CME Article

Economic evaluation

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ABSTRACT

Given the need to assess the value for money of healthcare treatments, economic evaluation has being gaining popularity over the past ten years. Studies comparing the costs and consequences of alternative healthcare interventions have been published in all fields of healthcare. This article describes the basic forms of economic evaluation and outlines the key methodological features to be considered in the critical appraisal of studies. Issues such as the appropriateness of the study question, the selection of alternatives to be compared, the measurement of costs and consequences, and the assessment of uncertainty are discussed. Additionally, an analytical critique of economic evaluations undertaken in Singapore is provided, and the prospects for economic evaluation in the future are discussed.

Keywords: cost-effectiveness analysis, economic evaluation, healthcare resources, resource allocation

Singapore Med J 2006; 47(6):456-462

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INTRODUCTION

Given the limitations in healthcare resources, there is increased interest in assessing the value for money, or economic efficiency, of healthcare treatment and programmes. This is achieved through economic evaluation, where the costs and consequences of alternative treatment strategies are compared. This article describes the basic forms of economic evaluation, outlines their key methodological features and provides an analytic critique of evaluations undertaken in Singapore. It also assesses the prospects for economic evaluation in the future.

THE BASICS OF ECONOMIC EVALUATION

The basic components of economic evaluation are shown in Fig. 1. In this example, a new drug is being compared with existing practice, which could be an older drug, a non-pharmacological intervention or, in the case of a "breakthrough"drug, no active therapy.

In considering the costs and consequences, the two types of treatment themselves will have acquisition costs, but the economic costs and consequences will be much broader. For example, if the new drug is more efficacious than the current therapy, there may be savings in other healthcare costs, such as hospitalisations. Alternatively, if the new drug has a better side-effect profile, fewer drugs and procedures will be consumed in dealing with adverse events.

Because the comparison of treatment types, in an economic evaluation, requires data on efficacy, the economic study usually builds on clinical assessments obtained from clinical trials. Sometimes, economic evaluations are conducted alongside, or concurrently with, a given clinical trial. These are called trial-based studies. However, economic evaluations are often undertaken based on a synthesis of data from a range of sources. If, additionally, they make use of decision-analytical or epidemiological models, they are called modelling studies. An important methodological feature of these studies is whether the assessments of clinical efficacy used in the model come from a systematic review of the relevant clinical literature. If the clinical data used in the economic evaluation do not accurately reflect the clinical evidence as a whole, the results of the economic study may be biased. See the paper on systematic reviews and meta-analysis in this series[1].

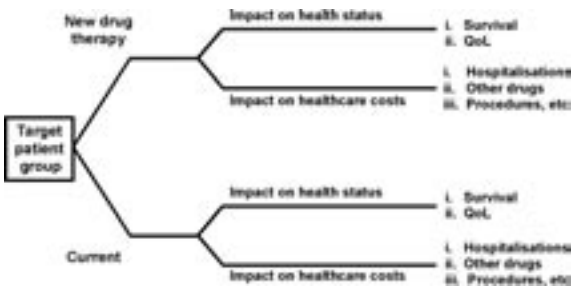

Fig. 1 Basic components of economic evaluation.

Table I. Forms of economic evaluation.

	Measure of costs	Measure of consequences
Cost-effectiveness analysis	Money	Natural units (e.g. life-years gained)
Cost-utility analysis	Money	Health status (e.g. quality-adjusted life-years gained)
Cost-benefit analysis	Money	Money

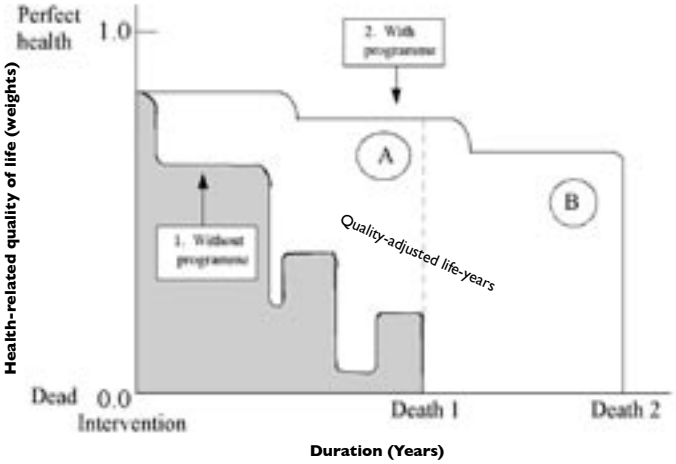

Fig. 2 QALYs gained from an intervention[3].
In the conventional approach to QALYs, the quality-adjustment weight for each health state is multiplied by the time in the state and then summed to calculate the number of quality-adjusted life-years. The advantage of the QALY as a measure of health output is that it can simultaneously capture gains from reduced morbidity (quality gains) and reduced mortality (quantity gains), and integrate these into a single measure. A simple example is displayed in the figure above, in which outcomes are assumed to occur with certainty. Without the health intervention, an individual's health-related quality of life would deteriorate according to the lower curve and the individual would die at time Death 1. With the health intervention, the individual would deteriorate more slowly, live longer, and die at time Death 2. The area between the two curves is the number of QALYs gained by the intervention. For instructional purposes, the area can be divided into two parts, A and B, as shown. Then part A is the amount of QALY gained due to quality improvements (i.e. the quality gain during the time that the person would have otherwise been alive anyhow), and part B is the amount of QALY gained due to quantity improvements (i.e. the amount of life extension, but adjusted by the quality of that life extension).

Finally, the consideration of costs in Fig. 1 is restricted to healthcare costs. However, some economic evaluations adopt a broader societal perspective and consider costs falling on other government budgets, the patient and their family, or the broader economy, through patients or their carers being able to return to work if the treatment is sufficiently successful.

In situations where the two treatment options being considered are identical from a clinical perspective (e.g. a comparison of a generic drug with a branded version of the same compound), the economic evaluation reduces to a comparison of costs only. However, such instances are quite rare and usually the difference in costs needs to be compared with an appropriate measure of the difference in consequences.

FORMS OF ECONOMIC EVALUATION

The main forms of economic evaluations are shown in Table I. In the first form, cost-effectiveness analysis (CEA), the consequences are measured in the most obvious natural units of effects. The choice of units of measurement depends on the clinical field being studied. For example, in life-saving therapy, such as treatment for chronic renal failure, the most appropriate effectiveness measure would be years of life gained. On the other hand, in a field such as asthma, the most appropriate measure may be "asthma-free days" or "symptom-free days".

However, such studies leave us with important issues of interpretation. For example, if one drug is superior in some measures of outcome and inferior in others, how would one outcome be valued relative to another? One way around this would be to turn the problem back to the decision-maker by just presenting the range of different consequences and asking him or her to give an overall assessment. Such studies are sometimes called cost-consequences analyses.

Alternatively, the various consequences could be combined in a single generic measure of health improvement. In another form of evaluation, cost-utility analysis (CUA), states of health are valued relative to one another through the use of health state preference values or health utilities. Then the superiority of one treatment over another can be expressed in terms of the quality-adjusted life-years (or QALYs) gained (see Fig. 2).

The use of a generic measure of outcome, like the QALY, enables us to compare the value for money of interventions in different fields of healthcare. The concept of the QALY is also quite useful when changes in quality of life are being traded with survival. For example, a new cancer drug may be more toxic than existing therapy, thereby reducing the patient's quality of life during treatment, but may produce gains in additional survival.

Finally, in a cost-benefit analysis (CBA), the various consequences may be valued, relative to one another, in monetary terms. In principle, CBA is the broadest form of economic evaluation, since all costs and consequences are expressed in the same unit (i.e. money). Therefore, we can assess whether the total costs of an intervention are justified by its total benefits. This contrasts with CEA and CUA, where the assessment of value for money requires some

judgment of what the unit of benefit (e.g. a life-year or QALY) is worth to society.

KEY METHODOLOGICAL FEATURES OF ECONOMIC EVALUATION

Determining the study question

In common with all forms of health services research, a study is greatly improved if a clear study question is posed. Since economic evaluation seeks to improve the allocation of healthcare resources, it is important that the question itself has some economic significance. For example, there is no point in undertaking an economic evaluation of two drugs that are quite similar, both in terms of their clinical effects and acquisition cost.

The other important attributes of the study question are that it should relate to a choice among two or more competing therapies and that the viewpoint (or perspective) should be clearly stated. The issue of viewpoint arose earlier when discussing the basic components of economic evaluation. That is, it is important to state whether the choice of therapies is being examined from the point of view of the healthcare system, all government budgets, or society at large. The latter is the broadest viewpoint and would include patient/family costs and productivity changes.

Selecting the alternatives for comparison

Normally, economic evaluations are prompted by the emergence of a new drug, device, or medical procedure. Therefore an important question is, "What do we compare the new technology with?" Consequently, analysts need to justify their choice of the comparator (to the technology of interest). Normally, this is on the grounds that it is "common practice" or "widely used" in the setting where the study is being conducted. Having said this, "current practice" may be hard to define and may itself be unevaluated, and hence potentially inefficient.

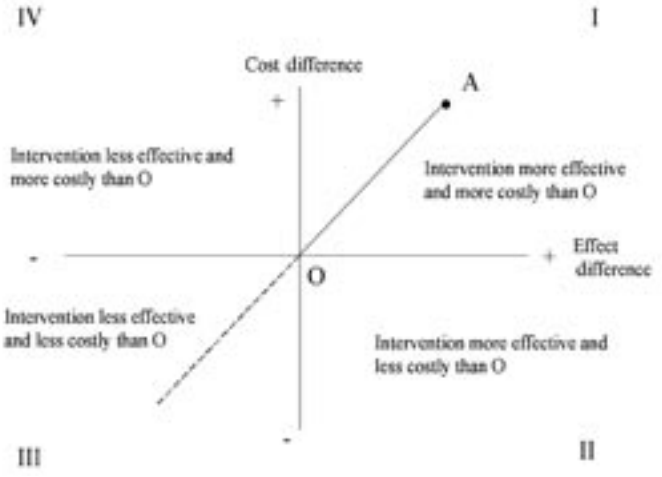

Fig. 3 The cost-effectiveness plane.

Measuring and valuing costs and consequences

This is probably the most important aspect of any economic evaluation and consists of several key components. A key point relates to the quality of the clinical evidence on which the economic evaluation is based. Normally, one would expect that the economic study is based on a randomised controlled trial (RCT) or a systematic review of the existing literature.

However, on occasions, economic evaluations will be based on lower quality evidence if RCTs do not exist at all, or the relevant head-to-head studies have not been conducted. Problems often arise in the case of devices or medical procedures, where there may not be RCTs available. Another difficult situation sometimes arises with new classes of drugs, where several compounds are being developed at the same time and head-to-head studies cannot easily be conducted. Here, economic evaluations frequently use more sophisticated methods of evidence synthesis in order to minimise the potential bias from making indirect comparisons[2]. The argument is that, while not perfect, the economic analysis should try to inform the decision-maker as best as possible, at the time when the decision has to be made.

Allowing for differential timing of costs and consequences

One of the important aspects of healthcare treatment choices is that not all the costs and consequences occur in the same year. The obvious example is the choice between a curative option and a preventive one. They both involve committing resources now, but the preventive option will only deliver benefits some time in the future. Are we indifferent to the timing of costs and benefits?

Most evidence suggests that as individuals, and as a community, we are not indifferent to when we make resource outlays, or receive benefits. Costs and benefits occurring in the future have less importance than costs and benefits today.

The process adopted in economic evaluations to account for this "positive rate of time preference" is called discounting to present values. It is beyond the scope of this article to go into detail, but in general terms, discounting gives less weight, in the analysis, to costs and benefits occurring in the future. A key component of the calculation is the choice of discount rate. In some countries, like the United Kingdom, the government advises the rate. In settings where there is no advised rate, analysts tend to use a rate similar

to the interest on long-term, riskless investments such as government bonds. For developed economies, discount rates are typically in the 3-5% range.

Assessing the incremental costs and consequences (of one alternative over the other)

The correct way to compare two alternatives is to assess what one receives in additional benefits from the option with higher costs. Normally, economists calculate the incremental cost-effectiveness ratio (ICER) as $(C_A - C_O)/(E_A - E_O)$, where A is the alternative of interest and O is current therapy. This can be seen in Fig. 3, known as the cost-effectiveness plane. The choice in quadrants II and IV is straightforward, as one therapy dominates the other in each case (e.g. has lower costs and superior effectiveness). The most interesting quadrant is quadrant I, where the new therapy is both more costly and more effective. The ICER is represented by the slope of the line joining OA.

If we have a threshold willingness-to-pay for a unit of effect (e.g. a life-year or a QALY) we might define a region of acceptable cost-effectiveness, as in Fig. 4. Then, the question is whether the ICER for our new therapy is in that region or not.

Allowing for uncertainty in estimates of costs and consequences

It is unlikely that all the parameters in an economic evaluation are known precisely. Indeed, it is normal and desirable to see a confidence interval around the estimate of clinical effectiveness, which represents an important input to the economic study. Other parameters may also be subject to uncertainty, such as the unit costs (or prices) for many of the resource inputs. These could vary by location, or by type of healthcare facility. Finally, there could be methodological uncertainty, such as whether it is appropriate to include productivity gains and losses in the study, or the method for determining the discount rate.

The normal approach for dealing with uncertainty in economic evaluations is to undertake a sensitivity analysis, where key parameters are varied, in order to see whether they have much impact on study results. Many of the sensitivity analyses conducted are one-way, namely, varying one parameter at a time in order to see how sensitive study results are to the variation. However, nowadays, many analysts undertake a probabilistic sensitivity analysis (PSA) to account for parameter uncertainty.

In PSA, each parameter is assigned a probability distribution, and random samples are drawn from these distributions to generate an empirical distribution for the incremental cost-effectiveness ratio. For further details, see chapters 3 and 5 of the book by Drummond et al[3].

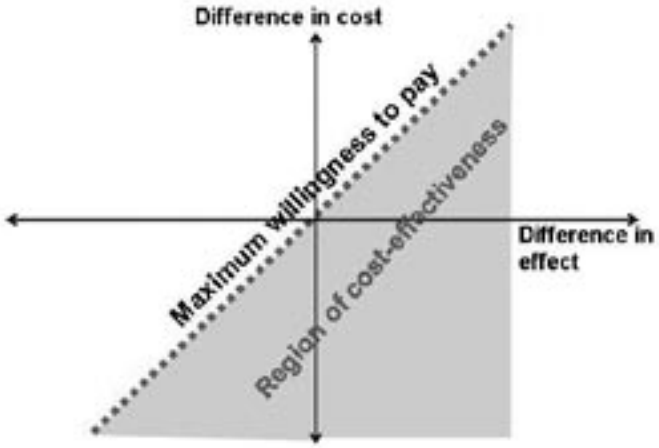

Fig. 4 The region of acceptable cost-effectiveness.

Table II. List of ten questions to ask of a study[3].

1. Was a well-defined question posed in an answerable form?
2. Was a comprehensive description of the competing alternatives given?
3. Was the effectiveness of the programmes or services established?
4. Were all important and relevant costs and consequences for each alternative identified?
5. Were costs and consequences measured accurately in appropriate physical units? (e.g. hours of nursing time, physician visits)
6. Were costs and consequences valued credibly?
7. Were costs and consequences adjusted for differential timing?
8. Was an incremental analysis of costs and consequences of alternatives performed?
9. Was allowance made for uncertainty in the estimates of costs and consequences?
10. Did the presentation and discussion of study results include all issues of concern to users?

Presenting study results

As in all health services research, an important aspect of presenting results is transparency. Namely, it is important that the user of the study can clearly see all the data, methods and assumptions. For example, in the United Kingdom, the British Medical Journal produced a set of guidelines on reporting of economic evaluations to be used by study authors and BMJ editors[4].

Another key aspect of economic studies is the extent to which the results are generalisable, or transferable, to other settings or locations. Since

Table III. Abbreviated NHS EED abstract for the full economic evaluation by Yang et al[15].

Bibliographical details	Yang K Y, Wang M C, Yeo S J, Lo N N. Minimally invasive unicondylar versus total condylar knee arthroplasty: early results of a matched-pair comparison. Singapore Medical Journal 2003; 44:559-562.
Study question	To compare effectiveness and costs of alternative treatments for patients with isolated medical compartmental osteoarthritis of the knee.
Alternatives compared	Unicompartmental knee arthroplasty (UKA) versus total knee arthroplasty (TKA).
Location/setting	Singapore/Secondary care.
Type of economic evaluation	Cost-effectiveness analysis (cost-consequences).
Methods	Source of effectiveness data: Prospective cohort study with matched controls that were comparable in terms of age, gender and prognostic features. The sample size included 100 patients (50 per group) and was followed up for six months. Primary outcomes: mean operating times, days required for independent ambulation, time to achieve 90 degree flexion, hospital stay, postoperative drainage, haemoglobin levels; motion. Cost analysis: The perspective of the economic analysis was not reported, although costs reflected hospital bills. No information was reported about categories of costs included, resource quantities used or the price year. Discounting was not performed, and was not relevant since costs were incurred within a short time. Analysis of uncertainty: Differences in effectiveness and costs between the two groups were appropriately tested for statistical significance.
Main findings	UKA was a more cost-effective procedure than TKA, with patients presenting lower postoperative drainage, quicker rehabilitation and independent ambulation, achieving flexion of 90 degrees faster and a greater range of motion at a lower cost (i.e. SGD$8,700 for a UKA patient versus SGD$12,000 for a TKA patient; $p<0.01$).
Commentary	Selection of comparator: The rationale for the choice of the comparators was clear: it represented traditional practice. Estimate of measure of effectiveness: Although the clinical data was derived from a prospective cohort study with well-matched patients, a randomised controlled trial would have minimised the potential for bias and confounding factors. It was not clear whether the study sample was representative of the study population, which would affect the external validity of the study results. Quality of life was not evaluated. Estimate of costs: The authors provided limited information on costing methodology. Consequently, it cannot be assessed whether all relevant costs were included in the costing. Additionally, resource utilisation was not reported separately from unit costs. Charges, instead of costs, were considered without further charge-to-cost adjustments. The costs were, appropriately, not discounted. The price year was not reported. Other issues: The issue of generalisability to other settings was not addressed.

there are reasons to suppose that economic study results are more location-specific than clinical ones, the issue of transferability has been widely debated in the economic evaluation literature[5,6].

These methodological principles have been formalised in several methodological checklists for how to undertake, or to critique, studies. One such checklist, by Drummond et al[3], is shown in Table II.

Analytical critiques of published economic evaluations

In order to provide practical illustrations of the various methodological features of economic evaluations, we searched the National Health Service Economic Evaluation Database (NHS EED) for economic evaluations conducted in Singapore. The NHS EED can be accessed either through the Cochrane Library[7] or the website of the Centre for Reviews and Dissemination at the University of York (www.york.ac.uk/inst/crd). The database contains structured abstracts, or reviews, of full economic evaluations, plus references of cost studies and methodological papers. The NHS EED abstract structure covers the main methodological features of the studies outlined above. Access to the database is free.

Eight studies were identified[8-15], covering topics as diverse as colorectal cancer screening[14], diagnosis of pulmonary tuberculosis[9] and knee arthroplasty[15]. However, one was excluded on the grounds that it covered several Southeast Asian countries, but only very superficially[12]. Overall, there was a well-posed question in all the studies. The comparators were generally chosen to represent current practice. The type of economic evaluation performed was cost-effectiveness analysis in all the cases, with two of the studies being cost-consequences analyses[11,15]. There were variations across the studies in terms of the sources of effectiveness data used: four of them used a single study[8,11,13,15] (with only one of them being a RCT[8]) and three were modelling studies based on literature reviews, which appeared to be non-systematic[9,10,14]. Overall, the estimation of costs was characterised by a limited reporting of the methods. Discounting was not applied due to the consideration of only short time horizons and there was lack of reporting of the price year. In most of the cases, the issue of the generalisability of the results to other settings was not addressed.

CRITICAL APPRAISAL OF AN ECONOMIC EVALUATION CONDUCTED IN SINGAPORE

We have chosen one of the previously-mentioned economic evaluations[15] to provide an example of how to critically appraise it. An abbreviated NHS

EED abstract for this study is shown in Table III. The paper can be openly accessed on the Internet (www.sma.org.sg/smj/4411/4411a1.pdf) and its corresponding NHS EED abstract can be consulted in the NHS EED database (144.32.150.197/scripts/WEBC.EXE/nhscrd/expand?saan=0000298809). Following the questions posed in Table II and the information provided by the NHS EED abstract, a critical appraisal of the study is presented below.

According to the information provided in the paper, a clear research question was presented and the importance of the economic analysis was highlighted, although the perspective adopted was not explicitly stated and the type of economic analysis undertaken (i.e. a cost-consequences analysis) was not identified. The alternatives compared (i.e. unicompartmental versus total knee arthroplasty) were described in detail and total knee arthroplasty was chosen as the comparator to represent traditional practice.

The effectiveness data were obtained from a prospective cohort study with well-matched patients, although a RCT would have been more appropriate in order to minimise potential biases and confounding factors. The clinical endpoints assessed (e.g. days required for independent ambulation, mobility, postoperative haemoglobin levels) were appropriate for the type of intervention analysed. An assessment of the number of life-years gained or QALYs gained was not performed, although this is common in studies evaluating the cost-effectiveness of knee arthroplasty.

Few details were reported about the methods used for the cost estimation and, as previously mentioned, the perspective was not identified. Consequently, it is difficult to assess whether all relevant costs were included. The follow-up period was short (i.e. six months) and therefore discounting was probably not performed. Appropriate statistical analyses were performed to test whether differences observed between the study groups were statistically significant.

As it can be observed from this critical appraisal, the study appeared to be internally valid in terms of the clinical outcomes, although the cost analysis presented some caveats that should be considered when interpreting the results.

FUTURE PROSPECTS FOR ECONOMIC EVALUATION

Economic evaluation has been gaining popularity over the past ten years and studies have been published in all fields of healthcare. Despite many methodological improvements in studies, several controversies remain. These include the role and measurement of productivity changes, the inclusion, in evaluations, of the costs in added years of life, the rate of discount for health benefits, and the pros and cons of the various methods of valuing health gains.

More jurisdictions are now using economic evaluation as part of their decision-making procedures for the pricing and reimbursement of health technologies, especially pharmaceuticals. This growth in use, which shows no sign of abating, will ensure that the remaining methodological challenges receive adequate attention in the future. In addition, databases of economic evaluation, such as NHS EED, greatly help the users of studies to assess their methodological quality[16]. If studies are well-conducted, and decision-makers interpret them correctly, they will lead to better informed decisions about the allocation of healthcare resources.

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
Multiple Choice Questions (Code SMJ 200606A)

	True	False
Question 1: Economic evaluations:		
(a) Often compare only the difference in costs between a new treatment and existing practice.	❑	❑
(b) May be biased if the data used does not accurately reflect the clinical evidence as a whole.	❑	❑
(c) May be based on clinical assessments obtained from a specific clinical trial, in which case it is known as a modelling study.	❑	❑
(d) May consider different costs and consequences depending on the perspective of the study.	❑	❑
Question 2: The following statements relate to forms of economic evaluation:		
(a) Cost-effectiveness analysis measures consequences in natural units of effects (e.g. years of life gained).	❑	❑
(b) Cost-benefit analysis measures consequences in health state preference values (e.g. quality-adjusted life-years gained).	❑	❑
(c) Cost-utility analysis measures consequences in monetary terms (i.e. the utility of an intervention is judged by the monetary difference between costs and consequences).	❑	❑
(d) Cost-consequences analysis presents a range of different consequences.	❑	❑
Question 3: The following are key methodological features of economic evaluations:		
(a) A clear study question should always be framed.	❑	❑
(b) The evaluation should compare the technology of interest with an alternative (e.g. a new drug compared with existing treatment).	❑	❑
(c) The US dollar is used as the standard currency to value costs and consequences.	❑	❑
(d) Economic evaluations must always discount costs and consequences to present values.	❑	❑
Question 4: Useful questions to ask when critically appraising an economic evaluation include:		
(a) Was a comprehensive description of competing alternatives given?	❑	❑
(b) Were all important and relevant costs and consequences for each alternative identified?	❑	❑
(c) Was an incremental analysis of costs and consequences of alternatives performed?	❑	❑
(d) Was allowance made for uncertainty in the estimates of costs and consequences?	❑	❑
Question 5: Indicate if the following statements are true or false:		
(a) Sensitivity analysis is an approach for dealing with uncertainty in economic evaluations, in which key parameters are varied to see whether they have much impact on study results.	❑	❑
(b) Economic evaluations should only be performed when there is evidence from randomised controlled trials available.	❑	❑
(c) The NHS EED contains structured abstracts or reviews of full economic evaluations. Access to the database is free.	❑	❑
(d) Well-conducted economic evaluations that are interpreted correctly will always lead to equitable allocation of healthcare resources.	❑	❑

Doctor's particulars:

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