

Chapter 4: Guide to the contents of a Cochrane protocol and review

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Key points

- Cochrane reviews have a highly structured format, and compliance with this format is facilitated by the use of RevMan. This chapter describes what an author is expected to include, and what a reader may expect to find, in each component of a Cochrane protocol or review.
- The chapter also serves as a guide to much of the *Handbook*, containing links to other chapters where further discussion of the methodological issues can be found.
- A ‘Review information’ (or ‘Protocol information’) section includes details of authors and important dates associated with maintaining and updating the review.
- The main text should be succinct and readable, so that someone who is not an expert in the area can understand it. The text of a protocol ends after the Methods section.
- A ‘Studies and references’ section provides a framework for classifying included, excluded and ongoing studies, as well as those for which insufficient information is available, and other references.
- Tables of characteristics of studies allow the systematic presentation of key descriptors of the studies considered for the review.
- A ‘Data and analyses’ section has a hierarchical structure, allowing data from included studies to be placed within particular subgroups of studies, which are in turn within meta-analyses of particular outcomes, which are in turn within particular intervention comparisons. For each meta-analysis, forest plots and funnel plots can be generated within RevMan.
- Further tables, figures and appendices can be included to supplement the inbuilt tables.

4.1 Introduction

Cochrane Intervention reviews all have the same format, and the preparation of a review with the required format is facilitated by the use of Review Manager (RevMan) software. In this chapter we

discuss the content of the entire review (or protocol) and outline what should appear in each section. Extensive references to other chapters in the *Handbook* are included to signpost advice relevant to each section. Guidance on *using* the RevMan software itself is available in the help system within the software.

4.2 Title and review information (or protocol information)

4.2.1 Title

The title succinctly states the intervention(s) reviewed and the problem at which the intervention is directed. Explicit guidance for structuring titles of Cochrane reviews is provided in [Table 4.2.a](#).

Table 4.2.a: Structure for Cochrane review titles

Scenario	Structure	Example
Basic structure.	[Intervention] for [health problem].	Antibiotics for acute bronchitis.
Comparing two active interventions.	[Intervention A] versus [intervention B] for [health problem].	Immediate versus delayed treatment for cervical intraepithelial neoplasia.
Type of people being studied or location of intervention mentioned explicitly.	[Intervention] for [health problem] in [participant group/location].	Inhaled nitric oxide for respiratory failure in preterm infants.
Not specifying a particular 'health problem' (e.g. 'Home versus hospital birth'), or if the intervention intends to influence a variety of problems (e.g. 'Prophylactic synthetic surfactant in preterm infants').	[Intervention] in OR for [participant group/location].	Restricted versus liberal water intake in preterm infants.
Sometimes it is necessary to specify that the intervention is for preventing, treating, or preventing and treating the health problem(s). If necessary, the word 'for' is followed by 'preventing', 'treating', or 'preventing and treating'. This is better than using 'for the prevention of' etc.		Pool fencing for preventing drowning in children; Amodiaquine for treating malaria; Vitamin C for preventing and treating the common cold.

4.2.2 Authors

Authorship of all scientific papers (including Cochrane protocols and reviews) establishes accountability, responsibility and credit (Rennie 1997, Flanagan 1998, Rennie 1998). When deciding

who should appear in the by-line of a Cochrane review, it is important to distinguish individuals who have made a substantial contribution to the review (and who should be listed) and those who have helped in other ways, which should be noted in the Acknowledgements section. Authorship should be based on substantial contributions to all of the following three steps, based on the ‘Uniform requirements for manuscripts submitted to biomedical journals’ (International Committee of Medical Journal Editors 2006). Authors must sign a ‘License for Publication’ form that affirms the following three contributions.

- Conception and design of study, or analysis and interpretation of data
- Drafting the review or commenting on it critically for intellectual content
- Final approval of the document to be published.

The specific contributions should be listed under the section ‘Contributions of authors’ (see below). The list of authors can be the name of an individual, several individuals, a collaborative group (for example, ‘Advanced Bladder Cancer Overview Collaboration’) or a combination of one or more authors and a collaborative group. Ideally, the order of authors should relate to their relative contributions to the review. The person who contributed most should be listed first.

4.2.3 Contact person

Contact details should be provided for the person to whom correspondence about the review should be addressed, and who has agreed to take responsibility for maintaining and developing the review. Most usually, this person would (i) be responsible for developing and organizing the review team; (ii) communicate with the editorial base; (iii) ensure that the review is prepared within agreed timescales; (iv) submit the review to the editorial base; (v) communicate feedback to co-authors; and (vi) ensure that the updates are prepared.

The contact person need not be the first listed author, and the choice of contact person will not affect the citation for the review. If an existing contact person no longer wishes to be responsible for a published review and another member of the review team does not wish to take responsibility for it, then contact details for the Review Group Co-ordinator (RGC) should be listed here. The contact person for a review need not be listed as an author.

4.2.4 Dates

4.2.4.1 Assessed as up to date

The date on which the review was last assessed as being up to date will often coincide with the date on which the authors submit the review for consideration to be published in the *Cochrane Database of Systematic Reviews (CDSR)*.

See also:

- Specific criteria for describing a review as up to date appear in Chapter 3 (Section 3.2).

4.2.4.2 Date of search

This date is used to help determine whether a review has been updated, and to inform the date on which the review is assessed as being up to date. It will not be published in the *CDSR*.

See also:

- Specific criteria for specifying the date of search appear in Chapter 3 (Section 3.3.3).
- Search methods are discussed in detail in Chapter 6 (Section 6.3).

4.2.4.3 Next stage expected

A date for internal use only (it will not be published in the *CDSR*) indicating when the completed review (for protocols) or the next review update (for reviews) is due.

See also:

- Policies for updating reviews are described in Chapter 3 (Section 3.1).

4.2.4.4 Protocol first published

The issue of the *CDSR* in which the protocol was first published (for example, Issue 2, 2004). The date cannot be edited in RevMan.

4.2.4.5 Review first published

The issue of the *CDSR* in which the full review was first published (for example, Issue 1, 2005). The date cannot be edited in RevMan.

4.2.4.6 Last citation issue

The issue of the *CDSR* in which the current citation version of the review was first published (for example, Issue 1, 2007). The date cannot be edited in RevMan.

See also:

- Citation versions are discussed in detail in Chapter 3 (Section 3.2)

4.2.5 What's new and History

The 'What's new' section should describe the changes to the protocol or review since it was last published in the *CDSR*. At each update or amendment of a review, at least one 'What's new' event should be recorded, containing the type of event, the date of the change and a description of what was changed. This description might be, for example, a brief summary of how much new information has been added to the review (for example, number of studies, participants or extra analyses) and any important changes to the conclusions, results or methods of the review. Entries from the 'What's new' table that do not relate to the current citation version of the review should be listed in the 'History' table.

See also:

- 'What's new' table events are discussed in detail in Chapter 3 (Section 3.5).

4.3 Abstract

All full reviews must include an abstract of 400 words or fewer. The abstract should be brief without sacrificing important content. Abstracts to Cochrane reviews are published in MEDLINE and the Science Citation Index, and are made freely available on the internet. It is therefore important that they can be read as stand-alone documents.

See also:

- Guidance for the content of an abstract is provided in Chapter 11 (Section 11.8).

4.4 Plain language summary

The plain language summary (formerly called the 'synopsis') aims to summarize the review in a straightforward style that can be understood by consumers of health care. Plain language summaries are made freely available on the internet, so will often be read as stand-alone documents. Plain

language summaries have two parts: a plain language title (a restatement of the review's title using plain language terms) and a summary text of not more than 400 words. Guidance for the content of a plain language summary is provided in Chapter 11 (Section 11.9).

4.5 Main text

The text of the review should be succinct and readable. Although there is no formal word limit for Cochrane reviews, review authors should consider 10,000 words an absolute maximum unless there is special reason to write a longer review. Most reviews should be substantially shorter than this. A review should be written so that someone who is not an expert in the area can understand it, in light of the following policy statement, stated in the Cochrane Manual (www.cochrane.org/admin/manual.htm):

“The target audience for Cochrane reviews is people making decisions about health care. This includes healthcare professionals, consumers and policy makers with a basic understanding of the underlying disease or problem.

It is a part of the mission and a basic principle of The Cochrane Collaboration to promote the accessibility of systematic reviews of the effects of healthcare interventions to anyone wanting to make a decision about health care. However, this does not mean that Cochrane reviews must be understandable to anyone, regardless of their background. This is not possible, any more than it would be possible for Cochrane reviews to be written in a single language that is understandable to everyone in the world.

Cochrane reviews should be written so that they are easy to read and understand by someone with a basic sense of the topic who may not necessarily be an expert in the area. Some explanation of terms and concepts is likely to be helpful, and perhaps even essential. However, too much explanation can detract from the readability of a review. Simplicity and clarity are also vital to readability. The readability of Cochrane reviews should be comparable to that of a well written article in a general medical journal.”

The text of a Cochrane review contains a number of fixed headings and subheadings that are embedded in RevMan. Additional subheadings may be added by the author at any point. Certain specific subheadings are **recommended** for use by all authors (and can be activated or deactivated in RevMan). However, these are not mandatory and should be avoided if they make individual sections needlessly short. Further, **optional** subheadings that may or may not be relevant to a particular review are also discussed below. Review authors who wish to mix recommended with optional subheadings should ensure that they are all displayed in appropriately consistent styles, which may require deactivating all of the recommended headings embedded in RevMan and creating them manually.

The following fixed headings are followed by fixed subheadings and can have no free text immediately after them: ‘Methods’, ‘Criteria for including studies’, ‘Results’, and ‘Authors’ conclusions’.

Background

[fixed, level 1 heading]

Well-formulated review questions occur in the context of an already-formed body of knowledge. The background should address this context, help set the rationale for the review, and explain why the questions being asked are important. It should be concise (generally around one page when printed) and be understandable to the users of the intervention under investigation. All sources of information should be cited.

Description of the condition [recommended, level 2 heading]

The review should begin with a brief description of the condition being addressed and its significance. It may include information about the biology, diagnosis, prognosis and public health importance (including prevalence or incidence).

Description of the intervention [recommended, level 2 heading]

A description of the experimental intervention(s) should place it in the context of any standard, or alternative interventions. The role of the comparator intervention(s) in standard practice should be made clear. For drugs, basic information on clinical pharmacology should be presented where available. This information might include dose range, metabolism, selective effects, half-life, duration and any known interactions with other drugs. For more complex interventions, a description of the main components should be provided.

How the intervention might work [recommended, level 2 heading]

This section might describe the theoretical reasoning why the interventions under review may have an impact on potential recipients, for example, by relating a drug intervention to the biology of the condition. Authors may refer to a body of empirical evidence such as similar interventions having an impact or identical interventions having an impact on other populations. Authors may also refer to a body of literature that justifies the possibility of effectiveness.

Why it is important to do this review [recommended, level 2 heading]

The background should clearly state the rationale for the review and should explain why the questions being asked are important. It might also mention why this review was undertaken and how it might relate to a wider review of a general problem. If this version of the review is an update of an earlier one, it is helpful to state this by writing, for example, “This is an update of a Cochrane review first published in YEAR, and previously updated in YEAR”. This may be supplemented with a brief description of the main findings of the earlier versions, with a statement of any specific reasons there may be for updating the review.

Objectives [fixed, level 1 heading]

This should begin with a precise statement of the primary objective of the review, ideally in a single sentence. Where possible the style should be of the form “To assess the effects of [*intervention or comparison*] for [*health problem*] for/in [*types of people, disease or problem and setting if specified*]”. This might be followed by a series of specific objectives relating to different participant groups, different comparisons of interventions or different outcome measures. It is not necessary to state specific hypotheses.

Methods [fixed, level 1 heading]

The Methods section in a protocol should be written in the future tense. Because Cochrane reviews are updated as new evidence accumulates, methods outlined in the protocol should generally be written as if a suitably large number of studies will be identified to allow the objectives to be met (even if it is known this is not the case at the time of writing).

The Methods section in a review should be written in the past tense, and should describe what was done to obtain the *results and conclusions of the current review*. Review authors are encouraged to cite their protocol to make it clear that there was one. Often a review is unable to implement all of the methods outlined in the protocol, usually because there is insufficient evidence. In such circumstances, it is recommended that the methods that were not implemented be outlined in the section headed

'Differences between protocol and review' (see below), so that it serves as a protocol for future updates of the review.

Criteria for considering studies for this review [fixed, level 2 heading]

Types of studies [fixed, level 3 heading]

Eligible study designs should be stated here, along with any thresholds for inclusion based on the conduct of the studies or their risk of bias. For example, 'All randomized controlled comparisons' or 'All randomized controlled trials with blind assessment of outcome'. Exclusion of particular types of randomized studies (for example, cross-over trials) should be justified.

See also:

- Eligibility criteria for types of study designs are discussed in Chapter 5 (Section 5.5).

Types of participants [fixed, level 3 heading]

The diseases or conditions of interest should be described here, including any restrictions such as diagnoses, age groups and settings. Subgroup analyses should not be listed here (see 'Subgroup analysis and investigation of heterogeneity' under 'Methods').

See also:

- Eligibility criteria for types of participants are discussed in Chapter 5 (Section 5.2).

Types of interventions [fixed, level 3 heading]

Experimental and comparator interventions should be defined here, under separate subheadings if appropriate. It should be made clear which comparisons are of interest. Restrictions on dose, frequency, intensity or duration should be stated. Subgroup analyses should not be listed here (see 'Subgroup analysis and investigation of heterogeneity' under 'Methods').

See also:

- Eligibility criteria for types of interventions are discussed in Chapter 5 (Section 5.3).

Types of outcome measures [fixed, level 3 heading]

Note that outcome measures do not always form part of the criteria for including studies in a review. If they do not, then this should be made clear. Outcome measures of interest should be listed in this section whether or not they form part of the eligibility criteria.

See also:

- Types of outcomes are discussed in Chapter 5 (Section 5.4).
- The importance of addressing patient-relevant outcomes is discussed further in Chapter 11 (Section 11.5.2); see also an extended discussion of patient-reported outcomes in Chapter 17.

Primary outcomes *[recommended, level 4 heading]*

The review's primary outcomes should normally reflect at least one potential benefit and at least one potential area of harm, and should be as few as possible. It is normally expected that the review should be able to analyse these outcomes if eligible studies are identified, and that the conclusions of the review will be based in large part on the effects of the interventions on these outcomes.

Secondary outcomes

[recommended, level 4 heading]

Non-primary outcomes should be listed here. The total number of outcomes addressed should be kept as small as possible.

The following *optional* (level 4) headings may be helpful, as supplements or replacements for the headings above:

Main outcomes for 'Summary of findings' table

Timing of outcome assessment

Adverse outcomes

Economic data

Search methods for identification of studies

[fixed, level 2 heading]

The methods used to identify studies should be summarized. The following headings are recommended. Before starting to develop this section, authors should contact their Cochrane Review Group (CRG) for guidance.

See also:

- Search methods are discussed in detail in Chapter 6 (Sections 6.3).

Electronic searches

[recommended, level 3 heading]

The bibliographic databases searched, the dates and periods searched and any constraints, such as language should be stated. The full search strategies for each database should be listed in an appendix to the review. If a CRG has developed a specialized register of studies and this is searched for the review, a standard description of this register can be referred to but information should be included on when and how the specialized register was most recently searched for the current version of the review and the search terms used should be listed.

See also:

- Search strategies are discussed in detail in Chapter 6 (Section 6.4).

Searching other resources

[recommended, level 3 heading]

List grey literature sources, such as internal reports and conference proceedings. If journals are specifically handsearched for the review, this should be noted but handsearching done by the authors to help build the specialized register of the CRG should not be listed because this is covered in the standardized description of the register. List people (e.g. trialists or topic specialists) and organizations who were contacted. List any other sources used, which may include, for example, reference lists, the World Wide Web or personal collections of articles.

The following *optional* headings may be used, either in place of 'Searching other resources' (in which case they would be level 3 headings) or as subheadings (level 4).

Grey literature

Handsearching

Reference lists

Correspondence

See also:

- Other search resources are discussed in Chapter 6 (Section 6.2).

Data collection and analysis

[fixed, level 2 heading]

This should describe the methods for data collection and analysis.

Selection of studies

[recommended, level 3 heading]

The method used to apply the selection criteria. Whether they are applied independently by more than one author should be stated, along with how any disagreements are resolved.

See also:

- Study selection is discussed in Chapter 7 (Section 7.2).

Data extraction and management

[recommended, level 3 heading]

The method used to extract or obtain data from published reports or from the original researchers (for example, using a data collection form). Whether data are extracted independently by more than one author should be stated, along with how any disagreements are resolved. If relevant, methods for processing data in preparation for analysis should be described.

See also:

- Data collection is discussed in Chapter 7, including which data to collect (Section 7.3), sources of data (Section 7.4), data collection forms (Section 7.5) and extracting data from reports (Section 7.6)

Assessment of risk of bias in included studies

[recommended, level 3 heading]

The method used to assess risk of bias (or methodological quality). Whether methods are applied independently by more than one author should be stated, along with how any disagreements are resolved. The tool(s) used should be described or referenced, with an indication of how the results are incorporated into the interpretation of the results.

See also:

- The recommended tool for assessing risk of bias is described in Chapter 8 (Section 8.5).

Measures of treatment effect

[recommended, level 3 heading]

The effect measures of choice should be stated. For example, odds ratio (OR), risk ratio (RR) or risk difference (RD) for dichotomous data; mean difference (MD) or standardized mean difference (SMD) for continuous data. The following *optional* headings may be used, either in place of 'Measures of treatment effect' (in which case they would be level 3 headings) or as subheadings (level 4):

Dichotomous data

Continuous data

Time-to-event data

See also:

- Types of data and effect measures are discussed in Chapter 9 (Section 9.2).

Unit of analysis issues

[recommended, level 3 heading]

Special issues in the analysis of studies with non-standard designs, such as cross-over trials and cluster-randomized trials, should be described. Alternatively, *optional* (level 3) headings specific to the types of studies may be used, such as:

Cluster-randomised trials

Cross-over trials

Studies with multiple treatment groups

See also:

- Unit of analysis issues are discussed in Chapter 9 (Section 9.3).
- Some non-standard designs are discussed in detail in Chapter 16, including cluster-randomized trials (Section 16.3), cross-over trials (Section 16.4), and studies with multiple intervention groups (Section 16.5). Non-randomized studies are discussed in Chapter 13.

Dealing with missing data

[recommended, level 3 heading]

Strategies for dealing with missing data should be described. This will principally include missing participants due to drop-out (and whether an intention-to-treat analysis will be conducted), and missing statistics (such as standard deviations or correlation coefficients).

See also:

- Issues relevant to missing data are discussed in Chapter 16 (Sections 16.1) and intention-to-treat issues in Chapter 16 (Section 16.2).

Assessment of heterogeneity

[recommended, level 3 heading]

Approaches to addressing clinical heterogeneity should be described, along with how the authors will determine whether a meta-analysis is considered appropriate. Methods for identifying statistical heterogeneity should be stated (e.g. visually, using I^2 , using a chi-squared test).

See also:

- Assessment of heterogeneity is discussed in Chapter 9 (Section 9.5).

Assessment of reporting biases

[recommended, level 3 heading]

This section should describe how publication bias and other reporting biases are addressed (for example, funnel plots, statistical tests, imputation). Authors should remember that asymmetric funnel plots are not necessarily caused by publication bias (and that publication bias does not necessarily cause asymmetry in a funnel plot).

See also:

- Reporting biases are discussed in Chapter 10.

Data synthesis

[recommended, level 3 heading]

The choice of meta-analysis method should be stated, including whether a fixed-effect or a random-effects model is used. If meta-analyses are not undertaken, systematic approaches to synthesizing the findings of multiple studies should be described.

See also:

- Meta-analysis and data synthesis are discussed in Chapter 9 (Section 9.4).

Subgroup analysis and investigation of heterogeneity

[recommended, level 3 heading]

All planned subgroup analyses should be listed (or independent variables for meta-regression). Any other methods for investigating heterogeneity of effects should be described.

See also:

- Investigating heterogeneity is discussed in Chapter 9 (Section 9.6).

Sensitivity analysis [recommended, level 3 heading]

This should describe analyses aimed at determining whether conclusions are robust to decisions made during the review process, such as inclusion/exclusion of particular studies from a meta-analysis, imputing missing data or choice of a method for analysis.

See also:

- Sensitivity analysis is discussed in Chapter 9 (Section 9.7).

The following further, *optional* (level 3) headings for the Methods section may be helpful:

Economics issues

Methods for future updates

Authors seeking to cover economics aspects of interventions in a review will need to consider economics issues from the earliest stages of developing a protocol.

See also:

- Economics issues are discussed in Chapter 15.
- Issues in updating reviews are discussed in Chapter 3.

Results [fixed, level 1 heading]

Description of studies [fixed, level 2 heading]

Results of the search [recommended, level 3 heading]

The results sections should start with a summary of the results of the search (for example, how many references were retrieved by the electronic searches, and how many were considered as potentially eligible after screening).

See also:

- Presentation of search findings is discussed in Chapter 6 (Section 6.6)

Included studies [recommended, level 3 heading]

It is essential that the number of included studies is clearly stated. This section should comprise a succinct summary of the information contained in the ‘Characteristics of included studies’ table. An explicit reference to this table should be included. Key characteristics of the included studies should be described, including the study participants, location (e.g. country), setting (if important), interventions, comparisons and outcome measures in the included studies and any important differences among the studies. The sex and age range of participants should be stated here except where their nature is obvious (for example, if all the participants are pregnant). Important details of specific interventions used should be provided (for radiotherapy, for example, this might summarize the total dose, the number of fractions and type of radiation used; for drugs, this might summarize preparation, route of administration, dose and frequency). Authors should note any other characteristics of the studies that they regard as important for readers of the review to know. The following *optional* (level 4) subheadings may be helpful:

Design
Sample sizes
Setting
Participants
Interventions
Outcomes

See also:

- The ‘Characteristics of included studies’ table is discussed in detail in Section 4.6.1.

Excluded studies [recommended, level 3 heading]

This should refer to the information contained in the ‘Characteristics of excluded studies’ table. An explicit reference to this table should be included. A succinct summary of why studies were excluded from the review should be provided.

See also:

- The ‘Characteristics of excluded studies’ table is discussed in detail in Section 4.6.3.

The following *optional* (level 3) headings may be used in the ‘Description of studies’ section:

Ongoing studies
Studies awaiting classification
New studies found at this update

Risk of bias in included studies [fixed, level 2 heading]

This should summarize the general risk of bias in results of the included studies, its variability across studies and any important flaws in individual studies. The criteria that were used to assess the risk of bias should be described or referenced under ‘Methods’ and not here. How each study was rated on each criterion should be reported in a ‘Risk of bias’ table and not described in detail in the text, which should be a concise summary.

See also:

- Presentation of ‘risk of bias’ assessments is addressed in Chapter 8 (Section 8.6).

For large reviews, aspects of the assessment of risk of bias may be summarized for the primary outcomes under the following headings.

Allocation [recommended, level 3 heading]

A summary of how allocation sequences were generated and attempts to conceal allocation of intervention assignment should be summarized briefly here, along with any judgements concerning the risk of bias that may arise from the methods used.

Blinding [recommended, level 3 heading]

A brief summary of who was blinded or masked during the conduct and analysis of the studies should be reported here. Implications of blinding of outcome assessment may be different for different outcomes, so these may need to be addressed separately. Judgements concerning the risk of bias associated with blinding should be summarized.

Incomplete outcome data [recommended, level 3 heading]

The completeness of data should be summarized briefly here for each of the main outcomes. Concerns of the review authors over exclusion of participants and excessive (or differential) drop-out should be reported.

Selective reporting [recommended, level 3 heading]

Concerns over the selective availability of data may be summarized briefly here, including evidence of selective reporting of outcomes, time-points, subgroups or analyses.

Other potential sources of bias [recommended, level 3 heading]

Any other potential concerns should be summarized here.

Effects of interventions [fixed, level 2 heading]

This should be a summary of the main findings on the effects of the interventions studied in the review. The section should directly address the objectives of the review rather than list the findings of the included studies in turn. The results of individual studies, and any statistical summary of these, should be included in 'Data and analysis' tables. Outcomes should normally be addressed in the order in which they are listed under 'Types of outcome measures'. Subheadings are encouraged if they make understanding easier (for example, for each different participant group, comparison or outcome measure if a review addresses more than one). Any sensitivity analyses that were undertaken should be reported.

Authors should avoid making inferences in this section. A common mistake to avoid (both in describing the results and in drawing conclusions) is the confusion of 'no evidence of an effect' with 'evidence of no effect'. When there is inconclusive evidence, it is wrong to claim that it shows that an intervention has 'no effect' or is 'no different' from the control intervention. In this situation, it is safer to report the data, with a confidence interval, as being compatible with either a reduction or an increase in the outcome.

See also:

- Presentation of results is addressed in Chapter 11 (Section 11.7).
- Interpretation of numerical results is discussed in Chapter 12 (Sections 12.4, 12.5 and 12.6).

Discussion [fixed, level 1 heading]

A structured discussion can aid the consideration of the implications of the review (Docherty 1999).

See also:

- Interpretation of results is discussed in Chapter 12.

Summary of main results [recommended, level 2 heading]

Summarize the main findings (without repeating the 'Effects of interventions' section) and outstanding uncertainties, balancing important benefits against important harms. Refer explicitly to any 'Summary of findings' tables.

Overall completeness and applicability of evidence [recommended, level 2 heading]

Describe the relevance of the evidence to the review question. This should lead to an overall judgement of the external validity of the review. Are the studies identified sufficient to address all of

the objectives of the review? Have all relevant types of participants, interventions and outcomes been investigated? Comments on how the results of the review fit into the context of current practice might be included here, although authors should bear in mind that current practice might vary internationally.

Quality of the evidence

[recommended, level 2 heading]

Does the body of evidence identified allow a robust conclusion regarding the objective(s) of the review? Summarize the amount of evidence that has been included (numbers of studies, numbers of participants), state key methodological limitations of the studies, and reiterate the consistency or inconsistency of their results. This should lead to an overall judgement of the internal validity of the results of the review.

Potential biases in the review process

[recommended, level 2 heading]

State the strengths and limitations of the review with regard to preventing bias. These may be factors within, or outside, the control of the review authors. The discussion might include the likelihood that all relevant studies were identified, whether all relevant data could be obtained, or whether the methods used (for example, searching, study selection, data collection, analysis) could have introduced bias.

Agreements and disagreements with other studies or reviews

[recommended, level 2 heading]

Comments on how the included studies fit into the context of other evidence might be included here, stating clearly whether the other evidence was systematically reviewed.

Authors' conclusions

[fixed, level 1 heading]

The primary purpose of the review should be to present information, rather than to offer advice. Conclusions of the authors are divided into two sections:

Implications for practice

[fixed, level 2 heading]

The implications for practice should be as practical and unambiguous as possible. They should not go beyond the evidence that was reviewed and be justifiable by the data presented in the review. 'No evidence of effect' should not be confused with 'evidence of no effect'.

Implications for research

[fixed, level 2 heading]

This section of Cochrane reviews is used increasingly often by people making decisions about future research, and authors should try to write something that will be useful for this purpose. As with the 'Implications for practice', the content should be based on the available evidence and should avoid the use of information that was not included or discussed within the review.

In preparing this section, authors should consider the different aspects of research, perhaps using types of study, participant, intervention and outcome as a framework. Implications for *how* research might be done and reported should be distinguished from *what* future research should be done. For example, the need for randomized trials rather than other types of study, for better descriptions of studies in the particular topic of the review, or for the routine collection of specific outcomes should be distinguished from the lack of a continuing need for a comparison with placebo if there is an effective and appropriate active treatment, or for the need for comparisons of specific named interventions, or for research in specific types of people.

It is important that this section is as clear and explicit as possible. General statements that contain little or no specific information, such as “Future research should be better conducted” or “More research is needed” are of little use to people making decisions, and should be avoided.

See also:

- Guidance on formulating conclusions is provided in Chapter 12 (Section 12.7).

Acknowledgements

[fixed, level 1 heading]

This section should be used to acknowledge any people or organizations that the authors wish to acknowledge, including people who are not listed among the authors. This would include any previous authors of the Cochrane review or previous sources of support to the review, and might include the contributions of the editorial team of the CRG. Permission should be obtained from persons acknowledged.

Contributions of authors

[fixed, level 1 heading]

The contributions of the current co-authors to the protocol or review should be described in this section. One author should be identified as the guarantor of the review. All authors should discuss and agree on their respective descriptions of contribution before the review is submitted for publication on the *CDSR*. When the review is updated, this section should be checked and revised as necessary to ensure that it is accurate and up to date.

The following potential contributions have been adapted from Yank et al. (Yank 1999). This is a suggested scheme and the section should describe what people did, rather than attempt to identify which of these categories someone’s contribution falls within. Ideally, the authors should describe their contribution in their own words.

- Conceiving the review.
- Designing the review.
- Coordinating the review.
- Data collection for the review.
 - Designing search strategies.
 - Undertaking searches.
 - Screening search results.
 - Organizing retrieval of papers.
 - Screening retrieved papers against eligibility criteria.
 - Appraising quality of papers.
 - Extracting data from papers.
 - Writing to authors of papers for additional information.
 - Providing additional data about papers.
 - Obtaining and screening data on unpublished studies.
- Data management for the review.
 - Entering data into RevMan.
- Analysis of data.
- Interpretation of data.

- Providing a methodological perspective.
- Providing a clinical perspective.
- Providing a policy perspective.
- Providing a consumer perspective.
- Writing the review (or protocol).
- Providing general advice on the review.
- Securing funding for the review.
- Performing previous work that was the foundation of the current review.

Declarations of interest

[fixed, level 1 heading]

Authors should report any present or past affiliations or other involvement in any organization or entity with an interest in the review that might lead to a real or perceived conflict of interest. Situations that might be perceived by others as being capable of influencing a review author's judgements include personal, political, academic and other possible conflicts, as well as financial conflicts. Authors must state if they have been involved in a study included in the review.

See also:

- A summary of the Collaboration's policy on conflicts of interest appears in Chapter 2 (Section 2.6).

Financial conflicts of interest cause the most concern, and should be avoided, but must be reported if there are any. Any secondary interest (such as personal conflicts) that might unduly influence judgements made in a review (concerning, for example, the inclusion or exclusion of studies, assessments of the validity of included studies or the interpretation of results) should be reported.

If there are no known conflicts of interest, this should be stated explicitly, for example, by writing 'None known'.

Differences between protocol and review

[fixed, level 1 heading]

It is sometimes necessary to use different methods from those described in the original protocol. This could be because:

- methods for dealing with a particular issue had not been specified in the protocol;
- methods in the protocol could not be applied (for example, due to insufficient data or a lack of information required to implement the methods); and
- methods are changed because a preferable alternative is discovered.

Some changes of methods from protocol to review are acceptable, but must be fully described in this section. The section provides a summary of the main changes in methods for the review over time.

- Point out any methods that were determined subsequent to the original published protocol (e.g. adding or changing outcomes; adding 'Risk of bias' or 'Summary of findings' tables).
- Summarize methods from the protocol that could not be implemented in the current review (e.g. because the review identified no eligible studies, or because no studies fell in a particular pre-defined subgroup).
- Explain any changes in methods from the protocol to the review, state when they were made and provide the rationale for the changes. Such changes should not be driven by findings on the effects

of interventions. Consider the potential effect on the review's conclusions of any changes in methods, and consider sensitivity analyses to assess this.

Published notes

[fixed, level 1 heading]

Published notes will appear in the review in the *CDSR*. They may include editorial notes and comments from the CRG, for example where issues highlighted by editors or referees are believed worthy of publication alongside the review. The author or source of these comments should be specified (e.g. from an editor or a referee).

Published notes must be completed for all withdrawn protocols and reviews, giving the reason for withdrawal. Only basic citation information, sources of support and published notes are published for withdrawn protocols and reviews.

4.6 Tables

4.6.1 Characteristics of included studies

The 'Characteristics of included studies' table has five entries for each study: Methods, Participants, Interventions, Outcomes and Notes. Up to three further entries may be specified for items not conveniently covered by these categories, for example, to provide information on length of follow-up, funding source, or indications of study quality that are unlikely to lead directly to a risk of bias (see Section 4.6.2 for including information on the risk of bias). Codes or abbreviations may be used in the table to enable clear and succinct presentation of multiple pieces of information within an entry; for example, authors could include country, setting, age and sex under the Participants entry. Footnotes should be used to explain any codes or abbreviations used (these will be published in the *CDSR*).

See also:

- Detailed guidance on 'Characteristics of included studies' tables is provided in Chapter 11 (Section 11.2).

4.6.2 Risk of bias

A 'Risk of bias' table is an optional, although strongly recommended, extension of the 'Characteristics of included studies' table. The standard 'Risk of bias' table includes assessments for sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting and 'other issues'. For each item, the table provides a description of what was reported to have happened in the study and a subjective judgement regarding protection from bias ('Yes' for a low risk of bias, 'No' for a high risk of bias; 'Unclear' otherwise).

See also:

- 'Risk of bias' tables are discussed in Chapter 8 (Section 8.6).

4.6.3 Characteristics of excluded studies

Certain studies that may appear to meet the eligibility criteria, but which were excluded, should be listed and the reason for exclusion should be given (for example, inappropriate comparator intervention). This should be kept brief, and a single reason for exclusion is usually sufficient.

See also:

- Selection of which studies to list as excluded is discussed in Chapter 7 (Section 7.2.5).

4.6.4 Characteristics of studies awaiting classification

The ‘Characteristics of studies awaiting classification’ table (formerly ‘Studies awaiting assessment’) has the same structure as the ‘Characteristics of included studies’ table. It should be used for two categories of study:

- Studies about which an inclusion or exclusion decision cannot be made because sufficient information is not currently available. All reasonable attempts to obtain information must be made before studies are left here on publication of the review, but the review should not be delayed excessively waiting for this information, especially if the inclusion or exclusion of the study is unlikely to have an impact on the review's conclusions. When information is not available for a table entry, the text ‘Not known’ should be inserted.
- Studies that have been identified but are awaiting an update to the review. In particular, it is appropriate to mention studies that have the potential to impact on the review’s conclusions, or studies that receive wide publicity, in the review in the period between updates. An amended review may therefore be produced with such studies summarized in this table. The full update, with such studies fully incorporated, should be completed as soon as possible. When information is not available for a table entry, the text ‘Not yet assessed’ or ‘Not known’ should be inserted, as appropriate.

4.6.5 Characteristics of ongoing studies

The ‘Characteristics of ongoing studies’ table has eight entries for each study: Study name, Methods, Participants, Interventions, Outcomes, Starting date, Contact information and Notes. The contents of these entries should be comparable to those in the table of ‘Characteristics of included studies’. Footnotes should be used to explain any abbreviations used in the table (these will be published in the *CDSR*).

4.6.6 Summary of findings

A ‘Summary of findings’ table is an optional, although strongly recommended, means of presenting findings for the most important outcomes, whether or not evidence is available for them. A ‘Summary of findings’ table includes, where appropriate, a summary of the amount of evidence; typical absolute risks for people receiving experimental and control interventions; estimates of relative effect (e.g. risk ratio or odds ratio); a depiction of the quality of the body of evidence; comments; and footnotes. The assessment of the quality of the body of evidence should follow the GRADE framework, which combines considerations of risk of bias, directness, heterogeneity, precision and publication bias.

See also:

- A full specification and discussion of ‘Summary of findings’ tables is provided in Chapter 11 (Section 11.5).
- The GRADE system is overviewed in Chapter 12 (Section 12.2).

4.6.7 Additional tables

Additional tables may be used for information that cannot be conveniently placed in the text or in fixed tables. Examples include

- information to support the background; and
- summaries of study characteristics (such as detailed descriptions of interventions or outcomes).

See also:

- Additional tables are discussed in Chapter 11 (Section 11.6).

4.7 Studies and references

4.7.1 References to studies

Studies are organized under four fixed headings. Each of these headings can include multiple studies (or no studies). A study is identified by a 'Study ID' (usually comprising the last name of first author and the year of the primary reference for the study). A year can be explicitly associated with each study (usually the year of completion, or the publication year of the primary reference), as can identifiers such as an International Standard Randomised Controlled Trial Number (ISRCTN). In addition, each study should be assigned a category of 'Data source' from among the following:

- published data only;
- published and unpublished data;
- unpublished data only; and
- published data only (unpublished sought but not used).

Each study can have multiple references. Each reference may be given identifiers such as a MEDLINE ID or a DOI. One reference for each study should be awarded the status of 'Primary reference'. Authors should check all references for accuracy.

4.7.1.1 Included studies

Studies that meet the eligibility criteria and are included in the review.

4.7.1.2 Excluded studies

Studies that do not meet the eligibility criteria and are excluded from the review.

4.7.1.3 Studies awaiting classification

Relevant studies that have been identified, but cannot be assessed for inclusion until additional data or information are obtained.

4.7.1.4 Ongoing studies

Studies that are ongoing and meet (or appear to meet) the eligibility criteria.

4.7.2 Other references

References other than those to studies are divided among the following two categories. Note that RevMan also includes a 'Classification pending' category to facilitate organization of references while preparing a review. All references should be moved out of this category before a review is marked for submission to the CDSR, since any references remaining in this category will not be published.

4.7.2.1 Additional references

Other references cited in the text should be listed here, including those cited in the Background and Methods sections. If a report of a study is cited in the text for some reason other than referring to the study (for example, because of some background or methodological information in the reference), it should be listed here as well as under the relevant study.

4.7.2.2 Other published versions of this review

References to other published versions of the review in a journal, textbook or the *CDSR* or elsewhere should be listed here.

Authors should check all references for accuracy.

4.8 Data and analyses

Results of studies included in a review are organized in a hierarchy: studies are nested within (optional) subgroups, which are nested within outcomes, which are nested within comparisons (see Figure 4.8.a). A study can be included several times among the analyses.

RevMan automatically generates forest plots illustrating data, effect estimates and results of meta-analyses (where selected) from the data entered into the ‘Data and analyses’ structure. The author is able to control whether, and how, meta-analyses are performed.

Note: The ‘Data and analyses’ should be considered as supplementary information because they may not appear in some formats of the published review. Key forest plots (containing data for each study) may be selected to be *always* included with the full text of the review by selecting them as figures (see Section 4.9). The full published Cochrane review in the *CDSR* will, however, contain all of the ‘Data and analyses’ section as a series of forest plots or tables.

Authors should avoid listing comparisons or outcomes for which there are no data (i.e. have forest plots with no studies). Instead, authors should note in the text of the review that no data are available for the comparisons. However, if the review has a ‘Summary of findings’ table, the main outcomes should be included in this irrespective of whether data are available from the included studies.

See also:

- Analyses are addressed in Chapter 9; including discussion of comparisons (Section 9.1.6), types of outcome data (Section 9.2) and subgroups (Section 9.6). Useful conversions from reported data to the required format are provided in Chapter 7 (Section 7.7).

4.8.1 Comparison

The comparisons should correspond to the questions or hypotheses under ‘Objectives’.

4.8.2 Outcome

Five types of outcome data are possible: dichotomous data, continuous data, ‘O – E’ and ‘V’ statistics, generic inverse variance (estimate and standard error) and other data (text only).

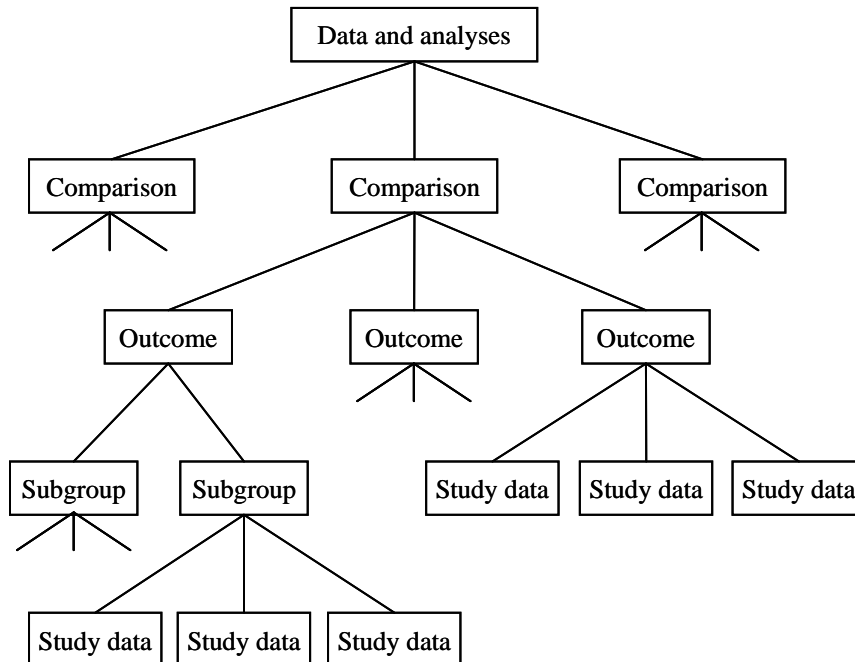
4.8.3 Subgroup

Subgroups may relate to subsets of studies (for example, trials using different durations of physiotherapy) or to a subdivision of the outcome (for example, short-term, medium-term, long-term).

4.8.4 Study data

Data for each study must be entered in a particular format specific to the type of outcome data (e.g. a sample size, mean and standard deviation for each group for continuous data).

Figure 4.8.a: Illustration of the hierarchy of the ‘Data and analyses’ section.



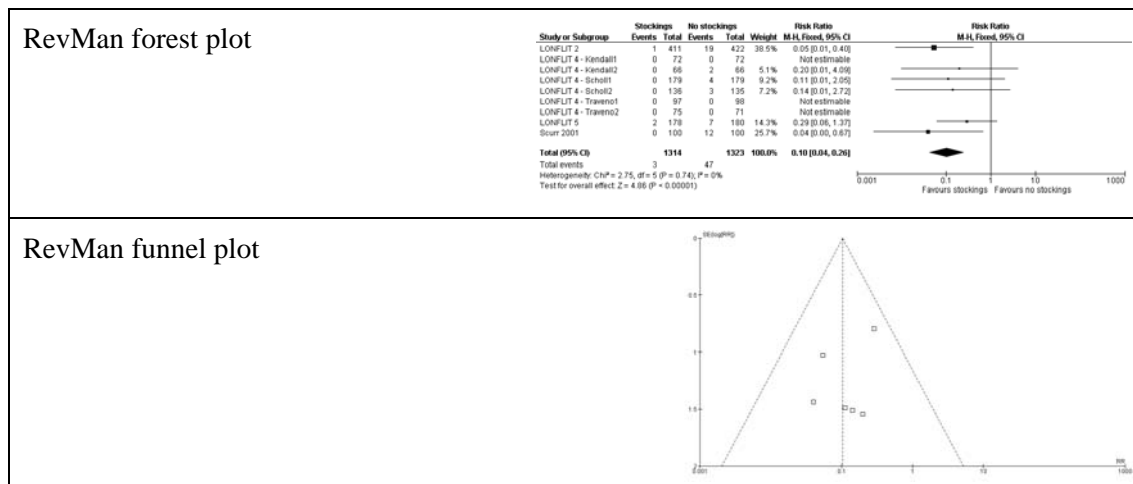
4.9 Figures

Five types of figures may be included within the text of the review (see [Table 4.9.a](#)). These figures will always be presented with the full-text publication of the review. Each figure must have a caption, providing a brief description (or explanation) of the figure, and must be referred to (with a link) in the review text.

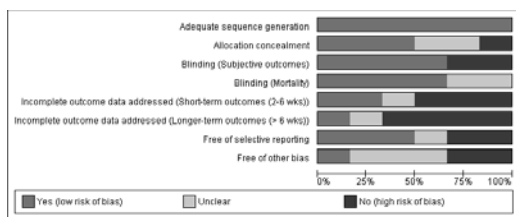
See also:

- Issues in the selection of figures are discussed in Chapter 11 (Section 11.4.2).

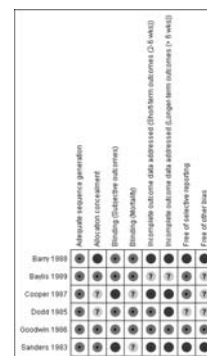
Table 4.9.a: Types of figures that can be included in a Cochrane review



RevMan 'risk of bias' graph



RevMan 'risk of bias' summary



Other figure



4.9.1 RevMan plots and graphs

Forest plots and funnel plots from among those in the 'Data and analyses' may be selected as Figures. Graphical representations of judgements on risk of bias can also be generated within RevMan and included as figures.

See also:

- Forest plots are discussed in Chapter 11 (Section 11.3.2).
- Funnel plots are discussed in Chapter 10 (Section 10.4).
- 'Risk of bias' graphs and 'Risk of bias' summaries are discussed in Chapter 8 (Section 8.6).

4.9.2 Other figures

Graphs and other images that are not generated by RevMan can be included as figures. These should never be used for content that can be generated in other ways within RevMan, for example as forest plots or as additional tables.

Authors are responsible for obtaining permission for images included in the review and for following guidance to ensure the images are fit for publication. If permission to publish a copyrighted figure is granted, the final phrase of the figure caption must be: "Copyright © [Year] [Name of copyright holder, or other required wording]: reproduced with permission."

See also:

- Figures showing statistical analyses should follow the relevant guidance prepared by the Statistical Methods Group (see Supplementary material on the *Handbook* web site: www.cochrane.org/resources/handbook).

4.10 Sources of support to the review

Authors should acknowledge grants that supported the review, and other forms of support, such as support from their university or institution in the form of a salary. Sources of support are divided into 'internal' (provided by the institutions at which the review was produced) and 'external' (provided by other institutions or funding agencies). Each source, its country of origin and what it supported should be provided.

4.11 Feedback

Each piece of Feedback incorporated into a review is identified by a short title and the date. **Summary, Reply and Contributors** are subheadings in this section. The summary should be prepared by the Feedback editor for the CRG in consultation, if necessary, with the person submitting the comment. The author(s) of the review should prepare a reply. The names of the people who contributed to the process of responding to the feedback should be given under 'Contributors'.

See also:

- Further information on Feedback is given in Chapter 3 (Section 3.6).

4.12 Appendices

Appendices provide a place for supplementary information such as:

- detailed search strategies (appendices are the recommended place to put these);
- lengthy details of non-standard statistical methods;
- data collection forms; and
- details of outcomes (e.g. measurement scales).

Appendices may not appear in some formats of the published review.

4.13 Chapter information

Editors: Julian PT Higgins and Sally Green.

This chapter should be cited as: Higgins JPT, Green S (editors). Chapter 4: Guide to the contents of a Cochrane protocol and review. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Intervention*. Version 5.0.1 [updated September 2008]. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.

Acknowledgements: This chapter builds on earlier versions of the *Handbook*. For details of previous authors and editors of the *Handbook*, please refer to Chapter 1 (Section 1.4). The list of recommended headings was developed by Julian Higgins in discussion with Mike Clarke, Sally Hopewell, Jacqueline Birks, numerous Review Group Co-ordinators, a working group on assessing risk of bias, and members of the Handbook Advisory Group. Contributing authors in recent updates have included Ginny Brunton, Mike Clarke, Mark Davies, Frances Fairman, Sally Green, Julian Higgins, Nicki Jackson, Harriet MacLehose, Sandy Oliver, Peter Tugwell and Janet Wale. We thank Lisa Askie, Sonja Henderson, Monica Kjeldstrøm, Carol Lefebvre, Philippa Middleton, Rasmus Moustgaard and Rebecca Smyth for helpful comments.

4.14 References

Docherty 1999

Docherty M, Smith R. The case for structuring the discussion of scientific papers. *BMJ* 1999; 318: 1224-1225.

Flanagin 1998

Flanagin A, Carey LA, Fontanarosa PB, Phillips SG, Pace BP, Lundberg GD, Rennie D. Prevalence of articles with honorary authors and ghost authors in peer-reviewed medical journals. *JAMA* 1998; 280: 222-224.

International Committee of Medical Journal Editors 2006

International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals: Writing and editing for biomedical publication [Updated February 2006]. Available from: <http://www.icmje.org> (accessed 1 January 2008).

Rennie 1997

Rennie D, Yank V, Emanuel L. When authorship fails. A proposal to make contributors accountable. *JAMA* 1997; 278: 579-585.

Rennie 1998

Rennie D, Yank V. If authors became contributors, everyone would gain, especially the reader. *American Journal of Public Health* 1998; 88: 828-830.

Yank 1999

Yank V, Rennie D. Disclosure of researcher contributions: a study of original research articles in *The Lancet*. *Annals of Internal Medicine* 1999; 130: 661-670.