

Chapter 15: Incorporating economics evidence

Authors: Ian Shemilt, Miranda Mugford, Sarah Byford, Michael Drummond, Eric Eisenstein, Martin Knapp, Jacqueline Mallender, David McDaid, Luke Vale and Damian Walker on behalf of the Campbell and Cochrane Economics Methods Group.

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Key points

- Economics is the study of the optimal allocation of limited resources for the production of benefit to society and is therefore relevant to any healthcare decision.
- Optimal decisions also require best evidence of effectiveness.
- This chapter describes methods for incorporating economics perspectives and evidence into Cochrane reviews, with a focus on critical review of health economics studies.
- Incorporating economics perspectives and evidence into Cochrane reviews can enhance their usefulness and applicability for healthcare decision-making and new economic analyses.

15.1 The role and relevance of economics evidence in Cochrane reviews

15.1.1 Introduction

Cochrane reviews assemble, select, critique and combine trustworthy data from multiple research studies on the effectiveness and other aspects of healthcare interventions. They can provide robust evidence on intervention effectiveness, resulting in less selectively biased, more statistically powerful information, which may be more likely to convince decision makers compared with evidence from single studies.

However, in the face of scarce resources, decision makers often need to consider not only whether an intervention works, but also whether its adoption will lead to a more efficient use of resources. The topics of Cochrane reviews cover a wide range of questions whose answers are important for the improvement of individual and public health and well-being in environments where resources are limited. Coverage of economic aspects of interventions can therefore enhance the usefulness and

applicability of Cochrane reviews as a component of the basis for healthcare decision-making (Lavis 2005).

It has been argued for many years that promoting effective care without taking into account the cost of care and the value of any health gain can lead to inefficient use of public and private funds allocated to health care, which may indirectly result in harm for individuals and the public (Williams 1987). Indeed, the case can be made that Archie Cochrane, who inspired much of the systematic review movement (and of course The Cochrane Collaboration), was in favour of decision-making informed by evidence on economics aspects of interventions as well as evidence on their effectiveness. The title of Cochrane's most famous work, his book of Rock Carling lectures, is *Effectiveness and Efficiency* (Cochrane 1972). [Box 15.1.a](#) contains two quotations from that book, illustrating the importance that Cochrane placed on the role of economic evidence in healthcare decision-making.

Box 15.1.a: Archie Cochrane on health economics (Cochrane 1972)

“Allocations of funds and facilities are nearly always based on the opinions of senior consultants, but, more and more, requests for additional facilities will have to be based on detailed arguments with ‘hard evidence’ as to the gain to be expected from the patients’ angle and the cost. Few can possibly object to this.” (p.82).

“If we are ever going to get the ‘optimum’ results from our national expenditure on the NHS we must finally be able to express the results in the form of the benefit and the cost to the population of a particular type of activity, and the increased benefit that would be obtained if more money were made available.” (p.2).

15.1.2 Economics and economic evaluation

Economics is the study of the optimal allocation of limited resources for the production of benefit to society (Samuelson 2005). Resources are human time and skills, equipment, premises, energy and any other inputs required to implement and sustain a given course of action (e.g. referral of an individual patient to a programme of healthcare treatment, and subsequent management of sequelae and complications). Health economics studies are defined here as full economic evaluation studies, partial economic evaluation studies, and single effectiveness studies that include more limited information relating to the description, measurement or valuation of resource use associated with interventions.

Full economic evaluation is the comparative analysis of alternative courses of action in terms of both costs (resource use) and consequences (outcomes, effects) (Drummond 2005). This definition distinguishes full economic evaluation from economic analyses which focus solely on costs and resource use, or partial economic evaluations. Full economic evaluation is not a single research method; it is a framework for structuring specific decision problems. This means that the appropriate type of full economic evaluation, and thus the approach to data collection and analysis, is determined primarily by the decision problem, or economic question, at issue and the viewpoint of the decision maker (see also [Section 15.2.1](#)). Full economic evaluation studies aim to describe, measure and value all relevant alternative courses of action (e.g. intervention X versus comparator Y), their resource inputs and consequences. Cost-benefit analysis (CBA) falls into this category. Some approaches fall short of full valuation of all consequences, but are still considered full economic evaluations, including cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). All types of full economic evaluation use a marginal approach to analysis. In other words, they aim to produce measures of *incremental* resource use, costs and/or cost-effectiveness. Brief descriptions of CEA, CUA and CBA are provided in [Box 15.1.b](#) (see also Chapter 2 of Drummond (Drummond 2005)).

Other types of studies of the use of healthcare resources do not make explicit comparisons between alternative interventions in terms of both costs (resource use) and consequences (effects). Such studies are not considered to be full economic evaluations but are known instead as partial economic evaluations. Partial economic evaluations can contribute useful evidence to an understanding of economic aspects of interventions. Health economics studies considered to be partial economic evaluations include cost analyses, cost-description studies and cost-outcome descriptions. In addition to full and partial economic evaluations, randomized trials and other types of single effectiveness studies may include more limited information relating to the description, measurement or valuation of resource use associated with interventions. Whilst the inclusion of this type of information may not always constitute a full or partial economic evaluation approach, it may still nevertheless contribute useful evidence to an understanding of economic aspects of interventions.

Economic evaluation studies both use, and are used in, systematic reviews of the effects of interventions. First, systematic reviews may include an economic component that incorporates a critical review of published and unpublished health economics studies (see Section 15.1.3). Second, as well as the increasing numbers of full and partial economic evaluations conducted alongside (and incorporating) single effectiveness studies, such as randomized trials (Maynard 2000, Neumann 2005), full economic evaluations are also increasingly based upon evidence of effects compiled using systematic review methods. Indeed, all of the types of full economic evaluation described above (CEAs, CUAs, CBAs) can be conducted alongside, and incorporating, a systematic review of effects, including use of a decision-analysis approach for pooling or modelling the available evidence on intervention costs and effects (Briggs 2006). Economic evaluation can be seen in this context as a further layer of evidence synthesis building on the systematic review process.

Cochrane reviews and other systematic reviews can therefore provide a useful source of data to inform subsequent, or parallel, full economic evaluation modelling exercises whether or not the review incorporates further coverage of economic aspects of interventions. In particular, a well-conducted meta-analysis of data on effect-size, adverse effects and complications assembled using a systematic review of randomized trials has been proposed as the least-biased source of data to inform effect-size and adverse effects parameters in an economic model (Cooper 2005). This needs to be supplemented by additional systematic searches of appropriate data sources to inform ranges of values for the other key parameters in the cost-effectiveness formula or economic model (Weinstein 2003, Philips 2004, Cooper 2005)

Box 15.1.b: Types of full economic evaluation

All types of full economic evaluation compare the costs (resource use) associated with one or more alternative interventions (e.g. intervention X versus comparator Y) with their consequences (outcomes, effects). All types value resources in the same way (i.e. by applying unit costs to measured units of resource use). The types differ primarily in the way they itemize and value effects. These differences reflect the different aims and viewpoints of different decision problems (or economic questions).

Cost-effectiveness analysis (CEA): the effects of an intervention (and its comparators) are measured in identical units of outcome (e.g. mortality, myocardial infarctions, lung function, weight, bleeds, secondary infections, revisional surgeries). Alternative interventions are compared in terms of 'cost per unit of effect'.

Cost-utility analysis (CUA): when alternative interventions produce different levels of effect in terms of both quantity and quality of life (or different effects), the effects may be expressed in utilities. Utilities are measures which comprise both length of life and subjective levels of

well-being. The best known utility measure is the quality-adjusted life year, or QALY. Alternative interventions are compared in terms of cost per unit of utility gained (e.g. cost per QALY).

Cost-benefit analysis (CBA): when both resource inputs and effects of alternative interventions are expressed in monetary units, so that they compare directly and across programmes within the healthcare system, or with programmes outside health care (e.g. healthcare intervention vs. criminal justice intervention).

15.1.3 Coverage of economics issues in Cochrane reviews

The overall aim of this chapter is to describe how authors of Cochrane and other systematic reviews might compile the best evidence on economic aspects of interventions in addition to the best evidence on their effectiveness.

There is currently no formal requirement for Cochrane reviews to include coverage of economic issues. This guidance is therefore presented as a series of optional methods to be considered by Cochrane review authors seeking to include coverage of economic issues. The principal element of the methodological framework outlined is a critical review of health economics studies, which can be conducted as a fully integrated component of a Cochrane review. This involves the assembly, selection, critical appraisal, summary and possibly synthesis of data from relevant health economics studies. Three core premises of the guidance are as follows:

1. Given the international audience of end-users of Cochrane reviews, the overall aim of economics components of reviews should be to summarize what is known from different settings about economic aspects of interventions, to help end-users understand key economic trade-offs between alternative healthcare treatments or tests;
2. Key secondary aims are to provide a framework for Cochrane reviews to present clinical and economic data in a format that facilitates their use in subsequent, or parallel, economic analyses;
3. Economics issues are relevant to decision-making even when evidence of intervention effectiveness is unclear. First, end-users often need to be aware of evidence regarding the incremental resource use and costs associated with an intervention, versus relevant comparators, as this can help to clarify the case for investing in future research on both effectiveness and cost-effectiveness. Second, it is important for end-users to be aware of whether or not existing full economic evaluations are based on robust evidence regarding effectiveness.

Authors of Cochrane reviews seeking to include coverage of economics aspects of interventions will need to consider in detail, and from the earliest stages of protocol development, how economics issues relate to their specific review topic. Use of the methods described in this chapter will also require at least some training in the use of health economics methods. Therefore, once a decision to include coverage of economics issues has been taken, it is advisable to consult with a health economist who has experience of systematic review methods as soon as possible.

Some Cochrane Review Groups (CRGs) already have access to one or more experienced health economists who regularly contribute work on economics components of reviews. The Campbell and Cochrane Economics Methods Group (CCEMG) will seek to help authors of Cochrane reviews identify health economists willing to contribute work, or to provide advice or peer review support (see [Box 15.10.a](#)).

15.2 Planning the economics component of a Cochrane review

15.2.1 Formulating an economic question

Following a decision to include coverage of economic aspects of interventions in a Cochrane review, the first stage of research is to formulate one or more questions, or objectives, that the economics component of the review will seek to address. Each economics question or objective will determine methodological decisions in subsequent stages of the critical review of health economics studies.

Formulating an economic question requires close consideration of the role and relevance of economic issues to the specific overall review topic. The *preliminary* questions below are intended to provide useful starting points to help authors and editors conceptualize the role and relevance of economic issues.

- What is the economic burden to society (e.g. health system, health or social care providers, individuals, families, employers) of the condition or illness that the intervention is seeking to affect?
- What types of incremental resource inputs are required to implement and sustain the intervention, versus comparators (e.g. staff, equipment, drugs, inpatient hospital care)?
- What are the incremental resource consequences of implementing the intervention, versus comparators? *or* How might the intervention impact on the subsequent (downstream) use of resources, versus comparators (e.g. complications, secondary procedures, outpatient visits, time-off-work)?
- What are the incremental costs associated with changes in resource use that may result from the intervention, versus comparators (e.g. direct and indirect medical costs, patient out-of-pocket expenses, income from employment)?
- What is the economic value associated with incremental beneficial or adverse effects (outcomes) that may result from the intervention, versus comparators (e.g. measures of willingness-to-pay, or utility)?
- What are the potential trade-offs between costs (resource use) and beneficial or adverse effects that may need to be considered in a decision to adopt or reject a given course of action?

In considering these preliminary questions, it is important to take the following key issues into account:

- *Magnitude*: What is the likely order of magnitude of different items of incremental resource use or incremental costs associated with the intervention, versus comparators? In other words, which items of resource use (resource inputs and resource consequences) and which costs are likely to be the most important when making choices between alternative interventions?
- *Time horizon*: What is the time horizon over which important costs (resource use) and effects (outcomes) are likely to accrue? Cochrane reviews implicitly establish a time horizon for effects by specifying intermediate and final endpoint measures of effects as target outcome measures. There is a parallel need to consider whether the same time horizon is applicable when all relevant costs (resource use) and effects are considered together.
- *Analytic viewpoint*: Who is likely to bear the incremental costs associated with an intervention, versus comparators, and who receives the incremental benefits (e.g. patient, patient's family, healthcare provider or third-party payer, healthcare system, society)? Some costs (resource use) are relevant from one analytic viewpoint, but not from another. For example, the cost of providing informal care may be relevant from a patient or a societal viewpoint, but may be excluded when a

narrower perspective is selected, such as that of the healthcare system. A further complication is that some resource use or cost categories may overlap between perspectives. Given the range of end-users of Cochrane reviews, a pragmatic approach is to consider the full range of perspectives and then to report not only measures of resource use and cost, but also who bears the cost or incurs the resource use.

Clinical event pathways can provide a further useful tool to help conceptualize the role and relevance of economic issues to a specific review topic. A clinical event pathway provides a systematic, explicit method of representing different health and social care processes and outcomes. The method involves describing the main pathways of events that have distinct resource implications or outcome values associated with them, from the point of introduction of the interventions, through subsequent changes in management of participants, to final outcomes (see also Chapter 2 of Donaldson (Donaldson 2002)). [Figure 15.2.a](#) shows an example clinical event pathway for the clinical event ‘stroke’. In developing a clinical event pathway, it is again important to consider the key issues of magnitude, time horizon and analytic viewpoint.

Once the role and relevance of economic issues has been considered carefully, one or more economic questions, or objectives, can be formulated. Review authors should avoid asking economic questions of the form ‘What is the cost-effectiveness of intervention X (compared with Y or Z)?’, since a critical review of health economics studies is unlikely to provide a credible answer to this type of question that is applicable across settings. Economic questions, or objectives, should be stated explicitly in the Objectives section of the protocol for a review, alongside other research questions and objectives.

Considerations of the role and relevance of economic issues can also be used to inform a commentary on economic aspects of interventions, to be included in the Background section of the review.

An ‘economics commentary’ can be included whether or not the authors intend to incorporate a critical review of health economics studies. This is useful to help set the interventions being studied in an economics context by highlighting their potential economic consequences for consideration by end-users of the review. The ‘economics commentary’ may highlight the economic burden of the illness or medical condition being addressed by interventions, the types of resources required to implement and sustain interventions (resource inputs), the potential impacts of interventions on the subsequent, downstream use of resources (resource consequences) and issues of cost-effectiveness. The commentary should be supported by appropriate references to, and critical comment on, relevant literature wherever possible. [Box 15.2.a](#) shows some examples of this type of commentary, extracted from Background sections of current Cochrane reviews.

Figure 15.2.a: Clinical event pathways

Event pathway	Example
Clinical event.	Stroke.
↓ Clinical event management + subsequent clinical events.	↓ Acute care and rehabilitation + sequelae and complications of treatment.
↓ Resources used to manage events and outcomes of events.	↓ Length of hospital stay, intensity of rehabilitation therapy, management of sequelae and complications (e.g. bleeding from secondary prophylaxis) and health outcomes associated with each stage.
↓ Cost of resources used and utilities of	↓ Valuation of resources using healthcare

outcomes.

(and other) pay and prices and valuation of outcomes, for example using quality-adjusted life years (QALYs) or willingness-to-pay (WTP).

Box 15.2.a: Background commentary highlighting economics aspects of interventions

“Faecal incontinence... can be a debilitating problem with medical, social and economic implications... In the United States more than \$400 million is spent each year on a range of both urinary and faecal incontinence products... During 1991 the direct costs of pads, appliances and other prescription items throughout hospitals and long term care settings in the UK for incontinence in general was estimated at £68 million... With the rise in numbers of elderly people in the world, this condition will be an increasing challenge to both healthcare services and home carers.” (Brown 2007).

“If such a new and relatively expensive treatment [Lamotrigine] is to be available for routine use, a clear understanding as to how it compares with a standard antiepileptic drug (AED) such as carbamazepine is needed. The potential cost implications are highlighted by a survey of epilepsy services in the North West, UK, which showed that almost 40% of drug costs (the largest single contributor of the direct costs of epilepsy) was accounted for by the new AEDs lamotrigine and vigabatrin, despite the fact they were only taken by seven per cent of patients.” (Gamble 2006).

“The cost of palliative chemotherapy treatment for advanced colorectal cancer includes not only the costs associated with the administration of chemotherapy, but also the provision of support to manage chemotherapy related complications. If palliative chemotherapy improves symptom control and quality of life this may reduce patient dependency and need for other symptomatic/ supportive care measures offsetting the cost of this treatment. On the other hand, if the incidence of chemotherapy related toxicity is high and there is a decrease in quality of life as a result of treatment, then the cost of palliative chemotherapy will become much greater than that of supportive care alone.” (Best 2000).

15.2.2 Including measures of resource use, costs and cost-effectiveness as outcomes

The process of formulating economic questions can also help to clarify the set of important measures of resource use, costs or cost-effectiveness (or a combination of these) to be included as target outcomes in a review. These outcomes should be included alongside other target outcomes in the ‘Types of outcome measures’ part of the ‘Criteria for considering studies for this review’ section of a review. Wherever possible, it is useful to break down measures of resource use and costs to the level of specific items or categories (e.g. length of hospital stay in days, duration of operation in minutes, number of outpatient attendances, bleeds from secondary prophylaxis at six-month follow-up, number of days off work, direct medical resource use, direct medical costs, indirect medical resource use or costs, patient out-of-pocket expenses) and to avoid the use of general descriptive terms for outcomes (e.g. ‘costs’, ‘resource utilization’, ‘health economics’). Measures of cost-effectiveness that may be included as target outcome measures in a review include incremental cost-effectiveness ratios (ICERs), incremental cost-per QALY and cost-benefit ratios (see also Section 15.1.2).

15.2.3 Specifying types of health economics studies and the scope of the economics component of a review

A critical review of health economics studies should specify at the outset which types of studies will be considered for inclusion (see also Section 15.1.2). This decision is driven primarily by the economic questions or objectives that have been formulated and the measures of resource use, costs and cost-effectiveness included as target outcome measures.

This decision should be made in consultation with a health economist, since it is not necessarily a straightforward exercise to map the analytic pathways between different forms of economic questions, 'economic' outcome measures and different types of health economics studies. For example, if a cost-effectiveness analysis includes reporting of results from all interim stages of analysis alongside final results, it may be possible to extract outcome data relating to measures of resource use, costs and cost-effectiveness; however if only final results are reported, it may only be possible to extract outcome data relating to measures of cost-effectiveness.

The types of health economics studies to be considered for inclusion in the review should be stated in the 'Types of studies' part of the 'Criteria for considering studies for this review' section. An illustrative statement featuring the full range of types of economics studies is as follows:

Types of studies

The following types of studies will be considered for inclusion in the critical review of health economics studies:

Full economic evaluation studies (i.e. cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses) of [intervention(s) versus comparator(s)]; partial economic evaluations (i.e. cost analyses, cost-description studies, cost-outcome descriptions) of [intervention(s) and comparator(s)]; and randomized trials reporting more limited information, such as estimates of resource use or costs associated with [intervention(s) and comparator(s)].

A final key methodological decision when planning a critical review of health economics studies is to set out the scope of this element of the review process. There are at least three options for the scope of a critical review of health economics studies:

1. Consider only relevant health economics studies conducted alongside effectiveness studies that meet eligibility criteria for the effectiveness component of the review;
2. Consider relevant health economics studies conducted alongside, and also those based upon data sourced from effectiveness studies that meet eligibility criteria for the effectiveness component of the review;
3. Consider all relevant health economics studies, whether or not conducted alongside, or based upon, effectiveness studies that meet eligibility criteria for the effectiveness component of the review.

The first option might typically allow only health economics studies conducted alongside high quality randomized trials to be considered for inclusion in the economics component of the review. The second option would *additionally* allow for consideration of economic modelling studies based on a meta-analysis of data from high quality randomized trials. A good example of a review of health economic models is the review of screening for abdominal aortic aneurysm conducted by Campbell and colleagues (Campbell 2007). The third option is clearly a more inclusive one that allows for consideration of all relevant health economics studies, including those based upon observational studies or analysis of large administrative databases, or regression-based cost and resource use analyses, for example.

Little is known about the impact of including these different types of health economics studies upon the results of a critical review. However, it is plausible that this type of decision regarding ‘scope’ at least has the potential impact on results, since different options may involve consideration of different sets of studies (see also Section 15.5.2). Also, where a review includes both economic evaluations based on single studies (e.g. randomized trials) and model-based economic evaluations, it may be optimal to consider each of these categories of studies separately, in order to retain comparability amongst studies.

In practice, a majority of current Cochrane reviews that set out to incorporate coverage of evidence from health economics studies restrict this coverage to economic studies conducted alongside effectiveness studies meeting eligibility criteria for the effectiveness component of the review (i.e. the first option), but do not state this explicitly (Shemilt 2007). Since the decision regarding scope has the potential to exclude some health economics studies without any recourse to critical appraisal of their methodological quality, the result of this decision should be stated in the ‘Types of studies’ part of the ‘Criteria for considering studies for this review’ section of a review, alongside details of the types of economic studies to be considered for inclusion, for example by appending “The review will consider only health economics studies conducted alongside effectiveness studies included in the effectiveness component of the review” to the illustrative statement above.

15.3 Locating studies

15.3.1 Use of electronic search filters

Search methods for locating relevant health economics studies will differ depending on the scope of a critical review of such studies and the types of studies to be considered for inclusion (see also Sections 15.2.3 and 15.1.2). However, in all cases the first stage of the search strategy will have the same objective: to identify effectiveness studies retrieved for initial screening and potential inclusion in a Cochrane review which include relevant health economics studies.

Electronic records of effectiveness studies retrieved from electronic literature databases can be filtered using search strategies designed to capture health economics studies. This can precede visual screening of abstracts and full texts of studies, acting as an aid to location of economic studies by limiting the number of records to be assessed. Electronic filtering is most useful in reviews where the number of records retrieved from electronic literature databases is large (i.e. where this number is relatively small, use of electronic filters may not be judged necessary, but explicit criteria would still need to be applied).

The Centre for Reviews and Dissemination (CRD) has developed a series of electronic search strategies designed to capture potential economic evaluation studies for inclusion in the NHS Economic Evaluation Database (NHS EED). MEDLINE (Ovid CD-ROM), CINAHL (Ovid CD-ROM), EMBASE (Ovid online) and PsychINFO (Ovid online) versions are published in the NHS EED Handbook (Craig 2007) and online at www.york.ac.uk/inst/crd/nfaq2.htm. Each of these search strategies can be appended to review-specific search strategies of the corresponding database using the ‘AND’ operator, to filter search results for records which also contain ‘economics’ search terms.

These NHS EED search strategies are very broad and will capture economics methods studies and reviews of economics studies, as well as the full range of types of health economics studies (see Section 15.1.2). For more specific searches, narrower adaptations of the search strategies and close reading of the scope notes of MeSH are advised. The search strategies can also be adapted, in consultation with information retrieval specialists, for use in other electronic literature databases.

Adaptation of the search strategies will need to take into account variations across databases in the indexing or classification of health economics studies. A useful annotated list of electronic literature databases that include coverage of health economics literature and details of internet sites containing relevant grey literature is available (Napper 2005).

An important procedural consideration when considering use of electronic search filters designed to capture health economics studies is that Cochrane reviews also frequently utilize other search filters designed to capture other specific study designs, such as randomized trials. These ‘study design search filters’ are also appended to review-specific search strategies using the ‘AND’ operator. Therefore, if the scope of the critical review is not restricted to health economics studies conducted alongside effectiveness studies included in the effectiveness component of the review (e.g. will also include model-based economic evaluations: see Section 15.2.3), then the ‘economics search filter’ should be appended to any other ‘study design search filter’ using the ‘OR’ operator, to ensure that all types of health economic studies to be considered are retrieved. Alternatively, if the scope of the critical review is limited to health economics studies conducted alongside effectiveness studies included in the effectiveness component of the review, then use of the ‘economics search filter’ is not required, since most of the economics studies to be considered will be retrieved using the ‘study design search filter’ (although, it is possible that in this case the search results may still omit some relevant economics studies, such as economic evaluations based on randomized trials but published separately from and usually after the trial results).

15.3.2 Use of specialist databases

The NHS Economic Evaluation Database (NHS EED) is published as part of *The Cochrane Library* (www.thecochranelibrary.com). Therefore, whenever users search *The Cochrane Library*, NHS EED records will be highlighted as well as Cochrane reviews. NHS EED is also available free online from the Centre for Reviews and Dissemination (CRD) web site (see www.york.ac.uk/inst/crd/crddatabases.htm). The version of NHS EED in *The Cochrane Library* is updated quarterly, whilst the CRD web site version is updated monthly.

A search of NHS EED and processing of these search results is recommended for all Cochrane reviews, especially those incorporating a critical review of health economics studies. NHS EED contains structured abstracts of full economic evaluations in health care, published in all languages, as well as bibliographic records of partial economic evaluations, methodology studies and reviews of economic studies. The NHS EED structured abstract format includes a critical commentary written by independent health economist peer reviewer and presents details of methods, results and other data in a summary format that is directly useful to inform critical appraisal and data collection in a critical review of health economics studies (see Sections 15.5.2 and 15.4.2).

It may sometimes be considered useful to include NHS EED abstracts of relevant full economic evaluation studies as an appendix to a published Cochrane review, as was done by Rodgers et al. and Fayter et al. (Rodgers 2006, Fayter 2007) (see also Section 15.6.2). If NHS EED does not contain a structured abstract of a full economic evaluation identified during searches conducted for a Cochrane review, it would be useful if the review authors could alert the Campbell and Cochrane Economics Methods Group (Box 15.10.a), so that NHS EED researchers can be made aware of the need to consider producing an abstract.

Searches of NHS EED and other specialist databases of health economics literature (see below) can be conducted using adaptations of review-specific search strategies, excluding both ‘economics search filters’ and other ‘study design search filters’. When searching *The Cochrane Library*, NHS EED is searched by default (i.e. unless the database is specifically excluded from the search using advanced

search options). Information on how to search the CRD web site version of NHS EED can be accessed in CRD help pages at www.crd.york.ac.uk/crdweb/html/help.htm.

The desire to extend the principles of the UK-based NHS EED database to other European countries has led to the establishment of the European Network of Health Economic Evaluation Databases (EURONHEED), which is also freely available online (see <http://infodoc.inserm.fr/euronheed/>). NHS EED provides links to EURONHEED full abstract records only (from 2000 forward), so although a search of NHS EED will retrieve all full abstract records from both databases, it will not retrieve bibliographic records of partial economic evaluations, methodology studies or reviews of economics studies that are held in EURONHEED only.

NHS EED, EURONHEED and other specialist databases of health economics literature that may be searched for Cochrane reviews (including The CEA Registry, the Health Economic Evaluations Database (HEED) and Econlit) are fully described in a paper published by the NHS EED project team (Aguiar-Ibanez 2005). CRD also publishes an annotated online list containing details of these databases, including links to each database web site, at www.york.ac.uk/inst/crd/econ4.htm, as part of their 'Information resources in health economics' pages (www.york.ac.uk/inst/crd/econ.htm). This annotated list also includes details of selected general databases which include coverage of health economics literature (see also Section 15.3.1).

If the scope of the critical review of health economics studies is limited to those studies conducted alongside effectiveness studies that meet eligibility criteria for the effectiveness component of the review (see Section 15.2.3), then the sole aim of a supplementary search of NHS EED and other specialist databases is to check whether they include any structured abstracts of full economic evaluation studies conducted alongside included effectiveness studies. However, if the scope of the critical review of health economics studies is broader (see Section 15.2.3), then an *additional* aim is to identify *further* economic studies for potential inclusion in the review.

15.4 Selecting studies and collecting data

15.4.1 Assessing relevance to the review topic

Once full-text papers of potentially relevant health economics studies have been obtained (and structured abstracts of full economic evaluations, where available), the next step is to assess the relevance of each of these studies to the specific review topic, as a preliminary stage to addressing the issue of risk of bias. Decisions to either include or exclude health economics studies on grounds of relevance should be based on whether or not they meet eligibility criteria relating to the target populations, interventions, comparisons and outcomes that were specified in the protocol for the review. Reasons for excluding health economics studies at this stage should be reported in 'Characteristics of excluded studies' tables.

15.4.2 Collecting data

Precise data collection requirements for the economics components of Cochrane reviews will need to be specified for each individual review, depending on the specific economics question or objective and on the measures of *incremental* resource use, costs or cost-effectiveness included as target outcomes. In general terms, two types of data will need to be collected: details of the characteristics of included health economics studies and details of their results. The potential to extract data as suggested below from published reports may be constrained by the quality of reporting of the health economics studies (where information is missing, a further option is to contact study authors to request additional details).

Useful data to be collected regarding the characteristics of each economic study are likely to include: year of study; details of interventions and comparators; study design and source(s) of resource use, unit costs and (if applicable) effectiveness data (see also Sections 15.1.2 and 15.2.3); decision-making jurisdiction, geographical and organizational setting; analytic viewpoint; and time horizon for both costs and effects (see Section 15.2.1).

For results, estimates of specific items of resource use associated with interventions and comparators and estimates of their unit costs should be extracted separately, if reported, as well as estimates of costs of the resource use (i.e. number of units of resource X unit cost). The type and quantity of each resource used should be extracted in natural units (e.g. length of hospital stay in days, duration of operation in minutes, number of outpatient attendances at six-month follow-up, number of days of work). It is also important to collect information on the price year and currency used to calculate estimates of costs and incremental costs. Measures of incremental resource use and costs should be collected at the individual patient level (i.e. resource use per patient, cost per patient), wherever possible. Both a point estimate and a measure of uncertainty (e.g. standard error or confidence interval) should be extracted for measures of incremental resource use, costs and cost-effectiveness, if reported. Additionally, it is useful to collect details of any sensitivity analyses undertaken, and any information regarding the impact of varying assumptions on the magnitude and direction of results.

CRD Report 6 (Craig 2007) includes a template for producing structured abstracts of full economic evaluations for inclusion in NHS EED (see also Section 15.3.2), together with notes to guide data collection and critical appraisal. These materials can provide a useful template for the design of data collection forms for use in the economics components of Cochrane reviews.

If a full economic evaluation already has a corresponding NHS EED structured abstract, this *may* obviate the need for researchers to undertake further data collection from the study. In parallel, given that critical appraisal and data collection from economic evaluation studies with no completed NHS EED abstract will need to be undertaken for the Cochrane review, authors are encouraged to consider registering with NHS EED to produce an abstract, in order to avoid duplication of effort. Please contact CCEMG for further information, or to initiate a request that a structured abstract is produced by NHS EED (see also Section 15.3.2).

15.5 Addressing risk of bias

15.5.1 Classification of studies by study design

A preliminary stage to be undertaken before addressing risk of bias is to classify the included health economics studies by study design. Methods underpinning critical appraisal of the methodological quality of health economics studies will vary slightly depending on study design.

Classification should consist of two stages:

1. Classification of the design of the health economics study.
2. Classification of the design of the study generating the effectiveness data on which the health economics study is based, if applicable.

Each health economics study may be classified (stage 1) as a type of full economic evaluation, a type of partial economic evaluation, or a type of effectiveness study (e.g. a randomized trial) reporting more limited information on the resource use or costs associated with an intervention (see Section 15.1.2). Classifying the design of the study that generates the effectiveness data on which the health economics study is based (stage 2) is only applicable in the case of health economics studies classified

as a full economic evaluation or as a cost-outcome description at the first stage of classification. The study generating the effectiveness data may be a single study design (e.g. a randomized trial, a non-randomized trial, an observational study) or a synthesis of several studies (e.g. a meta-analysis of randomized trials) (see also Section 15.1.2).

It is likely to be useful to consult with a health economist when undertaking classification of health economics studies. This is because health economics studies reported to use one type of study design (e.g. a cost-benefit analysis) may, on closer inspection, turn out to use another (e.g. a cost-effectiveness analysis). This means that particular care is required when classifying economic studies encountered during a review (Zarnke 1997).

Depending on the scope of the critical review of health economics studies and the types of studies that will be considered for inclusion (see Section 15.2.3), health economics studies may be excluded at this stage, based on classification by study design. Once again, reasons for excluding health economics studies at this stage should be reported in 'Characteristics of excluded studies' tables.

15.5.2 Critical appraisal of methodological quality

The next stage of research is to undertake critical appraisal of the methodological quality of the remaining health economics studies, in order to address risk of bias. Variability in the quality of the conduct and reporting in health economic analyses is well documented (Neumann 2005). The core objective of critical appraisal of health economics studies is to assess whether they describe methods, assumptions, models and possible biases in a way that is transparent and fully supported by available evidence, the strength of which is made easily accessible to any critical reader (Rennie 2000).

Critical appraisal of health economics studies can be informed by the use of checklists that have been developed to guide assessments of methodological quality. Where checklists are used to inform critical appraisal of health economics studies in a Cochrane review, bibliographic details of the checklist should be cited in the 'Data collection and analysis' section. Whichever checklists are used, it is also useful to consider including additional tables to summarize completed checklists for included health economics studies in the published review.

The reliability of a full economic evaluation (see Section 15.5.2) is in part predicated on its use of reliable effectiveness data, so part of the critical appraisal of a full economic evaluation conducted alongside a single effectiveness study (e.g. a randomized trial) involves considering all those sources of potential bias that may apply to the effectiveness study used (see Chapter 8). For this type of full economic evaluation study, the critical appraisal will therefore consist of the following two parts.

1. Assessment of the risk of bias in results of the single effectiveness study on which the full economic evaluation study is based, informed by a recognized checklist for effectiveness studies.
2. Assessment of the methodological quality of the full economic evaluation study, informed by a recognized checklist for economic evaluations conducted alongside single study designs.

A number of checklists have been developed to guide critical appraisal of health economics studies. Whilst no checklists have been formally validated, two have received more scrutiny than most:

- British Medical Journal Checklist for authors and peer reviewers of economic submissions (Drummond 1996);
- CHEC list for assessment of methodological quality of economic evaluations (Evers 2005).

These checklists are reproduced in [Figure 15.5.a](#) and [Figure 15.5.b](#). Use of the ‘Drummond checklist’ and the ‘Evers checklist’ is recommended in Cochrane reviews to inform appraisal of the methodological quality of full economic evaluations conducted alongside single effectiveness studies, and also to inform critical appraisal of partial economic evaluations using the subset of applicable checklist items (see also [Section 15.1.2](#)).

If the scope of the critical review of health economics studies encompasses relevant economic modelling studies (see [Section 15.2.3](#)), then assessments of the methodological quality of such studies will need to be informed by a different checklist, since the ‘Drummond checklist’ and ‘Evers checklist’ are relevant but not sufficient for modelling studies. The ‘Phillips checklist’ is recommended to inform critical appraisal of the methodological quality of economic modelling studies (Phillips 2004). Use of this checklist can be supplemented by referring to a published hierarchy of data sources which sets out the sources of data that are recognized as the best available sources to inform each parameter in an economic model (Cooper 2005).

Critical appraisal of the methodological quality of all types of full economic evaluation can usefully be informed by a corresponding NHS EED structured abstract, if available, to supplement the use of checklists (see also [Section 15.3.2](#)). This is because NHS EED structured abstracts include critical appraisal of study quality based on the same dimensions of quality reflected in the checklists recommended above.

There are as yet no widely validated minimum methodological criteria to be applied to screening economic studies for inclusion in systematic reviews. Decisions to include or exclude such studies will therefore need to be made on the basis of an overall judgement regarding their methodological quality, as well as their relevance in terms of the economic questions, interventions, populations and outcomes being studied (see [Section 15.4.1](#)). Eligibility criteria relating to dimensions of the methodological quality of health economics studies should be stated in the ‘Data collection and analysis’ section.

It is also important to highlight that, to date, there has been relatively little empirical research to investigate the impact upon the results of a critical review of health economics studies, of decisions to include economic studies that meet some but not all standards of methodological quality. However, as with choice of eligibility criteria relating to quality and design of effectiveness studies, and to the design of health economics studies (see also [Section 15.2.3](#)), it is plausible that use of different data sources for measures of resource use, cost and/or cost-effectiveness has at least the potential to impact on results (see also [Section 15.7](#)).

Figure 15.5.a: Drummond checklist (Drummond 1996)

Item	Yes	No	Not clear	Not appropriate
Study design				
1. The research question is stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. The economic importance of the research question is stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3. The viewpoint(s) of the analysis are clearly stated and justified.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. The rationale for choosing alternative programmes or interventions compared is stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5. The alternatives being compared are clearly described.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
6. The form of economic evaluation used is stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7. The choice of form of economic evaluation is justified in relation to the questions addressed.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Data collection				
8. The source(s) of effectiveness estimates used are stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

9.	Details of the design and results of effectiveness study are given (if based on a single study).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.	Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.	The primary outcome measure(s) for the economic evaluation are clearly stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12.	Methods to value benefits are stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.	Details of the subjects from whom valuations were obtained were given.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14.	Productivity changes (if included) are reported separately.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15.	The relevance of productivity changes to the study question is discussed.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16.	Quantities of resource use are reported separately from their unit costs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
17.	Methods for the estimation of quantities and unit costs are described.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
18.	Currency and price data are recorded.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
19.	Details of currency of price adjustments for inflation or currency conversion are given.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
20.	Details of any model used are given.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
21.	The choice of model used and the key parameters on which it is based are justified.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Analysis and interpretation of results					
22.	Time horizon of costs and benefits is stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
23.	The discount rate(s) is stated.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
24.	The choice of discount rate(s) is justified.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
25.	An explanation is given if costs and benefits are not discounted.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
26.	Details of statistical tests and confidence intervals are given for stochastic data.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
27.	The approach to sensitivity analysis is given.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
28.	The choice of variables for sensitivity analysis is justified.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
29.	The ranges over which the variables are varied are justified.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
30.	Relevant alternatives are compared.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
31.	Incremental analysis is reported.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
32.	Major outcomes are presented in a disaggregated as well as aggregated form.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
33.	The answer to the study question is given.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
34.	Conclusions follow from the data reported.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
35.	Conclusions are accompanied by the appropriate caveats.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Figure 15.5.b: Evers checklist (Evers 2005)

Item	Yes	No
1. Is the study population clearly described?	<input type="checkbox"/>	<input type="checkbox"/>
2. Are competing alternatives clearly described?	<input type="checkbox"/>	<input type="checkbox"/>
3. Is a well-defined research question posed in answerable form?	<input type="checkbox"/>	<input type="checkbox"/>
4. Is the economic study design appropriate to the stated objective?	<input type="checkbox"/>	<input type="checkbox"/>
5. Is the chosen time horizon appropriate to include relevant costs and consequences?	<input type="checkbox"/>	<input type="checkbox"/>
6. Is the actual perspective chosen appropriate?	<input type="checkbox"/>	<input type="checkbox"/>
7. Are all important and relevant costs for each alternative identified?	<input type="checkbox"/>	<input type="checkbox"/>
8. Are all costs measured appropriately in physical units?	<input type="checkbox"/>	<input type="checkbox"/>
9. Are costs valued appropriately?	<input type="checkbox"/>	<input type="checkbox"/>
10. Are all important and relevant outcomes for each alternative identified?	<input type="checkbox"/>	<input type="checkbox"/>

11.	Are all outcomes measured appropriately?	<input type="checkbox"/>	<input type="checkbox"/>
12.	Are outcomes valued appropriately?	<input type="checkbox"/>	<input type="checkbox"/>
13.	Is an incremental analysis of costs and outcomes of alternatives performed?	<input type="checkbox"/>	<input type="checkbox"/>
14.	Are all future costs and outcomes discounted appropriately?	<input type="checkbox"/>	<input type="checkbox"/>
15.	Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	<input type="checkbox"/>	<input type="checkbox"/>
16.	Do the conclusions follow from the data reported?	<input type="checkbox"/>	<input type="checkbox"/>
17.	Does the study discuss the generalizability of the results to other settings and patient/ client groups?	<input type="checkbox"/>	<input type="checkbox"/>
18.	Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	<input type="checkbox"/>	<input type="checkbox"/>
19.	Are ethical and distributional issues discussed appropriately?	<input type="checkbox"/>	<input type="checkbox"/>

15.6 Analysing and presenting results

The emphasis of guidance on analytic methods for the economics components of Cochrane reviews is upon tabulation of the characteristics and results of included health economics studies. This can be supplemented by a narrative summary which focuses on critical appraisal of included studies and discussion of their principal findings. Additionally, in some circumstances, a meta-analysis of resource use or cost data, or development of an economic model, may be considered. These options are described in more detail in the sections that follow. Further options for analysing health economics studies and presenting the results of these analyses need to be evaluated through further methodological research (see Section 15.9).

15.6.1 Presenting results in tables

‘Characteristics of included studies tables’ provide a natural place in a Cochrane review to present details of the characteristics of included health economics studies, such as year of study; details of interventions and comparators; study design; data sources; jurisdiction and setting; analytic perspective and time horizon (see also Section 15.4.2). Authors may also consider including additional tables to summarize checklists completed to inform assessments of the methodological quality of included health economics studies (see also Section 15.5.2).

The results of included health economics studies can be summarized using either ‘Characteristics of included studies’ tables, Additional tables, or both. In either case, where possible, point estimates of measures of items of resource use or costs should be presented with associated measures of uncertainty for both the target intervention and each of its comparators, as well as point estimates of *incremental* costs and/or cost-effectiveness, again with associated measures of uncertainty. It is also important to state the currency and price year alongside estimates of costs and/or incremental costs (if reported).

It may be possible to convert cost estimates to a common currency and price year, in order to facilitate comparison of estimates collected from different studies. An international exchange rate based on Purchasing Power Parities (PPPs) should be used to convert cost estimates to a target currency, and gross domestic product (GDP) deflators (or implicit price deflators for GDP) should be used to convert cost estimates to a fixed price year. Data sets containing PPP conversion rates and GDP deflator values are available from the International Monetary Fund in the World Economic Outlook Database

(updated biannually: see www.imf.org/external/data.htm). Conversion of cost estimates to a common currency and price year should only be performed in consultation with an experienced health economist. CCEMG will aim to issue further methods guidance on this topic in due course.

15.6.2 Narrative summary of results

Cochrane reviews may include narrative summaries of the main characteristics and results of included economic studies, including measures of incremental resource use, cost and cost-effectiveness, to supplement and provide a commentary on tabulated results. This can be located in the Results section, alongside narrative summary of the results of effectiveness studies (see Chapter 11, Section 11.7)

The central aim of this narrative summary is to make explicit, for the end-user, the extent to which cost and resource use estimates collected from multiple studies are homogeneous between studies. This can be accomplished by describing differences in methods for assessing, and patterns of, resource use and costs between comparison groups, both within and across included studies, with potential explanations for any inconsistencies in results between studies. As discussed earlier in this chapter, economic evaluation studies are constructed differently and for different purposes (see also Section 15.1.2). This is the one factor that may lead to heterogeneity between studies in their methods and results. Where there is heterogeneity between economics studies in their methods or results, drawing attention to these potential sources of *statistical* heterogeneity can help to summarize the international economics literature in an explicit way that is likely to be useful to the end-users of reviews (Gilbody 1999). It is important to avoid using this section as a form of analysis leading to recommendations regarding cost-effectiveness (see also Section 15.8).

Other features of good practice in a narrative summary of included health economics studies include:

- reporting the overall numbers of health economics studies selected for inclusion in the review, by study design;
- outlining the economic questions addressed within included studies;
- reporting the designs of included studies;
- reporting the analytic viewpoints adopted within included studies;
- reporting the time horizons adopted within included studies;
- discussion of measures of *incremental* resource use, costs and/or cost-effectiveness reported within included studies;
- reporting measures of uncertainty alongside measures of resource use, costs and/or cost-effectiveness extracted from reports of included studies;
- reporting currency and price year alongside estimates of costs extracted from included studies;
- adjusting cost estimates extracted from reports of each included study to a common currency and price year, if possible;
- highlighting key features of sensitivity analyses undertaken and consistency of results, both within sensitivity analyses and across included studies;
- discussion of the overall methodological quality and limitations of included studies;
- discussion of the relevance and generalizability of the results of included studies to other jurisdictions and settings; and
- discussion of the quality of effectiveness data used in included health economics studies and the relationship between outcomes used and those estimated in the effectiveness component of the Cochrane review.

A further option is to provide links to completed NHS EED or other structured abstracts of full economic evaluation studies, if available. NHS EED structured abstracts include information on both the characteristics and results of full health economic evaluations (see also Section 15.3.2). Some systematic reviews include NHS EED abstracts of included full economic evaluations in an appendix, as well as a narrative summary of the abstracts in the main text of the review (Rodgers 2006, Fayer 2007).

15.6.3 Meta-analysis of resource use and cost data

There are currently no agreed-upon methods for pooling combined estimates of cost-effectiveness (e.g. incremental cost-effectiveness, cost-utility or cost-benefit ratios), extracted from multiple economic evaluations, using meta-analysis or other quantitative synthesis methods. However, in principle, if estimates of measures of resource use and costs in a common metric (and associated measures of uncertainty) are available from two or more included studies, for an intervention and its comparator, these can be pooled using a meta-analysis. In practice, extreme caution is advised when considering whether to undertake a meta-analysis of resource use or cost data as part of a Cochrane review. Prior to any decision to pool estimates using a meta-analysis, particular attention should be given to whether the metric in question has equivalent meaning across studies.

Resource use and costs are sensitive to variability across settings, both *within* a country and *between* countries, in features of the local context, such as local prices or aspects of service organization and delivery (Drummond 2001, Sculpher 2004). This may limit the generalizability and transferability of estimates of cost, resource use and, by implication, estimates of cost-effectiveness, across settings. It is also the principal reason that resource use and cost data relating to specific target populations and jurisdictions of interest are regarded as the best available source of data for use in economic evaluations to be used in resource allocation decision processes in the specific setting (Cooper 2005). These issues have generated debate on whether meta-analysis of measures of resource use or costs across wider geographical and political boundaries is likely to generate meaningful results, how the results of such meta-analyses should be interpreted and what additional value the results may have for end-users of Cochrane reviews. (Further discussions around issues of applicability and transferability of health economic evaluations can also be found in texts by Hutubessy et al and Kumaranayake and Walker (Kumaranayake 2002, Hutubessy 2003).

On the other hand, whether specific estimates of resource use or costs are generalizable, or transferable, across settings may be regarded as an empirical question. In circumstances where there is evidence of little variation in resource or cost use between studies, it may be regarded as legitimate to present a pooled estimate. Otherwise it is important that the distribution of costs is clearly presented. Many completed Cochrane reviews include meta-analyses of resource use data. A small number of Cochrane reviews include meta-analyses of cost data, although these are not always accompanied by critical appraisal of the methods used to generate these data.

If meta-analyses of resource use or cost data are undertaken in a Cochrane review, this should always be supported by thorough critical appraisal of the methods used to derive such estimates within the corresponding health economics studies (see Sections 15.5.2, and 15.6.2), alongside use of statistical methods to investigate and incorporate between-study heterogeneity (e.g. I^2 , chi-squared; random-effects models: see Chapter 9, Section 9.5). Cost estimates collected from multiple studies should be adjusted to a common currency and price year before these data are pooled (see also Section 15.6.1). Authors should consult Chapter 9 for further guidance on the statistical procedures underpinning meta-analysis.

If meta-analyses of resource use or cost data are conducted, a narrative summary should be included in the Results section to comment on the direction and magnitude of results and their precision.

Similarly, if two or more health economics studies are included in a review, but a decision is taken not to pool (in a meta-analysis) resource use and/or cost data that have been collected from these studies, this can be stated in the Methods section (see [Box 15.6.a](#) for an example of this type of statement).

Box 15.6.a: Statement of a decision not to conduct a meta-analysis of resource use or cost data

“[Resource use and cost outcomes] were not pooled as the outcomes were not considered comparable across trials... The results are specific to the countries in which the studies were undertaken because of differences between the public health systems. The detailed reports show very different apportionment of costs between different items in different countries.”
(Birks 2006).

15.6.4 Developing an economic model

Cochrane reviews can contribute key components of the evidence required to develop a subsequent or parallel full economic evaluation, including use of a decision-analysis approach for pooling or modelling the available evidence on intervention costs and effects (see also [Sections 15.1.2](#) and [15.1.3](#)). This approach usually involves estimation of the point estimate, and description of the joint distribution, of incremental costs and effects resulting from an intervention (in terms of cost-effectiveness, cost-utility or cost-benefit), compared with a relevant alternative, in a defined population and setting, and with included costs and outcomes agreed to be relevant from a specific, stated analytic viewpoint (e.g. patient, healthcare provider or third-party payer, healthcare system, society).

Economic modelling methods are not covered in detail here, as their routine use as part of the Cochrane review process is not recommended. However, authors of Cochrane reviews wishing to pursue the ‘in-depth’ economics of interventions are encouraged to collaborate with researchers with expertise in developing economic models. It may sometimes be possible to develop a general structure for an economic model as part of a Cochrane review, where the basic model inputs and outputs are similar across different settings, but where some (or even all) of the data required to populate the model are specific to a local setting.

Also, notwithstanding issues already discussed regarding the generalizability and transferability of the results of economic evaluations across jurisdictions and settings (see [Section 15.6.3](#)), it cannot be ruled out that it may sometimes be considered worthwhile (although time, resource and expertise intensive) to develop one or more economic models for publication in a Cochrane review. For example, one motivation to develop an economic model as part of a Cochrane review may be an intention to use the review to inform directly the design of future research that will incorporate an economic evaluation component. In these circumstances, developing a model can help to clarify the structural assumptions and parameters that need to be considered in an economic evaluation, and the data that will need to be collected during the research. If this type of approach is pursued in a Cochrane review, it needs to be made clear that each example economic model aims to provide an illustrative assessment of the cost-effectiveness of the interventions being compared, in an example jurisdiction and at a given point in time.

Economic modellers are also encouraged to consider utilizing the evidence contained in Cochrane reviews to inform the development of economic models. Efforts to incorporate economics evidence into Cochrane reviews using the methods outlined in this chapter aim in part to increase the relevance and applicability of Cochrane reviews for use in subsequent, or parallel, full economic evaluation modelling exercises.

15.7 Addressing reporting biases

It is widely recognized that commercial and other pressures may affect the funding of studies and reporting of the results of studies which focus on the economic value of healthcare interventions (Drummond 1992). Despite this, until recently relatively little research attention has been focused on the issue of publication and related biases in economic evaluation studies, compared with coverage of this issue with respect to effectiveness studies. However, several recent studies have begun to examine this issue using systematic review and research synthesis methods.

Bell and colleagues undertook a systematic review of published cost-effectiveness studies in health care and found that studies sponsored by industry were more likely to report ratios that fall beneath, and cluster around, commonly proposed cost-effectiveness acceptability thresholds, when compared with studies sponsored by non-industry sources (Bell 2006). Miners and colleagues undertook a systematic review to compare evidence on cost-effectiveness submitted to the National Institute of Health and Clinical Excellence (NICE) by manufacturers of the relevant healthcare technologies and by contracted university-based assessment groups respectively (Miners 2005). This study found that estimated incremental cost-effectiveness ratios submitted by manufacturers were, on average, significantly lower than those provided by the assessment groups for the same technology. Friedberg and colleagues found that published economic analyses of new drugs used in oncology funded by pharmaceutical companies were one eighth as likely to reach unfavourable quantitative conclusions (and 1.4 times as likely to reach favourable qualitative conclusions) when compared to non-profit funded studies (Friedberg 1999). Other reviews focusing on this issue have reached broadly similar conclusions (Freemantle 1997, Azimi 1998, Lexchin 2003). A common theme of the discussion in these methodology review studies is the authors' suspicion that reporting or publication biases are likely to be instrumental in the observed patterns of results. The general hypothesis is that economic analyses with results that suggest an intervention may be economically unattractive are, consciously or unconsciously, not published by sponsors, authors, or journal editors.

However, all of the above methodology review studies are limited by their design (limitations are usually acknowledged and discussed by the authors). The ideal and most robust study design to investigate the presence of reporting and publication biases would involve direct comparison of published and unpublished findings within studies, or direct comparison of the findings of published and unpublished studies (Song 2000). As such, a systematic, comprehensive comparison is clearly difficult to achieve, due to the inherent difficulties of identifying all relevant unpublished economic analyses. In the absence of such data, it is not possible to rule out alternative explanations for the observed patterns of results (e.g. the results could reflect the true distributions of incremental cost-effectiveness ratios).

Methods for addressing publication bias in systematic reviews, which can be applied, with the same caveats, in systematic reviews of economic studies, are covered in Chapter 10. Proposals that have been suggested to help address publication and related biases in economic evaluation studies, such as those that may be encountered in Cochrane reviews, are:

1. to encourage a more transparent, consistent approach to the conduct and reporting of economic analyses, through the promulgation of good practice guidelines and checklists for use in critical appraisal of such studies – in particular review-based studies and modelling studies;
2. to increase scrutiny of journal submissions for potential conflicts of interest of study sponsors and authors; and
3. to increase access to all the underlying data used in an economic evaluation in order to increase transparency of methods.

15.8 Interpreting results

Interpretation of the results of a review of health economics studies is dependent on the specific economic questions and context of relevance to a given decision regarding the provision of health care. In Cochrane reviews – intended for an international audience – there are clearly a large number of potential economic questions and contextual factors that different decision-making constituencies may need to take into account. Given this global context, it is simply not feasible to interpret the results of a critical review of multiple economic evaluation studies in order to draw conclusions about the adoption or rejection of a healthcare treatment or diagnostic test, for example. However, whilst in these circumstances the Cochrane review is unlikely to provide the central aspect of any policy evaluation, it can still help to refine an economic discussion and to set this in an international context (Gilbody 1999).

In a review topic area with few or no relevant, high-quality economic evaluation studies, the critical review of health economics studies can serve to highlight a lack of economics evidence that future research may need to address. The need for further economic evaluation studies should be stated within the ‘Implications for research’ part of the ‘Authors’ conclusions’ section of the review. [Box 15.8.a](#) shows two examples of this type of statement. It should also be considered that since a full economic evaluation is predicated on the availability of reliable data on intervention effectiveness, a lack of robust effectiveness studies would clearly impact upon the feasibility and availability of full economic evaluation studies. Again, whilst Cochrane and other systematic reviews cannot overcome this limitation, they can draw attention to it within their conclusions sections.

Box 15.8.a: Highlighting a need for further economics studies in conclusions

“Most of the time, the cost of the intervention is not calculated [in included studies]. This information is crucial. In future studies, cost savings should be calculated and balanced against the potential costs of the intervention...The question of whether cost effective services can be delivered is a critical question for today’s healthcare environment. Thus studies that measure the costs as well as the effects of pharmacist interventions are needed.” (Beney 2000).

15.9 Conclusions

This chapter has outlined a methodological framework for incorporating evidence from health economics studies into the Cochrane review process. Whilst this exercise is extremely unlikely, and is not recommended, to produce statements about whether “intervention X is cost-effective”, it can help decision makers to understand the structure of the resource allocation problem they are addressing, the main parameters that need to be considered, variation between settings in terms of resource use, costs and cost-effectiveness, and potential reasons for these variations (Drummond 2002). Incorporating economics evidence can also enhance the usefulness and applicability of Cochrane reviews as a source of data for subsequent (or parallel) full economic evaluations. It is anticipated that this guidance will continue to be refined and updated as a result of being subjected to further criticism from a wider audience, and as the methods continue to develop based on experience of their use in Cochrane reviews and further methodological research.

The process of developing this guidance has also helped to clarify key priorities for further research aiming to develop and test alternative methods for the identification, appraisal, analysis and presentation of evidence on economic aspects of interventions. Key research priorities include: further development of a balance-sheet approach to summarizing the results of economics components of reviews, evaluation of the impact on the results of economic reviews of applying different methodological quality criteria or thresholds for inclusion of economic evaluation studies, and

evaluation of methods which utilize individual-level data to investigate and deal with heterogeneity between settings in resource use, costs and utilities (and other measures of preferences for health states). These and other methods research priorities are listed on the 'Research' pages of the CCEMG web site (see [Box 15.10.a](#)).

15.10 Chapter information

Authors: Ian Shemilt, Miranda Mugford, Sarah Byford, Michael Drummond, Eric Eisenstein, Martin Knapp, Jacqueline Mallender, David McDaid, Luke Vale, Damian Walker on behalf of the Campbell and Cochrane Economics Methods Group.

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Box 15.10.a: The Campbell and Cochrane Economics Methods Group

The Campbell and Cochrane Economics Methods Group (CCEMG) was formally registered as a Cochrane Collaboration methods group in 1998 and has been jointly registered as a Campbell Collaboration methods group since 2004. Core aims of the group include, within available resources, the following:

- to promote and support consideration of economics issues within systematic reviews;
- to develop economics methods for Cochrane reviews that are relevant to the consumers of reviews and appropriate, unbiased and objective in terms of their application; and
- to link review authors and editors with economists who can help with reviews or provide specialist advice and peer review.

Many Cochrane reviews already include coverage of economics aspects of interventions. However, this chapter is the first time that the *Handbook* has included detailed guidance on the use of economics methods in Cochrane reviews. Future versions of the chapter will be informed by an ongoing programme of methodological research and further experience of Cochrane reviews incorporating economics evidence.

E-mail: research@c-cemg.org

Web site: www.c-cemg.org

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