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REVIEW ARTICLE

Economic Evaluation for Ophthalmologists

Hannah Kuper
International Centre for Eye Health, London School of Hygiene & Tropical Medicine, London, UK

Mireia Jofre-Bonet
International Centre for Eye Health, London School of Hygiene & Tropical Medicine, London, UK, and Moorfields Eye Hospital, London, UK

Clare Gilbert
International Centre for Eye Health, London School of Hygiene & Tropical Medicine, London, UK

ABSTRACT *Purpose*: This review will describe the basic concepts of economic evaluation, using examples from the ophthalmic literature. The aim is to provide readers with knowledge about the fundamentals of economic evaluation to enable them to read papers critically, make healthcare funding and planning decisions, and understand the economic evaluation of interventions. *Review*: Ophthalmic services are often constrained by a lack of funding, and this is true in both high- and low-income countries. Ophthalmology also competes with other healthcare specialities for funding. Economic evaluation is used to identify the most efficient way of allocating and planning the use of these scarce resources among alternative activities. An economic evaluation is typically conducted by comparing two or more interventions in terms of their effectiveness and their cost. Cost is the value of all resources used in the intervention. Effects, or consequences of the intervention, can be measured in monetary terms, through disease-specific outcomes or using health-related quality of life measures. The four most commonly used types of economic evaluations are cost-minimization analysis, cost-benefit analysis, cost-effectiveness analysis and cost-utility analysis. There are a variety of intended and unintended consequences of a health intervention, and so the consequences of the intervention may be positive or negative. Economic models, such as decision trees and Markov models, calculate effectiveness and costs, taking into account all the consequences of the intervention, including complications. Uncertainties in the parameters of the models can be expressed through sensitivity analyses and confidence intervals. *Conclusions*: Economic evaluation may be used to identify the most efficient way of allocating scarce resources among alternative activities. Its use, if standardized in all areas, can improve the quality of care while enhancing efficiency and thereby enabling more programs to be funded.

KEYWORDS Cost effectiveness; cost utility; cost benefit analysis; economic evaluation; healthcare utilization; ophthalmology; quality-adjusted life years

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Correspondence to: Hannah Kuper, Int. Centre for Eye Health, London Sch. Hygiene & Tropical Med., Keppel Street, London, WC1E 7HT, U.K. Tel.: +44-(0)20-7958-8170; Fax: +44-(0)20-7958-8325. E-mail: hannah.kuper@lshtm.ac.uk

INTRODUCTION

What Is Economic Evaluation and What Are Its Uses?

Demand for ophthalmic services has increased throughout the world as the magnitude of visual impairment has risen.[1] At the same time, new diagnostic methods and interventions are being introduced, such as lasers for the treatment of diabetic retinopathy, expanding the range of conditions where treatment is now possible. This increased need for services is unlikely to be matched by increased funding, and so ophthalmic services will become constrained by a lack of resources, whether in high- or low-income countries. Difficult decisions therefore need to be made about how to allocate scarce resources between different activities, such as health promotion, screening, curative services, or rehabilitation. Ophthalmology also competes with other healthcare specialities for funding. Economic evaluation is a component of health economics, where the costs and consequences of alternative courses of action are compared to provide evidence to help policy makers and healthcare planners make these decisions.[2]

The growing financial constraints have occurred at the same time as an increasing interest in evidence-based practice, which includes the need to show value for resources consumed. This is done in a formal way in the UK by the National Institute for Health and Clinical Excellence (NICE), an independent organisation responsible for providing guidance to the National Health Service on the cost-effectiveness of health care interventions (www.nice.org.uk). NICE has made recommendations for ophthalmic care based on economic evaluations (e.g., recommending the use of photodynamic therapy for a specific modality of age-related macular degeneration). Economic evaluation components have been added to many health-related studies as a result of these developments.

TYPES OF ECONOMIC EVALUATION

An economic evaluation is typically conducted by comparing two or more interventions in terms of their consequences (effectiveness) and their cost. This allows identification of the intervention that produces the best results for a given cost, so that programme planners can choose where to invest their resources. Economists always use a comparator for the intervention that they are investigating. They usually compare a new intervention with the best possible practice, or else with the most commonly used intervention. Occasionally, economists compare the cost and effectiveness of the intervention with that of doing nothing.

There are four basic types of economic evaluations: cost-minimisation, cost-benefit, cost-effectiveness, and cost-utility. In a cost-minimisation study there is evidence that the various interventions are equally effective, so that the only difference between the interventions is their cost and the choice is then guided by the one that costs the least. In most circumstances we cannot assume that different interventions are equally effective and so we need to compare both the consequences and the costs. The consequences of an intervention can be measured in a number of ways, and this is the basis for the classification of different types of economic evaluation. In a cost-benefit analysis the outcomes are measured in terms of a monetary value, while in a cost-effectiveness analysis consequences are assessed through disease-specific outcomes (e.g., number of cases of blindness), and in a cost-utility analysis generic utility measures are used (e.g., Quality Adjusted Life Years–QALY).[3] This will be described in more detail below.

MEASURES OF COST

What Is Cost?

The cost of an intervention is measured in all types of economic evaluation.[3] Cost is the value of all the resources used in the intervention, including salaries, medication, time costs and so on. For instance, the costs of the Gambia Eye Care Programme include the costs of salaries for personnel, ophthalmic and other equipment, drug supplies and materials, water and electricity, land, rent, transport, training of eye and medical staff, running costs, telecommunication, equipment maintenance, patient feeding, administration, and hospital improvements.[4] The proper price for a resource should include the value of all the foregone benefits because the resource is not available for its best alternative use, and this is called the "opportunity cost".[3] For the Gambia Eye Care Programme the opportunity costs include the value of work-time, materials, medications, space, and so on, as they were not available for an alternative use. These costs should be valued by market prices.

Whose Cost Is It Anyway?

Costs (and consequences) of an intervention are incurred by patients, providers, and also by other third parties, such as insurance companies, governments, or family members who take care of the patients.[3] In an economic evaluation, the costs (and consequences) can be calculated from each of these perspectives. For instance, from the perspective of the provider, the costs of medical equipment are included, while from the perspective of the patient, the patient's travel costs are included, although they would not be from the perspective of the provider. The gold standard is the "societal" perspective, which includes the totality of costs incurred by the intervention. This will include the costs sustained by the healthcare providers, patients, governments, and all others, and so the societal viewpoint is always the broadest one. It is often very difficult to calculate costs from the societal perspective, as it is difficult to collect all the data on costs incurred, and so costs are often presented from the provider perspective, because these are more readily available and transparent. Costs should be calculated over the period during which all the resource impacts and main health effects are likely to occur.

Direct Costs, Indirect Costs and Productivity Costs

Costs are often divided into "direct" costs and "indirect" costs.[5] Direct costs are those that arise directly from delivering the intervention, plus the administrative and overhead costs of the hospital. The direct costs for cataract surgery may include capital costs (building, land, equipment, electrical installations); utilities (water, electricity); direct materials (intraocular lenses, medicines, consumables, surgical equipment); and labour, overheads, and patient's costs (spectacles and medicines).[6] Indirect costs arise from productivity gains or losses related to illness or death, but this term can be confusing because it has many different interpretations. Instead, we may wish to consider using the term "productivity" costs, which refers to changes in productivity on account of morbidity and mortality, such as the lost income that patients incur because of their time spent at the hospital.[5] This is the opportunity cost of time.

MEASURES OF OUTCOMES OR EFFECT

If we cannot assume that two interventions are equally effective then we must measure the consequences as well as the costs of the intervention.

Monetary Value of Outcomes

Economists attempt to assign a monetary value to the outcome of interventions, so that the consequences and costs of two interventions can be compared in a cost-benefit analysis.[3]

One way of assigning value to an intervention is through the "willingness to pay" approach, where people are asked how much they would pay for a certain treatment, such as a cure for their blindness.[3] Jampel et al. evaluated the amount that glaucoma patients were willing to pay for eyedrops with different characteristics.[7] They found that patients were willing to pay more for drops that did not produce blurring or drowsiness and did not inhibit sexual performance. An alternative method is the "human capital approach", where the outcome is valued in terms of the increased productivity generated by the treatment.[3] As an example, for a cataract surgical programme we can estimate how many people have regained their sight and how many of them are working again as a result of the surgery. We can then estimate the increased productivity generated by the programme by calculating how much money these people will earn over the remainder of their lifetimes, whereas without surgery they would have had no income.

Disease-Specific Outcome Measures

We cannot always convert outcomes of interventions into monetary benefits. Measuring the disease-specific outcomes, such as the number of cases of blindness averted, is often more intuitive.[3] Using a disease-specific outcome to measure the consequences of an intervention produces a cost-effectiveness analysis.

Health-Related Quality of Life and Health Utilities

Health-related quality of life and health utilities are generic measures that consider both the effect of a health intervention in terms of extension of life years and the impact on quality of life during those years.[3,8,9] These measures allow us to compare the value of different interventions targeted at different diseases, which is not possible with disease-specific outcome measures. This type of analysis is a cost-utility analysis.

The measurement of health-related quality of life usually requires the development of questionnaires to assess the patient's perception of illness and its impact on his/her life. This can be done through descriptive assessments or utility-based assessments. Descriptive assessments attempt to describe the different dimensions of living with a given disease for an individual. Typically, this type of assessment measures a person's physical and mental functioning using a battery of questions, which are then scored. An example of this kind of assessment is the EQ-5D, which scores an individual on five self-reported domains: pain/discomfort, anxiety/depression, mobility, self-care and usual activities.[10] A study in Spain showed that people with seasonal allergic conjunctivitis had significantly lower quality of life scores than age-matched controls on the domains of self-care, usual activities, pain/discomfort and anxiety/depression, but not for mobility.[9]

Utility-based assessments of health-related quality of life assess what it is like to live with a medical condition as reflected in an overall summary score. This approach tries to determine how patients value their health state. Scores for utilities range from zero (death) to one (perfect health) with all other health states lying between these boundaries. Scores for different conditions can be derived by a variety of methods: for instance, blindness has a utility value of 0.39, while systemic arterial hypertension has a utility value of about 0.95.[9,11,12] Two frequently used methods to assess utilities are the "Time Trade-Off" and the "Standard Gamble". In the "Time Trade-Off", the participant decides what proportion of their remaining years of life they would be willing to trade for perfect health instead of a particular health state. The utility value is calculated by subtracting the proportion of the remaining years of life they would be willing to trade from 1.0. Willingness to trade 7 of 20 remaining years of life to reverse visual impairment would imply a utility value of 0.65. The "Standard Gamble" approach uses hypothetical lotteries as a means of measuring people's preferences. An individual is asked to choose between the certainty of surviving for a fixed period in a particular state of ill health and a gamble between surviving for the same period without disability on the one hand and immediate death on the other. The probability of immediate death is then varied until the person shows no preference between the certain survival with the disability and the gamble. This percent risk accepted is subtracted from 1.0 to yield the utility value. For instance, willingness to accept a 15% chance of immediate death to ensure perfect vision among those with visually impairing cataract would imply a utility value of 0.85.

Once health-related quality of life measures are obtained, Quality Adjusted Life Years (QALY) can be calculated. A QALY is a function of length of life as well as the quality of life: living in perfect health for one year would score one QALY, equivalent to living at a health state of 0.5 for two years or a health state of 0.25 for four years. The impact of an intervention in terms of QALYs gained takes into account both the amount that life has been increased and the amount that quality of life has improved as a result of the intervention. QALYs gained can be compared for different interventions.

DISCOUNTING

We value current benefits more highly than future benefits, and future costs are less important to us than current costs. There are several reasons for this: first, inflation means that a unit of currency will buy more today than it will in ten years; second, we live in the moment and are unsure about the future and so we would like to defer costs to the future but enjoy benefits now. Lastly, there is the opportunity cost of investing money–a monetary unit that we have now can be invested and earn interest. As a result of this, economists discount future costs and benefits. The discount rate used is typically the real rate of interest, which subtracts the inflation rate from the interest rate, although other discount rates can be used.[13] As an example of discounting costs, the present value of an intervention that will cost \$100 today, \$200 next year and \$300 in the second year, with a discount rate of 5%, would be: $100 + .95 \times 200 + .90 \times 300 = \$563$ rather than \$600

$$PV\,Costs = 100 + \frac{200}{1+0.05} + \frac{300}{(1+0.05)^2} = \$563$$

if we had to pay for the total costs of the intervention today. Discounting may have a large effect on the results when costs or outcomes occur far in the future, such as for paediatric screening programmes or ocular hypertension treatment.

CHOOSING BETWEEN ALTERNATIVE INTERVENTIONS

Economic evaluators measure the costs and consequences of an intervention, so that they can compare different interventions to identify the best way to allocate scarce resources.

Cost-Minimisation Analysis

In a cost-minimisation study, there is evidence that the various interventions are equally effective. This evidence is usually obtained from equivalence trials or randomised controlled trials. This means that the only difference between the interventions is their costs and the choice is then guided by the one that costs the least. As an example, Rouland et al. conducted a randomised controlled trial to compare the costs and effectiveness of two methods to treat patients with ocular hypertension or primary open-angle glaucoma (brinzolamide or dorzolamide).[14] They found that the treatments were equally effective and so the only difference between the treatments was the medical costs accrued. One of the treatments (brinzolamide) was cheaper than the other (dorzolamide) in all four of the European countries included in the study, and so it became the recommended treatment.

Cost-Benefit Analysis

In a cost-benefit analysis, the costs and consequences of the intervention are assigned a monetary value and the net benefit is calculated, which is the total value of all the benefits minus the total value of all costs.[3,4] If the net benefit is greater than zero then the programme or treatment is worth undertaking, while if the net benefit is less than zero the money should be used elsewhere. The net benefit of two interventions can be compared, for instance by comparing the internal rate of return, which provides an indicator of the benefit per monetary unit invested in a programme. Not all programmes with a positive net benefit will necessarily be considered worth implementing if there is competition for limited resources, but the World Bank considers an internal rate of return on investment greater than 10% as very favourable.[15]

A cost-benefit analysis of the Gambian Eye Care Programme compared the cost of the programme to the monetary benefit in terms of life-time productivity gains.[4] The internal rate of return was 10%, making investment in the Gambian Eye Care Programme worthwhile, even using a limited measure of benefit.

Cost-Effectiveness Analysis

In a cost-effectiveness analysis, the costs and effectiveness (in terms of the disease-specific outcomes) of one intervention are compared to those of the benchmark intervention.[3] We do this by calculating the Incremental Cost-Effectiveness Ratio (ICER), which is the difference in cost between the benchmark and alternative interventions, divided by the difference in effectiveness. That is,

$$ICER_{\text{benchmark versus alternative}} = \frac{[Cost_{\text{alternative}} - Cost_{\text{benchmark}}]}{[Effect_{\text{alternative}} - Effect_{\text{benchmark}}]}$$

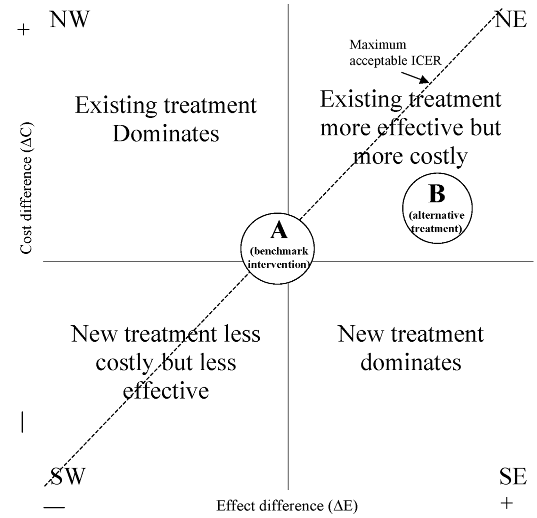

FIGURE 1 **The cost-effectiveness plane.**

This is illustrated by a cost-effectiveness plane, where the x-axis shows the difference in effectiveness and the y-axis the difference in costs between the two interventions (Fig. 1).[16] The benchmark intervention is placed at the origin (A) of the plane. We can use the difference in costs and effectiveness between the interventions to plot the alternative intervention in relation to the benchmark (B), with the slope of the straight line from the origin to the plotted point showing the ICER. If the alternative is both cheaper and more effective than the benchmark, it will be in the Southeast quadrant of the cost-effectiveness plane. In this instance, the alternative treatment would always be preferred to the benchmark treatment. If the alternative is more expensive and less effective than the benchmark, then it will be in the Northwest quadrant and the benchmark would always be preferred to the alternative intervention. The choice between the two interventions is more difficult when the alternative is in the Southwest quadrant (i.e., less effective but also less expensive) or the Northeast quadrant (i.e., more effective but also more expensive). In the case of the Northeast quadrant, we have to decide whether it is worth paying extra for the extra benefit. In the Southwest quadrant, we have to decide whether we are willing to accept an alternative that is cheaper but also less effective. The dashed line on the cost-effectiveness plane indicates the maximum acceptable ICER (or hypothesised ceiling ratio) in the Northeast and Southwest quadrants, which represents the maximum that society is willing to pay for a unit of effect, beyond which the gain in outcome is not considered to be worth the extra cost.

James et al. conducted a study to compare the cost-effectiveness of systematic photographic screening for sight-threatening diabetic eye disease to existing opportunistic programmes.[17] The systematic screening programme used primary-care-based photographic screening through a mobile screening unit together with a dedicated hospital assessment clinic. They calculated the cost-effectiveness of each method by dividing the total cost of the programme by the number of true positives detected. Since the standard practice in the UK was opportunistic detection, this was the benchmark intervention (A), while systematic screening was the alternative (B). They found that the total cost was slightly higher for systematic screening ($183,300) than for opportunistic screening ($174,600), but more cases were detected through systematic (502) than opportunistic screening (346). The cost per true positive case detected was lower for systematic screening ($365) than for opportunistic screening ($505). The incremental cost-effectiveness was calculated as the extra cost needed to generate each additional true positive result after replacing opportunistic screening by systematic screening. In this study, the incremental cost-effectiveness was $56, making systematic screening the more cost-effective option (i.e., it is in the NE quadrant but below the maximum ICER).

Cost-Utility Analysis

In a cost-utility analysis, the cost per QALY gained from one intervention compared to another is calculated. For instance, we can compare the cost per QALY gained of screening diabetics every two years versus every three years for diabetic retinopathy, or versus no screening programme. This can be compared to the cost per QALY of other interventions in a league table, which is a table ranking different types of medical interventions in terms of cost per QALY gained. To maximise health gains, interventions that provide QALYs at a lower cost should be prioritised first, before moving on to more expensive interventions until the maximum accepted cost per QALY is reached. Policy makers and society should decide what level of cost is affordable. The threshold is usually on the order of $100,000 per QALY gained in high-income countries,[18] although there is a lack of consensus about this threshold as some commentators argue that it is too restrictive and out-of-date.[19]

Busbee et al. compared the cost-utility of ocular interventions.[20] They found that the cost per QALY gained from paediatric ophthalmic interventions was relatively low–$786 per QALY gained for laser photocoagulation for threshold retinopathy of prematurity and $2,420 per QALY gained for combined medical and surgical management of amblyopia. Both initial cataract surgery ($2,143 per QALY gained) and second-eye cataract surgery ($2,893 per QALY gained) were cost-effective interventions, while Type 2 diabetic eye disease screening every second year ($117,457 per QALY gained) or every third year ($54,373 per QALY gained) were less worthwhile investments.

League tables do not take into account how many people are affected, and therefore ignore budgetary issues. Recommendations are usually based on both the use of league tables and the implied total costs of each intervention, using population-based estimates of the prevalence and/or incidence of disease.

MODELLING IN ECONOMIC EVALUATION

A variety of assumptions are made in economic evaluations, such as the probability that an outcome will occur or the costs of various components of the intervention. There are also a variety of intended and unintended consequences of a health intervention, and events may happen more than once. Economic models, such as decision trees and Markov models, calculate outcomes and costs taking these factors into account, and this may improve the validity of economic evaluations.

Decision Trees

Decision tree models can graphically represent the consequences and costs of one intervention compared to another, taking into account the inherent probabilities of each possible outcome (such as the occurrence of side effects).[21] For instance, Herpes Simplex Virus (HSV) eye diseases can be treated with long-term suppressive antiviral prophylaxis to reduce recurrence.[22] This medication may cause adverse effects, with consequent infection, stromal keratitis and the potential need for surgery. Infection may also occur among people

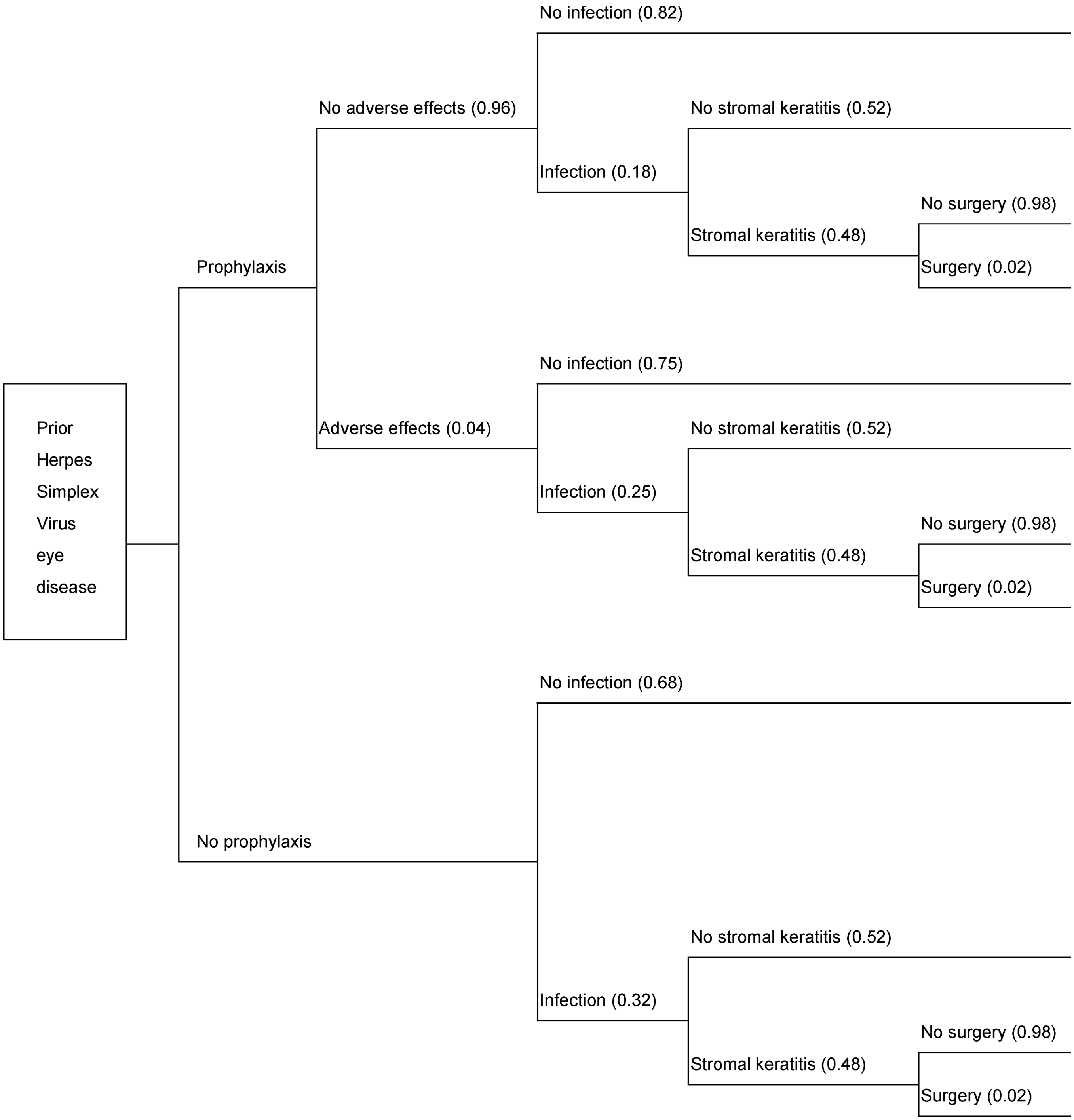

FIGURE 2 **A decision-tree model for one year of follow-up following randomisation to receive oral acyclovir prophylaxis or no chemoprophylaxis to prevent recurrence of herpes simplex eye disease. The figures in brackets indicate the probability of each event.**

who have not taken the prophylaxis. The probability of each of these outcomes can be calculated in a randomised clinical trial, and this information can be used to create a decision tree (Fig. 2). There are various costs associated with each possible outcome. By considering both the cost and consequences of the possible outcomes as well as their probabilities, Lairson et al. estimated that the expected costs of prophylaxis were $8,532 per ocular HSV episode averted. In this example of a cost-effectiveness study, the expected outcome and the expected cost for each therapeutic strategy (usually corresponding to a branch) are calculated separately and the ICERs are obtained using those expected outcomes and expected costs. In a cost-benefit analysis, the costs and consequences (both are expressed in monetary terms) are calculated for each possible end node, and the net benefit obtained is calculated by subtracting the costs from the consequences. The expected net benefit for each therapeutic strategy is then calculated as the weighted average of the corresponding final-nodes' net benefits using the corresponding probabilities as weights.

Markov Models

In many real-life scenarios, the timing of events determines the probability of the outcome, and events may happen more than once. Representing these situations using decision trees may require unrealistically simplistic assumptions, and in these cases Markov models can be used.[21] Markov models assume that a patient is always in one of a finite number of discrete health states (e.g., healthy, ill, dead), called Markov states, and as time goes by patients either stay in their original state or move to another. These options have an associated probability, and if the costs and outcomes of the options are known, then total costs and outcomes can be calculated and compared for different interventions. Markov models evaluate these events using Monte Carlo simulation, or less frequently matrix algebra or cohort simulations.[23]

Smith et al. used a Markov model to estimate the cost-effectiveness of photodynamic therapy with verteporfin for treating classic choroidal neovascular disease.[24] They built a Markov model that included 15 levels of visual acuity (VA) (ranging from 20/40 to <20/800) plus the "dead" state. There were two starting points: VA = 20/40 or VA = 20/100. The daily transition probabilities of moving to a lower state of VA were estimated, controlling for baseline VA, sex, and age. After five years of follow-up, the cost per QALY gained was $15,700 for people with a starting VA = 20/40 and $52,400 for people with a starting VA = 20/100, from the government's perspective of costs.

Dealing With Uncertainty in Economic Evaluation

There is uncertainty in every stage of an economic evaluation. Uncertainty can arise from sampling variation, because the data used in economic evaluations (such as the patient's costs incurred during an intervention) are usually obtained through surveys that rely on sampling from a wider population. Uncertainty incurred through sampling variation can be dealt with through statistical analysis, whereby economists provide confidence intervals around the estimates of costs and outcomes, based on the variation within the data.[25] Special techniques need to be used to estimate the confidence interval around the ICER since it is a ratio measure and its sampling distribution is usually not normal.

Uncertainty can also arise due to the assumptions made when constructing a model. For instance the results of the economic evaluation may be extrapolated to other populations or to future years, which means that assumptions need to be made about the generalisability. Economists may also use data from a variety of sources to construct their model, and there may be uncertainty about the applicability of their data. Economists can express levels of uncertainty in their estimates through sensitivity analyses, where various aspects of the model (e.g., the cost assumptions) are altered and the impact on the costs and outcomes of the intervention is presented.[20,25–26] There are various ways that this can be done. In a one-way sensitivity analysis, each variable is varied in turn across a plausible range of values, while the others are kept constant. In an extreme scenario analysis, all the variables are simultaneously set to their most optimistic (or most pessimistic) value, to estimate the best (or worst) case scenario. In a probabilistic sensitivity analysis, a large number of Monte Carlo simulations are conducted to vary the underlying variables simultaneously across a plausible range to examine the impact on the costs and effects. In the cost-effectiveness analysis comparing opportunistic and systematic screening for diabetic eye disease, the authors varied the assumptions about the prevalence of sight-threatening eye disease, the effectiveness of screening, compliance with systematic screening, and the number screened per year.[17] Under most assumptions, systematic screening remained more cost-effective.

CONCLUSIONS

Ophthalmic services are often constrained by lack of funding, and this is true in both high- and low-income countries; hence, difficult decisions have to be made about allocation of funding. Ophthalmology also competes with other healthcare specialities for funding. Economic evaluation is used to identify the most efficient way of allocating scarce resources among alternative activities. Increasingly, resources will flow to those procedures whose cost-effectiveness can be formally demonstrated. Use of economic evaluations, if standardised in all areas, can improve the quality of care while enhancing efficiency, so that more health programmes may be funded and more health benefits accrued.

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