COCHRANE CONSUMERS AND COMMUNICATION REVIEW GROUP
Standard Review Text and Additional Guidance for Review Authors

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General considerations in preparing your Cochrane review

Style of writing:

The text of the review should be clear and to the point. It should be written so that someone who is not an expert in the area can understand it. It must adhere to the *Style Guidelines for Cochrane Reviews* (found at http://www.cochrane.org/style/home.htm).

Data Extraction:

The Cochrane Consumers and Communication Review Group has developed a data extraction template; this template is recommended as a guide, and review authors should revise it as appropriate for their own review topic. The template can be downloaded at http://cccrg.cochrane.org/author-resources in word or excel formats.

Data entry:

RevMan 5 does not provide functionality for double data entry, but you can use a spreadsheet for doing this and then paste the verified data into RevMan. If data are entered by a single author they must be checked by another author.

Abstract

Refer to the Cochrane Handbook section 11.8.

Include an abstract of up to 1000 words (but ideally no more than 700 words). Abstracts to Cochrane reviews are published on MEDLINE and made freely accessible online, so will often be read as stand-alone documents. They should summarise the key methods and content of the review and not contain any material that is not in the review.

The content of the Abstract <u>must</u> be consistent with the text, data and conclusions of the review and not include references to any information outside the review.

Additionally, the content of the Abstract, Plain Language Summary (PLS) and 'Summary of findings' (SoF) table(s) <u>must</u> be consistent and meet each of the criteria on the 'Checklist for ensuring abstracts, PLS and SoF tables meet Cochrane Handbook guidance,' available at: <http://cccrg.cochrane.org/author-resources>

Please also note: although SoF tables are used to present a summary of the results of the review according to the outcomes identified as most important to decision makers, it is <u>essential</u> that the results reported in these tables are completely consistent with those presented throughout the review (Abstract, PLS, Effects of interventions, Discussion). We <u>strongly encourage</u> you to use the SoF tables (including the GRADE assessment of the quality of the evidence) as an organising principle or tool to help with reporting the findings throughout the different sections of the review (ie not just confining this to the SoF tables). This will help you to summarise results consistently, and will ensure that the quality of the evidence is reported alongside the data. These are both essential elements of reporting the findings.

Background: briefly explain the purpose and rationale for the review. If the review is an update consider including a sentence stating that it is an update of a Cochrane review first published and/or previously updated in [year].

Objectives: state the primary objectives of the review, ideally in a single sentence, and matching the Objectives section in the main part of the review. Use the format 'To assess the effects of…'

Search methods: list the sources and dates of the last search for each source (month and year), in the following order: the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*, Issue X, YEAR); MEDLINE (OvidSP) (date to date); EMBASE (OvidSP) (date to date); other databases (dates).

Selection criteria: describe the types of study; intervention or comparison; and type of people, disease or problem included in the review. Only include outcomes here if the review was restricted to particular outcomes. Include any extensions to the eligibility criteria (eg to address adverse effects or include qualitative research).

Data collection and analysis: describe how the data were extracted and assessed (not what data were extracted). Include details of how many people extracted data and assessed the risk of bias; whether contact with study authors was undertaken; and steps taken to identify adverse effects (if any). Indicate how rigorous the methods used were; for many reviews it may be sufficient to state 'We used standard methodological procedures expected by The Cochrane Collaboration.' Also mention here any non-standard methods (eg adaptation of the 'Risk of bias' tool).

Main results:

- Outline the total number of included studies and participants (preferably numbers analysed rather than numbers recruited/randomised) in the format 'We included X studies involving X participants.'

- Comment on the comparability of included studies (key characteristics that will determine the applicability of the body of evidence – eg age, setting).

- Comment on the 'Risk of bias' assessments. If this varies substantially by comparisons or by particular outcomes in the review then this might also be mentioned.

- Present the results of all the main outcomes, irrespective of the strength and direction of results and the availability of data. Select these based on what is most likely to help someone to make a decision about using the intervention. In general, the outcomes presented in the Abstract should be the same as those presented in the PLS and the Summary of findings tables. If no studies reported the outcome then this should be mentioned.

- Include information about the quality of the evidence for each reported outcome (GRADE rating).

- If any adverse effects, and the results associated with them, were identified, describe them. If adverse event data was sought by the review, but none identified, then this should also be reported.

- Explain the size and direction of the effects to accompany the numerical results presented, particularly if these are not intuitive.

- Present the summary statistics in a standard way that is consistent with the way they are presented in the review, eg 'odds ratio (OR) 2.31 (95% confidence interval 1.13 to 3.45).' Risk of events (percentages) or averages (continuous data) should be reported for both comparison groups where possible.

Authors' conclusions: briefly describe the main conclusions of the review, (Implications for practice and Implications for research). These should be drawn directly from the main findings of the review and so reflect the review's main results. Any important limitations of the data and/or analyses should be noted. This section should not make recommendations and must be consistent with the main results of the review.

Plain Language Summary

Refer to the [Cochrane Handbook](#) section 11.9 and '[Standards for the reporting of Plain Language Summaries in new Cochrane Intervention Reviews (PLEACS)](#)'

Summarise the review in an easily understood, Plain English style which would be understood by consumers of health care. Avoid jargon (clinical and Cochrane or reviewing jargon), hard words and potentially misunderstood words and regional words. Use the active voice, short paragraphs, and limit sentences to one key point each. Consider using the [SMOG Calculated Index](#).

Report the review's key messages consistently with other sections of the review, including re-expression of meta-analysis, results, the abstract, 'Summary of findings' tables, and the authors' conclusions.

PLS title: Restate the review title in plain language, including participants, interventions and outcomes (where these are included in the review title). The PLS title should <u>not</u> reflect the review's conclusions. It should not be in question form. It should be 256 or fewer characters in length.

PLS body: This may be up to 700 words in length and <u>should be divided into sections with standard headers, given in bold.</u> These are:

Review question

restates the question addressed by the review, including the population, interventions, comparisons and main outcomes, if applicable. eg 'We reviewed the evidence about the effects of X on Y in people with Z. We found # studies.'

Background

should briefly outline the topic to explain why the review is important to the population(s) of interest.

Study characteristics

- The date up to which some or all of the studies have been included in the review. For example 'We included the research published up to [DATE]' or 'The evidence is current to MM YYYY.' Details of the databases and search terms should <u>not</u> be included in the PLS.

- Key information to include is: the type of condition, details of the intervention(s), comparators, the population (such as age, gender, severity of disease) and setting. Not all features of the included studies need to be reported; however the total number of included studies and participants are key findings.

- Information about funding sources of included studies should also be reported, in summary form (for example, 10 out of 20 studies were funded by the drug manufacturer or by an agency with interests in the results of studies). If the review specifically assesses how funding sources affect the quality of the evidence then a statement indicating this impact should be given; otherwise if impact of funding sources is not considered then a statement to this effect should be provided.

Key results

- Results for each outcome should be reported in plain language.

- All primary, and key secondary outcomes that are important to patients, should be included, even where there is no data on all of these outcomes in the included studies.

- All important harms should also be reported, so that readers can evaluate the balance of benefits and harms. If no harms were reported then this should be stated.

- Where it is included, the 'Summary of findings' table should be used as the source of any quantitative data in the PLS, and in all cases this must be supported and consistent with what is reported elsewhere in the review.

- However it is not essential to provide numerical data in the PLS. For example, if the data are very uncertain or effects are very imprecise it may not be very helpful to readers.

- If numerical data are included in the PLS it is important that it is understandable to a lay audience:

  - statistical terms should be explained if used;

  - relative effects should be accompanied by a measure of absolute effects using natural frequencies (absolute risks or number needed to treat) for dichotomous outcomes; and as mean difference (with scales used) for continuous outcomes.

Quality of the evidence

- The overall quality of the evidence for each outcome, according to the GRADE criteria (ie ranging from very low to high quality), should be described.

- Main reasons for the level of evidence should be described – for example, poorly conducted studies; results not similar across studies; issues with study design; lack of data; only studied in population X.

- The impact of the quality of the evidence on key outcomes should be clear to authors, and any key limitations noted. However in the PLS this should only be stated briefly so only an overall assessment is needed. If the overall quality of the evidence is high then this should also be reported.

Note: for the Background, Objectives and Methods sections little should have changed between the protocol stage and the review stage, except a change to past tense where relevant, ie the review stage outlines what <u>was</u> done. Any change from what was planned (for instance, because new methods have become available during the review development stage) must be clearly described and justified in the section 'Differences between protocol and review' as well as in the relevant section of the Methods, and the Managing Editor advised during the review development process.

BACKGROUND

Refer to the Cochrane Handbook section 4.5.

This section should require minimal changes between the protocol and review stages.

OBJECTIVES

Refer to the Cochrane Handbook section 4.5.

This section should require minimal changes between the protocol and review stages.

METHODS

There are a number of key sections under the broad METHODS heading. See the [Cochrane Handbook](#) chapter 4.5.

Also consider the items on the Cochrane Equity Checklist
http://equity.cochrane.org/Files/equitychecklist.pdf

This section should require minimal changes from protocol to review stage, except for rewriting to the past tense, where needed. For example 'We will search the following databases…' should be rewritten to 'We searched the following databases…'.

Please note: Authors using CC&CRG standard text must tailor it to their review methods so that they accurately describe what was actually done to conduct the review.

Criteria for considering studies for this review

See the [Cochrane Handbook](#) chapter 4.5 and chapter 5.

Please note that the heading "Criteria for considering studies for this review" cannot have free text after it.

Types of studies

See the [Cochrane Handbook](#) chapter 4.5 and chapter 5.

Types of participants

See the [Cochrane Handbook](#) chapter 4.5 and chapter 5.

Types of interventions

See the [Cochrane Handbook](#) chapter 4.5 and chapter 5.

Types of outcome measures

See chapter 4.5, chapter 5 and chapter 7 of the [Cochrane Handbook](#).

Please note that even though outcomes on which to extract data will have been planned and pre-specified at protocol stage, there may be changes to this at review stage (ie. it is not always possible to anticipate all relevant outcomes related to complex interventions). Any changes (from protocol to review stage) to the outcomes to be sought, to the timepoints reported and/or to the outcomes selected for analysis (where more than one is reported) must be clearly explained and a rationale provided in the 'Differences between protocol and review section.'

Search methods for identification of studies

See the [Cochrane Handbook](#) chapter 4.5 and chapter 6.

Note: Searches that were planned at protocol stage but amended or not applied (for instance, because databases were not accessible) should noted briefly in the section 'Differences between protocol and review' as well as below.

Electronic searches [recommended level 3 heading]

Tailor the following CC&CRG standard text to your review:

'We searched:
- The Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, *latest issue*);
- MEDLINE (OvidSP) (*date* to *date*);
- EMBASE (OvidSP) (*date* to *date*);
- PsycINFO (OvidSP) (*date* to *date*); and
- *[List other databases].*

We present detailed search strategies in Appendices 1 to X.

[Cut and paste all search strategies as appendices, one database search per appendix, exactly as run]

There were no language nor date restrictions *[or specify any restrictions, giving reasons].'*

Note: Cochrane standards stipulate that searches are updated for all relevant databases within 12 months before publication of the review or review update, and the results screened for potentially eligible studies and incorporated into the review. If this is not likely to be possible for your review without excessively delaying publication, please contact the editorial base (cochrane@latrobe.edu.au).

Searching other resources [recommended level 3 heading]

Tailor the following CC&CRG standard text to your review:

'We searched *[list grey literature sources, such as reports and conference proceedings].*

[If journals were specifically handsearched for the review, describe this in the format] 'We handsearched the following journals: Title (dates), Title (dates), etc.'

We contacted experts in the field and authors of included studies for advice as to other relevant studies. We also searched reference lists of relevant studies and *(add other sources, e.g. personal collections of articles).*

We also searched online trial registers *(list them)* for ongoing and recently completed studies.

Specify any other search activities you undertook.'

If the review included additional studies such as qualitative research or those to identify adverse effects, describe the search methods used to identify these studies.

Data collection and analysis

Refer to the Cochrane Handbook section 4.5.

Note: Methods that were planned at protocol stage but not applied (for instance, because no trials were found, or results were not pooled) should summarised briefly in the section 'Differences between protocol and review' and the protocol cited there, for potential application in future updates of the review.

Note: Refer to the Review Group's *Study Quality Guide* (Ryan 2013) and the *Data Extraction Template,* available at http://cccrg.cochrane.org/author-resources.

Selection of studies

See the Cochrane Handbook section 7.2.

Authors should report study selection and flow using a modified PRISMA diagram, see **Figures** section below for more information.

Use the following CC&CRG standard text (tailored as necessary):

> 'Two authors independently screened all titles and abstracts identified from searches to determine which met the inclusion criteria. We retrieved in full text any papers identified as potentially relevant by at least one author. Two review authors independently screened full text articles for inclusion or exclusion, with discrepancies resolved by discussion and by consulting a third author where necessary to reach consensus. We collated duplicate publications and present these by individual study. All potentially-relevant papers excluded from the review at this stage are listed as excluded studies, with reasons provided in the 'Characteristics of excluded studies' table. We present citation details and any available information about ongoing studies in the 'Characteristics of ongoing studies' table. The screening and selection process is outlined in a PRISMA flow chart (Liberati 2009), see Figure X'

Data extraction and management

See the Cochrane Handbook chapter 7.

Use the following CC&CRG standard text (tailored as necessary):

> 'Two review authors extracted data independently from included studies. Any discrepancies were resolved by discussion until consensus was reached, or through consultation with a third author where necessary. We developed and piloted a data extraction form using the Cochrane Consumers and Communication Review Group Data Extraction Template (available at: http://cccrg.cochrane.org/author-resources). Data extracted included the following

items: Details of the study (aim of intervention, study design, description of comparison group…[*please add to this list as appropriate*]).* One review author entered all extracted data into RevMan, and another author working independently checked them for accuracy against the data extraction.'

[*Some details of the data extracted from included studies should be described but this can be relatively brief and can refer readers to the **Characteristics of included studies** table for full details of the data extracted, as well as mentioning that outcome data and results of studies were also extracted from included studies.]

* As part of the data extraction process it is now mandatory that details of the funding source for each included study and the declaration of interests for the primary investigators should also be collected and reported.

** Please note that it is essential that the data extraction form is piloted and usability of it is assessed before it is used to extract data from included studies.

Assessment of risk of bias in included studies

Refer to the Cochrane Handbook chapter 8 and to the CC&CRG *Study Quality Guide* (Ryan 2013)*, available at http://cccrg.cochrane.org/author-resources.

- Adapt the standardised text as needed. In particular:
  - o If the review is to include only RCTs then all studies rated at a 'high risk of bias' on the random sequence generation item of the risk of bias tool should be excluded from the review, because these studies are actually quasi-RCTs, not RCTs. Only reviews that expressly set out to include RCTs plus additional study designs should have any included studies at high risk of bias related to random sequence generation.
  - o If authors do not specifically exclude studies at unclear or high risk of bias on sequence generation in these cases, the protocol should also have planned how these studies will be dealt with at review stage: ie, either restricting meta-analyses to those studies with a low rating on this item; or conducting sensitivity analyses (excluding studies at unclear or high risk) to investigate the effects of this decision on effect estimates.
  - o If quasi-RCTs, cluster RCTs, CBA and/or ITS studies are included in the review, the additional standardised text outlining how these different designs were assessed must be added to the review.
  - o If 'other' sources of bias were assessed these need to be clearly described (ie what was assessed and why).
    - ▪ NOTE: validity and reliability of outcome measures and obtaining ethical approval do not affect study bias but might instead by collected under 'other measures of study quality' in the data extraction template.
  - o If studies were assigned an overall rating of 'higher' or 'lower' risk of bias (for example, as a basis for sensitivity analyses), describe here the way that these were defined. See the Cochrane Handbook section 8.8.3.1 for possible options – such as studies meeting particular

criteria, or defining a particular threshold point at which studies were considered at lower risk of bias.

o   Authors should summarise the risk of bias for each key outcome across the included studies. This approach links together aspects of the design of the study and the outcomes of the study, and is an important step in assessing the quality of the body of evidence.

Use the following CC&CRG standard text (tailored as necessary):

'We assessed and reported on the methodological risk of bias of included studies in accordance with the Cochrane Handbook (Higgins 2011) and the guidelines of the Cochrane Consumers and Communication Review Group (Ryan 2013), which recommends the explicit reporting of the following individual elements for RCTs: random sequence generation; allocation sequence concealment; blinding (participants, personnel); blinding (outcome assessment); completeness of outcome data, selective outcome reporting; and other sources of bias *[please specify].* We considered blinding separately for different outcomes, as appropriate. We judged each item as being at high, low or unclear risk of bias as set out in the criteria provided by Higgins 2011 and provided a quote from the study report and a justification for our judgement for each item in the 'Risk of bias' table.

Studies were deemed to be at the highest risk of bias if they were scored as at high or unclear risk of bias for either the sequence generation or allocation concealment domains [*or other domains of the tool; please adapt]*, based on growing empirical evidence that these factors are particularly important potential sources of bias (Higgins 2011).*

In all cases, two authors independently assessed the risk of bias of included studies, with any disagreements resolved by discussion to reach consensus. We contacted study authors for additional information about the included studies, or for clarification of the study methods as required. We incorporated the results of the 'Risk of bias' assessment into the review through standard tables, and systematic narrative description and commentary about each of the elements, leading to an overall assessment the risk of bias of included studies and a judgment about the internal validity of the review's results.'

If including quasi-RCTs insert this text:

'We assessed and reported quasi-RCTs as being at a high risk of bias on the random sequence generation item of the 'Risk of bias' tool.'

If including cluster RCTs insert this text:

'We assessed and reported cluster RCTs on the risk of bias associated with an additional domain: selective recruitment of cluster participants (described in Ryan 2013).'

If including controlled before and after studies insert this text:

'We assessed CBA studies' risk of bias systematically utilising adaptations to the above tool developed by the Effective Practice and Organisation of Care (EPOC) Group, outlined in Ryan 2013. Specifically, we assessed CBA studies against the same criteria as RCTs but reported them as being at high risk of bias on both the random sequence generation and allocation sequence concealment items; and we excluded CBA studies from the review if intervention and control groups were not reasonably comparable at baseline.'

If including interrupted times series analyses insert this text:

'We assessed the risk of bias of ITS studies systematically utilising adaptations to the above tool developed by the Effective Practice and Organisation of Care (EPOC) Group, outlined in Ryan 2013. Specifically, we assessed and reported the following individual items for ITS studies: intervention independence of other changes; pre-specification of the shape of the intervention effect; likelihood of intervention affecting data collection; blinding (participants, personnel); blinding (outcome assessment); completeness of outcome data, selective outcome reporting; and other sources of bias [please add].'

Measures of treatment effect

Refer to the Cochrane Handbook section 9.2

You may use the following *optional* headings, either in place of 'Measures of treatment effect' (ie. as level 3 headings) or as subheadings (level 4 headings):

> Dichotomous data
>
> Continuous data
>
> Time-to-event data

For RCTs, quasi-RCTs, cluster-RCTs and cross over trials: clearly describe which effect measures were used to summarise and present the data from included studies, at the study level, for each type of outcome (eg continuous outcomes (SMD, mean difference), dichotomous outcomes (OR, RR, RD) or other outcomes (ordinal, time-to-event)).

Also describe the effect measures that were used for each different type of study design that was included (ie RCTs and non-RCTs).

For cross-over studies other decisions are also needed, such as what data to include in the review (eg pre-crossover data, post-crossover data). This should have been specified in the protocol. See the Cochrane Handbook section 16.4.

An example of wording:

- For dichotomous outcomes, we analysed data based on the number of events and the number of people assessed in the intervention and comparison groups. We used these to calculate the risk ratio (RR) and 95% confidence interval (CI). For continuous measures, we analysed data based on the mean, standard deviation (SD) and number of people assessed for both the

intervention and comparison groups to calculate mean difference (MD) and 95% CI. Where the MD was reported without individual group data, we used this to report the study results. If more than one study measured the same outcome using different tools, we calculated the standardised mean difference (SMD) and 95% CI using the generic inverse variance method in Review Manager 5.

For non-RCTs (CBAs and ITS): clearly describe effect measures for each type of outcome

- For CBAs there are appropriate effect measures for dichotomous outcomes (RR, adjusted RR) and for continuous outcomes (relative % change post intervention, SMD).

- For ITS, effect measures typically include i) change in level of the outcome at the first point after the introduction of the intervention, and ii) the post-intervention slope minus the pre-intervention slope. These estimates are calculated from regression models adjusting for autocorrelation. It is not appropriate to present means and SDs of pre-intervention versus post-intervention time points.

  For further information see:

  - Brennan et al, Continuous quality improvement: effects on professional practice and healthcare outcomes (Protocol). Cochrane Database of Systematic Reviews 2009, Issue 4) – an example of how to structure a section on ITS data analysis.

  - Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. International Journal of Technology Assessment in Health Care 2003;19(4):613-23.

  - Clement S, Lassman F, Barley E, Evans-Lacko S, Williams P, Yamaguchi S, et al. Mass media interventions for reducing mental health-related stigma. Cochrane Database of Systematic Reviews 2013 (in press).

Unit of analysis issues

Refer to the Cochrane Handbook section 9.3.

Alternatively, *optional* (level 3) headings specific to the types of studies may be used in this section, such as:

> Cluster-randomised trials
>
> Cross-over trials
>
> Studies with multiple treatment groups

In this section authors describe how analysis was performed if the review included study designs, such as cluster RCTs and crossover trials, where the unit of analysis must take into the account the unit of randomisation. Describe here how the analysis was conducted to avoid unit-of-analysis errors. See section 16.3.4 of the Cochrane Handbook.

If appropriate, use the following CC&CRG standard text (tailored as necessary):

> 'We checked cluster RCTs for unit-of-analysis errors. Where errors were found, and sufficient information was available, we re-analysed the data using the appropriate unit of analysis, by taking account of the intracluster correlation (ICC). We obtained estimates of the ICC by contacting authors of included studies, or imputed them using estimates from external sources. Where it was not possible to obtain sufficient information to reanalyse the data we reported effect estimates and annotated 'unit-of-analysis error.'

Dealing with missing data

See the Cochrane Handbook section 16.1 and 16.2.

This section should describe how missing data were dealt with.

Missing outcome data may be imputed using different methods but these need to be specified (and for different study types). For dichotomous outcomes, imputation methods for missing outcome data in meta-analysis have been developed (see Higgins 2008) but these methods have not been extended to continuous data.

Further information:

- Higgins JP, White IR, Wood AM. Imputation methods for missing outcome data in meta-analysis of clinical trials. Clinical Trials 2008;5(3):225-39.

Use the following CC&CRG standard text (tailored as necessary):

> 'We attempted to contact study authors to obtain missing data (participant data, outcome data, or summary data). For participant data, we conducted analysis on an intention-to-treat (ITT) basis wherever possible; otherwise we analysed data as reported. We reported on the levels of loss to follow-up and assessed this as a source of potential bias.
>
> For missing outcome or summary data we imputed missing data where this was possible and reported any assumptions in the review. We investigated, through sensitivity analyses, the effects of any imputed data on pooled effect estimates.'

Assessment of heterogeneity

See the Cochrane Handbook section 9.5, and the 'Heterogeneity and subgroup analysis' Quick Guide at http://cccrg.cochrane.org/author-resources

Describe how the presence of heterogeneity (variation across studies) was assessed. This means considering how consistent the effects of an intervention on a particular outcome were across the included studies, which can be assessed formally in Cochrane reviews where meta-analysis has been conducted.

Please note that you will be expected to report why you decided to pool data using meta-analysis, or not, and exactly what these decisions were based on. This means that you will need to consider and

report exactly why studies were too variable to pool (if this is the decision made), or how the studies were similar enough to meta-analyse, so that these important decisions underpinning analyses in the review are transparent to readers.

Use the following CC&CRG standard text (tailored as necessary):

> 'We assessed that studies were similar enough to allow pooling of data using meta-analysis by considering *[please add reasons for this decision; it may include consideration of interventions, populations or other factors, for example]**. Where data was pooled using meta-analysis, we assessed the degree of heterogeneity by visual inspection of forest plots and by examining the Chi^2 test for heterogeneity. We quantified heterogeneity using the I^2 statistic. We considered an I^2 value of 50% or more to represent substantial levels of heterogeneity, but interpreted this value in light of the size and direction of effects and the strength of the evidence for heterogeneity, based on the P value from the Chi^2 test (Higgins 2011). Where heterogeneity was found in pooled effect estimates we explored possible reasons for variability by conducting subgroup analysis.'**
>
> '

Note: when there are few trials included in a meta-analysis (which is common in CC&CRG reviews) the Chi^2 test has little power to detect heterogeneity. Therefore a non-significant result should not necessarily be interpreted as evidence of no heterogeneity and should be instead interpreted with care.

* Please note that if you have made the decision not to pool data using meta-analysis then you should reword this entire section of text, using the text from this section of your protocol as a guide and providing a clear explanation as to why it was not possible and/or appropriate to undertake statistical pooling.

** Note that where heterogeneity in pooled effect estimates is low it may not be necessary to further investigate using subgroup analyses and in such cases this final sentence should be altered as needed. Similarly, if no subgroup analyses are planned this sentence should be amended.

Assessment of reporting biases

See the Cochrane Handbook chapter 10; also Guyatt *et al* (2011) GRADE guidelines 5. Rating the quality of evidence – publication bias, Journal of Clinical Epidemiology 1277-82, available at http://www.gradeworkinggroup.org/index.htm

Describe how the review assessed whether reporting biases were likely to have influenced the results. Reporting biases occur when the findings and type of results of a study influence the dissemination of the research (eg statistically significant, positive results are more likely to be published than non-significant results). Systematic reviews aim to identify and evaluate the entire body of evidence on the effects of a particular intervention (ie those with both statistically non-

significant and statistically results), yet reporting biases may make the identification of all available research, and so the assessment of the evidence available, more difficult.

One situation to look for when conducting a systematic review can be the inclusion of only small studies: large studies are less likely to remain unpublished or unknown, and are likely to provide more precise estimates of effect than smaller studies, whether results are positive or negative. However, larger studies are not immune from publication bias and so this aspect of the included literature does need to be assessed in all reviews.

Use the following CC&CRG standard text (tailored as necessary):

> 'We assessed the likelihood of reporting bias qualitatively based on the characteristics of the included studies (eg where only small studies that indicate positive findings were included in the review), and where information that we obtained from contacting experts and authors or studies suggested that there were relevant unpublished studies.'

If sufficient studies (at least 10) are included in the review it may be possible to construct a funnel plot to more formally assess reporting bias; please use the following standard text (tailored as needed):

> 'Sufficient studies were included in the review to allow construction of a funnel plot to investigate small study effects, which may indicate the presence of publication bias. We formally tested for funnel plot asymmetry, with the choice of test based on advice in Higgins 2011*.'

*See the Cochrane Handbook section 10.4.3.1 and Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011;343:d4002

If insufficient studies were identified please add the following text (tailored as needed):

> 'Insufficient studies were included in the review to allow construction of a funnel plot and formal testing of asymmetry, which may indicate publication bias. Should enough studies be included in future updates of the review we will plan to undertake these analyses, with the choice of test based on advice in Higgins 2011*.'

Data synthesis

See the Cochrane Handbook chapter 9.

Refer to the CCCG Guides on 'Analysis', 'Meta-analysis' and 'Examples of narrative synthesis' at http://cccrg.cochrane.org/author-resources

This section of the review describes how the data from included studies were analysed in the review. Describe here specific decisions about how the analysis was performed, such as how different types of data were dealt with and what methods were used to synthesise, summarise and analyse the data.

If meta-analysis was possible

Use the following CC&CRG standard text (tailored as necessary):

'The decision to meta-analyse data or not was based on an assessment of whether the interventions in the included trials were similar enough in terms of participants, settings, intervention, comparison and outcome measures to ensure meaningful conclusions from a statistically pooled result. Due to the variability in the [populations and interventions; *[please adapt]* of included studies, we used a random-effects model for meta-analysis.'

Inclusion of study designs other than RCTs add to the complexity of the review. If the review includes and meta-analyses results from these studies there needs to be a clear description of how this analysis was done. That is, as well as providing a clear description of the measures of effect for each study design (see earlier section – 'Measures of treatment effect') there also needs to be a clear description of how meta-analysis was done for non-RCTs.

One approach which could be used is for authors to include only RCTs, quasi-RCTs and cluster RCTs in any meta-analysis, and to provide descriptive statistics for CBA and ITS studies. Descriptive statistics could include median effect sizes, inter-quartile ranges or other measures, and this information could be presented graphically using bar charts or other approaches.

Also note (as stated earlier) if the review is restricted to RCTs only then authors should either plan to exclude all studies rated at a high risk of bias on sequence generation; or must plan how the possibility of studies with different ratings on this item will be dealt with in analyses ie, restricting meta-analysis to studies with a low risk of bias only; or conducting sensitivity analysis to investigate the effects of this decision (excluding studies with a high and unclear risk of bias on this item).

If meta-analysis was not planned and/or possible

In practice it may only be possible to statistically pool some data included in a review; or the data may be unsuitable for pooling statistically. It is necessary for authors to describe how data that could not be dealt with through meta-analysis was analysed.

Authors may wish to present data that is unable to be statistically pooled in graphs, tables, box plots or via a narrative summary and synthesis of the data.

Where a narrative summary was used authors should note that it is not sufficient to simply state that data was 'summarised narratively'. Instead, what is meant by a narrative summary should be explained and a how the narrative summary was structured and presented should be provided. An excellent guide of the different ways that Cochrane teams have done this can be found in 'Examples of narrative synthesis' at http://cccrg.cochrane.org/author-resources.

Some examples of how this might be described:

'We were unable to pool the data statistically using meta-analysis for the following reasons [*please outline your decisions*]. We therefore conducted a narrative synthesis of results. We presented the major outcomes and results, organised by intervention categories according to the major types and/or aims of the identified interventions. Within the data categories we explored the main comparisons of the review:
- o Intervention versus no intervention.
- o Intervention versus usual care.
- o One form of intervention versus another.

Where studies compare more than one intervention, we compared each separately to no intervention/ control; and with one another.'

'We were unable to pool the data statistically using meta-analysis for the following reasons [*please outline your decisions*]. We therefore grouped the data based on the category that best explores the heterogeneity of studies, in this case intervention type [or adapt]. Within each category we presented the data in tables and narratively summarised the results.'

Please note that if you are unable to pool data using meta-analysis you will need to provide a clear explanation of your reasoning, so that the decisions you reached are clear to readers of the review. You must also describe the methods of narrative (descriptive) synthesis that you used to analyse the data.

Subgroup analysis and investigation of heterogeneity

See the [Cochrane Handbook](#) section 9.5 and 9.6

See 'Heterogeneity and subgroup analysis' Quick Guide at http://cccrg.cochrane.org/author-resources

The effects of the intervention might vary in different populations or with different characteristics of the intervention itself (eg different durations or intensities of delivery). These different effect modifiers can be investigated in subgroup analyses (or using meta-regression) in the review.

Note that any such effect modifiers that will be investigated should have been pre-specified at protocol stage, along with thresholds for conducting the analyses and a strong rationale provided for each. If decisions are made post hoc to investigate particular effect modifiers in the review this needs to be clearly stated in this section, and also reported in the section 'Differences between protocol and review'.

Take care to clearly describe how subgroups were categorized in this case and provide a strong rationale for conducting post hoc analyses.

Note also that if subgroup analyses are undertaken at review stage, the subgroups should be compared formally using the appropriate statistical tests, and details of these methods reported in the review.

Sensitivity analysis

Refer to the [Cochrane Handbook](#) section 9.7.

Sensitivity analysis can be used to assess the robustness of results, such as the impact of assumptions, imputed data, borderline decisions, choice of meta-analysis method, and studies at high risk of bias. Sensitivity analyses repeat the primary analyses of the review, but with different assumptions or decisions, for example, changing the analysis method. The aim is to determine how robust the results of the review are to the decisions that were made in conducting the review. In this section of the review, describe any sensitivity analyses that were conducted, referring to the analyses planned at protocol stage.

Points to remember:
- If sensitivity analyses were performed based on 'Risk of bias' assessments, describe how the studies were classified as being at high or low risk of bias.
- A minimum of 10 studies is recommended for meta-regression for each variable that is included in the model.
- You must report in the review how any sensitivity analyses were conducted (ie what they were based on).

Summary of findings table

Refer to the [Cochrane Handbook](#) chapters 11 and 12, particularly section 11.5, and the 'Summary of findings' guide at http://cccrg.cochrane.org/author-resources

'Summary of findings' tables present the main findings of the review in a specialised table format. There are clear guidelines and requirements for these tables that must be met.

- Describe the methods that were used to prepare the 'Summary of findings' tables. Include information about: which populations (including the specification of low, medium or high risk populations), interventions and comparisons are being addressed, and why;

- the source of any external information used in the 'Assumed risk' column (ie the source of this information and a rationale for each assumed risk to be presented – for each outcome), see Handbook sections 11.5.6.3 and 11.5.6.4 for more;

- a brief comment that the GRADE approach for assessing the quality of the body of evidence was used; and

- any departures from the standard methods described in Chapters 11 and 12 of the Cochrane Handbook, along with a justification for such departures.

The review's main outcomes, ie those intended for inclusion in the 'Summary of findings' table, should be listed at the section 'Types of outcome measures'.

Use the following CC&CRG standard text (tailored as necessary):

'We prepared a 'Summary of findings' table to present the results for each of the major primary outcomes, including potential harms, as outlined in the 'Types of outcome measures' section (with meta-analysed results or results synthesised narratively). We converted results into absolute effects when possible, and provided a source and rationale for each assumed risk cited in the table(s) when presented, and used the GRADE criteria to rank the quality of the evidence based on the methods described in chapter 11 of the Cochrane Handbook for Systematic Reviews of Interventions (Schünemann 2011).'

If the GRADEpro software was used, also add the text:

'We used GRADEpro software to prepare the table (Schünemann 2011).'

Assessing the quality of the evidence (alternative heading to Summary of findings table)

If a formal 'Summary of findings' table is not produced, authors must still describe their methods for assessing the quality of the body of evidence in the review, and add a subheading ('**Assessing the quality of the evidence'**). The most widely accepted approach for assessing certainty in the quality of the evidence, by outcome, is the GRADE approach.

Authors should use the GRADE criteria to assess and summarise the quality of the evidence for each outcome. There are five criteria: risk of bias, inconsistency, imprecision, indirectness and publication bias, and they allow conclusions about the quality of the evidence to be drawn consistently across the different outcomes in a review. Ideally, two authors working independently should assess the quality of the evidence by considering each of the five GRADE criteria.

Use the following CC&CRG standard text (tailored as necessary):

'We assessed and reported the quality of the evidence, using the GRADE criteria to assess the quality of the evidence for each outcome: risk of bias, inconsistency, imprecision, indirectness and publication bias (Schünemann 2011). Two authors independently assessed the quality of the evidence (Cochrane Handbook, Chapter 11).'

Please note: We strongly encourage you to develop your SoF table(s) early in the process of considering the review findings. It can form the basis for reporting the findings consistently and clearly, together with a GRADE rating of quality of the evidence, throughout the review.

Other possible headings

You can also use the following optional level 3 headings here:

Economics issues

Methods for future update

Ensuring relevance to decisions in health care

This is the section of the review that highlights the vision for Cochrane reviews to inform real world decisions and the principle of assessing healthcare interventions using outcomes that matter to people making choices in health care. When practitioners are authors they bring an awareness of many pertinent issues. This awareness can be broadened by listening to health service users too. For reviews of interventions that require the authority, skills and resources of more than individual practitioners, policy makers and managers can also offer useful insights.

Outline how you took into account the views of people who make policy or practice decisions, implement decisions or experience the consequences of decisions related to the focus of your review, with the suggested subheading **'Ensuring relevance to decisions in health care'.**

This section should contain details of how the CC&CRG includes, as part of its editorial processes, input into protocols and reviews from people working in health services and people using health services. It should also include details of any other activities undertaken to seek the views of different people, and authors are encouraged to consider improving the quality of the review, in terms of its relevance to issues and outcomes for these people, in different ways. Listening to other people may help authors become more sensitive to important issues, choose how to frame the review when detailing the populations, interventions, comparators, outcomes and contexts to consider, choose appropriate subgroup analyses, or consider the implications of the findings.

This might have included undertaking one or more of the following as part of the review:

- Reading relevant reports and literature produced by organisations on issues for their members.

- Inviting members of relevant organisations or with personal experience to discuss issues pertinent to the review by telephone, email or round a table.

- Inviting members of organisations, including consumer organisations, to be part of the review team and to contribute as authors to drafting of the protocol and/or review.

- Forming an advisory group or panel to provide advice on the review and input to drafts.

None of these options are pieces of research. They broaden the ideas that authors bring to a review so any such input would be acknowledged appropriately in the protocol and/or review.

Another approach is to draw on existing research about people's views. This may be considered in the background to justify the importance of the review, or in the discussion to draw out the implications of the findings. There are increasing numbers of qualitative syntheses of people's views that are particularly appropriate to inform an effectiveness review. If so little research exists that there is not a good understanding of the issues authors may also choose to undertake additional research, using focus groups, interviews or questionnaires to support the analysis performed in the review. This could lead to important guidance for designing new randomised controlled trials.

Please include a section on ensuring relevance to healthcare decisions at the end of the methods section of your review, including (and expanding upon) the following text:

'The protocol and review received feedback from 1 to 2 consumer referees in addition to health professionals as part of the Cochrane Consumers and Communication Review Group's standard editorial process.'

RESULTS

Description of studies

Refer to the [Cochrane Handbook](#) chapter 4.5

Results of the search

Begin with a summary of the results of the search, referring to a PRISMA study flow diagram to describe the process if possible (eg numbers of records identified by the searches, numbers excluded after screening based on title and abstract, numbers retrieved in full text, and so on).

A PRISMA flow diagram can be created in RevMan; see also section 11.2.1 of the [Cochrane Handbook](#) and the section below under 'Figures.'

Included studies

State the number of included studies and briefly describe them, based on the information in the 'Characteristics of included studies' tables. Include a link or reference to the table in this section, which can be structured around the following (optional) subheadings:

> Design
>
> Sample sizes
>
> Setting
>
> Participants
>
> Interventions
>
> Outcomes

Note: if a study with several intervention arms is included (and not all the arms are relevant to the review's objectives), you should only include in the review those intervention and control arms which meet the review's eligibility criteria. Clearly report this in the 'Characteristics of included studies' table (ie that there were additional arms of the study that were not eligible for inclusion in the review).

Include a statement about the source of the data contained in the review– ie whether all were obtained from published literature, by correspondence, and so on.

Excluded studies

Refer (and link) to the information in the 'Characteristics of excluded studies' table and give a brief summary of the reasons that studies were excluded from the review. Note that the reasons outlined here must match those reasons for exclusion listed in the table.

You may also use the following optional headings:

Ongoing studies

Studies awaiting assessment

New studies found at this update

Risk of bias in included studies

See the Cochrane Handbook, chapter 4.5 and chapter 8 for a more detailed description of what to include in this section.

Briefly summarise the 'Risk of bias' assessments of the included studies, including variability across studies and any important flaws in included studies.

Provide detailed descriptions of the criteria used to assess the risk of bias under the Methods section of the review. Report how each study was rated on each individual risk of bias item in the 'Risk of bias' table for each study.

In this section, give a concise summary of the risk of bias, including its variability, as well as any important flaws in individual included studies.

You may also wish to generate 'Risk of bias' Figures and link to them from this section, see the Cochrane Handbook section 8.6.

NOTE: Refer to the CCCG's *Study Quality Guide* (Ryan 2013) in preparing this section,and/or to the Risk of bias section of the CCCG Data Extraction Template; both available at http://cccrg.cochrane.org/author-resources

Allocation (selection bias)

Summarise how allocation sequences were generated (random sequence generation) and intervention assignment was concealed (allocation concealment), and give judgements about the risk of bias arising from the methods used by included studies.

NOTE: for reviews of RCTs only, any studies with a high risk of bias rating for sequence generation should be excluded from the review, as these are quasi-RCTs; or should otherwise be dealt with by

restricting meta-analysis to those with a low risk of bias rating, or using sensitivity analysis to determine the effects of removing those at unclear or high risk of bias on effect estimates.

Blinding (performance bias and detection bias)

Briefly summarise who was blinded (kept unaware of group allocations after people are entered into the study) during the conduct and analysis of studies. Report your judgments about the risk of bias arising from the methods used by included studies. **Performance bias** is assessed by considering blinding of participants and personnel, while **detection bias** is assessed by considering blinding of outcome assessment.

Implications of blinding of outcome assessment may differ between different outcomes and so you should consider blinding separately for each outcome within included studies. For example, objective outcome measures might be less affected by a lack of blinding than the potential effect of unblinded outcome assessment on subjective outcomes. Similarly, for blinding of participants and personnel the risk of bias may be high for some outcomes if unblinded (eg behavioural, socially desirable or some self-reported outcomes) but less likely to affect others such as mortality.

Incomplete outcome data (attrition bias)

Briefly summarise how complete the data are for each main outcome. In assessing the likelihood of attrition bias you need to consider a number of factors, including the size (numbers) of exclusions and drop outs, as well as any differential effects (both numbers and reasons) between groups. See the Cochrane Handbook section 8.13.2.

Assessing the impact of missing data often cannot be done reliably for each study as a whole but may be different for different outcomes – for example, there may be lower attrition for an outcome assessed at three months than at two years. Multiple outcomes can be grouped (eg for a particular time point) but judgements of the risk of bias should be attempted for each outcome or set of outcomes.

Selective reporting (reporting bias)

Summarise briefly here whether data were only selectively available, including considerations of selective reporting of outcomes, timepoints, or analyses.

Other potential sources of bias

Summarise any other potential sources of bias here. This section should only report on sources of potential bias (eg baseline imbalances) that might change the effect estimate size. Other aspects of the quality of a study should not be summarised in this section, for example, reliability and/or validity of the outcome measures used.

Effects of interventions

See the Cochrane Handbook chapters 11 and 12.

Summarise the synthesised results of the effects of interventions, rather than describing the results study by study. The results should address the review's objectives.

Organising the results

Often this means organising this section by the review's comparisons, so that there is clear correspondence between the questions that the review asks and the findings. There are many other ways of organising this section, however, and the choice of options can depend on the review question as well as the complexity of the review.

See the 'Examples of Narrative Synthesis' guide at http://cccrg.cochrane.org/author-resources

For more information on comparisons in reviews of complex interventions, please refer to the CCCG guide on 'Identifying comparisons in CCCG reviews', available at http://cccrg.cochrane.org/author-resources

When reporting the results, for example within comparisons, outcomes should usually be reported in the order that they are listed under the 'Types of outcome measures' section, and should be separately identified as primary and secondary outcomes as appropriate.

Include the results of individual studies, and any statistical summary of these, in 'Data and analysis' tables rather than in the text here. The text should be about the summary of the results.

Subheadings can be useful to help to organise this section of the review (for example, for each different participant group, comparison or outcome measure if a review addresses more than one) – particularly if the review is complex and/or especially large.

You must report results for all pre-specified outcomes, irrespective of the strength and direction of the results, and the availability of data (including for harms).

Any post hoc decisions related to choice of outcomes or choice of outcome measures should be clearly described – for example, if post hoc decisions are made about the choice of outcomes from among multiple measures or multiple time points.

Presenting the results

This section of the review should clearly report the findings of the studies and analyses conducted (if appropriate), without interpretation. Authors should avoid making inferences about the findings.

Some common mistakes to avoid in describing the results here and later in the review when drawing conclusions, are described in the guide 'Describing results' available at http://cccrg.cochrane.org/author-resources. One particularly common mistake is to report an inconclusive result as 'evidence of no effect' or 'the intervention showed no effect', which are incorrect. Where there is inconclusive evidence about the effects of an intervention on an outcome (eg a statistically non-significant result) the conclusion should be that there is 'no evidence of effect';

or that the data suggest that either an increase or decrease in the outcome is possible as a result of the intervention.

If data are transformed for presentation in the review this should be explained, as should any methods for extracting numerical data from graphs.

Ensure that key findings are interpretable, or are re-expressed in an interpretable way; for example, as absolute values, or as units that are easily understandable.

Other data issues

- We encourage authors to undertake a simple check of the data included within the review. Authors should, for each included study, compare the data presented in the review with that presented in the study report. A basic check to ensure that both the direction and size of the effects are comparable is a simple way to double-check for errors in data extraction, interpretation or data entry into RevMan.

- Two authors should independently assign outcomes reported in each included study to the outcome categories and resolve any differences in categorisation, if they occur, by the involvement of a third author. This may lead to more than one outcome in each outcome category being selected for the review.

- The numbers of studies and participants contributing data to each outcome in the review should be stated, together with the proportion of the included studies and recruited participants that were potentially available for the relevant comparison.

- If results from studies are combined using different scales then authors must check that higher scores for all continuous outcomes have the same meaning – for example, sometimes a lower score will reflect a better outcome (eg lower symptom scores) and sometimes higher scores will be better (eg higher symptom-free days). Combining effect estimates that have opposite meanings leads to incorrect results. Authors should therefore check the meaning of scores, explain the direction of interpretation, and report any cases where they reversed the directions of the scales in the review.

- Effect estimates will need to be standardised so that scales and other outcome measures are concordant. Ratios greater than one, and differences between the intervention and comparator groups greater than zero should indicate benefit for the intervention group, so effect estimates may need to be multiplied by minus one where necessary.

- If studies with multiple arms are to be analysed, care must be taken to avoid double-counting of participants or omission of relevant groups, which can produce misleading results. Some alternatives include combining intervention groups or separating analyses, but authors should refer to the Cochrane Handbook (sections 7.7.3.8 and 16.5.4) and seek advice if this arises.

- Where subgroup analyses are to be compared, and there are enough studies to do this meaningfully, use a formal test to do so – as concluding that there is a difference on the basis of significantly different results can be misleading. See the Cochrane Handbook section 9.6.3.1.

- If multiple subgroup and/or sensitivity analyses are presented, the results of these are best presented in a summarised form (eg table or figure), rather than in multiple forest plots.

- Authors should also consider how the risk of bias for included studies might affect conclusions. This can be investigated formally in the review (eg restricting analyses to studies at low risk of bias), but can also be done narratively if meta-analysis is not performed.

- Please also note that if there are any post hoc decisions about which outcomes to report or prioritise (eg where there are multiple measures of the same outcome, or multiple time points at from which to choose) these need to be clearly reported and a rationale provided in the 'Differences between protocol and review' section.

Interpreting the results

When starting off this section it can be useful to consider:

1. What are the review findings? What is the direction of the findings (effects) for each outcome?

   For example, do they show positive, negative or no discernible effects of the intervention on specific outcomes? Are the results mixed – positive and negative effects for specific outcomes; or positive for some outcomes, negative or no effect for others?

   Answering these kinds of questions will mean considering the confidence intervals and P values associated with the results, see the Cochrane Handbook section 12.4 and section below on P values.

   Please note that in cases where two interventions are being compared, and results favour one over the other, it is critical to report clearly which intervention is favoured.

   This should lead to an overall summary of the effects of the intervention on the outcomes measured. Note that this should be considered systematically, especially if multiple comparisons are being made in a review, and multiple outcomes reported. You can use subheadings (eg according to comparisons made) to help to organise the results.

2. How large are the effects of the intervention?

   For example, are the effects on particular outcomes large and likely to be clinically or otherwise significant? eg a large change in screening test uptake or medication adherence.

   Are the effects on particular outcomes small but likely to be important because of the types of outcomes assessed? eg a small change in mortality may be important, whereas a similarly small change in another outcome such as a symptom score may be less so.

Are the effects large enough to be clinically or otherwise important/ meaningful? eg small changes in symptoms, pain or quality of life, or satisfaction that may not translate to a large difference for patients.

When considering the results of your included studies you must consider the size of the results when translated back to their clinical or social context. To be able to make this judgment, enough familiarity with the area, and with the outcome measures involved, is needed.

Please refer to the guide 'Describing results' for more information on thinking through the size of effects and the quality of evidence, available at http://cccrg.cochrane.org/author-resources

P values

A P value represents the probability that the observed or measured effect would occur when there is actually no effect. Hence, it is a measure of the likelihood of seeing the result if it did not really exist. This is why small P values are desirable: they mean that there is a very small chance that the observed effect (eg of an intervention) has arisen by chance alone and does not represent a real effect. For example, $P < 0.05$ means that there is a less than 5% chance, and $P < 0.01$ a less than 1% chance, that the effect observed has arisen by chance alone, and not as a result of the intervention.

P values are often misinterpreted. The first mistake is to misinterpret a large P value (eg $P > 0.05$) as meaning that the intervention has 'no effect.' A better way to interpret a large P value is to conclude that 'there is not strong evidence that the intervention has an effect,' Where possible, consider using this type of language to describe results, rather than using terms like 'not statistically significant' or 'non-significant.'

A second problem is to confuse the P value with the size or importance of the effect. Just because a statistically significant P value (difference) is found for the effects of a particular intervention does not mean that it is a clinically or otherwise important effect. This needs to be considered separately. The probability or P value gives an idea of the likelihood of observing an effect, relative to what would be seen by chance alone. The direction and size of the effect need to be considered to work out whether there are important benefits or harms for the people receiving the intervention.

Note: if reporting P values from meta-analysis in the review, then the exact P values generated by RevMan should be reported, ie rather than reporting '$P < 0.05$', report '$P = 0.045$'.

Imprecision

Another related factor to consider, with respect to the review findings, is how **precise** are the effects of the intervention?

Precision refers to the accuracy of the effect estimates. A precise estimate is exact, that is, there are a small number of possible values that the estimate could take (reflected by narrow measure of variability in the measure, such as narrow confidence intervals). On the other hand, less precise measures mean that there is a larger possible range of values that the effect estimate could take or in fact, that there were few participants or events in the analysis leading to wide confidence intervals. When interpreting results, precision is important to consider, because it can markedly

affect the size of the results. For example, considering precision of the effect estimates in your review means thinking about whether you would feel differently about the size of the effect of the intervention if the actual estimate lay at one end of the possible range? Does the variability measure include the possibility of clinically important changes with the intervention? Does the range of possible values for the effect estimate include the possibility of benefit and/or harm?

Note that all effect size estimates must be accompanied by a measure of statistical uncertainty – eg a 95% confidence interval.

For more on P values and their interpretation see the Cochrane Handbook, particularly section 12.4.2; and for more on precision and interpreting confidence intervals see section 12.4.1. You may also wish to refer to the section on imprecision in the 'How to GRADE' guide, available at http://cccrg.cochrane.org/author-resources.

3. Do the studies show inconsistent results – in different directions and/or with different estimated sizes?

The more similar in direction and similar in size the results of included studies are for the outcomes measured, the more confidence you can have in the results. This is because different individual studies are essentially replicating the effect of the intervention on an outcome.

Because a systematic review is selecting and combining different studies examining the effects of a particular intervention, there is likely to be variability in the effects of the interventions across studies. This is because there will inevitably be differences between studies – such as how and when the outcomes were assessed, who the outcomes were measured in, differences in the interventions, and so on. Assessing heterogeneity gives you a way of determining statistically whether the results are similar enough to have confidence in them, or that they are so inconsistent that additional factors affecting the outcomes might be at play – rather than reflecting only the effects of the intervention.

You should report the methods used in the review to identify the presence of heterogeneity, and the extent of variation between studies, and should take this into account when you are interpreting the results of studies.

See the 'Heterogeneity and subgroup analysis' guide, available at http://cccrg.cochrane.org/author-resources

Please note that GRADE includes structured assessment of both imprecision and inconsistency (heterogeneity) as part of the overall rating of quality of the evidence for a given outcome. This raises the important point that the GRADE ratings should be reported, wherever possible, alongside the findings (results) for a given outcome.

For example, 'Compared with usual care, the intervention increased adherence (RR 1.78 (95% CI 1.51 to 1.99; moderate certainty evidence)'. This enables a reader to interpret not only the result (size and direction of effect) but the quality of the evidence on which that specific result is based.

Assessing the quality of evidence using GRADE (part of which is assessing the risk of bias) is now a critical component of Cochrane reviews. We strongly encourage authors to use the ratings obtained from applying GRADE throughout their review, when describing the results in the Abstract, PLS, Summary of findings tables, Effects of interventions, and Discussion. This helps to ensure that there are consistent messages about the findings and quality of evidence throughout the review as a whole.

Reporting biases

Assessment of reporting biases should be reported alongside the results in this section of the review. This can include direct reference to the findings from funnel plots or other formal assessments of publication bias or other reporting biases if such tests are possible. Often there will be an insufficient number of included studies within a review to allow such formal tests but a qualitative assessment of the likelihood of reporting biases can still be undertaken and should be reported in this section.

Authors can report the on the likelihood of reporting biases for each outcome, or can elect to report this information in a summarised section for all outcomes at once, depending on the structure and complexity of the review.

For more on reporting biases see the *Cochrane Handbook* chapter 10.

Discussion

See the [Cochrane Handbook](http://), chapter 4.5 for a detailed description of what to include in this section, as well as chapter 12 on interpretation of results.

Also consider items on the Cochrane Equity Checklist <http://equity.cochrane.org/our-publications> and refer to the Review Group's 'Equity' Quick Guide, at <http://cccrg.cochrane.org/author-resources>

Use the recommended subheadings:

Summary of main results

Summarise the main findings without repeating the previous 'Effects of interventions section'. Also summarise any outstanding uncertainties about the balance of benefits and harms; refer to any 'Summary of findings' tables directly.

Overall completeness and applicability of evidence

In this section you should describe the relationship between the evidence reviewed and the review question, leading to a judgment about how externally valid the results of the review are. We strongly encourage authors to map systematically the outcomes reported in trials against those identified in their review protocol as being important and to comment on their assessment here.

Important questions to consider here include whether the included studies are able, and sufficient, to address all of the review's objectives; or whether all relevant participants and/or outcomes were

investigated in the included studies. Authors may also wish to comment on how the review's findings fit with current practice, although variations in practice internationally should also be kept in mind.

Quality of the evidence

Comment on whether robust conclusions can be drawn in response to the review's objectives; this section should be based on the information in the 'Summary of findings' tables, drawing on the GRADE approach to rating the quality of evidence (Refer to Summary of Findings and How to GRADE guides at http://cccrg.cochrane.org/author-resources). Authors should use the GRADE approach whether or not they also include a formal 'Summary of findings' table. Summarise the amount of evidence (in terms of numbers of studies and participants), along with key methodological limitations and the consistency or inconsistency of results, using the five GRADE considerations (risk of bias, inconsistency, imprecision, indirectness and publication bias). This should lead to an overall assessment of the quality of the evidence contributing to the review's results. Report all reasons for up- or down-grading the quality of the evidence so that the decisions are transparent to readers.

Potential biases in the review process

Describe the strengths and limitations of the review process, in terms of prevention of bias. This section is not about the limitations of the studies or data, but about the process authors used to conduct the review. This might include issues such as whether it was likely that all relevant studies were identified for assessment, whether all relevant data could be obtained, and whether the methods used (such as those for searching, selecting studies, collecting or analysing data) might have introduced bias.

One limitation that is easily overlooked in many reviews relates to adverse effects: in particular, if the review methods (e.g. including RCTs only) did not include studies which could have assessed serious and/or rare adverse events, then state this here as a limitation of the review.

Agreements and disagreements with other studies or reviews

Summarise how the included studies fit into the wider context of other evidence, and comment clearly on whether this other evidence was systematically reviewed or not.

Author's conclusions

See the Cochrane Handbook, chapter 4.5 and chapter 12.

The purpose of the review is to present information rather than to offer advice to readers: therefore the purpose of the conclusions or implications sections of the review is to present the overall findings of the review, <u>not</u> to make recommendations.

Implications for practice

The implications for practice should be as practical and unambiguous as possible. They should not go beyond the evidence that was reviewed, nor should they selectively report particular results based on the findings. Provide an overall summary of the quality of the evidence and the balance between benefits and harms (and costs) found by the review.

When writing this section, keep in mind what can and cannot be said from the data (evidence) in the review.

Implications for research

The implications for research aim to highlight those areas of research that are most needed, so that readers can make well-informed decisions about future research. Do not include vague statements such as 'more research is needed'. State exactly what research is needed, why and how urgently. Opinions on how the review might be improved with additional data or resources might also be included here.

When writing this section, it can be helpful to distinguish between _how_ future research should be done (eg RCTs in preference to other study designs, more comprehensive assessment of outcomes); and _what_ future research should be done (_ie_ based on gaps in the evidence in the review eg the need for head-to-head comparisons between interventions, or more research in specific populations or settings).

When writing this section, keep in mind what can and cannot be said based on the data in the review: information that has not been discussed previously should not make a first appearance here.

A format for structuring research recommendations (known as EPICOT; Brown 2006) is outlined below. You should, at a minimum, attempt to describe the PICO elements that should be investigated in future research, and if possible, also suggest particular study designs that would best suit the research.

- **E** (Evidence): What is the current evidence?
- **P** (Population): Diagnosis, disease stage, co-morbidity, risk factor, sex, age, ethnic group, specific inclusion or exclusion criteria, clinical setting;
- **I** (Intervention): Type, frequency, dose, duration, prognostic factors;
- **C** (Comparison): Placebo, routine care, alternative treatment/management;
- **O** (Outcome): Which clinical or patient-related outcomes will the researcher need to measure, improve, influence or accomplish? Which methods of measurement should be used?
- **T** (Time stamp): Date of literature search or recommendation.

Also consider the impact of any identified ongoing studies or those awaiting assessment and how these may affect the implications for research, bearing in mind that systematic reviewers need to be mindful of research waste.

Acknowledgements

Refer to the [Cochrane Handbook](#) chapter 4.5.

Acknowledge here any people or organisations that you wish. This would include any previous authors of the Cochrane protocol or review or previous sources of support to the review. Obtain permission from persons acknowledged. We encourage you to acknowledge the contribution of the Cochrane Consumers and Communication Review Group editors and staff.

> We thank the editors and staff of the Cochrane Consumers and Communication Review Group, particularly our contact editor [Name] for their input to this protocol. We thank XXXX…

If you have obtained independent statistical advice for your review, we suggest you include the statistician as a review author (rather than listing them in the Acknowledgements section).

Contribution of authors

Refer to the [Cochrane Handbook](#) chapter 4.5.

Describe the contributions of the co-authors to the protocol and review here. Identify which author is the guarantor of the review. All authors should discuss and agree on their respective contribution descriptions. Outline who will be responsible for conducting any update of the review.

Declarations of interest

Refer to the [Cochrane Handbook](#) chapter 2 and chapter 4.5.

If there are no conflicts of interest, state this explicitly, eg 'None known'.

Report any present or past affiliations or other involvement in any organisation or entity with an interest in the review that might lead to a real or perceived conflict of interest. It is impossible to abolish all conflict of interest, since the only person who does not have some vested interest in a subject is somebody who knows nothing about it at all, and who cannot be affected in any way. However, any interest that could unduly influence judgments in a review (such as deciding which studies can stay in, or what the results mean) needs to be declared.

Financial conflicts of interest in particular need to be declared. This includes 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.

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 that was included in the review, and how this was managed (eg that author was not be involved in assessing the study for inclusion, or extracting or analysing data from that study).

Ensure that the conflicts of interest reported here reflect the Declaration of Interest forms completed in Archie by each author.

Differences between protocol and review

Refer to the [Cochrane Handbook](#) chapter 4.5.

Methods that were planned at protocol stage but not applied (for instance, because no trials were found, or results were not pooled) should summarised briefly here, and the protocol cited.

Describe any other methods departing from those described in the original protocol here.

Published Notes

'This review draws on standard text and guidance provided by the Cochrane Consumers and Communication Review Group (CCCRG 2013b).'

Sources of support

Describe sources of funding (or in-kind support) for the review and what each source supported.

Tables

See the [Cochrane Handbook](#), chapter 4.6 and the Group's Data Extraction Template (http://cccrg.cochrane.org/author-resources).

Characteristics of included studies:

See the [Cochrane Handbook](#), chapters 4.6.1 and 11.2.

The 'Characteristics of included studies' table has five rows for each study: Methods, Participants, Interventions, Outcomes and Notes. Up to three further rows 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.

Subheadings 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 in the 'Participants' section. Authors can use codes or abbreviations, with footnotes used to explain these. The codes or abbreviations must be used consistently.

Authors can use additional tables (see below) to present further detailed information, for example, on interventions, outcomes or other aspects of included studies important to the review findings.

For ideas on how to organise the Characteristics of included studies tables and Additional tables, referring to published Consumers and Communication Group reviews may be useful.

'Risk of bias' table:

See the [Cochrane Handbook](#) chapters 4.6.2 and 8.6.

A 'Risk of bias' table is an extension of the 'Characteristics of included studies' table. The standard 'Risk of bias' table includes assessments for sequence generation, allocation sequence concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and 'other sources of bias'.

For each item, the authors provide a subjective judgement (low risk, unclear, high risk) and describe what was reported to have happened in the study (ie for information supporting the subjective judgement). Direct quotations from the studies can be used to support the judgement; while a comment is your interpretation of what was done/reported by the study and a judgement about whether the study is at risk of bias. It is highly desirable to provide to source information (eg through a direct quote from the study) on which the judgement is based. If judgements are based on information that is not readily publicly available (eg through author contact) this should be stated.

Do not leave cells blank. If no information is available from a study about a particular aspect of risk of bias (eg no details about allocation concealment) then there should be a statement about this (eg 'not reported'). Where details about the risk of bias are not reported by a study, this can be an important issue to raise with the study authors in author contact and when requesting further information about the study for the review.

'Other' sources of bias category:

Only use this category to capture specific aspects of study design that are clearly associated with bias, that is, that are able to change the size of the effect estimate, not its precision. Examples include contamination or baseline imbalances between groups (see the *Cochrane Handbook* section 8.15). In other cases there may be design-specific sources of bias that may need to be considered. For example, for cluster RCTs, it may be appropriate to report selective recruitment of cluster participants as an additional domain under this heading, and to consider adding other sources of bias (see the *Cochrane Handbook* section 16.3.2).

Do not assess aspects of conduct of the study, such as those associated with the 'quality' of a study in this domain. This might include aspects of the study such as ethical criteria (eg whether the study explicitly sought informed consent or obtained ethics approval), criteria related to precision of the study (eg use of a power calculation), reporting standards or other issues such as whether the validity and/or reliability of outcome measures was addressed.

What is captured in this domain in the review should be identified in the tables and in the methods, for example by using subheadings within the table if more than one aspect of other sources of bias is to be considered.

Characteristics of excluded studies:

See the [Cochrane Handbook](#) chapter 4.6.3.

Certain studies that may appear to meet the eligibility criteria, but which were excluded at the full-text stage of screening should be listed, and the reason for exclusion should be given (for example,

inappropriate comparator intervention, not an RCT). Keep this brief: a single reason for exclusion is usually sufficient. Reasons should be consistent and should match the inclusion/ exclusion criteria outlined under the 'Criteria for considering studies for this review' section.

Characteristics of ongoing studies:

See the [Cochrane Handbook](#) chapter 4.6.5.

This table has eight rows 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'. Use footnotes to explain any abbreviations used here. Report as many details under these fields as are available. Also consider whether these studies may be useful to consider and refer to in the Implications for research section.

Characteristics of studies awaiting classification:

This table reports any potentially relevant studies that might be eligible for inclusion in the review, but have not yet been incorporated. This is irrespective of whether the study is published or not. Any known details about these studies should be reported here, and you should also consider in the discussion that the impact of not including these studies may be a limitation of the review, and they may also affect the Implications for research.

Summary of findings

See the [Cochrane Handbook](#) chapters 4.6.6, 11.5, 12.2, and the 'Summary of Findings' Quick Guide at http://cccrg.cochrane.org/author-resources

See also Guyatt et al 2012 GRADE guidelines 12. Preparing Summary of Findings tables – binary outcomes. Journal of Clinical Epidemiology, available at http://www.gradeworkinggroup.org/index.htm

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 list of all important outcomes (benefits as well as harms), up to a maximum of seven

- a measure of the typical (baseline) burden of these outcomes (eg control group risk)

- a measure of the risk in the intervention group

- the relative size of the effect (eg risk or odd ratios)

- numbers of participants and studies addressing each outcome

- a rating of overall confidence in the effect estimates for each outcome (ie a measure of the quality of the evidence for each) – based on the GRADE framework (which combines considerations of risk of bias, directness, heterogeneity, precision and publication bias).

- comments and footnotes supporting the information presented in the tables.

PLEASE NOTE: 'Summary of findings' tables have a particular meaning within Cochrane reviews; they are <u>not</u> generic tables summarising the included studies' results. There are very clear guidelines on developing these tables. For more information and assistance with creating a 'Summary of findings' table for a review, contact the Managing Editor (m.prictor@latrobe.edu.au) in the first instance.

Additional tables

See the Cochrane Handbook chapters 4.6.7, 11.6.

Additional tables may be used for information that cannot be conveniently placed in the text or in fixed tables. Additional tables should generally be reserved for information that is highly relevant to the text of the review but cannot be easily slotted in elsewhere – such as tables of additional data or summaries of study characteristics (eg. detailed descriptions of interventions or outcomes).

In comparison, appendices are generally reserved for information that more generally supports the review, such as search strategies, information supporting the background, and so on.

Authors may choose to report details of author contact in an additional table (eg providing study ID, author contact successful, author replied, asked for additional information, additional information or data supplied by study author), or in an appendix or other table.

Studies and references

See the Cochrane Handbook, chapter 4.7 and the Style Guide.

Enter reference information in the appropriate Cochrane style; if this is not done we may return the review to you for correction.

Ensure that all studies and references are linked within the review text (by using 'ctrl+L'. Running a validation report to help you identify gaps in reference information.

References to studies are organised under four fixed headings (Included studies, Excluded studies, Studies awaiting classification, Ongoing studies). A study can have multiple references and these must appear together, with one being designated as the primary reference in the list.

You must also assign each study to a 'data source' category. In RevMan this can be done as follows:

- o Right click on the reference
- o Go to 'Edit study'
- o From the drop-down menu select the appropriate category:
  - Published data only (unpublished data not sought)
  - Published and unpublished data.
  - Unpublished data only.
  - Published data only (unpublished sought but not used).

A list of common references is found at the end of this document.

Data and analysis

For detailed guidance on analysis refer to the Cochrane Handbook, chapter 4.8 and chapter 9.

Results of studies included in a review are organised in a hierarchy: studies are nested within (optional) subgroups, which are nested within outcomes, which are nested within comparisons. 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.

Avoid listing comparisons or outcomes for which there are no data (ie have forest plots with no studies). Instead, 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.

Add links to relevant data and analyses graphs in the main text.

If forest plots are included in the review:

- the axes should be re-labelled from the automatically generated 'experimental' and 'control' labels to more specific labels that reflect the comparisons under investigation (ie with more specific intervention and comparison names)

- the direction of effects across forest plots should be used as consistently as possible within a review for ease of interpretation.

Figures

See the Cochrane Handbook, chapter 4.9.

Six different types of figures can be included in Cochrane reviews:

1. RevMan study flow diagram (PRISMA template) (see Cochrane Handbook chapter 11, especially 11.3.2)
2. RevMan forest plots (see Handbook chapter 11, especially 11.3.2)
3. RevMan funnel plots (see Handbook chapter 10, especially 10.4)
4. RevMan 'Risk of bias' graphs (see Handbook chapter 8, especially 8.6)
5. RevMan 'Risk of bias' summaries (see Handbook chapter 8, especially 8.6)
6. Other figures (see Handbook section 4.9.2)

All figures included in the review must be referred to in the text of the review.

Appendices

All search strategies need to be listed in full, for each database searched, in the appendices (one search strategy per appendix). These should be cut and paste so they are presented exactly as they were run.

You may also use the appendices to present other supplementary information not included in the additional tables or elsewhere in the review. Link appendices to the relevant sections of the main text.

Common References

How to cite this document in RevMan:

Reference ID: CCCRG 2016b
Reference Type: Other

Authors   Cochrane Consumers and Communication Review Group
English Title: Standard Review Text and Additional Guidance for Review Authors.
Journal/Book/Source: http://cccrg.cochrane.org
Date of Publication: 2016

How to cite the *Cochrane Handbook* in RevMan:

Reference ID: Higgins 2011
Reference Type: Other

Authors: Higgins JPT, Green S (editors)
English Title: Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011
Journal/Book/Source: Available from www.cochrane-handbook.org

How to cite **Liberati 2009** in RevMan:

Reference ID: Liberati 2009
Reference Type: Journal article

Authors: Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al
English Title: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration
Journal/Book/Source: PLoS Medicine
Date of Publication: 2009
Volume: 6
Pages: e1000100

How to cite the **RevMan software** in RevMan:

Reference ID: RevMan 2012
Reference type: Computer program
English title: Review Manager (RevMan)
Date of publication: 2012
Edition: 5.2
Publisher name: The Nordic Cochrane Centre, The Cochrane Collaboration
City of publication: Copenhagen

How to cite **Ryan 2013** in RevMan:

Reference ID: Ryan 2013
Reference Type: Other

Authors: Ryan R, Hill S, Prictor M, McKenzie J; Cochrane Consumers and Communication Review Group
English title: Study Quality Guide
Date of Publication: May 2013
Journal/book/source: http://cccrg.cochrane.org/authorresources (accessed *DATE*).

How to cite **Schünemann 2011** in RevMan:

Reference ID: Schünemann 2011
Reference Type: Other

Authors: Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Guyatt GH
English Title: Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of

Interventions Version 5.1.0 [updated March 2011]. The Cochrane
Collaboration, 2011

Journal/Book/Source: Available from www.cochrane-handbook.org.

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