**Session 9 – Value for money**

Welcome to this session on Value for Money in which we look at the most important concepts in health economics, pharmacoeconomics and value for money in terms of medicines. In this session you will be introduced to health economics and pharmacoeconomics principles, as well as methods of economic evaluation for value for money decisions. For each of these methods you will be referred to a reading as an example. You will also learn basic skills on how to interpret and appraise applied studies of health economics.

**Session Contents**

Session 5 will cover the following topics:

1. Introducing value for money
2. Defining Health Economics and pharmacoeconomics
3. Economic Evaluation Methods
4. Costing in economic evaluation
5. Interpretation of cost effectiveness
6. Clinical value of interventions/medicines
7. Critical appraisal of economic evaluations
8. Session summary
9. References and further reading

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| --- |
| **Learning Outcomes**  By the end of this session you should be able to:   * Understand the concept of value for money * Understand important concepts in health economics/pharmacoeconomics * Be able to distinguish different methods of economic evaluation * Know how to critically review published articles of economic evaluations |

**Readings**

Bijen, C.B.M., Vermeulen, K.M., Mourits, M.J.E. & de Bock, G.H. (2009). [Cost and Effect of Abdominal versus Laparoscopic Hysterectomy: Systematic Review of Controlled Trials](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2752190/pdf/pone.0007340.pdf). PLoS ONE, 4(10).

Hagberg, L.A., Brekke, H.K., Bertz, F., Winkvist, M.J.E. (2014). Cost-utility analysis of a randomized controlled weight loss trial among lactating overweight/obese women. *BMC Public Health* 2014, 14(38). Available at:

<http://www.biomedcentral.com/1471-2458/14/38>

O’Brien, B., Levine, M., Willan, A., Goeree, R. et al. (1999). [Economic Evaluation of Outpatient Treatment with Low-Molecular Weight Heparin for Proximal Vein Thrombosis](file:///C:\Users\pdaames\Downloads\Cost%20minimisation%20analysis.docx). *Arch Intern Med*. 1999, 159:2298-2304. Abstract available at

<http://www.ncbi.nlm.nih.gov/pubmed/10547169>

O’Byrne, P., Cuddy, L., Taylor, W.D., Birch, S. et al. (1996) Efficacy and cost-benefit of inhaled corticosteroids in patients considered to have mild asthma in primary care practice. *Canadian Respiratory Journal* 3:3 May/June 1996. Available at:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2255497/>

Ramsey, S.D., Wilke, R.J., Glick, H., Reed, S.D et al. (2015) Cost-Effectiveness Analysis Alongside Clinical Trials II—An ISPOR Good Research Practices Task Force Report. *Value in Health*. International Society for Pharmacoeconomics and Outcomes Research. Elsevier. Available at

<http://www.ispor.org/Cost-Effectiveness-clinical-trials-guideline.pdf>

Redekop, W.K., Orlewska, E., Maciejewski, P., Rutten, F.F.H. & Niessen, L.W. (2008). Costs and Effects of Secondary Prevention with Perindopril in Stable Coronary Heart Disease in Poland. *Pharmacoeconomics* 2008; 26(10): 861-877

Abstract available at

<http://www.ncbi.nlm.nih.gov/pubmed/18793033>

Tsuji, R.L., da Silva, G.V., Ortega, K.C., Ota´vio Berwanger, O. & Mion Ju´nior, D. (2012).An economic evaluation of antihypertensive therapies based on clinical trials.

*Clinics (Sao Paulo)* 2012. 67(1): 41-48. Available at

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3248600/>

**1 INTRODUCING VALUE FOR MONEY**

*To start the session, think about these questions; then read on through the notes:*

*What is “value for money”?*

*What is your understanding of “value for money” in relation to medicines?*

Value for money is defined as the utility derived from every purchase or every sum of money spent, and is used to judge whether or not maximum benefit is obtained from the goods and services provided within the finite resources available. For example when you go shopping for eggs you have a choice between organic eggs, free range eggs and grain fed eggs, at different prices. Your ultimate choice of which eggs to buy will depend on your perceived satisfaction of benefit in relation to what you will pay.

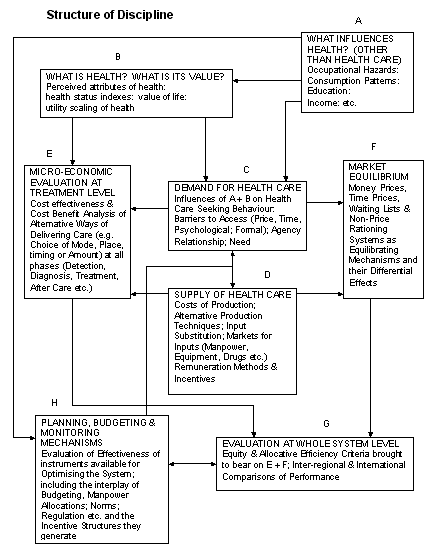
Value for money is not only based on the minimumpurchase price. In order to achieve true value for money one has to consider all of the following:

* **Economy** - careful use of resources to save expense, time or effort.
* **Efficiency** - delivering the same level of service for less cost, time or effort.
* **Effectiveness** - delivering a better service or getting a better return for the same amount of expense, time or effort

Value for money is not one and the same as consideration of only economy and efficiency; it is about finding the right balance between economy, efficiency and effectiveness. Reducing cost or improving efficiency may support or undermine value for money depending on whether effectiveness is considered.

**2 DEFINING HEALTH ECONOMICS AND PHARMACOECONOMICS**

In Health Economics, economic theory, models and empirical techniques are applied to the analysis of decision-making in terms of health and health care. Health Economics (HE) is concerned with scarcity of resources, and its application reflects the desire to obtain maximum value for money by considering not only clinical effectiveness, but also cost effectiveness. The figure below shows the structure of the Health Economics discipline.



**Fig 1. Structure of Health Economics discipline.**

Source: Cuyler, A.J. and Maynard, A. (1997) Being reasonable about the economics of health. Selected essays *by Alan Williams*.

Pharmacoeconomics is a branch of Health Economics which describes the analyses of costs of medicine therapy to health care systems and society. It identifies measures and compares the costs (resources consumed) and the outcomes (e.g. clinical, economic and humanistic) of pharmaceutical products and services.

In this session we will focus more on the micro level methods used to make decisions about utilisation of particular medicines by healthcare providers, Pharmaceutical and Therapeutic Committees, and Formulary committees based on the evaluation of value for the cost of these medicines or therapies.

**2.1 Basic economic theory**

If we accept that health is a “fundamental commodity”, analyses of the demand for health improvement can be done in the same way as the analyses of the demand for other goods and services. In the analysis of the demandfor most goods and services, a distinction is made between **wants**, which is the desire to consume something, andeffective **demand**which is wants linked to the willingness and ability to pay.

Unlike other goods and services such as food, electricity, cars, and clothes, healthcare is not usually demanded because it is pleasurable in itself. Instead it is demanded mainly for improvement of health. For this reason in health economics there is a widespread view that what matters in health care is not wants and demands, but needs, and that the need for healthcare is interpreted as the capacity to benefit from it, for valued improvement in health. In simple terms medicines are not taken for any other reason than to improve health e.g. Anti-tuberculosis medicines are used to treat and prevent the spread of tuberculosis. If not taken patients will die and more patients will then be infected.

In almost all economies people’s wants exceed the available resources. The diagram below shows that when there is scarcity of resources, choices have to be made between different wants. Hence, a clear balance must be struck between available resources and wants. To achieve this balance trade-offs are necessary. This is done by giving up something to provide something else.

How can we use

limited or scarce resources

more efficiently and effectively?

**2.2 Principles of economic evaluation in health care**

To strike a balance between wants and finite resources, economic analyses are used to provide a better understanding of the world. They do this by describing and explaining economic behaviour; i.e. economic evaluation provides information that assists people in making decisions about how to use scarce resources or how to choose between alternative ways of using these resources.

When a choice must be made about which resources to use for which activities, the choice of using resources for one activity instead of another means that the opportunity for using those resources for alternative activities is given up and the [benefits](http://www.nlm.nih.gov/nichsr/edu/healthecon/glossary.html#Benefit)associated with the alternative use of resources is foregone. This is called the [opportunity cost](http://www.nlm.nih.gov/nichsr/edu/healthecon/glossary.html#Opportunity_Cost). This is one of the most important concepts in economics in that it ensures that chosen activity’s benefits outweigh the opportunity cost.

*Example:*

*A hospital is given $2 000 000 to improve healthcare within their community. The hospital management has to choose between upgrading their emergency and trauma unit or building a new Maternal, Child and Neonatal (MCN) Unit at a cost of $2 000 000. If the hospital management decides to upgrade the Emergency and Trauma Unit the opportunity cost of this is the lives of mothers and children that could have been saved at this hospital by providing MCN Unit.*

Economic evaluation stems from the recognition that information on effectiveness of interventions, although necessary, is not adequate for decision-making and that it is evidently important to consider costs, in particular opportunity costs and benefits forgone by choosing different courses of action. Hence an economic approach such as economic evaluation provides a coherent and theoretically based approach to measuring and valuing cost and outcomes of competing alternatives. All economic evaluations compare alternative treatment options in terms of two dimensions, cost and consequences or benefits. Costs are considered as the value of resources involved in providing a treatment, and consequences are considered as the health effects of the treatment.

When performing an economic evaluation, the focus is on the joint consideration of differences in costs and consequences and/or benefits of two or more alternative treatments. The differences in costs and benefits of alternative treatments are referred to as incremental costs and incremental effects. This means that changes in cost and benefits are considered at the margin which provides important insights that can be obscured by using average costs and benefits.

The next activity will provide an example on how to consider costs at the margin and not the average or total cost.

***Activity 1 – Analysing costs at the margin***

1. *The Ministry of Health (MOH) intends to allot $1 000 000 for the prevention of disease A or disease B which are both prevalent in your country. Both diseases are fatal, but can be prevented with suitable interventions. You are requested to advise on how to spend their money to avert the maximum number of deaths. Evidence indicates that for: $1 000 000 used for Disease A*

***201*** *deaths from* ***Disease A*** *will be averted;*

*$1 000 000 used for Disease B*

***160*** *deaths from* ***Disease B*** *will be averted*

*What will be your advice?*

1. *After your advice the MOH indicates that due to budgetary constraints, only $500 000 will be allocated for the prevention of Disease A and Disease B. The MOH request you to review your recommendation in light of the new information. Evidence indicates that $500 000 dollars will avert:*

***120*** *deaths for* ***Disease A***

***100*** *deaths for* ***Disease B***

*What will you advise?*

1. *Your recommendation to the MOH was leaked to the press. However the MOH indicates that due to public pressure the original $1 000 000 will be allocated to the prevention of Disease A as per your original recommendation.*

*What would you advise, now?*

***Note****: In addition to looking at the feedback below, you can discuss this activity with the session convenor in the first Discussion Forum during this week.*

**Feedback**

The evidence suggested that:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Money Spent ($)** | **Deaths Averted** | | | **Average Cost per death averted ($)** | |
|  | **Disease A** | **Disease B** | **Total Deaths Averted** | **Disease A** | **Disease B** |
| $ 1 000 000 | 201 | 160 | 201 | 4975 | 6250 |
| $ 500 000 | 120 | 100 | 120 | 4166 | 5000 |
| $ 1 000 000 | 120 | 100 | 220 | 4166 | 5000 |

If $1 000 000 is used to prevent deaths (201) in Disease A instead of Disease B, 41 more additional deaths will be averted compared to $1000 000 used to prevent deaths in Disease B (160). However, spending $500 000 on both Disease A and B respectively provides better value for money in that an incremental (additional) 19 deaths are averted compared to the $1 000 000 spent on Disease A alone. In this case please note that additional deaths have been averted by using the same funds apportioned differently.

**3 ECONOMIC EVALUATION METHODS**

In the above activity we noticed that it is important to jointly consider both cost and effectiveness and that analysis at the margin provides critical insight, which may be missed if average or total cost were used.

Economic evaluation is considered a useful tool to present information on cost and effectiveness in a manner that can be used to inform decision making between two or more competing alternatives. As such, all methods of economic evaluation compare the cost and consequences or benefits between alternative options of treatments, interventions or programmes. Economic evaluations can be performed by collecting patient level data, which usually means collection of data alongside randomised controlled trials or by a decision analytic model incorporating information from various sources to inform a decision with regard to a medicine or treatment.

Rarely, all relevant evidence that is required for an economic evaluation comes from a single source such as a RCT. A critical requirement for economic evaluation is that all relevant evidence should be included. If relevant information is omitted from the evaluation, the risk of a wrong decision is likely. Decision analytic modelling is used when available evidence, particularly from RCTs, is not sufficient to make a decision with regard to the adoption of a treatment or intervention. For this reason there is a growing use of decision modelling as a vehicle for economic evaluation, as seen in the large number of economic modelling studies used in decision-making by the National Institute for Clinical Excellence in the UK (NICE, 2015). However, economic evaluation, occurring alongside randomised controlled trials, make up more than 30% of all evaluations and usually involve medicines. For this reason in this module we will only consider economic evaluations performed alongside randomised controlled trials.

**3.1 Cost consequence analysis**

The simplest way to present cost and consequences of two competing alternative treatment, intervention or programme options is to calculate and report all the various costs and consequences in a disaggregated manner. The information is presented in such a way that the decision maker has to interpret and synthesize the information in some or other way to come to a decision.

Click on the hyperlink below to read an example of a Cost Consequence Analysis:

[Cost and Effect of Abdominal versus Laparoscopic Hysterectomy: Systematic Review of Controlled Trials](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2752190/pdf/pone.0007340.pdf)

**3.2 Cost-minimisation analysis**

In a cost minimisation analysis (CMA) both costs and consequences are of interest. However, in this case it is assumed that the consequences/outcomes of the two or more interventions, treatments or programme options are identical. For this reason the option with the lower cost is favoured, as the objective of this evaluation is to minimise cost.

A CMA is at times implemented in very unique situations when a prospective economic evaluation conducted alongside a clinical trial fails to find any significant differences in the primary clinical outcomes (consequences). The applicability of CMA is very limited as very few clinical trials are designed to show equivalence or non-inferiority, as such a trial design requires much larger sample sizes. It is considered that CMA is most useful for comparing generic and therapeutic equivalents or “me too” medicines. Where there is no reliable equivalence between two products or if therapeutic equivalence cannot be demonstrated, CMA is inappropriate.

Click on the link below to view an example of CMA:

[Economic Evaluation of Outpatient Treatment with Low-Molecular Weight Heparin for Proximal Vein Thrombosis](file:///C:\Users\pdaames\Downloads\Cost%20minimisation%20analysis.docx)

**3.3. Cost-effectiveness analysis**

In a cost-effectiveness analysis (CEA) the cost and effects of each of the interventions, treatments or programmes are calculated. The difference in cost and difference in effects are then calculated. These differences are then presented in the form of a ratio i.e. cost per unit of health effect or outcome. The focus of a CEA is on the differences in cost and effects between two or more treatments, interventions and programme options, which are referred to as incremental cost and incremental effects. The ratio of incremental costs and incremental effects is known as the incremental cost effectiveness ratio (ICER). The mathematical relationship between ICER, cost and effects is shown below.

The effects for a CEA can be calculated in many different ways. For example when comparing two hypertension treatments, the effects of the treatments can be calculated in mmHg reduction in blood pressure, or when comparing two vaccines, effects can be measured as number of cases or deaths prevented.

Click on the link below for an example of a CEA:

Costs and Effects of Secondary Prevention with Perindopril in Stable Coronary Heart Disease in Poland

<http://www.ncbi.nlm.nih.gov/pubmed/18793033>

**3.4 Cost-utility analysis**

A cost–utility analysis (CUA) can be thought of as special type of CEA. The difference is that in a CUA the measure of effects or outcomes of interventions are captured in a metric that can be compared across different areas or programmes. One of these metrics is the Quality Adjusted Life Year (QALY), which captures a health intervention’s effect on survival in terms of life years and the effect in terms of quality of life. Each treatment, intervention and programme has an impact on life years and quality of life. QALY’s are referred to as a type of utility in economics. Hence cost effectiveness analyses which use QALY’s as an outcome are referred to as CUAs. The usefulness of this type of economic evaluation allows for comparison of cost effectiveness across different treatments, interventions and programmes.

*Quality Adjusted Life Years (QALY)*

Measuring improvement of health as QALY is considered one of the great innovations of health economics. As previously mentioned QALY endeavours to value the benefits of health care interventions in terms of a measure that combines the impact on length of life with quality of life into a numerical competence of year of full health. Health is a function of both longevity and quality of life and QALY provides a single index number to describe health.

QALY has been defined as a “measure of a health outcome which assigns to each period of time a weight, ranging from 0 to 1, corresponding to a health related quality of life during that period.

For example a patient diagnosed with severe angina and left main vessel disease has a life expectancy of 5 years with appropriate medical treatment and has a maximum quality of life score of 0.92 decreasing gradually over time. Evidence suggests that a patient undergoing coronary artery bypass grafting (CABG) will increase life expectancy to 11 years if the operation is successful; and increase quality of life to a maximum of 0.97 gradually decreasing over time. Hence it is clear that the number of QALY’s associated with CABG compared to medical management is considerably more.

In order to calculate QALY’s, death and full health are assigned values of 0 to 1; where death is presented as 0 and full health is presented as 1. In order to evaluate health states, various instruments are used for calculation of QALY. One of the most widely used instruments for estimating a value for health states is the generic preference-based measure of health - the EQ-5D. This instrument describes health in 5 dimensions:

* mobility
* self-care
* usual activities
* pain and discomfort
* anxiety and depression

Each dimension has three levels.

Level 1: no problem

Level 2: moderate or some problem

Level 3: severe problem

Together these 5 dimensions and three levels describe 243 different health states. These dimensions can be presented to patients or individuals in a short questionnaire to establish their level in each dimension. (See below)

**EQ-5D Questionnaire**

By circling one of the numbers (1 – 3) in each health state group below, please indicate which statements best describe your own health state today.

**Mobility**

1. I have no problems in walking about

2. I have some problems in walking about

3. I am confined to bed

**Self-Care**

1. I have no problems with self-care

2. I have some problems washing or dressing myself

3. I am unable to wash or dress myself

**Usual Activities** (*e.g. work, study, housework, family or leisure activities)*

1. I have no problems with performing my usual activities

2. I have some problems with performing my usual activities

3. I am unable to perform my usual activities

**Pain/Discomfort**

1. I have no pain or discomfort

2. I have moderate pain or discomfort

3. I have extreme pain or discomfort

**Anxiety/Depression**

1. I am not anxious or depressed

2. I am moderately anxious or depressed

3. I am extremely anxious or depressed

**Source**: www.euroqol.org/.../PDF/Languages/Sample\_UK\_\_English\_\_**EQ-5D**-3L.pdf

As per the instrument above, each health state profile is described as a 5 digit number. For example the health state 12112 indicates that the patient:

1. Has no problems walking about
2. Has some problems with self-care
3. Has no problems with performing usual activities

1 Has no pain and discomfort

2 Is moderately anxious or depressed

In order to assign a value to these health states, a population value set that provides an algorithm for the value of each of the 243 health states is calculated as a series of values less than 1.

**Methods for calculating health states**

The most used methods include the Time Trade Off (TTO) method and Standard Gamble Method (SGM) - which we will not cover in detail in this session - and the UK York TTO Tariff. This is shown in the table below and is the most widely used to score the EQ-5D health states.

This table can be used to calculate a value for each health state (243 in total) using the following guidelines:

* For all health states other than 11111, there is a constant decrement of 0.081;
* followed by a decrement for each level 2 and 3 that appears in the state;
* an additional decrement (N3) for states with a level 3.

**Table: UK TTO EQ-5D Tariff**

|  |  |  |
| --- | --- | --- |
| **Dimension** | **Level** | **Decrement** |
| Constant |  | 0.081 |
| **Mobility** | 2 | 0.069 |
|  | 3 | 0.314 |
| **Self-Care** | 2 | 0.104 |
|  | 3 | 0.214 |
| **Usual Activity** | 2 | 0.036 |
|  | 3 | 0.094 |
| **Pain/Discomfort** | 2 | 0.123 |
|  | 3 | 0.386 |
| **Anxiety/Depression** | 2 | 0.071 |
|  | 3 | 0.236 |
| N3 |  | 0.269 |

The impact of a health care intervention on perceived health is an important benefit. Hence using a metric such as QALY that can measure this impact is essential for comparison of programs, interventions and treatments, to ensure that resources are used optimally.

Click on the link below to read an example of CUA:

Cost-utility analysis of a randomized controlled weight loss trial among lactating overweight/obese women

<http://www.biomedcentral.com/1471-2458/14/38>

**3.5 Cost-benefit analysis**

A cost benefit analysis (CBA) attempts to place some monetary value on health outcomes and health resources. A CBA approach tries to estimate the monetary value of health outcomes, effects or benefits and calculates whether the monetary benefits of the treatment, intervention or programme exceeds the cost of obtaining these benefits. A CBA provides the opportunity to compare outcomes in healthcare to those outside of healthcare such as education, housing and social development. Although CBA’s are frequently used in other sectors, their use in health care is infrequent.

Click on the link below to see an example of CBA:

Efficacy and cost-benefit of inhaled corticosteroids in patients considered to have mild asthma in primary care practice

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2255497/>

**4 COSTING IN ECONOMIC EVALUATION**

As previously mentioned, when estimating relative cost effectiveness of treatments, interventions and programmes, reliable estimates of costs are of critical importance.

In economic evaluation, costs are calculated by quantifying the different types of resources required to produce particular goods or a service. For example the resources required to bake a cake include:

* Time spent by baker
* Ingredients (eggs, milk, flour, etc.)
* Oven
* Electricity
* Equipment (mixing bowl, egg-beater, spoon)

Once all the resources have been quantified they are multiplied by their respective unit costs.

Resource use in medicine can be based on patient specific or non-patient specific data. When costs are collected on a patient specific basis the resources used by each patient are subject to variability, which is influenced by a number of known and unknown factors and cannot be predicted. For example the number of days a person spends in hospital after a hip operation depends on age, gender, co-morbidities etc. On the other hand non-patient specific approaches allow for an assumption for a specific variable which may in practice vary substantially from the assumed value. For example we can assume that patients spend, on average, approximately 3-5 days in hospital after a hip operation.

**4.1 Performing Cost analysis**

A cost analysis involves 3 distinct stages which can be described as follows:

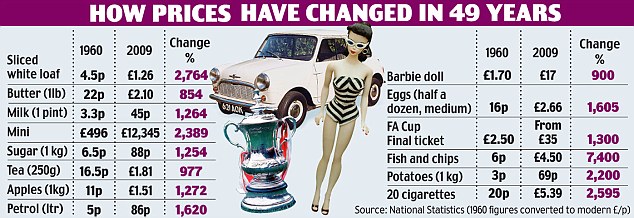
* **Identify:** estimate the different types of categories of resources likely to be required, e.g. theatre staff, consumables, equipment and medicine, surgical complications, adverse drug reactions
* **Measure:** estimate how much of each resource category is required e.g. type of staff, time involved, length of stay in hospital, medicine required
* **Value:** apply a unit cost to each resource category e.g. salary of staff, cost per hospital bed per day, unit cost of medicine

**4.2 Perspective**

The perspective from which the analysis is performed determines the costs (and outcomes) to be included in an economic evaluation. The main two perspectives used in economic evaluations are **payer** (usually the health service, ministry of health or medical insurance) and **societal**. The payer perspective includes only the cost incurred by the health services, while societal perspective includes all costs such as cost to patients, friends and family for informal care, social services, productivity loss incurred by employers, regardless of who incurs them. The National Institute for Health and Clinical Excellence (NICE) in the UK suggested that when performing an economic evaluation for consideration for reimbursement within the National Health Services (NHS), only the perspective of the health and social services should be used. The rationale behind this is that NICE is responsible for maximising the NHS budget. For this reason only cost and effects relevant to the NHS and social services are considered.

**4.3 Adjustments of costs**

Costs differ over time as illustrated below…



Source: http://www.thisismoney.co.uk/money/bills/article-1633409/Historic-inflation-calculator-value-money-changed-1900.html

As previously mentioned, economic evaluation compares the cost of two or more alternative options. These alternative options may not only differ on overall magnitude of cost and outcomes but also in when the cost and benefits occurs. Cost incurred today will not be the same for a product bought 3 years ago or being bought 3 years from now. For this reason costs are adjusted for the time horizon.

***For example:***

*When a 12 year old girl is vaccinated with Human Papilloma Virus (HPV) vaccine the costs are incurred at the time of administration. These costs include cost of the vaccine, staff costs, gloves, buildings etc. However the benefits of giving a HPV vaccine are only seen in the future, as the HPV vaccine is used to prevent cervical cancer which occurs much later in life.*

*In the case of cataract surgery, cost is incurred immediately and benefits (improved* *vision) are realised immediately and but also last for a period of time into the future.*

In both these scenarios you see that the health care interventions have distinct cost and benefits time profiles. This is critical to economic evaluation as people generally are motivated by the timing of cost and benefits. If I should lend you R1 000 today and tell that you can pay R1 000 back in 10 years’ time, will you take the deal? I would imagine all of you would. This is natural human behaviour as we are more inclined to enjoy benefits now and postpone costs till later and attach less value to future cost and benefits. For this reason economists agree that cost and benefits occurring at different times should not be given the same weighting.

In addition, when resources are not spent immediately, they can be invested over a period of time to generate an additional income. For example if you invest $100 now at a rate of return of 5% per annum for 5 years, an additional $28 will be earned and the investment will be equal to $128. Similarly if $100 is required in five years’ time, only $77 dollars need to be invested today. As you can see there is both a time preference and opportunity cost when money is spent over a period of time. For this reason discounting is used to account for this.

A discount rate is usually applied using the formula:

+ … +

Where is the present value, is the future cost value at year 1and is the future cost value at year n. Usually a discounting rate of 3%-6% is used. For example the UK treasury is recommending a discount rate of 3.5%.

***Activity 2: Calculating programme cost***

*A Ministry of Health wants to implement a vaccination programme over three years. The annual cost of the vaccination programme at present is $1 500 000. Using a discount rate of 5%, calculate the total cost of programme for the 3 years.*

**Feedback**

|  |  |  |
| --- | --- | --- |
| Period | Discount Formula | Cost |
| Present |  | **$1 500 000** |
| Year 1 |  | **$1 428 571** |
| Year 2 |  | **$1 360544** |
| Total cost over 3 years | | **$4 289116** |

You will able to see from the above that if discounting was not applied, the total cost of the programme over three years would have been over-estimated at $4 500 000.

**4.4 Inflation**

If health care costs are incurred over different time periods and in several instances where clinical trials run over many years, costs may be collected over different time periods. Therefore when performing economic evaluations it is critical to ensure that all costs incurred are placed in a common base year. To adjust cost incurred in the past to a present base value, a measure of inflation such as the consumer price index (CPI) can be used. The CPI is calculated by evaluating the change in cost to the consumer of purchasing a fixed basket of goods and services. Other inflation measures used include medical inflation, which reflects the change in cost in a basket of medical goods and services.

In summary, it is crucial for economic evaluations to consider both discounting and inflation when comparing costs of alternative programs that occur at different time periods.

**5 CLINICAL VALUE OF INTERVENTIONS/MEDICINES**

Randomised control trials are the gold standard for evaluation of medicines efficacy and effectiveness. Hence in recent years clinical trials have been used as a potential source for decisions about the value for the cost of medicines derived from clinical trials that measure efficacy and effectiveness. Frequently manufacturers of medicines incorporate economic evaluations in the drug development process in Phase III trials, as well as Phase IV trials (which occur after registration of medicines i.e. after the medicine is marketed). A large proportion of economic evaluations, especially for medicines, are conducted alongside clinical trials and are based on patient level data on cost and effect collected as part of the randomised controlled trial.

An economic evaluation alongside clinical trials should consider at least six of the following eight sets of issues:

*a) What pre-planning should be done?*

An economic assessment within a clinical trial should include consideration of length of follow-up. The length of follow-up is important as it will determine whether important economic and clinical endpoints are achieved. One approach to ascertain whether the length of follow-up is appropriate is to identify the economic episode of care for a condition. An episode of care is defined as the period between the patient’s diagnosis presentation of a clinical condition and when the condition is resolved or concluded.

*b) Estimation of average, variances and correlations of cost, health related quality of life and preference*

Average, variances and correlations of cost, health related quality of life and preference are required to assess the sample size required to answer economic questions posed in the study. It is very important to recognise that the sample size requirements of randomised controlled trials for clinical evidence may be very different to the sample size requirements for an economic assessment alongside a clinical trial. Usually when an economic evaluation is conducted alongside a RCT, much larger sample sizes are required. The methods to determine sample size have been dealt with in earlier sessions, however, it is imperative to remember that economic assessments require more information than what is needed to calculate the sample sizes for clinical outcomes and cost differences alone. The simplest data required for sample size calculations in economic assessments include the size of the incremental cost and effects expected and the standard deviations of cost and effects.

*c) Identifying the medical services used by study participants and what medical services should be measured.*

An important activity in economic assessments in clinical trials is to identify the type of medical services that participants will be likely to use during the study period. This can be performed by reviewing medical charts, administrative data, or log books of patients keeping track of their medical service use. This will provide information of what medical services should be measured.

Once these services have been identified, decisions have to be made on what proportion of medical services should be measured and also the cost that should be measured. Based on whether data is collected prospectively or not, it is unrealistic to measure each and every service use and cost. Hence the objective should be to measure services that make up a large portion of the differences in treatment between the randomised groups and also measure those services that make up a large portion of the total cost. Furthermore, data collection should be limited to disease related services and no “unrelated” service use should be collected.

*d) In what form should the data be collected?*

A strategy commonly adopted for costs in trials is to measure medical service occurrence in trials, and multiply the count of medical service use by a set of price weights to determine the cost.

The level at which medical services are aggregated, depends on a number of factors, such as whether we expect the medicine to improve the number of hospitalisations, length of hospitalisation or the intensity of medical services use. When making decisions on whether data will be collected at aggregate or less aggregate level, consideration should be given to the likely difference more or less aggregated information will have on the result, as well as the cost implications of collecting more or less aggregated data.

*e) Which price weight or unit cost?*

Sources of price weight differ by country. For example in the United Kingdom there are a number of publicly available sources that provide prices for specific treatments, hospital charges and medicine. However in some countries such information is not readily available and should then be estimated through primary data collection.

*f) How naturalistic should the study design be?*

The primary purpose of a cost-effectiveness analysis is to inform real world decision makers on how to respond to real world health care needs. Hence, clinical trials used to inform economic evaluations should be designed as close to real world situation as possible.

*g) What should be done if the full cost and benefits are not expected to be observed during the full duration of the trial?*

In most trials evaluating chronic treatments and conditions, the studies end prematurely. When trials are ended prematurely, the cost and effects should only reflect the in-trial cost and effects. Hence if the trial follow-up was for one year, the cost and benefits for one year should be measured. However, if long term use yields outcomes are normally observed in the long term, therapeutic decisions based solely on results observed within short term trials may be inappropriate. These long term effects are usually addressed using decision analytic models from various information sources.

*h) Whether an economic evaluation is inappropriate within a trial*

The decision to perform an economic evaluation within a trial should not be based on whether an economic advantage can be observed or not. However one of the most common reasons for not performing an economic evaluation within a trial is that no unbiased evidence about economic value will be observed.

Furthermore, it is inappropriate to perform economic evaluations when it is believed that the result of an economic evaluation will not affect the decision to use the therapy. When a therapy is very effective, society will not worry about the cost e.g therapy for a disease that is highly fatal, was previously untreatable but only adds a year of life expectancy. Similarly, clinicians will use treatments/interventions that are novel, even if they are not cost effective.

**6 INTERPRETATION OF COST EFFECTIVENESS**

When one therapy is compared to another in terms of costs and effects, nine possible outcomes can be observed. Look at how these are represented in the matrix below:

1. Reduced cost, more effective

2. Increased cost, less effective

3. Same cost, more effective

4. Increased cost, same effect

5. Same cost, less effective

6. Reduced cost, same effectiveness

7. Increased cost, more effective

8. Reduced cost, less effective

9. Same cost, same effect

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Incremental effectiveness of treatment compared to control** | | |
|  |  | **More** | **Same** | **Less** |
| **Incremental cost of treatment compared to control** | **More** | **7** | **4** | **2** |
| **Same** | **3** | **9** | **5** |
| **Less** | **1** | **6** | **8** |

*Source:* Drummond, et al. (2005) *Methods for the Economic Evaluation of Health Care*

In outcome 1 and 2 there is a strong dominance for a decision. In case of outcome 1 it is clear that treatment is preferred over control. In case of outcome 2 the treatment is rejected, (it is less effective and costs more). In cases 3, 4, 5 and 6 we say that there is weak dominance for decision, and in cases 7, 8 and 9 there is non-dominance and no obvious decision can be made. In case of outcome 7 the question arises whether the added incremental effect is worth the added cost. In outcomes 8 the question is whether the reduced effect is acceptable given the reduced cost. In outcome 9 there is no difference in cost and effects, hence other reasons are needed to adopt treatment. From the above it is evident that to choose between alternatives is not an easy task and the need for a systematic approach to decision making is imperative.

**6.1 Cost-effectiveness plane**

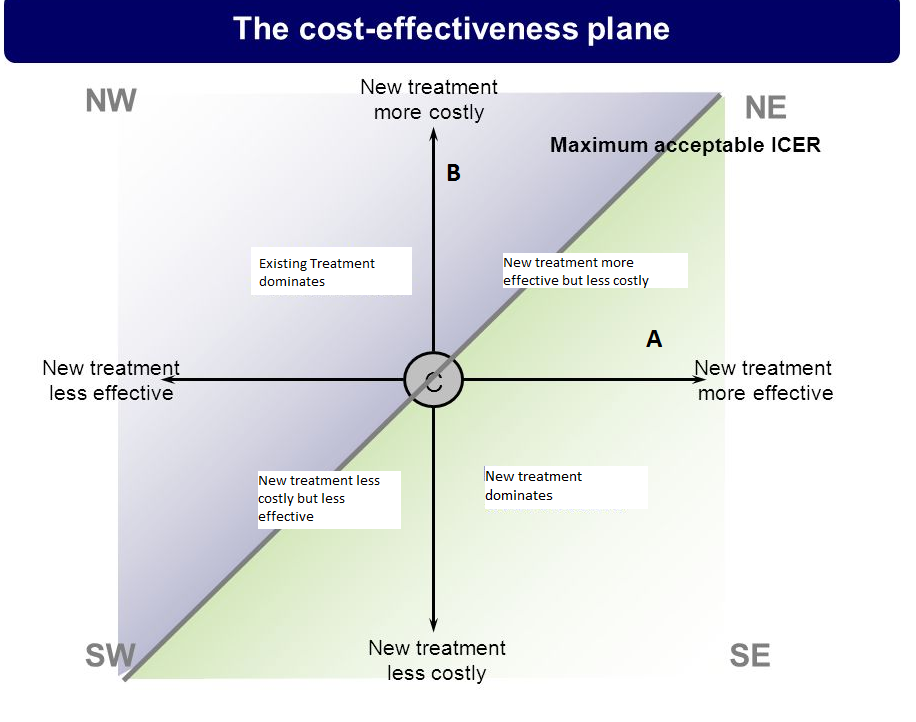
Cost-effectiveness analysis (CUAs and CEAs) resides in a two dimensional world of costs and effects and is represented graphically with the cost effectiveness plane. CUAs and CEAs are the most commonly used methods of economic evaluation of health care to determine value for money. Whether an intervention is good value for money depends on analysis of the comparison of the Cost Effectiveness Ratio (CER) against a “benchmark” CER which is referred to as the ceiling benchmark or cost-effectiveness threshold, which is indicative of the society’s willingness to pay.

The graphic presentation below, referred to as the cost effectiveness plane, shows the incremental cost and incremental benefits of new intervention vs the comparator (which can be current treatment, no treatment or alternative treatments). The incremental effectiveness is shown on the x-axis and the costs on the Y-axis, with C being the point of comparison or control. Hence compared to the central point the new treatment can be less costly or more costly and more effective or less effective which can be represented by the four quadrants of the figure below.

The marginal analysis which is the appraisal of the added benefits and costs is the cornerstone for decision making. If it is ascertained that the new treatment is less costly and more effective it will be in the South-East (SE) quadrant. In this case decision makers will have no problem in adopting the new treatment. If the new treatment is considered more costly and less effective, a decision to reject the new treatment can be made easily. More difficult decisions have to be made when a new treatment is either in North-East (NE) or South-West (SW) quadrants. In these areas there is a trade-off between effects and costs. Additional health benefits can be obtained with higher cost (NE quadrant) or savings can be achieved by having lower health benefit (SW Quadrant). Hence the important question in these situations is whether the health gain (or cost saving) is worth the additional cost (or health loss).

However, in the NE quadrant we can have a treatment (B) very costly and marginally more effective and on the other hand may have a treatment (A) marginally costly but very effective. As one moves from Treatment A to Treatment B, a case arises where decision makers are no longer prepared to pay the additional cost for an additional benefit. This point is referred to as the maximum acceptable ICER and is represented by the line C to NE.

Hence, when working in the two dimensional plane of cost-effectiveness analysis, there will be uncertainty around how much more or less effective and how much more or less costly a new treatment is with respect to the current treatment. There is also an uncertainty about how much a decision maker is willing to pay for the health gain.

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**Fig. 2: Cost-Effectiveness Plane**

Source: Gray A.M. et al (2011) *Applied methods of Cost-Effectiveness Analysis in Health Care*.

**6.2 Cost Effectiveness Acceptability Curve (CEAC)**

In simplifying the decision about whether a treatment is cost effective, a cost effectiveness acceptability curve can be used to answer the question “What is the probability that a specific treatment is cost effective?” Whilst confidence intervals for ICER’s are a valid approach to address uncertainty in cost effectiveness analysis, in some situations problems with the interpretation of the ICER may arise. For example, when an ICER is negative (a cost-effect pair in the SE Quadrant), difficulty arises in interpreting such an ICER. Similarly a cost-effect pair in the NW quadrant will also have negative ICER’s for precisely the opposite reason (more costly and less effective). From this it is evident that two clearly radically different situations could have identical ICER’s.

Similarly, the interpretations of ICER’s in the SW and NE quadrants also differ. As you will recall an ICER is indicative of the additional funds that must be paid to gain one additional health benefit and that treatments with an ICER below the ceiling ratio (acceptable MAX ICER) is considered cost effective. However, an ICER in the SW quadrant indicates the amount of savings that can be gained by one unit loss of health. Also, a higher ICER is preferred in the SW quadrant, as more money will be saved and only those treatments above the ceiling should be adopted. For this reason an ICER of $10 000/QALY in the NE quadrant may be considered cost effective, whereas a $10/QALY ICER in the SW quadrant may not be considered cost effective.

As a result ICER’s are not helpful in differentiating between desirable and undesirable outcomes and the additional limitation is that confidence intervals of ICER’s are not informative. A solution to this problem is provided by the Cost Effectiveness Acceptability Curve (CEAC) which is used to determine the probability at which a treatment will be cost effective. By displaying uncertainty in cost-effectiveness the CEAC provides several pieces of useful information, for example:

* The point estimate of cost effectiveness
* The significance of cost difference
* The significance of the effect difference

Furthermore, the CEAC can be used to find the strength of evidence in support of a treatment being cost-effective.

**Fig. 3: Cost effectiveness Acceptability Curve**

Source: Gray, A.M. et al (2011)*Applied methods of Cost-Effectiveness Analysis in Health Care*.

**7 CRITICAL APPRAISAL OF ECONOMIC EVALUATIONS**

We have seen that many variables are considered when conducting an economic evaluation. Hence the quality of economic evaluations is variable and necessitates the need to evaluate the quality of these applied studies to ensure that the correct decision is made.

In order to further understand quality problems associated with economic evaluations, read the following, which discusses the quality issues specifically related to economic evaluations performed alongside clinical trials:

Cost-Effectiveness Analysis alongside Clinical Trials II: An ISPOR Good Research Practices Task Force Report

<http://www.ispor.org/Cost-Effectiveness-clinical-trials-guideline.pdf>

It is important that evidence on efficiency, effectiveness and cost are reliable and that when an economic evaluation is performed it is critical that the economic evaluation is relevant to one’s own setting. For this reason the reliability of the economic evaluation should be checked against:

* Quality of the methodology
* Accuracy of the reporting of results
* Whether the results of the study can be generalised to your setting.

Critical appraisal of economic evaluations can be done through a standard checklist of which many are available. For the purposes of this course, in the activity below you will use the CASP checklist for guidance on the critical appraisal of economic evaluations.

|  |
| --- |
| ***Activity 3 – Critical appraisal of an economic evaluation***  *Now that we have covered all the information required to make judgement on the quality of an economic evaluation, you are required to perform a critical appraisal of an economic evaluation. Please use the critical appraisal checklist (see Module Resources) to assist you to obtain the relevant information.*  *You have been provided with an economic evaluation which you will appraise (see Module Resources):*  Tsuji, R.L., et al. (2012). *An economic evaluation of antihypertensive therapies based on clinical trials.*  <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3248600/>  *Please critically appraise the economic evaluation and recommend whether the treatment or interventions could be adopted in your setting. As you perform your critical appraisal of the economic evaluation, give careful consideration to:*   * *The research question addressed by the study* * *The estimation of resource use and cost* * *The evidence or estimated benefits of the interventions* * *Has discounting been considered* * *Whether uncertainty has been dealt with effectively (sensitivity analysis).*   *Submit your critical appraisal via File Sharing. You will have an opportunity to engage with your convenor if you would like to during the week.* |

**8 SESSION SUMMARY**

In this session our focus was on value for money and the use of economic evaluation in the context of it being used as a tool to ensure the adoption of the most cost-effective interventions and treatments.

Economic evaluations are generally used:

* To maximise the benefits for money spent
* As a tool to assist/ improve decision-making

Economic evaluations are usually commissioned by stakeholders who have an interest in the provision of goods and services, such as pharmaceutical manufacturers, clinicians and ministries of health.

The type of economic evaluation performed is dependent on how the benefits and consequences of interventions or treatments are measured.

Notwithstanding the widespread use of economic evaluation there are still issues with quality of economic evaluations. Therefore critical appraisal of economic evaluations is of utmost importance to ensure good decisions are taken to adopt interventions.

**9 REFERENCES AND FURTHER READING**

Cuyler, A.J. and Maynard, A. (1997) Being reasonable about the economics of health. Selected essays *by Alan Williams*.

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