

Introduction

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The assessment of pharmaceuticals has, in recent years, expanded beyond efficacy and safety to cover economic implications and other consequences. The incorporation of an economic perspective into the decision-making process as to which therapies will be reimbursed and made available by respective healthcare systems has aroused much debate and discussion, which at times has been quite heated. Newspaper headlines of people having to re-mortgage their houses to pay for “life-saving” therapies and media frenzy when “effective” treatments are denied to desperate patients are becoming all too common occurrences. The intention of this introductory Chapter is to explore some of the concepts that underpin the economic assessment of pharmaceuticals in order to appreciate the rationale for economic considerations and how the approaches and instruments used in undertaking the economic assessments can be applied to everyday decision-making processes.

Healthcare Dilemma

It cannot have escaped the attention of anyone involved in Health Services that there is a shortage of more or less everything that is needed to adequately provide services. The nature of the healthcare dilemma, which confronts all healthcare systems, is a microcosm of the basic economic problem: that of reconciling infinite wants, needs, and demands with finite resource availability, in terms of income, time, expertise, and so on. The exponential increase in demand for healthcare services has been occurring at the same time as pressures on governments and funding agencies to carefully manage the volume of resources available for healthcare services. It is not simply a lack of finance—although that does feature prominently—but as individuals we are continually faced with the consequences of not having enough time to fit in everything that needs to be done and would very much like to do. In addition,

¹ This chapter, which was originally written by Ceri Phillips, has been updated by Lorenzo Pradelli

shopping lists far exceed abilities to purchase everything they contain, while good intentions to maintain strict exercise routines are often thwarted by the lack of energy after a busy day at the office, in the surgery, or in the operating theatre!

The fundamental economic problem is that while we all have unlimited wants and desires, we only have limited resources (time, energy, expertise, and money) at our disposal to satisfy them. This situation has become particularly evident in healthcare and has been compounded by factors such as increasing expectations of people in relation to what can actually be delivered by healthcare services, continuing advancements in health technology and medical science, and the increasing health needs and demands of an ageing population. As individuals we are constantly making choices as to how we use our time, into which activities we channel our energies, and on what we spend our available funds. Spending time on one activity or purchasing a certain commodity means that period of time and those funds are not available for other activities and other purchases. The same issues relate to health systems: Which patients to treat, when, and with what therapies? The answers do not lie in spending more money: How do we know whether any additional expenditure will actually produce additional healthcare benefits? Healthcare systems will never be a position to meet everyone's healthcare needs, let alone people's wants and desires. The politicians, managers, and other officials who run the services veer between trying to contain costs and defusing the anger of patients, families, and the electorate for the inadequacies in the services that are provided. Media focus on the pressures and problems, rather than the successes, do little to remedy the situation, while professionals' frustration and anger with what they see as the inadequacies in the systems and their effects on patient care are increasingly apparent.

Opportunity Cost

It is therefore apparent that in making a choice to use funds and resources in one way means that they are not available for other purposes. As a result, the benefits, which would have been derived, are sacrificed. These sacrifices are referred to as **opportunity cost**. Their very existence provide a rationale for economists to take an interest in all resources that are used, whether by individuals, governments, Health Services, or societies, regardless of whether or not money is paid for them, in order to achieve the maximum benefit.

Questions of resource allocation, that is how scarce resources are, could be or should be allocated amongst the infinite variety of competing activities, are therefore fundamental to any study of economics. The wide range of economic systems, which have existed and evolved over time, have all attempted to address the basic economic problem of allocating resources in such a way as to maximize the benefits for society. Similarly, the variety of approaches employed to fund and finance healthcare by different countries all have the same basic aim of seeking to maximize the health benefits for their citizens, given the resources they have available at that point of time. The nature, type, and funding of healthcare systems continue to exercise the minds of many policy makers and stimulate debate in academic institutions, the media, and other popular centers of debate and discussion.

In developing a cost profile, it is important that the resource implications associated with the particular therapy being appraised in comparison with treatments that are currently provided should be identified, measured, and valued within a relevant context and should include a comment on the validity of using resource data from other locations, if local data are not available. The appraisal should present direct healthcare resource usage for the therapy and its comparator(s) separately and in natural units, such as hospital days, dosage, and duration of treatment, with data sources cited. These would constitute the costs to the respective healthcare system. However, patient resource use in accessing and using treatment should also be included where felt to be significant, particularly where there are major differences between the therapy and its comparator(s). Other resource use may also be presented separately where differences arise between the therapeutic agent and its comparator(s), e.g., direct non-healthcare resource use, such as those by other agencies, while productivity losses attributable to changes in health outcomes might also warrant some discussion.

Efficiency and Equity

The term **efficiency** is used by economists to consider the extent to which decisions relating to the allocation of limited resources maximize the benefits for society. The concept of efficiency embraces inputs (costs) and outputs and/or outcomes (benefits) and the relationship between them, with a society being judged in efficiency terms by the extent to which it maximizes the benefits for its population given the resources at its disposal. The sim-

plest notion of efficiency is the one synonymous with economy, and is often referred to as **efficiency savings**, where output is expected to be maintained, while at the same time making cost reductions, or where additional output is generated with the same level of inputs. This type of efficiency has also been referred to as **cost-effectiveness**. It is applied where a choice needs to be made between alternatives, which seek to achieve the same goal, and exists when output is maximized for a given cost or where the costs of producing a given output are minimized. It is widely used in the context where new therapies are compared against existing treatments and authorities have to decide whether it is worth paying more for the potential additional benefits which the new therapy offers.

However, cost-effectiveness is not sufficient in order to establish priorities, both within healthcare systems, and when comparing the provision of healthcare with other publicly funded services. In order to determine whether and how much of certain services should be provided and in order to establish priorities, allocative efficiency must be used. This type of efficiency exists when it is impossible to make one person better off without at the same time making someone else worse off. It represents a situation where no input and no output can be transferred so as to make someone better off without at the same time making someone else worse off.

However, it is impossible to separate the drive towards an efficient allocation of resources from its impact on income distribution. A move towards efficiency may well result in a redistribution of income in favour of the well off, which may not be acceptable on grounds of fairness and equity. Virtually all healthcare systems employ a mix of libertarian and egalitarian values. The notion of equity is inextricably linked with notions of fairness and justice, but it is important to distinguish it from the concept of equality. Policies designed to achieve equality of opportunity, or access, or utilization or outcome may well be desirous but they need not necessarily be equitable.

The extent of health inequalities within countries and across international boundaries continues to ensure that equity remains high on the list of health policy objectives. Many influential national and international policy documents highlight the importance of equity as a goal of policy and the on-going need to implement remedial measures to reduce inequalities both between and within populations, which remain frustratingly large. It is widely acknowledged that people's environment, social status, educational achievements, ethnic origin, age, gender, etc. affect their state of health, and equally that their conditions and characteristics result in some being better able to respond to treatments and enjoy longer life expectancy.

An issue which has really polarized opinion, both within the healthcare professions and among decision-makers, for example, is whether people who knowingly engage in health-damaging behavior should receive treatment—is it fair and equitable that limited healthcare resources are allocated to these people, while others, who have attempted to live healthy lives, have to wait for treatment or access the services of the private sector? The very fact that service provision is limited makes it inevitable that some people will not receive all that is wanted or even required. The decision-making process as to who should receive services, treatments, and interventions is littered with casualties, who can lay legitimate claim to claiming that such decisions are unfair and inequitable. In addition, there is a lack of consensus on how to deal with policies that improve efficiency while increasing inequalities or those that improve fairness while decreasing efficiency.

It is therefore very evident that in setting the economic objectives of healthcare systems, both efficiency and equity considerations are vital components and must be given serious consideration. However, it is inevitable that in seeking to achieve a more equitable allocation of resources, a level of efficiency will have to be sacrificed, or, in attempting to move to a more efficient healthcare system, inequalities in provision or access to services may have to be compromised.

HTA and Pharmacoeconomics

The containment of public spending means that more attention is required in the allocation of resources to health technologies (drugs, medical devices, procedures, organizational, and management models).

The Health Services challenge is to respond to the stable increase in needs and demands faster than the available resources.

The increase in needs can be attributed to various causes. First of all, the aging of the population involves the management of diseases which, thanks to scientific progress, have become chronic.

However, the increase in needs is also associated with the introduction of new technologies. For instance, in the context of a previously incurable or under-treated pathology, the introduction of a novel effective intervention inevitably results in the onset of new needs.

The Health Services funders can control the increase in needs in a relative manner, by influencing, above all, the careful management of new technolo-

gies while promoting the abandonment of the most obsolete and redundant ones, thus ensuring the maximum value from the resources invested.

To promote the entry of a technology on the market, it is essential to demonstrate an adequate cost-benefit ratio to justify and promote the sustainability of current and future innovative technologies.

The Health Technology Assessment (HTA) is a multidimensional and multidisciplinary approach which is useful for evaluating the effectiveness, safety, costs, and impact of a new technology. For this reason, the HTA can support the decisions of payers and health professionals in making informed decisions about the adoption or rejection of a technology.

Therefore, it is configured as a bridge between the technical-scientific world and that of decision makers.

It also promotes the development of safe, effective, and patient-focused health policies by answering questions such as:

- Should this health technology be reimbursed by Health Services?
- Which patients would benefit from it?
- How long should they use it?

Three levels can be distinguished in which HTA activities can be carried out.

1. Macro: health policy decisions at national or international level. National governments evaluate how much funds should be allocated to health-care and how these should be distributed among the different Regions, taking into account the different needs and requirements.
2. Meso: political and operational decisions at regional or Health Authority level.
3. Micro: strictly related to operational decisions of the single department/area/healthcare professional.

The various situations have different needs, thus an HTA evaluation has to answer to questions regarding different problems.

Depending on the objective and the type of health technology to be evaluated, full reports or rapid reports may be created.

The choice of the assessment type to be conducted is dictated by the “policy question” (question to be answered by decision makers), by the “research question” (definition of the survey dimensions and expected results) as well as by the economic and human resources available.

In the case of a very broad policy question, such as the positioning of a technology within the National Health System (NHS), the full report is appropriate. It has to investigate different dimensions—domains—and to arrange the results in clinical practice by bringing out the scientific evidence, market analysis, and economic impact.

On the other hand, when there is a need to express a recommendation quickly (for example, a new technology just released on the market), the rapid report is more suitable as it addresses a more limited analysis on a lower number of domains with respect of the full report.

The European Union network of HTA organizations (EUnetHTA), that is the European network that connects many of the European HTA organizations, has developed the HTA Core Model to standardize the areas of assessment.

Each domain—or element of evaluation—provides an evaluation perspective and is organized into topics, each of which defines a more specific aspect of the analysis and comes from the answer to a series of questions (issues). Nine domains have to be analyzed in a full report, whilst for the drafting of a rapid HTA report, EUnetHTA suggests focusing on the first four domains as they are considered the most important and are easily extensible to other contexts.

Below, we report the list of domains to be analyzed in a full report.

1. Health problem and current use of technology (CUR): Provides important background information by giving an appropriate definition of the disease and the target population to which the technology is addressed. It defines health problem, epidemiology, impact of the disease on the individual and the community, way of use, life cycle, and regulatory aspects of the technology under consideration and its alternatives.
2. Description and technical characteristics of the technology (TEC): Describes the technology and its technical characteristics, outlining when it was developed and introduced, for what purpose, for what conditions, and at what levels of the NHS it will be used. The investments required for use in terms of equipment and staff are also reported. By means of small improvements, the evolution of a technology can lead to large changes in performance and indications. An accurate description of the technical characteristics of a technology allows differentiation from competitors.
3. Safety (SAF): Describes unwanted or harmful effects caused by the use of technology to patients, healthcare professionals, and the environment.
4. Effectiveness (EFF): Information relating to efficacy, safety, and efficacy-safety ratio are of greatest interest to the decision maker. Here, the clinical benefit (net of adverse events) deriving from the use of the technology in normal clinical practice (effectiveness) is evaluated. Patient-relevant outcomes such as mortality, morbidity, and quality of life are mainly considered.

5. **Costs and economic evaluation (ECO):** Is an important tool that can be used by decision makers, administrators, and health professionals to distribute the available resources effectively and responsibly. By identifying, measuring, evaluating, and comparing costs and outcomes of the technology under consideration, decisions are supported based on the “value for money” criterion. The information reported concerns the various types of costs (direct and indirect) and health outcomes. Data may be the result of systematic reviews of the literature or the critical review of one or more economic evaluation studies presented by the manufacturer. Data can also be based on the evaluations of *ex novo* studies based on decision-making models. Different economic analyses can contribute to the creation of a report (e.g., Cost-Effectiveness Analysis—CEA and Cost-Utility Analysis—CUA) and can differ on the basis of the measurement and enhancement of health outcomes. However, they all provide guidance on the most efficient way to allocate resources.
6. **Ethical aspects (ETH):** Addresses considerations regarding the social and moral norms relevant to the consequences of introducing and adopting the technology. It is particularly important, for example, for those technologies intended for fragile and seriously ill categories. In addition, it investigates the possible ethical consequences coming from that technology (e.g., genetic-based diagnostic tests or infertility treatments).
7. **Organizational aspects (ORG):** The implementation of the new technology may require a reorganization of the management of various resources—knowledge, economic resources, infrastructures, and health personnel. The organizational aspects considerably influence the possibilities of adoption and the performance of the technology in the clinical practice (e.g., a new drug that allows home administration instead of outpatient administration).
8. **Patient perspective and social aspects (SOC):** The perspective of patients and caregivers on the pathology and the technology provides a global view of the technology impact on daily life. Patient’s experiences with the previous technologies as well as expectations about the new one are reported. The information that patients receive regarding the use of the new technology is shown. On the other hand, social aspects are linked to groups of individuals who share a specific interest in the evaluation of technology (e.g., patients’ societies).
9. **Legal aspects (LEG):** The decision-making process requires that the legal aspects relevant to the introduction of the new technology be considered in addition to the roles and responsibilities of the actors involved.

The regulations that protect the patients' rights (informed consent, privacy) and those about the rights and duties of health professionals relating to the correct management of the new technology are identified (e.g., off-label use of the drug).

Pharmacoeconomics is one of the disciplines of HTA, through which it is possible to identify, measure, enhance, and compare the costs and consequences of the alternatives considered, with the aim of rationalizing health-care costs and freeing up resources to make the system sustainable.

Pharmacoeconomics

It is these issues that health economic evaluation seeks to address and, specifically in relation to pharmaceuticals, provides the underlying premise on which pharmacoeconomics is based. The term **pharmacoeconomics** has been coined to depict the economic assessment of pharmaceuticals, to evaluate the extent to which they provide additional benefits relative to the additional costs incurred. What is required is information that guides decision-makers as to which therapy provides the greatest bang per buck! In other words, is it worth paying more for the potential additional benefits which a new therapy offers when compared with existing treatments? The term **cost-effectiveness** has become synonymous with pharmacoeconomics and has been used (and misused) to depict the extent to which interventions measure up to what can be considered to represent value for money—what is the additional bang and what is the additional buck? Strictly speaking, however, CEA is one of a number of techniques of economic evaluation, where the choice of technique depends on the nature of the benefits specified. CEA has been defined by NICE as an economic study design in which consequences of different interventions are measured using a single outcome, usually in “natural” units (for example, life-years gained, deaths avoided, heart attacks avoided, or cases detected) and the interventions are compared in terms of cost per unit of effectiveness.

However, given that outputs and outcomes are highly specific and differ according to the nature of the condition, it is necessary to utilize “common currencies” so that apples and pears can be compared—that is outputs in obstetrics and gynecology need to be compared with outputs and outcomes in renal disease, care of the elderly, musculoskeletal disorders, etc.—so that the cost-effectiveness of an intervention in one therapeutic area can be

compared with the cost-effectiveness of an intervention in a different area. The usual common currency that is employed is that of the Quality-Adjusted Life-Year (QALY), which is derived by the combination of the impact of the intervention on both quantity and quality of life. A QALY embraces both quantity and quality of life and is the arithmetic product of life expectancy and a measure of the quality of the remaining life-years. It provides a common currency for measuring the extent of health gain that results from healthcare interventions and, when combined with the costs associated with the interventions, can be used to assess their relative worth from an economic perspective. The quantity of life, expressed in terms of survival or life expectancy, is a traditional measure that is widely accepted and has few problems of comparison—people are either alive or not. Quality of life, on the other hand, embraces a whole range of different facets of people's lives, not just their health status. Even restricting the focus to a person's health-related quality of life will result in a number of dimensions relating to both physical and mental capacity. A number of approaches have been used to generate these quality of life valuations, referred to as health utilities: for example, standard gamble, time trade-off, and the use of rating scales. The utilities that are produced represent the valuations attached to each health state on a continuum between 0 and 1, where 0 is equivalent to being dead and 1 represents the best possible health state, although some health states are regarded as being worse than death and have negative valuations. The specific type of cost-effectiveness analysis that is undertaken when using QALYs is referred to as CUA.

There may be occasions when the outcomes generated by interventions are virtually equal or at least very similar. In such circumstances it might be possible for a Cost-Minimization Analysis (CMA) to be undertaken, where only the cost differences between the interventions are needed to establish which of them provides the best value for money. However, caution should be exercised in relation to what is meant by equivalence or similarity—the condition for use of CMA is that the outcomes should be identical—since while both oral and IV modes of a drug can provide equivalent therapeutic outcomes, the outcomes from a patient's perspective can be very different.

In Cost-Benefit Analysis (CBA) the costs and outcomes are expressed in monetary terms, so as well as being able to make comparisons across all areas of healthcare, comparisons can also be made with programmes and schemes in education, transport, and the environment, for example. The difficulty arises, however, when trying to place a monetary value on the intangible benefits, where market prices do not exist. There are two main techniques

that can be used here: these are willingness-to-pay and discrete choice experiments.

What is important to bear in mind is that the aim of all approaches used to undertake pharmacoeconomic assessments is to maximize the level of benefits—health effects—relative to the level of resources available. However, the complexities and contentions relating to the assignment of monetary valuations to healthcare outcomes and the inadequacies of CEA and CMA has meant that CUA has become the primary technique used in conducting pharmacoeconomic evaluations.

Further discussion on these approaches forms the basis of the remainder of this book.

Sensitivity Analysis

Pharmacoeconomics is far from being a precise science and the findings emerging from such evaluations should be treated with a degree of caution. There is often considerable uncertainty associated with the findings with wide variation surrounding the results generated and it is therefore imperative that all pharmacoeconomic assessments should be subjected to a sensitivity analysis. The need for sensitivity analysis arises because of a number of factors:

- Methodological issues arising from different approaches and methods employed in the evaluation;
- Potential variation in the estimates of costs and effects used in the evaluation;
- Extrapolation from observed events over time or from intermediate to final health outcomes;
- Transferability of results and the validity of results from different populations/patient groups.

Therefore, the findings from cost-effectiveness assessments require some indication of the confidence that can be placed in them. What would happen, for example, if the “true cost” of one of the treatment strategies was somewhat higher or lower than the estimate used in the investigation or if there were significant changes in the life-years gained or other parameters used? Sensitivity analysis tests all the assumptions used in the model and enables the impact of changes on the baseline estimates.

More information on sensitivity analysis will be provided later in the book.

Summary

The decision-making process in determining which services and treatments should be provided is highly complex and involves a number of different, often conflicting, factors. The utilization of pharmacoeconomics can assist decision makers to utilize the information relating to the effectiveness and efficiency of an intervention. They can also go some way to contributing to the process of determining healthcare priorities and in seeking to ensure that the most efficient use is made of resources available within limited healthcare budgets. Healthcare professionals are increasingly being exposed to extremely powerful and emotive choices, and in no way can pharmacoeconomics provide the solution to such complex and difficult issues. What it does offer is a mode of thinking which can assist in arriving at possible solutions (notice the use of the term “assist” here—pharmacoeconomics cannot by itself offer the solutions, it has to be part of a wide-ranging approach to decision-making) to these often contentious problems. It aims at identifying which therapies would provide the maximum healthcare benefit for society within the envelope of resources available. It is the same process as we go through as individuals, in making that decision between a holiday abroad or a new kitchen—the one will provide us with significant benefits within a short period of time but the duration of these will soon diminish as we return to our normal existence. The kitchen, on the other hand, will provide fewer benefits immediately in comparison, but the duration of the benefits will extend for a number of years. The prices of the alternatives are basically the same but we can only afford one of them. What factors should be considered in making the decision? How should these difficult choices be made? How should it be decided which therapies to fund? The use of pharmacoeconomics techniques can help in making these decisions but they should always be just one part of a multi-faceted process, with other factors also being considered.

Questions

1. Tick all the correct sentences

- A. The opportunity costs are the benefits that are sacrificed when funds are used for other purposes
- B. In developing a cost profile, using resource data from other locations if local data are not available is wrong
- C. The term “efficiency” refers to the extent to which decisions relating to the allocation of limited resources maximize the benefits for society
- D. Cost-effectiveness is a type of efficiency

2. Tick the correct sentence about Health Technology Assessment

- A. It evaluates just the effectiveness of a new technology
- B. It cannot answer a question such as “Should this health technology be reimbursed by Health Services?”
- C. Full reports or rapid reports may be created
- D. It can be carried out just at national or international level

3. Tick all that apply to the EUnetHTA

- A. It is the European network that connects many of the European HTA organizations
- B. It has developed the HTA Core Model to standardize the areas of assessment
- C. It connects European and American HTA organizations
- D. It suggests focusing on the first two domains when drafting rapid HTA reports

4. Tick all the correct sentences

- A. A cost-effectiveness analysis is an economic study design in which consequences of different interventions are measured using a single outcome and the interventions are compared in terms of cost per unit of effectiveness
- B. QALY considers just the quality of life, while the quantity of life is taken into account by other measures
- C. QALY is the arithmetic product of life expectancy and a measure of the quality of the remaining life-years
- D. The Cost-Utility Analysis is a cost-effectiveness analysis undertaken when using QALYs

5. Tick all the correct sentences

- A. A Cost-Minimization Analysis may be undertaken if the outcomes are identical
- B. The Cost-Minimization Analysis permits to make comparisons across all areas of healthcare
- C. The Cost-Minimization Analysis has become the primary technique used in conducting pharmaceconomic evaluations
- D. All pharmaco-economic assessments should be subjected to a sensitivity analysis

Answers

- 1. A, C, D
- 2. C
- 3. A, B
- 4. A, C, D
- 5. A, D

References and Further Readings

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