Prioritizing Investments in Health: Can We Assess Potential Value for Money?

INTRODUCTION

Several jurisdictions now use economic data in making decisions about the reimbursement of health technologies. Typically, guidelines for the conduct of economic evaluation accompany these policies[1]. These serve as guidance to manufacturers and sponsors of health technologies in making submissions to the relevant decision-making bodies[2].

The growing use of economic evaluation has led to increased scrutiny of the methodology and conduct of the studies. Therefore, this article assesses the capability of economic evaluation to deliver reliable and relevant estimates of the value for money of new health technologies by outlining the main methodological challenges and, where possible, indicating how they are being tackled. Where possible, examples are given from the rheumatology field.

KEY METHODOLOGICAL CHALLENGES

Making Indirect Clinical Comparisons

It is widely recognized that the most appropriate, and least biased, method for comparing alternative therapies is the randomized controlled clinical trial (RCT). However, in the context of reimbursement decisions, the relevant RCT may not have been performed. There are several reasons for this.

First, for reimbursement purposes, the relevant alternative to the drug, or other health technology, of interest is "current practice" (i.e., the most widely used therapy in the jurisdiction concerned). However, since most clinical trials of drugs are undertaken for licensing purposes, the new drug may have been compared with placebo, or an older therapy[3].

Second, decision makers may wish to compare 2 newly available therapies, e.g., two cyclooxygenase-2 (COX-2) inhibitors, where head-to-head studies may not be available. (This could be because such studies are difficult or costly to undertake, or because it is not possible to undertake trials of 2 investigational therapies.)

Third, the range of existing therapies may be quite wide, with different drugs being the therapy of choice in different jurisdictions. Therefore it is unlikely that the new drug will have been compared with every conceivable alternative [e.g., the first COX-2 inhibitors were only compared with a limited number of existing nonsteroidal antiinflammatory drugs (NSAID)].

When indirect comparisons are made, it is important to adjust for differences in the patients enrolled in the various trials, especially baseline risk. However, there is always the possibility that biases may be present. Nevertheless, a recent review of metaanalyses indicates that the results from indirect comparisons may not differ substantially from those obtained from head-to-head studies[4].

Determining Cost-Effectiveness by Patient Subgroup

Whereas the licensed indications for a new therapy may be quite broad [e.g., treatment of osteoarthritis (OA)], the criteria for reimbursement are often more restrictive. This is because the payers for health care want to direct the use of the therapy towards those patients for whom it represents good value for money. For example, the National Institute for Clinical Excellence in the UK decided that: "COX-2 selective inhibitors are not recommended for routine use in patients with rheumatoid arthritis or osteoarthritis. They should be used in preference to standard NSAID only in patients who may be at 'high risk' of developing serious gastrointestinal adverse effects"[5].

Whereas one might understand the authorities' interest in examining patient subgroups, existing trials may not be designed to enable a reliable subgroup analysis, nor sufficiently powered to detect clinically important differences between the therapies in each subgroup. Therefore, in the absence of trials focussing on the relevant subgroups, it will again be necessary to model comparisons using the best available data.

Projecting Beyond the Duration of Clinical Trials

In order to estimate the life-years or quality-adjusted life-years (QALY) gained by therapy, it is necessary to track benefits over a patient's lifetime. However, most clinical trials are of a shorter duration. For example, one of the clinical trials of anti-tumor necrosis factor therapy for RA lasted for one year, with an open-label extension[6].

Therefore the issue for economic analysis is what happens to patient benefit beyond the period observed in the trial. Is the effect seen at one year maintained, in which case the survival curves (of benefit over time) can be projected in a parallel fashion? Alternatively, is there a gradual decline in treatment effect over time (i.e., the curves moving together)? Finally, an extremely conservative assumption would be that no benefit is obtained beyond that observed in the trial (i.e., the curve for active therapy drops to that of placebo).

Although the projection of benefit beyond the period of the trial is probably the most important issue, other issues include the following: At what rate do patients discontinue therapy? If patients discontinue therapy do they experience the same benefit in the future as placebo patients, or is there a "catch-up" effect?

Measuring and Valuing Treatment Benefits

This issue has 2 elements. Whose values are the most relevant? Which is the most appropriate way to make the measurements? Regarding the first issue, health economists

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are fairly unanimous that society's values are the most relevant for reimbursement decisions[7]. However, patients' values might be the most relevant for choosing treatment clinical options within a given funding envelope (e.g., at the level of a clinical department).

With regard to the issue of measurement, the first question is whether health states should be valued relative to one another (e.g., through the estimation of health state preference or "utility" values), or whether they should be valued in money terms (e.g., through willingness-to-pay estimations). Currently, most reimbursement agencies prefer the "utility" approach, which enables the estimation of the QALY gained from therapy[1,2].

The second question relates to the choice of instrument. Currently, 2 generic instruments are in widespread use, the EQ-5D[8] and the Health Utilities Index[9]. Often, the choice between the 2 will be determined by the setting for the study, as the instruments derive their health state preference valuations (or "tariff") from different general populations.

Transferring/Generalizing Economic Data

Understandably, decision-makers expect to see data relevant to their own setting. It is usually assumed that, while clinical data may be generalizable across settings, economic data may not. For example, differences in the relative prices of resources, and differences in clinical practice patterns, can affect the relative costs, and cost-effectiveness, of therapies in different settings.

The most common way of producing economic data relevant to different locations is to build a flexible generic model that can be populated with data from different settings. An example in the field of rheumatology is the ACCES model, which has been used to estimate the cost-effectiveness of celecoxib, as compared with various NSAID, in a range of settings[10].

Dealing with Equity Issues

Whereas cost-effectiveness is a primary concern in reimbursement decisions, an analysis of decisions made by the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia suggests that other criteria are taken into account[11]. Many of these relate to equity concerns, such as the seriousness of the health condition and the cost that would be borne by the patient in the absence of reimbursement.

Some approaches to estimating health state valuations, such as the "person trade-off"[12], incorporate equity concerns relating to the seriousness of the health condition. Other economists have proposed a weighting of QALY, and positive discrimination in favor of those individuals who have not yet had the opportunity to live a long and healthy life[13]. This is known as the "fair innings" argument.

CONCLUDING REMARKS

Whereas the general methodology of economic evaluation in health care is fairly well specified, its use in reimbursement decisions has raised additional methodological challenges. This article has outlined a number of these challenges and the ways in which they are being addressed.

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