Drug and Therapeutics Committee
Training Course

Session 6.
Evaluating the Cost of Pharmaceuticals

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

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

Outline

- Introduction
- Definitions
- Cost-Evaluation Methods
  - Cost-Minimization Analysis (CMA)
  - Cost-Effectiveness Analysis (CEA)
- Evaluating Pharmacoeconomic Studies
- Activities
- Summary

Preparation and Materials

- Read Trainer’s Guide and Participants’ Guide, and review visual aids (VAs).
- Instruct participants to read the Participants’ Guide the evening before the session presentation.
- Do all the calculations yourself before teaching the session.
- Ensure that there are at least two calculators per table (of five to eight people).
Further Readings


Visual Aid Listing

1. Title slide
2. Introduction
3. Objectives
4. Outline
5. Key Definitions (1)
6. Key Definitions (2)
7. Direct Costs of a Medicine
8. Indirect Costs of a Medicine
9. Cost-Minimization Analysis
11. Cost-Minimization Analysis: Example 1
12. Cost-Minimization Analysis: Example 2
13. Cost-Effectiveness Analysis (CEA)
14. CEA: Steps
15. Incremental Cost Effectiveness Ratio
16. Example of CEA: Medicine Costs
17. Example of CEA: Benefits
18. Example of CES: Incremental Cost-Effectiveness
19. CEA of Two Thrombolytics in MI in Australia (1)
20. CEA of Two Thrombolytics in MI in Australia (2)
21. CEA of Two Thrombolytics in MI in Australia (3)
22. CEA of Two Thrombolytics in MI in Australia (4)
23. CEA of Two Thrombolytics in MI in Australia (5)
24. CEA of Two Thrombolytics in MI in Australia (6)
25. Other Controversial Cost Analyses
26. Sensitivity Testing
27. Discounting
28. Evaluating Pharmacoeconomic Studies (1)
29. Evaluating Pharmacoeconomic Studies (2)
30. Evaluating Pharmacoeconomic Studies (3)
31. Activities
32. Summary
Organization of the Session

Total time: 3 hours

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.

First Component: 15 minutes
VAs 1–6: Introduction

Start the session by asking the participants how much it costs to treat someone for a disease such as pneumonia or hypertension. Elicit from them answers that illustrate that treatment involves many more expenses than just the price of the medicine. Then carefully go over the outline of the session and the definitions. Mention that medicine cost analyses are becoming increasingly important because medicine costs consume an increasing proportion of health care costs—maybe up to half.

Second Component: 30 minutes
VAs 7–12: Cost of Using a Medicine and Cost-Minimization Analysis

Review the costs of using a medicine on VAs 7 and 8. These slides are important because they give details of the true cost of using a medicine over and above the acquisition cost. Explain the method of CMA (VAs 9 and 10), and mention that it is the method of cost evaluation used most often by pharmacy departments. Emphasize that cost minimization can only be used to compare two products that have been shown to be equivalent in dose and therapeutic effect. Therefore, this method is most useful for comparing generic and therapeutic equivalents or “me too” medicines. CMA cannot be used when there is not a reliable equivalence between the products being compared. Work through the examples (VAs 11 and 12) with the participants, getting them to follow the calculations step by step. The cost of salary for pharmacy and nursing will be controversial. Explain that this cost is necessary only when these costs have a significant impact on the cost of the medicine. If there is no difference between the two medicines, it is not necessary to actually calculate these costs.

Third Component: 30 minutes
VAs 13–24: Cost-Effectiveness Analysis

Explain that cost-effectiveness introduces medicine effectiveness into the analysis. Effectiveness is measured in terms of intermediate clinical outcomes (e.g., blood pressure, blood sugar, asthma attacks) or long-term clinical outcomes (e.g., years of life saved). This form of analysis can be used to compare medicines that are not equivalent in terms of dose or therapeutic effect, but that
are used to treat the same clinical condition. Such analyses are difficult for a DTC to do, but it is important to understand the principles to be able to judge pharmacoeconomic studies when assessing new medicines for the formulary. Work through the example with the participants getting them to follow the calculation step by step. Explain that the example from Australia was an actual analysis done at the national level.

**Fourth Component: 15 minutes**  
**VAs 25–27: Other Cost Analyses, Sensitivity Analysis, and Discounting**

Briefly explain other cost analyses and how controversial they are. Ask the participants to list some of the assumptions people make in cost analyses and what they think of the accuracy of these assumptions. Ask how they might deal with such assumptions. Then explain how to vary these assumptions in a sensitivity analysis to see if the cost analyses change. Briefly mention that only national health economists, not DTCs, use discounting, but that it will be encountered in the literature.

Discounting is used in cost evaluations to establish present value of a future benefit. This method is necessary to take into account the effects of inflation and aging (life span). Actual benefits of a medicine today or this year will not have the same value 5 to 10 years from now. Discounting is an important concept to give validity to the pharmacoeconomic calculations that have benefits ranging over prolonged periods of time.

**Fifth Component: 15 minutes**  
**VAs 28–30: Pharmacoeconomic Studies**

Ask the participants what sort of problems they might expect to encounter in pharmacoeconomic articles. Then briefly summarize the information in the VAs.

- Discuss how the literature will provide valuable cost information from pharmacoeconomic studies.

- Discuss the shortcomings of this type of literature, such as influences of pharmaceutical companies, methodological shortcomings of the study, and occasionally incorrect conclusions.

- Discuss briefly those areas that are involved in a more comprehensive evaluation (if time permits and interest is great). This information is not on the VAs, but is included in the Participants’ Guide.

Briefly present and discuss the checklist in the Participants’ Guide. There are no VAs for the checklist, but it is important to let the participants know about it and that they need to review carefully. This checklist will be of value when reviewing pharmacoeconomic literature.
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 adverse drug reactions (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 1. (Table 2 provides solutions in italics.)

**Table 1. Acquisition Costs**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose</th>
<th>Cost per Dose (USD)</th>
<th>Cost per Day (USD)</th>
<th>Cost for 7 Days (USD)</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 costs associated with giving NSAIDS include—*
- Syringe/needle: 0.90 U.S. dollars
- Nursing cost to administer one dose: USD 1.00

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

   *Answer: Diclofenac (see table 2)*
Table 2. Acquisition Costs (with Solutions)

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose</th>
<th>Cost per Dose (USD)</th>
<th>Cost per Day (USD)</th>
<th>Cost for 7 Days (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>400 mg tid</td>
<td>0.0077</td>
<td>0.0231</td>
<td>0.16</td>
</tr>
<tr>
<td>Naproxen</td>
<td>500 mg bid</td>
<td>0.0216</td>
<td>0.0432</td>
<td>0.30</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>50 mg tid</td>
<td>0.0057</td>
<td>0.0171</td>
<td>0.12</td>
</tr>
<tr>
<td>Diclofenac injection</td>
<td>75 mg IM × 1 dose only</td>
<td>0.07</td>
<td></td>
<td>1.97</td>
</tr>
<tr>
<td>+ Diclofenac</td>
<td>50 mg tid</td>
<td>0.0057</td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total diclofenac tablets and injection</td>
<td>2.09</td>
</tr>
</tbody>
</table>

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

   Answer: USD 2,090 vs. USD 120 for a cost savings of USD 1,970

3. Perform a sensitivity analysis on your analysis by changing the cost of syringe/needle to USD1.50.

   Total cost for diclofenac injections = USD 2,570
   Total cost of diclofenac tablets = USD 120
   Total cost = USD 2,690 for the injection + tablets

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

   Discontinue the use of the injection or limit its use to a well-defined population.

   • There is little evidence of improved efficacy compared to oral NSAIDs.

   • ADRs are well documented for this injection, including pain on administration and neuropathies (sciatic nerve injury).

   • Cost is significantly higher than oral preparations.

   • Increased nursing time is needed to administer the injection.
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 tablet 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 a 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.

   The calculation is as follows:

   **Medicine costs**
   
   **Cost for A+L at USD 5 per pack of 24 tablets per patient**
   Medicine cost of A+L for 100 patients = USD 5 × 100 = USD 500

   **Cost for A+M at USD 1.54 per pack A + USD 4.57 per pack of M = USD 6.11/patient**
   Medicine cost for A+M for 100 patients = 6.11 × 100 = USD 611

   **Benefits**
   Treatment failure defined as parasitemia at 28 days
   A+L: Failure rate 4 percent, so cure rate = 100 – 4 = 96 percent
   A+M: Failure rate 0 percent, so cure rate = 100 – 0 = 100 percent

   Incremental cost-effectiveness ratio (ICER) = (611 – 500) ÷ (100 – 96) = 27.75
   That is, USD 27.75 extra per patient cured treating with A+M as 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 a such a medicine to the formulary?

   The calculation is as follows:

   Sensitivity analysis where benefits changed to the following cure rates
   A+L: Failure rate 4 percent as before, so cure rate remains 96 percent.
A+M: Failure rate changed to 5 percent less than A+L, so cure rate = 96 – 5 = 91%

\[
\text{ICER} = (611 - 500) \div (91 - 96) = \text{USD } -22.2
\]
That is, USD 27.75 less per patient cured treating with A+M as compared to A+L.

A+M is more expensive, and on these data, more effective, but this analysis does not include ADRs or ease of dosing. As the sensitivity analysis shows, the results are sensitive to the estimate of effectiveness difference. As soon as both products are equivalently effective, A+L is more cost-effective—as shown by the negative result for the ICER on sensitivity analysis, since in this scenario it is both cheaper and more effective. If you were not sure about the difference in treatments, then you would go with the cheaper product.

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

If effectiveness is most important, then paying an extra USD 27 per additional patient cured might be value for money. But if your hospital treats a lot of patients, then the total cost of buying enough treatment may be an important factor in your decision and the cheaper less effective treatment might be an alternative.

The answers are provided in table 3.

**Table 3. Cost Effectiveness Analysis for Activity 2**

<table>
<thead>
<tr>
<th>Medicine Costs</th>
<th>Per Patient</th>
<th>For 100 Patients</th>
<th>Sensitivity Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A+L</td>
<td>USD 5.00</td>
<td>USD 500</td>
<td>—</td>
</tr>
<tr>
<td>A+M</td>
<td>USD 6.11</td>
<td>USD 611</td>
<td>—</td>
</tr>
<tr>
<td>Benefits (cures)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A+L</td>
<td>—</td>
<td>96%</td>
<td>96%</td>
</tr>
<tr>
<td>A+M</td>
<td>—</td>
<td>100%</td>
<td>91%</td>
</tr>
<tr>
<td>ICER: A+M compared to A+L:</td>
<td>USD 27.75/extra</td>
<td>—22.20/extra</td>
<td></td>
</tr>
<tr>
<td>First analysis:</td>
<td>(611 – 500) \div (100 – 96) = 27.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity analysis:</td>
<td>(611 – 500) \div (91 – 96) = -22.2</td>
<td>Patient cured</td>
<td>Patient cured</td>
</tr>
</tbody>
</table>
Seventh Component: 15 minutes
VAs 32: Summary

Summarize the key points of the session. Emphasize that cost minimization analysis is the most common type of analysis done by DTCs and can be used only to compare therapeutically equivalent medicines.