

Editorial

The use of quality-adjusted life-years in cost-effectiveness studies

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In this issue of *Allergy*, Briggs and colleagues present a cost-effectiveness (CE) analysis of salmeterol in combination with fluticasone propionate compared with fluticasone propionate alone in asthma patients. This is a CE analysis of the GOAL study,(1) which used a treatment strategy of aiming for guideline-defined Totally Controlled asthma. An important feature of that study is that health benefits to patients are expressed in terms of quality-adjusted life-years (QALYs). This editorial considers the growing use of QALYs to inform health service decision makers.

Unavoidable decisions

It is a reality for all health care systems that they need to make decisions about which interventions and programmes should be made available to patients from within their limited budgets. Internationally, many systems now use evidence on CE to inform these decisions. Such arrangements started with the public health systems of Australia (2) and Ontario, Canada (3) but now extend to a large proportion of systems in the developed world (4).

One feature of the use of CE studies in this context is that decision makers are usually having to assess competing bids for limited resources across a number of different specialties and clinical areas. For example, the National Institute for Health and Clinical Excellence (NICE) in the UK has recently used CE analyses to inform decisions about whether to support the use of new interventions in diverse areas such as Alzheimer's disease, asthma, various types of cancer, dermatology and heart disease (<http://www.nice.org.uk>). Given limited budgets,

if decision makers decide to cover or reimburse a new medicine in, say, Alzheimer's disease, any additional resources needed to do this will have to be found from existing activities. This might involve, for example, doing fewer hip replacements or coronary artery bypass grafts. The real cost of the decision to reimburse the new therapy for Alzheimer's is, therefore, the health benefits forgone by having to do less of some other activity elsewhere in the system – economists call this the 'opportunity cost'. The task of CE studies is to assess whether the benefits of reimbursing a new drug are greater or less than its opportunity cost. In order to do this, studies need to be able to compare the health benefits to Alzheimer's patients with the health disbenefits to patients who will not get (or will have to wait longer for) their hip replacement or CABG. This needs measures of health benefit which are 'generic'; that is, they can be meaningfully used in the full range of clinical areas. In other words, decision makers need CE studies to compare apples and apples rather than apples and pears!

What is a QALY?

The QALY is the most widely used generic measure of health benefit in CE studies. It has two important features which support its use to evaluate interventions across disparate areas of health care. The first is that it is able to combine the two dimensions of health: life expectancy and health-related quality of life (HRQoL). Figure 1 illustrates how these are brought together. The horizontal axis represents a patient's survival duration in terms of life-years. The vertical axis shows a patient's HRQoL on a scale running from 0 to 1 with higher scores represent-

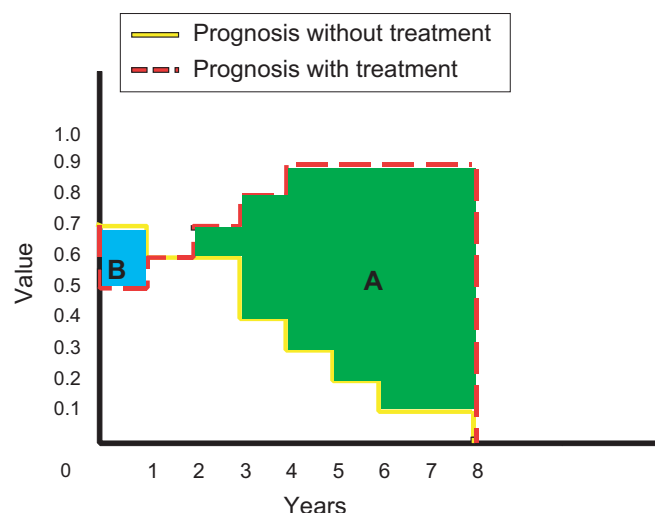


Figure 1. How quality-adjusted life-years are calculated.

ing better levels of HRQoL. An important feature of HRQoL for QALYs (which is sometimes called utility, preference or valuation) is that the 0 and 1 mean something very specific: these anchors are taken as equivalent to death and good health, respectively. It should be noted that the QALY also permits negative HRQoL values to represent extreme states of health which are considered worse than death.

Figure 1 shows the stylized prognoses of two patients – one who receives treatment (dotted line) and one who does not (continuous line). Without treatment the patient begins with reasonable HRQoL (around 0.7), continues at that level for about a year at which point it declines to around 0.6 for 2 years and then progressively worsens until the patient dies after 8 years. With treatment the prognosis is rather different. From the same HRQoL starting point as with no treatment, in this example it is assumed that the patient initially worsens (perhaps because of an adverse event) after which they progressively improve, reach a level of about 0.9 by year 4 where they remain until they too die after 8 years. A key feature of this example is that treatment confers no mortality benefit; but there is a difference in HRQoL. The QALYs for the two prognoses are the areas under the two curves, so the *difference* in QALYs between treatment and no treatment is the area A (the gain in HRQoL from treatment once the patient has recovered from the adverse event) minus area B (the HRQoL decrement of the adverse event).

The QALY, then, is a measure of life expectancy weighted by an index of HRQoL. It can be used to represent health benefits of interventions when there is no mortality effect which applies in the Briggs et al. asthma application in this journal, when there is a change in mortality but not in HRQoL, and when there is a (positive or negative) change in both. The QALY construct incorporates some strong assumptions about individuals' preferences regarding the trade-off between length and quality

of life (5). For example, in terms of QALYs, 5 years in good health is equivalent to 10 years at HRQoL of 0.5 and 20 years at 0.25 on the scale. Although these assumptions may be considered crude for *individual* decision making, it can be argued that these are necessary to make the measure a practical tool for group decisions about resource allocation.

Measuring HRQoL for QALYs

In order to calculate QALYs, suitable evidence is needed on mortality (available in most trials) and HRQoL. The latter is increasingly measured in trials in many clinical fields but, to be used in QALYs, HRQoL needs to be expressed on the 0–1 utility scale. One approach that has been used in trials is to use methods to get patients to give utility scores for their own health state at a given point of time. An increasingly popular alternative is to ask patients to complete a questionnaire which records information on their HRQoL using a set of standardized descriptions. For a given response, a utility can be attached based on the preferences of a separate group of individuals. The EQ5D is such an instrument which is widely used in trials (6). The instrument categorizes HRQoL into five dimensions each of which has three response categories. These describe health generically such that the instrument can be completed by a wide range of patients and nonpatients. On this basis, patients effectively define their HRQoL as one of 245 possible 'health states'. A utility score has been previously estimated for each of these health states based on interviews with representative samples of the general public. Such values are available for a number of countries including the UK, USA and Denmark (<http://www.euroqol.org/web/>). So from the HRQoL data from patients and the utility scores based on public preferences, QALYs can be calculated for samples of patients. There are arguments for and against the use of utilities elicited from the public as opposed to patients (7), and some health service decision makers have a stated preference about the source of these data (4). EQ5D data have been captured in trials and other studies in a range of clinical areas (<http://www.euroqol.org/web/>).

In the Briggs et al. CE study in asthma in this journal, no utilities were available from data directly collected in the GOAL trial. Given the importance of QALYs for CE analysis, however, these data were estimated from other HRQoL data collected in the trial, the Asthma Quality of Life Questionnaire (AQLQ), which does not generate utilities directly. This estimation was on the basis of a sample of nontrial patients who completed both the AQLQ and the EQ5D.

Making decisions with QALYs

Decision makers need to establish which of the range of new technologies available to the system, across a range

Table 1. Estimated incremental costs per quality-adjusted life-year (QALY) gained of a sample of health care interventions. Note that ratios will vary according to the comparator and the relevant patient group and are estimated with uncertainty [source Devlin and Parkin (10) and Ganz et al. (12)]

Relevant technology	Cost per QALY, £ (€)
GP advice to stop smoking	270 (397)
Seretide vs fluticasone (depending on strata)	7400–14700 (10878–21609)
Statins (simvastatin)	13995 (20573)
Donepezil in Alzheimers	15100 (22197)
Riluzole in motor neurone disease	34000–44000 (49980–64680)
Beta inteferon for MS	35000–105000 (51450–154350)

of technologies, represent sufficient value for money to be reimbursed or covered. Table 1 shows the estimated incremental costs per QALY gained of a sample of healthcare interventions, and places the results of the Briggs et al. comparison of Seretide and Fluticasone in the context of some other studies. How do decision makers decide which technologies to support? As described above, the value of the QALY is to make it possible to compare the benefits of new interventions with the benefits forgone from those programmes which have to be down-scaled or displaced to fund them. In practice, however, it is rarely possible to quantify the opportunity costs directly; indeed, these will vary between localities within a given jurisdiction. As a result, many healthcare systems seek to proxy the process by establishing a threshold monetary value for an extra QALY. If a particular intervention generates additional QALYs, compared with the other options available for the relevant patient group, at an additional cost which is less than the threshold, then it would be considered cost-effective. Such threshold values have been referred to in the literature for many years. Some healthcare systems are beginning to state their threshold. In the UK, for example, NICE has indicated that this lies in the range of £20 000 to £40 000 per QALY gained (8), although it emphasizes that there are additional factors that it takes into account in deciding whether a new technology should be recommended for the NHS.

Table 2. Classification of decisions made between 1999 and May 2002 by the National Institute for Clinical Excellence in the UK according to the estimated incremental costs per quality-adjusted life-year (QALY) gained [source Towse et al. (9)]

Cost per QALY, £ (€)	Accepted	Restricted	Rejected
<20000 (<29000)	14	3	1
20000–30000 (29000–43500)	0	4	0
>30000 (>43500)	1	4	3

This conceptual framework is supported in practice. Analyses of decisions made by NICE (9, 10) and the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia (11) suggest that the likelihood of positive decisions about new technologies is inversely related to the estimates of their incremental cost per QALY but, rather than a single threshold operating, there is more of a 'threshold region'. This is illustrated in Table 2 which shows the decisions of NICE between 1999 and May 2002 according to the estimated costs per QALY gained. Over time, the idea of a threshold becomes engrained in decision making about resource allocation, but it is important to recognize that, in principle, the threshold should change as the global budget changes and as healthcare technology develops.

In summary, CE analyses are increasingly being used to inform real decisions about the availability of new interventions in healthcare systems. The need to compare the benefits of new technologies with their opportunity costs requires a common measure of health benefit across different clinical areas. The QALY is widely used for this purpose, and the Briggs et al. CE study in this journal is an important contribution to the body of evidence on the CE of asthma therapies. The use of salmeterol/fluticasone propionate compared with fluticasone propionate alone results in an incremental cost per QALY gained that, based on what was described earlier, compares favourably with other uses of scarce healthcare resources that have recently been recommended by NICE.

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