

CHAPTER 1

Principles and methods

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INTRODUCTION TO PHARMACOECONOMICS



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This introduction describes the basic forms of economic evaluation, outlines the formal requirement for such studies and assesses whether the increased interest in economic analysis is favourable for patients, their physicians and society at large.

Given the limitations on healthcare resources, there is increased interest in assessing the value for money, or economic efficiency, of healthcare treatments and programmes. This is achieved through economic evaluation, where the costs and consequences of alternative treatment strategies are compared [1]. When economic evaluation is applied to pharmaceuticals, such studies often go under the term ‘pharmacoeconomics’.

WHAT IS PHARMACOECONOMICS?

The basic components of economic evaluation are shown in Figure 1. Here a new drug is compared with existing practice, which could be an older drug, a non-pharmacological intervention or, in the case of a ‘breakthrough’ drug, no active therapy.

In considering the costs and consequences, the two treatments will have acquisition costs, but the economic costs and consequences will be much broader. For example, if the new drug is more efficacious than current therapy, there may be savings in other healthcare costs, such as hospitalisations. Alternatively, if it has a better side effect profile, fewer drugs and procedures will be used in dealing with adverse events.

Since the comparison of treatments requires data on efficacy, the economic study usually builds on assessments obtained from clinical trials. Sometimes economic evaluations are conducted alongside a given clinical trial; these are trial-based studies. However, economic evaluations are

often undertaken based on data from a range of sources. If they make use of decision-analytical or epidemiological models they are called modelling studies.

Some economic evaluations adopt a broader societal perspective and consider costs falling on other government budgets, the patient, their family, or the broader economy, through patients or their carers being able to return to work if the treatment is sufficiently successful.

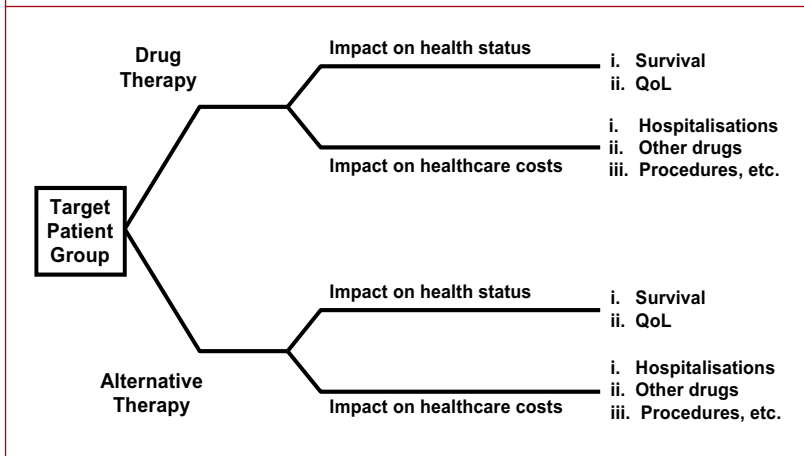
When the two treatment options being considered are clinically identical, the economic evaluation reduces to a comparison of costs only. However, this is rare and usually the difference in costs needs to be compared with an appropriate measure of the difference in consequences.

There are three main forms of economic evaluation. In cost-effectiveness analysis (CEA), the consequences are measured in the most obvious natural units of effects. In treatments for chronic renal failure, the most appropriate effectiveness measure would be years of life gained. But in a field such as asthma, the most appropriate measure may be ‘asthma-free days’ or ‘symptom-free days’.

However, this has important issues for interpretation, for instance if one drug is superior in some measures of outcome and inferior in others, how would one outcome be valued relative to another? One way around this would be to turn the problem back to the decision maker by just presenting the range of different consequences and asking for an overall assessment.

It is important to understand pharmacoeconomics methods and how these can be used to demonstrate value for money.

Figure 1: Basic components of economic evaluation



Alternatively, the various consequences could be combined in a single generic measure of health improvement. In cost-utility analysis (CUA), states of health are valued relative to one another through the use of health state preference values or health utilities. Then the superiority of one treatment over another can be expressed in terms of the quality-adjusted life years (QALYs) gained.

The use of a generic measure of outcome, like QALY, enables comparison of the value for money of interventions in different fields of health care. The QALY is useful when changes in quality of life are being traded with changes in survival. For example, a new cancer drug may be more toxic than existing therapy, thereby reducing the patient's quality of life during treatment, but may produce gains in additional survival.

In a cost-benefit analysis (CBA), the various consequences may be valued, relative to one another, in monetary terms. CBA is the broadest form of economic evaluation, since all costs and consequences are expressed in the same unit, i.e. money. Therefore, we can assess whether the total costs of an intervention are justified by its total benefits. This contrasts with CEA and CUA, where the assessment of value for money requires some judgment of what the unit of benefit, e.g. a life year or QALY, is worth to society.

WHO IS ASKING FOR PHARMACOECONOMIC STUDIES?

Australia was the first to use pharmacoeconomic studies as part of decision-making processes for new drugs. Since 1993 economic analysis has been a requirement in the information submitted by manufacturers to the Pharmaceutical Benefits Advisory Committee (PBAC), which advises ministers on whether new drugs go on the national formulary, the Pharmaceutical Benefits Schedule (PBS). Listing on the PBS ensures that the drug will be reimbursed [2].

Now Canada, Finland, New Zealand, Norway, Sweden and Scotland request economic data as part of their formal decision-

making procedures. In these jurisdictions all drugs, or all drugs used outside public hospitals, are included and in most cases the decision relates to reimbursement. In Scotland all drugs with a licence are reimbursed, but the Scottish medicines consortium issues guidance on their use under the National Health Service (NHS). In some cases the guidance is against use of the drug at all or for a range of indications narrower than those mentioned in the licence.

In England, Germany, Hungary, The Netherlands and Portugal, pharmacoeconomic studies are used for selected new drugs. In The Netherlands, a pharmacoeconomic study is requested only in situations where the manufacturer argues that the drug should not be clustered with existing drugs under the reference pricing scheme.

The National Institute for Health and Clinical Excellence (NICE) in England only requests an economic study if the new drug is likely to have a major impact on the NHS, either because it represents a 'breakthrough' in therapy, or because it has a much higher acquisition cost than existing medications for a given condition. Whether it is better to have a comprehensive or selective use of economic analysis is still a matter of debate [3].

In several jurisdictions pharmacoeconomic analyses are not required, but are used by manufacturers and decision makers on a voluntary basis. In the US economic data can be supplied by manufacturers according to a format devised by the Academy of Managed Care Pharmacy [4]. Voluntary use of economic analysis also takes place in Denmark, France and Italy. Whether there will ever be a formal requirement in these jurisdictions is uncertain, but the trend is for more jurisdictions to use economic analysis rather than less [5].

When pharmacoeconomic studies are formally required, the authorities usually issue a specification, or set of guidelines, for the submission of data. The existing published guidelines are broadly similar, but do differ in detail [6]. The set of guidelines developed by NICE [7] gives advice on the therapeutic strategies to be confirmed, the perspective for costing, the measurement and valuation of health outcomes and the characterisation of uncertainty.

A major issue arising from the formal use of pharmacoeconomics is that of deciding on what constitutes good value for money. More specifically, do decision makers have a threshold value, or maximum willingness-to-pay, for a unit of health improvement such as a QALY? Decision makers from NICE have suggested that the important range for decision-making is in the region of GBP 20,000 to GBP 30,000 (Euros 25,000 to Euros 38,000) per QALY [8, 9].

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The results of a study of 26 decisions on new drugs [10], made by the PBAC in Australia showed that if the incremental cost per life year gained is less than AUS\$ 40,000 (Euros 24,000), the Committee's decision is highly likely to be positive, whereas above AUS\$ 80,000 (Euros 48,000) it is highly likely to be negative.

The PBAC decision is largely related to the incremental cost-effectiveness ratio, however, there were several exceptions. A number of possible explanations have been offered for this. Firstly, although the results were presented as point estimates, there may be differing amounts of uncertainty associated with each estimate. Secondly, the Committee may be more likely to recommend listing if the drug is the only therapy available for a given group of patients, or if their health condition is very serious. Thirdly, they may be more likely to list if, in the absence of listing, the cost falling on patient is very high. The Committee may be less likely to list if, despite a favourable cost-effectiveness ratio, the overall budgetary impact is likely to be large due to the size of the patient population or if the drug is for a disease partly determined by lifestyle.

HOW DO NEW DRUGS FARE IN PHARMACOECONOMIC STUDIES?

The anti-tumour necrosis factors (TNFs) in rheumatology have been widely studied from an economic perspective. For example, in a CUA based on the ATTRACT study, Kobelt et al [11] found that infliximab had an incremental cost per QALY of GBP 34,800 (Euros 44,200) for two years' treatment, or GBP 29,900 (Euros 37,900) per QALY if productivity gains were included. This result is very close to the threshold, of around GBP 30,000 (Euros 38,000) per QALY, set by NICE and other reimbursement bodies. This suggests that the cost-effectiveness of the anti-TNFs for rheumatoid arthritis is close to the limits of what decision makers are willing to pay.

PHARMACOECONOMICS: FRIEND OR FOE?

Pharmacoeconomics represents another obstacle to the availability of new medicines. In jurisdictions using pharmacoeconomics, once a drug obtains a licence, or approval to market, a dossier must be submitted to a separate committee that will decide on reimbursement.

Often the indications for reimbursement, or guidance for use, will be narrower than the licensed indications. For example, NICE ruled that Cox-2 selective inhibitors should not be used routinely in patients with rheumatoid or osteoarthritis, but should be reserved for those patients that are at high risk of developing serious gastrointestinal adverse effects [12].

The requirement to undertake pharmacoeconomic studies gives manufacturers the opportunity to demonstrate the cost-effectiveness of their products. It is worth noting that many of those jurisdictions currently using pharmacoeconomics

have always imposed some limitations on the reimbursement of new medicines. It is by no means certain that the use of pharmacoeconomics makes these restrictions tougher.

Even in jurisdictions with no apparent restrictions on the availability of new medicines, covert rationing takes place because of financial considerations. In the UK this is called 'postcode rationing' since patients in one location can gain access to expensive new drugs whereas in another they cannot, because of the view decision makers take on the budgetary impact. Indeed this was one of the prime motivations for establishing NICE.

An alternative view of pharmacoeconomics is that, rather than limiting expenditure on drugs, it directs funds to those patients who

will benefit the most from new medications. It is generally true that expenditure on drugs is not decreasing in the richest European countries [13]. Therefore, in a world where reimbursement is driven by value for money considerations, the successful manufacturers will be those who focus on developing products that are cost-effective in a wide range of indications and patients. Indeed, this should be one of the main factors driving the drug development process. Such a shift in research priorities could be beneficial to patients, their physicians and society at large.

CONCLUSION

Depending on one's perspective, pharmacoeconomics could be considered to be a friend and a foe. However, the trend appears to be that more jurisdictions are using economic analysis as part of their decision-making procedures. Thus, it is important that those developing, or seeking to use, expen-



sive new medicines understand pharmacoeconomic methods and how these can be used to demonstrate value for money. Armed with this knowledge, hospital pharmacists can make well-informed recommendations for the hospital formulary.

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