CRITICAL APPRAISAL SKILLS
Making Sense Of Evidence

12 questions to help you make sense of economic evaluations

CRIB sheet for: cost effectiveness of intensive glycaemic control, intensified hypertension control, and serum cholesterol lever reduction for type 2 diabetes. CDC Diabetes Cost effectiveness group.
JAMA 2002 187 (19): 2543-2551, updated on 18 May 2004

General comments

- Three broad issues need to be considered when appraising an economic evaluation.

  A/ Is the economic evaluation valid?

  B/ How were costs and consequences assessed and compared?

  C/ Will the results help in purchasing services for local people?

  The 12 questions on the following pages are designed to help you think about these issues systematically.

- The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions.

- There is a fair degree of overlap between several of the questions.

- You are asked to record a "yes", "no" or "can't tell" to most of the questions.

- Beneath each question there are hints that may help you understand the question better. They will remind you why the question is important. In the small group concentrate on answering the main question – it is not necessary for the group to answer all the detailed points.

- The 12 questions are adapted from Drummond MF, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford: Oxford University Press, 1987 by the Critical Appraisal Skills Programme (CASP), Oxford, UK and CASP Spain (CASPe).

A/ Is the economic evaluation valid?

1 Was a well-defined question posed? *HINT: Is it clear what the authors are trying to achieve?* • *What is the perspective?* • *How many options are compared?* • *Are both costs and consequences considered?* • *What is the time horizon?*	**Yes** **Can't tell** **No** √ ❑ ❑ The perspective of the analysis was the health service (page 2542, paragraph 3). It is a complete economic evaluation, with effects measured in QALYs (page 2542, paragraphs 2-3). In fact it is really three studies of cost utility, which are then ranked in order of their ICER. All compare two options: intensive treatment versus standard treatment (page 2542, paragraph 2). The time horizon is life-long.
2 Was a comprehensive description of the competing alternatives given? *HINT: Is there a clear decision tree (or similar given):* *Can you tell* • *who did what, to whom, where and how often?*	**Yes** **Can't tell** **No** √ **or** **(√)** ❑ The decision tree/s **can** be identified unambiguously. However, you may have found this hard work because it is not explicitly stated. The implicit decision tree for each analysis (glycaemic control, control of hypertension, and control of cholesterol) has a decision node with two branches: intensive treatment and conventional treatment (see last page of this cribsheet for details). In the description of drugs for hyperglycaemia they do not mention Metformin, this is commonly used in the UK so the interventions given may not reflect current practice well. The intervention and other details are not fully defined but the authors refer to the UKPDS and the NHANESIII. They also give all the information in a technical document available from the authors. The CASP International Network has a copy of this document, which was received from the authors two days after its request by email.

3 Does the paper provide evidence that the programme would be effective (i.e. would the programme do more good than harm)? *HINT: Consider if an RCT or systematic review was used; if not, consider how strong the evidence was.* *(Economic evaluations frequently have to integrate different types of knowledge stemming from different study designs.)*	**Yes** **Can't tell** **No** √ ❑ ❑ The estimates of effectiveness are obtained from RCTS. There was no Cochrane review on this subject at the time this paper was written. (Note: When the best economic evaluation you can find to inform a commissioning decision is a few years old, you should always check whether there could be more up-to-date evidence that would significantly change any of the parameters, such as change in costs, a new systematic review on effectiveness etc.) The UKPDS study is a large cohort study with nested RCTs. The authors state "because intensified hypertension did not have a statistically significant effect on CHD (in the UKPDS) our base case analysis assumed that the intervention has no effect on the CHD transition probability"; however if the estimate of effect size was clinically significant, but the particular part of UKPDS underpowered; then to assign a null effect may arguably not have been the most sensible decision for the base case.

4 Were the effects of the intervention identified, measured and valued appropriately HINT: Effects can be measured in natural units (e.g. years of life) or more complex units (e.g. years adjusted for quality of life such as QALYs) or monetary equivalents of the benefit gained (e.g. $).	Yes √ Can't tell ❑ No ❑ The effectiveness outcomes (from RCTs and UKPDS) were measured in surrogate outcomes (mmHg, mg cholesterol, glycaemic levels). (There is evidence that these correlate well with clinical outcomes.) In order to be incorporated into the model (i.e. how do transition probabilities change), these results need to be converted into a risk reduction. This is described for glycaemic control on p2543, 2nd column, 4th paragraph. For hypertension, the authors make an assumption on risk reduction based on UKPDS data (p2543, 3rd column, 3rd paragraph). For cholesterol, the authors modelled the risk reduction based on two trials (p2545, 1st column, 3rd paragraph). Little information is given on how the QALYs were obtained but there are references to the sources. Years of life gained are also used. Utility values are given for various health states (e.g. 0.69 for blindness). The references for these may be incomplete: does ref 25 provide the utilities for blindness, ERD, and lower extremity amputation or just for amputation? - it is important to know the validity of these as the ascribed utility is an important parameter when calculating the incremental cost/QALY. Data on distribution of patients at diagnosis and transition probabilities were taken from the UKPDS study, previous referenced models and studies contained within the technical report. Utility data used to estimate QALYs were referenced (but was this complete?) The authors assumed that data on progression for type 1 diabetes could be used for type 2 diabetes (p 2543, 2nd column, 4th paragraph).

B/ How were consequences and costs assessed and compared?

5. Were all important and relevant resources required and health outcome costs for each alternative identified, measured in appropriate units and valued credibly? *HINTS:* *Identified?* • *Remember the perspective being taken.* *Measured accurately in appropriate units prior to evaluation?* • *Appropriate units may be hours of nursing time, number of physician visits, years-of-life gained etc.* *Valued credibly?* • *Are the values realistic?* • *How have they been derived?* • *Have opportunity costs been considered?*	**Yes** √ or **Can't tell** √ **No** ❑ There is little information in the article on resources, how they were measured nor prices. Nonetheless the article refers to references in the public domain and in particular the technical report. The opportunity cost is implicitly considered when producing a cost/QALY because a QALY in one disease or condition is equivalent to a QALY from a different disease or decision. (The patient perspective and societal perspective may also be important depending on the context of the decision being made.)
6 Were costs and consequences adjusted for different times at which they occurred (discounting)?	Yes √ Can't tell ❑ No ❑ There is a long time horizon, which means that both cost and benefits in the future will have a lower present day value and the authors have applied a discount rate of 3% to both (page 2545, 3rd column). (Note: From 2005 NICE has required the use of 3.5% both costs and benefits, based on the recommendations of the UK Treasury.)
7. What were the results of the evaluation? *HINTS:* *What is the bottom line?* *What units were used (e.g. cost/life year gained, cost/QALY, Net benefit)*	The units used were cost per QALY. In table 4 on page 2547 both discounted costs/QALY and undiscounted years of life gained are shown. One can see the ICERs • Glycaemic control $41,000/QALY • Control of blood pressure, $-2,000/QALY • Control of cholesterol $52,000/QALY It is important to realise the ***minus*** in the $-2,000/QALY for hypertension is because there are cost savings and increased QALYs, that is the ICER falls in the South-East quadrant (comparator is dominated). A minus would also occur due to greater cost AND fewer QALYs (and the ICER then would be in the North-West quadrant – not the case here). The ICER is also presented for different age groups.

8 Was an incremental analysis of the consequences and costs of alternatives performed?	**Y Yes** √ **Can't tell** ❑ **No** ❑ Yes, there was a set of univariate sensitivity analyses in which many variables were changed (page 2458). However the point estimates of effectiveness for CHD of intensive hypertensive therapy from the clinical trial was not used because it did not reach statistical significance. Using the UKPDS figures (which are particularly relevant in the UK) in the scenario for the control of glucose levels, intensive treatment became cost saving with a cost per QALY of approximately $-6,000/QALY (page 2549 figure 3A) **(**NB the **minus)**. This which would make this the most cost effective option of the three in the UK.
9. Was an adequate sensitivity analysis performed? *HINT: Consider if all the main areas of uncertainty were considered by changing the estimate of the variable and looking at how this would change the result of the economic evaluation?*	**Yes** √ **Can't tell** ❑ **No** ❑ Yes

C/ Will the results help in purchasing for local people?

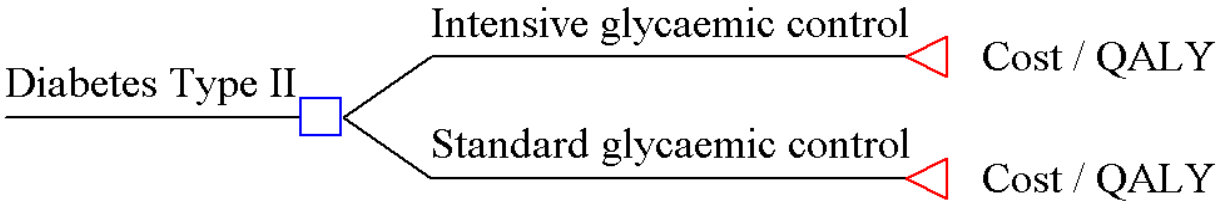
10. Is the programme likely to be equally effective in your context or setting? *HINT: Consider whether* *a) the patients covered by the review could be sufficiently different to your population to cause concern b) your local setting is likely to differ much from that of the review.*	**Yes** √ **Can't tell** ❑ **No** ❑ There is no reason to think that the UK population response to diabetic treatment and control of risk factors would be radically different from that of the US population. However we must be cautious about the data for glycaemic control because of the uncertainty, noted above, about the extent to which the treatment of diabetes represents current practice.

11. Are the costs translatable to your setting?	**Yes** √ **Can't tell** ❑ **No** √ "No" in that the cost and resources of the American Health Service are very different from the European. The authors use a top-down (reference cost) approach based on US data. "Yes" in that the UKPDS scenario is probably applicable to the UK.
12. Is it worth doing in your setting?	**Yes** √ **No** ❑ Controlling hypertension is probably cost saving in the UK, which suggests that it ought be implemented. From the scenario used in the UKPDS data it would seem that the intensive control of glycaemia is also cost saving and ought to be implemented.

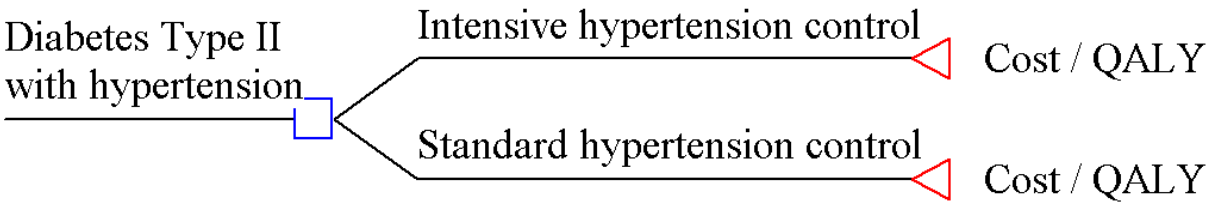
This article is a typical article and perhaps should be avoided for novices in EBM. However it worked well in two workshops to date where there were participants with very little experience in economical evaluation but some training in EBM.

Decision trees

1. Glycaemic control



2. Control of hypertension



3. Control of cholesterol