The Joanna Briggs Institute
Reviewers’ Manual 2014
The Systematic Review of Economic Evaluation Evidence
Foreword

Every year the Joanna Briggs Institute publishes a Reviewers’ Manual, which is designed to support individuals who are undertaking systematic reviews following JBI methodologies and methods. This chapter represents the latest work and methodological development of the Institute that was not ready for inclusion in the 2014 edition of the Reviewers’ Manual that was published in January.

As with the Reviewers’ Manual we recommend that this chapter be utilized in conjunction with the JBI SUMARI User Guide. Please note that this chapter makes reference to forthcoming analytical modules that do not currently exist in the JBI SUMARI software suite, but should be available in 2015. For advice on how to best apply the current software to accommodate this new methodology please contact the Synthesis Science Unit of the Institute at jbisynthesis@adelaide.edu.au

We hope that the information contained herewith provides further insight into how to analyze and synthesise different types of evidence to inform clinical and policy decisions to improve global health outcomes.

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## Contents

1. Background .................................................................................................................. 6  
   1.1 Introduction: Purpose ............................................................................................... 6  
   1.2 Key concepts ........................................................................................................... 7  
   1.3 Method and validity in evaluation research ............................................................ 10  
   1.4 The debate over the utility or futility of systematic reviews of economic evaluations .................................................................................................................. 13  

2. Title and protocol development ....................................................................................... 15  
   2.1 Title development .................................................................................................... 15  
   2.2 Reviewers ................................................................................................................ 16  
   2.3 Background ............................................................................................................. 16  
   2.4 Review objective(s)/question(s) ............................................................................. 17  
   2.5 Method ................................................................................................................... 18  
      Assessment of methodological quality .................................................................... 22  
   2.6 Conflicts of interest ................................................................................................. 22  
   2.7 Acknowledgements ................................................................................................. 22  
   2.8 References ............................................................................................................. 22  
   2.9 Appendices ............................................................................................................. 22  

3. Conduct and write-up of a systematic review of economic evaluations ......................... 23  
   3.1 Structure of the systematic review report ............................................................... 24  
   3.2 Guidance for systematic review conduct and report writing .................................. 25  

4. References ..................................................................................................................... 34  

5. Appendices .................................................................................................................... 36  
   5.1 Appendix I JBI Critical Appraisal Checklist for Economic Evaluations .................. 36  
   5.2 Appendix II JBI Data Extraction Form for Economic Evaluations ......................... 37  
   5.3 Appendix III - Guidance for critical appraisal of economic evaluations using the JBI ACTUARI assessment tool ................................................................. 39
The Systematic Review of Economic Evaluation Evidence

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1. Background

1.1 Introduction: Purpose

In late 2012 a methodological working group, comprised of representatives from the Joanna Briggs Institute (JBI) Head Office in Adelaide and the JBI Collaboration, was established to review and enhance its methodology for systematic reviews of evidence from health economic evaluations. This document presents the updated methodological guidance for JBI systematic reviews of economic evaluation evidence that emerged from the work of this group.

There are two broad approaches to using systematic reviews as a tool to promote evidence-based decision-making in policy and/or practice relating to decisions of costs. The first deals with the synthesis of economic evaluations. The other is a systematic review to inform the development of a jurisdiction specific decision model. Whilst JBI acknowledges that systematic reviews of quantitative evidence to support development of decision models can make a substantial contribution to promoting evidence-based health care (EBHC) and that methodological guidance in this area is critical, its guidance for review of economic evidence at this stage covers only systematic reviews of economic evaluations.

This guidance has been developed to support reviewers: (i) conducting reviews with the limited objective of identifying and summarizing the best available evidence for a question about intervention costs or costs relative to benefits; (ii) conducting mixed method reviews, aiming to identify and synthesize the best available evidence for questions about intervention resource use/costs and/or cost effectiveness in addition to a range of other questions about the intervention, including effectiveness, meaningfulness, barriers and facilitators using a range of study types (qualitative and quantitative).

The process and steps in a JBI systematic review of economic evaluations mirror those used in JBI reviews of other evidence types. The steps are:

(i) Formulating the review objective/question(s), defining inclusion/exclusion criteria for the review in a protocol, which is then submitted for review and publication.
(ii) Searching the evidence.
(iii) Study selection (objective based on inclusion criteria as specified in the protocol).
(iv) Assessment of identified study quality using standardized instruments by two reviewers.
(v) Data extraction using a pre-determined proforma/data extraction template.
(vi) Analysis/synthesis of findings to answer the review questions and drawing of inferences for policy/practice and future research.
(vii) Drafting the systematic review report.
1.2 Key concepts

Economics

Resources, including people’s time and skills, raw materials, land and energy, are necessary inputs required for the production of goods, services and programs required to meet health needs.\textsuperscript{1,2} However, they are scarce. Economics focuses on the problem of how best to allocate societies’ scarce resources in the context of competing needs, unlimited wants and different preferences. It is the study of optimal allocation of limited resources for the production of maximum benefit to society.\textsuperscript{1}

Efficiency opportunity costs/trade-offs equity and perspective

The concept of efficiency lies at the heart of neoclassical economics, the traditional and dominant paradigm in economics. It was developed by Vilfredo Pareto (1848 -1923), the father of neoclassical Welfare Economics. In Neoclassical Welfare Economics, Pareto efficiency refers to the hypothetical state in which resources are allocated by markets such that no change in allocation can be made that makes someone better off without making someone else worse off.\textsuperscript{1} It is a state in which resources are used in a way that generates the maximum level of output or welfare/health possible. Neoclassical economic theories illustrate that if the economy is in a state of efficiency using all of its resources and the existing production of goods or services is changed – for example, due to a minister supporting a new health intervention – then some existing output will be lost. This loss is called “opportunity cost”.\textsuperscript{2} In the real world, markets are not perfect for reasons including imperfect information and hence there is potential for government to improve resource allocation and outcomes by intervening and changing resource allocation.

The concepts of efficiency and opportunity cost facilitate understanding why it is beneficial from a maximizing health outcomes perspective for decision makers to have access to the best available evidence on costs and costs relative to benefits of different health intervention alternatives. Systematic reviews of economic evaluation evidence are aimed at helping to meet this need.

The direction and magnitude of the costs and benefits associated with introducing a new program or intervention (or not introducing it) depends on the perspective. Hence definition of the perspective in conception definition and measurement of costs and benefits is critical in primary economic evaluation research as well as in systematic reviews of economic evidence. Perspectives commonly used when measuring costs and benefits in health economic evaluations commonly include (but are not limited to): (i) Individual patient; (ii) patient and his/her family; (iii) patient group(s); (iv) health care provider(s), third party payer and societal.

The distribution of costs and benefits across different groups in society has become a central issue in economics. Decision makers are interested not only in estimates of intervention costs and costs relative to effects but also how they will be distributed and in particular whether they will be equally shared among the most vulnerable and those in need. This is important to consider when reviewing economic evaluations to provide useful recommendations for decision makers and future research.
Health economic evaluation research

Health economic evaluation research is the comparative analysis of alternative interventions with regard to their resource use, costs and health effects. It focuses on identifying, measuring, valuing and comparing resource use, costs and benefit/effect consequences of two or more alternative intervention options.

Economic evaluation research involves the following steps:

- Defining the intervention whose costs and benefits are to be measured and selecting a relevant comparator.
- Defining the perspective(s) or analytical viewpoint(s) from which costs and benefits are to be measured (e.g. patient, patient’s family, healthcare provider, health system, community and societal).
- Specification of the time frame over which costs and effects are to be measured.
- Deciding what costs are relevant and will be included and measured.
- Deciding which outcomes and measures are most appropriate and will be used to measure the effect(s).
- Selecting the prices to be used to value costs and how to value effects.

Often these decisions are constrained by data availability.

Economic evaluations’ data sources are characterized by plurality. Whilst some health economic evaluations draw their effectiveness and resource use data from a single study, for example, a randomized controlled trial (RCT), others use data from a range of quantitative studies, which may include RCTs. Many economic evaluations incorporate a modeling component.

Economic evaluation research responds to the need for decision makers to have knowledge on not only the health effects (and harmful effects) associated with an intervention/program or strategy and its primary comparator(s) to make decisions that promote optimal health outcomes, but also on resource use and costs.

The Dominance Ranking Matrix classification tool

The Dominance Ranking Matrix (DRM) refers to a simple classification system/tool developed by JBI for summarizing and interpreting the results of economic evaluations in systematic reviews of economic evaluations. The tool is included in the Analysis of Cost, Technology and Utilisation Assessment and Review Instrument ACTUARI module of the Institute’s software for conducting systematic reviews (CReMS).

The DRM (see also Figure 1) is a three-by-three matrix with the following classification options:

- **Strong dominance** for the intervention. To be selected when the incremental cost effectiveness measure shows the intervention as: (i) more effective and less costly; or (ii) effective and less costly; or (iii) equal cost and more effective.

In this case the evidence may be interpreted as suggesting decision makers should, from an efficiency perspective, favor the intervention over the comparator (at least in circumstances similar to those of the evaluation[s]).
• **Weak dominance** for the intervention. Selected when the measure shows the intervention as: (iv) equally costly and effective; or (v) more effective and more costly; or (vi) less effective and less costly.

In this case no conclusion may be drawn about whether the intervention is preferable from an efficiency perspective without further information on the priorities/preferences of decision makers in the particular decision making context. Decision makers – clinicians, health managers/administrators, policy makers and patients – are left to judge whether the cost/benefit trade-offs are worth the introduction of the intervention in their particular context.

• **Non-dominance** for the intervention. This is when the measure shows the intervention as: (vii) more costly and less effective; or (viii) equally as costly and less effective; or (ix) more costly and as effective.

In this case the evidence may be interpreted as suggesting the comparator is favorable from an efficiency perspective (at least in circumstances similar to those of the evaluation[s]).

<table>
<thead>
<tr>
<th>Cost</th>
<th>No. of studies</th>
<th>Health benefit</th>
<th>Implication for decision makers</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>0</td>
<td>-</td>
<td>Reject intervention</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>-</td>
<td>Reject intervention</td>
</tr>
<tr>
<td>+</td>
<td>0</td>
<td>0</td>
<td>Reject intervention</td>
</tr>
<tr>
<td>-</td>
<td>0</td>
<td>-</td>
<td>Unclear – Judgment required on whether intervention preferable considering incremental cost effectiveness measures and priorities/willingness to pay</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Unclear – Judgment required on whether intervention preferable considering incremental cost effectiveness measures and priorities/willingness to pay</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Unclear – Judgment required on whether intervention preferable considering incremental cost effectiveness measures and priorities/willingness to pay</td>
</tr>
<tr>
<td>-</td>
<td>0</td>
<td></td>
<td>Favor intervention</td>
</tr>
<tr>
<td>0</td>
<td>+</td>
<td></td>
<td>Favor intervention</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
<td></td>
<td>Favor intervention</td>
</tr>
</tbody>
</table>

Note: + implies the intervention has a greater cost, or greater health effect than the comparator. 0 the intervention has equal cost or health effect/benefit as comparator. - that the intervention is less costly or less effective than comparator. Read matrix by row left to right.

**Figure 1: Three-by-three dominance ranking matrix**
1.3 Method and validity in evaluation research

There are four main research design types in primary economic evaluation research. Conceptualization, definition and measurement of costs are similar across the four types. The types differ in their conceptualization, definition and measurement of health effects/outcomes.

Method 1: Cost minimization analysis (CMA)

This is a partial economic evaluation method in which the effects of the alternative interventions examined are assumed to be identical. Resource use and costs are measured in monetary units.

Method 2: Cost effectiveness analysis (CEA)

This is an economic evaluation method in which the effects of the intervention and its comparator are measured in identical units of outcome (e.g. mortality, myocardial infarctions, lung function, weight, height for age and secondary infections). Alternative interventions are then compared in terms of costs (expressed in monetary terms) per unit of effect (expressed in the natural unit of clinical significance, e.g. mmHg for blood pressure and mg/dl for blood glucose level).

Method 3: Cost benefit analysis (CBA)

This method measures resource inputs/costs and effects in monetary units. Alternative interventions are then compared in terms of costs per unit of effect measured in monetary units using the Incremental Net Benefit (INB) measure.

Method 4: Cost utility analysis (CUA)

In this method the effects/benefits of the intervention and its comparator(s) are expressed and measured in utility units, of which the most commonly used one is Quality Adjusted Life Years (QALYs). Quality Adjusted Life Years are a product of length of life and quality of life. Quality of life is measured subjectively using one of a range of commonly used methods. Costs are expressed and measured in monetary units. The alternative interventions are compared in terms of costs per QALY.

Hoch et al. (2005) provide an example-based description of the different economic evaluation methods and it is recommended that reviewers wanting to gain additional understanding on economic evaluation research methods read them.
Table 1 summarizes the main features of the four economic evaluation design types.

<table>
<thead>
<tr>
<th>Method</th>
<th>Measurement approach and outcome measures</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMA</td>
<td>Measures costs of intervention compared to comparator with costs expressed in monetary units (e.g. US $). Assumes benefits equal. Outcome measures: Relative resource use and cost expressed in monetary units.</td>
<td>The assumption of equal benefits/effects is only realistic for a small number of specific interventions, e.g. generic versus non-generic drugs.</td>
</tr>
<tr>
<td>CEA</td>
<td>Measures relative costs and benefits of intervention and comparator with costs expressed in monetary units (e.g. US $) and effects in clinical outcome units (e.g. years of life and mortality). Outcome measures: Relative resource use, cost and Incremental Cost Effectiveness Ratio (ICER).</td>
<td>ICER measure may vary significantly depending on clinical outcome used. Underscores importance of evaluations testing robustness of outcome measures to changes in clinical outcomes selection.</td>
</tr>
<tr>
<td>CBA</td>
<td>Measures relative costs and benefits with both expressed in monetary units. Outcome measures: Relative resource use, costs and Incremental Net Benefit Ratio (NBR) or Net Present Value (NPV).</td>
<td>Heroic assumptions need to be made in the valuation of benefits. Underscores importance of sensitivity testing for robustness/validity of findings.</td>
</tr>
<tr>
<td>CUA</td>
<td>Measures relative costs and benefits with costs expressed in monetary units and effects in Quality Adjusted Life Years (QALYs) or Disability Adjusted Life Years (DALYs). Outcome measures: Resource use; costs and Incremental Cost Effectiveness Ratio with costs expressed in monetary units and effects in QALYs or DALYs.</td>
<td>Debate over assumptions made in measurement of DALY and QALY and best practice method for measuring QALY or DALY. Testing sensitivity of measures to change in assumptions in DALY/QALY measurement critical.</td>
</tr>
</tbody>
</table>
Aspects of economic evaluation research key for validity

The software for conducting a JBI systematic review of economic evaluations, ACTUARI, includes a general critical appraisal checklist for appraising economic evaluations (see also Appendix 1). The tool is informed by consideration of the features that affect the internal validity of economic evaluations, as well as consideration of two validated checklists commonly used for appraising economic evaluations. The JBI critical appraisal tool has not been designed for the purpose of appraising models. Hence it is recommended that reviewers also use the Philips et al. (2006) tool designed for appraisal of models if they are considering evaluations that include a modeling exercise.

The following are design aspects that promote validity of findings from economic evaluations and the quality criteria in the JBI critical appraisal:

- Comprehensive coverage of costs and health outcomes/effectiveness for the selected perspective.
- Credible valuation of costs and health outcomes/effectiveness.
- Inclusion of an incremental analysis which shows differences in costs and outcomes for one specific intervention/program compared to another.
- Time period of analysis that is sufficient in length to capture all relevant future effects (costs and consequences) and discounting of costs and clinical outcomes.
- Use of sensitivity analysis to test robustness of cost/effect findings with clear explanation about which assumptions are critical for validity of the cost/effectiveness results.
- Clear definition of perspective in cost and effect measurement. Best practice is usually the societal perspective as it incorporates the broadest range of costs and minimizes cost shifting, which relates to the underestimation of true costs by narrowing the perspective of analysis, such that the full cost of an intervention is not captured and it appears less costly to society than it actually is in reality. However, in some cases it may be appropriate to take a purely organizational perspective (e.g. the hospital) or individual patient perspective. Provided this is stated and the results are interpreted only for the chosen perspective, validity is not compromised.
1.4 The debate over the utility or futility of systematic reviews of economic evaluations

Whilst the value of primary economic evaluation research in EBHC is not disputed, a systematic review of this evidence is.\textsuperscript{12,13,14}

Arguments against

Three main arguments are put forward against systematic reviews of this kind of economic evidence.

The first argument starts from the premise that the purpose of such systematic reviews is to generate an average generalizable incremental cost/effectiveness measure from individual cost/effectiveness measures of the included studies. This narrow conceptualization purpose is shaped by the focus in systematic reviews on effectiveness evidence in the form of RCTs using meta-analysis to generate a robust generalizable measure of effect size and direction. It then proceeds by identifying the following three reasons why a meta-analysis of the findings from economic evaluations studies is unwise (unlikely to yield a robust or scientific result):\textsuperscript{2,12,13,14}

- Resource use and costs (the product of factor prices and resource use) vary from country to country, in different regional settings as well as over time, which makes the cost component of cost-effectiveness measures incomparable.

- There is also a high likelihood that differences in context (including institutional delivery capacity) and populations (behavior and culture) will translate into differences in how interventions work in different settings, undermining the comparability of even the effectiveness elements in cost-effectiveness measures of included studies. This problem, it is noted, will be particularly relevant when the intervention in question is a complex multi-component public health type intervention.

- High level of plurality of methods across studies – common in economic evaluations – is likely to generate a level of heterogeneity in cost effectiveness measures.

The second argument against systematic reviews of economic evaluations is that they are not valuable because differences between the interventions/comparators, populations and context of the included studies and the decision maker’s intervention/comparators, populations and context are likely to undermine transferability of findings. In other words, valuable lessons from systematic reviews that summarize results of economic evaluation studies conducted in other contexts cannot be drawn because resources, opportunity costs, interventions and relevant comparators are so different. The third is that as there is a dearth of primary studies, reviews often generate empty systematic review reports rather than strong evidence-based recommendations to support decision making that improves health outcomes.
Arguments for the JBI position

Advocates of systematic reviews of economic evaluations aimed at addressing questions about resource use, costs and costs relative to the effectiveness of interventions acknowledge that differences in evaluation contexts and populations imply that such reviews are unlikely to yield “one size fits all” type answers. However, this does not make them futile. They argue that they can still offer policy makers, clinicians, community leaders, patients and other decision maker’s useful information. Moreover that they can do this by:

- Identifying for decision makers the range and quality of available studies related to a particular resource use/cost and or cost effectiveness questions and gaps in the evidence base. The evidence base gap identification and the research directions offered in systematic reviews linked to this are seen as particularly valuable as they facilitate understanding of the kind of evidence base (or decision model) that can be developed to support evidence-based decision making and stimulates their development.

- Alerting decision makers to results that may be relevant to the intervention choice/trade-offs they are grappling with.

- Providing decision makers with an enhanced understanding of the conditions which are conducive to interventions/models to be cost effective. This contribution is achieved if the objective of the reviews is not limited to only summarizing the range of resource use, cost and cost/effectiveness measures from existing studies but also to learning lessons about the circumstances (contextual intervention and population factors) that promote cost effectiveness.

This argument about the value of systematic reviews of economic evaluations for EBHC is reflected in Donaldson et al.’s (2004) publication on how to use systematic reviews of economic evidence as a tool to promote evidence informed health care. They suggest that the value of systematic review of economic evaluation evidence is not to generate a single authoritative result/recommendation about cost relative effectiveness, but rather to help decision makers understanding the structure of the resource allocation problem and potential impacts. Further, that the focus in such reviews should be less on trying to generate a summarized estimate of the cost-effectiveness ratio, and more on demonstrating by how much this varies from setting to setting, and why it varies.

Archie Cochrane was a strong advocate for considering evidence from costing studies and economic evaluations in systematic reviews as a means to improve health outcomes.\(^2\)
2. Title and protocol development

The Joanna Briggs Institute systematic reviews of economic evaluation evidence are conducted using the JBI Comprehensive Review Management System (CReMS) software and the ACTUARI analytical module within it. These are both parts of the JBI System for the Unified Management, Assessment and Review of Information (SUMARI) which includes modules for reviews of different evidence types. The ACTUARI module is designed to assist reviewers to appraise, extract and analyze data from economic evaluations. To use the software reviewers need to register through the JBI website and obtain a username and password.

Before developing their protocol, to prevent review duplication, reviewers should search at least the Cochrane Library, JBI Database of Systematic Reviews and Implementation Reports (JBISRIR), MEDLINE, NHS EED and the PROSPERO database to establish whether a similar protocol or review has recently been published. Reviewers should also establish whether the size of the evidence base warrants conducting the review. A review with findings from a couple of studies that offers useful directions for future research may be worthwhile. However, an empty review with no studies is less useful and difficult to justify from a cost/benefit perspective.

The importance of this first step in the systematic review process cannot be overstated. This is for two reasons: (i) because the development of the background section in the review, which includes providing the rationale for the review and definition of key concepts, helps reviewers to define the scope of the review and establishes its value (i.e. its contribution to the evidence base and potential offerings to decision makers); (ii) because a priori setting of inclusion and exclusion criteria reduces the risk of introducing bias into the review, thereby promoting validity of its findings.

This guidance for developing the protocol for a JBI systematic review of economic evidence is organized to meet the structure/template requirements in CReMS. Reviewers should develop their protocol using the CReMS software. It is critical that the template/structure in CReMS (and outlined below) is followed.

American spelling and the Vancouver style referencing should be used.

2.1 Title development

The title should be short and simple but still provide the reader with a clear understanding of what the review is about. The title should not be phrased as a question or conclusion. There should be congruency between the review title, objective, question(s) and inclusion criteria. If possible the population, setting and comparator to be examined in the review should be indicated in the title. The title should end with: “a systematic review protocol”.
An example of a title for a review examining cost effectiveness evidence for one intervention compared to another:

“Cost effectiveness of paclitaxel and cisplatin versus cyclophosphamide and cisplatin as first line therapy in advanced ovarian cancer: a systematic review protocol”

An example of a title for a review examining evidence on cost-effectiveness evidence of a one health intervention compared to a range of alternatives:

“Cost effectiveness of vitamin A supplementation for improving health outcomes in very young children (age 0-2): a systematic review protocol”

An example of a title for a review examining economic evidence from economic evaluations as part of a mixed method systematic review with a broad scope:

“Effectiveness, cost effectiveness and acceptability of Chronic Kidney Disease management programs/models for Aboriginal and Torres Strait Islander Australians: a systematic review protocol”

2.2 Reviewers

Reviewer names and post-nominal qualifications should be listed beneath the review title. An e-mail address for the corresponding review author should be provided beneath the list. Reviewer affiliations should also be listed.

2.3 Background

To develop a protocol that is implementable and a useful systematic review report, reviewers should invest time in developing this section of the protocol, which should be around 1000 words.

The background should include: (i) definition of concepts including a detailed explanation of the intervention whose costs/cost effectiveness are being examined; (ii) the review topic and motivation; (ii) introduction to the health setting, population and outcomes of interest in the review; (iii) a motivation for the review, with reference to current debates among policy makers and/or clinicians relating to the topic, gaps in the evidence base and user needs.

JBI recommends, like Cochrane, that reviewers developing protocols examining economic evidence for simple clinical interventions develop an event pathway diagram for the intervention (program) and condition (problem/issue) for inclusion in the background (as part of the intervention description). This is because it facilitates defining of appropriate objectives for the review as well as outcomes of interest and relevant sub-group analysis. A clinical event pathway provides a systematic, explicit method of representing the main pathways of events and distinct resource implications or outcome values associated with them, from the point of introduction of the intervention/program through subsequent changes in management to final outcomes.

For reviews examining costs and cost effectiveness of complex multi-component interventions, developing a program logic model that describes how the intervention works and the causal mechanism that links the intervention to different outcomes (immediate proximal and ultimate) is recommended.

The background should be written scientifically. This requires careful definition of concepts, avoiding colloquial language, and using references to support definitions of key concepts as
well as statements of findings from the existing research literature. It is appropriate to use expert opinion to make statements; however, these should be acknowledged. When referring to existing findings from the literature, it is important that they are not presented as reviewer conclusions. Instead the statements should be presented as judgments of a third party, for example: “Smith indicates that acupuncture is more effective and more costly than splint treatment for rheumatoid arthritis in the hand in adults”. This is because the literature has not yet been critically appraised and analyzed. This is to be done in the systematic review. When direct quotes are used a page number is required for in-text citations.

It is recommended that reviewers refer to a couple of existing studies they have identified on the topic, as this will allay fears that a lack of evidence may result in a completely empty review. The background section should conclude with a statement that a preliminary search for existing systematic reviews on the topic has been conducted (state the databases searched) and that no review identical to that proposed was found. If an existing systematic review that is similar and conducted within the last three years is identified, it should be specified how the proposed review will differ.

The JBI CReMS software transfers the background developed for the protocol to the final systematic review report when it builds the report.

2.4 Review objective(s)/question(s)

The objective(s) of the review should be clearly stated and flow naturally from the background section. The objective statement should, if length permits, reflect the health intervention/model and comparator, context and population to be examined in the review. It should signal whether the review aims to identify and synthesize the best available evidence for questions about cost only or cost and benefit.

Reviewers may add a list of questions to the review objectives – if it is a review with a large scope requiring much sub-group analysis and addressing a range of questions. However, this is not necessary as comprehensive and clear objectives statements in most cases can also serve the role of being the questions for the review.

The key to developing appropriate/useful review objective(s) is developing an understanding of: (i) the intervention and how it works on which outcomes; and (ii) the existing evidence base in the area as well as the information needs of policy makers, clinicians, researchers and/or patients. This requires:

- A cursory consideration of the literature (focusing on systematic reviews and literature reviews)
- Consultation with users and considering current debates in policy and practice relating to the topic.

In defining the review objective it is important to consider resources available to implement the review (reviewer skill set and time). There are advantages and disadvantages with respect to the breadth of the review objectives. Adopting an ambitious objective that implies a broad scope of coverage with respect to the comparators, geographical context and population range to be considered has the advantages of helping to ensure that there will be a large amount of data to analyze and synthesize in the review, and increasing the usability of the review internationally. However, such an approach is demanding on time and resources.
Reviewers should judge for themselves how to limit the scope of the review to ensure it is feasible to implement with the available time/resources whilst still ensuring that it will still be useful for their and other users (i.e. researchers, policy makers, patients and/or clinicians).

The review objective and question should be consistent with the title and the PICO elements specified in the protocol inclusion criteria (see below).

An example objective statement for a review with a narrow objective:

“The objective of this review is to identify and summarize the best available Australian evidence on resource use and costs (all perspectives) of the total versus specific surface bearing socket design type in prosthetic prescription for Australian trans-tibial adult amputees.”

An example of an objective statement for a review aimed at synthesizing evidence on costs and effectives as well as drawing lessons about factors that promote cost effectiveness:

“The objectives of this review are to identify and synthesize the best available evidence on CKD management programs delivered to Indigenous people in Australia, the United States, New Zealand and Canada to:

1. Determine cost-effectiveness in terms of the costs and costs relative to the benefits of the programs/models from the perspectives of individual patients and their families, the primary health services that deliver them, tertiary health services and society as a whole;
2. Draw inferences from the review findings about the programs/models design features and implementation contexts that are conducive to lower cost and high effectiveness of the programs/models.”

2.5 Method

Inclusion criteria
This section, which details the basis on which economic evaluation studies will be considered for inclusion in the review, sets the boundaries of the review. The eligibility criteria should be comprehensive in coverage and pay attention to the fine details of definitions of the participant/population, intervention and comparator(s), context (geographical health setting and culture), and outcome measures.

The “P (population) I (intervention and comparator) C (context/setting) O (outcomes) S (study design)” mnemonic is used to structure the inclusion criteria.

Population/participants of interest
To define this aspect of the inclusion criteria, reviewers should first reflect on the target audience of the intervention for which measures of cost and/or cost effectiveness is being examined in the review.
Secondly, consideration should be given to whether the entire world/international population is to be considered or only a population (or sub-population) of a particular country. In specifying the characteristics of the population to be considered, the statements about exclusion criteria should be made with reference to clear scientific or policy related justification rather than unsubstantiated personal or clinical justification.

An example of a statement for the population inclusion criteria:

“The population of interest in the review includes the trans-tibial adult (individuals age 18 or older) population living in Australia, regardless of cause of amputation, age, sex, socio-economic status, co-morbidities or ethnic origin.”

**Intervention of interest and comparator**

In this section, reviewers should describe in a comprehensive and clear manner, the intervention and comparator(s) for which evidence on resource use, costs and/or cost effectiveness is to be sought. The description should include details of the key characteristics of the intervention including nature of services/care delivered, time period of delivery, dosage/intensity, co-interventions, and personnel undertaking delivery. The reviewer(s) should clarify whether measures of resource use, cost and/or cost effectiveness will be sought for the intervention/program implemented as a standalone, or also in addition for the intervention/program in combination with others.

In addition, reviewers should identify clearly the comparator(s) to be considered.

**Context**

In this section the health setting(s) to be considered should be specified, for example, primary health care, community based or hospital based. If the review is focusing on a particular cultural setting or differences between two cultural settings this should be noted. If only low resource settings are to be considered this should be clarified and the concept of “low resource setting” defined.

**Outcomes and outcome measures**

Here the outcomes and outcome measures the review seeks to identify and summarize should be described. First in this regard is a statement to clarify whether the review will identify and synthesize study results only on resource usage and costs of the intervention and its comparator(s) or additionally on cost-effectiveness. Second, if the scope includes cost effectiveness outcomes and measures, reviewers should explain whether the review aims to identify and synthesize estimates of: (i) cost per unit of effect expressed in clinical outcome units (from CEA), cost per QALY or DALY (from CUA) and NBR (from CBA) or only one or two of these.

As estimates from measures of resource use of interventions compared to comparators are more likely to be transferable across contexts than those from measures of costs and cost effectiveness, it is advised that reviewers always include resource use measures in the range of outcomes to be considered.
In some instances it may be appropriate to organize outcomes into primary and secondary categories.

The analytic viewpoints for which estimates of resource use, costs and cost effectiveness for the range of measures are to be included should be stated. If reviewers wish to adopt an inclusive approach, and seek estimates of resource use, costs and cost effectiveness from all viewpoints/analytic perspectives, this should be stated. The viewpoint selected for the review should be justified.

**Study design**

What should be specified here is first, the types of economic evaluation research designs to be considered for inclusion (CMA, CEA, CBA and/or CUA), and second, whether the review will consider only studies based on empirical data alone or also those that include modeling.

An example statement for the description of study types to be considered in the review is as follows:

“Full economic evaluation studies (i.e. CEA, CUA, CBA, and CMA) of [intervention versus comparators(s)] as well as partial economic evaluations (i.e. cost analysis, cost-description studies, and cost-outcome descriptions) of [intervention versus comparator(s)] will be considered for inclusion in the review. Modeling studies will be considered in addition to those that rely only on empirical data.”

**Search strategy**

This section should detail how the reviewers plan to search for relevant studies. The date and language limitations to be applied in the search should be stated and motivated. The databases to be searched should be listed along with initial keywords to be used for the search.

The following statement, which is a set text in CReMS should be inserted to describe the process:

“The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of MEDLINE and CINAHL will be undertaken followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe articles. A second search using all identified keywords and index terms will then be undertaken across all included database. Thirdly, the reference list of all identified reports and articles will be searched for additional studies. Studies published in #insert language(s)# will be considered for inclusion in this review. Studies published from #insert dates# will be considered for inclusion in this review.

The databases to be searched include:

#insert text#

The search for unpublished studies will include:

#insert text#

Initial keywords to be used will be:

#insert text#
As economic evaluation studies are frequently conducted for government or by government, searching databases of grey literature is particularly important in a review of economic evaluations. Hence, it is important that appropriate sources of grey literature are identified and that the protocol includes description of a strategy to access this type of evidence. Conversations with experts on the intervention being considered in the review may also be useful and if this to be part of the strategy it should be noted here in the protocol.

A list of databases that are particularly useful for identifying evidence on resource usage, costs and cost effectiveness of health interventions is provided in Table 2. It is recommended that in addition to selecting relevant databases from Table 2, reviewers search at least the following: protocol: PubMed, CINAHL, Cochrane (CENTRAL), and Scopus. To identify unpublished studies, MedNar or Google Scholar, ProQuest Dissertations, and the Online clinical trials registers will need to be searched.

<table>
<thead>
<tr>
<th>Database</th>
<th>Coverage</th>
<th>Availability</th>
<th>Value features</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHS Economic Evaluation Database (NHS EED)</td>
<td>Health care economic evaluations (worldwide)</td>
<td>Free at <a href="http://www.crd.york.ac.uk/crdweb/">http://www.crd.york.ac.uk/crdweb/</a></td>
<td>Detailed summaries plus critical appraisal</td>
</tr>
<tr>
<td>Health Economic Evaluations Database</td>
<td>Economic evaluations (worldwide)</td>
<td>Subscription service: <a href="http://www3.interscience.wiley.com/cgi-bin/mrwhome/114130635/HOME">http://www3.interscience.wiley.com/cgi-bin/mrwhome/114130635/HOME</a></td>
<td>Extensive categorizations; detailed abstracts</td>
</tr>
<tr>
<td>Cost effectiveness analysis (CEA) registry</td>
<td>Health care cost utility analysis</td>
<td>Free at: <a href="https://research.tufts-nemc.org/clear/default.aspx">https://research.tufts-nemc.org/clear/default.aspx</a></td>
<td>Extracts cost-effectiveness ratios and utility weights</td>
</tr>
<tr>
<td>Health Technology Assessment (HTA) database</td>
<td>Health care technology assessments</td>
<td>Free at: <a href="http://www.crd.york.ac.uk/crdweb/">http://www.crd.york.ac.uk/crdweb/</a></td>
<td>Bibliographic details; links to technology assessments with economic evaluations</td>
</tr>
<tr>
<td>Pediatric Economic Database Evaluation (PEDE)</td>
<td>Pediatric economic evaluations</td>
<td>Free at: <a href="http://pede.biinfo.sickkids.on.ca/pede/index.jsp">http://pede.biinfo.sickkids.on.ca/pede/index.jsp</a></td>
<td>Categorizations</td>
</tr>
<tr>
<td>COnnaissances et Décision en Économie de la Santé (CODECS)</td>
<td>French health care economic evaluations</td>
<td>Free at: <a href="http://infodoc.inserm.fr/codecs/codecs.nsf">http://infodoc.inserm.fr/codecs/codecs.nsf</a></td>
<td>Summaries plus critical appraisal</td>
</tr>
</tbody>
</table>
Assessment of methodological quality

This section should explain that critical appraisal will be undertaken independently by two individuals, and also that if any disagreements arise they will be discussed and if need be resolved by a third party.

Reviewers should explain in this section that they will be using the JBI critical appraisal tool for economic evaluations in ACTUARI and the Phillips et al. (2004) tool for appraising models if relevant. If an additional or substitute appraisal tool is to be used it should be identified.

Data extraction

In this section reviewers should explain that data from included papers is to be extracted from included studies using the standardized data extraction tool for economic evaluations in ACTUARI. If any additional data is to be extracted this should be clarified.

The following text may be useful to help inform the description of the data to be extracted from included papers:

“Data will be extracted from papers included in the review using the standardized data extraction tool in JBI-ACTUARI. The data extracted will cover: firstly descriptive data about the (i) study population/participants, intervention, comparator(s) and outcomes; (ii) study methods including evaluation design type, analytic viewpoint(s), source of effectiveness data, prices and currency used for costing, time period of analysis; sensitivity testing; measures of resource use, cost and health effect/clinical and cost effectiveness; (iii) study context (geographical, health care and broader service delivery setting and culture); secondly results for the resource use and/or cost and/or cost effectiveness measures; thirdly where possible author conclusions about factors that promote intervention cost effectiveness”

Data analysis and synthesis method

Reviewers should explain that the data extracted from included studies will be analyzed and summarized to answer the review objective using the JBI Dominance Ranking Matrix (DRM), narrative and tables.

2.6 Conflicts of interest

A statement, which either declares the absence of any conflicts of interest or describes a specified or potential conflict, should be made in this section.

2.7 Acknowledgements

Acknowledgements should be made in this section, e.g. sources of external funding or the contribution of colleagues/ institutions.

2.8 References

All the sources used in the protocol (which would have been entered into the CReMS software) should be listed here, in numeric order and the order in which they were used. The references should be provided using the Vancouver referencing style.

2.9 Appendices

Two appendices need to be attached to the protocol:

Appendix I - ACTUARI critical appraisal tool, and, if used, Appendix II - ACTUARI data extraction pro form
3. Conduct and write-up of a systematic review of economic evaluations

This third section of this guide is aimed at providing information to support JBI reviewers with the conduct and write-up of their reports. It has two sections: Section 3.1 outlines the structure that reviewers should follow when writing the systematic review report, and Section 3.2 offers reviewers some guidance for each step in the review implementation (post protocol publication).

This section of the Reviewers Manual should be read in conjunction with the CReMS User Manual: Version 5.0 and in particular the ACTUARI chapter in the Manual. The latter provides guidance on using the CReMS module for systematic review of economic evidence. Reviewers should also refer to the Author Guidelines in the JBISRIR [http://www.joannabriggslibrary.org/index.php](http://www.joannabriggslibrary.org/index.php).

The Author Guidelines lay out the language convention and style requirements for a JBI Systematic Review. Key requirements are:

- Use American spelling.
- Use abbreviations sparingly; use only where they ease the reader’s task by reducing repetition of long, technical terms. Initially, use the word in full, followed by the abbreviation in parentheses.
- Vancouver style referencing should be used throughout the review with superscript numbers without brackets used for in-text citations.

It is expected that when conducting their review, and developing their systematic review report, JBI reviewers remain true to the original research plan specified in the protocol published in the JBISRIR. The peer review process includes considering congruency between the systematic review report and the protocol. As explained in Section 2, staying true to the protocol is important because it reduces risk of bias and enhances the validity of review findings. Deviations from approved protocols are rare, and if a report has deviated from the protocol, this should be made explicit in the methods section and justification provided.

The ACTUARI module in CReMS is designed to facilitate ease of systematic review protocol implementation and report writing. As long as reviewers’ work through the systematic review steps in ACTUARI, the report generated in the <Report Builder> function will include the essential structure/template required in a JBI economic evidence systematic review report. All sections marked with an * in the software are transferred by CReMS into the report that is generated by the <Report Builder> function.

The review report generated by CReMS is a word document that is best understood as a first draft of the systematic review report which requires editing and extending. With respect to editing, firstly, the tense needs to be changed from future to past tense. This is because the text transferred is that used in the protocol (written in the future tense). A second editing task is reviewing the content and headings of the Tables transferred and making adjustments where necessary. A third is reviewing and finalizing the references. With respect to additional work to develop the content of the report generated by CReMS, there is a need to add narrative description and interpretation in the results section to develop the discussion, conclusions and inferences for research, practice and/or policy.
3.1 Structure of the systematic review report

Box 1 shows the essential headings and organizational structure of a JBI systematic review report for a systematic review of economic evaluations. The report builder in the JBI CReMS software generates the report using this basic structure. Reviewers can then edit the report and add to the structure once the software has generated the report. However, the basic structure set out in Box 1 is a requirement.

<table>
<thead>
<tr>
<th>Box 1: Structure of the systematic review report</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title</strong></td>
</tr>
<tr>
<td><strong>Reviewers</strong></td>
</tr>
<tr>
<td><strong>Executive summary</strong></td>
</tr>
<tr>
<td><strong>Background</strong></td>
</tr>
<tr>
<td><strong>Objective(s)/question(s)</strong></td>
</tr>
<tr>
<td><strong>Method</strong></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
</tr>
<tr>
<td><strong>Search strategy</strong></td>
</tr>
<tr>
<td><strong>Methodological quality assessment</strong></td>
</tr>
<tr>
<td><strong>Data extraction and synthesis method</strong></td>
</tr>
<tr>
<td><strong>Results</strong></td>
</tr>
<tr>
<td><strong>Description of studies</strong></td>
</tr>
<tr>
<td>Search and study selection</td>
</tr>
<tr>
<td>Key characteristics of included studies</td>
</tr>
<tr>
<td>Methodological quality</td>
</tr>
<tr>
<td><strong>Findings</strong></td>
</tr>
<tr>
<td><strong>Discussion</strong></td>
</tr>
<tr>
<td><strong>Conclusions</strong></td>
</tr>
<tr>
<td>Implications for practice</td>
</tr>
<tr>
<td>Implications for research</td>
</tr>
<tr>
<td><strong>References</strong></td>
</tr>
<tr>
<td><strong>Appendices</strong></td>
</tr>
<tr>
<td>Appendix 1: Search strategy</td>
</tr>
<tr>
<td>Appendix 2: Articles excluded at full text appraisal with reasons</td>
</tr>
<tr>
<td>Appendix 3: Critical appraisal tool(s)</td>
</tr>
<tr>
<td>Appendix 4: Data extraction tool</td>
</tr>
<tr>
<td>Appendix 5: Table of characteristics of included studies</td>
</tr>
</tbody>
</table>
3.2 Guidance for systematic review conduct and report writing

Title
See section on title development in Section 2.

Reviewers
See section on reviewer names in Section 2.

Executive summary
The executive summary should be a comprehensive yet concise summary of the purpose, scope, methods, findings and implications of the systematic review. It should contain no abbreviations or references, be limited to 500 words and accurately reflect the review content. The executive summary should include the following headings:

Background
Objectives
Inclusion criteria:
- Participants
- Intervention/comparators
- Context
- Outcomes
- Study types

Search strategy
Methodological quality
Data collection
Data synthesis
Results
Conclusions
Implications for practice
Implications for research
Background
At the JBI CReMS software transfers the background from the protocol to the systematic review report, reviewers simply need adjust the tense used and edit the text to check for grammatical errors. See the section titled background development in Section 2 for guidance on the content of this section in the systematic review report. It is recommended that all JBI systematic reviews contain a sentence clearly indicating: “The objectives, inclusion criteria and methods of analysis for this review were specified in advance and documented in a protocol. Ref” (The reference should be to the appropriate citation in JBISRIR). This sentence should appear as the final line of the background/introduction section of the review report and complies with the recommendations for reporting of systematic reviews detailed in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.

Review Objective/Review question(s)
The objective and review question(s) section of the systematic review report is transferred by the JBI review management software from the protocol into the systematic review report. Hence when writing up the report all reviewers should do is review the objective and questions for grammatical and layout errors.

Method
The JBI review management software also transfers the description of the review method from the protocol when reviewers ask the software to build the report.

When finalizing the method description section in the systematic review report reviewers should:
- Adjust the tense from future to past and check the text for accuracy of content and grammar.
- Check that the inclusion criteria coverage is comprehensive and accurate.
- Check that the description of the search strategy is congruent with the approach used. Any adjustment to the approach outlined in the protocol should be explained and justified.
- Check that the tool(s) used to appraise the quality of included studies has been correctly identified and attached as an appendix to the systematic review report.
- Check that the data extraction sheet has been attached as an appendix to the systematic review report. Also, that any additional data extraction/amendments to the data extraction form have been explained. If two reviewers had conducted the data extraction with cross checking conducted to ensure accuracy and comprehensiveness (the best practice approach), this should be explained.
- Check that the description of the approach used to synthesize/summarize the findings of the included studies for the outcomes and outcome measures of interest is congruent with the actual approach used. It is expected that in most cases reviewers would have used the three-by-three Dominance Ranking Matrix (DRM), narrative and tables. This should be explained. If any additional approach was used to analyze, synthesize and interpret the data, this should be explained.
Have the tool(s) used to assess the quality of considered economic evaluations and the data extraction proforma used been appended to the systematic review report?

The JBI ACTUARI data extraction tool is appended as Appendix 2 to this guide. Reviewers will notice that the data extraction proforma is designed to assist reviewers to:

- Extract from each study information on the key characteristics (population, intervention/comparator, outcomes, setting and methods).
- Extract from each study the results for the outcomes of interest (cost/resource use, effectiveness and cost effectiveness) outcome measures.
- Extract from each study the author conclusions and note any differences between these and the reviewer interpretation.
- Using the Dominance Ranking Matrix as a tool, classify the study results as showing strong dominance, non-dominance or weak dominance for the intervention.

With respect to the final stage of the extraction, the three-by-three matrix asks reviewers to classify the cost effectiveness outcome/result of each study as one of nine options (labeled as A-I) based on what the findings are about the costs and effects of the intervention relative to the comparator. For example, if the study cost effectiveness outcome shows the intervention as more costly and more effective ‘A’ needs to be selected. If it shows the intervention to be more effective and less costly, then ‘G’. Figure 2 illustrates that A-I options reviewers need to select between for the classification.

Figure 2: The nine options for classifying cost effectiveness findings of included studies (select one)

<table>
<thead>
<tr>
<th>Cost</th>
<th>+</th>
<th>0</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>A</td>
<td>B</td>
<td>C</td>
</tr>
<tr>
<td>0</td>
<td>D</td>
<td>E</td>
<td>F</td>
</tr>
<tr>
<td>-</td>
<td>G</td>
<td>H</td>
<td>I</td>
</tr>
</tbody>
</table>

Clinical Effectiveness

The descriptive information that is extracted from the included studies as well as the author/reviewer conclusions are used in the CReMS software to generate a Table of Key Characteristics of Included Studies that needs to be included as an Appendix. This table is critical for two reasons: firstly it helps readers to understand the main features of studies; secondly it provides information on the similarities and differences between studies that are vital for reviewers to understand in order to summarize and interpret the results.
Have the cost effectiveness measure outcomes of each study been classified using the three-by-three matrix? Is the descriptive data extracted from each study on the population, intervention/comparator, context, outcomes and methods sufficient to populate the Table of Key Characteristics of included studies that needs to be appended to the systematic review report?

Results
As explained above, the results section of the systematic review report should include two main sections, “Description of included studies” and “Findings”. Guidance for these is provided below.

Description of included studies
This first section in the results section has the purpose of providing readers with an overview of the number of studies identified by the search, and the nature and quality of the evidence base. It is comprised of three sub-sections.

The first should present the results of the search and study selection. This should include a flow chart that presents the search results (see Figure 3). This section should also refer readers to an appendix (usually Appendix III) that reports the search strategies used to search each electronic database as well as an appendix (usually Appendix IV) that lists all the studies excluded at full text examination or critical appraisal with reasons for their exclusion.
Figure 3: Search results

1. Potentially relevant papers identified by literature search
   \( n = \) 
   \( n = \)
   \( n = \)
   \( n = \)

2. Duplicate citations removed

3. Citations excluded after evaluation of title and abstract
   \( n = \)
   \( n = \)

4. Papers retrieved for full text examination
   \( n = \)

5. Papers excluded after review of full text
   \( n = \)

6. Papers assessed for methodological quality
   \( n = \)

7. Papers excluded after assessment of methodological quality
   \( n = \)

8. Papers included in the systematic review
   \( n = \)
The second section in this descriptive results section has the purpose of describing the evidence base/included studies identified and used in the systematic review. It should refer readers to a Table of Characteristics of Included Studies included as an Appendix (usually appendix V). It should also, using narrative, the key characteristic of the set of studies identified and included in the review. The narrative description of the included studies should highlight similarities and differences across the studies. It should cover methods (for example whether CMA, CEA, CBA or CUA) as well as the PICO’s and contexts of studies.

Directly below an example template for the Table of Characteristics of included studies is provided. It is advised that reviewers include a description in the table of at minimum each characteristic in the table below.

### Table 3: Table of characteristics of included studies

<table>
<thead>
<tr>
<th>Author, design type (CMA, CEA, CBA, CUA) and date</th>
<th>Population, Intervention Comparator and Outcomes</th>
<th>Methods (incl. perspective, measure of costs and health effects, time horizon, discounting, sensitivity testing, data sources, modeling if used)</th>
<th>Context (geographical location, health care and broader service delivery setting including human resource availability and capacity, technology and culture)</th>
<th>Author conclusion and reviewer reflection</th>
</tr>
</thead>
<tbody>
<tr>
<td>− Author(s) ref</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The importance of this section of the systematic review report cannot be overemphasized. This is for the following reasons:

- Describing, understanding and comparing the characteristics of the included studies facilitate reviewer understanding whether the study circumstances and cost effectiveness results are sufficiently similar to conduct meta-analysis. As argued above, in most cases they will not be.

- Describing each study’s characteristics in an accessible manner increases the usability and impact of the review by facilitating decision makers/users identifying the contexts of the study(ies) that are the most similar to theirs and whose cost effectiveness results they should hence focus on in drawing inferences for policy/practice.

- The description of study characteristics lays the foundation for the third step in the synthesis, namely, the development of the narrative summary of what the cost effectiveness outcomes and characteristics of included studies suggest about the circumstances conducive to the intervention being more effective and less costly than the comparator.
The third and final section in the descriptive part of the results reporting has the purpose of presenting the results of the assessment of methodological quality of the included studies. It should report only on the methodological quality/risk of bias as determined by the critical appraisal checklist actually used. There should be a narrative summary of the overall methodological quality of the included studies, which can be supported (optional) by a table showing the results of the critical appraisal (see Table 4 for an example). Where only few studies are identified, or there are specific items of interest from included studies, these should be addressed in the narrative also, particularly where studies were deficient, or particularly good, i.e. with clear narrative regarding risk of bias/rigor of included studies. Use of N/A should also be justified in the text.

Table 4: Critical appraisal results for included studies using the JBI-ACTUARI Critical Appraisal Checklist

<table>
<thead>
<tr>
<th>Study</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q5</th>
<th>..</th>
<th>..</th>
<th>..</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s) ref</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>U</td>
<td></td>
</tr>
</tbody>
</table>

Y - Yes, N - No, U - Unclear

Findings of the review

Although there is no defined structure for this section, the findings of the review should flow logically from the review objective and question(s). A guiding rule for organizing the results is to arrange them so that a persuasive story flows that is clearly based on the evidence and linked to the review questions.

The presentation of the findings from a review of economic evaluations using the JBI methodology should preferably include the following three sub-sections:

- **Classification of studies using the dominance ranking framework**
  In this section of the systematic review report, a visual and narrative description of the dominance classification of each study generated in the synthesis should be presented. Reviewers may want to use the figure below as a guide.

- **Presentation of findings on incremental cost effectiveness measures**
  In this section the range of incremental cost effectiveness results of the included studies should be presented and compared using narrative and tables.

- **Drawing of inferences on factors promoting intervention efficiency**
  In this section a narrative summary should be provided about what the results of the included studies together with the study characteristics suggest about the circumstances conducive to the intervention being more effective and less costly than the comparator.
### Figure 4: Three-by-three matrix dominance classifying for cost effectiveness outcomes/findings of economic evaluations

<table>
<thead>
<tr>
<th>Cost</th>
<th>No. of studies</th>
<th>Health benefit</th>
<th>Implication for decision makers</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>0</td>
<td>-</td>
<td>Reject intervention</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>-</td>
<td>Reject intervention</td>
</tr>
<tr>
<td>+</td>
<td>0</td>
<td>0</td>
<td>Reject intervention</td>
</tr>
<tr>
<td>-</td>
<td>0</td>
<td>-</td>
<td>Unclear – Judgment required on whether intervention preferable considering incremental cost effectiveness measures and priorities/willingness to pay</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Unclear – Judgment required on whether intervention preferable considering incremental cost effectiveness measures and priorities/willingness to pay</td>
</tr>
<tr>
<td>+</td>
<td>2</td>
<td>+</td>
<td>Unclear - Judgment required on whether intervention preferable considering incremental cost effectiveness measures and priorities/willingness to pay</td>
</tr>
<tr>
<td>-</td>
<td>3</td>
<td>0</td>
<td>Favor intervention</td>
</tr>
<tr>
<td>0</td>
<td>3</td>
<td>+</td>
<td>Favor intervention</td>
</tr>
<tr>
<td>-</td>
<td>2</td>
<td>+</td>
<td>Favor intervention</td>
</tr>
</tbody>
</table>

If all the studies are very similar with respect to population, intervention, comparator and outcome, and they have similar methods and results, then this should be explained. If they all show strong dominance then this should be explained. In this case it may be legitimate to undertake a meta-analysis. If this is the case the findings of the meta-analysis should be presented.

### Discussion

This section should reflect on the systematic review’s contribution and limitations with reference to the existing knowledge base/literature and debates in policy and practice. The discussion should conclude by identifying the gaps in the evidence base. The discussion should not bring in new literature to support the argument about the findings from the review. It should only refer to studies/literature not included in the review to explain the contribution the systematic review has made and to reflect on its findings, and compare to findings from other reviews and studies.

Points to consider when developing the discussion:

- Were any problems experienced in implementing the search which resulted in difficulty in accessing potential studies? If so these should be reported and their implications for the robustness of findings discussed.
- What limitations were there in the included studies – were the populations, settings, interventions and outcomes as well as the outcome measures used similar? Or was there a high level of heterogeneity?
• Were the findings from the review generalizable to many different populations and settings? If not why not?
• What were the findings about the conditions conducive to the intervention being cheaper/less costly and more effective than the comparator? Or did the studies not allow for the drawing of any evidence-based answers to this question?
• What did the evidence suggest in regards to the important sub-groups to consider when reflecting on the cost and benefit trade-offs of the intervention/comparator considered?

Conclusion
The conclusion to the systematic review should present a paragraph that summarizes succinctly review findings and contribution. It should also include the following two subsections:

• *Implications for practice and/or policy* – This should draw out the implications of the review for policy and/or practice. Careful attention should be paid to ensuring that the generalizations take into consideration the contexts of included studies. The appropriate JBI Level of Evidence should be assigned to each recommendation.

• *Implications for research* – This should explain future research priorities. The research priorities should flow from the knowledge gaps identified in discussion.

Conflicts of interest
In this final section a statement which either declares the absence of any conflicts of interest or which describes a specified or potential conflict is required.

Acknowledgements
Any acknowledgements should be made in this section, e.g. sources of external funding or the contribution of colleagues or institutions. It should also be noted if the systematic review is to count towards a degree award.

References
All references should be listed in full using the Vancouver referencing style. They should be listed numerically and in the order in which they appear in the review.

Appendices
The five appendices that should be included at minimum in a JBI Systematic Review of Economic Evidence are listed below. The appendices should be numbered using Roman numerals in the order in which they have been referred to in the body of the text.

The systematic review report should include at minimum the following in the appendix:

• **Appendix I:** JBI critical appraisal instrument (and additional if used e.g. Philips et al. (2004) tool for assessing models

• **Appendix II:** JBI- ACTUARI data extraction instrument

• **Appendix III:** Search strategy (for at least one database searched and preferably all)

• **Appendix IV:** List of studies excluded at full text and critical appraisal with reasons

• **Appendix V:** Table of characteristics of included studies
4. References


9. NHMRC. How to compare the costs and benefits: evaluation of the economic evidence. 2001. Canberra; Biotex Production.


12. Centre for Reviews and Dissemination. Systematic Reviews: CRD’s guidance for undertaking reviews of health care. 2008. Centre Reviews and Dissemination, University of York, Published by CRD.


## Appendices

### 5.1 Appendix I JBI Critical Appraisal Checklist for Economic Evaluations

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not Applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is there a well defined question?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Is there comprehensive description of alternatives?</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>3. Are all important and relevant costs and outcomes for each alternative identified?</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>4. Has clinical effectiveness been established?</td>
<td></td>
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<tr>
<td>5. Are costs and outcomes measured accurately?</td>
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<tr>
<td>6. Are costs and outcomes valued credibly?</td>
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<td></td>
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<tr>
<td>7. Are costs and outcomes adjusted for differential timing?</td>
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<tr>
<td>8. Is there an incremental analysis of costs and consequences?</td>
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<tr>
<td>9. Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?</td>
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<tr>
<td>10. Do study results include all issues of concern to users?</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>11. Are the results generalisable to the setting of interest in the review?</td>
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</tbody>
</table>

Overall appraisal: Include □ Exclude □ Seek further info. □

Comments (Including reasons for exclusion)

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## 5.2 Appendix II JBI Data Extraction Form for Economic Evaluations

**JBI Data Extraction Form for Economic Evaluations**

<table>
<thead>
<tr>
<th>Reviewer</th>
<th>Date</th>
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</thead>
<tbody>
<tr>
<td>Author</td>
<td>Year</td>
</tr>
<tr>
<td>Journal</td>
<td>Record Number</td>
</tr>
</tbody>
</table>

**Method of Evaluation**
- Cost Minimisation
- Cost Utility
- Cost Effectiveness
- Cost Benefit

**Interventions**

**Comparator**

**Setting**

**Geographical**

**Participants**

**Source of effectiveness data**

**Authors Conclusions**

**Reviewers Comments**

**Extraction Complete**
- Yes
- No
Clinical Effectiveness Results

Study design

Year range of primary studies

Analysis used

Clinical outcome results

Economic Effectiveness results

Date/s of economic data

Modeling used

Measure of benefits used in economic evaluation

Direct costs

Indirect costs

Currency

Statistical analysis

Estimated benefits used in EE

Cost results

Synthesis of costs and results

Outcome category

<table>
<thead>
<tr>
<th>Clinical effectiveness</th>
<th>Cost</th>
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</thead>
<tbody>
<tr>
<td>+ A B C</td>
<td>+</td>
</tr>
<tr>
<td>0 D E F</td>
<td>0</td>
</tr>
<tr>
<td>- G H I</td>
<td>-</td>
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</tbody>
</table>

Key

<table>
<thead>
<tr>
<th>Effectiveness</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better</td>
<td>Lower</td>
</tr>
<tr>
<td>Equal</td>
<td>Equal</td>
</tr>
<tr>
<td>Poorer</td>
<td>Higher</td>
</tr>
</tbody>
</table>
5.3 Appendix III - Guidance for critical appraisal of economic evaluations using the JBI ACTUARI assessment tool

1. Is there a well-defined question/objective?
Consider the following before marking the study as compliant with this quality criterion:
- Is the objective/question of the study clearly stated?
- Does the statement reflect the perspective (e.g. patient or community or societal or health provider) used in measurement of costs or/and cost effectiveness?
- Was the study placed in a particular decision making context?

2. Is there a comprehensive description of alternatives?
To be marked as compliant with this criterion the authors of the study should offer a clear description of the intervention or interventions considered in the economic evaluation and the comparator or comparators. Compliance does not require that a broad range of interventions and comparators was considered. What is important here is clear description of the nature of the intervention and comparator whose cost/effectiveness was measured.

3. Are all important and relevant costs and outcomes for each alternative identified?
This quality criterion assesses the comprehensiveness and relevant of the cost and cost effectiveness outcomes measured in the economic evaluation. When deciding whether all important costs and outcomes have been identified/measured in the study reflect on whether the outcomes are sufficient in light of the objectives of the study. It is appropriate for a study that has the objective of measuring a narrow range of costs and benefits to identify and measure a limited range. However, the limits of the narrow approach should be drawn out in the study. It is not appropriate for a study which implies in its objective statement that it measures a broad range of costs for a broad range out outcomes to include only a very limited range of relevant costs and outcomes.

4. Has clinical effectiveness been established?
To assess compliance with this quality criterion requires considering whether the study has reported the evidence used to derive the effectiveness estimate and the level of this evidence. If it is not clear how the effectiveness estimate was derived, the study cannot be marked as compliant. To achieve compliance for this criterion the effectiveness estimate in the evaluation does not need to be derived from the same study as the resource use/cost estimate. What is important is the there is a solid evidence base under-pinning the assumptions about the direction and magnitude of the effectiveness measure(s) used in the evaluation.
5. Are costs and outcomes measured accurately?
This quality criterion assesses whether the study has used appropriate/best practice measurement method to measure costs and effectiveness. To decide whether a study should be marked as compliant consider whether the methods section of the paper offers a detail description of the measures used for costs and outcomes and how it justifies them. In addition, consider whether the authors/study implementers discussed any limitations associated with the measures used and concerns about the accuracy of measurement. In economic evaluations it is often difficult to measure costs and outcomes accurately, and hence in many cases this quality criterion will be difficult to achieve.

6. Are costs and outcomes valued credibly?
This quality criterion assesses whether appropriate prices were used to value costs and the validity of the valuation of benefits. It requires considering the method description and judging where there is a sufficient explanation about how costs and outcomes were valued and whether the justification for it is persuasive.

7. Are costs and outcomes adjusted for differential timing?
To be marked compliant for this question the study should have identified and justified the discount rate used. The time frame over which the study was conducted should also have been identified and justified.

8. Is there any incremental analysis of costs and consequences?
To achieve compliance the paper should report a measure that shows the change in costs and benefits for the intervention and comparator for a marginal shift in resources from the comparator to the intervention.

9. Were sensitivity analysis conducted to investigate uncertainty in estimates of costs or outcomes?
Sensitivity analysis is critical for establishing the validity of any economic evaluations results. To be compliant a study must present sensitivity testing results that describe how the study findings vary with changes in key variables (for example relative prices, and intervention estimates? conducted to check the robustness of findings.

10. Do study results include all issues of concern to users?
This question reflects on the comprehensiveness of coverage in the reporting of results. In deciding whether to mark the study as compliance consider whether the range of measures presented provider answers to all the questions users/decision makers would want to know when taking a decision about whether to implement the program examined (or cutting it)?

11. Are the results generalizable to the setting of interest in the review?
To be marked as compliant for this last quality criterion the paper should: (i) have described the study setting adequately; (ii) discuss the issue of transferability of findings and how the results are generalizable to other settings with similar characteristics.