Methodological Expectations of Cochrane Intervention Reviews (MECIR)

Standards for the *conduct* and *reporting* of new Cochrane Intervention Reviews 2012

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THE COCHRANE COLLABORATION®

Preface

Cochrane Reviews are seen as exemplifying best practice in the quality of both their conduct and reporting. To maintain this position we need to improve and maintain the quality of our output as standards and expectations for systematic reviews increase generally; we also need to ensure consistency across all Cochrane Review Groups (CRGs) and all reviews. To this end we have undertaken within The Cochrane Collaboration to define Methodological Expectations for Cochrane Intervention Reviews (MECIR).

The documents associated with the MECIR project form a major step forward aimed at ensuring that both researchers and editorial teams have a shared understanding of the expectations of conduct and reporting for reviews in the *Cochrane Database of Systematic Reviews* (CDSR).

The standards in this booklet summarize attributes of the conduct of reviews of interventions described in the *Cochrane Handbook* that we have established should be either Mandatory* or highly desirable** for new Cochrane Reviews. Also here are standards that summarize attributes of reporting that we consider should be either Mandatory or highly desirable for new Cochrane Intervention Reviews. The judgments are accompanied by a rationale and reference to the appropriate section of the *Cochrane Handbook*. Additional standards for new protocols and considerations for updates will be addressed. There is a separate project that has clarified expectations for plain language summaries led by the Consumer Network with support from the MECIR Co-ordinating team. Please see separate booklet.

Please note some minor amendments have been made to the standards since the previous booklet V1: C24, C25, C33, C35, C44, C76 R36, R38, R105, and R108.

In order to provide the user with a succinct and relevant document, the methodology of a review should be reported in such a way that links the methods directly to the results of the present version of the review. Thus, details of methods that were planned in the protocol but were not implemented should generally be reported in the dedicated section for differences between the protocol and the review, or in an appendix.

The Cochrane Collaboration has adopted recommendations provided in the PRISMA statement [http://www.prisma-statement.org/]. We believe the reporting standards will ensure compliance with these recommendations. Some items have been included specifically to enable this (e.g. the standard relating to mentioning that the review has a published protocol). Extensions to the PRISMA statement may also be relevant to particular reviews, such as reviews addressing equity issues [http://equity.cochrane.org/equity-extension-prisma].

The ordering of the standards reflects the position in which each issue might be expected to be addressed in the main text of the review. In some items we have specified where things should be reported (e.g. for contents of the table of 'Characteristics of included studies'). For other items, review authors should consider whether information should be reported in the main text, in tables, figures or appendices.

We have described the process for determining the expectations for conducting and reporting of Cochrane Reviews of interventions, including the methods used to develop the initial list and the management of all feedback received during the consultation process (see: www.editorial-unit.cochrane.org/mecir). This booklet is a draft format and comments are welcome, please contact jchandler@cochrane.org.

Finally, I want to pay tribute to my colleagues who have contributed to this work so far. Julian Higgins and Rachel Churchill have led this initiative with great expertise, perseverance and energy. An important feature of this project, at all levels, has been to reflect the importance of CRG teams and methodologists working alongside one another. Rachel and Julian have been supported by Jackie Chandler and Toby Lasserson, both of whom have made major contributions. In addition, scores of people from within the Collaboration either contributed to the working groups, without which we would have had no 'long-list' of proposed expectations to build on, or the consultation that succeeded the working groups. Additionally, I thank invited external stakeholders for comments received on a draft set of reporting standards. I hope that the Collaboration recognises the efforts of all the individuals involved and the true sense of collaboration that the work has engendered.

David Tovey, Editor in Chief of *The Cochrane Library*

Status: *Mandatory means that a new review should not be published if this is not reported.
****Highly desirable means that this should generally be done, but that there are justifiable exceptions.**

To cite these Methodological Expectations of Cochrane Intervention Reviews (MECIR) please see citation at the beginning of each section.

Methodological Expectations of Cochrane Intervention Reviews (MECIR)

Standards for the **conduct** of new Cochrane Intervention Reviews 2012 V2.3

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Setting the research question(s) to inform the scope of the review

Standard	Rationale and elaboration
C1 Formulating review questions	**Mandatory**
Ensure that the review question and particularly the outcomes of interest, address issues that are important to stakeholders such as consumers, health professionals and policy makers.	Cochrane reviews are intended to support clinical practice and policy, not just scientific curiosity. The needs of consumers play a central role in Cochrane Reviews and they can play an important role in defining the review question. Qualitative research, i.e. studies that explore the experience of those involved in providing and receiving interventions, and studies evaluating factors that shape the implementation of interventions, might be used in the same way. See *Handbook* 2.3.2, 2.3.4, 17.2, 20.2.2
C2 Pre-defining objectives	**Mandatory**
Define in advance the objectives of the review, including participants, interventions, comparators and outcomes.	Objectives give the review focus and must be clear before appropriate eligibility criteria can be developed. If the review will address multiple interventions, clarity is required on how these will be addressed (e.g. summarized separately, combined or explicitly compared). See *Handbook* 5.1.1
C3 Considering potential adverse effects	**Mandatory**
Consider any important potential adverse effects of the intervention(s) and ensure that they are addressed.	It is important that adverse effects are addressed in order to avoid one-sided summaries of the evidence. At a minimum, the review will need to highlight the extent to which potential adverse effects have been evaluated in any included studies. Sometimes data on adverse effects are best obtained from non-randomized studies, or qualitative research studies. This does not mean however that all reviews must include non-randomized studies. See *Handbook* 5.4.3, 14.1.1, 14.3
C4 Considering equity and specific populations	**Highly desirable**
Consider in advance whether issues of equity and relevance of evidence to specific populations are important to the review, and plan for appropriate methods to address them if they are. Attention should be paid to the relevance of the review question to populations such as low socioeconomic groups, low or middle income regions, women, children and older people.	Where possible reviews should include explicit descriptions of the effect of the interventions not only on the whole population but also describe their effect upon the disadvantaged and/or their ability to reduce socio-economic inequalities in health and to promote their use to the community.

Setting eligibility criteria for including studies in the review

Standard	Rationale and elaboration
C5 Pre-defining unambiguous criteria for participants	**Mandatory**
Define in advance the eligibility criteria for participants in the studies.	Pre-defined, unambiguous eligibility criteria are a fundamental pre-requisite for a systematic review. The criteria for considering types of people included in studies in a review should be sufficiently broad to encompass the likely diversity of studies, but sufficiently narrow to ensure that a meaningful answer can be obtained when studies are considered in aggregate. Considerations when specifying participants include setting, diagnosis or definition of condition and demographic factors. Any restrictions to study populations must be based on a sound rationale, since it is important that Cochrane reviews are widely relevant. See *Handbook* 5.2
C6 Pre-defining a strategy for studies with a subset of eligible participants	**Highly desirable**
Define in advance how studies that include only a subset of relevant participants will be handled.	Sometimes a study includes some 'eligible' participants and some 'ineligible' participants, for example when an age cut-off is used in the review's eligibility criteria. In case data from the eligible participants cannot be retrieved, a mechanism for dealing with this situation should be pre-specified. See *Handbook* 5.2
C7 Pre-defining unambiguous criteria for interventions and comparators	**Mandatory**
Define in advance the eligible interventions and the interventions against which these can be compared in the included studies.	Pre-defined, unambiguous eligibility criteria are a fundamental pre-requisite for a systematic review. Specification of comparator interventions requires particular clarity: are the experimental interventions to be compared with an inactive control intervention (e.g. placebo, no treatment, standard care, or a waiting list control), or with an active control intervention (e.g. a different variant of the same intervention, a different drug, a different kind of therapy)? Any restrictions on interventions and comparators, such as regarding delivery, dose, duration, intensity, co-interventions and features of complex interventions should also be pre-defined and explained. See *Handbook* 5.3
C8 Clarifying role of outcomes	**Mandatory**
Clarify in advance whether outcomes listed under 'Criteria for considering studies for this review' are used as criteria for including studies (rather than as a list of the outcomes of interest within whichever studies are included).	Outcome measures typically should not always form part of the criteria for including studies in a review. However, some reviews do legitimately restrict eligibility to specific outcomes. For example, the same intervention may be studied in the same population for different purposes (e.g. hormone replacement therapy, or aspirin); or a review may address specifically the adverse effects of an intervention used for several conditions. If authors do exclude studies on the basis of outcomes, care should be taken to ascertain that relevant outcomes are not available because they have not been measured rather than simply not reported. See *Handbook* 5.1.2
C9 Pre-defining study designs	**Mandatory**
Define in advance the eligibility criteria for study designs in a clear and unambiguous way, with a focus on features of a study's design rather than design labels.	Pre-defined, unambiguous eligibility criteria are a fundamental pre-requisite for a systematic review. This is particularly important when non-randomized studies are considered. Some labels commonly used to define study designs can be ambiguous. For example a "double blind" study may not make it clear who is blind; a "case control" study may be nested within a cohort, or be undertaken in a cross-sectional manner; or a "prospective" study may have only some features defined or undertaken prospectively. See *Handbook* 5.5, 13.2.2

C10 Including randomized trials	Mandatory
Include randomized trials as eligible for inclusion in the review, *if they are feasible for the interventions and outcomes of interest.*	Randomized trials are the best study design for evaluating the efficacy of interventions. If they are feasible for evaluating questions that are being addressed by the review, they must be considered eligible for the review. However, appropriate exclusion criteria may be put in place, for example regarding length of follow-up. See *Handbook* 5.5, 13.1.3
C11 Justifying choice of study designs	Mandatory
Justify the choice of eligible study designs.	It might be difficult to address some interventions or some outcomes in randomized trials. Authors should be able to justify why they have chosen either to restrict the review to randomized trials or to include non-randomized studies. The particular study designs included should be justified with regard to appropriateness to the review question and with regard to potential for bias. See *Handbook* 13.1.2, 13.2.1.3
C12 Excluding studies based on publication status	Mandatory
Include studies irrespective of their publication status, unless explicitly justified.	Obtaining and including data from unpublished studies (including grey literature) can reduce the effects of publication bias. However, the unpublished studies that can be located may be an unrepresentative sample of all unpublished studies. See *Handbook*
C13 Changing eligibility criteria	Mandatory
Justify any changes to eligibility criteria or outcomes studied. In particular, *post hoc* decisions about inclusion or exclusion of studies should keep faith with the objectives of the review rather than with arbitrary rules.	Following pre specified eligibility criteria is a fundamental attribute of a systematic review. However unanticipated issues may arise. Review authors should make sensible *post hoc* decisions about exclusion of studies, and these should be documented in the review, possibly accompanied by sensitivity analyses. Changes to the protocol must not be made on the basis of the findings of the studies or the synthesis as this can introduce bias. See *Handbook* 5.2, 5.7

Selecting outcomes to be addressed for studies included in the review

Standard	Rationale and elaboration
C14 Pre-defining outcomes	Mandatory
Define in advance which outcomes are primary outcomes and which are secondary outcomes.	Pre-definition of outcome reduces the risk of selective outcome reporting. The *primary outcomes* should be as few as possible and should normally reflect at least one potential benefit and at least one potential area of harm. It is expected that the review should be able to synthesize these outcomes if eligible studies are identified, and that the conclusions of the review will be based in large part on the effects of the interventions on these outcomes. See *Handbook* 5.4.2
C15 Choosing outcomes	Highly desirable
Keep the total number of outcomes selected for inclusion in the review as small as possible. Choose outcomes that are relevant to stakeholders such as consumers, health professionals and policy makers. Avoid trivial outcomes and biochemical, interim and process outcomes, but consider the importance of resource-use outcomes.	Cochrane reviews are intended to support clinical practice and policy, and should address outcomes that are important to consumers. These should be specified at protocol stage. Where they are available, established sets of core outcomes should be used. Patient-reported outcomes should be included where possible. It is also important to judge whether evidence on resource use and costs might be an important component of decisions to adopt the intervention or alternative management strategies around the world. Large numbers of outcomes, while sometimes necessary, can make reviews unfocussed, unmanageable for the user, and prone to selective outcome reporting bias. See *Handbook* 5.4.2

C16	Pre-defining outcome details	Highly desirable
Define in advance details of what are acceptable outcome measures (e.g. diagnostic criteria, scales, composite outcomes).	Having decided what outcomes are of interest to the review, authors should clarify acceptable ways in which these outcomes can be measured. It may however be difficult to pre-define adverse effects. See *Handbook* 5.4.1	
C17	Pre-defining choices from multiple outcome measures	Highly desirable
Define in advance how outcome measures will be selected when there are several possible measures (e.g. multiple definitions, assessors or scales).	Pre-specification guards against selective outcome reporting, and allows users to confirm that choices were not overly influenced by the results. A pre-defined hierarchy of outcomes measures may be helpful. It may however be difficult to pre-define adverse effects. A rationale should be provided for the choice of outcome measure. See *Handbook* 5.4.1	
C18	Pre-defining time points of interest	Highly desirable
Define in advance the timing of outcome measurement.	Pre-specification guards against selective outcome reporting, and allows users to confirm that choices were not overly influenced by the results. Authors may consider whether all time frames or only selected time-points will be included in the review. These decisions should be based on outcomes important for making healthcare decisions. One strategy to make use of the available data could be to group time-points into pre-specified intervals to represent 'short-term', 'medium-term' and 'long-term' outcomes and to take no more than one from each interval from each study for any particular outcome. See *Handbook* 5.4.1	

Planning the review methods at protocol stage

Standard		Rationale and elaboration
C19	Planning the search	Mandatory
Plan in advance the methods to be used for identifying studies. Design searches to capture as many studies as possible meeting the eligibility criteria, ensuring that relevant time periods and sources are covered and not restricting by language or publication status.		Searches should be motivated directly by the eligibility criteria for the review, and it is important that all types of eligible studies are considered when planning the search. There is a possibility of publication bias and/or language bias (whereby the language of publication is selected in a way that depends on the findings of the study) if searches are restricted by publication status or by language of publication. Removing language restrictions in English-language databases is not a good substitute for searching non-English language journals and databases. See *Handbook* 6.3, 6.4
C20	Planning the assessment of risk of bias in included studies	Mandatory
Plan in advance the methods to be used for assessing risk of bias in included studies, including the tool(s) to be used, how the tool(s) will be implemented, and the criteria used to assign studies, for example, to judgements of low risk, high risk and unclear risk of bias.		Pre-defining the methods and criteria for assessing risk of bias is important since analysis or interpretation of the review findings may be affected by the judgements made during this process. For randomized trials, the Cochrane risk of bias tool is Mandatory, so it is sufficient (and easiest) simply to refer to the definitions of low risk, unclear risk and high risk of bias provided in the *Cochrane Handbook*. See *Handbook* 8.3
C21	Planning the synthesis of results	Mandatory

Plan in advance the methods to be used to synthesize the results of the included studies, including whether a quantitative synthesis is planned, how heterogeneity will be assessed, choice of effect measure (e.g. odds ratio, risk ratio, risk difference or other for dichotomous outcomes), and methods for meta-analysis (e.g. inverse variance or Mantel Haenszel, fixed-effect or random-effects model).	Pre-defining the synthesis methods, particularly the statistical methods, is important since analysis or interpretation of the review findings may be affected by the judgements made during this process. See *Handbook* 9.1.2
C22 Planning the subgroup analyses	**Mandatory**
Pre-define potential effect modifiers (e.g. for subgroup analyses) at the protocol stage; restrict these in number; and provide rationale for each.	Pre-specification reduces the risk that large numbers of undirected subgroup analyses lead to spurious explanations of heterogeneity See *Handbook* 9.6.5
C23 Planning a 'Summary of findings' table	**Mandatory**
Plan in advance the methods to be used for summarizing the findings of the review, including the assessment of the quality of the body of evidence. If a formal 'Summary of findings' table is anticipated, specify which outcomes will be included, and which comparisons and subgroups will be covered (if appropriate).	Methods for 'Summary of findings' tables should be pre-defined, particularly with regard to choice of outcomes, to guard against selective presentation of results in the review. The table should include the essential outcomes for decision making (typically up to seven), which should generally not include surrogate or interim outcomes. These outcomes should not be chosen on the basis of any anticipated or observed magnitude of effect, or because they are likely to have been addressed in the studies to be reviewed. See *Handbook* 11.5

Searching for studies

Standard	Rationale and elaboration
C24 Planning the search	**Mandatory**
Search the Cochrane Review Group's Specialized Register (internally, e.g. via the Cochrane Register of Studies, or externally via CENTRAL). Ensure that CENTRAL, MEDLINE (e.g. via PubMed) and Embase, if it is available to either the CRG or the review author, have been searched (either for the review or for the Review Group's Specialized Register).	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. The minimum databases to be covered are the Cochrane Review Group's Specialized Register (if it exists and was designed to support reviews in this way), CENTRAL, MEDLINE and Embase, if it is available to either the CRG or the review author. Expertise may be required to avoid unnecessary duplication of effort. Some, but not all, reports of eligible studies from MEDLINE, Embase and the Cochrane Review Groups' Specialized Registers are already included in CENTRAL. Supplementary searches should be performed as described in sections 6.3.2 and 6.3.3 of the *Cochrane Handbook*.
C25 Searching specialist bibliographic databases	**Highly desirable**
Search appropriate national, regional and subject specific bibliographic databases.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. Databases relevant to the review topic should be covered (e.g CINAHL for nursing-related topics, PsychINFO for psychological interventions), and regional databases (e.g. LILACS) should be considered. See *Handbook* 6.2.1.4, 6.2.1.5, 6.4.1
C26 Searching for different types of evidence	**Mandatory**
If the review has specific eligibility criteria around study design to address adverse effects, economic issues or qualitative research questions, undertake searches to address them.	Sometimes different searches will be conducted for different types of evidence, such as for non-randomized studies for addressing adverse effects, or for economic evaluation studies. See *Handbook* 13.3, 14.5, 15.3, 20.3.2.1
C27 Searching trials registers	**Mandatory**

Search trials registers and repositories of results, where relevant to the topic through ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) portal and other sources as appropriate.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. Although ClinicalTrials.gov is included as one of the registers within the WHO ICTRP portal, it is recommended that both ClinicalTrials.gov and the ICTRP portal are searched separately due to additional features in ClinicalTrials.gov. See *Handbook* 6.2.3.1, 6.2.3.2, 6.2.3.3
C28 Searching for grey literature	**Mandatory**
Search relevant grey literature sources such as reports/dissertations/theses databases and databases of conference abstracts.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. See *Handbook* 6.2.1.7, 6.2.1.8, 6.2.2
C29 Searching within other reviews	**Highly desirable**
Search within previous reviews on the same topic.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. See *Handbook* 6.2.2.5
C30 Searching reference lists	**Mandatory**
Check reference lists in included studies and any relevant systematic reviews identified.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. See *Handbook* 6.2.2.5
C31 Searching by contacting relevant individuals and organisations	**Highly desirable**
Contact relevant individuals and organisations for information about unpublished or ongoing studies.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible. It is important to identify ongoing studies, so that when a review is later updated these can be assessed for possible inclusion. See *Handbook* 6.2.3
C32 Structuring search strategies for bibliographic databases	**Mandatory**
Inform the structure of search strategies in bibliographic databases around the main concepts of the review, using appropriate elements from PICO and study design. In structuring the search, maximize sensitivity whilst striving for reasonable precision. Ensure correct use of the AND and OR operators.	Inappropriate or inadequate search strategies may fail to identify records that are included in bibliographic databases. Expertise may need to be sought, in particular from the Cochrane Review Group's Trials Search Coordinator. The structure of a search strategy should be based on the main concepts being examined in a review. In general databases, such as MEDLINE, a search strategy to identify studies for a Cochrane Review will typically have three sets of terms: 1) terms to search for the health condition of interest, i.e. the population; 2) terms to search for the intervention(s) evaluated; and 3) terms to search for the types of study design to be included (typically a 'filter' for randomized trials). There are exceptions, however. For instance, for reviews of complex interventions, it may be necessary to search only for the population or the intervention. Within each concept, terms are joined together with the Boolean 'OR' operator, and the concepts are combined with the Boolean 'AND' operator. The 'NOT' operator should be avoided where possible to avoid the danger of inadvertently removing from the search set records that are relevant. See *Handbook* 6.4.2, 6.4.4, 6.4.7
C33 Developing search strategies for bibliographic databases	**Mandatory**

Identify appropriate controlled vocabulary (e.g. MeSH, Emtree, including 'exploded' terms) and free-text terms (considering, for example, spelling variants, synonyms, acronyms, truncation and proximity operators).	Inappropriate or inadequate search strategies may fail to identify records that are included in bibliographic databases. Search strategies need to be customized for each database. It is important that MeSH terms are 'exploded' wherever appropriate, in order not to miss relevant articles. The same principle applies to Emtree when searching Embase and also to a number of other databases. The controlled vocabulary search terms for MEDLINE and Embase are not identical, and neither is the approach to indexing. In order to be as comprehensive as possible, it is necessary to include a wide range of free-text terms for each of the concepts selected. This might include the use of truncation and wildcards. Developing a search strategy is an iterative process in which the terms that are used are modified, based on what has already been retrieved. See *Handbook* 6.4.5, 6.4.6, 6.4.8

C34 Using search filters	**Highly desirable**
Use specially designed and tested search filters where appropriate including the Cochrane Highly Sensitive Search Strategies for identifying randomized trials in MEDLINE, but do not use filters in pre-filtered databases e.g. do not use a randomized trial filter in CENTRAL or a systematic review filter in DARE.	Inappropriate or inadequate search strategies may fail to identify records that are included in bibliographic databases. Search filters should be used with caution. They should be assessed not only for the reliability of their development and reported performance but also for their current accuracy, relevance and effectiveness given the frequent interface and indexing changes affecting databases. See *Handbook* 6.4.11, 6.4.2, 13.3.1.2, 14.5.2, 15.3.1, 17.5, 20.3.2.1

C35 Restricting database searches	Mandatory
Justify the use of any restrictions in the search strategy on publication date, publication format.	Date restrictions in the search should only be used when there are date restrictions in the eligibility criteria for studies. They should be applied only if it is known that relevant studies could only have been reported during a specific time period, for example if the intervention was only available after a certain time point. Searches for updates to reviews might naturally be restricted by date of entry into the database (rather than date of publication) to avoid duplication of effort. Publication format restrictions (e.g. exclusion of letters) should generally not be used in Cochrane reviews, since any information about an eligible study may be of value. See *Handbook* 6.4.9
C36 Documenting the search process	Mandatory
Document the search process in enough detail to ensure that it can be reported correctly in the review.	The search process (including the sources searched, when, by whom, and using what terms) needs to be documented in enough detail throughout the process to ensure that it can be reported correctly in the review, to the extent that all the searches of all the databases are reproducible. See *Handbook* 6.6.1
C37 Rerunning searches	Mandatory
Rerun or update searches for all relevant databases within 12 months before publication of the review or review update, and screen the results for potentially eligible studies.	The published review should be as up to date as possible. The search must be rerun close to publication, if the initial search date is more than 12 months (preferably 6 months) from the intended publication date, and the results screened for potentially eligible studies. Ideally the studies should be fully incorporated. If not, then the potentially eligible studies will need to be reported, at a minimum as a reference under 'Studies awaiting classification' or 'Ongoing studies'.
C38 Incorporating findings from rerun searches	Highly desirable
Incorporate fully any studies identified in the rerun or update of the search within 12 months before publication of the review or review update.	The published review should be as up to date as possible. After the rerun of the search, the decision whether to incorporate any new studies fully into the review will need to be balanced against the delay in publication.

Selecting studies into the review

Standard	Rationale and elaboration
C39 Making inclusion decisions	Mandatory
Use (at least) two people working independently to determine whether each study meets the eligibility criteria, and define in advance the process for resolving disagreements.	Duplicating the study selection process reduces both the risk of making mistakes and the possibility that selection is influenced by a single person's biases. The inclusion decisions should be based on the full texts of potentially eligible studies when possible, usually after an initial screen of titles and abstracts. It is desirable, but not Mandatory, that two people undertake this initial screening, working independently. See *Handbook* 7.2.4
C40 Excluding studies without useable data	Mandatory
Include studies in the review irrespective of whether measured outcome data are reported in a 'usable' way.	Systematic reviews typically should seek to include all relevant participants who have been included in eligible study designs of the relevant interventions and had the outcomes of interest measured. Reviews must not exclude studies solely on the basis of *reporting* of the outcome data, since this may introduce bias due to selective outcome reporting. While such studies cannot be included in meta-analyses, the implications of their omission should be considered. Note that studies may legitimately be excluded because outcomes were not *measured*. Furthermore, issues may be different for adverse effects outcomes, since the pool of studies may be much larger and it can be difficult to assess whether such outcomes were measured. See *Handbook* 5.4.1

C41 Documenting decisions about records identified	**Mandatory**
Document the selection process in sufficient detail to complete a PRISMA flow chart and a table of 'Characteristics of excluded studies'.	A PRISMA flow chart and a table of 'Characteristics of excluded studies' will need to be completed in the final review. Decisions should therefore be documented for all records identified by the search. Numbers of records are sufficient for exclusions based on initial screening of titles and abstracts. Broad categorizations are sufficient for records classed as potentially eligible during an initial screen. Studies listed in the table of 'Characteristics of excluded studies' should be those which a user might reasonably expect to find in the review. At least one explicit reason for their exclusion must be documented. Authors will need to decide for each review when to map records to studies (if multiple records refer to one study). Lists of included and excluded studies must be based on studies rather than records. See *Handbook* 6.6.1*, 11.2.1*
C42 Collating multiple reports	**Mandatory**
Collate multiple reports of the same study, so that each study rather than each report is the unit of interest in the review.	It is wrong to consider multiple reports of the same study as if they are multiple studies. Secondary reports of a study should not be discarded, however, since they may contain valuable information about the design and conduct. Review authors must choose and justify which report to use as a source for study results. See *Handbook* 7.2.1, 7.2.2, 7.6.4

Collecting data from included studies

Standard	Rationale and elaboration
C43 Using data collection forms	**Mandatory**
Use a data collection form, which has been piloted.	Review authors often have different backgrounds and level of systematic review experience. Using a data collection form ensures some consistency in the process of data extraction, and is necessary for comparing data extracted in duplicate. The completed data collection forms should be available to the CRG on request. Piloting the form within the review team is highly desirable. At minimum, the data collection form (or a very close variant of it) must have been assessed for usability. See *Handbook* 7.5
C44 Describing studies	**Mandatory**
Collect characteristics of the included studies in sufficient detail to populate a table of 'Characteristics of included studies'.	Basic characteristics of each study will need to be presented as part of the review, including details of participants, interventions and comparators, outcomes and study design. Details of funding source for each study and the declarations of interest for the primary investigators should also be collected during this process. See *Handbook* 7.3, 11.2
C45 Extracting study characteristics in duplicate	**Highly desirable**
Use (at least) two people working independently to extract study characteristics from reports of each study, and define in advance the process for resolving disagreements.	Duplicating the data extraction process reduces both the risk of making mistakes and the possibility that data selection is influenced by a single person's biases. Dual data extraction may be less important for study characteristics than it is for outcome data, so it is not a Mandatory standard for the former. See *Handbook* 7.6.2, 7.6.5
C46 Extracting outcome data in duplicate	**Mandatory**
Use (at least) two people working independently to extract outcome data from reports of each study, and define in advance the process for resolving disagreements.	Duplicating the data extraction process reduces both the risk of making mistakes and the possibility that data selection is influenced by a single person's biases. Dual data extraction is particularly important for outcome data, which feed directly into syntheses of the evidence and hence to conclusions of the review. See *Handbook* 7.6.2

C47 Making maximal use of data	**Mandatory**
Collect and utilize the most detailed numerical data that might facilitate similar analyses of included studies. Where 2×2 tables or means and standard deviations are not available, this might include effect estimates (e.g. odds ratios, regression coefficients), confidence intervals, test statistics (e.g. t, F, Z, chi-squared) or P values, or even data for individual participants.	Data entry into RevMan is easiest when 2×2 tables are reported for dichotomous outcomes, and when means and standard deviations are presented for continuous outcomes. Sometimes these statistics are not reported but some manipulations of the reported data can be performed to obtain them. For instance, 2×2 tables can often be derived from sample sizes and percentages, while standard deviations can often be computed using confidence intervals or P values. Furthermore, the inverse-variance data entry format can be used even if the detailed data required for dichotomous or continuous data are not available, for instance if only odds ratios and their confidence intervals are presented. The RevMan calculator facilitates many of these manipulations. See *Handbook* 7.7
C48 Examining errata	**Highly desirable**
Examine any relevant retraction statements and errata for information.	Some studies may have been found to be fraudulent or may for other reasons have been retracted since publication. Errata can reveal important limitations, or even fatal flaws, in included studies. All of these may potentially lead to the exclusion of a study from a review or meta-analysis. Care should be taken to ensure that this information is retrieved in all database searches by downloading the appropriate fields together with the citation data. See *Handbook* 6.4.10
C49 Obtaining unpublished data	**Highly desirable**
Seek key unpublished information that is missing from reports of included studies.	Contacting study authors to obtain or confirm data makes the review more complete, potentially enhancing precision and reducing the impact of reporting biases. Missing information includes details to inform 'Risk of bias' assessments, details of interventions and outcomes, and study results (including breakdowns of results by important subgroups). See *Handbook* 7.4.2
C50 Choosing intervention groups in multi-arm studies.	**Mandatory**
If a study is included with more than two intervention arms, include in the review only intervention and control groups that meet the eligibility criteria.	There is no point including irrelevant intervention groups in the review. Authors should however make it clear in the 'Table of characteristics of included studies' that these intervention groups were present in the study. See *Handbook* 16.5.2
C51 Checking accuracy of numeric data in the review.	**Mandatory**
Compare magnitude and direction of effects reported by studies with how they are presented in the review, taking account of legitimate differences.	This is a reasonably straightforward way for authors to check a number of potential problems, including typographical errors in studies' reports, accuracy of data collection and manipulation, and data entry into RevMan. For example, the direction of a standardized mean difference may accidentally be wrong in the review. A basic check is to ensure the same qualitative findings (e.g. direction of effect and statistical significance) between the data as presented in the review and the data as available from the original study. Results in forest plots should agree with data in the original report (point estimate and confidence interval) if the same effect measure and statistical model is used.

Assessing risk of bias in included studies

Standard	Rationale and elaboration
C52 Assessing risk of bias	**Mandatory**
Assess the risk of bias for each included study. For randomized trials, the Cochrane 'Risk of bias' tool should be used, involving judgements and supports for those judgements across a series of domains of bias, as described in Chapter 8 of the Cochrane Handbook (version 5 or later).	The risk of bias of every included study in a Cochrane review must be explicitly considered to determine the extent to which its findings can be believed, noting that risks of bias might vary by outcome. Recommendations for assessing bias in randomized studies included in Cochrane Reviews are now well-established. The new tool – as described in the *Cochrane Handbook* – must be used for all randomized trials in new reviews and all newly included randomized trials in updated reviews. This does not prevent other tools being used. The discussions in Chapters 8 and 13 of the Cochrane Handbook should be used to inform the selection of an appropriate tool for non-randomized studies. See *Handbook* 8.5, 8.9, 8.10, 8.11, 8.12, 8.13, 8.14, 8.15*
C53 Assessing risk of bias in duplicate	**Mandatory**
Use (at least) two people working independently to apply the risk of bias tool to each included study, and define in advance the process for resolving disagreements.	Duplicating the risk of bias assessment reduces both the risk of making mistakes and the possibility that assessments are influenced by a single person's biases. See *Handbook* 7.6.2, 8.3.4
C54 Supporting judgements of risk of bias	**Mandatory**
Justify judgements of risk of bias (high, low and unclear) and provide this information in the 'Risk of bias' tables (as 'Support for judgement').	Providing support for the judgement makes the process transparent. Items which are judged to be at an unclear risk of bias but without accompanying information supporting the judgment appear as empty cells in the graphical plots based on the risk of bias tool in the published review. See *Handbook* 8.5.1, 8.5.2
C55 Providing sources of information for risk of bias assessments	**Highly desirable**
Collect the source of information for each risk of bias judgement (e.g. quotation, summary of information from a trial report, correspondence with investigator etc).Where judgements are based on assumptions made on the basis of information provided outside publicly available documents, this should be stated.	Readers/editors/referees should have the opportunity to see for themselves where supports for judgments have been obtained. See *Handbook* 8.5.2
C56 Differentiating between performance bias and detection bias.	**Highly desirable**
Consider separately the risks of bias due to lack of blinding for (i) participants and study personnel (performance bias), and (ii) outcome assessment (detection bias).	The use of mutually exclusive domains of bias (e.g. selection bias, performance bias, detection bias, attrition bias and reporting bias) provides a more comprehensive framework for considering biases in randomized trials. The changes to RevMan in March 2011 made this framework a more central part of the process than it was previously. See *Handbook* 8.5.1, 8.11.1*, 8.12.1*
C57 Assessing risk of bias due to lack of blinding for different outcomes	**Highly desirable**
Consider blinding separately for different key outcomes.	The risk of bias due to lack of blinding may be different for different outcomes (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different from that for a patient-reported pain scale). When there are multiple outcomes, they should be grouped (e.g. objective versus subjective). See *Handbook* 8.5.1, 8.11.2, 8.12.2*

C58	Assessing completeness of data for different outcomes	**Highly desirable**
Consider the impact of missing data separately for different key outcomes to which an included study contributes data.	When considering risk of bias due to incomplete (missing) outcome data, this often cannot reliably be done for the study as a whole. The risk of bias due to missing outcome data may be different for different outcomes. For example, there may be less drop-out for a three-month outcome than for a six-year outcome. When there are multiple outcomes, they should be grouped (e.g. short term versus long term). Judgements should be attempted about which outcomes are thought to be at high or low risk of bias. See *Handbook* 8.5.1	
C59	Summarizing risk of bias assessments	**Highly desirable**
Summarize the risk of bias for each key outcome for each study.	This reinforces the link between the characteristics of the study design and their possible impact on the results of the study, and is an important pre-requisite for the GRADE approach to assessing the quality of the body of evidence. See *Handbook* 8.7	
C60	Addressing risk of bias in the synthesis	**Highly desirable**
Address risk of bias in the synthesis (whether qualitative or quantitative). For example, present analyses stratified according to summary risk of bias, or restricted to studies at low risk of bias.	Review authors should consider how study biases affect conclusions. This is useful in determining the strength of conclusions and how future research should be designed and conducted. See *Handbook* 8.8	
C61	Incorporating assessments of risk of bias	**Mandatory**
If randomized trials have been assessed using one or more tools in addition to the Cochrane 'Risk of bias' tool, use the Cochrane tool as the primary assessment of bias for interpreting results, choosing the primary analysis, and drawing conclusions.	For consistency of approach across Cochrane reviews, the Cochrane risk of bias tool should take precedence when two or more tools are used. The Cochrane tool also feeds directly into the GRADE approach for assessing the quality of the body of evidence. See *Handbook* 8.5	

Synthesizing the results of included studies

Standard		Rationale and elaboration
C62	Combining different scales	**Mandatory**
If studies are combined with different scales, ensure that higher scores for continuous outcomes all have the same meaning for any particular outcome; explain the direction of interpretation; and report when directions were reversed.	Sometimes scales have higher scores that reflect a 'better' outcome and sometimes lower scores reflect 'better' outcome. Meaningless (and misleading) results arise when effect estimates with opposite clinical meanings are combined See *Handbook* 9.2.3.2	
C63	Ensuring meta-analyses are meaningful	**Mandatory**
Undertake (or display) a meta-analysis only if participants, interventions, comparisons and outcomes are judged to be sufficiently similar to ensure an answer that is clinically meaningful.	Meta-analyses of very diverse studies can be misleading, for example of studies using different forms of control. Clinical diversity does not necessarily indicate that a meta-analysis should not be performed. However, authors must be clear about the underlying question that all studies are addressing. See *Handbook* 9.1.4	

C64 Assessing statistical heterogeneity	**Mandatory**
Assess the presence and extent of between-study variation when undertaking a meta-analysis.	The presence of heterogeneity affects the extent to which generalizable conclusions can be formed. It is important to identify heterogeneity in case there is sufficient information to explain it and offer new insights. Authors should recognise that there is much uncertainty in measures such as I-squared and tau-squared when there are few studies. Thus, use of simple thresholds to diagnose heterogeneity should be avoided. See *Handbook* 9.5.2
C65 Addressing missing outcome data	**Highly desirable**
Consider the implications of missing outcome data from individual participants (due to losses to follow up or exclusions from analysis).	Incomplete outcome data can introduce bias. In most circumstances, authors should follow the principles of intention to treat analyses as far as possible (this may not be appropriate for adverse effects or if trying to demonstrate equivalence). Risk of bias due to incomplete outcome data is addressed in the Cochrane risk of bias tool. However, statistical analyses and careful interpretation of results are additional ways in which the issue can be addressed by review authors. Imputation methods can be considered (accompanied by, or in the form of, sensitivity analyses). See *Handbook* 16.2
C66 Addressing skewed data	**Highly desirable**
Consider the possibility and implications of skewed data when analysing continuous outcomes.	Skewed data are sometimes not usefully summarized by means and standard deviations. While statistical methods are approximately valid for large sample sizes, skewed outcome data can lead to misleading results when studies are small. See *Handbook* 9.4.5.3
C67 Addressing studies with more than two groups	**Mandatory**
If multi-arm studies are included, analyse multiple intervention groups in an appropriate way that avoids arbitrary omission of relevant groups and double-counting of participants.	Excluding relevant groups decreases precision and double counting increases precision spuriously; both are inappropriate and unnecessary. Alternative strategies include combining intervention groups, separating comparisons into different forest plots and using multiple treatments meta-analysis. See *Handbook* 7.7.3.8, 16.5.4
C68 Comparing subgroups	**Mandatory**
If subgroup analyses are to be compared, and there are judged to be sufficient studies to do this meaningfully, use a formal statistical test to compare them.	Concluding that there is a difference in effect in different subgroups on the basis of differences in the level of statistical significance within subgroups can be very misleading See *Handbook* 9.6.3.1
C69 Interpreting subgroup analyses	**Mandatory**
If subgroup analyses are conducted, follow the subgroup analysis plan specified in the protocol without undue emphasis on particular findings.	Selective reporting, or over-interpretation, of particular subgroups or particular subgroup analyses should be avoided. This is especially a problem when multiple subgroup analyses are performed. This does not preclude the use of sensible and honest post hoc sub group analyses. See *Handbook* 9.6.5.2
C70 Considering statistical heterogeneity when interpreting the results	**Mandatory**
Take into account any statistical heterogeneity when interpreting the results, particularly when there is variation in the direction of effect.	The presence of heterogeneity affects the extent to which generalizable conclusions can be formed. If a fixed-effect analysis is used, the confidence intervals ignore the extent of heterogeneity. If a random-effects analysis is used, the result pertains to the mean effect across studies. In both cases, the implications of notable heterogeneity should be addressed. It may be possible to understand the reasons for the heterogeneity if there are sufficient studies. See *Handbook* 9.5.4

C71 Addressing non-standard designs	**Mandatory**
Consider the impact on the analysis of clustering, matching or other non-standard design features of the included studies.	Cluster-randomized trials, cross-over trials, studies involving measurements on multiple body parts, and other designs need to be addressed specifically, since a naive analysis might underestimate or overestimate the precision of the study. Failure to account for clustering is likely to overestimate the precision of the study - i.e. to give it confidence intervals that are too narrow and a weight that is too large. Failure to account for correlation is likely to underestimate the precision of the study - i.e. to give it confidence intervals that are too wide and a weight that is too small. See *Handbook* 9.3, 16.3, 16.4
C72 Sensitivity analysis	**Highly desirable**
Use sensitivity analyses to assess the robustness of results, such as the impact of notable assumptions, imputed data, borderline decisions and studies at high risk of bias.	It is important to be aware when results are robust, since the strength of the conclusion may be strengthened or weakened. See *Handbook* 9.7
C73 Interpreting results	**Mandatory**
Interpret a statistically non-significant P value (e.g. larger than 0.05) as a finding of uncertainty unless confidence intervals are sufficiently narrow to rule out an important magnitude of effect.	Authors commonly mistake a lack of evidence of effect as evidence of a lack of effect. See *Handbook* 12.4.2, 12.7.4
C74 Investigating reporting biases	**Highly desirable**
Consider the potential impact of reporting biases on the results of the review or the meta-analyses it contains.	There is overwhelming evidence of reporting biases of various types. These can be addressed at various points in the review. A thorough search, and attempts to obtain unpublished results, might minimize the risk. Analyses of the results of included studies, for example using funnel plots, can sometimes help determine the possible extent if the problem, as can attempts to identify study protocols, which should be a more routine feature of a review. See *Handbook* 10.1, 10.2

Summarizing the findings

Standard	Rationale and elaboration
C75 Including a 'Summary of Findings' table	**Highly desirable**
Include a 'Summary of Findings' table according to recommendations described in Chapter 11 of the Cochrane Handbook (version 5 or later). Specifically: • include results for one population group (with few exceptions); • indicate the intervention and the comparison intervention; • include seven or fewer patient-important outcomes; • describe the outcomes (e.g. scale, scores, follow-up); • indicate the number of participants and studies for each outcome; • present at least one baseline risk for each dichotomous outcome (e.g. study population or median/medium risk) and baseline scores for continuous outcomes (if appropriate); • summarize the intervention effect (if appropriate); and • include a measure of the quality of the body of evidence.	These are standards which should be consistently applied across reviews. Authors should justify why a 'Summary of Findings' table is not included if this is the case. See *Handbook* 11.5
C76 Assessing the quality of the body of evidence	**Mandatory**
Use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome, and to draw conclusions about the quality of evidence within the text of the review.	GRADE is the most widely used system for summarising confidence in effects of the interventions by outcome across studies. It is preferable to use the GRADE tool (as implemented in GRADEprofiler and described in the help system of the software). This should help to ensure that author teams are accessing the same information to inform their judgments. Ideally, two people working independently should assess the quality of the body of evidence. The five GRADE considerations should be addressed irrespective of whether the review includes a 'Summary of Findings' table See *Handbook* 12.2
C77 Justifying assessments of the quality of the body of evidence	**Mandatory**
Justify and document all assessments of the quality of the body of evidence (for example downgrading or upgrading if using the GRADE tool).	By adopting a structured approach, transparency is ensured in showing how interpretations have been formulated and the result is more informative to the reader. See *Handbook* 12.2.1

Reaching conclusions

Standard	Rationale and elaboration
C78 Formulating implications for practice	**Mandatory**
Base conclusions only on findings from the synthesis (quantitative or narrative) of studies included in the review.	The conclusions of the review should convey the essence of the synthesis of included studies, without selective reporting of particular findings on the basis of the result, and without drawing on data that were not systematically compiled and evaluated as part of the review. See *Handbook* 12.7.4

C79	Avoiding recommendations	Mandatory
Avoid providing recommendations for practice.		Cochrane reviews should not attempt to tell people which interventions should or should not be used, since local considerations may be relevant. However, the implications of the findings should be discussed, and decision-making can be helped by laying out different scenarios. See *Handbook* 12.7.2
C80	Formulating implications for research	Highly desirable
Structure the implications for research to address the nature of evidence required, including population intervention comparison, outcome, and type of study.		Anyone wishing to conduct a study in the topic area of the review should be provided with a clear sense of what the remaining uncertainties are. A useful framework for considering implications for research is EPICOT (evidence, population, intervention, comparison, outcome and time stamp). See *Handbook* 12.7.3

*These Handbook section numbers are specific to Version 5.1.
All other section numbers apply equally to the 2008 edition (and 2009 reprints) published by Wiley-Blackwell.

Methodological Expectations of Cochrane Intervention Reviews (MECIR)

Standards for the **reporting** of new Cochrane Intervention Reviews 2012 V.1.2

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Title and Authors

Standard		Rationale and elaboration
R1	Format of title	**Highly desirable**
Follow the standard template for a Cochrane review title.		See *Handbook* Table 4.2.a.
R2	Authors	**Mandatory**
List names and affiliations of all authors		See *Handbook* 4.2.2.

Abstract

Standard		Rationale and elaboration
R3	Writing the abstract	**Mandatory**
Prepare a structured abstract to provide a succinct summary of the review. In the interests of brevity it is highly desirable for authors to provide an abstract of less than 700 words, and it should be no more than 1000 words in length.		Abstracts are a prominent, publically accessible summary of the review. They should convey key information about the review question and its findings, and be informative to readers. [PRISMA item 2]
R4	Abstract, Background	**Mandatory**
Summarize the rationale and context of the review.		See *Handbook* 11.8
R5	Abstract, Objectives	**Mandatory**
State the main objective(s), preferably in a single concise sentence		The objective(s) should be expressed in terms that relate to the population(s), intervention comparison(s) and, where appropriate, outcomes of interest. See *Handbook* 11.8
R6	Abstract, Search methods	**Mandatory**
Provide the date of the last search from which records were evaluated and any studies identified were incorporated into the review, and an indication of the databases and other sources searched.		Abstracts should aim to give readers brief but key information about the comprehensiveness of the search and the currency of the information summarised by the review. The abstract must include the month and year of the set of searches up to which the conclusions of the review are valid. This date should reflect the date of the most recent set of searches from which all records have been screened for relevance and any studies meeting the eligibility criteria have been fully incorporated into the review (studies may be awaiting classification if, for example, the review authors are awaiting translation or clarification from authors or sponsors). Abstracts do not need to report on recent repeat or 'catch-up' searches whose results have not been fully incorporated into the review. However, discretion should be applied if such searches identify a large body of evidence whose absence from the review findings may affect the reliability of the conclusions. The amount of information regarding the search should be indicative of the process rather than provide specific details. In the interests of brevity certain details regarding the overall process may need to be moved to the full text of the review. Example: "CENTRAL, MEDLINE, Embase, five other databases and three trials registers were searched on [date] together with reference checking, citation searching and contact with study authors to identify additional studies".

R7	Abstract, Selection criteria	Mandatory
Summarize eligibility criteria of the review, including information on study design, population and comparison.	Any extensions to eligibility criteria to address adverse effects, economic issues or qualitative research should be mentioned.	

R8	Abstract, Data collection and analysis	Mandatory
Summarize any noteworthy methods for selecting studies, collecting data, evaluating risk of bias and synthesizing findings. For many reviews it may be sufficient to state "We used standard methodological procedures expected by The Cochrane Collaboration."	This section of the abstract should indicate the rigour of the methods that underpin the results reported subsequently in the abstract. It does not need to replicate detailed description of the methods in the main text of the review. Details of how many people were involved in the screening process and collection of information about any included studies are not necessary in the abstract. Key statistical methods may be given if not clear from the results that follow. The abstract should prioritize the disclosure of non-standard approaches. For example, rather than disclosing all domains applied in the assessment of bias, notable variations on the standard approach should be given, such as non-standard tools that were used.	

R9	Abstract, Main results: number of studies and participants	Mandatory
Report the number of included studies and participants.	The total number of included studies should be stated. It might be appropriate to provide numbers of studies and participants for specific comparisons and main outcomes if the amount of evidence differs substantially from the total. Numbers of participants *analysed* should generally be presented in preference to numbers *recruited* (e.g. randomized); more important is to be clear which numbers are being reported. For some types of data there may be preferable alternatives to the number of participants (e.g. person-years of follow-up, number of limbs).	

R10	Abstract, Main results: study characteristics	Highly desirable
Provide a brief description of key characteristics that will determine the applicability of the body of evidence (e.g. age, severity of condition, setting, study duration).	Summarizing the study characteristics will provide readers of the abstract with important information about the applicability of the included studies. This is particularly important if the included studies reflect a subgroup of those eligible for inclusion in the review, for example, if the review intended to address the effects of interventions across all age groups, but included studies that only recruited adolescents.	

R11	Abstract, Main results: bias assessment	Mandatory
Provide a comment on the findings of the bias assessment.	The risk of bias assessments are a key finding and form a fundamental part of the strength of the conclusions drawn in the review. If risks of bias differ substantially for different comparisons and outcomes, this may need to be mentioned.	

R12	Abstract, Main results: findings	Mandatory
Report findings for all primary outcomes, irrespective of the strength and direction of the result, and of the availability of data.	Findings should typically include concise information about the quality of the body of evidence for the outcome (such as study limitations, consistency of effect, imprecision, indirectness and publication bias), for example using GRADE. Outcomes should not be selected solely on the basis of the findings. If no studies measured the primary outcomes, then a comment should be made to that effect.	

R13	Abstract, Main results: adverse effects	Mandatory
Ensure that any findings related to adverse effects are reported. If adverse effects data were sought, but availability of data was limited, this should be reported.	The abstract of the review should aim to reflect a balanced summary of the benefits and harms of the intervention. See *Handbook* 11.8	

R14	Abstract, Main results: format of numerical results	Mandatory
Present summaries of statistical analyses in the same way as they are reported in the review and in a standard way, ensuring that readers will understand the direction of benefit and the measurement scale used, and that confidence intervals are included where appropriate.	The standard format for reporting the results of statistical analysis includes an indication of the summary measure, point estimate and confidence interval (e.g. odds ratio 0.75 (95% confidence interval 0.62 to 0.89)).	
R15	Abstract, Main results: interpretability of findings	Highly desirable
Ensure that key findings are interpretable, or are re-expressed in an interpretable way. For instance, they might be re-expressed in absolute terms (e.g. assumed and corresponding risks, NNTs, group means), and outcomes combined with a standardized scale (e.g. SMD) might be re-expressed in units that are more naturally understood.	Absolute effects provide a useful illustration of the likely impact of intervention, and are usually easier to understand than relative effects. Units expressed on a standardized scale reflect the effect estimate as the number of standard deviations. This is not intuitive to many readers who may be more familiar with specific scales. Any re-expressed findings must have been presented in the same way in the main text of the review (see previous standard).	
R16	Abstract, Authors' conclusions	Mandatory
State key conclusions drawn.	Authors' conclusions may include both implications for practice and implications for research. Care must be taken to avoid interpreting lack of evidence of effect as evidence of lack of effect (See *Handbook* 12.7.4). *Recommendations* for practice should be avoided (See *Handbook* 11.8).	
R17	Completeness of main review text	Mandatory
Ensure that all findings reported in the abstract and plain language summary, including re-expressions of meta-analysis results, also appear in the main text of the review.	See *Handbook* 11.8 and 11.9	
R18	Consistency of summary versions of the review	Mandatory
Ensure that reporting of objectives, important outcomes, results, caveats and conclusions is consistent across the text, the abstract, the plain language summary and the 'Summary of findings' table (if included).	Summary versions of the review should be written on the assumption that they are likely to be read in isolation from the rest of the review.	

Background

Standard		Rationale and elaboration
R19	Background	Mandatory
Provide a concise description of the condition or problem addressed by the review question, definition of the intervention and how it might work, and why it is important to do the review.		Systematic reviews should have a clearly defined and well-reasoned rationale which has been developed in the context of existing knowledge. Outlining the context of the review question is useful to readers and helps to establish key uncertainties that the review intends to address. [PRISMA item 3]
R20	Background headings	Highly desirable
Include the four standard headings when writing the Background.		Four standard headings are included in RevMan ('Description of the condition', 'Description of the intervention', 'How the intervention might work', and 'Why it is important to do this review'). See *Handbook* 4.5

R21	Background references	Mandatory
Back up all key supporting statements with references.	Claims or statements regarding aspects such as disease burden, morbidity, prevalence and mechanisms of action should be substantiated and, where available, supported by external evidence.	
R22	Background text	Mandatory
Avoid the use of plagiarized text.	Unacknowledged copying from the work of other people is not acceptable. There may however be situations in which the same text appears in different reviews, for example when the reviews are prepared by the same team. A formal policy on plagiarism in Cochrane reviews is in development. Content that is identical to, drawn or copied from standard texts may be acceptable but must be referenced. Ensure any verbatim quotations of more than a few words are shown in quotation marks and clearly acknowledge (i.e. cite) all sources.	
R23	Main objective	Mandatory
State the main objective, where appropriate in a single concise sentence.	The primary objective of a Cochrane review should be to assess the effects of one or more healthcare interventions on stakeholder-important outcomes, both intended and unintended. The objective should be expressed in terms that relate to the population(s), intervention comparison(s) and, where appropriate to specify explicitly, the outcomes of interest. Stakeholders may be patients, carers, policy makers, clinicians or others. *MECIR conduct standard 2* (Define in advance the objectives of the review, including participants, interventions, comparators and outcomes.) Where possible, the format should be of the form "To assess the effects of *[intervention or comparison]* for *[health problem]* for/in *[types of people, disease or problem and setting if specified]*". [PRISMA item 4]	
R24	Secondary objectives	Highly desirable
State explicitly (as secondary objectives) any specific questions being addressed by the review, such as those relating to particular participant groups, intervention comparisons or outcomes.	The objectives should be expressed in terms that relate to the population(s), intervention comparison(s) and, where appropriate, outcomes of interest. *MECIR conduct standard 4* (Consider in advance whether issues of equity and relevance of evidence to specific populations are important to the review, and plan for appropriate methods to address them if they are. Attention should be paid to the relevance of the review question to populations such as low socioeconomic groups, low or middle income regions, women, children and older people.)	
R25	Economic evidence	Mandatory
If health economics evidence is being reviewed, state this explicitly in the Objectives (as secondary objectives).	The primary aim of a Cochrane review should be to assess the effects of one or more healthcare interventions on stakeholder-important outcomes, both intended and unintended. These outcomes may include economic outcomes. If health economics evidence is being reviewed as an integrated economics component (see Handbook section 15.2.3), this should be stated as a secondary objective.	
R26	Qualitative research evidence	Mandatory
If qualitative research evidence is being reviewed, state this explicitly in the Objectives (as secondary objectives).	The primary aim of a Cochrane review should be to assess the effects of one or more healthcare interventions on stakeholder-important outcomes, both intended and unintended. If qualitative research evidence is being included to 'extend' the review (see *Handbook* section 20.2.1), this should be stated as a secondary objective.	

Methods

Standard		Rationale and elaboration
R27	Reference protocol	**Highly desirable**
Cite the protocol for the review.		The reader should be made aware that the review is based on a published protocol. This is particularly important if the review has been split into multiple reviews since the protocol was published. Since the protocol is usually no longer included in the CDSR once the review is published, it should be cited using the last publication citation for the protocol. Archived versions of protocols can be accessed via the current version of the review. [PRISMA item 5]

Criteria for considering studies for this review

Standard		Rationale and elaboration
R28	Eligibility criteria for types of study: study designs	**Mandatory**
State eligible study designs, and provide a justification for the choice.		It is not necessary to explain why randomized trials are eligible (if that is the case), although it may be important to explain the eligibility or non-eligibility of other types of study. *MECIR conduct standard 9* (Define in advance the eligibility criteria for study designs in a clear and unambiguous way, with a focus on features of a study's design rather than design labels.) *MECIR conduct standard 11* (Justify the choice of eligible study designs.) [PRISMA item 6]
R29	Eligibility criteria for types of study: study reports	**Mandatory**
If studies are excluded on the basis of publication status or language of publication, explain and justify this.		Studies should be included irrespective of their publication status and language of publication, unless explicitly justified. *MECIR conduct standard 12* (Include studies irrespective of their publication status, unless explicitly justified.) [PRISMA item 6]
R30	Eligibility criteria for types of participants	**Mandatory**
State eligibility criteria for participants, including any criteria around location, setting, diagnosis or definition of condition and demographic factors, and how studies including subsets of relevant participants are handled.		Any notable restrictions on the eligibility criteria of the review should be given and explained (e.g. exclusion of people under or over a certain age, specific settings of intervention). *MECIR conduct standard 5* (Define in advance the eligibility criteria for participants in the studies.) *MECIR conduct standard 6* (Define in advance how studies that include only a subset of relevant participants will be handled.) [PRISMA item 6]
R31	Eligibility criteria for types of interventions	**Mandatory**
State eligibility criteria for interventions and comparators, including any criteria around delivery, dose, duration, intensity, co-interventions and characteristics of complex interventions.		*MECIR conduct standard 7* (Define in advance the eligible interventions and the interventions against which these can be compared in the included studies.) [PRISMA item 6]

R32 Role of outcomes	Mandatory
If measurement of particular outcomes is used as an eligibility criterion, state and justify this.	Studies should never be excluded from a review solely because no outcomes of interest are *reported*. However, on occasion it will be appropriate to include only studies that *measured* particular outcomes. For example, a review of a multi-component public health intervention promoting healthy lifestyle choices, focussing on reduction in smoking prevalence, might legitimately exclude studies that do not measure smoking rates. *MECIR conduct standard 8* (Clarify in advance whether outcomes listed under 'Criteria for considering studies for this review' are used as criteria for including studies (rather than as a list of the outcomes of interest within whichever studies are included).) [PRISMA item 6]
R33 Outcomes of interest	Mandatory
State primary and secondary outcomes of interest to the review, and define acceptable ways of measuring them.	Explain how multiple variants of outcome measures (e.g. definitions, assessors, scales, time points) are addressed. *MECIR conduct standard 14* (Define in advance which outcomes are primary outcomes and which are secondary outcomes.) Also *MECIR conduct standards 15 – 18*.

Search for methods of identification of studies

Standard	Rationale and elaboration
R34 Search sources	Mandatory
List all sources searched, including: databases, trials registers, web sites and grey literature. Database names should include platform/provider name and dates of coverage; web sites should include full name and URL. State whether reference lists were searched and whether individuals or organizations were contacted.	*MECIR conduct standard 36* (Document the search process in enough detail to ensure that it can be reported correctly in the review.) *Also MECIR conduct standards 24 – 31*. [PRISMA item 7]
R35 Latest searches	Mandatory
Provide the date of the last search and the issue / version number (where relevant) for each database whose results were evaluated and incorporated into the review If a search was re-run prior to publication, the results of which were not incorporated, explain how the results were dealt with and provide the date.	The review should provide the search date from which studies have been retrieved and assessed for inclusion. This is the date up to which the conclusions of the review are valid. It should reflect the date of the most recent set of searches from which all records have been screened for relevance and any studies meeting the eligibility criteria have been fully incorporated into the review (studies may be awaiting classification if, for example, the review authors are awaiting translation or clarification from authors or sponsors). Since the review is likely to have drawn on searches conducted across multiple databases, it is possible that searches were performed on more than one date. The earliest date of the most recent set of searches should be provided in the review text and as the hard-coded date of the last search. The remaining dates for other databases should be reported in an appendix. If a 'catch-up' search was run subsequent to the review being written up, any relevant studies not yet assessed for inclusion should be listed in the section 'Studies awaiting assessment'. *MECIR conduct standard 37* (Rerun or update searches for all relevant databases within 12 months before publication of the review or review update, and screen the results for potentially eligible studies.) *MECIR conduct standard 38* (Incorporate fully any studies identified in the rerun or update of the search within 12 months before publication of the review or review update.) [PRISMA item 7]

R36	Search restrictions	Mandatory
Specify and justify any restrictions placed on the time period covered by the search.	*MECIR conduct standard 35* (Justify the use of any restrictions in the search strategy on publication date, publication format or language.)	

R37	Searches for different types of evidence	Mandatory
If the review has specific eligibility criteria to include additional studies such as studies of adverse effects, health economics evidence or qualitative research evidence, describe search methods for identifying such studies.	Some reviews extend beyond a focus on the effects of healthcare interventions and address specific additional types of evidence. These are discussed in Chapters 14, 15 and 20 of the *Handbook*. *MECIR conduct standard 26* (*If the review has specific eligibility criteria around study design to address adverse effects, economic issues or qualitative research questions*, undertake searches to address them.)	

R38	Search strategies for bibliographic databases	Mandatory
Present the exact search strategy (or strategies) used for each database in an Appendix, including any limits and filters used, so that it could be replicated.	Search strategies that are available elsewhere (e.g. standard methodological filters, or strategies used to populate a specialized register) may be referenced rather than reproduced. Including numbers of hits for each line in the strategy is optional. *MECIR conduct standard 36* (Document the search process in enough detail to ensure that it can be reported correctly in the review.) Also *MECIR conduct standards 32 – 35*. [PRISMA item 8]	

R39	Search strategies for other sources	Highly desirable
Report the search terms used to search any sources other than bibliographic databases (e.g. trials registers, the web), and the dates of the searches.	Some of this information might be best placed in an Appendix. *MECIR conduct standard 36* (Document the search process in enough detail to ensure that it can be reported correctly in the review.)	

Data collection and analysis

Standard		Rationale and elaboration
R40	Inclusion decisions	Mandatory
State how inclusion decisions were made (i.e. from search results to included studies), clarifying how many people were involved and they worked independently.	*MECIR conduct standard 39* (Use (at least) two people working independently to determine whether each study meets the eligibility criteria, and define in advance the process for resolving disagreements.) [PRISMA item 9]	
R41	Data collection process	Mandatory
State how data were extracted from reports of included studies, clarifying how many people were involved (and whether independently), and how disagreements were handled. Describe data collection process for any reports requiring translation.	*MECIR conduct standard 43* (Use a data collection form, which has been piloted.) *MECIR conduct standard 45* (Use (at least) two people working independently to extract study characteristics from reports of each study, and define in advance the process for resolving disagreements.) [PRISMA item 10]	
R42	Requests for data	Highly desirable
Describe attempts to obtain or clarify data from individuals or organizations.	*MECIR conduct standard 49* (Seek key unpublished information that is missing from reports of included studies.) [PRISMA item 10]	
R43	Data items	Mandatory
State the types of information that were sought from reports of included studies.	*MECIR conduct standard 44* (Collect characteristics of the included studies in sufficient detail to populate a table of 'Characteristics of included studies'.) [PRISMA item 11]	

R44	Transformations of data	Mandatory
Explain any transformations of reported data prior to presentation in the review, along with any assumptions made. Explain any procedures for extracting numeric data from graphs.	*MECIR conduct standard 47* (Collect and utilize the most detailed numerical data that might facilitate similar analyses of included studies. Where 2×2 tables or means and standard deviations are not available, this might include effect estimates (e.g. odds ratios, regression coefficients), confidence intervals, test statistics (e.g. t, F, Z, chi-squared) or P values, or even data for individual participants.)	
R45	Missing outcome data	Highly desirable
Explain how missing outcome data were handled.	Describe how assumptions are applied for missing data, e.g. last observation carried forward, or assumptions of particular values such as worst-case or best-case scenarios.	
R46	Tools to assess risk of bias in individual studies	Mandatory
State the tool(s) used to assess risk of bias for included studies, how the tool(s) was implemented, and the criteria used to assign studies, for example, to judgements of low risk, high risk and unclear risk of bias.	If the *Handbook* guidance for undertaking risk of bias assessments was followed in its entirety, then a reference to the *Handbook* is sufficient to provide the criteria used to assign judgements (see Sections 8.9 to 8.15*). Justify any deviations from the tool. *MECIR conduct standard 52* (Assess the risk of bias for each included study. For randomized trials, the Cochrane 'Risk of bias' tool should be used, involving judgements and supports for those judgements across a series of domains of bias, as described in Chapter 8 of the Cochrane Handbook (version 5 or later).) *MECIR conduct standards 53 – 61*. [PRISMA item12]	
R47	Effect measures	Mandatory
State the effect measures used by the review authors to describe effect sizes (e.g. risk ratio, mean difference) in any included studies and/or meta-analyses.		
R48	Quantitative synthesis	Mandatory
Describe any methods for combining results across studies (e.g. meta-analysis, subgroup analysis, meta-regression, sensitivity analysis), including methods for assessing heterogeneity (e.g. I^2, tau-squared, statistical test). Reference the software and command/macro/program used for analyses performed outside of RevMan.	*MECIR conduct standard 63* (Undertake (or display) a meta-analysis only if participants, interventions, comparisons and outcomes are judged to be sufficiently similar to ensure an answer that is clinically meaningful.) *MECIR conduct standard 64* (Assess the presence and extent of between-study variation when undertaking a meta-analysis.) [PRISMA items 12, 13, 14 and 16]	
R49	Addressing risk of bias	Mandatory
Describe how studies with high or variable risks of bias are addressed in the synthesis.	*MECIR conduct standard* 60 (Address risk of bias in the synthesis (whether qualitative or quantitative). For example, present analyses stratified according to summary risk of bias, or restricted to studies at low risk of bias.)	
R50	Non-standard designs	Mandatory
If designs other than individually randomized, parallel-group randomized trials are included, describe any methods used to address clustering, matching or other design features of the included studies.	*MECIR conduct standard 71* (Consider the impact on the analysis of clustering, matching or other non-standard design features of the included studies.)	
R51	Studies with more than two groups	Mandatory
If multi-arm studies are included, explain how they are addressed and incorporated into syntheses.	*MECIR conduct standard 67* (*If multi-arm studies are included*, analyse multiple intervention groups in an appropriate way that avoids arbitrary omission of relevant groups and double-counting of participants.)	

R52	Risk of reporting bias across studies	**Highly desirable**
Describe any methods used for assessing the risk of reporting biases such as publication bias.	[PRISMA item 15]	

R53	Subgroup analyses	**Mandatory**
If subgroup analysis (or meta-regression) was performed, state the potential effect modifiers with rationale for each, stating whether each was defined *a priori* or *post hoc*.	*MECIR conduct standard 22* (Pre-define potential effect modifiers (e.g. for subgroup analyses) at the protocol stage; restrict these in number; and provide rationale for each.) [PRISMA item 16]	

R54	Summary of findings	**Highly desirable**
State any methods for summarizing the findings of the review, including the assessment of the quality of the body of evidence for each outcome.	*MECIR conduct standard 75* (Include a 'Summary of Findings' table according to recommendations described in Chapter 10 of the Cochrane Handbook (version 5 or later). Specifically: •include results for one population group (with few exceptions); •indicate the intervention and the comparison intervention; •include seven or fewer patient-important outcomes; •describe the outcomes (e.g. scale, scores, follow-up); •indicate the number of participants and studies for each outcome; •present at least one baseline risk for each dichotomous outcome (e.g. study population or median/medium risk) and baseline scores for continuous outcomes (if appropriate); •summarize the intervention effect (if appropriate); and •include a measure of the quality of the body of evidence) *MECIR conduct standard 76* (Use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome, and to draw conclusions about the quality of evidence within the text of the review.) [PRISMA item 12]	

Results

Description of studies

Standard		Rationale and elaboration
R55	Flow of studies	**Mandatory**
Provide information on the flow of studies from the number(s) of references identified in the search to the number of studies included in the review, ideally using a flow chart. Clarify how multiple references for the same study relate to the individual studies.		*MECIR conduct standard 41* (Document the selection process in sufficient detail to complete a PRISMA flow chart and a table of 'Characteristics of excluded studies'.) *MECIR conduct standard 42* (Collate multiple reports of the same study, so that each study rather than each report is the unit of interest in the review.) [PRISMA item 17]
R56	Lack of included studies	**Highly desirable**
If a review identifies no eligible studies, restrict the Results section to a description of the flow of studies and any brief comments about reasons for exclusion of studies.		Under 'Risk of bias in included studies' and 'Effects of interventions', state "No study met the eligibility criteria'. Any discussion of evidence not meeting the eligibility criteria of the review should be in the Discussion section.
R57	Excluded studies	**Mandatory**
List key excluded studies and provide justification for each exclusion.		The table of 'Characteristics of excluded studies' is intended as an aid to users rather than a comprehensive list of studies that were identified but not included. List here any studies that a user might reasonably expect to find in the review to explain why it is excluded. See *Handbook* 7.2.5.
R58	Studies awaiting classification	**Highly desirable**
List the characteristics of any studies that have been identified as potentially eligible but have not been incorporated into the review.		Users of the review will be interested to learn of any potentially relevant studies that have been conducted which are known to the review team but have not yet been incorporated in to the review. This will help them to assess the stability of the review findings. These should be listed in the table of 'Characteristics of studies awaiting classification', along with any details that are known.
R59	Ongoing studies	**Mandatory**
Provide details of any identified studies that have not been completed.		Users of the review will be interested to learn of any potentially relevant studies that have not been completed. This will help them to assess the stability of the review findings. These should be listed in the table of 'Characteristics of ongoing studies', along with any details that are known.
R60	Table of 'Characteristics of included studies'	**Mandatory**
Present a table of 'Characteristics of included studies' using a uniform format across all studies.		*MECIR conduct standard 44* (Collect characteristics of the included studies in sufficient detail to populate a table of 'Characteristics of included studies'.) [PRISMA item 18]
R61	Included studies	**Mandatory**
Provide a brief narrative summary of any included studies. This should include the number of participants and a summary of the characteristics of the study populations and settings, interventions, comparators and funding sources.		See *Handbook* 4.5

R62	Table of 'Characteristics of included studies': sample sizes	**Mandatory**
Include the sample size for each included study in the table of 'Characteristics of included studies'.	If sample sizes are available for each intervention group, these should be included. A convenient place is often within the box for Interventions (e.g. inserting "(n=.))" after each listed intervention group.	
R63	Table of 'Characteristics of included studies': methods	**Mandatory**
Provide the basic study design or design features (e.g. parallel group randomized trial, cluster-randomized trial, controlled before and after study).	Even if the review is restricted to one study design, these tables should provide a comprehensive summary of each study. It is important that labels used to describe study designs are clearly defined in the review (see *Handbook* section 13.2). [PRISMA item 18]	
R64	Table of 'Characteristics of included studies': participants	**Mandatory**
Provide sufficient information about the study populations to enable a user of the review to assess the applicability of the review's findings to their own setting.	Information presented in this table should reflect the baseline demographics of the study sample. In addition, it is helpful to state the eligibility criteria of the study. [PRISMA item 18]	
R65	Table of 'Characteristics of included studies': interventions	**Mandatory**
Provide sufficient information to enable users of the review to assess the applicability of the intervention to their own setting, and if possible in a way that allows the intervention to be replicated.	For example, for drug interventions, consider dose, route, frequency, and duration; or for complex interventions, specify the core components of the intervention. Lengthy explanations of interventions should be avoided. Citations to sources of detailed descriptions can be included. [PRISMA item 18]	
R66	Table of 'Characteristics of included studies': outcomes	**Mandatory**
Provide clear and consistent information about outcomes measured (or reported), how they were measured and the times at which they were measured.	It should be clear whether main outcomes of interest in the review were measured in the study.	
R67	Table of 'Characteristics of included studies': dates	**Highly desirable**
Include the dates when the study was conducted in the table of 'Characteristics of included studies'.	If dates are not available then this should be stated (e.g. "Study dates not reported"). [PRISMA item 18]	
R68	Table of 'Characteristics of included studies': funding source	**Mandatory**
Include details of funding sources for the study, where available.	Details of funding sources should be placed in this table rather than as part of the 'Risk of bias' table. Including an extra row in the table of 'Characteristics of included studies' is encouraged.	
R69	Table of 'Characteristics of included studies': declarations of interest	**Mandatory**
Include details of any declarations of interest among the primary researchers.	Declarations of interest should be placed in this table rather than as part of the 'Risk of bias' table. Including an extra row in the table of 'Characteristics of included studies' is encouraged.	

R70	Choice of intervention groups in multi-arm studies.	**Highly desirable**
If a study is included with more than two intervention arms, restrict comments on any irrelevant arms to a brief comment in the table of 'Characteristics of included studies'.	Intervention arms that are not relevant to the review question should not be discussed in detail, although it is useful to clarify (in this table) that such arms were present. *MECIR conduct standard 50* (*If a study is included with more than two intervention arms*, include in the review only intervention and control groups that meet the eligibility criteria.)	
R71	References to included studies	**Mandatory**
List all reports of each included study under the relevant Study ID.	[PRISMA item 18]	

Risk of bias in included studies

Standard		Rationale and elaboration
R72	'Risk of bias' table	**Mandatory**
Present a 'Risk of bias' table for each included study, with judgements about risks of bias, and explicit supports for these judgements.	The 'Risk of bias' table in RevMan should be used, which is an extension of the table of 'Characteristics of included studies'. *MECIR conduct standard 52* (Assess the risk of bias for each included study. For randomized trials, the Cochrane 'Risk of bias' tool should be used, involving judgements and supports for those judgements across a series of domains of bias, as described in Chapter 8 of the Cochrane Handbook (version 5 or later).) Also *MECIR conduct standards 54 – 61*. [PRISMA item 19]	
R73	Summary assessments of risk of bias	**Highly desirable**
Summarize the risk of bias across domains for each key outcome for each included study, and ensure that these are supported by the information presented in the 'Risk of bias' tables.	*MECIR conduct standard 59* (Summarize the risk of bias for each key outcome for each study.) [PRISMA item 22]	
R74	Risk of bias in included studies	**Mandatory**
Provide a brief narrative summary of the risks of bias among the included studies.	It may be helpful to identify any studies considered to be at low risk of bias for particular key outcomes. [PRISMA items 22 and 25]	

Effects of interventions

Standard		Rationale and elaboration
R75	Use of 'Data and analysis' headings	**Mandatory**
Ensure appropriate use of the hierarchy of Comparisons / Outcomes / Subgroups / Study data in the 'Data and analysis' section.	Appropriate use of the hierarchy ensures consistency of structure across reviews. It is confusing for the user if outcomes are listed against the heading 'Comparison' and interventions listed against the heading 'Outcome or subgroup'.	
R76	Presenting data	**Highly desirable**
Ensure that simple summary data for each intervention group, as well as estimates of effect size (comparing the intervention groups), are available for each study for each outcome of interest to the review. These appear by default when dichotomous	Simple summaries such as numbers of events, means and standard deviations should be presented for each treatment group when available. This is achieved primarily by using the 'Data and analyses' section of the review, for dichotomous and continuous outcomes. For other outcomes, these should typically be presented in tables of 'Other data'. When data for each separate intervention group are available for outcomes analysed as 'Generic inverse variance' data, these might be presented in Additional tables.	

or continuous outcome data are analysed within RevMan. [PRISMA item 20]

R77	Number of studies and participants	Mandatory
State how many studies and how many participants contributed data to results for each outcome, along with the proportion of the included studies and recruited participants potentially available for the relevant comparison.	It is unlikely that the same number of studies will contribute data to every outcome of interest. Specific studies may contribute different numbers of participants for different outcomes. Therefore, for each comparison, it is helpful to indicate to readers what proportion of the relevant included studies and recruited participants contribute data to each outcome. Failing to disclose this may be misleading. [PRISMA item 9]	
R78	Source of data	Highly desirable
State the source of all data presented in the review, in particular, whether it was obtained from published literature, by correspondence, from a trials register, from a web-based data repository, etc.	Transparency of data source enables validation or verification of data by others including editors or readers of the review.	
R79	Multiple outcome data	Mandatory
Describe any *post hoc* decisions that might give rise to accusations of selective outcome reporting, for example when there are multiple outcome measures (e.g. different scales), multiple time points or multiple ways of presenting results.	Transparent disclosure of post-hoc decisions will enable readers of the review to assess the credibility of the results of the review for themselves. *MECIR conduct standard 16* (Define in advance details of what are acceptable outcome measures (e.g. diagnostic criteria, scales, composite outcomes).) *MECIR conduct standard 17* (Define in advance how outcome measures will be selected when there are several possible measures (e.g. multiple definitions, assessors or scales)). *MECIR conduct standard 18* (Define in advance the timing of outcome measurement.)	
R80	Ordering of results and 'Data and analysis' section	Highly desirable
Organize results to follow the order of comparisons and outcomes specified in the protocol, following in particular the distinction between primary and secondary outcomes.	Review authors must avoid selectively reporting analysis results in a way that depends on the findings. The best way to achieve this is to follow a well-structured protocol and present results as outlined in that protocol. However, sometimes a pragmatic decision needs to be made that an alternative arrangement is preferable, particularly with regard to comparisons. This choice should be explicitly justified.	
R81	Pre-specified outcomes	Mandatory
Report synthesis results for all pre-specified outcomes, irrespective of the strength or direction of the result. Indicate whether data were not available for outcomes of interest, including whether harms were identified.	To avoid selective outcome reporting (in truth or in perception), the review should address all outcomes specified in the protocol. [PRISMA item 20]	
R82	Statistical uncertainty	Mandatory
Accompany all effect size estimates with a measure of statistical uncertainty (e.g. a confidence interval with a specified level of confidence such as 90%, 95% or 99%).	Confidence intervals are the preferred method for expressing statistical uncertainty. [PRISMA item 20]	
R83	P values	Highly desirable
If reporting P values, provide exact P values (e.g. P = 0.08 rather than P > 0.05).	Effect estimates with confidence intervals are the preferred method of presenting numeric results. P values should not be used as an alternative to confidence intervals and should not be used to divide results into 'significant' or 'non-significant'; exact P values portray the strength of evidence against the null hypothesis. See *Handbook* Section 12.4.2..	
R84	Tables and Figures	Mandatory
Link to each Table and Figure.		

R85	Number of Tables and Figures	**Highly desirable**
Restrict the number of Tables and Figures to a small number to convey key findings without affecting the readability of the review text.	Tables (typically implemented as Additional Tables) and Figures (including RevMan flow charts, RevMan forest plots and imported graphics) may be added to reviews and included in the body of the text. Reviews should try and avoid including more than six such Tables and Figures. Further Tables and Figures can be included as supplementary material (e.g. as 'Data and analysis' forest plots or within appendices).	
R86	Consistency of results	**Mandatory**
Ensure that all statistical results presented in the main review text are consistent between the text and the 'Data and analysis' tables.		
R87	Different scales	**Mandatory**
Explain how studies measuring an outcome of interest using different scales (such as alternative rating scales that measure symptoms or behaviour) were combined, stating whether positive or negative values reflect benefit or harm.	If data from different scales are combined and presented on a standardized scale (such as a standardized mean difference), it is important to clarify that a positive effect size has the same meaning for every study. The direction of benefit or harm must be stated. . *MECIR conduct standard 62* (*If studies are combined with different scales*, ensure that higher scores for continuous outcomes all have the same meaning for any particular outcome; explain the direction of interpretation; and report when directions were reversed.)	
R88	Interpretability of results	**Mandatory**
Ensure that key findings are interpretable, or are re-expressed in an interpretable way. For instance, they might be re-expressed in absolute terms (e.g. assumed and corresponding risks, NNTs, group means), and outcomes combined with a standardized scale (e.g. SMD) might be re-expressed in units that are more naturally understood. If clinically important effect sizes are well understood, these should be provided to aid interpretation.	Absolute effects provide a useful illustration of the likely impact of intervention, and are usually easier to understand than relative effects. They may need to be accompanied, however, with information about assumed baseline risks. Confidence intervals should be presented for NNTs and similar summary measures. Re-expressing relative effects as absolute effects often requires the specification of assumed (e.g. untreated) risks, and the source of these should be provided. Results expressed as standardized mean differences reflect the number of standard deviations' difference between mean responses. This is not intuitive to many readers who may be more familiar with specific scales. Clinically important effect sizes should ideally be specified in the protocol.	
R89	Studies without usable data	**Mandatory**
Comment on the potential impact of studies that apparently measured outcomes but did not contribute data that allowed the study to be included in syntheses.	There is good evidence of selective outcome reporting among clinical trials. Outcomes that are believed to have been measured but are not reported in a usable format may therefore be systematically different from those that are usable, introducing bias. 'Usable' in this sense refers both to incorporation in a meta-analysis and to consideration in non-statistical syntheses of findings. Authors might consider using a table to indicate which studies contribute data to the outcomes of interest in the review. *MECIR conduct standard 40* (Include studies in the review irrespective of whether measured outcome data are reported in a 'usable' way.	
R90	Missing outcome data	**Highly desirable**
Discuss the implications of missing outcome data from individual participants (due to losses to follow up or exclusions from analysis).	*MECIR conduct standard 65* (Consider the implications of missing outcome data from individual participants (due to losses to follow up or exclusions from analysis).)	
R91	Skewed data	**Highly desirable**
Discuss the possibility and implications of skewed data when analysing continuous outcomes.	*MECIR conduct standard 66* (Consider the possibility and implications of skewed data when analysing continuous outcomes)	

R92	Forest plots	Highly desirable
Present data from multiple studies in forest plots (using the 'Data and analyses' structure in RevMan) wherever possible, providing it is reasonable to do so.	Presenting data in forest plots can be useful even if the studies are not combined in a meta-analysis. [PRISMA item 20]	
R93	Multiple subgroup analyses and sensitivity analyses	Highly desirable
If presenting multiple sensitivity analyses or different ways of subgrouping the same studies, present these in summary form (e.g. a single Table or Figure) and not in multiple forest plots.	[PRISMA item 23]	
R94	Labels on plots	Mandatory
Label the directions of effect and the intervention groups in forest plots with the interventions being compared.	By default, RevMan currently uses 'Experimental' and 'Control' as labels. It is helpful to replace these with more specific intervention names, and essential if the ordering is swapped (or for head-to-head comparisons). Directions of effect should be used as consistently as possible within a review.	
R95	Risk of bias across studies	Highly desirable
Present results of the assessment of risk of bias across studies (and across domains) for each key outcome, and state whether this leads to concerns about the validity of the review's findings.	Considerations of risk of bias across studies are required for assessments of the quality of the body of evidence (e.g. using GRADE). [PRISMA item 22]	
R96	Reporting biases	Highly desirable
Present results of any assessment of the potential impact of reporting biases on the review's findings.	*MECIR conduct standard 74* (Consider the potential impact of reporting biases on the results of the review or the meta-analyses it contains.) [PRISMA item 22]	
R97	'Summary of findings' table	Highly desirable
Present a 'Summary of Findings' table according to recommendations described in Chapter 11 of the Cochrane Handbook (version 5 or later). Specifically: include results for one clearly defined population group (with few exceptions); indicate the intervention and the comparison intervention; include seven or fewer patient-important outcomes; describe the outcomes (e.g. scale, scores, follow-up);indicate the number of participants and studies for each outcome; present at least one baseline risk for each dichotomous outcome (e.g. study population or median/medium risk) and baseline scores for continuous outcomes (if appropriate); summarize the intervention effect (if appropriate); and include a measure of the quality of the body of evidence for each outcome.	*MECIR conduct standard 75* (Include a 'Summary of Findings' table according to recommendations described in Chapter 11 of the Cochrane Handbook (version 5 or later). Specifically: •include results for one population group (with few exceptions); •indicate the intervention and the comparison intervention; •include seven or fewer patient-important outcomes; •describe the outcomes (e.g. scale, scores, follow-up); •indicate the number of participants and studies for each outcome; •present at least one baseline risk for each dichotomous outcome (e.g. study population or median/medium risk) and baseline scores for continuous outcomes (if appropriate); •summarize the intervention effect (if appropriate); and •include a measure of the quality of the body of evidence.) [PRISMA item 24]	

R98	Assessments of the quality of the body of evidence	**Mandatory**
Provide justification or rationale for any measures of the quality of the body of evidence for each key outcome. If a 'Summary of findings' table is used, use footnotes to explain any downgrading or upgrading according to the GRADE system.	*MECIR conduct standard 76* (Use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome, and to draw conclusions about the quality of evidence within the text of the review.) *MECIR conduct standard 77* (Justify and document all assessments of the quality of the body of evidence (for example downgrading or upgrading if using the GRADE tool).)	

Discussion

Standard		Rationale and elaboration
R99	Discussion headings	**Highly desirable**
Include the standard headings when writing the Discussion.	Five standard headings are included in RevMan ('Summary of main results', 'Overall completeness and applicability of evidence', 'Quality of the evidence', 'Potential biases in the review process, 'Agreements and disagreements with other studies or reviews'). See *Handbook* 4.5	
R100	Limitations	**Mandatory**
Discuss limitations of the review at study and outcome level (e.g. regarding risk of bias), and at review-level (e.g. incomplete identification of studies, reporting bias).	Review authors must explicitly state the limitations of their review. One aspect that is easily overlooked is that of adverse effects. In particular, if the review methods do not allow for detection of serious and/or rare adverse events, the review authors must explicitly state this as a limitation. *MECIR conduct standard 74* (Consider the potential impact of reporting biases on the results of the review or the meta-analyses it contains.) [PRISMA item 25]	

Authors' conclusions

Standard		Rationale and elaboration
R101	Conclusions: implications for practice	**Mandatory**
Provide a general interpretation of the evidence so that it can inform healthcare or policy decisions. Avoid making recommendations for practice.	*MECIR conduct standard 79* (Avoid providing recommendations for practice.)	
R102	Conclusions: implications for research	**Mandatory**
If recommending further research, structure the implications for research to address the nature of evidence required, including population, intervention comparison, outcome, and type of study.	Researchers and research funders are an important user group of Cochrane reviews. Recommendations for future research should offer constructive guidance on addressing the remaining uncertainties identified by the review. This is particularly important for reviews that identify few or no studies. *MECIR conduct standard 80* (Structure the implications for research to address the nature of evidence required, including population intervention comparison, outcome, and type of study).	

Acknowledgements

Standard		Rationale and elaboration	
R103	Acknowledgements		**Mandatory**
Acknowledge the contribution of people not listed as authors of the review, including any assistance from the Cochrane eview Group, non-author contributions to searching, data collection, study appraisal or statistical analysis, and the role of any funders.		[PRISMA item 27]	

Contributions of authors

Standard		Rationale and elaboration	
R104	Contributions of authors		**Mandatory**
Describe the contributions of each author		See *Handbook* 4.2.2	

Declarations of interest

Standard		Rationale and elaboration	
R105	Declarations of interests		**Mandatory**
Report any present or past affiliations or other involvement in any organization or entity with an interest in the review's findings that might lead to a real or perceived conflict of interest.		The nature and extent of the affiliation or involvement (whether financial or non-financial) should be described. Potential conflicts of interest can also arise from non-financial sources including academic competition and affiliations with professional bodies or learned societies. An additional consideration for authors of systematic reviews is the declaration of involvement in studies that were included in the review. See *Handbook* 2.6	

Differences between protocol and review

Standard		Rationale and elaboration	
R106	Changes from the protocol		**Mandatory**
Explain and justify any changes from the protocol (including any *post hoc* decisions about eligibility criteria or the addition of subgroup analyses).		*MECIR conduct standard 13* (Justify any changes to eligibility criteria or outcomes studied. In particular, post hoc decisions about inclusion or exclusion of studies should keep faith with the objectives of the review rather than with arbitrary rules.)	
R107	Methods not implemented		**Highly desirable**
Document aspects of the protocol that were not implemented (e.g. because no studies, or few studies, were found) in the section 'Differences between protocol and review', rather than in the Methods Section.		See *Handbook* 2.1	

Sources of Support

Standard		Rationale and elaboration	
R108	Sources of support		**Mandatory**
List sources of financial and non financial support for the review and the role of the funder, if any.		See *Handbook* 4.10. [PRISMA item 28]	

*These Handbook section numbers are specific to Version 5.1.
All other section numbers apply equally to the 2008 edition (and 2009 reprints) published by Wiley-Blackwell

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