Session 6.
Evaluating the Cost of Pharmaceuticals

Participants’ Guide
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Developed in Collaboration with the
World Health Organization
Geneva, Switzerland
ABBREVIATIONS AND ACRONYMS

A+L       artesunate plus lumefantrine
A+M       artesunate plus mefloquine
ADR       adverse drug reaction
AIDS      acquired immunodeficiency syndrome
AUD       Australia, dollars
bid       twice a day (bis in die)
CD4       human T helper cells expressing CD4 antigen (T helper cell)
CEA       cost-effectiveness analysis
CER       cost-effectiveness ratio
CMA       cost-minimization analysis
CUA       cost-utility analysis
DALY      disability-adjusted life year
DTC       Drug and Therapeutics Committee
HbA1c     glycosylated hemoglobin
HIV       human immunodeficiency virus
ICER      incremental cost-effectiveness ratio
IM        intramuscular
kg        kilogram
MI        myocardial infarction
NSAID     non-steroidal anti-inflammatory drug
QALY      quality-adjusted life year
SK        streptokinase
tid       three times a day (ter in die)
tPA       tissue plasminogen activator
UC        usual care
USD       U.S. dollar
VA        visual aid
WHO       World Health Organization
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SESSION 6. EVALUATING THE COST OF PHARMACEUTICALS

Purpose and Content

Session 6 is designed to provide participants with basic information about analyzing the cost of pharmaceuticals and, to a limited extent, pharmacoeconomic principles. Participants will learn the value of a basic cost analysis and its importance to the Drug and Therapeutics Committee (DTC) in evaluating and selecting medicines for the formulary.

Objectives

After attending this session, participants will be able to—

- Define and understand the different types of cost analysis methods relevant to choosing medicines for the formulary
- Understand how to read and assess journal articles concerning an economic study
- Apply session materials to conduct a basic cost analysis for a medicine being requested for the formulary

Preparation and Materials

Read the Participants’ Guide.

Further Readings


Key Definitions

Pharmacoeconomics—The description and analysis of the cost of pharmaceutical therapy to health care systems and society

Cost—The total resources consumed in producing a good or service

Price—The amount of money required to purchase an item
**Medicine effectiveness**—The effects of a medicine when used in real-life situations

**Medicine efficacy**—The effects of a medicine under clinical trial conditions

## Introduction

The Drug and Therapeutics Committee (DTC) is responsible for careful evaluation of new medicines before they are added to the formulary. As discussed in previous sessions, this evaluation must involve efficacy, safety, quality, and cost. Session 6 provides information on how to evaluate the cost of a medicine, not only its procurement cost, but also the cost impact on the entire health care system including the patient. The discussion is important so that the overall evaluation of a medicine is complete and the DTC knows all of the cost implications when considering the addition of a new medicine. Economic evaluation techniques are used not only for medicines, but also for health care services such as disease management programs. Two questions can be answered by economic evaluation—

- Is this health procedure, service, or program worth doing compared with other things the DTC could do with these same resources?
- Is the DTC satisfied that the health care resources should be spent in this way rather than some other way?

The medicine information literature has an excess of articles, from research to clinical practice, describing the various uses of cost analysis in pharmaceutical management programs. The science of pharmacoeconomics is relatively new, however, and many of the concepts are not well understood by practitioners. When applied appropriately, pharmacoeconomic principles are useful to determine which medication or other intervention will provide the most benefit. Many pharmacoeconomic studies, however, are sponsored by a pharmaceutical company to prove economic superiority of its produce over a competing medication, especially when comparing medicines of similar efficacy and safety. The nature of the pharmacoeconomic discipline allows for the development of a study to meet a particular outcome and, therefore, the reader of economic studies must evaluate them carefully.

The quality of pharmacoeconomic studies is frequently poor, and the reader of any study must take quality into consideration. This session concentrates on the basic aspects of pharmacoeconomics so that participants will be able to use key concepts and ideas to evaluate medicines for the formulary. Participants are referred to the key readings to provide more detailed information on the pharmacoeconomic discipline.

## Cost of a Medicine

What actually goes into the cost of a medicine? The most basic cost of a pharmaceutical is reflected in the acquisition price from a supplier. Acquisition cost is one of the most important aspects in calculating a medicine’s cost, but it is only a start in the total evaluation. It is
becoming more important to look beyond the acquisition cost of a medicine and obtain all costs associated with using the medicine.

There are three types of costs associated with medicines in a health care system: direct, indirect, and intangible. These three types of costs, when taken collectively, will give the most comprehensive assessment of actual medicine cost.

- **Direct costs** are costs that are directly related to the resource use associated with a service or commodity in dealing with a health care intervention and include—
  - Acquisition cost of the medicine (medicine price)
  - Transportation (shipping and insurance)
  - Supplies and equipment to administer the medicine
  - Supply management (storage facilities, supply personnel)
  - Medical and allied health consultations
  - Costs of managing adverse effects of therapy
  - Hospitalization costs related to adverse events or treatment effectiveness
  - Laboratory services
  - Outpatient visits
  - Nonmedical costs such as travel costs, community assistance, and palliative care

- **Indirect costs** are costs associated with lost production capacity and include—
  - Time lost from work for the patient
  - Time lost from work for the caregiver

- **Intangible** costs are costs associated with pain and suffering, usually incorporated in the utilities assigned to health states that reflect quality of life.

**Economic Evaluation Methods**

Economic evaluation is about relating the cost of a service or program to the outcomes delivered. Usually, analysts are interested in comparing one health product or intervention with another. There are generally four technical types of economic evaluations—

- **Cost minimization analysis** (CMA) assumes that the effects of the two interventions being compared are equal and therefore compares costs.

- **Cost effectiveness analysis** (CEA) is used when the effects of the two interventions being compared are different (i.e., one intervention is superior to the other).

- **Cost-utility analysis** (CUA) is a special type of cost effectiveness analysis, in which the outcome is expressed as a utility measure (e.g., quality-adjusted life year [QALY]).

- **Cost-benefit analysis** (CBA) is derived from transport economics; both costs and benefits are expressed in monetary terms.
For assessing pharmaceuticals, the first three types of evaluation are commonly used. Cost-benefit analysis is far more challenging to carry out and interpret for health interventions, so papers describing cost-benefit analyses of pharmaceuticals should be interpreted with care.

**Cost-Minimization Analysis**

CMA is appropriate when two interventions have been shown to produce the same, or similar, effects. In such a situation, only the costs of the interventions need to be considered. For comparing two pharmaceutical products, cost minimization can be used only for products that have been shown to be equivalent in therapeutic effect. Therefore, this method is most useful for comparing generics and their therapeutic equivalents or “me too” medicines. This type of comparison can be difficult for many products because there may not be a reliable equivalence between the two products. If therapeutic equivalence cannot be demonstrated, then this particular type of cost comparison should not be used.

The costs to be included in the analysis include the intervention, or medicine costs, along with other health service costs including medical staff costs (e.g., physicians, nurses), laboratory costs, and equipment costs (e.g., syringes, IV sets). The inclusion of indirect costs related to such things as time off work and lost productivity is not straightforward because the valuation of indirect costs is problematic. If such costs are included, then care should be taken in the valuation process.

To perform a CMA, the following costs should be identified, measured, and then valued—

- Acquisition cost of the medicine
- Pharmacy, nursing, and physician costs (if they contribute significantly to the cost of using the medicine)
- Cost of equipment and supplies (e.g., syringes, needles, IV sets, sterile water for dilution)
- Cost of laboratory services (if a significant cost is involved)
- Indirect costs (such as time off work), but only if they can be measured and valued reliably

Table 1 is an example of a CMA of two injectable antibiotics for treating meningitis.
Table 1. Sample CMA (Based on Course of Treatment)

<table>
<thead>
<tr>
<th>Cost Centers</th>
<th>Medicine A (USD)</th>
<th>Medicine B (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquisition price</td>
<td>8.00</td>
<td>15.00</td>
</tr>
<tr>
<td>Pharmacist salary (to prepare the medicine)</td>
<td>2.50</td>
<td>1.50</td>
</tr>
<tr>
<td>Nursing salary (to administer the medicine)</td>
<td>2.50</td>
<td>2.00</td>
</tr>
<tr>
<td>Supplies (to administer the medicine)</td>
<td>9.00</td>
<td>2.25</td>
</tr>
<tr>
<td>Laboratory services</td>
<td>4.00</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>26.00</strong></td>
<td><strong>21.75</strong></td>
</tr>
</tbody>
</table>

*Note: USD = U.S. dollars.*

The CMA in table 1 shows that medicine B is slightly less costly to use than medicine A. Just looking at acquisition price of the medicines, however, would have shown that medicine A was less costly and probably preferred if all other criteria for selection were equal. Completing the CMA provides information indicating that the real cost of the two medicines is significantly different from the acquisition price and that medicine B has a lower overall cost.

Table 2 shows another example of a CMA. In this example, the total annual cost is included, a fact that is also important for the DTC to consider.

Table 2. Hypothetical Example of Cost Minimization Analysis of Three Injectable Antibiotics

<table>
<thead>
<tr>
<th>Cost Categories</th>
<th>Ampicillin (500 mg)</th>
<th>Ceftriaxone (1 g)</th>
<th>Gentamicin (80 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquisition price for one vial</td>
<td>USD 1.00</td>
<td>USD 8.00</td>
<td>USD 2.00</td>
</tr>
<tr>
<td>Doses per day</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Price per day</td>
<td>USD 4.00</td>
<td>USD 8.00</td>
<td>USD 6.00</td>
</tr>
<tr>
<td>Nursing salary at USD 0.75 per injection</td>
<td>USD 3.00</td>
<td>USD 0.75</td>
<td>USD 2.25</td>
</tr>
<tr>
<td>Equipment: IV set at USD 1.00 per set</td>
<td>—</td>
<td>USD 1.00</td>
<td>—</td>
</tr>
<tr>
<td>Syringe + needle USD 0.50 per set</td>
<td>USD 2.00</td>
<td>—</td>
<td>USD 1.50</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>USD 2.00</td>
<td>USD 2.00</td>
<td>USD 4.00</td>
</tr>
<tr>
<td><strong>Total medicine costs/day</strong></td>
<td>USD 11.00</td>
<td>USD 11.75</td>
<td>USD 13.75</td>
</tr>
<tr>
<td><strong>Total medicine costs/3,000 treatment-days/year</strong></td>
<td><strong>USD 33,000</strong></td>
<td><strong>USD 35,250</strong></td>
<td><strong>USD 41,250</strong></td>
</tr>
</tbody>
</table>

Sensitivity analyses are important in any kind of economic analysis. Such an analysis tests how sensitive the conclusions are to the different assumptions made. For example, in table 2, if we change the assumption that giving an IV injection by IV infusion takes the least nursing time, and assume instead that such infusions take slightly more nursing time than ampicillin or gentamicin, such that the nursing salary would be USD 4 instead of USD 0.75, then the overall cost of using ceftriaxone would be USD 15 per day and total annual cost USD 45,000. In this scenario, ceftriaxone would be the most costly option.
Cost-Effectiveness Analysis

CEA is a type of economic evaluation that compares the costs and outcomes of health programs or treatments when the interventions have a common health outcome but differ in effectiveness. The health outcomes are measured in natural units (e.g., lives saved, life years gained, cases of illness avoided) or changes in functional status (e.g., units of blood pressure in hypertension, cholesterol in hypercholesterolemia). The results of a CEA are generally displayed as a cost per unit of effect. With regard to medicines, CEA is used to compare two or more medicines that are not exactly equivalent in terms of dose or therapeutic effect, but that are used to treat the same clinical condition. This form of analysis is difficult and is often done only at the national level. It requires measuring the cost per defined measurable clinical outcome (effect) for each of the medicines. The cost of the medicine should include indirect as well as direct costs, and some examples of measures for clinical outcomes include—

- Hypertension—blood pressure measurements
- Diabetes—glycosylated hemoglobin (HbA1c), blood glucose results
- Coronary heart disease—frequency of angina attacks
- Urinary tract infections—incidence of infections
- Obesity—weight measurement
- Seizures disorders—frequency of seizures
- HIV/AIDS—CD4 counts
- Heart failure (and any other disease)—years of life saved, QALYs, or disability-adjusted life years (DALYs)

Cost-effectiveness measurement can be presented in many different ways, for example, for—

- Acute illness: cost per course of treatment or cost per cure
- Chronic illness: cost per month of satisfactory control
- Disease prevention: cost per case prevented
- Health promotion: cost per month of desired outcome

Steps to Complete a Basic CEA

1. Define the objective of the analysis. For example, which pharmaceutical regimen should be the treatment of choice?
2. Identify the different ways to achieve the objective. For example, should a cheaper, slightly less efficacious medicine or a more expensive, slightly more efficacious medicine be chosen?
3. Identify and measure the intervention and pharmaceutical costs of each option.
4. Identify and measure the benefits (clinical outcomes) of each option.

5. Calculate and interpret the benefits of each option. The cost-effectiveness ratio (CER), or the cost per unit of benefit of the health care intervention (e.g., medicine), is estimated by dividing the total intervention or medicine cost by the number of units of outcome. The incremental cost-effectiveness ratio (ICER) is the change in costs and health benefits when one health care intervention (e.g., medicine A) is compared with the alternative intervention (e.g., medicine B). The formula below demonstrates how the ICER is calculated.

\[
\text{ICER} = \frac{\text{Cost of intervention A} - \text{Cost of intervention B}}{\text{Effect of intervention A} - \text{Effect of intervention B}}
\]

If intervention A is superior to intervention B and costs less, then intervention A is said to be dominant. If intervention A has greater benefit but also costs more than intervention B, then the ICER is used in determining whether the benefits gained from intervention A are worth the additional cost.

6. Perform a sensitivity analysis on the conclusions. A sensitivity analysis varies some of the assumptions in the analysis (e.g., costs of staff salaries and hospital overheads) to see if changing these assumptions also changes which medicine is found to be most cost-effective. If the conclusion about which medicine is most cost-effective does not change with varying the assumptions, then the conclusion is likely to be valid. If however, the conclusion is very sensitive to changing the assumptions, then the study result is likely to be subject to error and no firm conclusion can be drawn.

**Example: Using CEA for Pharmaceutical Treatment of Type II Diabetes**

Table 3 provides a summary of the cost information needed to perform a simple cost-effectiveness analysis of two drugs, A and B, used in the treatment of Type II diabetes, assuming a treatment duration of one year. The desirable outcome from treatment is more patients with a lower HbA1c, a measure of control of diabetes. Table 4 provides the incremental cost, benefit (percentage of patients with ≥ 1% decrease in HbA1c), and resultant ICER.

**Table 3. Cost Information for CEA**

<table>
<thead>
<tr>
<th>Cost</th>
<th>Cost/Unit (USD)</th>
<th>No. of Units</th>
<th>No. of Patients</th>
<th>Total Cost (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicine A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicine cost</td>
<td>40</td>
<td>12</td>
<td>100</td>
<td>48,000</td>
</tr>
<tr>
<td>Laboratory cost</td>
<td>20</td>
<td>1</td>
<td>100</td>
<td>2,000</td>
</tr>
<tr>
<td>Adverse event</td>
<td>50</td>
<td>2</td>
<td>100</td>
<td>10,000</td>
</tr>
<tr>
<td>Physician</td>
<td>25</td>
<td>2</td>
<td>100</td>
<td>5,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>65,000</strong></td>
</tr>
<tr>
<td>Medicine B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicine cost</td>
<td>25</td>
<td>12</td>
<td>100</td>
<td>30,000</td>
</tr>
<tr>
<td>Laboratory cost</td>
<td>20</td>
<td>2</td>
<td>100</td>
<td>4,000</td>
</tr>
<tr>
<td>Adverse event</td>
<td>50</td>
<td>3</td>
<td>100</td>
<td>15,000</td>
</tr>
<tr>
<td>Physician</td>
<td>25</td>
<td>3</td>
<td>100</td>
<td>7,500</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>56,500</strong></td>
</tr>
</tbody>
</table>
Table 4. Results of CEA

<table>
<thead>
<tr>
<th></th>
<th>Medicine A</th>
<th>Medicine B</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cost</strong></td>
<td>USD 65,000.00</td>
<td>USD 56,500.00</td>
<td>USD 8,500.00</td>
</tr>
<tr>
<td><strong>Number of patients per 100 treated with</strong></td>
<td>25</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>$\geq 1%$ decrease in HbA1c</td>
<td>$\frac{65,000}{25}$</td>
<td>$\frac{56,500}{19}$</td>
<td>$\frac{8,500}{6}$</td>
</tr>
<tr>
<td><strong>Cost-effectiveness ratio</strong></td>
<td>$2,600$</td>
<td>$2,973.70$</td>
<td></td>
</tr>
<tr>
<td><strong>Cost per extra patient with $\geq 1%$ decrease in HbA1c with medicine A compared to medicine B:</strong></td>
<td>$\frac{(65,000 - 56,500)}{(25 - 19)} = \frac{8,500}{6} = 1,416.67$</td>
<td>USD 1,416.67</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 demonstrates that medicine A is more effective than medicine B because more patients get a desirable response (i.e., 25 patients per 100 with medicine A as compared to 19 patients per 100 with medicine B). The CER is lower with medicine A—USD 2,600.00 to treat one patient successfully (by reducing HbA1c $\geq 1$ percent), than with medicine B—USD 2,973.70 to treat one patient successfully. A CER, however, expresses only the cost-effectiveness of an intervention compared to no intervention and cannot be used directly to make comparisons between different interventions. The DTC, by contrast, wants to compare medicine A directly with medicine B and for this comparison, the ICER must be calculated. In this example, the incremental cost per extra patient with $\geq 1$ percent decrease in HbA1c is calculated as USD 8,500.00/6, which is USD 1,416.67, meaning that the health care system would have to pay an extra USD 1,416.67 (over a year) for each extra patient with a desirable response. The judgment that needs to be made is whether this estimate represents value for money.

Table 5 below provides the components of a CEA and a brief description of each component.

Table 5. Components of a CEA

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Context</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Intervention</td>
<td>Pharmaceutical treatment or health program</td>
<td>The population should be relevant to or comparable to the population in which the treatment will be used.</td>
</tr>
<tr>
<td>2. Population</td>
<td>Based on clinical history, age, gender, other characteristics</td>
<td></td>
</tr>
<tr>
<td>3. Setting</td>
<td>Location, type of institution</td>
<td>Does the trial setting correspond to the setting in which medicine or treatment will be used?</td>
</tr>
<tr>
<td>4. Comparator</td>
<td>Treatment most likely to be replaced; standard medical management</td>
<td>The basis on which comparator is chosen is important (i.e., more expensive comparator may make new treatment more cost-effective).</td>
</tr>
</tbody>
</table>
| 5. Source of evidence | • Published literature  
                     | • Clinical trials                                                | The source of evidence should be evaluated using the following criteria— |
|                  |                                                  | • Quality of evidence—randomization, trial size,                   |
### Session 6. Evaluating the Cost of Pharmaceuticals

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Component</strong></td>
<td><strong>Description</strong></td>
<td><strong>Issues</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>effect size</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Relevance of evidence—similarity of trial settings, populations, and other characteristics to the situation in which treatment will be used</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Comprehensiveness of evidence—representative of medical literature as a whole or selective</td>
</tr>
</tbody>
</table>

#### 6. Outcomes used
- Surrogate or final outcome
  - Surrogate outcomes must be relevant.
  - Surrogate and final outcomes must be linked.

### Costs

#### 7. Identification
- Perspective of the analysis (societal, patient, government)
- Type of costs
  - The following costs should be identified—
    - Medicine or treatment costs
    - Physician costs
    - Administration costs
    - Laboratory monitoring costs
    - Adverse event costs
    - Other medical services
    - Indirect costs

#### 8. Measurement
- Number of units consumed
  - Does use in trials represent use in real life?
  - The accuracy of medical records should be checked.

#### 9. Valuation
- Cost per unit
  - The source of cost should be determined.

#### 10. Discounting
- Rate used to convert the value of future costs and consequences into equivalent present values
  - WHO recommends a discount rate of 3% for costs and benefits and a sensitivity analysis using 6% for costs and 0% for benefits.

#### 11. Sensitivity analyses
- Determines the sensitivity of the estimates to variations in cost and treatment effects
  - The following elements need to be considered—
    - Confidence interval of the point estimate of treatment effect
    - Costs
    - Discount rate
    - Duration

---

Box 1 shows a real-life example of how two different kinds of thrombolytic agent for the treatment of myocardial infarction were compared from the point of view of efficacy and cost-effectiveness in Australia. The treatment of myocardial infarction in the usual way was compared with usual treatment plus the use of either streptokinase or tissue plasminogen activator.
Comparison was done in terms of (a) total treatment costs, (b) death rates, and (c) cost per life saved (or death averted). The treatment costs included all the direct and indirect costs.

**Box 1. Economic Analysis of Two Thrombolytics in Acute Myocardial Infarction in Australia**

A review of the literature was conducted in Australia concerning the cost effectiveness of different thrombolytics in the treatment of myocardial infarction (MI). The cost of the various treatments and the mortality rate following MI were evaluated, and the results are shown below.

**Cost of treatment and mortality rates**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost (AUD)</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual care (UC) of MI</td>
<td>3.5 million</td>
<td>120</td>
</tr>
<tr>
<td>UC of MI + streptokinase (SK)</td>
<td>3.7 million</td>
<td>90</td>
</tr>
<tr>
<td>UC of MI + tissue plasminogen activator (tPA)</td>
<td>5.5 million</td>
<td>80</td>
</tr>
</tbody>
</table>

**Comparison of the different treatments**

- **Difference between SK and UC of MI:**
  - Cost of treatment = AUD 3.7 – 3.5 million/1,000 cases = AUD 0.2 million/1,000 cases = AUD 200 per case
  - Number of deaths that will be prevented = 120 – 90 = 30 deaths/1,000 cases treated
  - Cost effectiveness of SK = AUD 0.2 million/30 lives = AUD 6,700 per life saved

- **Difference between tPA and usual care of MI:**
  - Cost of treatment = AUD 5.5 – 3.5 million/1,000 cases = AUD 2.0 million/1,000 cases = AUD 2,000/case
  - Number of deaths that will be prevented = 120 – 80 = 40 deaths/1,000 cases treated
  - Cost effectiveness of tPA = AUD 2.0 million/40 lives = AUD 50,000 per life saved

- **Difference between tPA and SK treatments for MI:**
  - Cost of treatment = AUD 2.0 – 0.2 million/1,000 cases = 1.8 million/1,000 cases = AUD 1,800 per case
  - Number of deaths that will be prevented = 90 – 80 = 10 deaths/1,000 cases treated
  - Increased cost effectiveness of tPA over SK = AUD 1.8 million/10 lives = AUD 180,000 per life saved

- **If one has a budget of only AUD 500,000, which medicine should one use?**
  - For SK: number of cases that can be treated = 500,000/200 = 2,500 cases
    - Number of lives that can be saved = (30/1000) x 2500 = 75 lives
  - For tPA: number of cases that can be treated = 500,000/2000 = 250 cases
    - Number of lives that can be saved = (40/1000) x 250 = 10 lives

**Conclusion**

This study concluded that though tPA had slightly better efficacy and saved marginally more lives, when cost was taken into account, more patients could be treated and more lives saved using SK. In other words, the extra cost effectiveness of tPA over SK was so high (AUD 180,000 per life saved) that fewer people could be treated, and fewer lives saved, using tPA as compared to SK, with the limited budget available.

Other Types of Economic Evaluation

Cost-Utility Analysis

CUA is a type of economic evaluation that uses utilities as a measure of the value of an intervention. Utilities, which are measured as the preferences individuals or society may have for any particular set of health outcomes, are expressed as numerical values between 0 (worst) and 1 (full health). The outcome used in a cost utility evaluation is a QALY or DALY that includes the length of life gained and a measure of the subjective levels of well-being. QALYs are determined by adjusting the length of time affected through the health outcome by the utility value of the resulting level of health status. In a CUA the incremental cost of an intervention is compared to the incremental health improvement attributable to the intervention, with the health improvement measured in QALYs gained. The results of CUAs are usually expressed in terms of the cost per QALY gained.

A number of methods are used to measure and estimate utilities. The sources of values used in the analysis can come from patients, health care providers, or the general public. Further details of these methods can be found in Drummond et al. (2005) and are beyond the scope of this session.

Using CUA in relation to pharmaceuticals has three weaknesses: (a) utility as a strength of preference may not be a reliable or comprehensive index of health-related quality of life; (b) QALY calculations may not capture precisely the real trade-offs between quantity and quality of life; and (c) the methods used to work out numerical values for utilities are not comparable, may be unreliable, and may not translate well from one setting to another. If a DTC wants to use CUA in decision making, it should make sure that the study can be evaluated by an expert.

Cost-Benefit Analysis

A CBA is an economic evaluation that measures both the costs and benefits of treatment alternatives in monetary amounts. The results of a CBA can be stated as a ratio of benefits to costs or as a simple difference representing the net benefit of one alternative over another. Results of such analyses are expressed as benefit-to-cost ratios. They are difficult to carry out reliably for pharmaceuticals and should not be used in decision making by DTCs without expert advice on their validity and interpretation.

Two Important Components of Economic Evaluations

Sensitivity Analysis

Sensitivity analysis should be done for all kinds of economic evaluation—whether cost minimization, cost-effectiveness, or some other type. This technique is used to quantify the uncertainty in an economic evaluation by varying the values given to a key variable in the valuation. Key variables are identified, a plausible range of values is determined, and then the analysis is re-run using different values of the key variables, and the impact of these changes on the results is observed. Sensitivity analysis can be conducted changing one variable at a time.
(one-way) or several (multi-way). If the results of an economic evaluation change significantly with sensitivity analysis, they are generally less reliable for use in decision making.

Examples of variables in a cost-analysis study include cost of physician visits, price of medicines, cost estimate of adverse drug reactions (ADRs) as well as the number of ADRs experienced, laboratory tests required in the treatment, and duration of treatment. In a sensitivity analysis, different estimates of cost can be applied to the variables and the analysis performed to confirm or refute the original results. (See the example following table 2 in “Cost-Minimization Analysis” above.)

Discounting

Discounting is a technique used in economic evaluations that allows the adjustment of calculations of costs and benefits over time for the different preference we have for having costs in the present or in the future. The discount rate is the rate used to convert the value of future costs and benefits into equivalent present values. The choice of discount rate and whether it should be applied to costs, benefits, or both are controversial issues—some authors argue that benefits should not be discounted. Typical discount rates range from 3 to 6 percent. The important point to note is that different discount rates can dramatically alter the final result of any cost-effectiveness calculation, a point to consider when deciding whether a DTC can rely on an analysis.

Evaluating Pharmacoeconomic Studies

Unlike clinical studies that involve medicine comparisons for efficacy, there is no “gold standard” for pharmacoeconomic studies. Several different methods of performing these studies are used, and outcomes are highly dependent on how the analysis was performed. Using published pharmacoeconomics studies has a number of potential pitfalls, so readers of this literature must be careful when interpreting results and take the following into account.

- One significant problem is the applicability of a study for one’s home country or community—what may make sense economically in one area of the world may not be applicable in other areas.

- The randomized controlled study is the most reliable medicine study design. Unfortunately the rigorous nature of a clinical trial frequently does not reflect what will happen in other locations that do not have the same constraints as the study (i.e., blinding, monitoring, laboratory testing, intense medical follow-up).

- The rush to conduct pharmacoeconomic studies has resulted in variations in the quality of many studies performed. Problems include using incorrect methodology, arriving at incorrect conclusions, and defining important pharmacoeconomic terms incorrectly.

- Many studies are conducted by pharmaceutical companies. There is always the possibility of bias being introduced concerning the information about the company’s medicine.
• Negative outcome research seldom gets into the literature. This omission again may relate back to the sponsor of the study, who may want to suppress any results that are not useful in promoting a particular medicine.

Readers should interpret published data cautiously. Some fundamental questions that a reader must ask about an economic evaluation are—

• Are the patients and therapies selected for the study similar to those in my community?
• Is the study applicable to my setting?
• Are costs of the therapies fully described and similar to those for my patients?
• Are costs of benefits or assumptions of effectiveness fully disclosed?
• Has a sensitivity analysis been done?
• Who is the sponsor?
• Are all of the costs associated with pharmaceutical treatment including good and bad outcomes described (not just prices)?
• Has discounting been used to reflect the cost of future benefits or consequences in present day values?

A checklist for assessing economic evaluations was adapted from one found in *Methods for the Economic Evaluation of Health Care Programmes, 3rd ed.* by M. J. Drummond, G.W. Sculpher, B.J. Torrance, et al. 2005, Oxford University Press. Systematic application of the points on the checklist (appendix 1) will allow readers to identify and assess the strengths and weaknesses of individual studies.

**Activity 1. Cost Minimization Analysis of NSAIDs**

Your hospital outpatient department sees a large volume of patients with back pain, minor trauma, and arthralgias. A medicine use indicator study in this department indicated that a high percentage—25 percent—of patients receive injections. An in-depth review showed that diclofenac injection is extensively used for all type of pain syndromes. Typically, patients are given diclofenac 75 mg intramuscular (IM) followed by diclofenac 50 mg three times a day for one week.

Review of the literature on use of this injection shows that it is no more effective than oral non-steroidal anti-inflammatory drugs (NSAIDs) and has significant ADRs including pain on injection and occasional neuropathies. Your DTC asks that a cost minimization study be done to evaluate the four NSAIDs that are available in the outpatient department. For activity 1, perform a cost analysis (cost-minimization) of these medicines based on the usual treatment regimen of seven days. Acquisition costs of these products are listed in table 6.
Table 6. Acquisition Costs

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose</th>
<th>Cost per Dose (Acquisition)</th>
<th>Cost per Day (Treatment)</th>
<th>Cost for 7 Days (Treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>400 mg tid</td>
<td>0.0077</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naproxen</td>
<td>500 mg bid</td>
<td>0.0216</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diclofenac</td>
<td>50 mg tid</td>
<td>0.0057</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diclofenac injection</td>
<td>75 mg IM × 1 dose only</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Diclofenac 50 mg tid</td>
<td>50 mg tid</td>
<td>0.0057</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Other cost associated with administering NSAIDs injections include—
- Syringe/needle: USD 0.90
- Nursing cost to administer one dose (salary): USD 1.00

1. What is the least costly treatment regimen according to your analysis?

2. What is the cost savings for 1,000 patients treated with diclofenac tablets compared to regimen of diclofenac injection + diclofenac tablets?

3. Perform a sensitivity analysis on your analysis by changing the cost of syringe/needle to USD 1.50

4. What would your DTC recommend concerning the NSAIDs in this health facility?

Activity 2. Cost-Effectiveness Analysis of Two Antimalarial Treatments

Your DTC is considering adding an artemisinin combination therapy for the treatment of uncomplicated malaria. You have two choices to consider: artesunate plus lumefantrine (A+L) or artesunate plus mefloquine (A+M).

The effectiveness of both medicines has been summarized in a systematic review—

- A+L, 6 doses: number of patients with parasitemia at 28 days was 11 of 289 (4 percent)
- A+M, 3 days: number of patients with parasitemia at 28 days was 0 of 100 (0 percent)

The dose of A+L in adults is six doses of four tablets (20 mg + 120 mg). The dose of A+M in adults is four tablets of artesunate daily for three days (200 mg per day), and 500 mg of mefloquine on day 2 and 250 mg on day 3 (for 50 kg adult).

The cost of one pack of 24 A+L tablets is USD 5.00. The cost of A+M (two separate packets) is USD 1.54 for 12 artesunate 50 mg tablets and USD 4.57 for six mefloquine 250 mg tablets.

1. Evaluate the cost-effectiveness of A+M compared to A+L.
2. Carry out a simple sensitivity analysis, by reducing the effectiveness of A+M to 5 percent lower than that of A+L. What other important criteria should be considered when adding such a medicine to the formulary?

3. Which of these two medications is the preferable product for the formulary?

Summary

Economic evaluation is an important component in evaluating the usefulness of a medicine for the formulary. A simple determination of a medicine’s price is frequently inadequate for determining the actual cost of a medicine to the health care system.

Basic economic evaluations can be done by the DTC, most commonly cost-minimization analysis. Cost-effectiveness can also be done but usually only in large centers or at the national level where there is sufficient expertise. Nevertheless, the DTC can also use pharmacoeconomic information from clinical trials or reasonable extrapolations of these trials in assessing medicines for the formulary.

Most likely, health care practitioners will increasingly be faced with the need to conduct or evaluate medicine costs in the future because health care systems will demand that such data be carefully considered before adding a new medicine to the formulary.
APPENDIX 1. CHECKLIST FOR ASSESSING ECONOMIC EVALUATIONS

The following 10-point checklist for assessing economic evaluations has been adapted from Drummond et al. (2005). Systematic application of the points on the checklist will allow readers to identify and assess the strengths and weaknesses of individual studies. This checklist is made available by permission of Oxford University Press (www.oup.com).

1 Was a well-defined question posed in answerable form?
   1.1 Did the study examine both costs and effects of the service(s) or program(s)?
   1.2 Did the study involve a comparison of alternatives?
   1.3 Was a viewpoint for the analysis stated, and was the study placed in any particular decision-making context?

2 Was a comprehensive description of the competing alternatives given (i.e., can you tell who did what to whom, where, and how often)?
   2.1 Were any relevant alternatives omitted?
   2.2 Was (should) a do-nothing alternative (be) considered?

3 Was the effectiveness of the programs or services established?
   3.1 Was effectiveness established through a randomized, controlled clinical trial? If so, did the trial protocol reflect what would happen in regular practice?
   3.2 Were effectiveness data collected and summarized through a systematic overview of clinical studies? If so, were the search strategy and rules for inclusion or exclusion outlined?
   3.3 Were observational data or assumptions used to establish effectiveness? If so, what are the potential biases in results?

4 Were all the important and relevant costs and consequences for each alternative identified?
   4.1 Was the range wide enough for the research question at hand?
   4.2 Did it cover all relevant viewpoints? (Possible viewpoints include the community or social viewpoint, and those of patients and third-party payers. Other viewpoints may also be relevant depending upon the particular analysis.)
   4.3 Were capital costs, as well as operating costs, included?
5 Were costs and consequences measured accurately in appropriate physical units (e.g., hours of nursing time, number of physician visits, lost workdays, gained life years)?

5.1 Were the sources of resource utilization described and justified?

5.2 Were any of the identified items omitted from measurement? If so, does this mean that they carried no weight in the subsequent analysis?

5.3 Were there any special circumstances (e.g., joint use of resources) that made measurement difficult? Were these circumstances handled appropriately?

6 Were costs and consequences valued credibly?

6.1 Were the sources of all values clearly identified? (Possible sources include market values, patient or client preferences and views, policy makers’ views and health professionals’ judgments.)

6.2 Were market values employed for changes involving resources gained or depleted?

6.3 Where market values were absent (e.g., volunteer labor) or market values did not reflect actual values (such as clinic space donated at a reduced rate) were adjustments made to approximate market values?

6.4 Was the valuation of consequences appropriate for the question posed (i.e., has the appropriate type or types of analysis—cost-effectiveness, cost-benefit, cost-utility—been selected)?

7 Were costs and consequences adjusted for differential timing?

7.1 Were costs and consequences that occur in the future discounted to their present values?

7.2 Was any justification given for the discount rate used?

8 Was an incremental analysis of costs and consequences of alternatives performed?

8.1 Were the additional (incremental) costs generated by one alternative over another compared to the additional effects, benefits, or utilities generated?

9 Was allowance made for uncertainty in the estimates of costs and consequences?

9.1 If patient-level data on costs or consequences were available, were appropriate statistical analyses performed?

9.2 If a sensitivity analysis was employed, was justification provided for the range of values (for key study parameters) and the form of sensitivity analysis used?
9.3 Were the conclusions of the study sensitive to the uncertainty in the results, as quantified by the statistical or sensitivity analysis or both?

10 Did the presentation and discussion of study results include all issues of concern to users?

10.1 Were the conclusions of the analysis based on some overall index or ratio of costs to consequences (e.g., cost-effectiveness ratio)? If so, was the index interpreted intelligently or in a mechanistic fashion?

10.2 Were the results compared with those of others who have investigated the same question? If so, were allowances made for potential differences in study methodology?

10.3 Did the study discuss the generalizability of the results to other settings and patient/client groups?

10.4 Did the study allude to, or take account of, other important factors in the choice or decision under consideration (e.g., distribution of costs and consequences, or relevant ethical issues)?

10.5 Did the study discuss issues of implementation, such as feasibility of adopting the preferred program given existing financial or other constraints, and whether any freed resources could be redeployed to other worthwhile programs?