Cochrane Anaesthesia Review Group's "Tips for Peer Reviewers"

Introduction

Welcome to the Cochrane Anaesthesia Review Group's (CARG's) guide to peer reviewing a Cochrane intervention protocol and a review. We hope you will find it helpful.

This guide is split into five parts.

(1) A brief introduction to The Cochrane Collaboration
(2) Overview
(3) The CARG editorial process
(4) Common errors which authors make
(4) How to peer review a Cochrane Protocol
(5) How to peer review a Cochrane Review

A Brief Introduction to The Cochrane Collaboration and CARG

The Cochrane Collaboration is an international non-profit organization. It aims to help people make well-informed decisions about healthcare by producing and publishing systematic reviews of health care interventions.

The Collaboration is made up of five different entities or 'groups'.

(1) Collaborative Review Groups
(2) Cochrane Centres
(3) Methods Groups
(4) Networks or fields
(5) The Consumer Network

CARG is a Cochrane Review Group (CRG). We prepare systematic intervention and diagnostic test accuracy reviews in:

(1) anaesthesia
(2) intensive care medicine
(3) perioperative medicine
(4) prehospital medicine
(5) resuscitation
(6) emergency medicine

This guide deals with intervention reviews. A separate guide will be developed for diagnostic test accuracy reviews.

There are 51 CRGs world-wide, each focusing on a particular area of health. CARG's editorial base is in Copenhagen, Denmark. Our scope is wide and overlaps with many other Cochrane Groups, for example: the Pregnancy and Childbirth Group and the Pain, Palliative Care and Supportive Care Group. We work closely with other CRGs.

For a more detailed introduction to The Cochrane Collaboration: http://www.cochrane.org

The CARG editorial team:

(1) Co-ordinating Editors:	Ann Møller and Nathan Pace
(2) Managing Editor (ME):	Jane Cracknell
(3) Trials Search Co-ordinator:	Karen Hovhannisyan
(4) Editorial adviser and treasurer:	Tom Pedersen
(5) Secretary:	Annette van Hauen
(6) PhD students:	Arash Afshari and Georgina Imberger
(7) And 13 editors	

CARG Editors:

Senior Statistical Editor:	Nathan Pace (USA)
Statistical Editor:	Marialena Trivella (UK)
Statistical Editor:	Cathal Walsh (IRE)
Feedback Editor:	John Carlisle (UK)
Consumer Editor:	Janet Wales (Australia)

Content Editors: Mike Bennett (Australia); John Carlisle (UK); Harald Herkner (Austria); Stephan Kettner (Austria); Anna Lee (Hong Kong, China); Mark Neuman (USA); Nicola Petrucci (Italy); Andrew Smith (UK); Mathew Zacharias (New Zealand).

Overview

Critical evaluation is essential to ensure and maintain a high scientific standard throughout the process of making a systematic review.

Please note all CARG protocols and reviews are edited following the process outlined in the Cochrane Reviewers' Handbook, which can be downloaded or browsed by visiting:
http://www.cochrane.org/resources/handbook/

It is our goal that protocols and reviews prepared through the CARG will be published electronically in *The Cochrane Library's Database of Systematic Reviews*.

The *Cochrane Library's Database of Systematic Reviews* moved to monthly publication in 2010.

You can access The *Cochrane Library's Database of Systematic Reviews via The Cochrane Library www.thecochranelibrary.com*

The aim of a Cochrane review is to systematically assess the best possible scientific evidence about the effects of a health care intervention. The review should aim to minimize the possibility of bias.

(1) The conduct of the review and its analyses must follow clear, pre-specified criteria.
(2) The review must be clearly written and easy to understand.
(3) Any conflict of interest must be declared.
(4) Efforts must be made to find every possible study that may be eligible for the review.
(5) The studies included in the review's final analyses must have as little bias as possible.
(6) Outcomes that are important to consumers must be considered: whether or not researchers have measured them. This is to avoid conclusions that are based on a narrow picture.
(7) The final review must follow the pre-specified criteria, addressing all the important issues raised by the researchers at the beginning of the review, and highlighting any issues and gaps in the information that should be addressed by researchers in the future.

The title

All intervention titles should conform to Cochrane standards: an intervention for a specific health problem. For example: "Drugs for preventing postoperative nausea and vomiting"

Cochrane reviews should not duplicate work already published in *The Cochrane Library.*
Generally, only randomized or controlled clinical trials are suitable for inclusion in the review.

In brief, the stages of a Cochrane Review are:

(1) Registered Title
(2) Protocol
(3) Review
(4) Updated review

The Editorial Process

The editorial process is similar for both protocol and review. For ease both documents will be referred to as 'reviews' in this part of the booklet.

CARG operates an open editorial process. All members of the editorial team (content editor, statistical editor, peer reviewers and consumers) are identified, as are the authors. **All peer reviewers' comments will be directly returned to the author of the review unblinded (with the peer reviewer's name on them).**

All CARG reviews are submitted to the editorial office in RevMan 5.1 (The Cochrane Collaboration's software.) The reviews are then saved to pdf and sent out to a content editor, and a statistical editor (statistical editors only comment on the second draft of a protocol), a minimum of two peer reviewers

and a member of the Cochrane Consumer Network.

The peer reviewers, consumer referee and statistical editor are asked to return their comments (in an evaluation form) to the ME within 28 days of receiving the review. Comments should be written in a constructive manner.
Your comments will then be sent to the content editor. The content editor will (from the editorial evaluations) outline a plan of action for the author to follow. Please remember that we operate an open editorial process. This means that the authors will receive copies of the original unblinded (with your names on them) comments. All peer reviewers will be sent that plan plus copies of the unblinded individual comments of all the members of the editorial team.
We ask that authors respond to their editor's comments within three months of receipt. They are asked to revise their review on the strength of the editor's comments. They should submit their revised review, along with a detailed covering letter describing the changes they have made. This covering letter should answer all comments made by the editor. It should clearly outline the changes they have made to their review. It should clarify how they have responded to the editor's comments (or their reasons for not implementing the editor's suggested changes).
The peer reviewers and consumer representatives will not see the revised review again, nor will they see the author's replies to their comments. Peer reviewers and consumers are only asked to comment on the first draft of protocols, reviews and updated reviews. You will be sent a pdf copy of the published review as a way of thanking you for your help. You will also be mentioned in the acknowledgement section of the published protocol or review and in CARG's published module. (The module appears in the 'About Cochrane' section of *The Cochrane Library*.)
The authors 'work' with the statistical and content editors until they approve the review. This can take several drafts. Once the editors have approved the review, it will then be sent to the Co-ordinating editors (Ann Møller and Nathan Pace) for final publication approval. The Co-ordinating Editors may request further changes before approving the review for final publication. Once the review is approved it will be internally and externally copyedited to conform to Cochrane style. As with all journals, Cochrane has its own 'style', the final review must follow Cochrane's style guidelines.

COMMON ERRORS AUTHORS MAKE IN REVIEWS

1. If the protocol is thorough the chances of the review producing results that misrepresent the evidence will be minimized. Therefore the most likely sources of error are either that the authors do not follow their protocol (acts of omission or commission) or that the protocol was inadequate.
2. There will always be errors of style in the first draft of a review. You will find errors on the Cover sheet and in the Tables as well as in the main text of the review (or protocol).
3. The Background is usually too long. The sentences are usually too long. The words are usually too long.
4. There are usually too many outcomes and proposed subgroup analyses.
5. The authors fail to proof read the tabular text. The format of some of the references will be incorrect.

The Protocol

The protocol is the outline of the systematic review the authors are planning to conduct. The protocol acts as a template for their review. A systematic review is rather like a primary clinical research study, in that it is setting out what the authors propose to do; how they intend to deal with expected findings and how they will deal with unexpected problems. A well-written protocol will guide you through the review. It is like writing a protocol for a research proposal.
The protocol should be written in the future tense and active voice: "we will search".

How to peer review a protocol

The aim of your comments is to assist an editor in identifying any areas of weakness in a protocol, and suggesting improvements. We appreciate that you may not feel comfortable to comment on all areas, for example: the search strategy.
Please write your comments in the **separate protocol evaluation form** and email them to:
jane_cracknell@yahoo.com

What to look for:
A. The Cover Page
This must be completed. It should contain the review title and authors' affiliations.

B. The Background
The background section is designed to explain to people what is going to be reviewed and why. It must explain why the question needing to be answered is important. For example, it should indicate the areas of uncertainty in relation to the intervention and highlight issues that are controversial or the subject of public concern. It must define all terms and interventions clearly, and should try to use a balanced tone that does not pre-judge the value of the intervention.
The background should be concise and easy to understand. It should provide enough detail to understand the review and no more (i.e. not a detailed literature review of the topic). As a guide, it should be one page long. It should avoid unnecessary abbreviations, be readable, discuss important issues and avoid repetition. The authors should describe the health issues to be addressed by the protocol, including how they occur, where they occur, who is affected (including high risk groups), diagnosis, symptoms and consequences.
The authors should describe the intervention, including how it works, how it is different from the control or other interventions, the context of usual practice in this field, and known adverse effects.

The authors should support all facts, figures and statements with references.

Please indicate in your comment sheet whether you think the author has covered these issues adequately?

C. The Objectives
This section should contain a precise statement of the primary objectives of the review, including the intervention(s) reviewed and the problem(s) addressed preferably in simple sentences. It can also mention why the review is being done, and how it might relate to a wider review of a general problem. Sub-group analysis should be explicitly stated in this section.
Please indicate in your comment sheet whether you think the author has covered these issues adequately?

D. The Selection criteria

This section has four parts (please see below). Together, they should make it clear which studies will be included in the authors' review, and which will be excluded. The aim is to come up with very specific, reproducible guidelines for deciding whether a study addresses the objective of the review. Later, the quality of included studies will also be assessed. The author should have biological rationale or empirical evidence for inclusion and exclusion criteria and all subgroup analyses. The authors should define all the criteria they are using e.g. what does 'critically ill' mean, what does 'intensive care' mean, what does 'food' mean etc.

1 **Types of studies:** The design of the studies that will be eligible for inclusion is usually randomized controlled trials. The aim is to include study designs that minimize the chances of the results being biased.

2 **Types of participants**: The author should briefly describe which types of people would be included in the studies. They should also include their exclusion criteria.

3 **Types of interventions:** The authors should describe what interventions they intend to include. An intervention is anything that is meant to change the course of events (e.g. surgery, a drug, a test, a treatment, counselling).

4 **Types of outcomes:** These are the most important outcomes that need to be considered in order to make decisions about the particular intervention. These need to be specified in advance. The studies may not address particular outcomes: in which case, it is important for the authors to know that important topics have been overlooked.

- The authors should consider including adverse effects among the outcomes to be reported
- The authors should describe appropriate methods of measuring each outcome (e.g. validated tools, meaningful process measures) and appropriate time points for measurement
- The authors should consider the minimally important difference for each outcome
- The authors should select a maximum of seven key important outcomes, including adverse effects, to be included in the '**Summary of findings**' tables when the review is complete

Please indicate in your comment sheet whether you think the author has covered these issues adequately? Are the reasons for excluding studies clearly reported?

E. Search strategy for the identification of studies

This section explains how and where the authors will look for studies that may be eligible for inclusion in their review. They should include: *The Cochrane Library*, MEDLINE, EMBASE and all other relevant databases. The CRG's specialized register should be referenced. The date ranges of searches should be included (it should include the start year and then 'to date'.).

The authors should include their MEDLINE search terms in the appendices. The relevant appendix should be linked to the search strategy section. The authors should state whether they will search conference proceedings of important meetings and abstracts; and if efforts will be made to contact experts in order to identify unpublished research and trials still underway. Any speciality journals that have been hand searched should be identified and referenced. The name of the journal should, be entered in full.

The search strategy must be reproducible. The search must not be limited by language or publication status.

The inclusion criteria for the review, including the types of studies, should be consistent with the search strategy.

Do you think the search strategy is adequate? Please describe in your comment sheet any inadequacies.

F. Methods

This section should describe both the steps of the review process and its standards and criteria. It should clarify how the quality of studies is going to be assessed, what the criteria are going to be, and what checks there will be on these steps. As with the selection criteria, the aim is to be clear, specific and reproducible.

1 **Explicit criteria for inclusion and exclusion of studies**:

The authors need to explicitly state their inclusion and exclusion criteria. They should state how they will identify the trials, which authors will retrieve the trials and how they will resolve disagreements.

2 **Data collection:**

This section should contain details of the methods the authors will use to identify published and unpublished data to be included in their review. They need to explicitly state how many authors will extract the data. At least two persons should extract data independently. This is to assure objectivity. Quality assessment tends to be subjective, value-laden and surprisingly heterogeneous. They need to state which authors will check and enter those data into Review Manager (RevMan) 5.1.
Transcription errors in entering data into the data extraction form are a common problem. The authors should explain how they would deal with missing information or data inconsistencies.
NOTE: We expect all authors to insert a copy of their data extraction form in their review's appendices and link the relevant appendix to the methods' section.

WHY?

A data extraction form provides a quick overview of each study and helps the authors complete their tables of "**Characteristic of Included", "Characteristics of Excluded Studies" and "Risk of bias"** at review stage.

3. Appropriate criteria for assessing the quality of the studies:

Randomized controlled trials (RCTS) should be selected, analysed and considered for inclusion and graded for their methodological quality, using concealment of randomizations, blinding of patients, blinding of caregivers, blinding of assessors, handling of dropouts and use of intention-to-treat analysis.
We do **not** recommend that authors give 'points' in the process of quality assessment.

4. Appropriate methods:

The authors should state whether the data would be combined qualitatively or quantitatively. They should include the statistical methods they will use, and any sensitivity or subgroup analyses they plan to do (see below). As with outcomes, these need to be specified in advance. Developing theories about what causes any differences in results afterwards is less reliable than establishing a rationale for differences in advance.

- A sensitivity analysis involves re-analysing the results having excluded particular studies, to see if they are skewing the results. Sensitivity analyses try to find out if there are reasons to explain heterogeneity in the results (differences in results from study to study).
- A subgroup analysis means looking for differences in particular groups of people.
- Statistical handling should foresee problems with multiplicity and subgroup analysis

The authors should describe a strategy for assessing and addressing heterogeneity

The authors should describe a strategy for dealing with missing data, unit of analysis error and intention-to-treat analysis.

Review Manager version 5 has implemented two new tables. The risk of bias (ROB) table is a tool for assessing risk of bias in included studies. The summary of findings (SOF) table is a tabular listing

of important outcomes and quality of evidence (GRADE). The Anaesthesia Review Group now requires inclusion of ROB and SOF tables in a review. The authors should state that a risk of bias table will be constructed for each study. They should provide a brief explanation of how a summary of findings table will be constructed (i.e. GRADE Profiler software).

The authors should describe appropriate methods of measuring each outcome (e.g. validated tools, meaningful process measures) and appropriate time points for measurement. The authors should state how they would grade the evidence and formulate a recommendation.

Is there an adequate description of: the methods used to select trials; the criteria and methods used to assess the methodological quality of the included trials; the methods used to collect data from the included trials; the qualitative and quantitative methods used to combine data? Please describe in your comment sheet any inadequacies.

G: Conflict of interest:
Sponsorship of a Cochrane review by any commercial source or sources is prohibited.
The authors should report any conflict of interest that is capable of influencing their judgement. This would include personal, political, academic, and particularly, financial conflicts. Financial conflicts of interest include the receipt of any benefit in cash or kind, any hospitality, or any subsidy derived from any source with an interest in the results of the review. Any sponsorship or funding of the review needs to be declared. If there are no conflicts they should write: "none known".
H: References:
References for every article or book identified in the text must be listed. At protocol stage the references should be found under 'Additional references'.

How to peer review a Cochrane Review

The aim of your comments is to assist an editor in identifying any areas of weakness in a review, and suggest improvements.
The review should follow the same format as the published protocol. You will be sent a copy of the published protocol with the draft review. Any changes to the published protocol should be noted (and reasons for those changes) in the section ' "Differences between the published protocol and review".
The protocol will have been written in the active voice and future tense. The review should be written in the active voice and the **past** tense.

Please write your comments on the review in the **separate review evaluation form** and email to: jane_cracknell@yahoo.com

The completed review should include the following sections

A. Plain language summary:
The synopsis is a brief summary of the results of the review, written in plain language that could easily be understood by consumers and non-specialist readers.
It should contain:

- Information on the number of included studies, the risk of bias, and any possible adverse effects.
- A summary of the most important outcomes for answering the review question, including those that were not statistically significant or for which no results were found
- Results and conclusions that are consistent with those in the **Abstract** and the main text of the review
- No references.

B. Abstract

The abstract is a stand-alone document and should summarize the results of the review. It needs to be suitable for publication in PubMed and other abstracting services.

It should contain:

- Information on the number of included studies, the risk of bias, and any possible adverse effects.
- A summary of the most important outcomes for answering the review question, including those that were not statistically significant or for which no results were found
- Results and conclusions that are consistent with those in the main text of the review.
- No additional information not found else where in the review
- No references.

C. Background:

The background section is designed to explain to people what is going to be reviewed and why. It must explain why the question being answered is important. For example, it should indicate the areas of uncertainty in relation to the intervention and highlight issues that are controversial or the subject of public concern. It must define all terms and interventions clearly, and should try to use a balanced tone that does not pre-judge the value of the intervention.

The background should be concise and easy to understand. It should provide enough detail to understand the review and no more (i.e. not a detailed literature review of the topic). As a guide, it should be one page long. It should avoid unnecessary abbreviations, be readable, discuss important issues and avoid repetition.

It should describe:

- The condition or health issue to be addressed by the review, including how it occurs, where it occurs, who is affected (including high risk groups, vulnerable/disadvantaged groups), diagnosis, symptoms, consequences and significance;
- The intervention, including its context in relation to usual practice in this field, the context of comparison interventions, the treatment regiment or intervention components, and known adverse effects;
- Any likely differences in the use or outcomes of the intervention for specific populations (e.g. children, vulnerable/disadvantaged groups);
- How the intervention might work to achieve the desired outcomes;

In addition:

- All facts, figures and statements should be supported with references
- **Technical and medical terms should be clarified for non-specialist readers.**

Please indicate in your comment sheet whether you think the author has covered these issues adequately?

D. Objectives: The objectives remain the same as in the protocol. They should be rewritten in the past tense. They should contain a precise statement of the primary objectives of the review, including the intervention(s) reviewed and the problem(s) addressed preferably in single sentences. This section can also mention why the review is being done, and how it might relate to a wider review of a general problem. Sub-group analysis should be explicitly stated.

If there are hypotheses for the review (specific theories or suggestions being tested), these should be explicitly stated here. The comparisons that are listed later in the review should be consistent with any hypotheses described in the objectives section

Please indicate in your comment sheet whether you think the author has covered these issues adequately?

E. Criteria for considering studies for this review

Again this section remains the same as in the published protocol, but rewritten in the past tense. This section has four parts (please see below). Together, they should make it clear which studies are included in the authors' review, and which are excluded. The aim is to come up with very specific, reproducible guidelines for deciding whether a study addresses the objective of the review. Later, the quality of included studies will also be assessed. The author should have biological rationale or empirical evidence for hypotheses, inclusion and exclusion criteria and all subgroup analyses. The authors should define all the criteria they are using e.g. what does 'critically ill' mean, what does 'intensive care' mean, what does 'food' mean etc.

1 Types of studies: The design of the studies eligible for inclusion is usually randomized controlled trials. The aim is to include study designs that minimize the chances of the results being biased.

2 Types of participants: This should briefly describe which types of people are included in the studies.

3 Types of interventions: An intervention is anything that is meant to change the course of events (e.g. surgery, a drug, a test, a treatment, counselling).

4 Types of outcomes: These are the most important outcomes that need to be considered in order to make decisions about the particular intervention. These need to be specified. The studies may not address particular outcomes: in which case, it is important for the authors to state that important topics have been overlooked.

- The authors have considered including adverse effects among the outcomes to be reported
- The authors have described appropriate methods of measuring each outcome (e.g. validated tools, meaningful process measures) and appropriate time points for measurement
- The authors have considered the minimally important difference for each outcome
- The authors have selected a maximum of seven key important outcomes, including adverse effects, to be included in the '**Summary of findings**' tables when the review is complete

Please indicate in your comment sheet whether you think the author has covered these issues adequately?

F. Search strategy for identification of studies

This section should be the same as the protocol except the authors provide the dates they searched the databases. This section should be rewritten in the past tense.

This section should explain how and where the authors looked for studies that are eligible for inclusion in their review. They should include: *The Cochrane Library*, MEDLINE, EMBASE and all other relevant databases. The CRG's specialized register should be referenced. The date ranges of searches should be included.
All of the authors' search terms should be included in the appendices and linked to the text.

The authors should state whether they searched conference proceedings of important meetings and abstracts; and if efforts were made to contact experts in order to identify unpublished research and trials still underway. Any speciality journals that have been hand searched should be identified and referenced. The name of the journal should, be entered in full.

The search strategy must be reproducible. The search must not be limited by language or publication status.
The search strategy should be consistent with the inclusion criteria for the review, including the types of studies to be included.

The search should incorporate a broad range of appropriate sources (e.g. subject-specific databases, sources in multiple languages, sources relevant to health equity, contact with experts, references and citations, handsearching)

The authors have entered the last date on which every component of their search was up-to-date in. If their sources were searched on several different dates, the earliest of those searched determines how up to date a review is .The latest search date in a draft review should be about six months before the date the review is accepted in the editorial process.
Do you think the search strategy is adequate? Please describe in your comment sheet any inadequacies?

G. Methods of the review
This section should describe both the steps of the review process and its standards and criteria. It should clarify how the quality of studies was assessed, what the criteria were and what checks there were. In other words the authors need to describe what they did and how they did it. As with the selection criteria, the aim is to be clear, specific and reproducible. This section should be written in the past tense.
1 **Explicit criteria for inclusion and exclusion of studies**:
The authors should explicitly state their inclusion and exclusion criteria. They
should state how they identified the trials; which authors retrieved the trials and how they resolved disagreements.

2 **Data collection:**
This section should contain details of the methods the authors used to identify published and unpublished data included in their review. They need to explicitly state how many authors' extracted data. (At least two persons should extract data independently. This is to assure objectivity. Quality assessment tends to be subjective, value-laden and surprisingly heterogeneous.) They should state which authors checked and entered the data into Review Manager (RevMan) 5.1. Transcription errors in entering data into the data extraction form are a common problem. The authors should explain how they dealt with missing information or data inconsistencies.
Appropriate criteria for assessing the quality of the studies:
Randomized controlled trials (RCTS) should be selected, analysed and considered for inclusion and graded for their methodological quality, using concealment of randomizations, blinding of patients, blinding of caregivers, blinding of assessors, handling of dropouts and use of Intention-to-Treat analysis. We do **not** recommend that authors give 'points' in the process of quality assessment.
Appropriate methods:
The authors should state whether the data was combined qualitatively or quantitatively.
They should include the statistical methods they used and any sensitivity or subgroup analyses they did (see below).

- A sensitivity analysis involves re-analysing the results having excluded particular studies, to see if they are skewing the results. Sensitivity analyses try to find out if there are reasons to explain heterogeneity in the results (differences in results from study to study).
- A subgroup analysis means looking for differences in particular groups of people.

- Statistical handling should foresee problems with multiplicity and subgroup analysis
- They have described a strategy for dealing with missing data, unit of analysis error and intention-to-treat analysis.

Is there an adequate description of: the methods used to select trials; the criteria and methods used to assess the methodological quality of the included trials; the methods used to collect data from the included trials; the qualitative and quantitative methods used to combine data?

H. Description of studies:
This should refer to the information contained in the **Characteristics of Include**d **Studies** and the **Characteristics of Excluded Studies tables**. The author should provide you with a summary of the **trial selection process. You should be informed how many citations the search revealed, how many studies are included (and duplicates of), excluded (and duplicates of), awaiting assessment, ongoing. You should be referred to a searching figure.**
Is the result of the search adequately described? Is the reader directed to the 'Table of characteristics of included studies' and the 'Table of characteristics of excluded studies'? Are the participants in the included studies adequately described (in text or table)? Are the interventions adequately described (in text or table)? Are the outcomes adequately described (in text or table)? Are these elements consistent with the criteria?

I. Methodological Quality:
This section should describe the general quality of the included studies and any important flaws in individual studies that may affect bias (e.g. randomization, concealment of random allocation, blinding, drop-outs, etc.). It should include: the number of included and excluded studies, included patients, studies awaiting assessment, on-going trials, and individuals or companies that are providing data.
Are the methodological criteria described in the Methods adequately followed and reported? Is the reader directed to the 'Table of characteristics of included studies'?

J. Results:
This should be a summary of the main findings of the review and any sensitivity analyses that were undertaken. It should describe results in the same order as they appear in the **Table of Comparisons**. All results, both quantitative and qualitative, should be included.
Are the results presented in a format consistent with the objectives of the review, any stated hypotheses and the criteria for inclusion? Is the result of the primary hypothesis presented first? This is the overall effect of the intervention(s) on the incidence/value of the outcome in the population, and it should precede any subgroup or sensitivity analyses.
Are the results presented in the text consistent with the results presented in the Table of characteristics of included studies, in the Table of comparisons and in the analytical graphs (Forest and Funnel plots)?
Are the subgroup analyses the same as those proposed in the Protocol? Are the sensitivity analyses the same as those presented in the Protocol? Is the possibility of publication bias reported?
Please indicate in your comment sheet whether you think the author has covered these issues adequately?

K. Discussion:
This should include brief comments on any methodological limitations of the included studies and the issues that are important for decisions about practice or future research. It should briefly summarize the included studies and their results in plain language, including the risk of bias, areas of uncertainty and completeness of the available evidence. This

section should not include any new results not reported in the previous section.

- The authors should refer to their '**Summary of findings**' table(s) and include links as appropriate.
- The authors should consider both the statistical significance and clinical significance of the results.
- The authors should consider both the applicability and context of the results.
- They should discuss the strengths and limitations of their review.
- They should discuss their findings in the context of current knowledge, including the findings of other reviews in the area.

Is the discussion section consistent with the results? Is the uncertainty of the results discussed? The discussion should not drift into areas that were not addressed in the Protocol. In particular, reviewers should refrain from making statements that are not supported by the evidence that they have found.
Please indicate in your comment sheet whether you think the author has covered these issues adequately?

L. Reviewers' conclusions:
This should present information, not offer advice. It should avoid platitudes such as "more research is needed". The authors should summarize their findings clearly, stating exactly what research is needed and why. Opinions on how the review might be improved with additional data or resources can also be noted. If recommending additional research, the authors should include specific recommendations for how the research should be conducted (e.g. study designs, outcome measurements) as well as what research should be conducted (e.g. different populations, interventions).

- **Implications for practice:** This should include any important finding that may influence clinical practice.
- **Implications for research:** If trials show nothing useful, the authors should constructively criticize previous research and lay down guidelines for future trials.

Conclusions should be conservative. They should be contained with the certainty limits (95% confidence intervals) of the results. Implications for research should logically follow on from the conclusion.

M. Acknowledgements: This section should be used to acknowledge individuals or organizations (e.g. editor, researcher or company that provided additional data).

N. Potential conflict of interest:
The authors should report any conflict of interest that is capable of influencing their judgement. This would include personal, political, academic, and particularly, financial conflicts. Financial conflicts of interest include the receipt of any benefit in cash or kind, any hospitality, or any subsidy derived from any source with an interest in the results of the review. Any sponsorship or funding of the review needs to be declared. If there are no conflicts the authors should write: "none known".
Sponsorship of a Cochrane review by any commercial source or sources is prohibited.

O. References.
References for every article or book identified in the text must be listed. Authors should indicate whether included and excluded studies are primary references; they need to do this even if there is only one version of the study.