence, natural history of disease, etc. that are used to populate models (see **modelling**).

**EQ-5D** is a **preference- based generic instrument**, developed by the EuroQoL Foundation to measure health related quality of life that can be affected by a wide-range of health conditions and treatments. The instrument consists of a descriptive system with five dimensions; mobility, self-care, usual activities, pain or discomfort, and anxiety or depression; and EQ visual analogue scale which records patient's self-rated health on a vertical visual analogue scale to be used as a quantitative measure of health outcome that reflects the patient's own judgement. The scores on the five dimensions can be presented as a health profile or can be converted to a single summary index or utility reflecting preferences compared to other health profiles. There are currently three versions of EQ-5D: ED-5D-3L with three levels of severity (no problems, some problems and extreme problems), EQ-5D-5L with five levels of severity (no problems, slight problems, moderate problems, severe problems and extreme problems) for each dimension and the EQ-5D-Y for use in children and young adults. There are also EQ-5D proxy versions for use in patients who are not capable of reporting their health related quality of life (e.g. children ( see Matza et al. (2005) and dementia patients(see Coucill

et al. (2001) ) and EQ-5D 'bolt-on' items for use in some conditions such as vision and hearing problems (see Yang et al. (2015).

**Extended dominance** also known as weak dominance is a principle applied in economic evaluations (with more than 2 alternatives) to compare mutually exclusive alternatives (i.e. only one alternative is available to each patient); ICERs after **strongly dominated** alternatives have been ruled out (i.e. alternatives are not dominated by one another) are calculated based on comparisons of moving from a lower cost to the next costly and effective alternative. If the ICER obtained from moving to more costly alternative falls, then the lower cost alternative is extendedly dominated and should be ruled out as well (REF).Failure to apply this principle in evaluating more than two mutually exclusive alternatives may "lead to acceptance of alternatives that are not **cost effective**"(Drummond et al., 2015).

**Expected value of perfect information (EVPI)** is a **value of information analysis** method used to estimate the difference between the expected value of the decision made using existing current information(with uncertainty) and a situation of perfect information (i.e. no uncertainty). The expected cost of uncertainty is estimated jointly with the probability that a decision made based on existing information will be wrong and the consequences of the wrong decision (Briggs et al., 2012, Tuffaha et al., 2014).

**Expected value of partial perfect information (EVPPI)** also known as partial EVPI is calculated for some selected **parameters** in an **economic evaluation**. This helps identifies parameters that are worth studying to resolve uncertainty around them. EVPPI is estimated as the difference between the expected value of a decision made with perfect information on a parameter or parameters and the decision made based on current information (Claxton and Sculpher, 2006).

**Expected value of sample information (EVSI)** is calculated as the difference between the EVPI at the time of decision-making and the expected future **EVPI** with additional information from a given study or trial with a given or known sample size.

**Expected net benefits of sample (ENBS)** is the difference between the expected benefits of research as in **EVSI** and the expected cost of the sampling (Briggs et al., 2006).

**Externality** refers to the third party effects (positive or negative) that usually arise as a result of the consumption and production of goods and services. In health care externalities refers to any effect of an **intervention** on individuals or groups that do not receive or provide the intervention.

**External validity** refers to the extent to which the results of a study can be transferred or generalised to other patient populations and settings (Drummond et al., 2015)

**Extrapolation** refers to a set of mathematical procedures in which the values of a variable are estimated over a time horizon not yet observed by making and using predictions based on observed or existing data.

**Evidence-based medicine** describes the systematic and rigorous use of methods to evaluate existing clinical studies, in order to deliver best clinical care to individuals or groups

of patients. It includes the following steps: asking a relevant clinical question, performing a target-oriented literature search, critically appraising the literature using established **guidelines**, and applying the recommendations based on information or evidence gathered to clinical practice.

**Fee for service** is a method of remuneration by which health providers are given payment in return for specific medical treatment.

**Financial incentive** refers to the potential to influence professional behaviour by affecting either their income or their expenditure related to alternative decisions.

**Fixed costs** include the costs incurred in providing a particular intervention that do not vary with the scale or number of people benefiting from the intervention (i.e. increase in number of patients treated or screened). For example, the building used for screening or vaccination is a fixed cost since a small increase in the number of people turning up would not require a bigger building in the 'short- run. Fixed costs are only fixed in the short run but are variable in the 'long-run'.

**Generalizability** of results is similar to **external validity** in that it refers to the extent to which information (both clinical and economic) can be extrapolated either to a patient group with different characteristics or to a similar patient group treated in a different geographic, political or time structure. See also **transferability**.

**Grey literature** refers to documents and other research-based material issued in limited amounts outside formal channels of publication and distribution. Examples include scientific and technical reports, government documents, doctoral theses and unpublished material.

**Guidelines** refer to statements that reflect the suggested course or procedure to follow usually based on best current evidence or practice.

**Health economics** is the study of the economics aspects of health care. It combines methods and theories from traditional economics and epidemiology and can serve as an important supplement to the routine clinical information used by medical and health care programs.

**Health Technology Assessment (HTA)** is the systematic evaluation of the properties, effects and/or other impacts of health care technology. It is designed to provide objective information to support healthcare decisions and policy-making.

**Health-Related Quality of Life (HRQOL)** refers to the physical, social and emotional aspects that are relevant and important to a patient's well-being. It can be assessed using a disease-specific, generic or a preference-based measurement tool.

**Health Utility Index (HUI)** is a generic preference based measure of health benefit that consist of two systems, HUI2 and HUI3, each includes a health status classification system and a scoring formula based on **standard gamble utilities**. The descriptive system of HUI3 is more detailed and well-structured with eight attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain) making it the preferred HUI for **primary studies**. The

HUI2 on the other hand has just six attributes including self-care and fertility hence it may be useful in studies with these specific conditions. It can also be used in secondary studies and for sensitivity analysis.

Hedonic pricing method (see **revealed preference approach**) uses the economic value of a surrogate good or service to make inference on the price of a non-market good. This method is typically used to implicitly measure the value /amount of premium individuals pay to purchase a property close to 'an environmental amenity or away from the amenity' (Champ et al., 2003), i.e. house prices are usually used to value environmental quality. E.g. individuals may be willing pay a premium for a house located close to a country park but they may wish to have a discount on a house that is close to factories.

**Heterogeneity** usually refers to differences in participants' characteristics in a study (e.g. **RCT, economic evaluation**.) or variability among studies in a **systematic review.** 

**Human capital approach**: The use of healthcare is considered an investment in a person's human capital. The returns on this investment is measured as the value of the healthy time, quantified in terms of a person's increased production in the market place. Monetary weights are then placed on healthy time using market wage rates and the value of a health (care) programme is assessed in terms of the present value of future earnings.

**Incentives** are designed to encourage individuals and health care professionals with the aim of improving health or health outcome. They can either be monetary or non-monetary. See **financial incentives**, **fee for service** and **capitation**.

**Incremental** (e.g. incremental resource use, or costs, or effectiveness, or benefits, or cost effectiveness) refers to the additional/less resource use, costs and effectiveness, benefit or cost effectiveness associated with an **intervention** in comparison to a comparator.

**Incremental cost-effectiveness ratio** (ICER) is the ratio of the difference in costs between an intervention and a specified comparator to the difference in effectiveness between that intervention and the specified comparator. From the results of a cost-effectiveness analysis, an **incremental cost-effectiveness ratio** can be calculated that depicts the extra cost per unit of outcome obtained, in comparing one treatment option to another. In this case, a value judgement will be required to assess whether the extra unit of outcome is worthwhile (see **cost-benefit analysis**).

Incremental net (health) benefit (INHB) is another summary measure of the results of an economic evaluation (see ICER). This measure rescales the measure of cost effectiveness into health by subtracting the value from the differences in costs ( $c_1-c_2$ )divided by the cost effectiveness threshold (k) from the differences in health benefit ( $h_1-h_2$ ). The intervention is cost effective if INHB is greater than zero and vice versa (see Drummond et al. (2015) pages 80-82).

**Incremental net monetary benefit (INMB) is** similar to **incremental net benefit.** It is calculated by subtracting the differences in costs from the product of cost effectiveness threshold and the differences in health benefit. An intervention is cost effective if INMB is greater than zero and vice versa (Drummond et al. (2015).

**Indirect comparison** refers to the analytical methods that may be used to compare costs and effects or efficacy of alternative interventions based on data from separate primary studies when there is no evidence or sufficient evidence from a single **randomised controlled trial**. Indirect comparison methods include **systematic reviews** and **network meta-analyses**.

**Intention-to-treat (ITT):** An intention-to-treat analysis involves an assessment of participants of an experimental research or a trial based on participants' initial treatment assignment on entry to a study (random allocation), regardless of whether or not they completed or received that treatment or fully adhered to treatment or switched to an alternative treatment. This is conducted in order to avoid the effects of crossover, dropouts and non-compliance, which may produce risk of bias if such effects are not randomly distributed between comparison groups.

**Indirect costs** refer to any losses incurred to society as a result of the impact of disease, illness, and treatments. They include losses incurred from an inability to engage in normal daily activities, work, domestic responsibilities and social and recreational activities.

**Internal validity** refers to whether the results obtained from a study are valid and true for the group of patients that were treated within a specific trial. Sources of **bias** (including **selection bias**) should be minimized to enhance the internal validity of a study. Guidelines have been developed (see <u>Chapters 8 and 13 of Cochrane Handbook 6.0</u>) to enable readers of clinical trials to determine whether the studies have any features that threaten internal validity.

**Intervention** refers to any treatment (drugs), devices, therapy, or policy that is used or attempts to improve health or health outcome.

**Iterative bidding method** also termed 'bidding game' is used to elicit preferences in a **contingent valuation.** The iterative question takes the form of an auction where the interviewer presents the respondent with a 'first bid amount and, depending on whether they accept or reject that bid, this bid is either raised or lowered till the respondent's maximum WTP is reached'(Edwards and McIntosh, 2019).

Mapping or 'cross walking' (Wailoo et al., 2017) involves the development and use of an algorithm to predict health utility values by using data from other measures of health outcome.

**Marginal benefit** is the additional satisfaction derived from the consumption of an additional unit of a service or product. In healthcare, this is the additional/less health outcome produced by an additional unit of the intervention or programme.

**Marginal cost** is additional cost incurred by producing or providing one more unit of the product or service.

**Markov model**: In this type of **modelling**, patients with a specific clinical problem can exist in a finite set of health states (e.g. alive in well, with no problems, alive with a reduction in health related quality of life, or dead) between which they can move over time. Movement between these health states occurs over a discrete time interval, for example yearly (known as a Markov cycle) based on pre-set transition probabilities. By attaching resource costs and health outcome consequences to each Markov state (which may vary based on use of an

intervention), it is possible to test how such an intervention might influence outcomes and resource use (on average) for a group of patients with a clinical problem.

**Meta-analysis** is a quantitative form of **systematic review** consisting of searching for, evaluating and combining numerically the results of relevant studies that examine the effect of the same intervention on a defined outcome to derive an overall estimate of the clinical effect.

**Meta-regression analysis (MRA)** involves the use of a multivariate statistical model to analyse data collected from several studies, in order to investigate the impact of study characteristics on study results. In principle, this allows the effects of multiple characteristics to be investigated simultaneously (See Chapter 10 of Cochrane Hand book 6.0).

**Modelling** is a tool used by health economists to determine the most likely health outcome and resource consequences of choosing to use an intervention to treat a hypothetical cohort of patients with a defined clinical condition. It often involves the use of **decision analysis**; modelling enables the extrapolation of costs and effectiveness results beyond trial data, (e.g. over a lifetime horizon).

**Micro-simulation models** usually consider the individual patient characteristics and variability between patients as individuals are moved through the model one at a time. The accumulated patient history can then be used to determine transitions, costs and health related quality of life (Briggs et al., 2006).

**Monte Carlo simulation** is used in **decision analysis**. It uses simulation methods to simultaneously deal with the potential uncertainty surrounding each important clinical or costing variables. In this method, each transition probability, effect size, utility or cost, is represented as a variable quantity with a range of possible values described by a probability distribution function (pdf).

Multi-Criteria Decision Analysis (MCDA) is a method that is used alongside economic evaluations, to help decision-makers evaluate 'alternative courses of action' that require consideration of multiple criteria, e.g. to incorporate benefits/outcomes of interventions beyond QALYs (as done in CUA) in an explicit, transparent and consistent manner. MCDA is defined as 'a set of methods and approaches to aid decision making, where decisions are based on more than one criterion, which make explicit the impact of the decision of all the criteria applied and the relative importance attached to them' (Devlin and Sussex, 2011).

**Network meta-analysis is** a technique used in **systematic reviews** to compare the relative effectiveness of three or more interventions simultaneously that have not been compared in a single randomised trial or a single analysis by combining both direct and indirect effectiveness across a network of studies (see <u>Chapter 11 of Cochrane Handbook 6.0</u>).

**Observational studies** are non-intervention studies (usually case-control or cohort studies) that usually examine the effect of exposure to risk factors on specified health outcomes.

**Open-ended question** is a **contingent valuation method** where the participants are asked to state their **WTP** for a health care intervention without any clues from the interviewer. For e.g. 'what is the maximum amount you would be willing to pay to attend a community-based walking imitative?' (Edwards and McIntosh, 2019).

**Opportunity cost**, a concept central to economics and health economics, rests on two principles, scarcity of resources and **choice**. Due to the scarcity of resources, society must make choices about what health programs to fund and which ones to forgo. The benefits of the next best alternative health programme (s) that is/are foregone because the funds are not spent on that programme constitute the opportunity cost.

**Payment scale or payment-ladder question** (used in **CVM**) presents participants with a range of values/amounts (typically from lowest bids to highest bids in a vertical order) to choose, and the value chosen represents the amount the respondent's **WTP**.

**Pay for performance** is a method of payment where financial **incentives**/ disincentives are made based on provider performance (physicians, hospitals and other healthcare providers). See also **capitation**, **fee for service** and **financial incentives**.

**Perspective** is a key point to consider in planning an economic evaluation. It is the **viewpoint** (patient, health system or society) from which the study should be conducted that is which costs and effects should be included in the analysis. From the perspective of the health service/health care provider, patient related costs such as time off work due to illness are not included, but from the societal perspective, all costs and benefits are considered regardless of whom they fall on. The societal perspective is thus broader as all important costs are included. However, healthcare decision-makers are usually faced with budget constraints and hence have the incentive to focus on or consider healthcare costs in evaluating interventions.

Primary studies are studies, which rely on original data to answer study questions.

**Probabilistic sensitivity analysis (PSA)** represents parameters (inputs) as distributions of possible mean values instead of single point estimates in a **deterministic analysis**. These distributions are then sampled, often using **Monte Carlo simulation**, which samples from the assigned distribution at random.

**Programme budgeting and marginal analysis (PBMA)** is a process that may help decision-makers 'maximise the impact of healthcare resources on the health needs of a local population' or meet other specified goals such as equity. Programme budgeting involves an appraisal of the past resource allocation in specified programmes with the aim of tracking future resource allocation in those same areas while marginal analysis involves the appraisal of the added /incremental benefits and added costs of a proposed investment or the lost benefits/ lower costs of a proposed disinvestment (Brambleby and Fordham, 2003).

**Publication bias** is a form of reporting bias observed when studies suggesting a beneficial intervention **effect size** are selected for publication while studies without a beneficial effect are not selected for publication.

**Quality-Adjusted Life Year (QALY)** is a measure of health outcome, which captures both length of life and the quality of life. QALYs are calculated by multiplying the total time

(years) in a specific health state (or the number of life years remaining) by the "utility" of those years (measured from zero, representing the worst imaginable health (values less than zero represents health states worse than death), to one, representing perfect health). QALYs may be calculated using **generic health measures** such as EQ-5D or **condition specific measures** such as Glaucoma utility index in glaucoma and King's Health Questionnaire in incontinence.

**Randomized Controlled Trial (RCT) or randomised trial** is an experimental study that investigates the **efficacy or effectiveness** and side effects of at least two interventions. Participants of the study are randomly allocated to the study groups (experimental and control or comparison) to ensure the two groups are similar in terms of the characteristics of participants. Random allocation of participants reduces **selection bias**.

**Resources** refer to all the components that are used in the production of a good or service. Within health care, resources refer not only to financial resources, but also to other resources such as doctors, nurses, buildings, equipment and supplies.

**Revealed preference approach** is a benefit valuation technique used to measure the economic value that individuals place on goods and services; this approach uses observed data, i.e. data gathered from individuals' actual **choices** in the market (see **hedonic price, travel cost, defensive and damage cost methods**) (Champ et al., 2003). However, in the health sector, because of the characteristics of health care programmes such as the public good nature of these programmes and asymmetric information, it may not be possible for consumer preferences to be revealed by the purchases that they make, and as such **stated preferences methods** that are based on hypothetical questions and surveys are mostly used in the health sector.

**Scarcity**: **resources** are limited but society needs and wants are unlimited making priority setting in decision making inevitable.

**Selection bias** refers to systematic differences between comparison groups in prognosis or responsiveness to treatment, resulting from the manner in which subjects are selected. Random allocation with adequate concealment of allocation protects against selection bias.

Sensitivity analysis is a technique used in economic evaluation or decision analysis to determine how and/or whether plausible changes in uncertain clinical or costing variables affect the main results of the analysis. This could also include altering the structural assumptions and methodological approaches (e.g. discount rates)

Short form 36 (SF-36) is a questionnaire used to measure health status of particular populations to help service planning and also measure the impact of clinical and social interventions. The questionnaire generates scores for eight domains of health status: physical functioning, physical role limitations, bodily pains, general health perceptions, vitality, social functioning, emotional role limitations and mental health. These scores are then transformed to a range from zero, the worst possible health to 100, the best possible health. While such domain scores provide a means to measure the effectiveness of an intervention, they cannot be used to conduct a **cost-utility analysis** because they are not based on preferences.

Short form 12 (SF-12) is an abridged form (subset) of the SF-36 that may be more appropriate for large-scale surveys. The 12 items are summarised as two scores; the physical component summary (PCS) and the mental component summary (MCS).

Short Form 6D (SF-6D) is a preference-based instrument that is based on Short Form 36. The SF-6D was developed as a tool to convert results of studies that used the SF-36 questionnaire to health state preference values needed to calculate QALYs. The instrument consists of a multi-attribute health status classification system with six attributes (physical functioning, role limitations, social functioning, pain, mental health and vitality) and a scoring table, which contains scores for each of the attributes.

**Standard gamble** is a direct method for eliciting patient preferences (health states utilities/weights). In the standard approach an individual is offered a hypothetical choice between two alternatives, the certainty outcome, A (living his remaining life expectancy in the chronic state for life) and the gamble, B. The gamble alternative has two possible outcomes; either the patient is returned to perfect health for the remaining life expectancy with probability P or the patient dies immediately with probability 1-p. Probability P is varied until the respondent is indifferent between the two alternatives (A & B), at which point the utility of the certainty outcome (chronic state) is equal to the value at the point of indifference.

**State transition models** (see **modelling**) considers the 'health states' that the population (cohort) or individual is in or can be in and the 'transitions'/movement between or among the health states' See **Markov models** and **microsimulation models**.

**Social cost benefit analysis (SCBA)** differs from the traditional **CBA** in the way in which health outcomes are measured and valued; 'a life satisfaction' or individuals reported wellbeing approach, but not a **stated** or **revealed preference approach**, is used to value outcomes. This approach estimates the value of 'non-market' goods by taking into consideration how they affect individuals reported well-being (Edwards and McIntosh, 2019). For example in the UK, from 2011, UK Office for National Statistics will include four subjective wellbeing questions in the Integrated Household Survey (IHS) to value over all 'life satisfaction'.

**Social return on investment (SROI)** is based on the concept of return on investment. In measuring outcomes ('financial value'), the economic, social and environmental impacts of interventions are taken into account. Similar to CBA outcome is measured in monetary units with the SROI outcomes covering a broader range with stakeholders' involvement as a key component.

Stated preference methods involve the valuation of healthcare interventions and health benefits by directly asking individuals to state their preferences in a hypothetical or virtual market. The best-known monetary stated preferences techniques are contingent valuation method and discrete choice experiments or conjoint analysis. Non-monetary stated preference methods include TTO and Standard gamble.

**Systematic review** refers to the application of explicit methods to comprehensive identification, as well as subsequent review and either a qualitative or a quantitative synthesis of all the literature on a specific topic, usually using a defined search strategy and reporting framework. When the results of studies can be combined quantitatively using appropriate

statistical methodology, rather than in just a narrative summary, this is usually termed a **meta-analysis**.

**Subgroup analyses** are additional analyses that are ideally pre-planned that are conducted in addition to the main analysis of a primary or modelled based study to investigate whether the effect of the intervention differs by particular groups of patients. For example, whether treatment is more or less effective in women or treatment effectiveness is better or worse among older people.

**Technical efficiency**: Within economics, technical efficiency refers to the production of the maximum level of output for a certain combination of input factors (i.e. raw material, working hours, etc.). Within health care, it refers to choosing a programme or an intervention to achieve a given set of objectives or a level of outcome with the fewest resources.

**Time Trade-off** is a direct technique for eliciting health state utilities. Respondents are asked to choose between a given remaining life expectancy in the 'alive' state (chronic state) and a shorter life span in normal health. They are asked whether they would be willing to trade years of remaining life expectancy to avoid the chronic condition.

**Transferability** refers to the ability to extrapolate results obtained from one setting or context to another. See also **generalisability**.

**Travel cost method /model** (see **revealed preference approach**) typically estimates the economic values for recreational activities or amenities that are free to enter and use. The value of these amenities is therefore derived from goods or services which are complementary to consumption of the free recreational amenity by assuming that the travel and time cost is the value of the trip to the recreational facility. Within health care, this method is used to estimate the travel time and travel costs associated with receiving an **intervention** 

Utility is a measure of the preference for a specific health outcome. A utility can be derived from a direct measurement approach (such as a standard gamble or time-trade off exercise), an indirect approach (such as discrete choice experiment), or from a preference-based instrument (including the EQ-5D, Health-Utilities Index or Short Form 6D). All approaches result in a number where zero represents death and one represents perfect health with less than zero representing states worse than death. Utilities can be directly used to estimate QALYs, which can then be used in cost-utility analysis.

**Uncertainty** exists when we do not know for a fact what the expected costs and effects of an intervention will be in a particular population of patients, even if all patients within the population have the same characteristics as far as we can observe them. This could be around either the value a parameter takes or the relationship between parameters (structural uncertainty). Additional evidence can reduce uncertainty and provide a more precise estimate of expected outcomes in the whole population or within subgroups.

**Viewpoint** refers to the **perspective** of the likely readers and users of the economic evaluation. Analyses can be done from the **perspective** of the health care provider (in which case patient-related expenses such as time off work due to illness are not included), society (

all costs/benefits are considered, regardless of to whom they accrue), a medical insurer or the patient. Thus, the analyses differ with respect to what costs and benefits are considered.

Willingness to Pay (WTP) is the maximum amount of money that an individual is willing to pay or give up to benefit from a particular intervention (i.e. receive a given intervention). This is elicited by direct questioning, using contingent valuation method and indirectly using discrete choice experiment or conjoint analysis.

**Willingness to accept (WTA)** is the minimum amount of money an individual is willing to accept to not benefit from an intervention.

Value of information (VOI) analysis is an approach used to reduce the expected costs or risks of uncertainty associated with decisions informed by economic evaluations. Decisions are made on existing information that are uncertain (see **uncertainty**) and so there is the chance that wrong decisions could be made which comes with consequences in terms of the health risks/loss associated with treating people with interventions that are not optimal and inefficient use of health care resources (Steuten et al., 2013, Tuffaha et al., 2014).VOI analysis therefore helps decision-makers to simultaneously decide whether to adopt an intervention and the need for further research for adequate evidence by using a **Bayesian approach** to **sensitivity analysis**.

**Variable cost** include costs that vary with the quantity of output. In healthcare variable costs include costs of an intervention or programme that vary with the size of the intervention or programme or the number of patients that benefit from the intervention. For example cost incurred on vaccines vary with the number of people screened and vaccinated.

**Visual Analogue Scale (VAS)** is a technique in which respondents are asked to rate their health states by placing a mark on a (most commonly) 10cm horizontal or vertical line, anchored by optimal health and death or by possible best health and worst possible health. The score is the number of centimetres from death/worst possible health to the mark, divided by 10. This technique does not reflect a trade-off that a subject is willing to make in order to obtain better health, in terms of time or risks or any other construct.

## **Bibliography and references**

- ABDELHAMID, A. & SHEMILT, I. 2010. Glossary of terms. *Evidence-Based Decisions and Economics Health Care, Social Welfare, Education and Criminal Justice. 2nd ed. Oxford: Wiley-Blackwell*, 186-197.
- BRAMBLEBY, P. & FORDHAM, R. 2003. Implementing PBMA. Evidence Based Medicine. What is Series. *EPRINTS-JOURNAL*.
- BRAZIER, J., PAPAIOANNOU, D., CANTRELL, A., PAISLEY, S. & HERRMANN, K. 2010. *Identifying and reviewing health state utility values for populating decision models*, Wiley-Blackwell, Oxford.
- BRAZIER, J., ROBERTS, J. & DEVERILL, M. 2002. The estimation of a preference-based measure of health from the SF-36. *Journal of health economics*, 21, 271-292.
- BRIGGS, A., SCULPHER, M. & CLAXTON, K. 2006. *Decision modelling for health economic evaluation*, OUP Oxford.
- BRIGGS, A. H., WEINSTEIN, M. C., FENWICK, E. A., KARNON, J., SCULPHER, M. J. & PALTIEL, A. D. 2012. Model parameter estimation and uncertainty analysis: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force Working Group–6. *Medical decision making*, 32, 722-732.
- CHAMP, P. A., BOYLE, K. J., BROWN, T. C. & PETERSON, L. G. 2003. *A primer on nonmarket valuation*, Springer.
- CLAXTON, K. P. & SCULPHER, M. J. 2006. Using value of information analysis to prioritise health research. *Pharmacoeconomics*, 24, 1055-1068.
- COLLABORATION, C. 2008. Cochrane handbook for systematic reviews of interventions, Cochrane Collaboration.
- COUCILL, W., BRYAN, S., BENTHAM, P., BUCKLEY, A. & LAIGHT, A. 2001. EQ-5D in patients with dementia an investigation of inter-rater agreement. *Medical care*, 39, 760-771.
- CURRIE, G. 2002. Glossary of Terms for Health Economics and Systematic Review In: BOOKS, B. (ed.) Evidence Based Health Economics: From Effectiveness to Efficiency in Systematic Review (Evidence-Based Medicine)

London: BMJ Publishing Group.

- DEVLIN, N. & SUSSEX, J. 2011. Incorporating multiple criteria in HTA. *Methods and processes. London: Office of Health Economics*.
- DRUMMOND, M. 2010. Evidence-based decisions and economics: an agenda for research. *Evidence-Based Decisions and Economics: Health Care, Social Welfare, Education and Criminal Justice*, 181-182.
- DRUMMOND, M. F., SCULPHER, M. J., CLAXTON, K., STODDART, G. L. & TORRANCE, G. W. 2015. *Methods for the economic evaluation of health care programmes*, Oxford university press.
- EDWARDS, R. T. & MCINTOSH, E. 2019. Applied health economics for public health practice and research, Oxford University Press.
- EUROQOL GROUP. 2017, April 28. *EQ-5D instruments | About EQ-5D* [Online]. Available: <u>https://euroqol.org/eq-5d-instruments/</u> [Accessed].
- FREW, E. 2010. Applied methods of cost-benefit analysis in health care, Oxford University Press.
- FURLONG, W. J., FEENY, D. H., TORRANCE, G. W. & BARR, R. D. 2001. The Health Utilities Index (HUI<sup>®</sup>) system for assessing health-related quality of life in clinical studies. *Annals of medicine*, 33, 375-384.
- GLENNY, A., ALTMAN, D., SONG, F., SAKAROVITCH, C., DEEKS, J., D'AMICO, R., BRADBURN, M. & EASTWOOD, A. 2005. Indirect comparisons of competing interventions.
- HUSEREAU, D., DRUMMOND, M., PETROU, S., CARSWELL, C., MOHER, D., GREENBERG, D., AUGUSTOVSKI, F., BRIGGS, A. H., MAUSKOPF, J. & LODER, E. 2013. Consolidated health economic evaluation reporting standards (CHEERS) statement. *Cost Effectiveness and Resource Allocation*, 11, 6.

- KARNON, J., STAHL, J., BRENNAN, A., CARO, J. J., MAR, J. & MÖLLER, J. 2012. Modeling using discrete event simulation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–
  4. *Medical decision making*, 32, 701-711.
- MATZA, L. S., SECNIK, K., MANNIX, S. & SALLEE, F. R. 2005. Parent-proxy EQ-5D ratings of children with attention-deficit hyperactivity disorder in the US and the UK. *Pharmacoeconomics*, 23, 777-790.
- RYAN, M., GERARD, K. & AMAYA-AMAYA, M. 2007. Using discrete choice experiments to value health and health care, Springer Science & Business Media.
- SHEMILT, I., MUGFORD, M., VALE, L., MARSH, K. & DONALDSON, C. 2011. *Evidence-based decisions and economics: health care, social welfare, education and criminal justice,* John Wiley & Sons.
- SHIELL, A., DONALDSON, C., MITTON, C. & CURRIE, G. 2002. Health economic evaluation. *Journal of epidemiology and community health*, 56, 85.
- STEUTEN, L., VAN DE WETERING, G., GROOTHUIS-OUDSHOORN, K. & RETÈL, V. 2013. A systematic and critical review of the evolving methods and applications of value of information in academia and practice. *Pharmacoeconomics*, 31, 25-48.
- TUFFAHA, H. W., GORDON, L. G. & SCUFFHAM, P. A. 2014. Value of information analysis in healthcare: a review of principles and applications. *Journal of medical economics*, **17**, 377-383.
- WAILOO, A. J., HERNANDEZ-ALAVA, M., MANCA, A., MEJIA, A., RAY, J., CRAWFORD, B., BOTTEMAN, M. & BUSSCHBACH, J. 2017. Mapping to estimate health-state utility from non-preferencebased outcome measures: an ISPOR good practices for outcomes research task force report. *Value in Health*, 20, 18-27.
- YANG, Y., ROWEN, D., BRAZIER, J., TSUCHIYA, A., YOUNG, T. & LONGWORTH, L. 2015. An exploratory study to test the impact on three "bolt-on" items to the EQ-5D. *Value in Health*, 18, 52-60.