

The models used for health economic analysis

By Mark Greener, BSc, and Julian Guest, PhD

This article examines the techniques used to compare the relative costs of pharmaceutical interventions. An understanding of these models can help pharmacists critically review data to make the most effective use of drug budgets



Purchasers and providers need to ensure the effective and equitable distribution of limited health care resources. Health economic analyses assess whether resource allocation fulfils these two critical criteria. In this article, the second of three introducing health economics for pharmacists, we explore the ways in which economists estimate the costs of competing technologies. We also review the most widely used measures that allow purchasers and providers to compare diverse interventions — for example, the relative health gain arising from screening for cervical cancer compared with active pharmacological intervention for reducing high blood pressure. Understanding the strengths and weaknesses of the different approaches should enable pharmacists to make their decisions on a rational basis and critically review the often conflicting claims made by different stakeholders.

— Economic modelling

Resource use is one of the building blocks that economists use to construct health economic models. Ideally, researchers collect resource use data prospectively alongside clinical data during a phase III study. This allows economists to correlate resources used with the associated clinical outcomes.

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When health-related quality of life (HRQoL) measures are used as an outcome, economists may be able to derive quality-adjusted life years (QALYs) or other utility measures (see below). Such studies are the gold standard economic evaluations, from which arguments for a particular technology may be compelling.

Economists generally perform such analyses after clinical studies have been completed and develop, for example, models which can examine the costs of a subgroup or simulate a patient population over a longer period than is practical or ethical in a clinical study.

In other cases, a pharmaceutical company may commission a health economic analysis to meet the requirements of the National Institute for Health and Clinical Excellence or to address a specific marketing issue, such as the launch of a competing therapy. In other cases, pharmaceutical companies commission evaluations years before a drug's possible launch to help inform the decision on whether to progress the drug into expensive and protracted clinical studies. In these cases, economists collect resource use from a range of sources, including statistics published by the Department of Health, interviews with clinicians and published, peer reviewed studies.

Economists use computer programs to model the drug's use in a clinic. They can employ any one of a number of programs depending on the nature of the study, the type of resources used, the study period and so on. This article will consider two of the most common health economic models: decision analytic models and Markov models.

— Decision analytic models

Decision analytic models employ a tree-like structure with a probability associated with each bifurcation. The clinician makes a decision at the initial node. Based on a series of subsequent events, the associated probabilities and resource use, an economist can associate a cost with each possible outcome. For example, we used a decision tree to compare three treatments for erectile dysfunction, Viridal Duo, MUSE and Viagra.¹

In the model, treatment could be successful or fail. Seven out of 10 patients are expected to respond, so the probability that the clinician will decide to continue treatment is 0.7 (we assume the clinician is rational). Experiencing an adverse event — another bifurcation — could have a probability of 0.2. Therefore, the clinician needs to decide whether to withdraw therapy or switch. This forms another bifurcation, each with an associated probability: 0.2 and 0.8, respectively. Ultimately, the economist can determine which represents the best value for money.

— Markov models

Markov models are a different type of analytic model that economists use in particular circumstances, such as when some events are time sensitive. For example, Markov models allow economists to examine probabilities that are continuous over time rather than being associated with the need to make a decision. Markov models are also valuable

when the timing of clinical events is important and when the key events potentially occur at least twice. Incorporating time-sensitive events in a traditional decision tree often means over-simplifying assumptions² undermining a study's validity.

Markov simulations, decision analytic trees and other computer models include numerous assumptions and inferences. As a result, well-designed economic studies include sensitivity analyses, which vary key assumptions to test the robustness of the results. For example, sensitivity analyses for the erectile dysfunction study varied assumptions about GP consultations, hospital outpatient visits, and the probabilities of successful treatment, continued treatment or switching treatment. We found that the results were insensitive to changes in the use of most clinical outcomes and resources, but sensitive to the unit cost of outpatient consultations and the probabilities of successful and continued treatment.¹ A comprehensive sensitivity analysis is one hallmark of a well-designed study. The final article in this series considers some others and discusses how pharmacists can evaluate economic analyses.

— QALYs

Most health economic studies aim to define which of several competing technologies produce the greatest health gain for each pound invested. This requires a common measure that translates health gains into a common value across different diseases, conditions, outcomes and interventions.⁴

The QALY is the most widely used of these measures. By definition, death or a year in a coma is zero QALYs. A year in perfect health is one QALY. Almost all of us experience minor physical and psychological ailments and injuries over a year. Therefore, an individual's QALY falls between these two extremes and can, in theory at least, have a negative value ("a fate worse than death"). The importance of QALYs arises, in particular, from their ability to encompass a variety of factors that potentially impact on HRQoL, including physical mobility, the ability to perform activities of daily living, the absence of pain, anxiety and depression and so on.⁵ As a result, QALYs are based on HRQoL assessments.

NICE, which uses this approach exten-

sively, regards a QALY lost or gained in a particular disease as being equivalent to that in another.⁵ Furthermore, NICE regards QALYs as equivalent regardless of how many QALYs a patient had in the past or has to come, their age and sex, how "deserving" they are and any deprivation in other aspects of health.⁵

— QALY thresholds

In other words, a QALY gained by screening for cancer represents the same "value" as that gained by a potent new antihypertensive. However, if screening costs £5,000 per QALY and a new antihypertensive costs £50,000, the former is the better value: it produces the greatest health gain and the lowest opportunity costs (see p42) for each pound invested. Purchasers can invest the other £45,000 in other interventions. Decisions based on economic studies rarely save money. Rather, they release money for investment elsewhere.

In other words, the implicit assumption is that purchasers and providers should prefer technologies with a low cost per QALY to those with a high cost. Transferring resources from high to low cost per QALY interventions will increase overall health gain (other things being equal). Eventually, the cost per QALY for each technology will reach equity.⁶

Following this logic, a threshold emerges above which a technology will not be used.⁶ NICE generally considers interventions that show incremental cost-effectiveness ratios between £5,000 and £15,000 per QALY as being cost-effective. It probably would not reject a technology with a cost-effectiveness ratio in this range on cost grounds alone.⁵ On the other hand, it tends to judge technologies with cost-effectiveness ratios over £25,000 as not being cost-effective.⁵ As a result, NICE would need compelling reasons to accept the technology, such as proven efficacy and a lack of any alternative.⁵

In between these two thresholds, the judgement about whether to recommend a technology depends on numerous factors, such as the uncertainty surrounding the estimate, the condition and patient population as well as how innovative the approach is. NICE also considers, when appropriate, wider societal costs and benefits, and previous appraisals.⁵ As a result, in some cases, the cost per QALY can be well above the upper threshold, such as the screening of donated blood for pathogens.⁷

Nevertheless, implementing decisions based on QALYs is not always easy and purchasers and providers can find themselves on the horns of an ethical dilemma. Assume for the sake of argument, that a licensed medicine for a chronic disease shows a cost per QALY of £80,000. The treatment is not cost-effective and purchasers take the decision not to fund the medicine. However, assume some people are already on treat-

ment. Should treatment be withdrawn from patients already receiving it? Should people established on treatment be allowed to continue but new courses stopped? Should everyone be allowed to receive it? This choice between these competing options is not economic: it is a value judgement.⁶

For example, is it ethical to withdraw treatment from patients who are already benefiting? Allowing some patients to receive the drug may, strictly, go against the ideas of equity and distributive justice that lie at the heart of the NHS. Economists can only provide information to inform choice. The decision cannot be based on analysis alone.

— Risk and QALYs

Some economists criticise QALYs on various grounds. One of the most fundamental arguments is that QALYs do not account for attitudes towards risk. Assume, for the sake of argument, I offer you £100 now or £200 if I flip a coin and it comes up heads. If the coin comes up tails, you get nothing. If you take the £100, you are risk averse.⁸

Conventional QALYs assume that people are risk neutral. Imagine the Grim Reaper gives you the choice of living five years or 10 years if he flips a coin and it comes up heads. If it is tails, he wields the scythe now. Conventional QALYs assume that, other things being equal, people do not care one way or the other. They have no preference for living five years or for flipping the coin. The Grim Reaper can choose.

Numerous studies, however, suggest that patients and society are risk averse when comparing choices that influence life span. Most people would choose to live the "guaranteed" five years, rather than flip the coin. In other words, the utility that a patient gains from an extra year of life is lower than the utility lost if life is a year shorter. To put it another way: assume a drug produces a range of outcomes. Group one experiences a below average level of benefit. Group two experiences an above average level of benefit. Because we tend to be risk averse, group one loses more utility than group two gains.⁹

To reflect this risk adversity, economists sometimes modify QALYs to place more weight on immediate than delayed outcomes. Once you consider risk adversity, a study's result can change dramatically. QALYs derived using a risk-neutral Markov model suggested surgical management was superior to expectant management (watchful waiting) for benign prostatic hypertrophy. However, after including mild risk aversion expectant management emerged as superior. Weighting QALYs in this way seems particularly appropriate for decision models where one or more options is associated with a short-term risk of morbidity or mortality.¹⁰

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— Rivals to QALYS

Due to the limitations of QALYS, economists have devised other utility measures. Disability-adjusted life years (DALYs), for example, measure loss of healthy life rather than life years gained.¹¹ However, DALYs attracted considerable criticism. Critics note, for example, that DALYs are based on limited data. DALYs may also obscure the distribution of disease and include social and economic value judgements. Critics contend that these issues compromise DALYs' ability to act as a rationale guide to resource allocation.¹²

Healthy year equivalents (HYEs) consider a sequence of health states, rather than considering each year individually as is the case with QALYS. Furthermore, HYE, unlike QALYS, fully represent individuals' preferences.¹³ Assume for the sake of argument that economists enrol a group of patients who have lived with a disabling disease for three years. Using specific measures, the economists can determine how many years of healthy life the three years with the disability is equivalent to — six HYE for example. In contrast, QALYS rate a disease's impact over a year irrespective of how many years the patient has suffered. However, HYE are complex to measure and economists rarely use them in economic studies.³

In other words, QALYS are far from perfect but so, too, are the main alternatives. In addition, QALYS benefit from the support of a wide and growing evidence base. To paraphrase Churchill's comment about democracy: no one pretends that QALYS are perfect or all-wise. Indeed, QALYS are the worst way to compare competing health care technologies — except all those other forms that have been tried from time to time.

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