

Basics and principles of Pharmacoeconomics



- ☐ Pessimist: bottle ½ empty متشائم
- ☐ Optimist: bottle ½ full
- ☐ Economist: bottle ½ wasted

Health economic problem



- 1- Unlimited healthcare “wants” with rapid growth in health expenditure.
- 2- Insufficient health sector resources.
- 3- Choosing between ‘wants’ we can ‘afford’ our resource ‘budget’.

Introduction

- The United States spent about \$2.7 trillion on health care in 2010, for an average of about \$8,000 per person. About 12% (over \$900 per person) of health care expenditures were for medications.
- The gross domestic product (GDP) is one the primary indicators used to gauge the health of a country's economy. The proportion حصة of GDP (Gross Domestic Product) إجمالي الناتج المحلي spent on total health care has climbed steadily over the past 30 years.
- Although private health insurance and government programs cover a growing portion of drug expenditures, approximately 36% of drug costs are still paid directly by the consumers.
- Despite the general evidence supporting the use of pharmaceuticals, few data exist regarding the actual costs and benefits attributed to specific drug therapies. A primary reason is the lack of defined methodologies to evaluate medical interventions.

إجمالي الناتج المحلي (GDP) هو القيمة السوقية لكل السلع النهائية والخدمات المعترف بها بشكل محلي والتي يتم إنتاجها في دولة ما خلال فترة زمنية محددة. غالبًا ما يتم اعتبار إجمالي الناتج المحلي للفرد مؤشرًا لمستوى المعيشة في الدولة

Definitions

- **Health economics** is the science of assessing cost and benefits, not to make decisions about resource use, but to inform those decisions makers.
- The aim is to identify what is most efficient, so that the greatest amount of benefit can be bought for a given amount of money or resources.
- Remember that in health care, efficiency may not be the most important objective (we might for instance prioritize caring for dying patients or treating patients with serious disease who have relatively little hope of surviving).

- **Pharmacoeconomics** has been defined as “the description and the analysis of the cost of drug therapy to health care systems and society”. It identifies, measures, and compares the costs (i.e., resources consumed) and consequences (clinical, economic, and humanistic) of pharmaceutical products and services.
- Figure 1 the left hand side of the equation represents the input (costs) used to obtain and use the pharmaceutical products or service. The right hand side of the equation represents the health related outcomes produced by the pharmaceutical product or service. The center of the equation the drug product or service assessed is symbolized by R . If just the left hand side is measured without regard to outcomes, it is a cost analysis (or partial economic analysis). If just the right hand side of the equation is measured without regard to costs, it is a clinical analysis or outcome study (not an outcome analysis). To be a true pharmacoeconomic analysis both sides of the equation must be considered and compared.

COSTS (\$) → R → OUTCOMES

Figure 1. Pharmacoeconomic studies compare the cost (left box) associated with providing a pharmacy product or service (represented by R) to the outcome of the or service.

- **Outcomes** is increasingly being used to describe the results and value of healthcare intervention.
- However, depending on perspective, the outcomes of health care are multidimensional.
- The clinician has traditionally been most concerned with clinical outcomes of treatments.
- Patients, on the other hand, are seeking more information regarding the humanistic outcomes of therapy.
- Healthcare payers and administrators have focused on the resource use or economic outcome of healthcare decisions.
- **Resources** **موارد** it is intended **مقصود**, people and their time and skills, and the facilities and the equipment needed to deliver effective health promotion **ترويج** programs. It does not mean money.

- In economics, resources are believed to be insufficient relative to what can be done with them and so it is necessary to choose where best to invest those resources.
- It is essential to know whether the programs that are supported do indeed make best use of the limited resources that are available to them.

Perspective: وجهة نظر, انطباع The “point of view” considered in economic analyses which influences the outcomes

- Provider
- Patient
- Payer
- Society

Once a perspective is chosen, the costs and consequences associated with a given product or service can be identified and measured services

- **Patient perspective:** is vital because patients are the ultimate اساسي consumers of healthcare services.
- Cost from the perspective of patients are essentially what patients pay for a product or service, that is, the portion not covered by insurance.
- Consequences, from a patient’s perspective, are the clinical effects, both positive and negative, of a program or treatment alternative.
- **Provider Perspective:** المجيز The actual expense of providing a product or service, regardless of what the provider charges.
- Providers can be hospitals, managed-care organizations (MCOs), or private-practice physicians.
- From this perspective, direct costs such as drugs, hospitalization, laboratory tests, supplies, and salaries of healthcare professionals can be identified, measured, and compared.
- Indirect costs can be of less importance to the provider.
- **Payer Perspective:** Payers include insurance companies, employers, or the government.
- From this perspective, costs represent the charges for healthcare products and services allowed, or reimbursed عوض, by the payer.
- The primary cost for a payer is of a direct nature. However, indirect costs, such as lost workdays and decreased productivity, also can contribute to the total cost of healthcare to the payer.

- **Societal Perspective:** It is the broadest of all perspectives because it is the only one that considers the benefit to society as a whole.
- Theoretically, all direct and indirect costs are included in an economic evaluation performed from a societal perspective.
- Costs from this perspective include patient morbidity and mortality and the overall costs of giving and receiving medical care.
- **Cost:** is defined as the value of the resources consumed by a program or drug therapy of interest.
- **Consequence:** is defined as the effects, outputs, or outcomes of the program or drug therapy of interest.

Types of Pharmacoeconomic studies

There are four basic types of pharmacoeconomic studies (Table 1) cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA). Each method measures cost in dollars, but they differ regarding how health outcomes are measured and compared.

Table 1. The four basic types of pharmacoeconomic analysis

Methodology	Cost measurement unit	Outcome unit
Cost minimization	Dollars	Various- but equivalent in comparative groups
Cost benefit	Dollars	Dollars
Cost effectiveness	Dollars	Natural units (life years, mg/dl blood sugar, LDL cholesterol)
Cost utility	Dollars	Quality adjusted life years

How should I treat my patient?

- NSAIDs are inexpensive compared to Cox-II inhibitor:
- But the more expensive agent pay for itself many times over by preventing an expensive GI bleed in my patient?
- Dyspeptic symptoms are decreased by 15%
- Clinically significant ulcer

Risk of GI bleed: how much can it be altered? complications are reduced by 50%

- Not all osteoarthritis patients have an equal risk of developing a GI bleed
- Is paying extra for GI protection justified in all patients?
- How much can the risk of GI bleed be altered by using a Cox-II inhibitor instead of an NSAID?
- What value is really purchased for the extra cost?
- The relative risk reduction of GI complications with Cox-II inhibitor catches our eye- but actual risk reduction is small.
- 1-2% for overall ulcer complications.
- 1% for serious hemorrhage.

Measuring and estimating costs

Costs are calculated to estimate the resources (or inputs) that are used in the production of a good or service. Resources used for one good or service are no longer available to be used for another. According to economic theory, the “true” cost of a resource is its **opportunity cost**—the value of the best-forgone option or the “next best option”—not necessarily the amount of money that changes hands.

The “price” or the amount that is charged to a payer is not necessarily synonymous with the **cost** of the product or service. For example, if a hospital system wanted to calculate how much it cost to treat a patient with a specific diagnosis, there may be a substantial difference in what the total cost is to the hospital when compared with the amount the hospital charges the payer and what is actually collected from the payer after allowable amounts are factored in.

Cost categorization

Pharmacoeconomic categorizes costs into four types: **direct medical costs**, **direct nonmedical costs**, **indirect costs**, and **intangible costs** (Table 1).

Direct Medical Costs

Direct medical costs are the most obvious costs to measure. These are the medically related inputs used directly to provide the treatment. Examples of direct medical costs include the costs associated with the pharmaceuticals, diagnostic tests, physician visits, pharmacist visits, emergency department visits, and hospitalizations.

For chemotherapy treatment, for example, direct medical costs may include the chemotherapy products themselves, other medications given to reduce side effects of the chemotherapy, intravenous supplies, laboratory tests, clinic costs, and physician visits.

Direct Nonmedical Costs

Direct nonmedical costs are costs to patients and their families that are directly associated with treatment but are not medical in nature. Examples of direct nonmedical costs include the cost of traveling to and from the physician’s office, clinic, or the hospital; child care services for the children of a patient; and food and lodging required for the patients and their families during out-of-town treatment.

For the chemotherapy treatment, patients may have increased travel costs related to traveling to the clinic or hospital. They may also have to hire a babysitter for the time they are undergoing treatment.

Table 1 contains examples of these costs. Again, the costs that are identified, measured, and ultimately compared vary depending on the perspective

TABLE 1-1 Example of Healthcare Cost Categories	
Cost Category	Costs
Direct medical costs	Medications
	Supplies
	Laboratory tests
	Healthcare professionals' time
	Hospitalization
Direct nonmedical costs	Transportation
	Food
	Family care
	Home aides
Indirect costs	Lost wages (morbidity)
	Income forgone because of premature death (mortality)
Intangible costs	Pain
	Suffering
	Inconvenience
	Grief
Opportunity costs	Lost opportunity
	Revenue forgone

Indirect Costs

Indirect costs involve the costs that result from the loss of productivity because of illness or death. **Indirect benefits**, which are savings from avoiding indirect costs, are the increased earnings or productivity gains that occur because of the medical product or intervention. In the chemotherapy example, some indirect costs result from time the patient takes off from work to receive treatment or reduced productivity because of the effects of the disease or its treatment. On the other hand, some indirect benefits may accrue at a later time because of the increased productivity allowed by the success of the treatment in decreasing morbidity and prolonging life.

Intangible Costs

Intangible costs include the costs of pain, suffering, anxiety, or fatigue that occur because of an illness or the treatment of an illness. Intangible benefits, which are avoidance or alleviation of intangible costs, are benefits that result from a reduction in pain and suffering related to a product or intervention. It is difficult to measure or place a monetary value on these types of costs. In the example of chemotherapy, nausea and fatigue are common intangible costs of treatment.

Perspective منظور

To determine what costs are important to measure, the **perspective** of the study must be determined. Perspective is an economic term that describes *whose costs* are relevant based on the purpose of the study. Conventional economic theory suggests that the most appropriate and comprehensive perspective is that of society. **Societal costs** include costs to the insurance company, costs to the patient, costs to the provider/institution, other sector costs, and indirect costs because of the loss of productivity.

Resources for cost estimations

Sources of estimates for four types of common direct medical cost categories are addressed: medications, medical services, personnel costs, and hospitalizations.

1- Medications

The **average wholesale price** (AWP) is often used when calculating the cost of pharmaceutical products in the United States. This is considered the “list price” or “sticker price” of medications.

The **average manufacturer’s price** (AMP), calculated to reflect the average amount paid to manufacturers by wholesalers after discounts are included, is a more precise estimate of what buyers (pharmacies) pay for medications, but the AMP calculations are proprietary and not available to the general public. Researchers should be clear about the source they use to estimate pharmacy costs, to enhance comparability of studies.

2- Medical Services

Medical services, such as office or clinic visits and outpatient laboratory and surgical procedures, are frequently included in direct medical cost estimates. As mentioned, providers have a list of charges for these types of services, but payers usually pay less than this “list price.”

3- Personnel

When the perspective of the study is that of the provider of health services (e.g., hospital, clinic, physician's office, pharmacy) and the provision of different health care alternatives involves a difference in the amount of time spent by medical personnel, attributing a cost to this difference is warranted. For example, if a hospital wanted to determine the cost-effectiveness of instituting a pharmacy discharge counseling service, an important cost estimate would include the time of the pharmacists who would provide this service.

4- Hospitalizations

The level of the precision of estimates varies widely for studies that include hospital costs as part of their evaluation. In order from least precise (gross or macrocosting) to most precise (micro-costing), four methods for estimating hospital costs are **per diem**, **disease-specific per diem**, **diagnosis-related group (DRG)**, and **micro-costing**.

Per Diem

The least precise method of estimating hospital costs is the per diem method of costing. For each day that a patient is in a hospital setting, an average cost per day for all types of hospitalizations is used as a multiplier.

Disease-Specific Per Diem

It would be more precise to use estimated costs per day for specific diseases, or a disease-specific per diem.

Diagnosis-Related Group

A relatively available and often-used method of estimating hospital costs to the payer is the payment rate for DRGs. This method is used to classify clinically cohesive diagnoses and procedures that use similar resources.

Each patient is assigned one of more than 500 DRGs based on factors such as principal diagnosis, specific procedures involved, secondary diagnoses, and age, and the average reimbursement for each DRG can be used to approximate the cost to the payer.

Micro-costing

The most precise method of estimating hospital costs is micro-costing. Microcosting involves collecting information on resource use for each component of an intervention (in this example, each component of a hospitalization) to estimate and compare alternative interventions.

Cost of minimization analysis

Cost minimization analysis (CMA) measures and compares input costs and assumes output to be equivalent. Thus the type of interpretation that can be evaluated with this method are limited.

A common example of a CMA is the comparison of generic equivalents of the same drug entity. When comparing medications that are the same chemical entity and the same dose and have the same pharmaceutical properties as each other (brand versus generic or generic made by one company compared with a generic made by another company) only the cost of the medication itself needs to be compared because outcomes should be the same.

Another example of a CMA analysis includes measuring the costs of receiving the same medication in different settings. For example, researchers could measure the costs of receiving intravenous antibiotics in a hospital and compare this with receiving the same antibiotics (at the same doses) at home via a home health care service.

There is some debate about the use of the term CMA. Some contend that if outcomes are *not measured*, the study is considered to be a partial economic analysis that is termed a **cost analysis** and not a full pharmacoeconomic analysis. In addition, when both costs and clinical outcomes are *measured*, yet clinical outcomes are found to be *equivalent*, some categorize the study as a CMA because outcomes were equivalent, but others categorize the study as a **cost-effectiveness study**, or because clinical outcomes were measured. (If outcomes were measured and found to be equivalent, I would tend to refer to the study as a CEA.).

Example

Cost-Minimization Analysis (CMA) That Compares Outpatient and Inpatient Costs

The costs in the following table are based on a study, by Farmer et al., that estimated the costs associated with administering prostaglandin E2 gel intracervically to expectant mothers on the day before labor was to be induced (to help ripen the cervix). They compared the costs of (1) application of the gel, followed by a 2-hour monitoring period and then sending the expectant mother home for the night compared with (2) application of the gel followed by a 2-hour monitoring period and then sending the expectant mother to the maternity unit overnight. Both groups received oxytocin the next day at the hospital to augment or induce labor.

The perspective was that of the payer, so only direct medical costs were included. The authors used “usual and customary charges” from one hospital as a proxy for costs because they were readily obtainable. The authors collected and compared the costs associated with labor and delivery but specifically did not include the cost of infant care because newborn outcomes (e.g., Apgar scores) were the same between the two groups. Because the same drug was being administered in the same dose, the authors expected the outcomes for both groups to be the same. In addition, they measured maternal outcomes (e.g., percent of cesarean sections performed, amount of oxytocin needed) and found that there were no statistical differences between the groups. The authors said they conducted a CMA because outcomes were expected to be the same, but others (including me) might have labeled it a cost-effectiveness analysis because outcomes were measured but found to be the same.

Type of the costs	Cost of outpatients Mean (n=40)	Cost of inpatients Mean (n=30)	Statistical difference
Labor costs	\$ 575	\$ 902	Yes $p= 0.002$
Delivery costs	\$ 471	\$ 453	No $p= 0.754$
Pharmacy costs	\$ 150	\$ 175	No $p= 0.384$
Hospital costs	\$ 3,835	\$ 5,049	Yes $p= 0.015$

Summary

Cost-minimization analysis is the simplest of the four types of pharmacoeconomics analyses because the focus is on measuring the left-hand side of the pharmacoeconomic equation in chapter 1—costs—and the right hand side of the equation—outcomes—is assumed to be the same (or is found to be the same). But this method has limited use because it can only compare alternatives with the same outcomes.

Cost Effectiveness Analysis

Background

- Cost effective analysis is a technique designed to assist a decision maker in identifying a preferred choice among possible alternatives.
- Cost effective analysis is defined as a series of analytical and mathematical procedures that aid in the selection of a course of action **مسار العمل** from various alternative approaches.
- Cost is measured in dollars, and outcomes are measured in terms of obtaining a specific therapeutic outcome (lives saved, cases cured, life expectancy, or drop in blood pressure).
- The results of CEA are also expressed as a ratio—either as
 - ❖ an average cost-effectiveness ratio (ACER) or as
 - ❖ an incremental **زيادة ربح** cost-effectiveness ratio (ICER).

Average cost-effectiveness ratio (ACER)

- An ACER represents the total cost of a program or treatment alternative divided by its clinical outcome to yield a ratio representing the dollar cost per specific clinical outcome gained, independent of comparators.
- The ACER can be summarized as follows

$$\text{ACER} = \frac{\text{health care costs (\$)}}{\text{clinical outcome (not in \$)}}$$

- This allows the costs and outcomes to be reduced to a single value to allow for comparison.
- Using this ratio, the clinician would choose the alternative with the least cost per outcome gained.
- The most cost-effective alternative is not always the least costly alternative for obtaining a specific therapeutic objective.
- Cost-effectiveness need not be cost reduction but rather cost optimization.

Incremental cost-effectiveness ratio (ICER)

- Incremental CEA can be used to determine the additional cost and effectiveness gained when one treatment alternative is compared with the next best treatment alternative.
- Thus, instead of comparing the ACERs of each treatment alternative, the additional cost that a treatment alternative imposes **يفرض** over another

treatment is compared with the additional effect, benefit, or outcome it provides.

- This formula yields the additional cost required to obtain the additional effect gained by switching from drug A to drug B.
- The ICER can be summarized as follows:

$$ICER = \frac{\text{cost}_A(\$) - \text{cost}_B(\$)}{\text{effect}_A(\%) - \text{effect}_B(\%)}$$

(Strong) Dominance

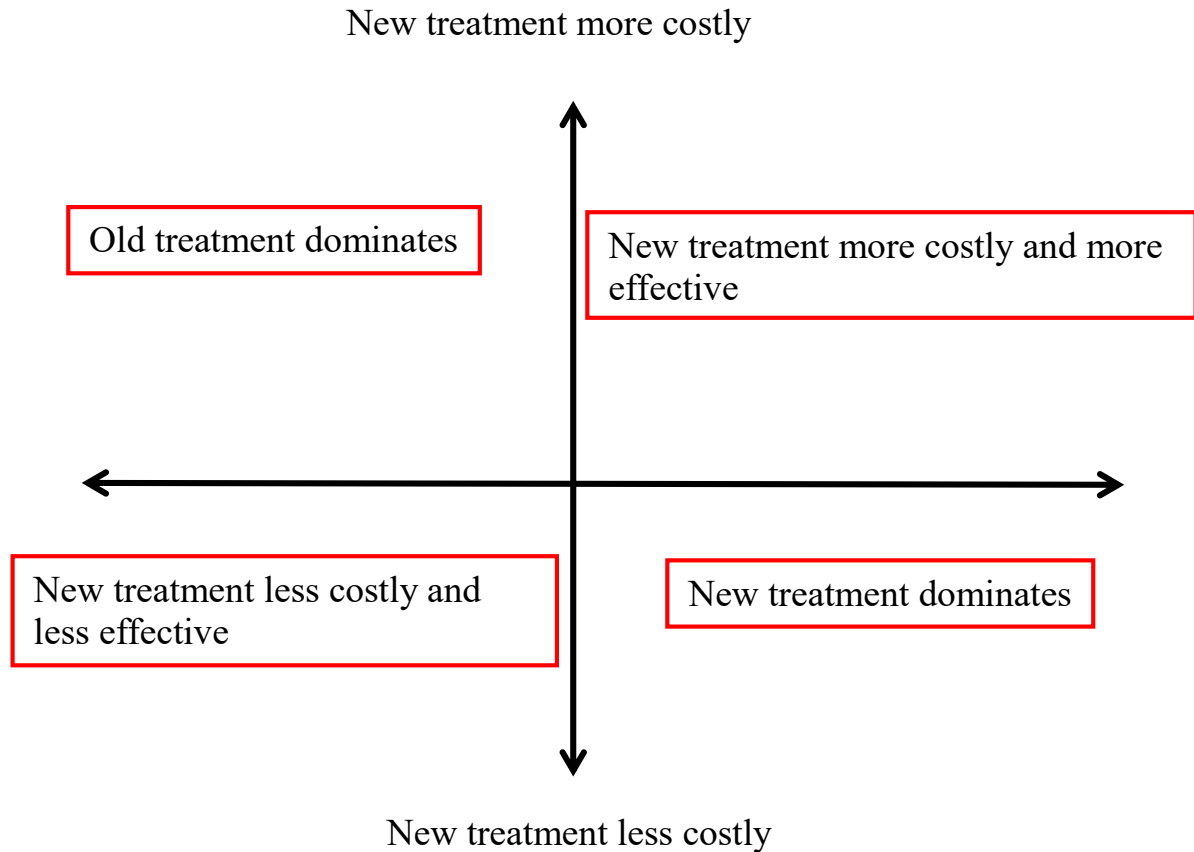
<u>Management of angina</u>				
Programme	Costs	Effects		
A	20	8		
B	30	4	→	Dominated: B has lower effects and higher cost than A
C	50	1		
D	60	9		

Average vs. incremental cost-effectiveness ratios

<u>Breast screening</u>					
Programme	Costs	Effects	C/E	$\Delta C/\Delta E$	
A	110	20	5.50	----	
B	120	29	4.14	1.11	
C	150	50	3.00	1.43	
D	190	60	3.17	4.00	
E	240	70	3.42	5.00	

Average ratios have no role in decision making

Incremental cost-effectiveness plane



Cost effectiveness analysis (CEA)

- There is no 'magic' cut-off number that establishes whether or not an intervention is '**cost-effective**'.
- It will depend on what is termed the decision maker's '**ceiling ratio**'.
- The ceiling ratio can be inferred **بستندل** (indirect) from the amount that decision-makers are **willing to pay**.
- To make a decision:
 - If ICER of the program \leq ceiling ratio \rightarrow adopt **يُتبنى** the program
 - If ICER of the program $>$ ceiling ratio \rightarrow do not adopt the program

Benefits of CEA

1. Balancing cost with patient outcome,
2. Determining which treatment alternatives represent the best health outcome per dollar spent,
3. Deciding when it is appropriate to measure outcome in a specific therapeutic objective.
4. CEA can provide valuable data to support drug policy, formulary management, and individual patient treatment decisions.
5. Globally ^{عالمياً}, CEA is being used to set public policies regarding the use of pharmaceutical products (national formularies).

Why does cost-effectiveness matter (issue)? ^{موضوع}

1. Money can only be spent once
2. If a particular service is not achieving what it sets out to do (improving life for children and families) that money could be better spent in future
3. A service could be reduced or discontinued and extra resources could be delivered in another way
4. Positive evidence of cost-effectiveness provides support for a continuation of services.

When should this happen?

- If it is done too early there are no outcomes to consider
- If it is done too late, there will not be time to reallocate ^{إعادة توزيع} resources in the light of evaluation findings
- Ideal time is probably after around 18 months – 2 years of operation, with periodic reviews after that

Cost Utility Analysis

Basics

- A cost-utility analysis is defined as a type of cost-effective analysis that compares different procedures and outcomes relative to a person's quality of life.
- Two measures used to assume CUA are costs per Quality-Adjusted Life Years (QALY) and costs per Disability-Adjusted Life Years (DALY).
- Results of CUA are also expressed in a ratio, a cost-utility ratio (C:U ratio).
- Most often this ratio is translated as the cost per QALY gained or some other health-state utility measurement.
- The preferred treatment alternative is that with the lowest cost per QALY (or other health-status utility).
- For example, a full year of health in a disease-free patient would equal 1.0 QALY, whereas a year spent with a specific disease might be valued significantly lower, perhaps as 0.5 QALY, depending on the disease.

Quality-adjusted life years (QALY)

- Quality-adjusted life years (QALY) is a mathematical measurement that combines quantity and quality of health to calculate outcomes based on treatment or other activities that influence health
- The measure of QALY describes the cost of producing one year of quality living existence.
- The scoring range of QALY is from 0 (death) to 1 (perfect health); however, a score that is a negative number may be derived when a person is living with an extremely low quality of life

Disability-Adjusted Life Years (DALY)

- DALY is another CUA measure which can be used to measure the effect of ill health (i.e., hip fracture) in regard to function and premature mortality.
- In other words, one DALY is one lost year of healthy life.
- The goal of measurement of DALY is to use an assessment of the residual burden of disease and/or injury as an outcome measure.
- Two mathematical equations are used to calculate DALY, years of life lost (YLL) and years lived with disability (YLD).
- YLL is the number of years of life lost due to premature death.
- YLD is the number of healthy years lost due to disability from the condition until remission or death. These are then summed together to provide years living with disability.

- The DALY scale range is the reverse of the QALY scale, with 1 indicating death and 0 indicating the best possible state of health.
- Unlike QALY, DALY reverse scaling would not allow for negative values because 0 is equivalent to perfect health.
- To better understand DALY, consider this hypothetical example. Assume that 150 eighteen-year-olds die as a result of motorcycle accidents in a state with no helmet law. ^{خوذة}
- The life expectancy for the birth cohort of 1990 is 71.8 years.
- Therefore, YLL (for the total sample) was 8070 (150 X 53.8 years).
- For YLD, let's assume these teenagers did not die, but sustained severe brain trauma with disabilities similar to someone with severe cerebral palsy. As a result, their life expectancy, due to this injury, is decreased to 31 years.

Cost utility analysis (CUA)

- CUA is the most appropriate method to use when comparing programs and treatment alternatives that are life extending with serious side effects (e.g., cancer chemotherapy), those which produce reductions in morbidity rather than mortality (e.g., medical treatment of arthritis), and when HRQOL is the most important health outcome being examined.
- CUA is employed less frequently than other economic evaluation methods because of a lack of agreement on measuring utilities, difficulty comparing QALYs across patients and populations, and difficulty quantifying patient preferences.

Box 2. Calculating QALYs - a simple example

With treatment X

Estimated survival = 10 years

Estimated quality of life

(relative to 'perfect health') = 0.7

QALYs = (10 X 0.7) = 7.0

Without treatment X

Estimated survival = 5 years

Estimated quality of life

(relative to 'perfect health') = 0.5

QALYs = (5 X 0.5) = 2.5

QALY gain from treatment X = 7 - 2.5 = 4.5 QALYs

If the cost of treatment X is £18,000 then the cost per QALY is £4,000 per QALY (£18,000 divided between 4.5 additional QALY's)

Cost utility analysis (CUA)

- In Europe the tool used is the EQ5D (Euroqol). This is the method required by NICE (The National Institute for Health and Care Excellence).
- The EQ5D has been designed to be straightforward for an individual to complete and uses utility values obtained from several thousand members of the British public.
- It is the individual who answers the questions upon how they are feeling, rather than being determined by an external clinical measure.
- This is to take into account subjectivity: eg people tolerate pain differently; the loss of a leg will end the career of a footballer, but not that of a health economist and as a result the loss will be valued differently by the two individuals.
- Cost per QALY can be compared across many different health care interventions

Advantages

- 1- On the plus side, CUA allows comparison across different health programs and policies by using a common unit of measure (money/QALYs gained).
- 2- CUA provides a more complete analysis of total benefits than simple cost benefit analysis does. This is because CUA takes into account the quality of life that an individual has, while CBA does not.

Disadvantages

- 1- Societal benefits and costs are often not taken into account.
- 2- Some economists believe that measuring QALYs is more difficult than measuring the monetary value of life through health improvements, as in cost-benefit analysis.
- 3- Some people believe that life is priceless and there are ethical problems with placing a value on human life.

Exercises in cost utility analysis

5. When the objective is to compare an intervention with others that have already been evaluated in terms of cost per QALY (or equivalent) gained.

WORKED EXAMPLE 6.1 (ex: 5.2 contin...)

Economic evaluation of management of anaemia in haemodialysis patients:

Patients with chronic renal failure who are on haemodialysis suffer from profound anaemia, which is often extremely debilitating. This is due to a reduction in the production of erythropoietin in these patients, and loss of blood during haemodialysis. Historically, these patients have been managed by the use of blood transfusions. Now, synthetic erythropoietin is available. It is considered to be highly effective, but is very expensive. So the alternatives are to either give erythropoietin or to give blood transfusions when the patient's haemoglobin level is below 8g/dl.

Cost information:

Total costs to manage the 1000 patients for 1 year using blood transfusions: £3,128,000.

Total costs to manage the 1000 patients for 1 year using erythropoietin: £5,547,100.

Outcome information:

Utility data for the two alternatives available from the literature suggest that patients maintained on erythropoietin value their health states at a higher level than those maintained on blood transfusions. In a study, 100 patients stated that for a treatment period of 10 years, their utility value for each year (when valued from 0 to 1) on erythropoietin was 0.80, whereas on blood transfusions it was 0.75.

1. What is the difference in cost between the two alternatives for the 1000 patients?

£2,419,100.

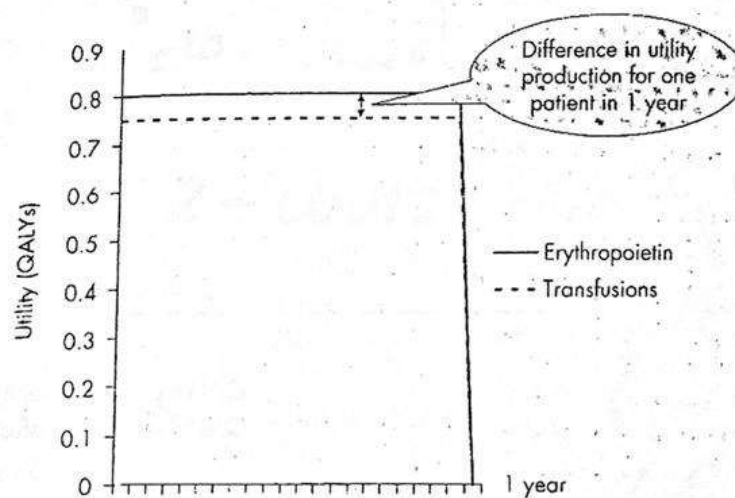
2. What is the difference in utility production of the two alternatives, i.e. how many extra QALYs are produced by erythropoietin per year of treatment, for the 1000 patients?

Change in utility = $0.80 - 0.75$

= 0.05 QALYs per patient per annum

= 50 QALYs per 1000 patients per annum.

Figure 6.1 illustrates the difference in utility production for the two alternatives.



QALYs (transfusions) for 1000 patients = $1000 \times 0.75 = 750$ QALYs

QALYs (erythropoietin) for 1000 patients = $1000 \times 0.80 = 800$ QALYs

Figure 6.1 Utility produced over 1 year for erythropoietin vs blood transfusions.

3. Calculate an incremental cost-utility ratio for erythropoietin.

$$\begin{aligned} \text{ICER} &= \frac{\text{Change in cost}}{\text{Change in outcome (utility)}} \\ &= \frac{£2,419,100}{50} \\ &= £48,382 \text{ per extra QALY gained by erythropoietin.} \end{aligned}$$

This cost per QALY can be plotted on a cost-effectiveness plane (Figure 6.2). You can see that this ICER is in the northeast quadrant because erythropoietin is more effective and more costly.

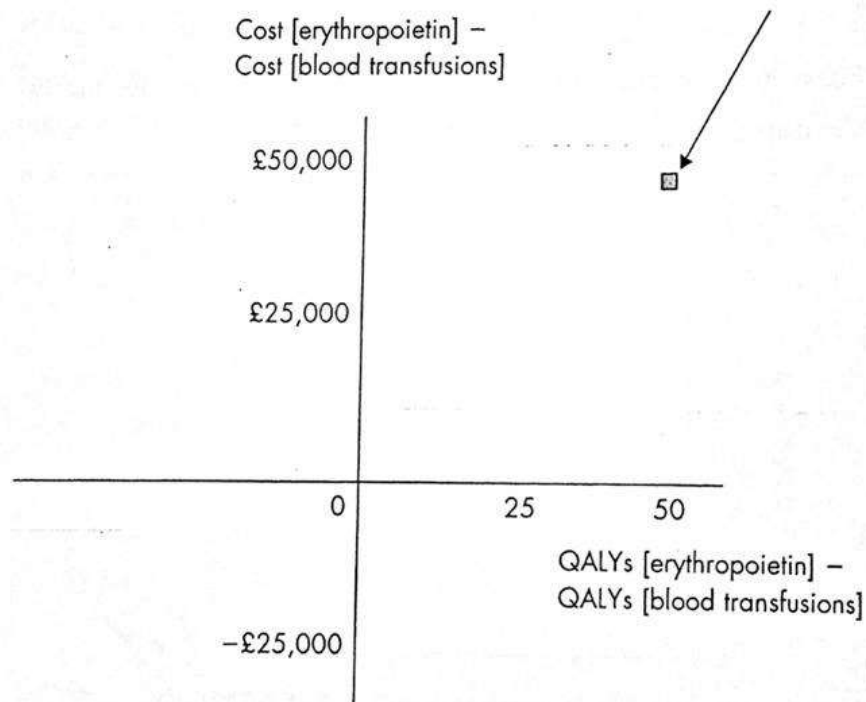


Figure 6.2 Cost-effectiveness plane for erythropoietin Vs blood transfusions

Pharmacoeconomics

WORKED EXAMPLE 6.2 Cost-utility analysis of two different types of service

A group of community nurses (Group A) wants to set up an asthma patient monitoring service for a GP practice which has 200 asthma patients.

Results from a study suggest that the practice will have cost reductions and the patients will have improved outcomes (Table 6.1)

Table 6.1 Impact of a nurse-led asthma monitoring service

<i>Costs and outcome measures for 1 year</i>	<i>Before asthma service</i>	<i>With asthma service</i>	<i>Difference</i>
Prescribing costs (£)	20,000	16,000	-4,000
Hospital costs (£)	2,000	1,000	-1,000
Nurse service costs (£)	0	4,000	4,000
Total costs (£)	22,000	21,000	-1,000
Emergency hospital admissions due to asthma	20	10	-10

Another group of community nurses (Group B) wants to set up an ischaemic heart disease (IHD) patient monitoring service for the same GP practice, which has 250 IHD patients. Results from a study suggest that the service will be cost neutral and the patients will have improved outcome (Table 6.2).

Table 6.2 Impact of a nurse-led ischaemic heart disease monitoring service

<i>Costs and outcome measures for 1 year</i>	<i>Before IHD service</i>	<i>With IHD service</i>	<i>Difference</i>
Prescribing costs (£)	25,000	20,000	-5,000
Hospital costs (£)	10,000	5,000	-5,000
Nurse service costs (£)	0	10,000	10,000
Total costs (£)	35,000	35,000	0
Emergency hospital admissions due to chest pain	50	25	-25

The practice has to decide whether to reduce emergency admissions due to asthma by 10 a year and save £1,000, or reduce emergency admissions due to chest pain by 25 a year at no change in costs to the practice.

How can the GP objectively compare and choose between improving the health of asthma and IHD patients?

Groups A and B elicit utility values from the 200 asthma and 250 IHD patients. Time trade-off was used to elicit the utility values and these were used to calculate QALYs.

The groups obtain the following results:

	<i>Asthma patients</i>	<i>IHD patients</i>
Mean QALYs before intervention	0.75	0.60
Mean QALYs after intervention	0.85	0.75
Incremental QALY change caused by intervention	0.10	0.15

The results refer to a 1-year period. The asthma patients improved their quality of life per year by 0.10 QALYs each. The IHD patients improved their quality of life per year by 0.15 QALYs each.

Incremental cost-effectiveness ratio (ICER):

$$\begin{aligned}\frac{\Delta \text{Cost}}{\Delta \text{QALY}} &= \frac{\text{Cost}_{\text{IHD service}} - \text{Cost}_{\text{asthma service}}}{\text{QALY}_{\text{IHD service}} - \text{QALY}_{\text{asthma service}}} \\ &= \frac{0 - (-1000)}{(250 \times 0.15) - (200 \times 0.10)} = \frac{1000}{17.5} \\ &= \text{£57 per QALY gained from the IHD service over the asthma service.}\end{aligned}$$

If the GP practice funds the IHD service it will cost them £1,000 per year more than the asthma service, but they will obtain 17.5 more QALYs for their patients.

EXERCISE 1: Calculating a cost per QALY:

Several treatments exist to treat fungal toenail infections. Four oral medicines used are drugs A, B, C and D. The table below shows the costs (£) associated with treating one patient with each of these four treatments:

	<i>Drug A</i>	<i>Drug B</i>	<i>Drug C</i>	<i>Drug D</i>
Total costs (£)	1,301	1,503	1,570	1,200

You then find some evidence to suggest that two of these agents have differing effects on patients' quality of life owing to difference in their side-effect profiles. This evidence is summarized below:

Agents	Increase in QALYs per patient per year
Drug C	0.10
Drug D	0.05

What is the difference in utility production of the two alternatives, per year of treatment, for the 100 patients?

0.05 QALYs per patient per year = 5 QALYs per 100 patients per year.

Calculate an incremental cost-utility ratio for drug C compared with drug D.

$$\begin{aligned} \text{ICER} &= \frac{\text{Cost (drug C)} - \text{Cost (drug D)}}{\text{Outcome (drug C)} - \text{Outcome (drug D)}} \\ &= \frac{100(1,570 - 1,200)}{10 - 5} = \frac{37,000}{5} \\ &= \text{£7,400 per extra QALY.} \end{aligned}$$

Draw a cost-effectiveness plane and place the ICER you have calculated on that graph. You should have a point plotted in the northeast quadrant (Figure 6.4).

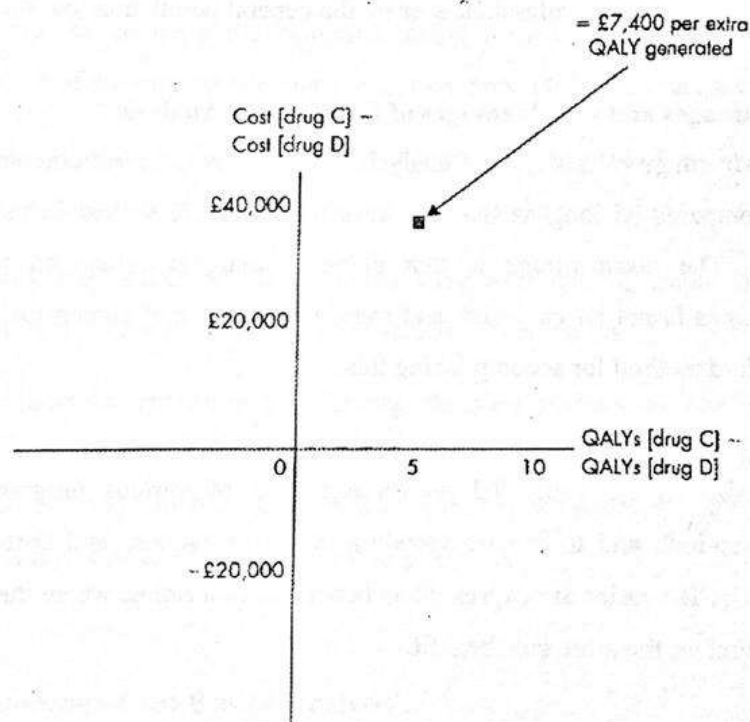


Figure 6.4 Cost-effectiveness plane for drug C versus drug D.

Which treatment will you recommend to your Trust, and why?

Either could be recommended, depending on the driving force for the choice. Is cost containment most important? Then choose drug D. Is improved patient outcome most important? Then choose drug C.

Cost Benefit Analysis

- Is a method that allows for the identification, measurement, and comparison of the benefits and costs of a program or treatment alternative.
- The benefits realized from a program or treatment alternative are compared with the costs of providing it.
- Both the costs and the benefits are measured and converted into equivalent dollars in the year in which they will occur. These costs and benefits are expressed as a ratio (a benefit-to-cost ratio), a net benefit, or a net cost.
- A clinical decision maker would choose the program or treatment alternative with the highest net benefit or the greatest benefit-to-cost (B:C) ratio.

Guidelines for the interpretation of the benefit to cost ratio

- 1- If B/C ratio > 1 , the program or treatment is of value. The benefits realized by the program or treatment alternative outweigh the cost providing it.
- 2- If B/C ratio $= 1$, the benefits equal the cost. The benefits realized by the program or treatment alternative are equivalent to the cost of providing it.
- 3- If B/C ratio < 1 , the program or treatment is not economically beneficial. The cost of providing the program or treatment alternative outweighs the benefits realized by it.

Value of life

- The phrase **value of life** refers to the monetary worth **القيمة النقدية** of a human life.
- The concept of assigning **تعيين** worth or value to an individual life is a crucial part **القسم الحاسم** of cost-benefit analysis involving health and the healthcare industry.
- These decisions, like other economic decisions, require comparing the marginal costs of the healthcare to the marginal benefits received.
- Based on the fact that most medical care is performed with the aim of extending or improving the quality of life, one must know the value of life in order to make effective medical decisions.

Cost Benefit Analysis (CBA)

Cost-benefit analysis is the most comprehensive **شاملة** method of economic evaluation available which involves the estimation of value of life and it can be applied in two ways.

The human capital approach means that the value of people's contributions is linked to what they are paid.

Willingness to pay based on individuals' observed or stated preference ^{التفضيل} ^{المعلن} which means how much money they are prepared to accept for an increased risk or to pay for a particular service.

- ❑ The main difference between cost-benefit analysis and other methods is that it seeks to place monetary values on both the inputs (costs) and outcomes (benefits) of health care.
- ❑ It is possible to say whether a particular procedure or program offers an overall net gain to society in the sense that its total benefits exceed its total costs.
- ❑ Cost-effectiveness and cost utility analysis do not do this because they measure costs and benefits in different units.

Human capital approach

- It compares the value of a human life to the economical value of the output produced by an individual over an expected lifetime. It estimates the economical value of future earnings ^{كسب} that result from an extension or improvement in life.
- The general trend of economical lifetime earnings initially increases as an individual ages from infancy through mid- 20's. The peak economical value of lifetime earnings for females is approximately \$644, 000 at the age 24 compared to \$1.16 million at age 20 for males.

Willingness to Pay Approach

- It attempts to account for the shortcomings of the human capital approach by considering more than just the workplace output of an individual.
- The willingness to pay approach determines the value of life based on a person's willingness to pay for small reductions in the probability of dying. A person's willingness to pay is expressed through choices such as wearing or not wearing a seat belt, installing carbon monoxide and/or smoke detectors, and choosing to engage in unhealthy behaviors such as smoking or excessive drinking.
- The willingness to pay approach generally estimates the value of life to be higher than that estimated using the human capital method.

Example of CBA

- A simple illustration of cost benefit analysis can be seen in the decision whether to get Lasik eye surgery or not.
- The joy of being able to see without glasses and the benefit of not having to spend money on corrective vision eye wear are compared to the amount of money it may cost to have the surgery performed, the risk of the surgery not going well, and the amount of time spent in the surgery room that could have

been spent doing something else possibly more productive are all weighed against each other.

This illustration shows the use of cost benefit analysis, weighing the costs and benefits and then making a decision depending on which one has a greater value than the other.

The Five Steps of Benefit / Cost Analysis

1. Identify the resources and state the goal
2. List alternative uses of the resources to achieve the goal
3. Identify the advantages and disadvantages of each alternative
4. Identify the choice and the opportunity cost of the choice
5. Review the decision, was your choice right for you?

Summary

- CBA is most commonly used for *public decisions*– policy proposals, programs, and projects, e.g., dams, bridges, traffic circles, riverfront parks, libraries, drunk driving laws, and anything else the government might fund
- Takes a community-wide perspective *انطباع ، رأي*
- Allows the consideration of a range of policy options
- Determines which policy maximizes net benefits to the community
- Allows benefits and costs to be compared over time
- Can show the costs and benefits accruing *استحقاق* to different groups within the community

Calculating Results of Costs and Benefits

After all costs and benefits have been identified and quantified, the results of the analysis must be presented in ways that help decision makers understand the value of the program or intervention.

CBA can be presented in the following three formats: **net benefit calculations**, **benefit-to-cost ratios**, and **internal rates of return (IRR)**.

When evaluating interventions, it is important to consider the *time horizon* for the project. If retrospective data are collected for more than 1 year or if the project inputs or outcomes are estimated for more than 1 year into the future, it is important to adjust or discount these costs one point in time.

Net Benefit (or Net Cost) Calculations.

The net benefit (or net cost) calculation simply presents the difference between the total costs and benefits.

Net benefit = total benefits — total costs;

Net cost = total costs — total benefits.

Interventions would be considered to be cost beneficial if:

Net Benefit > 0 or Net Cost < 0

Benefit-to-Cost (or Cost-to-Benefit) Ratio Calculations.

CBA results can also be calculated by summing up the total benefits and dividing by the total costs. The ratio may be expressed as a benefit-to-cost ratio or a cost to-benefit ratio. Depending on how the ratio is calculated, interventions are cost beneficial if:

Benefit-to-cost > 1 or Cost-to-benefit < 1

Example Using Different Calculation Techniques.

Suppose a decision maker had to choose between two proposals for implementation. Also assume that the projects are for 1 year, so discounting is not needed.

Proposal A: Cost = \$1000; Benefit = \$2000

Proposal B: Cost = \$5000; Benefit = \$7500

TABLE 7.4. COMPARISON OF TWO PROPOSALS USING NET AND RATIO CALCULATIONS

	<i>Proposal A</i>	<i>Proposal B</i>
Net benefit	$\$2000 - \$1000 = \$1000$	$\$7500 - \$5000 = \$2500$
Net cost	$\$1000 - \$2000 = -\$1000$	$\$5000 - \$7500 = -\$2500$
Benefit/cost ratio	$\$2000/\$1000 = 2.0$	$\$7500/\$5000 = 1.5$
Cost/benefit ratio	$\$1000/\$2000 = 0.5$	$\$5000/\$7500 = 0.7$

Table 7.4 shows the net and ratio calculations for both proposals. Although four calculations are shown in the table, the benefit-to-cost ratio (when compared with the cost-to-benefit ratio) and the net benefit calculation (when compared with the net cost calculation) are used most often because the higher the result, the more cost beneficial an option becomes.

Using the criteria outlined above for cost-beneficial programs, it is apparent that both programs are cost beneficial using both the net and ratio methods of calculations. However, when comparing net calculations, proposal B is more cost beneficial than proposal A (net benefit = \$2500 versus \$1000), but proposal A is more cost beneficial than proposal B (benefit-to-cost ratio = 2.0 versus 1.5) when using ratio calculations.

In this example, in which both proposals are cost beneficial, the decision maker may consider other issues, such as the **amount of money available for**

investment. Whereas A would require \$1000 input costs, proposal B would require \$5000.

Another consideration may involve **the return on investment.** Proposal A, with a 2:1 benefit-to-cost ratio, has a higher return than proposal B (i.e., 1.5:1 benefit-to-cost ratio).

اي ان الدولار الواحد المصروف على Proposal A يعود دولارين
وان الدولار الواحد المصروف على Proposal B يعود دولار ونصف

A third consideration is **the actual net benefit amount.** Proposal B has a higher net benefit than proposal A (\$2500 versus \$1000).

WORKED EXAMPLE 7.1 Economic evaluation of management of anaemia in haemodialysis patients

Patients with chronic renal failure who are on haemodialysis suffer from profound anaemia, which is often extremely debilitating. This is due to a reduction in the production of erythropoietin in these patients, and loss of blood during haemodialysis. Historically, these patients have been managed by the use of blood transfusions. Now, synthetic erythropoietin is available. It is considered to be highly effective, but is very expensive. So, the alternatives are either to give erythropoietin or to give blood transfusions when the patient's haemoglobin level is below 8 g/dl.

Total costs to manage the 1000 patients for 1 year using blood transfusions: £3,128,000.

Total costs to manage the 1000 patients for 1 year using erythropoietin: £5,547,100.

Outcome information

A willingness-to-pay study for the two alternatives available from the literature suggests that patients maintained on erythropoietin are

'willing to pay' for the extra perceived health benefits over blood transfusions. In a study, 50 patients stated that they would be willing to pay a mean of £2,000 a year for the extra health benefits associated with erythropoietin.

1. What is the difference in cost between the two alternatives for the 1000 patients?
£2,419,100.

2. What is the difference in benefit between the two alternatives, expressed in monetary terms, i.e. how much are patients willing to pay for the health benefits for erythropoietin per year of treatment, for the 1000 patients?

Change in benefit = £2,000 more benefit per annum per patient when given erythropoietin.

Change in benefit = £2,000,000 more benefit per annum per 1000 patients when given erythropoietin.

3. What is the overall net benefit of erythropoietin compared with blood transfusions?

$$\begin{aligned}\text{Overall net benefit} &= \text{Change in benefit} - \text{Change in cost} \\ &= 2,000,000 - 2,419,000 \\ &= -£419,000.\end{aligned}$$

Therefore, the overall net benefit from giving erythropoietin is -£419,000.

If the net benefit is negative, the net cost (to society) is positive, so the preferred option must be the blood transfusions.

Using cost-benefit analysis to allocate resources to different services

Worked example 7.1 shows how WTP can be used in a CBA to generate net benefit. However, in that example we were trying to decide between two ways of treating the same illness. We could also have used a common outcome

such as the presence of anemia, and the resulting economic evaluation would have been a CEA (see 5, worked examples).

It is more difficult to compare two healthcare interventions that do not have comparable outcome measures. CEA cannot be used in this situation, and we have to use an outcome measure that can be used across different diseases, such as WTP. CBA can be used to generate net benefit in different disease areas, and so diseases with different clinical outcomes can be compared. This means that CBA can be used to allocate resources to different services. Worked example 7.2 illustrates how this can be carried out.

WORKED EXAMPLE 7.2 Cost-benefit analysis of two different types of service

A group of community nurses (Group A) wants to set up an asthma patient monitoring service for a GP practice which has 200 asthma patients. Results from a study suggest that the practice will have cost reductions and the patients will have improved outcomes (Table 7.1).

Table 7.1 Impact of a nurse-led asthma monitoring service

<i>Costs and outcome measures for 1 year</i>	<i>Before asthma service</i>	<i>With asthma service</i>	<i>Difference</i>
Prescribing costs (£)	20,000	16,000	-4,000
Hospital costs (£)	2,000	1,000	-1,000
Nurse service costs (£)	0	4,000	4,000
Total costs (£)	22,000	21,000	-1,000
Emergency hospital admissions due to asthma	20	10	-10

Another group of community nurses (Group B) wants to set up on ischaemic heart disease (IHD) patient monitoring service for the same GP practice, which has 250 IHD patients. Results from a study suggest that the service will be cost neutral and the patients will have improved outcome (Table 7.2).

Table 7.2 Impact of a nurse-led ischaemic heart disease monitoring service

<i>Costs and outcome measures for 1 year</i>	<i>Before IHD service</i>	<i>With IHD service</i>	<i>Difference</i>
Prescribing costs (£)	25,000	20,000	-5,000
Hospital costs (£)	10,000	5,000	-5,000
Nurse service costs (£)	0	10,000	10,000
Total costs (£)	35,000	35,000	0
Emergency hospital admissions due to chest pain	50	25	-25

The practice has to decide whether to reduce emergency admissions due to asthma by 10 a year and save £1,000, or reduce emergency admissions due to chest pain by 25 a year at no change in costs to the practice.

How can the GP objectively compare and choose between improving the health of asthma and that of IHD patients?

Groups A and B elicit WTP values from the 200 asthma and 250 IHD patients (Table 7.3).

Table 7.3 WTP values for asthma and IHD patients

<i>Service</i>	<i>Mean WTP per patient (£)</i>	<i>Range of WTP values (£)</i>	<i>Total WTP for group (£)</i>
Asthma monitoring (200 patients)	250	50-1,500	50,000
IHD monitoring (250 patients)	350	40-2,500	87,500

What do these results mean?

The asthma patient group has a combined WTP of £50,000. The IHD patient group has a combined WTP of £87,500. Therefore, £37,500 more benefit will be obtained by funding the IHD monitoring service.

$$\text{Net cost to society} = \text{Cost of service} - \text{Benefit of service.}$$

The asthma service costs -£1000 and provides £50,000 of benefit. The IHD service costs £0 and provides £87,500 of benefit. This equates to -£51,000 for the asthma service and -£87,500 for the IHD service. Therefore the IHD service provides £36,500 more benefit. It has an incremental net cost of -£36,500 to society.

So, this CBA would suggest that, because both services have a net negative cost (positive net benefit) to society, both are 'worth it'. It would then go on to recommend the IHD service over the asthma service.

Cost-Benefit or Cost-Effectiveness Analysis

Cost-benefit and cost-effectiveness analyses are useful tools for assessing the clinical economic impact of medical care programs or interventions. There are, however, several important distinctions between the two approaches.

First, CBA may be applied to single or multiple programs, while cost-effectiveness analysis is applied to multiple programs.

Second, CBA may be used to compare programs with disparate outcomes. In contrast, cost-effectiveness analysis is a method for identifying the least costly approach to achieving a single outcome.

A third distinction is that CBA requires that all the outcomes or benefits be assigned a dollar value. The outcome or effect is not valued in cost-effectiveness analysis.

Which approach should you use in the pharmacy arena? It depends. A general guideline is that cost-effectiveness analysis is most appropriate when a single effect or outcome can be defined.

CBA is usually most appropriate when a single program is to be evaluated or when budget allocation decisions must be made among programs with unrelated outcomes.

Decision Analysis

Decision analysis is the application of an analytical method for systematically comparing different decision options. It assists with selecting the best or most cost-effective alternative.

Steps in Decision Analysis

Step 1: Identify تحديد the Specific Decision

The specific decision to be evaluated should be clearly defined by answering the questions: What is the objective of the study? Over what period of time will the analysis be conducted (e.g., the episode حدث of care, a year)? Will the **perspective** be that of the patient, the medical care plan, an institution or organization, or society?

Step 2: Specify Alternatives

Ideally, the most effective treatments or alternatives should be compared. In pharmacotherapy evaluations, makers of innovative يتكرر new products may compare or measure themselves against a standard (i.e., older, more well-established) therapy.

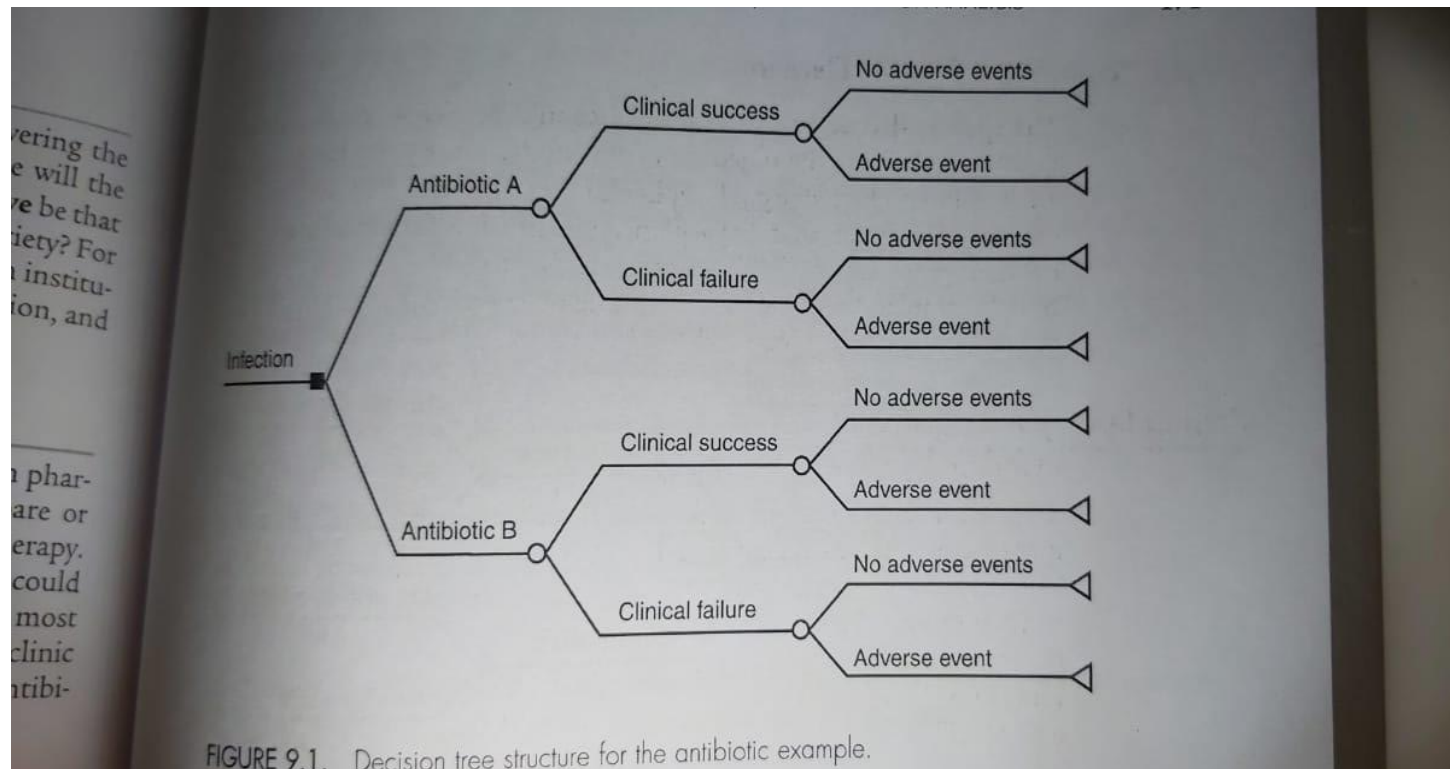
Step 3: Draw the Decision Analysis Structure

Lines are drawn to joint decision points (branches or arms of a decision tree), represented as choice nodes نقطة اللقاء, chance nodes, or terminal (final outcome) nodes. Nodes are places in the decision tree where different options occur; branching becomes possible at this point.

There are three types of nodes: (1) in a choice node, a choice is allowed (e.g., treatment A versus treatment B); (2) in a chance node, chance comes into the equation (e.g., the chance or probability of cure or adverse events for different treatment options); and (3) in a terminal node, the final outcome of interest for each

option in the decision is represented. The units used to measure final outcomes (e.g., dollars or quality-adjusted life years [QALYs]) must be the same for each option being considered.

By convention ^{بالاتفاق}, software programs use a square box to represent a choice node, a circle to represent a chance node, and a triangle for a terminal branch or final outcome. Figure 1. illustrates the decision tree for the antibiotic example.



Step 4: Specify Possible Costs, Outcomes, and Probabilities

For each option, information should be obtained for the probability of occurrence and the consequences of the occurrence. Probabilities are assigned for each branch of the chance nodes, and the sum of the probabilities for each branch must add up to 1.00.

Consequences are reported as monetary outcomes, health related outcomes, or both. Decision analysis articles should provide a listing of the probability, cost, and outcome estimates used in the analysis, including where or how the estimates were

obtained (e.g., literature review, clinical trial, expert panel). Table 1 lists these data for the antibiotic example.

	<i>Antibiotic A</i>	<i>Antibiotic B</i>
Probability of clinical success (%)	90	80
Cost of antibiotic per course of therapy (\$)	600	500
Probability of adverse events (%)	10	15
Cost of treating adverse events (\$)	1,000	1,000

Step 5: Perform Calculations

At each terminal node, the probability of a patient having that outcome is calculated by multiplying the probability of each arm from the choice node to the terminal node. The total costs for each terminal node are calculated by adding up the costs over all of the branches from the choice node to the terminal node. The product of the costs multiplied by the probability ($C \times P$) is calculated for each node and then summed for each option.

In our example, each of the two options (antibiotic A versus antibiotic B) has four possible terminal endpoints: success/no adverse events, success/adverse events, failure/no adverse events, and failure/adverse events. Table 2 and Figure 2 show the calculations used to estimate the average expected cost per treatment. Note that the sum of the probabilities for the four terminal endpoints equals 1.00.

For patients taking antibiotic A, the costs can range from \$600 (for medication and no adverse events) to \$1,600 (for medication and treatment of adverse events), and the average cost is \$700 per patient.

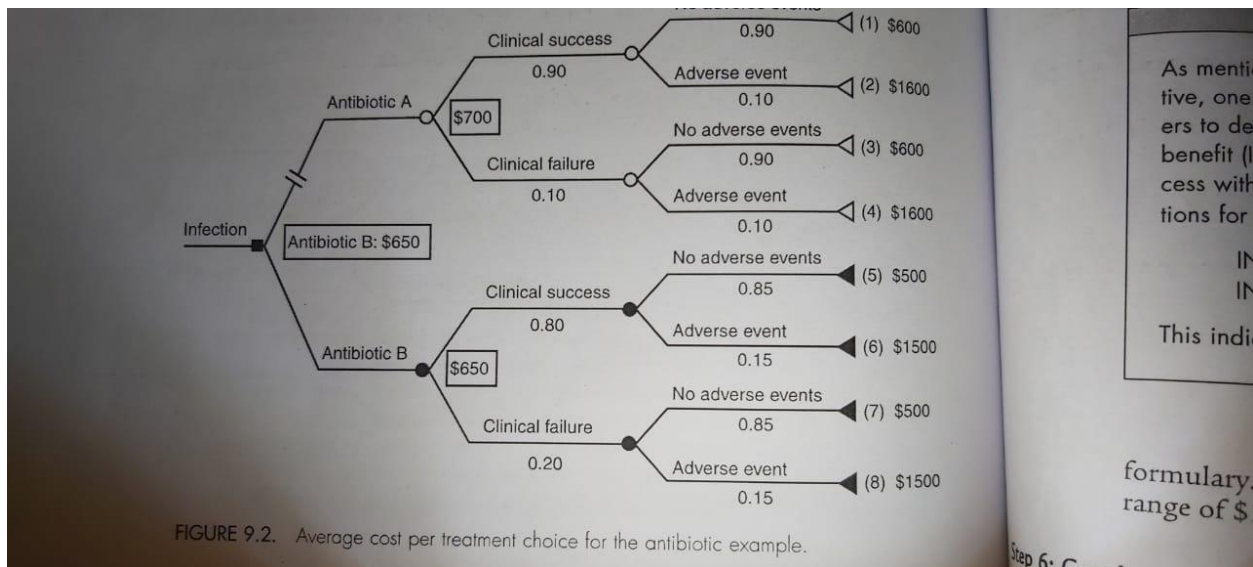
Similarly, for patients taking antibiotic B, the costs can range from \$500 (for medication and no adverse events) to \$1,500 (for medication and treatment of adverse events), and the average cost is \$650 per patient.

These calculations show that antibiotic B is less expensive even when including the costs of treating adverse events. But because antibiotic A is a better clinical option (higher probability of success and lower probability of adverse events), decision makers could use either the **incremental cost-effectiveness ratio (ICER)** or the **incremental net benefit (INB)** calculations to determine whether to add antibiotic A to the formulary. The calculated ICER would be:

ICER = $\Delta \text{Costs} / \Delta \text{Outcomes} = \$700 - \$650 / 0.090 - 0.80 = \500 more per extra success

If it is decided that each extra successful outcome is worth at least \$500 (patient discharged from the hospital faster, prevention of second round of treatment costs with another antibiotic, and so on), then antibiotic A would be added to the formulary.

	<i>Outcome</i>	<i>Cost (\$)</i>	<i>Probability</i>
<i>Cost × Probability (\$)</i>			
Antibiotic A			
Success with no adverse events	600	$0.9 \times 0.9 = 0.81$	486
Success with adverse events	$600 + 1,000 = 1,600$	$0.9 \times 0.1 = 0.09$	144
Failure with no adverse events	600	$0.1 \times 0.9 = 0.09$	54
Failure with adverse events	$600 + 1,000 = 1,600$	$0.1 \times 0.1 = 0.01$	16
Total for antibiotic A		1.00	700
Antibiotic B			
Success with no adverse events	500	$0.8 \times 0.85 = 0.68$	340
Success with adverse events	$500 + 1,000 = 1,500$	$0.8 \times 0.15 = 0.12$	180
Failure with no adverse events	500	$0.2 \times 0.85 = 0.17$	85
Failure with adverse events	$500 + 1,000 = 1,500$	$0.2 \times 0.15 = 0.03$	45
Total for antibiotic B		1.00	650



Step 6: Conduct a Sensitivity Analysis

Because some uncertainty surrounds the estimates used to construct these models, a **sensitivity analysis** is conducted. High and low estimates of costs and probabilities are inserted into the decision model to determine the range of answers. These estimates should be sufficiently varied to reflect realistic variations in values.

In the base case analysis of our antibiotic example, the total cost of using antibiotic A averaged to \$700 versus \$650 for antibiotic B. By choosing possible high and low ranges for probabilities and costs, numerous one-way sensitivity analyses were conducted.