Course 1:

INTRODUCTION TO ECONOMIC EVALUATIONS I

Basic Course

OBJECTIVES (of the basic Course)

- To understand the role of health technology assessment (HTA) as a means of relating research with healthcare decision making.
- To familiarize participants with the most important definitions related to HTA.
- To recognize the main features of Economic Evaluations (EE).
- To identify the usefulness and necessity of EE in the decision making process.
- To understand the concept of opportunity cost and benefits.

CONTENTS (of the basic Course)

- General introduction to HTA and EE.
- Definitions of health technology and HTA.
- Differential characteristics of HTA.
- HTA as a connection between research and healthcare decision making.
- General introduction to EE.
- Utility of EE in healthcare decision making.
- Opportunity cost.
- Contextualization, equity and social values.
- Examples of utilization.

Advanced Course

OBJECTIVES (of the advanced Course)

- To recognize the different types of economic evaluations and their use.
- To recognize the different tools or vehicles for performing EE.
- To understand the main concepts related to Markov models and decision trees.
- To analyze the transferability of EE.

CONTENTS (of the advanced Course)

- Introduction to the concept of disability-adjusted life years (DALY) and quality-adjusted life years (QALY).
- Perspective of analysis of EE.
- Cost categories.
- EE vehicles.
- Introduction to model-based EE: Decision trees and Markov models.
- Transferability / generalizability in economic evaluations.
BASIC COURSE

GENERAL INTRODUCTION TO HEALTH TECHNOLOGY ASSESSMENT AND ECONOMIC EVALUATIONS

In recent decades the use of health technologies in all of their forms, whether they are pharmaceutical products, diagnostic equipment or therapeutic devices, has increased in healthcare systems worldwide. Today, technologies are a critical part of every healthcare system. In many cases, the introduction of new technologies has brought significant benefits, either in terms of prevention, safety, improvements in health and quality of life or fewer adverse effects. However, in a context of limited resources, proper adoption and dissemination of technologies has proven to be a challenge to every healthcare system and, in many cases, a serious problem. There are many interventions and health technologies for which evidence exists regarding their effectiveness and cost-effectiveness. In spite of this, their use ends up being less than expected and this underuse represents loss of potential health benefits.

In addition, and in contrast to this situation, healthcare systems face another, even more widespread and fundamental problem: the effectiveness and cost-effectiveness of many medical practices currently in use have never been evaluated. There are estimates that show that over 90% of medical procedures have never been evaluated in terms of their cost-effectiveness. The definition of cost-effectiveness will be discussed later on, but a simple definition is that it is the relationship between the benefits provided and the costs incurred with the use of a certain type of technology. For example, a very cost-effective technology would be one for which great health benefits are reported at a relatively low cost, while a type of technology that is not very cost-effective would be one that offers relatively small health benefits, but entails high costs.

In recent years, many of the innovations that have been incorporated in healthcare systems have resulted in improvements in effectiveness and quality with significantly lower costs. Others have resulted in health improvements, but have also been responsible for increases in healthcare costs (Cutler & McClellan, 2001; Newhouse, 1992), while yet others have not resulted in any reported benefits or have been harmful. Greater development of health technologies has been accompanied by other factors that have influenced healthcare systems in recent decades. The emergence of new diseases, aging of the population, greater expectations regarding access to the health system and more informed users have resulted in greater demand for new health products (Deyo 2002).

In this context, healthcare decision makers have increasingly begun to demand more reliable and detailed information that enables them to make transparent and legitimate decisions when setting priorities in their search to obtain the maximum benefit from limited budgets.

The growth and development of health technology assessment (HTA) reflects this demand for sound and transparent information that supports decisions on the development, inclusion and dissemination of health technologies. Precisely, HTA has its origins in this growing concern about the expansion of new and costly health technologies in the 1970s and the capacity of healthcare systems to finance their use (Jonsson & Banta 1999).
Health technology assessment has evolved since the seventies, becoming a multidisciplinary specialty whose purpose is to gather available evidence for helping healthcare decision makers, health professionals and patients to understand the relative value of technologies (Gabbay 2006). In this process, HTA evaluates the safety, effectiveness and costs of technologies and, ideally, also makes a broad evaluation of their impact from an ethical and social perspective.

SOME DEFINITIONS

Health technologies
The term “health technology” is used to refer to things as disparate as drugs, medical devices, diagnostic methods and surgical procedures.

A cancer drug, the organization of a primary healthcare system, a laparoscopic surgical technique, a system for prioritizing patients for cardiovascular surgery, a cardiac pacemaker, an educational program to promote physical activity, a program to track breast cancer or a vaccine is a health technology that can be assessed.

Currently, the concept of health technology is defined very broadly and encompasses every intervention that can be used to promote health; to prevent, diagnose or treat diseases; or for rehabilitation or long-term care. This includes drugs, devices, procedures and organizational systems used in health care (INAHTA, HTA glossary prepared jointly with HTAi. http://www.inahta.org/HTA/Glossary/).

Health technology assessment

While there are several definitions, approaches and interpretations regarding exactly what HTA is, simply put, it can be said that HTA is the evaluation of health effects associated with the use of a technology by means of analysis of available knowledge. This evaluation is made using a scientific method, with the clear purpose of obtaining useful information for decision making in the real world.

Health technology assessment is generally defined as the systematic evaluation of properties, effects and/or other impacts of health technologies (International Society of Technology Assessment in Health Care, 2002).

More specifically, HTA is the evaluation of an intervention through the production, synthesis and/or systematic review of a wide range of scientific evidence. This evaluation systematically examines the technical characteristics of a health technology, its clinical safety, efficacy and effectiveness, costs, cost-effectiveness, organizational implications, social consequences and ethical and legal considerations of its application (EUR-ASSESS Report 1997).

WHY PERFORM A HEALTH TECHNOLOGY ASSESSMENT?

The objective of HTA is to provide decision makers (especially those involved in decision making on health financing, planning, purchasing and investments) with evidence-based information that is accessible and easy to use, for the purpose of guiding decisions on the use
and dissemination of health technologies and efficient resource allocation. For this reason, HTA has been considered as “a bridge between the world of scientific evidence and the world of healthcare decision making” since it provides information for healthcare decision makers at the macro-, meso- and micro-levels (Battista 1999).

If high-quality information is not available for decision making, the inclusion and dissemination of new technologies will more likely be influenced by a wide range of social, financial, professional, political or institutional factors that surely produce neither optimal results nor efficient use of limited health resources.

Providing healthcare for the population has become a very complex process; for this reason, it is no longer possible to make good decisions without adequate information. Attaining the best health results with available resources in a scenario of limited resources and the constant appearance of new and costly technologies is a challenge for every country in the world.

HTA is one of the main tools available to those wishing to provide the population with healthcare services that are efficient and equitable. The development of HTA has been especially noteworthy in the last 20 years and is now an indispensable part of the healthcare systems of many countries, especially wealthy countries. In the region of Latin America and the Caribbean (LAC) as well, a number of HTA initiatives have emerged. The majority have characteristics very similar to developments observed in Europe, Canada, Australia and other regions (Pichon-Riviere 2011). However, the level of development of HTA in the region is still insufficient. In a nearly generalized manner, a lack of researchers capable of performing HTA and economic evaluations (EE); healthcare decision makers that are still unaware of the existence, principles and applications of HTA; and healthcare systems that have not completed the explicit inclusion of scientific evidence in their decision making processes have been observed.

**In a broader sense, it can be stated that the ultimate objective of HTA is to improve the quality of healthcare the population receives, promoting the use of effective and cost-effective health technologies and interventions and protecting patients treated with interventions.**

*The fourth hurdle*

In the vast majority of the world’s countries, there are three so-called hurdles that must be overcome before a new technology, especially a new drug, can be licensed and prescribed by professionals and commercialized in pharmacies or drugstores.

These three traditional hurdles are:

1. **Quality**: the manufacturer of a technology must guarantee that it complies with high quality manufacturing standards and that quality standards are followed in the manufacture of the technology.

2. **Safety**: as a result of the different phases of clinical research (especially phases I, II and III of clinical trials), technology that comes onto the market must offer a profile of reasonable safety. In these phases, relatively frequent adverse effects can be detected;
however, there are some less frequent adverse events that, for now, can only be detected in pharmacovigilance (or phase IV) studies once the technology has come onto the market.

3. **Efficacy**: the last traditional hurdle is that of efficacy. In order to obtain licensing for a new technology, its efficacy must be demonstrated; that is, it must be better than (or sometimes similar to) its comparator in clinical trials. Although the Comparative Effectiveness Research movement advocates the use of one or several relevant comparators used for a given condition, often regulatory agencies are satisfied (for now) if the new technology is superior to a placebo. For example, approval for a new anti-inflammatory drug can be obtained based on demonstration that its effects are better than the placebo, rather than by comparing it to ibuprofen or diclofenac. Although there are differences among regulatory agencies in different countries, this third hurdle, efficacy, is not always applied with the same rigorousness. In cases in which a new technology entails risks (for example, cancer drugs) the proof of efficacy requirement is greater. However, there are many other cases of interventions where the risk is considered to be low (for example, vitamins) and efficacy requirements tend to be more lax. Once these three hurdles are overcome, in many countries the technology obtains a license and can be marketed. Examples of these agencies are the FDA in the USA, ANMAT in Argentina and INVIMA in Colombia.

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**Figure 1. The four hurdles or barriers**

The world is increasingly becoming aware that these three hurdles are insufficient and that no healthcare system is capable of covering every effective technology. For this reason, many countries have incorporated some type of fourth hurdle, or a cost-effectiveness hurdle.
Demonstrating that a technology is of good quality, safe and effective is not sufficient; evidence of its cost-effectiveness must also be shown. In other words: Does this new technology produce relevant health benefits (over and above the treatments currently available) in relation with its additional cost? Is the cost of this new technology justifiable in relation with the budget available in the healthcare system? It is not the same to consider the inclusion of a drug for the treatment of a very infrequent condition affecting one out of every 10,000 citizens, as it is to consider a new drug for hypertension, from which one out of every 3 adults suffers.

Although the country that pioneered the establishment of this type of hurdle was Australia, over fifteen years ago, perhaps the best known case is that of NICE (an agency serving England and Wales) which was established a decade ago. In our region, Brazil’s ANVISA agency is the primary example of the application of this system in which pharmacoeconomic requirements have been added to the traditional hurdles.

For further details on the concept of the fourth hurdle, we suggest reading the article published by Taylor in 2004.

INTRODUCTION TO ECONOMIC EVALUATIONS

Let’s begin this introduction to EE with a case study that facilitates discussion of the main concepts related to EE.

CASE STUDY: a new vaccine for “tropical pneumonitis”

In this hypothetical case, let’s suppose that we are developing a new vaccine to prevent a disease caused by pneumobacillus. This disease of bacterial origin particularly affects children between 0 and 5 years of age. Above all, this germ produces respiratory infections. The risk of suffering a respiratory infection caused by a pneumobacillus at some point in life is very high, nearly 20%. As we can see, this is a very common germ!

These respiratory infections tend to be mild or moderate and can be managed on an outpatient facility with antibiotics in most cases. However, there are also severe forms that can even be fatal. In addition to respiratory infections, pneumobacillus can cause neurological infections (meningitis), which are always very serious. They require hospitalization in order to administer antibiotics intravenously, and they are also potentially fatal. In addition, a percentage of the patients who suffer from meningitis may have permanent neurological sequelae. If a person who has suffered an infection due to pneumobacillus (whether respiratory or neurological) survives, he or she will have permanent immunity to this germ.

The context

We are in Provacland, a low-to-middle income country. The symptoms of disease caused by pneumobacillus are treated regularly in the public health system by means of medical visits and antibiotic treatment for patients with mild to moderate respiratory infections, and with in-patient treatment for patients with severe respiratory infections or meningitis.
A vaccine to prevent infections due to pneumobacillus has been available for several years. The vaccine is called Anti-pneumobacillus-A1. It is administered in three doses in the first year of life and its effectiveness in preventing infections throughout a person’s life is quite acceptable, since it stimulates a long-lasting immune response. It is also a safe vaccine, without significant adverse effects, and relatively inexpensive, since its development process involves traditional vaccine development technologies. For these reasons, the majority of the world’s countries introduced it some time ago and it is part of their official vaccination schedules. In Provacland, this vaccine has been administered to every newborn for the last 15 years.

Recently, a new pneumobacillus vaccine called Anti-pneumobacillus-B2 was developed. This new vaccine has demonstrated effectiveness superior to that of the old vaccine in preventing both respiratory and neurological infections. Although the difference in effectiveness is not great, due to the fact that the incidence of infections caused by pneumobacillus is relatively high, the additional number of cases and deaths averted with the new vaccine is significant when considering the entire population. However, this new vaccine is also much more costly, which is why many countries continue providing the old Anti-pneumobacillus-A1 vaccine in their vaccination schedules. However, some countries have decided to replace the Anti-pneumobacillus-A1 with the Anti-pneumobacillus-B2, considering that the additional cost of this vaccine is justified by the additional benefits it provides.

In the country in our example, there is a public healthcare system that provides coverage for the entire population. This public system guarantees access, free of charge, to drugs, devices, diagnostic methods and other health technologies included in the “National List of Guaranteed Health Technologies”. In order for a drug, device or any other health technology to be included on this national list, it must be approved by a special national immunization committee, which accepts the inclusion based on a set of criteria, the most important of which are, as stated in the law that regulates its operation, “…that the technology has been shown to be effective, safe and cost-effective”.

The company that produces the new vaccine makes a presentation to the committee in order to request the inclusion of the Anti-pneumobacillus-B2 vaccine on the National List. This new vaccine has actually been available in the country for more than a year, but its high cost impedes a large part of the population’s access to it (since it is not officially included in the national vaccination schedule).

The decision that the National Committee must make is relevant, because if it is included on the National List of Guaranteed Health Technologies, all the population will have access to this vaccine free of charge.

For these reasons, the National Committee has commissioned the preparation of a health technology assessment report that includes an economic evaluation, in order to know what the costs and consequences of incorporating this vaccine in Provacland would be, and to use this information to make a decision.

1) Why is it necessary to have an EE in this particular case?

2) In general, what are the reasons for which EE are important in healthcare decision making on resource allocation?
As we have seen, this country’s committee decides to include a new technology on the National List if it has been shown to be effective, safe and cost-effective.

From the evidence available, it is clear that the new vaccine is effective. In this case, “effective” means that greater results have been obtained in comparison with the old vaccine. This does not necessarily mean that the results are revolutionary, as preventing 100% of the cases would be. Strictly speaking, effective only means that there was a difference in the proportion of cases prevented, and that this difference was statistically significant.

As an example, we will assume that the old vaccine is able to prevent 40% of the cases. It may be that the new vaccine is slightly more effective; let’s say 43%, for example. If this small difference was scientifically demonstrated, we are authorized to say that the new vaccine is more effective. However, it is a difference that may have little clinical relevance.

For these reasons, and intelligently, this country’s rules indicate that being effective is a requirement, but it is not sufficient for deciding on the inclusion of a technology. This makes it possible to avoid, for example, allowing a drug that may be effective from a technical point of view, but whose benefit is very small in clinical terms, to be included for use in the health care system, especially if its cost is high. Another requirement imposed by the committee is that the technology must also be cost-effective, but what does this mean exactly?

Although later on we will discuss the concept of cost-effectiveness in greater detail, for now we can say that this requirement demands the existence of a “reasonable” relationship between the benefit of a technology and the cost it entails. That is, in this context, a technology that is very costly and whose clinical benefit is very small will not be considered “cost-effective” and will have a greater chance of being rejected by the committee.

As you are surely thinking, this criterion sounds reasonable in general, but entails many difficulties. To start with, defining what is a small clinical benefit or a significant clinical benefit is no simple matter.

Is increasing survival by two months a significant or small clinical benefit? More importantly, what is that “reasonable” relationship between costs and benefits? In addition, we can assume that this rule that only provides for the inclusion of technologies that have been shown to be effective, safe and cost-effective inherently allows the possibility that some technologies which have been shown to be safe and effective could be rejected, even when there are no other alternatives. We will come back to all of these points later on. For now, let’s concentrate on discussing why having an EE is necessary in this particular case.

Does the new vaccine fulfill this requirement of cost-effectiveness? If it is included on the National List, it will be a new expenditure that the healthcare system must cover. Is it reasonable to pay the additional cost it entails, given the benefit it produces? Is it a good investment of health resources?

These questions can only be answered adequately by means of an Economic Evaluation (EE). EE analyze the costs and consequences of the application of a health technology by contributing the information necessary to determine whether the relationship between the costs and benefits is within acceptable limits according to the committee’s judgment.
What are the committee’s information requirements? Basically, it can be said that it is necessary to know the costs and benefits of these vaccines in order to establish whether this “reasonable” relationship exists between them. Later on, we will come back to this point to discuss what “reasonable” means in further detail. For now, we will work with the concept that, for example, a very high cost to obtain a very small clinical benefit is not “reasonable”.

In simpler terms, the committee’s reasoning could be stated in the following manner: “Currently, we’re using the Anti-pneumococillus-A1 vaccine. Today, this entails certain costs and clinical results. What would happen if we included the Anti-pneumococillus-B2 vaccine? What additional benefits would we obtain? What new costs to the healthcare system would this entail? Are these additional costs justified based on the benefits to be obtained?”

We have thus tried to answer the first question: In this particular case, why was it necessary to have an EE? Now we will go to the second question, which has to do with a more general matter: What are the reasons why EE are important in healthcare decision making on resource allocation?

In the country in our example, the decision to include a new technology on the National List is made when it has been shown to be effective, safe and cost-effective. As we have seen, this means that it is possible that a health technology that has, for example, a relatively small clinical benefit and a high cost may be rejected even when there are no other alternatives. What reasons can there be for impeding the population’s access to a technology that has been shown to be safe and effective?

To explain this situation, we will now introduce an important concept: opportunity cost. Every healthcare system, in poor countries as well as wealthy countries, must face the situation of limited resources. This limitation of resources is evident in a number of areas, from limitations in the number of physicians or diagnostic equipment to budget limitations. Beyond the amount budgets are increased or efficiency is improved, there will always be a limitation imposed by the resources available. For the time being, this dilemma appears to be far from being resolved. The aging of the population, the emergence of new diseases and technological innovation, among other factors, have driven health spending in recent decades faster than the growth of economies, forcing countries to allocate higher percentages of their gross domestic product to healthcare. For these reasons, every country will continue facing the dilemma of growing needs and insufficient resources, even in wealthier countries (recall, for instance, the intense debate in the USA in 2009 over President Obama’s healthcare reform plan).

This limitation of resources has a fundamental first consequence: the resources we use in a given intervention, with the expectation of obtaining certain health benefits, will no longer be available for use in other potential interventions, which in turn could have provided health benefits. If these “lost” benefits are smaller than those to be obtained with the intervention chosen, the right decision was made.

Let’s look at a highly simplified example to illustrate this point. Let’s assume that a certain region of the country suffers from high child mortality. The national government has decided to budget an additional US$ 2,000,000 to deal with this problem. That is, the following year this region will have the same resources as the year before, plus this additional amount on which an investment decision must be made. Following preliminary analysis, three alternatives on how to use this additional amount are proposed. Each of these alternatives has a cost of US$ 2,000,000, due to which only one of them could be implemented in the following year:
1. Expand the capacities of Intensive Neonatal Therapy units. Expected effect: a 15% reduction in child mortality.
3. Improvements and additions to operating room and delivery room equipment. Expected effect: an 8% reduction in child mortality.

The three interventions proposed represent improvements in the healthcare system and are effective in reducing child mortality. Health authorities in this region would probably like to implement all of them, but their budget only allows them to choose one. Which would be the correct choice?

Based on the information we have, the answer is obvious. Option 2 (strengthen primary care) is our best alternative, since it is the one that offers the greatest health benefit.

As we have indicated, when resources are limited, choosing an alternative means that there are other things that we will not be able to do. This is opportunity cost. Using resources in a certain intervention means that we have lost the opportunity to use them in other interventions.

If we decide to implement alternative 2, strengthening primary care, what is our opportunity cost? The answer is easy. Choosing this alternative means, for example, that we will not be able to expand the capacities of neonatal intensive therapy units this year. Therefore, we will no longer be able to obtain the benefits of this intervention. In other words, we are losing the opportunity to reduce child mortality by 18% through improvements in intensive therapy. But what are we gaining? We are obtaining a very significant benefit, since we begin to reduce child mortality by 30% through the intervention chosen. As we can see, the opportunity cost we are paying (not being able to reduce child mortality by 18%) is compensated by the benefit that we will obtain as a consequence of our choice (reducing child mortality by 30%).

Having limited resources, we cannot avoid the fact that there will be an opportunity cost. There will always be something we have to give up doing as a consequence of our choice. As we have seen in this example, we have opted for an alternative whose benefits are greater than the opportunity cost; therefore, our choice was on target. It would have been different if we had opted to use the resources to equip operating rooms and delivery rooms (option 3). Although it is true that we would also have obtained benefits (an 8% reduction in child mortality), our opportunity cost would have been higher, since we would be giving up the opportunity to obtain the benefits of other interventions with a greater impact. It would not have been an on-target choice, at least from a perspective of efficiency in resource allocation.

Therefore, in this example we see that even when all three potential interventions are effective, an erroneous choice entails a loss of benefits with regard to what could have been obtained. Take note of something that can be a little confusing: despite the fact that we are talking about opportunity cost, we are referring to benefits that we would be giving up.

**How does this situation relate to the case of pneumobacillus vaccines?**

This is a more complex situation, but it is easy to make an analogy with the preceding case. In the country in the example, as in every country in the world, resources are limited. Incorporating a new technology entails using resources which will not be available for other interventions.
How can we ensure that the right decision is being made? In other words, how can we ensure that the opportunity cost of including the new technology will be offset by the benefits to be obtained?

Unfortunately, reality is much more complex than the situation presented in the child mortality example, in which we had a specific additional budget (US$ 2,000,000), a single health problem on which to focus and three alternatives whose costs and benefits were known. Healthcare systems must make hundreds of decisions related to very diverse health problems and interventions, and without complete information in most cases. Therefore, it is not as clear as we stated in the example. However, we can see that the criterion of requiring that a technology be cost-effective; that is, that there be a “reasonable” relationship between the costs it entails and the benefits it provides, is based on the same concepts. If the committee were to accept the inclusion of very costly new technologies with very small clinical benefits on the National List, it would not be making efficient use of the resources, since this would imply losing the benefits of other more cost-effective interventions that could not be included.

This introduction focused on EE and for this reason we have centered on discussing the application of these economic criteria when making decisions. However, it should be noted at this point that efficiency in resource allocation is an important criterion, but it is not the only one that societies need to take into account. There are also other values that influence decisions.

It may be the case that an intervention is less efficient from the perspective of the clinical benefits it provides, but results in a reduction in inequity regarding a particular matter, due to which it may be preferable to another more intervention that is more efficient but does not improve on, or even increases, inequity in the healthcare system.

However, it is clear that it is not possible to make on-target decisions without information and if not all of the aspects of decisions are known. Economic evaluations compare the costs and consequences of two or more health interventions, and aid in making an in-depth analysis of the framework in which they are carried out. It is for these reasons that, in recent years, there has been growing production of EE throughout the world, greater demand for EE on the part of decision makers and a growing interest in these matters when setting priorities in resource allocation.

However, in our region there are still few explicit mechanisms to guide these decisions. This is reflected in practice in the implicit rationing that is evident, for example, in waiting lists, the unavailability of drugs and treatments, or the deterioration of equipment and infrastructure. Given the lack of transparent rules, the manner in which resources end up being allocated is often the result of other forces operating in the system: each patient’s capacity to stand up for his or her rights, the power of the area in that hospital to obtain a turn for surgery, judicial intervention, the availability of a certain prosthesis through the purchasing system, market pressure to disseminate a particular technology, nearness to healthcare facilities or the availability of a certain technology in the geographical area, to list some examples. The result is implicit rationing in which many people may not have access to basic and highly cost-effective medical services, with the further difficulty that this takes place without transparent rules that can be discussed and changed, which is reflected in greater inequity and inefficient use of limited health resources.
As a number of experts coincide, and as stated in the words of the World Health Organization, “...throughout the world, resources are insufficient to deal with the demand for healthcare. The gap between what is needed and the needs that can be fulfilled make it necessary to introduce the establishment of priorities as an essential aspect of every healthcare system, whether rich or poor...” Until another solution to this gap between available resources and needs is found, those who want more equitable and efficient healthcare systems must deal with the challenge of setting priorities sooner or later. In these cases, the role of EE will be fundamental. Making decisions based on scientific evidence, taking care of the resources generated by society, requires optimum use of available resources.

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REFERENCES


ADVANCED COURSE

ECONOMIC EVALUATIONS: DEFINITION AND MAIN TYPES

The two most important aspects of informed healthcare decision making are the effectiveness of treatments and their costs.

When referring to effectiveness, we do so in a broad sense, considering aspects such as reduction in mortality, increased survival rates, improvement in symptoms, reduction in adverse effects and improvement in quality of life, as well as any other aspect that affects the longevity or quality of life of a specific group of patients. As we will see shortly, the measure of effectiveness chosen will depend on the type of economic evaluation to be performed.

When referring to costs, we include the monetary valuation of all of the relevant resources entailed in the use of the technologies to be evaluated. As the measure of effectiveness indicates the type of EE, the type of costs to include will define the so-called perspective of the study, which may be a more limited perspective, such as that of a hospital, or even a perspective as broad as that of society as a whole. In the following paragraphs, we will take a closer look at these concepts.

TYPES OF ECONOMIC EVALUATIONS (EE)

As we have seen, EE can take into account two dimensions of health interventions: their effects and their costs. Studies that only take one of these two dimensions into account are called partial EE.

In a scenario where we compare different interventions for the same disease, in some cases we can only compare how much each one costs us. However, it is evident that the lack of information on the effectiveness of the interventions is a very significant limitation.

At the other extreme, we can have the case of comparisons where only clinical results are evaluated, regardless of the resources employed. These are the classical studies found regularly in medical literature, which contribute very valuable information regarding the effectiveness of different interventions, but they tell us nothing about the costs to the health system that these interventions entail.

Lastly, and most recommendable, we can incorporate both dimensions and evaluate the costs as well as the consequences or effects. If we perform this analysis on a single intervention, we will be giving a thorough description of it, but in order for it to be a true, full EE, it must compare two or more interventions, including effects as well as costs. This is the type of EE that really interest us and is a valuable tool for decision making, since it contributes information that makes it possible to compare two or more interventions in their most relevant dimensions. Now we will
cover full EE in greater detail, since within this group there are different types that we need to be familiar with.

**Table 1. Classification of Partial and Full Economic Evaluations**

As shown on the following chart, there are five types of full economic evaluations:

**Table 2. Classification of Full Economic Evaluations**
All full economic analyses use the same cost identification, measurement and valuation methods; the difference is in the way they measure consequences or benefits.

The following paragraphs explain each type:

**Cost-minimization analysis**

In these studies, both alternatives produce the same result; that is, there are no differences with regard to their effectiveness (i.e. they are equi-effective). It should be kept in mind that effectiveness must be considered in a broad sense; it does not only refer to a single clinical result. For example, if two drugs are equally effective with regard to their capacity to reduce mortality caused by a certain condition, but one of these two drugs produces severe adverse effects, it cannot be stated that they are equivalent.

The primary objective of cost-minimization studies is to find the least costly alternative, given that the consequences are the same.

An additional use of these studies is to identify the cost distribution and explain why an alternative is less costly. For example, corrective surgery for myopia can be an outpatient or inpatient procedure. The efficacy and effectiveness of both are the same, but the former is less costly. Of course, these evaluations are rare, since there are few equi-effective interventions.

Cost-minimization analysis is used when two interventions are compared and previous studies have demonstrated that their efficacy and effectiveness is the same.

**Cost-effectiveness analysis**

In this type of analysis, benefits are measured in natural units. Some examples are: life years gained, millimeters of mercury of blood pressure lowered, kilograms of weight lost, cases of breast cancer detected or heart attacks averted.

In this case, the measure of evaluation of benefits is common to both alternatives. In order to compare them, the difference in costs and the difference in effects between them will be estimated and the cost-effectiveness rate will be calculated.

In cost-effectiveness studies, a natural parameter common to both alternatives being evaluated is selected. The comparison of options that do not have a common result is not permitted.

Cost-effectiveness studies are very useful, but they have some drawbacks. The following are the two main drawbacks:

1) There may be interventions that produce more than one clinical result (this is quite usual), due to which the final result cannot be summarized in a single value.

2) Cost-effectiveness studies do not permit comparing interventions in different areas or even in similar areas if different cost-effectiveness measures were selected.
It is partly due to these reasons that cost-effectiveness studies have been gradually replaced by the next category we will address: cost-utility studies.

Cost-utility analysis

In cost-utility studies, the type of EE of choice preferred these days, the way of measuring consequences is a combination of years lived and quality of life. This type of analysis is used for three fundamental reasons in different situations:

• When interventions have multiple consequences and all of them are of concern to us; for example, in the treatment of sedentariness, we may be interested in evaluating physical training, kilograms of weight lost, prevention of cardiovascular events (number of heart attacks prevented, life years gained), improvement in dyslipidemia, and reduction in depression and anxiety.

• When we are interested in obtaining a result that will allow us to compare alternatives that are unrelated to each other and do not share consequences. For example, we are interested in being able to decide on or compare the utility cost of a malnutrition treatment with other unrelated interventions, such as a heart attack treatment, for instance.

• When we are particularly interested in measuring both the survival rate and the quality of life that survival entails.

The major advantage of cost-utility studies is that they make it possible to summarize all of the effects of an intervention as a single value. A given treatment may prolong life, avert hospitalization and improve symptoms at the same time that it produces a serious adverse effect or a certain complication.

There are different measures proposed for use in this type of studies that give us an idea of healthy life, or from a complementary perspective, burden of disease.

In simplified form, a given disease or condition can negatively affect health in two ways:

• Reducing life years (when it involves a risk of death)
• Causing disability

For these reasons, losses of health include both deaths attributable to health problems and disabilities caused by disease among the population. In order to evaluate the global burden of disease in a population (attributable to all diseases), the World Health Organization (WHO) defines it as a population’s state of health, taking into account not only the number of deaths, but also the impact of premature deaths and disabilities caused by different diseases, injuries or risk factors.

One of the indicators used most frequently to evaluate burden of disease is disability-adjusted life years (DALY), which is recommended by WHO.
DALY is a metric that comprises both premature mortality and disability due to morbidity, and this is the metric ordinarily used to estimate burden of disease.

Let's look at the following example:

Life expectancy WITHOUT the disease:

```
65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81
```

Let's assume that each of these 17 green boxes represents a year lived in full health and that this is how long we would expect a 65-year-old person to live in an ideal situation without health problems. That is, we are going to assume that a 65-year-old person should live to be 81 years old (17 years in full health).

```
65 66 67 68 69
```

In this other example, we see how a given disease, contracted at age 65, affects a person’s life. On the one hand, it affects his/her quality of life, producing a 20% disability (represented by the red color) for 5 years. On the other, it causes premature death, shortening his/her life by 12 years (these lost years of life are the blank boxes).

If we compare the two cases, how many “disability-adjusted life years” were lost?

It is easy to see that 12 years were lost, since the person could expect to live 17 years without the disease, but only lived 5. However, this is not the only “harm” caused by the disease. In addition, the disease caused a disability for 5 years, making those 5 years “less valuable”. If we add all of the red portions in each of the boxes, given that we have rated this disability a 20% disability, we can say that this loss (red section) is equivalent to a year of life.

In summary, this condition can be deemed to have caused a total loss of 13 years: a 12-year loss due to premature mortality (blank boxes) + a 1-year loss due to disability (red portion of the boxes). That is, the burden of disease was 13 DALYs.

This is a simplified version of the concept of DALYs, since the calculation of DALYs can be somewhat more complex, incorporating different weighted values in which a year of life lived at a certain age (for example, a person’s productive age) has a greater value than a year of life at other ages.

Another measure that combines the concepts of length and quality of life that is widely disseminated, particularly for economic evaluations, is quality-adjusted life years or QALY.

As we have indicated, a given treatment can prolong life, avert inpatient admissions and improve a symptom at the same time that it produces a serious adverse effect or a certain complication. All of these effects can be summarized in a single measure, QALY, and this value can be used to compare it with another treatment, which in turn can have multiple effects, even different ones, but also summarized in this manner.

So what do these QALY mean and where do they come from?
QALY is a measure intended to state how much a year living with a given condition is worth. The “unit” used for this comparison is a year lived in full health. For example, if we say that the QALY of renal dialysis is 0.65, what we are saying is that living a year with chronic renal insufficiency (CRI) with the need to undergo renal dialysis is equal to 0.65 years in full health.

Why? This is due to the fact that renal dialysis affects one’s quality of life. For these reasons, a year in dialysis “is worth” less than a year without dialysis. This has significant implications when evaluating the cost-utility of interventions.

Due to these reasons, it is currently preferable that EE be cost-utility studies, unless there are good reasons for choosing another type of design. However, the term “cost-effectiveness” is so well disseminated that it is common to refer in a general manner to EE as cost-effectiveness studies, encompassing both true cost-effectiveness studies and cost-utility studies in this term.

**In Cost Utility analysis, the following can be used as a measure of results:**
- DALY (Disability-adjusted life years)
- QALY (Quality-adjusted life years)

**Cost-benefit analysis**

In this case, clinical results are converted to monetary units. A monetary value needs to be assigned to the consequences. For example, it implies defining the monetary value of a life. It is a point that neither physicians nor the general public care for, which is why this type of studies is not found frequently in the literature. Cost-benefit analysis measures results in monetary units.

**PERSPECTIVE OR POINT OF VIEW OF THE ANALYSIS / COST CATEGORIES**

This is a specific ingredient of EE that is relatively unknown to those in the healthcare field, but better known by those in the field of management or economics. The perspective of a study, or its point of view, refers to the position from which we evaluate the problem. It is not the same if we use the perspective of the president of a country or that of the Ministry of Economy or Finance, as if we look at a problem from the perspective of the director of a hospital or of a private health insurance company. Defining the perspective of a study starting with its design is fundamental, since it determines what type of costs must be considered.

For example, for a private health insurance company, the out-of-pocket costs that patients have to pay in order to receive treatment are not directly relevant. However, for a decision maker at the governmental level, it may be relevant.

So the perspective of a study mainly defines what types of costs are included in the study and which ones are not. Some of the possible perspectives are:
- The patient’s
- The physician’s
- The hospital’s
- The financier’s
- The government’s
• Society’s

The vast majority of economic evaluations are made from the point of view of the financier, although there is an increasing tendency to consider the social perspective.

The types of costs included in each perspective are those corresponding to it. For example, a private health financier will include costs that have to do with it (costs of outpatient care, inpatient admissions, laboratory work, etc.), but will not include other types of costs that have nothing to do with it (for example, the costs of transportation that patients and their families incur, or those related to lost productivity).

So, before we continue outlining the different perspectives, let’s define the types of costs that economic evaluations consider. The first differentiation that must be made is between direct and indirect costs (which have different meanings in the context of economic evaluations than in accounting). As their name indicates, direct costs are all costs directly related to the implementation of a given program or the administration of a given drug. Direct costs are classified as:

• Direct costs to the healthcare system (medical visits, nursing, drugs and other technologies, equipment, use of space)
• Direct costs to the patient and the family (out-of-pocket expenses for transportation, for hiring informal help)
• Direct costs to other agencies or sectors (considered less frequently in EE; for example, an addiction prevention program would have direct effects on reducing crime and this would reduce costs to the legal or penitentiary system)

With regard to indirect costs, more aptly referred to as lost productivity costs, these refer to the value assigned to the time that a patient must stop working due to the intervention considered, or to the time that a family member stops working due to this intervention (for example, any pediatric treatment for which parents or caretakers inevitably lose productive hours in order to accompany their children).

The following table shows the types of costs included for each perspective of EE.
Table 3. Main Perspectives and Types of Costs to be included in each

<table>
<thead>
<tr>
<th>Examples of costs</th>
<th>Perspectives of the study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient</td>
</tr>
<tr>
<td>Direct medical cost</td>
<td>yes</td>
</tr>
<tr>
<td>Physician’s time</td>
<td>no</td>
</tr>
<tr>
<td>Other staff members’ time (nurses, technicians)</td>
<td>yes</td>
</tr>
<tr>
<td>Drugs</td>
<td>no</td>
</tr>
<tr>
<td>Disposable material and medical devices</td>
<td>no</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>no</td>
</tr>
<tr>
<td>Non-medical direct costs</td>
<td>no</td>
</tr>
<tr>
<td>Administration</td>
<td>no</td>
</tr>
<tr>
<td>Facilities/Physical plant</td>
<td>no</td>
</tr>
<tr>
<td>Services (telephone, electricity, etc.)</td>
<td>no</td>
</tr>
<tr>
<td>Patient’s per diem expenses</td>
<td>yes</td>
</tr>
<tr>
<td>Temporary companion / caretaker</td>
<td>yes</td>
</tr>
<tr>
<td>Indirect cost</td>
<td>yes</td>
</tr>
<tr>
<td>Time off work for medical visits</td>
<td>yes</td>
</tr>
<tr>
<td>Time off work due to illness</td>
<td>yes</td>
</tr>
<tr>
<td>Temporary household help</td>
<td>yes</td>
</tr>
</tbody>
</table>


Therefore, if we conduct or read a study from a financier’s perspective, only the direct costs to the healthcare system, including those listed by the table as medical costs as well as the financier’s administrative costs will be included. Other costs, such as the patient’s loss of earnings or the costs of transportation and caretakers will not be included.

The social perspective is the most complete and all-encompassing. If we consider this perspective, all of the resources consumed should be included in the study, regardless of who consumes them, since all costs are relevant from the social perspective.

MAIN VEHICLES OF ECONOMIC EVALUATIONS

How are economic evaluations conducted in real life? There is no single answer. We could try to simplify it by saying that there are two ways to conduct an economic evaluation: there are economic evaluations that are based on individual patient data (for example, in a clinical trial),
and others (the majority), model-based economic evaluations (mathematical models that synthesize data from different sources to estimate consumption of resources, as well as the results to be obtained). We will introduce these main types and further analyze model-based economic evaluations.

Economic evaluations piggybacked on clinical trials

A type of economic evaluation used increasingly is the so-called “piggyback” study, or economic evaluation “piggybacked” on a clinical trial.

Alongside clinical trials, in any phase of the development of a technology, at the same time that regular data are gathered (effectiveness or safety, for example), data on the consumption of patients’ resources are collected, and in the case of cost-utility studies, a questionnaire is also used periodically (for example, the EuroQol EQ-5D) in order to assess quality of life and QALY. This makes it possible to obtain estimates of cost-effectiveness or cost-utility using only data from the primary study (on individual patients). Often, and in many places in the world, final decisions on the launch of a new product in the market or approval by the regulatory authorities depend on this economic information, in addition to information on efficacy and safety.

Introduction to model-based economic evaluations

There are situations in which conducting a research study to answer questions of concern is not feasible, for example, situations where the timeframe of concern is the entire life of the subjects. On other occasions, data from different sources are synthesized (for example, administrative databases, medical histories, databases of complementary studies) and an attempt is made to analyze them from a new perspective in order to obtain conclusions on a concrete problem. For these cases, appropriate mathematical models are created to facilitate the obtainment of information for timely decision making.

A “model” is a real world simplification that only considers important components of the health problem to be evaluated from the perspective one wishes to analyze. A good model makes it possible to estimate the costs and benefits of the different decisions that could be taken, incorporating all relevant information. Models aid in the analysis of decisions and foster an explicit and encompassing rationale, considering existing alternatives. In addition, they facilitate the identification of weaknesses in the evidence available at the time a decision is made.

The following figure shows the different types of information generally included in model-based economic evaluations:

Information necessary for the construction of models

The techniques used in economic models are increasingly used in EE to aid in decision making regarding the conducts of healthcare or the introduction of new technologies. Models can be useful in a number of situations, particularly:
- For synthesizing data from different sources for an EE.
- For extrapolating data beyond the conclusions of clinical studies (for example, a treatment for depression based on studies that tracked patients for six months, and one is interested in the long-term trend for decision making).
- For relating intermediate developments with final results (for example, blood pressure and cardiovascular death; bone density and hip fractures; or glycosylated hemoglobin with micro or macrovascular events in diabetes).
- For generalizing the results of a study with other situations (for example, situations in which there are changes in the cost of a medical hour or treatments, or the prevalence of disease).
- For synthesis and “head-to-head” comparison of treatments for which no direct comparison has been made in clinical studies (for example, there is no study comparing all hypertension treatments head-to-head, although an EE should include and compare all relevant treatments).
- When a decision must be made in the absence of convincing evidence in the data available.
- To indicate the need for further research.

A good model should reflect ordinary practice; therefore, a good comparator should be used and it should be based on the best information available.

A crucial characteristic of models is their transparency and reproducibility, so that they can adapt to different scenarios. It is essential that models have internal validity. Increasingly, governments (England, Australia, Portugal, Brazil and Mexico) require economic evaluations before approving a new technology to be covered by the healthcare system.

**In summary, the main characteristics of “models” for economic evaluations are:**

- They provide a way to represent the complexity of the real world in a simple and understandable manner.
- They are a mathematical structure that represents clinical and economic of alternative strategies in relation with patients or populations under different scenarios.
- They synthesize data from different sources.
- They account for uncertainty.
- They focus on the decision to be made.
- They are increasingly accepted as vehicles for EE by regulatory agencies.
- A good model is intended to appear sufficiently similar to a real situation for it to be used as a decision-making tool.

The creation of a model implies simplifying a clinical/economic problem by turning it into a mathematical structure, usually in a computer, whether through spreadsheets or specific programs. Once the structure of the model has been outlined, the following step is to incorporate parameters (epidemiological, effectiveness, cost, utility) in the model, using the best evidence available.

In summary, model-based EE “are here to stay”, and they are accepted – and sometimes required – instruments for decision making in many countries around the world. Unlike the classic measurement paradigm (clinical trials, systematic reviews) that seek to precisely measure a given result (such as the relative risk of an event with one drug vs.
another), models are incorporated in the paradigm of decision making, and are intended to respond to the question of what to do based on all current sources of knowledge, taking into account that decisions cannot be avoided and must always be made under uncertain conditions.

The two most common types of models are:

**Economic evaluations based on decision trees**

Decision trees are relatively simple tools that were frequently used for making EE in the past, but less so now. They seek to reflect a relevant sequence of events, both clinically and economically, of the problem at hand. A series of events is associated with each option, and they are represented as branches. Subsequent events can be modeled as branches that are “conditional” on previous events.
Limitations of decision trees:

A problem with the use of decision trees is that they are not very useful when one wishes to model the long-term prognosis of a health problem, since decision trees do not explicitly consider the passage of time, although the time dimension is available when the unit of measurement for evaluating results is selected.

It is not a practical tool for modeling recurring events either, since a decision tree may have too many branches, or for modeling chronic diseases where one may be interested in modeling events over time (complications, recurrences, remission, mortality), since this also involves numerous branches. Nor is it easy to incorporate matters related to discounted benefits and costs in decision trees.

For these reasons, in the majority of cases these days, another type of model is used, the most common being the Markov model.

Its main use is for comparing two or more interventions over time, as well as to extrapolate results of clinical trials to a long-term horizon. This will be explained in the following paragraphs.

Markov Models

Markov models, which are also called state transition models, are those most frequently used in model-based economic evaluations today.

In what cases is a Markov model recommended?

• When a decision has to do with the risk over time.
• When “time” or the timing of events is important.
• When events may recur.
• When a disease progresses from stage to stage.
• When one wishes to extrapolate results beyond clinical trials.

Although there are many ways to analyze it, one of the most frequently used is the so-called cohort method, in which a hypothetical cohort is followed over time.

EXAMPLE:

Schematically, it could be illustrated as follows (a cohort that comprises three different states of health) over the cycles/years:
TRANSFERABILITY / GENERALIZABILITY IN ECONOMIC EVALUATIONS

Let’s change the subject a little. The topic we are going to approach now is perhaps the Achilles heel of economic evaluations, or the reason why they have not been more widely disseminated.

For example, take the case of low back pain or lumbalgia. When prescribing a drug to calm the pain, we would not hesitate to prescribe one that has been evaluated in high-quality randomized clinical trials, even though none of these studies was conducted in our country, or with a population such as ours. This is due to general consensus that the relative effect of interventions “travels” easily from one setting to another. Therefore, the vast majority of interventions that we use in our countries, from vaccines to treatments for hypertension or cancer, are widely used based on efficacy data from other countries or settings.

Now, imagine that we are reviewing an economic evaluation made in the United Kingdom. Can we apply it directly to our decision in Brazil, Mexico, Peru or some other country in our region? If your thought is a resounding NO, you weren’t off base...

First, let’s try to define these terms. Although they are often used interchangeably, they can be defined as follows:

- Generalizability: “the extent to which the results of a study based on measurement in a particular patient population and/or a specific context hold true for another population and/or in a different context” without any type of adaptation or adjustment [Sculpher 2004].
• Transferability: “the potential to adapt or adjust analysis of a study to make the results relevant in different settings” [Drummond 2008].

There are diverse factors that cause the cost-effectiveness of technologies to vary from one place to another. They can be grouped according to aspects related to the behavior of a health problem in a local setting (for example, the incidence or severity of the problem at hand); the availability of health resources (for example, treatments available for it); local treatment practices (for example, in the USA, there are more “invasive” practices for managing coronary disease than in the majority of European countries); and also the difference in costs (for example, in most of the countries in our region, the cost of the physician’s time or of inpatient care are much lower in relative terms than in the USA or other developed countries, while the costs of new technologies are often similar to their costs in those countries).

In a systematic review that our team conducted jointly with researchers from the University of York to evaluate the transferability of EE in Latin America, of the 521 studies reviewed, 72 met the study’s criteria for inclusion. More than a third of these (36%) did not specify the type of economic evaluation. Nearly 40% were based on the data of individual patients in clinical trials, and a third was model based. We observed that, in general, it was very difficult to transfer results from one setting to another, due to the fact that the vast majority of the studies had methodological or reporting problems that impeded transferability to other settings (Augustovski 2009).

For those interested in the different methodologies for improving the transferability or generalizability of EE, including those based on individual patients and those based on models, we recommend reading the ISPOR (International Society of Pharmacoeconomics and Result Research) Task Force’s report on this subject [Drummond 2009].
REFERENCES


