

The evaluation and application of pharmacoeconomic studies

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This article, the final in the series introducing health economics for pharmacists, examines factors that pharmacists should consider when evaluating pharmacoeconomic studies and determining whether or not they are complete, accurate and relevant



This article describes some factors that pharmacists should consider when evaluating pharmacoeconomic studies and determining whether they apply to their endeavours to manage the entry of new drugs and develop formularies, for example. These principles can be applied to the published literature, National Institute for Health and Clinical Excellence guidance and promotional material produced by pharmaceutical companies. Furthermore, the issues raised in this article may help readers to design an economic element to their studies and audits.

No hiding place

The ideal health economic study should leave no hiding place. Economic analysis should reveal the assumptions and strategies surrounding resource allocation, which traditionally were implicit or covert.

Researchers should describe clearly the costs and consequences that were collected or estimated, the analysis they used¹ and the assumptions they made. If these are not stat-

ed and justified, a study's value in determining resource allocation for your trust may be limited, for the reasons described in this article. When reading promotional material, you may need to ask the company to justify and explain its methods, especially if some of the information is presented at meetings or "held on file".

Increasingly, companies use economic models run on spreadsheets that purport to quantify a drug's influence on your budget. It is just as important — perhaps even more so — to question the model underlying these bespoke programs as when reading a paper. After all, the assumptions may well be embedded in the program rather than set out in the methods section.

In particular, pharmacists need to consider whether the method used was appropriate, first, to answer the researchers' question, and secondly to answer the questions that arise in their daily work. For example, in a cost-minimisation analysis did the authors justify the supposition that the drugs were equally effective? A societal model, which considers the costs to the UK economy, may help decision making on a national level, but it may be of less value to an individual trust deciding whether the local drug budget can sustain the cost of a new medicine.

We estimated, for example, that the cost of providing and transfusing blood products was £898m during 2000–01.² Blood donors incurred a direct cost of £8.1m per year. Used leisure time and lost productivity accounted for £3.1m and £7.2m, respectively (see p42). Our study forms part of an accumulating evidence base that blood donation consumes considerable resources. Together with reductions in supply due to demographic changes and the risk of transmission of infections, this helped encourage a greater emphasis on blood conservation in the UK and Europe more widely.

However, pharmacists should consider the wider context if they wish to continue to influence the national debate about health policy. Pharmacists also need to consider how the data used in an analysis were collected. For example, were estimates collected alongside the clinical data in a prospective study or in an observational survey or from longitudinal databases, or did a panel of experts reach a consensus on the resources used in practice? The former is more rigorous; nevertheless, the other approaches can form the basis of valuable studies, provided the results are subjected to an extensive sensitivity analysis (see below).

The method section needs to justify the choice of any model — such as decision tree

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or Markov modelling (see p45).³ Models are invaluable in economic analysis, allowing researchers to examine costs of a subgroup or simulate a patient population over a longer period than is practical or ethical in a clinical study. For example, in the initial NICE deliberations about biopharmaceuticals for multiple sclerosis (MS), clinical trial data covered two years' use and there were no data for more than five years' follow-up.⁴ However, differences in the models used and the data included meant that results from the cost-effectiveness models often showed considerable variation, a point often noted by NICE. In other cases, a pharmaceutical company might commission a health economic analysis to meet NICE's requirements or to address a specific marketing issue, such as the launch of a competing therapy. Pharmacists must rely on their index of suspicion for any methodological or, more commonly, unintentional bias in these analyses.

Quality-adjusted life years (QALYs, see p46) are intended to offer a lingua franca for comparing costs of competing interventions. Nevertheless, pharmacists still need to cast a critical eye over the methodology. For example, in cost-utility analyses, disease-specific quality of life measures may be more likely than generic measures to reflect clinical benefits in that condition.⁵ As a result, quality of life comparisons of drugs for the same disease — asthma or depression, for example — may be better derived from disease-specific measures. However, generic measures help pharmacists compare the costs and benefits of competing studies from different therapeutic areas, for example, smoking cessation counselling, vaccination for a viral infection and increasing access to cholesterol lowering agents. Once again, pharmacists need to consider which is the most appropriate method to answer the research question.

— Fundamental questions

Thoma and colleagues suggest asking some other fundamental questions about each economic study.⁶ First, did the analysis provide a full economic comparison of the health care strategies and from which viewpoint? For example, was the study performed from the perspective of the NHS or society as a whole? Did it focus on direct costs to the NHS? Did it include indirect costs to the patient or society? Were costs to carers included?

These issues are of more than academic interest. A study that includes both direct and indirect costs can paint a different picture of cost-effectiveness to one that focuses on either alone. NICE estimated that the cost per quality-adjusted life year for drugs for MS was between £248,000 and £810,000, assuming five years' treatment.³ Based on the usual economic criteria, the MS treatments were not cost-effective.

However, some drugs — such as those for MS, Alzheimer's disease and some cancers — may have their greatest economic impact on areas outside the health budget. For instance, a new cancer chemotherapeutic agent may consume a large proportion of your drug budget but, because it allows people to remain at work longer, the increased cost is more than offset by tax revenues. In the case of MS, advocates of the biopharmaceuticals suggested that the treatment's impact on severity and (by avoiding severe disability) the personal social services budgets potentially offset much of the additional cost. As a result, the Department of Health implemented a collaborative risk sharing agreement with the manufacturer to fund the agent while further studies assessed the long-term effects.⁴ It is important to note, however, that arguments for and against funding a particular intervention on economic grounds potentially generate tensions between health care professionals' duty of care, the rights of the patient to receive care and the need to maximise the utility gained from each pound invested.

As mentioned above, a societal perspective or one that includes the costs to both the patient and the trust may be less relevant to a pharmacist's daily practice than an analysis that focuses on direct costs alone. However, a perspective is relative rather than absolute. As Richardson and Nord wrote: "Perspectives are not right or wrong; rather, each represents a different ethical position with respect to the appropriate basis for the evaluation of health states."⁷

Secondly, pharmacists should consider whether an analysis compared all the relevant clinical strategies and whether the study establishes the relative clinical effectiveness of each intervention. The latter is, perhaps, an especially salient point for new technology. A study that compares a drug with placebo, for example, to fulfil a regulatory requirement, may not be appropriate if a better agent is used in clinical practice. As a rule, the comparator should be the most widely used intervention, the most cost-effective or both.³ If the subject of an analysis is the gold standard, the next most commonly used or cost-effective approach should act as the comparator. This suggests that economic evaluations need to be up dated to stay relevant to the evolving evidence base. Against this background, pharmacists may need to examine the studies used as the basis of the analysis. There are relatively few studies in some areas, for example, mental health. In part, this dearth of data may reflect the problems associated with measuring effectiveness in these conditions.¹

Thirdly, did the study measure costs accurately and were data on costs and outcomes integrated appropriately? For example, did the study, if outcomes were assessed for more than a year, include discounting. In general, benefits that accrue more quickly are pre-

ferred to those that occur further in the future. On the other hand, we prefer to pay in the future — a tendency exploited in the high street with "buy now pay later" offers and customer credit. As a result, economic analyses discount costs and benefits. The annual discount rate recommended by NICE is currently 3.5 per cent.

— Relevance to practice

Moreover, pharmacists need to consider the costs and patterns of resources used in the study and compare these with those in their hospitals.³ Such an analysis helps answer other questions posed by Thoma and colleagues: do the results help care for patients in my hospital?² Can my patients expect similar benefits? Are the costs similar? You might need to perform a new "back of the envelope" analysis using the data in the paper to examine these issues.

Health economic studies performed in one country may not be directly applicable to another. In particular, researchers may not be able to export resource use collected in one country to another country. It is difficult, for example, to extrapolate conclusions from the US to the UK: the costs of drugs and other resources, the intervention thresholds and the insurance structure are radically different. Much the same applies to analyses performed in other countries in the EU. The acquisition cost of drugs is similar but, as parallel importing shows, not necessarily the same. Moreover, the cost of a clinician's time in, for example, Central and Eastern Europe is considerably less than in the UK. Indeed, the lower costs make Central and Eastern Europe an increasingly important site for clinical studies.

— Allowing for uncertainties

Fourthly, Thoma and colleagues suggest asking whether a study makes appropriate allowances for uncertainties. How much, for example, does changing the uncertain outcomes alter the results?⁶

Economic analyses are often surrounded by considerable uncertainty. For example, in some studies a panel of experts estimate costs that are not available from the literature. In other cases, the economists might have used non-randomised studies. As a result, a sensitivity analysis is essential. This varies the key results by a suitable amount — for example, two standard deviations — and determines the effect on the results. Economists regard those results that do not change significantly as being robust. For example, in an erectile dysfunction study, we performed sensitivity analyses on GP consultations, hospital outpatient visits and the probabilities of successful or continued treatment or switching treatment.⁸ We found that the results were insensitive to changes in most clinical outcomes and resource use, but sensitive to

the unit cost of outpatient consultations and the probabilities of successful and continued treatment.

Finally, are the estimates of costs and outcomes related to the baseline risk? Do incremental costs and consequences differ among subgroups? A compelling body of clinical and experimental evidence now suggests that toxicity and efficacy may differ according to patients' age, race, sex and genotype. This will, in turn, influence cost-effectiveness. Such stratification could become more important in the future following the increasing use of pharmacogenomic analysis.

For example, BiDil (isosorbide dinitrate plus hydralazine) recently became the first drug licensed specifically by the US Food and Drug Administration for a particular ethnic population.⁹ Some cases of non-response to antidepressants could result from patients expressing polymorphisms of cytochrome P450 isozymes that degrade the substrate drug more rapidly than the average rate in the population. In other cases, the polymorphism encodes a relatively ineffective variant, raising the prospect of increased toxicity.¹⁰ The impact of the genomic stratification on health economics will be an area of active research in the future, although maintaining equity as well as equality will be important. A study that suggests, for example, a new treatment is cost-effective one group of people but not another could become politically charged.

In the meantime, health economics will remain as influential as efficacy, safety and quality in determining whether, how widely and to whom, clinicians prescribe a drug. Pharmacists' growing influence on formulary decisions makes understanding the strengths and weaknesses of health economic studies essential. In the final analysis, however, the results of health economic studies are relativist rather than absolute, heuristic rather than didactic, they can guide but not dictate resource allocation. Pharmacists will still need to bring their clinical and scientific skills to bear when deciding which drugs to include on a formulary and how to make the most effective and efficient use of their drugs budget.

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