Cochrane Methods

Methodological Expectations of Cochrane Intervention Reviews (MECIR)

Standards for the conduct and reporting of new Cochrane Intervention Reviews, reporting of protocols and the planning, conduct and reporting of updates

Julian PT Higgins, Toby Lasserson, Jackie Chandler, David Tovey and Rachel Churchill

Version 1.02
Last updated: January 2018

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Publication date 2016

Publication citation:
Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. *Methodological Expectations of Cochrane Intervention Reviews*. Cochrane: London, Version 1.02, 2016.

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INTRODUCTION

Key points

- **The MECIR standards represent a true collaborative effort across our community.**
- **They are an essential part of Cochrane's quality assurance strategy.**
- **The MECIR standards represent a living programme of work, and will be adapted over time as methods, and expectations change.**

Ensuring that Cochrane Reviews represent the highest possible quality is critical if they are to inform decision making in clinical practice and health policy (*Strategy to 2020* goals 1 and 2). Methodological Expectations of Cochrane Intervention Reviews (MECIR) are standards that should guide the conduct and report of Cochrane Intervention Reviews. They are drawn from the *Cochrane Handbook for Systematic Reviews of Interventions* (the '*Handbook*'). The development of the standards has been a collaborative effort over several years, involving review authors, editors and methodologists from all corners of our community. We have implemented both conduct and reporting standards for new intervention reviews and they have formed the basis for the quality assurance work that has taken place over the past two to three years. In this document we present a complete set of standards for intervention reviews.

Development and consultation

We established working groups in 2011 to develop minimum standards based on early proposals and groundwork by many groups and individuals within Cochrane. We agreed the need to identify methodological expectations for Cochrane protocols, reviews and updates of reviews on the effects of interventions that could be implemented across Cochrane. Six Working Groups covered six core methodological aspects of Cochrane Intervention Reviews:

1. developing a question and deciding the scope of the review;
2. searching for studies;
3. selecting studies and collecting data;
4. assessing risk of bias in studies;
5. analysing data and undertaking meta-analyses;
6. interpretation and presenting results.

For each of these areas, we set out to identify the following in respect of intervention reviews:

A. essential minimum standards (*must do*);

B. desirable standards (*should do*);

C. common errors (*should not do*);

D. fatal flaws (*must not do*) and identification of any important methodological uncertainties.

The standards cover A and B, whilst work on C and D is ongoing. At least one methodologist and one Co-ordinating Editor (clinical specialist) jointly led each working group. We sought to ensure that groups reflected divergent views and had access to appropriate expertise. We co-opted other people from across Cochrane as necessary to ensure co-ordination and consistency of approach (training and knowledge translation). From an initial draft set of standards, we consulted widely throughout Cochrane, after which the MECIR co-ordinating author team collated responses to produce this final set of standards. Although primarily drawn from the current (2011) version of the *Handbook*, the standards proposed have also required amendment to the *Handbook*. Thus, the *Handbook* will incorporate these standards.

Implementation of the standards

Cochrane Review authors and the Cochrane Review Groups (editorial bases) are expected to meet these minimum quality standards in their reviews. These standards guarantee consistency of methodological practice across Cochrane Intervention Reviews and are an important element of the quality assurance of individual reviews. All standards are qualified with the status of 'mandatory' or 'highly desirable'. Mandated standards are essential and compliance is expected, or an appropriate justification should be provided. Reviews that do not meet these standards should not be published. Earlier versions of these MECIR standards for conduct and reporting are currently in use and used to audit new Review abstracts and reviews. The Cochrane Editorial Unit (CEU) used a subset of the standards in its prepublication screening programme of new reviews. Since this initial implementation, the standards have undergone review and revision. We have now developed standards for updates and protocols.

We introduce each set of standards with key points and, where necessary, additional explanatory notes.

The MECIR standards represent a considerable amount of work from many people within the Cochrane community. However, it seems appropriate to single out Julian Higgins, Rachel Churchill, Toby Lasserson and Jackie Chandler for their commitment and resolve in pushing the process through to this resolution. That said, of course this does not represent the final word. Methods change and these standards will continue to be refined over time. We therefore welcome feedback from all of you who are responsible for delivering the standards, and hope that they are useful to you in producing and maintaining high quality, relevant reviews that can guide decision makers throughout the world, in pursuit of better health outcomes.

David Tovey
Editor in Chief
The Cochrane Library

These standards are also available on our website http://methods.cochrane.org/resources. They will also be available in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.2 and subsequent versions.

Acknowledgements

We thank the following working group leads and contributors for their early development of the standards: Doug Altman, **Mohammed Ansari (Methods lead),** Sally Bell-Syer, Patrick Bossuyt, Deborah Caldwell, Christopher Cates, **Rachel Churchill (Co-ordinating Editors (Co-Eds) lead, Co-ordinating team)**, **Mike Clarke (Co-Eds co-lead)**, **Jan Clarkson (Co-Eds co-lead)**, Philippa Davies, **Marina Davoli (Co-Eds lead)**, Ruth Foxlee, Chantelle Garritty, **Davina Ghersi (Co-Eds co-lead)**, **Julie Glanville (Methods co-lead)**, Peter Herbison, Julian Higgins (Co-ordinating team), **Sophie Hill (Co-Eds lead)**, Toby Lasserson (Co-ordinating team), Edith Leclercq, **Carol Lefebvre (Methods co-lead)**, Jessie McGowan, Rachel Marshall, Ruth Mitchell, Donal O'Mathuna, Anna Noel-Storr, **Georgia Salanti (Methods lead)**, Doug Salzwedel, Margaret Sampson, Jelena Savovic, **Holger Schünemann (Methods lead)**, Ian Shemilt, Nandi Siegfried **Jonathan Sterne (Methods lead)**, **Britta Tendal (Methods lead)**, David Tovey (Co-ordinating team), Peter Tugwell, Lucy Turner, Claire Vale, Julia Walters, **Helen Worthington (Co-Eds lead)**, and Janelle Yorke. We also thank all those Cochrane members of Review Groups, Methods Groups, Fields, Centres and Training who responded in some detail to MECIR Standard consultations, allowing us to improve these standards to ensure relevance and comprehension.

Standards for the **conduct** of new Cochrane Intervention Reviews

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Please cite this section as: Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. Standards for the conduct of new Cochrane Intervention Reviews. In: Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. *Methodological Expectations of Cochrane Intervention Reviews*. Cochrane: London, 2016.

Introduction

Key points

- **The conduct standards should be consulted during preparation of the protocol for a Cochrane Intervention Review.**
- **They describe the methods that should be implemented throughout the review process.**
- **Few specific methods are mandatory, one notable exception being use of the Cochrane tool for assessing risk of bias when randomized trials are included in the review.**

The MECIR standards for conduct of a Cochrane Intervention Review provide expectations for the general methodological approach to be followed from designing the review up to interpreting the findings at the end. They should be consulted particularly when preparing the protocol for the review. The protocol describes the review question, the criteria for considering studies for the review, and the methods that will be followed to identify, appraise, summarize and synthesize the studies. Cochrane led the way in making protocols available to readers of the Cochrane Library. They ensure transparency in how reviews are prepared and allow the planned methods to be critiqued. Specification of the review question (through setting the review's objectives) and the criteria for including studies are critical to the success of the review and the first two sections of the standards address these tasks. The following section addresses selection of the outcomes of interest, an important aspect that should be prespecified carefully to avoid the need for post hoc decisions that could be influenced by the data.

The remaining standards address the detailed methodology that will be followed during the review, covering the search for studies, selection of studies into the review, data collection, 'Risk of bias' assessment, synthesis (including any meta-analysis approaches), and overall assessment of the evidence. With few exceptions (such as use of the Cochrane 'Risk of bias' tool for randomized trials), the precise methods to be used are not prescribed. For example, authors are free to use any meta-analysis method, although there is a potential convenience to both authors and readers if those implemented in Review Manager (RevMan) software are used.

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DEVELOPING THE PROTOCOL FOR THE REVIEW

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 review users such as healthcare 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, 17.2, 20.2.2
C2 Predefining objectives	**Mandatory**
Define in advance the objectives of the review, including participants, interventions, comparators and outcomes (PICO).	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 upon the whole population, but also on the disadvantaged, and/or the ability of the interventions to reduce socioeconomic inequalities in health, and to promote use of the interventions to the community.

Setting eligibility criteria for including studies in the review

Standard	Rationale and elaboration
C5 Predefining unambiguous criteria for participants	**Mandatory**
Define in advance the eligibility criteria for participants in the studies.	Predefined, unambiguous eligibility criteria are a fundamental prerequisite 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	Predefining 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 addressed.		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. If data from the eligible participants cannot be retrieved, a mechanism for dealing with this situation should be prespecified. See *Handbook* 5.2
C7	Predefining 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.		Predefined, unambiguous eligibility criteria are a fundamental prerequisite 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, for example, regarding delivery, dose, duration, intensity, cointerventions and features of complex interventions should also be predefined 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 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	Predefining 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.		Predefined, unambiguous eligibility criteria are a fundamental prerequisite 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 was blinded; 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 it is feasible to conduct them to evaluate interventions and outcomes of interest.*	Randomized trials are the best study design for evaluating the efficacy of interventions. If it is feasible to conduct them to evaluate 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 exclusion is 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 10.3.2*
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 prespecified 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 Predefining outcome domains	**Mandatory**
Define in advance which outcomes are primary outcomes and which are secondary outcomes.	Full specification of the outcomes includes consideration of outcome domains (e.g. quality of life) and outcome measures (e.g. SF-36). Predefinition 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 largely on the effects of the interventions on these outcomes. It is important to identify up to seven outcomes from the primary and secondary outcomes that will form the basis of the GRADE assessment. See *Handbook* 5.4.2
C15 Choosing outcomes	**Mandatory**
Choose only outcomes that are important to users of the review such	Cochrane Reviews are intended to support clinical practice and policy, and should address outcomes that are important to consumers. These

as healthcare consumers, health professionals and policy makers.	should be specified at protocol stage. Where 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 of 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. Biochemical, interim and process outcomes should be considered where they are important to decision makers. See *Handbook* 5.4.2
C16 Predefining outcome measures	**Mandatory**
Define in advance details of what will constitute 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 be difficult, however, to predefine adverse effects. See *Handbook* 5.4.1
C17 Predefining 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).	Prespecification guards against selective outcome reporting, and allows users to confirm that choices were not overly influenced by the results. A predefined hierarchy of outcomes measures may be helpful. It may be difficult, however, to predefine adverse effects. A rationale should be provided for the choice of outcome measure. See *Handbook* 5.4.1
C18 Predefining time points of interest	**Highly desirable**
Define in advance the timing of outcome measurement.	Prespecification 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 prespecified 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 that meet the eligibility criteria, ensuring that relevant time periods and sources are covered and not restricted 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. If searches are restricted by publication status or by language of publication, there is a possibility of publication bias, or language bias (whereby the language of publication is selected in a way that depends on the findings of the study), or both. 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.	Predefining 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, use of 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 *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).	Predefining 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 subgroup analyses	Mandatory
Predefine potential effect modifiers (e.g. for subgroup analyses) at the protocol stage; restrict these in number, and provide rationale for each.	Prespecification reduces the risk that large numbers of undirected subgroup analyses will lead to spurious explanations of heterogeneity. See *Handbook* 9.6.5

C23 Planning the GRADE assessment and 'Summary of findings' table	Mandatory
Plan in advance the methods to be used for assessing the quality of the body of evidence, and summarizing the findings of the review.	Methods for assessing the quality of evidence for the most important outcomes in the review need to be prespecified. In 'Summary of findings' tables the most important feature is to predefine the choice of outcomes in order 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 generally should not include surrogate or interim outcomes. The choice of outcomes should not be based on 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

PERFORMING THE REVIEW

Searching for studies

Standard	Rationale and elaboration
C24 Planning the search	**Mandatory**
Search the Cochrane Review Group's (CRG'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 Embase 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 CRG's Specialized Register (if it exists and was designed to support reviews in this way), CENTRAL, MEDLINE and Embase (if Embase 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 CRGs' 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 *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	**Highly desirable***
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

*C28: changed from 'Mandatory' to '**Highly desirable**'

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 organizations	Highly desirable
Contact relevant individuals and organizations 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 these can be assessed for possible inclusion when a review is updated. 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 CRG's Information Specialist. 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 records that are relevant from the search set. 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 and 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 which 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 six months) from the intended publication date, and the results screened for potentially eligible studies. Ideally the studies should be incorporated fully in the review. 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' if they have not yet completed).
C38 Incorporating findings from rerun searches	**Highly desirable**
Fully incorporate 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 to include in 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 and risk undermining the systematic review process. 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 that 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 that 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 using a sample of included studies is highly desirable. At a 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. TiDieR (Hoffman 2014) will assist selection of which characteristics of interventions should be sought. 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 study characteristics. 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 the 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^2) 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	Mandatory
Examine any relevant retraction statements and errata for information.	Some studies may have been found to be fraudulent or may have been retracted since publication for other reasons. Errata can reveal important limitations, or even fatal flaws, in included studies. All of these may lead to the potential 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 enhances precision and reduces 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 the intervention and control groups that meet the eligibility criteria.	There is no point including irrelevant intervention groups in the review. Authors, however, should 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 support for those judgements across a series of domains of bias, as described in Chapter 8 of the *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 tool – as described in the *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 *Handbook* should be used to inform the selection of an appropriate tool for non-randomized studies. See *Handbook* 8.2.1, 8.5, 8.9 to 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* 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 that are judged to be at an unclear risk of bias but are 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* 8.5.2	
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 and referees should have the opportunity to see for themselves from where supports for judgments have been obtained. See *Handbook* 8.5.2	
C56	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	
C57	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.	Often, considering risk of bias due to incomplete (missing) outcome data cannot be done reliably for a 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 dropout 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 8.13.2	

C58 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 prerequisite for the GRADE approach to assessing the quality of the body of evidence. See *Handbook* 8.7
C59 Addressing risk of bias in the synthesis	**Highly desirable**
Address risk of bias in the synthesis (whether quantitative or non-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* 8.8.1
C60 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 Intervention 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* 8.8.1

Synthesizing the results of included studies

Standard	Rationale and elaboration
C61 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 are 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
C62 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 where studies use different forms of control. Clinical diversity does not indicate necessarily 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
C63 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 recognize that there is much uncertainty in measures such as I^2 and Tau^2 when there are few studies. Thus, use of simple thresholds to diagnose heterogeneity should be avoided. See *Handbook* 9.5.2

C64 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
C65 Addressing skewed data	Highly desirable
Consider the possibility and implications of skewed data when analysing continuous outcomes.	Skewed data are sometimes not summarized usefully 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
C66 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
C67 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
C68 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 a problem especially when multiple subgroup analyses are performed. This does not preclude the use of sensible and honest post hoc subgroup analyses. See *Handbook* 9.6.5.2
C69 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

C70 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
C71 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
C72 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
C73 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 of the problem, as can attempts to identify study protocols, which should be a routine feature of Cochrane Reviews. See *Handbook* 10.1, 10.2

Assessing the quality of evidence and summarizing the findings

Standard		Rationale and Elaboration
C74	Assessing the quality of the body of evidence	**Mandatory**
Use the five GRADE considerations (risk of bias, 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 approach for summarizing confidence in effects of interventions by outcome across studies. It is preferable to use the online GRADEpro tool, and to use it as 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 and reach a consensus view on any downgrading decisions. The five GRADE considerations should be addressed irrespective of whether the review includes a 'Summary of findings' table. It is helpful to draw on this information in the Discussion, in the Authors' conclusions and to convey the certainty in the evidence in the Abstract and Plain language summary. See *Handbook* 12.2
C75	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 GRADE).		The adoption of a structured approach ensures transparency in formulating an interpretation of the evidence, and the result is more informative to the user. See *Handbook* 12.2.1

Reference

Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. (2014) Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014;348:g1687. doi: 10.1136/bmj.g1687

Standards for the **reporting of protocols** for new Cochrane Intervention Reviews

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Please cite this section as: Lasserson T, Churchill R, Chandler J, Tovey D, Higgins JPT. Standards for the reporting of protocols of new Cochrane Intervention Reviews. In: Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. *Methodological Expectations of Cochrane Intervention Reviews*. Cochrane: London, 2016.

Introduction

Key points

- **Publishing a protocol for a Cochrane Review establishes a public record of the review question and planned methods.**
- **Reporting clear definitions will help authors to adhere to a well formulated approach.**
- **Readers need to determine how far the review will address their own questions of interest.**
- **Changes to the review question or methods will need to be clearly described and justified in the full review.**

Publishing the protocol for a Cochrane Systematic Review is a key milestone in the review process. As with any other form of research, it finalizes the development of the research question and sets out the different methods that will be used to address it.

Preparing and publishing a clearly conceived and well-written protocol serves a number of purposes. Investment of effort in the development of the review question and methods and the definition of the different aspects of the eligibility criteria will provide review authors with a clear plan to guide implementation of methods and reporting the full review, reducing their reliance on post hoc decisions. Publishing the protocol gives readers access to the plan from which the review will develop. It also helps them to judge how the eligibility criteria of the review, stated outcomes and planned methods will address the intended question of interest.

The protocol is a public record of the question of interest and the intended methods before results of the studies are fully known. This helps anyone who evaluates the review to judge how far it fulfils the original objectives. One of the key parts of the CEU review prepublication screening programme involves the comparison between the intended methods with those implemented during the preparation of the review. It is crucial that review authors acknowledge and justify important differences between methods stated in the protocol and those used to produce the review findings. This is key to supporting replication, and provides users of the review with a sense of how far the review preserves the research question. Particularly important changes concern eligibility criteria, the definition or status of outcome measurements and methods relating to effect measures, data analysis and exploration of heterogeneity. Any changes that are made to these aspects of the review could potentially impact on the overall objectives as well as the interpretation of the evidence summarized by the review.

On publication Cochrane systematic review protocols are automatically assigned a record on PROSPERO, the register of ongoing and completed systematic reviews. For more information see www.crd.york.ac.uk/PROSPERO/

Toby Lasserson
Senior Editor
Cochrane Editorial Unit

REPORTING THE REVIEW PLAN

Title and authors

Standard	Rationale and Elaboration
PR1 Format of title	**Highly desirable**
Follow the standard template for a Cochrane Review title.	See *Handbook* 4.2.1 and table 4.2a
PR2 Authors	**Mandatory**
List names and affiliations of all authors.	See *Handbook* 4.2.2

Background

Standard	Rationale and elaboration
PR3 Background	**Mandatory**
Provide a concise description of the condition or problem addressed by the review question, a definition of the intervention and how it might work, and why it is important to do the review. Include the four standard RevMan headings when writing the Background.	Systematic reviews should have a clearly defined and well-reasoned rationale that 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. 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*
PR4 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 evidence.

Objectives

Standard	Rationale and elaboration
PR5 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 user-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 (PICO). Review users may be patients, carers, policy makers, clinicians, practitioners or others. The format should be: "To assess the effects of *[intervention or comparison]* for *[health problem]* for/in *[types of people, disease or problem and setting if specified]*". *MECIR conduct standard 2:* Define in advance the objectives of the review, including participants, interventions, comparators and outcomes.

PR6 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 outcome.	The secondary objectives should be expressed in terms that relate to the population(s), intervention comparison(s) and, where appropriate, outcomes of interest. The format might be: "To assess whether the effects of *[intervention or comparison]* differ according to *[types of people, intervention or comparator characteristic, disease, problem, setting etc.]*". Secondary objectives should be kept succinct, since they will be published in the front sheet of the review protocol on the Cochrane Library. *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.
PR7 Economic evidence	Mandatory
If health economics evidence is to be reviewed, state this explicitly in the Objectives (as a secondary objective).	The primary aim of a Cochrane Review should be to assess the effects of one or more healthcare interventions on outcomes, both intended and unintended, that are important to review users. These outcomes may include economic outcomes. If health economics evidence is being reviewed as an integrated economics component, this should be stated as a secondary objective. See *Handbook* section 15.2.3.
PR8 Qualitative research evidence	Mandatory
If qualitative research evidence is to be reviewed, state this explicitly in the Objectives (as a secondary objective).	If qualitative research evidence is being included to 'extend' the review, this should be stated as a secondary objective. See *Handbook* section 20.2.1.

Criteria for considering studies for this review

Standard	Rationale and elaboration
PR9 Eligibility criteria for types of study: study designs	Mandatory
State eligible study designs, using key study characteristics, 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. Particular care may be needed to explain whether cross-over trials and cluster-randomized trials are to be considered. Study characteristics might include details such as "with blind assessment of outcomes" or "with prospective identification of participants", rather than ambiguous labels such as "double blind" or "prospective study". If 'conditional' eligibility criteria are used that are based on absence of particular types of evidence (e.g. when no randomized trials are found), this must be stated unambiguously (and

	detailed methods for addressing all *potentially* eligible studies will need to be described). *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.
PR10 Eligibility criteria for types of study: study reports	**Mandatory**
If studies will be 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 exclusion is explicitly justified. *MECIR conduct standard 12:* Include studies irrespective of their publication status, unless exclusion is explicitly justified.
PR11 Eligibility criteria for types of participants	**Mandatory**
State eligibility criteria for participants, including any criteria around location, setting, diagnoses or definition of condition and demographic factors, and how studies including subsets of relevant participants will be addressed.	*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 addressed.
PR12 Eligibility criteria for types of interventions	**Mandatory**
State eligibility criteria for interventions and comparators, including any criteria around delivery, dose, duration, intensity and cointerventions. Criteria for complex interventions should be made explicit, e.g. by stating mandatory components.	Eligible interventions, and particularly the comparators, must address the stated objectives of the review. For example, inclusion of studies with an active comparator intervention is not consistent with an objective to look only at whether an experimental intervention is effective compared with an inactive control. *MECIR conduct standard 7:* Define in advance the eligible interventions and the interventions against which these can be compared in the included studies.
PR13 Role of outcomes	**Mandatory**
Be explicit about the role of outcomes in determining eligibility of studies for the review.	For most Cochrane Reviews of randomized trials of the intended effects of interventions, the aim should be to identify and include all relevant participants who have been randomized to the intervention comparisons of interest. The extent to which outcome data are available for these people can be affected by decisions made by the trialists – i.e. there is a risk of selective outcome reporting bias. An important distinction should be made between whether outcomes were measured, and whether the measured outcome data are available. Studies should not be excluded from a review solely because no outcome data are available. 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. Often it is difficult to know whether unreported outcomes were measured, so it is generally appropriate to include all studies irrespective of whether outcomes are reported. *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).
PR14 Outcome domains of interest	**Mandatory**
State which outcomes are primary outcomes and which are secondary outcomes.	Up to seven outcomes should be prespecified for inclusion in a 'Summary of findings' table (see PR40); it may be convenient to highlight them here. *MECIR conduct standard 14:* Define in advance which outcomes are primary outcomes and which are secondary outcomes. Also *MECIR conduct standards 15–18*
PR15 Outcome measures of interest	**Mandatory**
Define relevant outcome measures and time points for measurement, and any hierarchy for choosing among them.	Explain how multiple variants of outcome measures (e.g. definitions, assessors, scales, time points) will be addressed.
PR16 Minimally important difference	**Highly desirable**
Define minimally important differences for key outcome measures.	To facilitate interpretation of the size of effect of an intervention, it is important to understand the size of difference that is important to review users.

Search methods for identification of studies

Standard	Rationale and elaboration
PR17 Search sources	**Mandatory**
List all sources that will be searched, including: CRG specialized register(s), CENTRAL, other databases, trials registers, websites and grey literature. State whether reference lists will be searched and whether individuals or organizations will be contacted.	*MECIR conduct standard 19:* Plan in advance the methods to be used for identifying studies. Design searches to capture as many studies as possible that meet the eligibility criteria, ensuring that relevant time periods and sources are covered and not restricted by language or publication status. *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*
PR18 Search restrictions	**Mandatory**
Specify and justify any restrictions to be placed on the search (e.g. time period or publication format).	*MECIR conduct standard 35:* Justify the use of any restrictions in the search strategy on publication date or publication format.

PR19	Searches for different types of evidence	**Mandatory**
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.	
PR20	Search strategies for bibliographic databases	**Mandatory**
Present the complete search strategy (or strategies) to be implemented for at least one database in an Appendix, including any limits and filters to be used.	The line-by-line search string should be presented to facilitate peer review. 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. Note that when the full review is published, it is mandatory to report search strategies used for all databases. *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*	
PR21	Search strategies for other sources	**Highly desirable**
Report search terms that will be used to search any sources other than bibliographic databases (e.g. trials registers, the web).	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. See *Handbook* 8.2.3.1	

Data collection and analysis

	Standard	Rationale and elaboration
PR22	Inclusion decisions	**Mandatory**
State how inclusion decisions will be made (i.e. from search results to included studies), clarifying how many people will be involved and whether they will work 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.	
PR23	Data collection process	**Mandatory**
State how data will be extracted from reports of included studies, clarifying how many people will be involved (and whether they will work independently), and how disagreements will be resolved.	*MECIR conduct standard 43:* Use a data collection form that 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.	

PR24 Requests for data	Highly desirable
Describe what attempts will be made 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.
PR25 Data items	**Mandatory**
State the types of information that will be sought from reports of included studies.	This information is a useful basis for the design of data collection forms and also indicates what sort of information about the included studies readers might anticipate seeing in the full text of the review. Detailed lists are not necessary. Instead, a broad outline of the summary information that authors might collect will suffice, for example: "We will collect information on study design and setting, participant characteristics (including disease severity and age), study eligibility criteria, details of the intervention(s) given, the outcomes assessed, the source of study funding and any conflicts of interest stated by the investigators." *MECIR conduct standard 44:* Collect characteristics of the included studies in sufficient detail to populate a table of 'Characteristics of included studies'.
PR26 Missing data	**Highly desirable**
Comment on how missing data will be addressed.	Briefly describe any planned strategies that will be used to address missing data. This might include imputation of missing outcome data for individuals within studies (such as worst-case or best-case scenarios), or imputations of missing standard deviations. Note that standard deviations can sometimes be computed from other reported statistics. *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^2) or P values, or even data for individual participants. *MECIR conduct standard 64:* Consider the implications of missing outcome data from individual participants (due to losses to follow-up or exclusions from analysis). See *Handbook* 7.7
PR27 Tools to assess risk of bias in individual studies	**Mandatory**
State and reference the tool(s) that will be used to assess risk of bias for included studies, how the tool(s) will be implemented, and the criteria that will be used to assign study results to judgements of low risk, high risk and unclear risk of bias.	Different tools are likely to be appropriate for different types of studies (e.g. randomized trials and non-randomized studies). If the current *Handbook* guidance for undertaking 'Risk of bias' assessments will be followed in its entirety, then a reference to the *Handbook* is sufficient to provide the criteria used to assign judgements (see *Handbook* Sections 8.9 to 8.15). Justify any intended deviations from the tool.

	MECIR conduct standard 20: 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 study results to judgements of low risk, high risk and unclear risk of bias. *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 *Handbook* (version 5 or later). Also *MECIR conduct standards 53–60*
PR28 'Risk of bias' assessment process	**Mandatory**
State how risk of bias will be assessed, clarifying how many people will be involved (and whether they will work independently), and how disagreements will be resolved.	*MECIR conduct standard 53:* 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.
PR29 Measures of effect	**Mandatory**
State the effect measures that will be used to describe effect sizes in any included studies or meta-analyses, or both (e.g. risk ratio or odds ratio, mean difference or standardized mean difference).	
PR30 Unit of analysis issues	**Mandatory**
If designs other than individually randomized, parallel-group randomized trials are likely to be included, describe any methods that will be used to address clustering, matching or other design features of the included studies.	In some circumstances, specific study designs are likely to be identified in which unit-of-analysis errors might arise. This includes cluster-randomized trials, cross-over trials, trials involving multiple body parts and non-randomized studies with clustered designs. *MECIR conduct standard 70*: Consider the impact on the analysis of clustering, matching or other non-standard design features of the included studies.
PR31 Studies with more than two groups	**Highly desirable**
If multi-arm studies are likely to be included, explain how they will be addressed and incorporated into syntheses.	Note that it is mandatory to describe these methods in the full version of the review if studies with more than one arm are identified and included. *MECIR conduct standard 66: 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.
PR32 Quantitative synthesis	**Mandatory**
Describe any intended statistical 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^2, statistical test).	In the majority of reviews, most of this information is located under the subheading 'Data synthesis'. Note, however, that additional subheadings should be used to provide details of subgroup analyses, assessment of heterogeneity and sensitivity analysis.

	MECIR conduct standard 21: 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). *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.
PR33 Non-quantitative synthesis	**Mandatory**
Describe any intended non-statistical methods for synthesizing findings across studies (sometimes referred to as narrative or qualitative synthesis).	It may be apparent that a meta-analysis is unlikely, in which case methods should be prespecified for how the findings of the included studies will be compared and contrasted.
PR34 Risk of reporting bias across studies	**Highly desirable**
Describe any methods that will be used for assessing the risk of reporting biases such as publication bias.	
PR35 Addressing risk of bias	**Mandatory**
Describe how studies with high or variable risks of bias will be addressed in the synthesis.	Several options are available for addressing risk of bias in a synthesis, including reporting separate syntheses for studies at different risks of bias, restricting analysis to studies at low (or low and unclear) risk of bias only, and undertaking sensitivity analysis to examine the impact of risks of bias on the conclusions. An understanding of the impact of risks of bias is important to inform GRADE assessments. *MECIR conduct standard* 59: Address risk of bias in the synthesis (whether quantitative or non-quantitative). For example, present analyses that are stratified according to summary risk of bias, or restricted to studies at low risk of bias.
PR36 Subgroup analyses	**Mandatory**
If subgroup analysis (or meta-regression) are planned, state the potential effect modifiers with rationale for each.	*MECIR conduct standard 22:* Predefine potential effect modifiers (e.g. for subgroup analyses) at the protocol stage, restrict these in number, and provide rationale for each.
PR37 Methods for economic evidence	**Mandatory**
If health economics evidence is to be reviewed, state the methods to be used to assess and synthesize this evidence.	See *Handbook* 15.2-15.9
PR38 Methods for qualitative research evidence	**Mandatory**
If qualitative research evidence is to be reviewed, state the methods to be used to assess and synthesize this evidence.	See *Handbook* 20.3-20.3.2.7

PR39 Quality of the evidence	Mandatory
State the methods to be used to assess the quality of the body of evidence (using the five GRADE considerations).	If the current GRADE guidance for these assessments will be followed in its entirety (see *Handbook* Chapter 12), then a reference to this is sufficient to provide the criteria used to make judgements. *MECIR conduct standard 74:* Use the five GRADE considerations (risk of bias, 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.

PR40 'Summary of findings' table	Mandatory
State which outcomes and comparisons it is planned will be included in a 'Summary of findings' table.	A maximum of seven important outcomes should be prespecified for inclusion in a 'Summary of findings' table. If possible, sources of any assumed risks to be presented in a 'Summary of findings' table should be explained. *MECIR conduct standard 23*: Plan in advance the methods to be used for assessing the quality of the body of evidence, and summarizing the findings of the review.

Acknowledgements

PR41 Acknowledgements	Mandatory
Acknowledge the contribution of people not listed as authors of the protocol, including any assistance from the Cochrane Review Group, non-author contributions and the role of any funders.	

Contribution of authors

PR42 Contributions of authors	Mandatory
Describe the contributions of each author to the protocol.	See *Handbook* 4.2.2

Declarations of interest

PR43 Declarations of interests	Mandatory
Report relevant present or recent (three years prior to declaration) 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 detailed policy for declaring relevant interests is available in the Cochrane Editorial and Publishing Policy Resource (EPPR). In brief, the nature and extent of the affiliation or involvement (whether financial or non-financial) should be described. Declarations of interest should be stated according to the relevant criteria from the International Committee of Medical Journal Editors (ICMJE), and must be consistent with interests declared on the Disclosure of Potential Conflicts of Interest form. See *Handbook* 2.6

Sources of support

PR44 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.

Standards for the **reporting** of new Cochrane Intervention Reviews

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Please cite this section as: Churchill R, Lasserson T, Chandler J, Tovey D, Higgins JPT. Standards for the reporting of new Cochrane Intervention Reviews. In: Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. *Methodological Expectations of Cochrane Intervention Reviews*. Cochrane: London, 2016.

Introduction

Key points

- **Authors should consult the MECIR reporting standards before and during writing up of their review.**
- **The reporting standards are compatible with key reporting guidelines developed by different bodies, including PRISMA.**
- **Abstracts and Plain language summaries need to be consistent with each other, and with the main text of the review.**
- **Clear and consistent reporting supports replication of systematic reviews and should make updating easier.**

Authors should consult these reporting standards before and during writing up of their review. Adherence to the standards will help authors to prepare an informative, readable review. It will also help to make editorial evaluation of their work efficient. It is especially important to declare and justify differences to the planned question or eligibility criteria, since these may indicate important changes to the scope of the review. Where any search, data collection and analysis methods used are different from those planned, this also needs to be reported and explained. The reporting standards are available from within Review Manager (RevMan) software according to the heading or subheading to which they relate.

Several reporting guidelines are already available for primary studies and systematic reviews, and have been compiled by the Equator Network[1]. MECIR standards are compatible with the core items in two key sources of reporting guidance for systematic reviews: the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA), and the US Institute of Medicine's standards for systematic reviews.

Accurately summarizing the key findings of a Cochrane Review in its Abstract and Plain language summary serves an important purpose in knowledge translation. These standalone summaries help to convey the results of the review to a broad audience. Authors should take particular care to ensure that conclusions drawn in the main text of the review under 'Implications for practice' and 'Implications for research' take account of the strength of evidence presented in the review, and are appropriately distilled in the Abstract and Plain language summary.

Authors and editors should ensure that all parts of the review are succinct and readable, so that someone who is not an expert in the area can understand it. The published review needs to signpost and structure information clearly to help orientate readers. Review methods should be reported in sufficient detail that others are in principle able to reproduce the findings. Clear reporting of the eligibility criteria and methods will also help future efforts to update and maintain the published version of the review.

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[1] The Equator Network is a Library for health research reporting that provides a searchable database and can be found at http://www.equator-network.org/

REPORTING REVIEW CONDUCT

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 that need to stand alone. They should convey key information about the review question and its findings, and be informative to readers.
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 that 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 summarized 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, the absence of which 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 Cochrane."	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 the detailed description of the methods given 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 use of non-standard tools.
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); it is important 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 should be mentioned.	

R12	Abstract, Main results: findings	Mandatory
Report findings for all important outcomes, irrespective of the strength and direction of the result, and of the availability of data.	Findings should typically include concise information about the size of effect and quality of evidence for the outcome (such as risk of bias, consistency of effect, imprecision, indirectness and publication bias), for example using GRADE. Outcomes reported in the Abstract should not be selected solely on the basis of the findings. In general, the same outcomes in the Abstract should be presented in the Plain language summary and 'Summary of findings' tables. If no studies measured the outcome, 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, NNTBs, group means), and outcomes combined with a standardized scale (e.g. standardized mean difference) 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 main 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 that 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.
R20 Background headings	Highly desirable
Include the four standard RevMan 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 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 user-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 the outcomes of interest explicitly. Review users may be patients, carers, policy makers, clinicians, practitioners 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]*".
R23 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.
R24 Economic evidence	**Mandatory**
If health economics evidence is being reviewed, state this explicitly in the Objectives (as a secondary objective).	The primary aim of a Cochrane Review should be to assess the effects of one or more healthcare interventions on user-important outcomes, both intended and unintended. These outcomes may include economic outcomes. If health economics evidence is being reviewed as an integrated economics component, this should be stated as a secondary objective. See *Handbook* section 15.2.3
R25 Qualitative research evidence	**Mandatory**
If qualitative research evidence is being reviewed, state this explicitly in the Objectives (as a secondary objective).	The primary aim of a Cochrane Review should be to assess the effects of one or more healthcare interventions on user-important outcomes, both intended and unintended. If qualitative research evidence is being included to 'extend' the review, this should be stated as a secondary objective. See *Handbook* section 20.2.1

Methods

Standard	Rationale and elaboration
R26 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. The most convenient place to reference the protocol for the review is under 'Other published versions of this review'. 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.

Criteria for considering studies for this review

Standard	Rationale and elaboration
R27 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 why other types of study meet the eligibility criteria of the review. *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.
R28 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 exclusion is explicitly justified.
R29 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 addressed.	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 addressed.
R30 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.
R31 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).

R32 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 methods for identification of studies

Standard	Rationale and elaboration
R33 Search sources	**Mandatory**
List all sources searched, including: databases, trials registers, websites and grey literature. Database names should include platform or provider name (or both), and dates of coverage; websites 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*
R34 Latest searches	**Mandatory**
Provide the date of the last search and the issue or version number (where relevant) for each database for which results were evaluated and incorporated into the review. If a search was rerun prior to publication, and its results were not incorporated, explain how the results were dealt with, and provide the date of the search.	The review should provide the search date up to which studies have been retrieved and assessed for inclusion. This is the date 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.

R35 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 or publication format.
R36 Searches for different types of evidence	**Mandatory**
If the review has specific eligibility criteria concerning inclusion of 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.
R37 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 the number 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*
R38 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 better 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
R39 Inclusion decisions	**Mandatory**
State how inclusion decisions were made (i.e. from search results to included studies), clarifying how many people were involved and whether 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.
R40 Data collection process	**Mandatory**
State how data were extracted from reports of included studies, clarifying how many people were involved, whether they worked independently, and how disagreements were resolved. Describe data collection process for any reports requiring translation.	*MECIR conduct standard 43:* Use a data collection form that 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.
R41 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.

R42	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'.

R43	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^2) or P values, or even data for individual participants.

R44	Missing outcome data	Highly desirable
Explain how missing outcome data were addressed.		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.

R45	Tools to assess risk of bias in individual studies	Mandatory
State and reference 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 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 *Handbook* 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 *Handbook* (version 5 or later). *MECIR conduct standards 53–61*

R46	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 or meta-analyses, or both.		

R47	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 70:* Consider the impact on the analysis of clustering, matching or other non-standard design features of the included studies.

R48	Studies with more than two groups	Mandatory
If multi-arm studies are included, explain how they were addressed and incorporated into syntheses.		*MECIR conduct standard 66: 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.

R49 Assessing heterogeneity	Mandatory
Describe the methods used to identify the presence of heterogeneity between the studies in the review (e.g. non-quantitative assessment, I^2, Tau^2 or statistical test).	*MECIR conduct standard 69:* Take into account any statistical heterogeneity when interpreting the results, particularly when there is variation in the direction of effect. *MECIR conduct standard 62:* 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 63:* Assess the presence and extent of between-study variation when undertaking a meta-analysis.
R50 Risk of reporting bias across studies	**Highly desirable**
Describe any methods used for assessing the risk of reporting biases such as publication bias.	
R51 Data synthesis	**Mandatory**
Describe any methods used for combining results across studies. Where data have been combined in statistical software external to RevMan, reference the software, commands and settings used to run the analysis.	Decisions to depart from intended methods, for example an alternative statistical model, should be reported and justified. *MECIR conduct standard 62:* 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.
R52 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 and how they were compared (e.g. statistical tests).	*MECIR conduct standard 22:* Predefine potential effect modifiers (e.g. for subgroup analyses) at the protocol stage, restrict these in number, and provide rationale for each. *MECIR conduct standard 67:* 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.
R53 Addressing risk of bias	**Mandatory**
Describe how studies with high or variable risks of bias are addressed in the synthesis.	*MECIR conduct standard 59*: Address risk of bias in the synthesis (whether quantitative or non-quantitative). For example, present analyses that are stratified according to summary risk of bias, or restricted to studies at low risk of bias.
R54 Sensitivity analysis	**Mandatory**
State the basis for any sensitivity analyses performed.	*MECIR conduct standard 71:* 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.

ADDENDUM: Description of studies.
New standard inserted at R55 with subsequent renumbering of standards in this section

R55	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
R56	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.
R57	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.
R58	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 they are excluded. See *Handbook* 7.2.5.
R59	Studies awaiting classification	**Highly desirable**
List the characteristics of any completed 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 and are known to the review team, but have not yet been incorporated in to the review irrespective of their publication status. 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. Authors should also consider the impact of not including these studies on the review findings as a potential limitation, and the extent to which they affect the implications for research.
R60	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. Cochrane Reviews should be mindful of research waste so it is useful to consider how ongoing studies might address the review question under 'Implications for research'.
R61	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'.

R62	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	

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).	

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.	

R65	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.	

R66	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.	The components of all interventions (drug, non-drug, simple or complex) should be reported. Reporting guidelines have been developed for describing interventions used in primary research and review authors may find it useful to structure their description of interventions around the core attributes highlighted by TIDieR (Hoffman 2014). Lengthy explanations of interventions should be avoided. Citations to sources of detailed descriptions can be included.	

R67	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.	

R68	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").	
R69	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.	
R70	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.	
R71	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.)	
R72	References to included studies	**Mandatory**
List all reports of each included study under the relevant Study ID.	It is important that all reports are listed, and are grouped by study. Marking one report as the primary reference is helpful where appropriate.	

Risk of bias in included studies

Standard		Rationale and elaboration
R73	'Risk of bias' table	**Mandatory**
Present a 'Risk of bias' table for each included study, with judgements about risks of bias, and explicit support for these judgements.		The 'Risk of bias' table in RevMan should be used, this 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 *Handbook* (version 5 or later). Also *MECIR conduct standards 54–61*
R74	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		*MECIR conduct standard 58:* Summarize the risk of bias for each key outcome for each study.

are supported by the information presented in the 'Risk of bias' tables.

R75	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.

Effects of interventions

Standard	Rationale and elaboration
R76 Use of 'Data and analysis' headings	Mandatory
Ensure appropriate use of the heading hierarchy of Comparisons, Outcomes, Subgroups and 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'.
R77 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 or continuous outcome data are analysed within RevMan.	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 labelled '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.
R78 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. Failure to disclose this may be misleading.
R79 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.
R80 Multiple outcome data	Mandatory
Describe any post hoc decisions that might give rise to accusations of selective outcome reporting, for example when there were 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. Post hoc decisions to change the definition or priority of outcome measures must be reported and justified under 'Differences between the protocol and review'.

	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.
R81 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 selective reporting of 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.
R82 Prespecified outcomes	**Mandatory**
Report synthesis results for all prespecified outcomes, irrespective of the strength or direction of the result. Indicate when data were not available for outcomes of interest, and whether adverse effects data were identified.	To avoid selective outcome reporting (in truth or in perception), the review should address all outcomes specified in the protocol.
R83 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.
R84 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.
R85 Tables and Figures	**Mandatory**
Link to each Table and Figure.	All tables and figures should have a brief descriptive caption and must be referred to in numerical order in the review text.
R86 Number of Tables and Figures	**Highly desirable**
Keep the number of Tables and Figures low 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 in total. Further Tables and Figures can be included as supplementary material (e.g. as 'Data and analysis' forest plots or within Appendices).

R87 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.	Errors can be introduced, particularly when analyses are rerun.
R88 Direction of effect	**Mandatory**
State whether findings indicate a clear direction of benefit.	Where results indicate that an intervention is better or worse than another intervention, it is important to make it clear which intervention is favoured. This is the case particularly when different scales are combined using standardized mean differences.
R89 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, NNTBs, group means), and outcomes combined with a standardized scale (e.g. standardized mean difference) might be re-expressed in units that are more naturally understood. If minimally important differences were prespecified or are available, these should be provided to aid interpretation.	Absolute effects provide a useful illustration of the likely impact of an 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 NNTBs 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. Ideally, minimally important effect sizes should be specified in the protocol.
R90 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, and introduce 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 contributed 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.
R91 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 64:* Consider the implications of missing outcome data from individual participants (due to losses to follow-up or exclusions from analysis).
R92 Skewed data	**Highly desirable**
Discuss the possibility and implications of skewed data when analysing continuous outcomes.	*MECIR conduct standard 65:* Consider the possibility and implications of skewed data when analysing continuous outcomes.
R93 Forest plots	**Highly desirable**
Present data from multiple studies in forest plots (using the 'Data and analyses' structure in RevMan)	Presenting data in forest plots can be useful, even if the studies are not combined in a meta-analysis.

wherever possible, providing it is reasonable to do so.

R94	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.		

R95	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' within 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.	

R96	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).	

R97	Reporting biases	**Highly desirable**
Present results of any assessment of the potential impact of reporting biases on the review's findings.	*MECIR conduct standard 73:* Consider the potential impact of reporting biases on the results of the review or the meta-analyses it contains.	

R98	'Summary of findings' table	**Highly desirable**
Present a 'Summary of findings' table according to recommendations described in Chapter 11 of the *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. Efforts should be made to incorporate information presented in 'Summary of findings' tables (such as absolute effects, quality ratings and downgrading decisions) in other parts of the review including the Abstract, Plain language summary, Effects of interventions, Discussion and Authors' conclusions.	

R99	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	*MECIR conduct standard 74:* Use the five GRADE considerations (risk of bias, 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.	

or upgrading according to the GRADE approach.	*MECIR conduct standard 75:* Justify and document all assessments of the quality of the body of evidence (for example downgrading or upgrading if using GRADE).

Discussion

Standard		Rationale and elaboration
R99	Discussion headings	**Highly desirable**
Include the standard RevMan 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
R101	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 or rare adverse events, or both, the review authors must explicitly state this as a limitation. Additional considerations here include currency and completeness of the search, completeness of data collection processes, assumptions made regarding classification of interventions, outcomes or subgroups, and methods used to account for missing data. *MECIR conduct standard 74:* Consider the potential impact of reporting biases on the results of the review or the meta-analyses it contains.

Authors' conclusions

Standard		Rationale and elaboration
R102	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.		See *Handbook* sections 4.5 and 12.7
R103	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. Include any information about completed or ongoing studies that are likely to address the review question.

Acknowledgements

Standard		Rationale and elaboration
R104	Acknowledgements	**Mandatory**
Acknowledge the contribution of people not listed as authors of the review, including any assistance from the Cochrane Review Group, non-		

author contributions to searching, data collection, study appraisal or statistical analysis, and the provision of funding.

Contributions of authors

Standard		Rationale and elaboration	
R105	Contributions of authors		**Mandatory**
Describe the contributions of each author to the review.		See *Handbook* section 4.2.2	

Declarations of interest

Standard		Rationale and elaboration	
R106	Declarations of interests		**Mandatory**
Report any present or recent (three years prior to declaration) 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. Include the dates of the involvement.		The full policy on conflicts of interest is available in the Cochrane Editorial and Publishing Policy Resource (EPPR). In brief, the nature and extent of the affiliation or involvement (whether financial or non-financial) should be described to promote transparency. Strategies to clarify how commercial and intellectual conflicts of interests (such as review authors who are trialists) were handled in the review process may be needed. Declarations of interest should be stated according to the relevant criteria from the International Committee of Medical Journal Editors (ICMJE), and must be consistent with interests declared on the Disclosure of Potential Conflicts of Interest form. See *Handbook* section 2.6	

Differences between protocol and review

Standard		Rationale and elaboration	
R107	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.	
R108	Methods not implemented		**Mandatory**
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.		Including a record of methods that were not implemented helps to retain specific details of the protocol. By doing so, the next version of the review can be seen to be coherent with what was planned in the protocol. See *Handbook* section 2.1	

Sources of support

	Standard	Rationale and elaboration	
R109	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* section 4.10.	

Reference

Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. (2014) Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014;348:g1687. doi: 10.1136/bmj.g1687

Standards for the **planning, conduct and reporting of updates** of Cochrane Intervention Reviews

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Please cite this section as: Chandler J, Lasserson T, Higgins JPT, Tovey D, Churchill R. Standards for the planning, conduct and reporting of updates of Cochrane Intervention Reviews. In: Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. *Methodological Expectations of Cochrane Intervention Reviews*. Cochrane: London, 2016.

Introduction

Key points

- **Before undertaking an update, authors should consider the currency and relevance of the question, as well as the methodology used to address it.**
- **A new protocol will be required if important changes are made to the review question or the general methodology.**
- **Standards for updates should be used in conjunction with the conduct and reporting standards.**

Since its inception, Cochrane has advocated for the routine updating of systematic reviews, in order to take account of new evidence. Before undertaking an update, several important decisions are required. The first is whether the original review question is still relevant. The second is whether the general methodological approach is still appropriate to answer the review question: this will need a review of the original protocol. Third, authors need to address whether the scope of the review is appropriate, whether it should be split into two or more reviews, or whether it should be merged with other reviews. Important changes of this nature indicate a need for a new protocol.

The following updating standards reflect three discrete review stages: planning, conducting and reporting. Expectations are that review authors will consider each of these sections before updating a review. Authors should examine and address any feedback on the original review before embarking on an update or a new derivative review. Planning an update should involve discussion with the Cochrane Review Group (CRG) over the adoption of new methods or changes to the review question proposed. The following standards for updates should be used in conjunction with the conduct and reporting standards for new Cochrane Reviews and these are cited where necessary. All CRGs are encouraged to classify their reviews by their update status, to denote whether the review is up to date, an update is pending or no update is planned (See explanatory note 1).

Jackie Chandler
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Cochrane Editorial Unit

DECIDING ON AND PERFORMING AN UPDATE

Planning the update

Standard	Rationale and elaboration
U1 Reconsidering review questions	**Mandatory**
Confirm or amend review question (PICO) and objectives.	Consider whether it is important to modify or add new objectives to make the review relevant to its users. Consider whether the review will be split, merged with another review or otherwise changed substantially. If so, a new protocol might be warranted and the *MECIR conduct standards* should be followed rather than these *update standards*. It will be necessary to agree the approach to updating the review with the CRG. *MECIR conduct standards C1, C2* See explanatory note 1
U2 Reconsidering outcomes	**Mandatory**
Confirm or amend outcomes of interest.	Consider whether it is necessary to modify or add outcomes to ensure all user-important outcomes, including adverse effects, are addressed. Define which outcomes are primary outcomes and which are secondary outcomes. Keep the total number of outcomes as small as possible. Consider core outcome sets where available. Prioritize outcomes that will be assessed with the GRADE considerations. *MECIR conduct standards C3, C14-C18, C23*
U3 Reconsidering eligibility criteria	**Mandatory**
Confirm or amend eligibility criteria.	Changes to the review objectives (e.g. additional consideration of rare adverse effects, economic issues or qualitative issues) may require modification of the eligibility criteria, possibly extending the scope to additional types of studies.
U4 Planning the search	**Mandatory**
Decide appropriate search methods.	There are four considerations in planning search methods for updates: 1. Changes to eligibility criteria may require the search methods to be modified, or additional search strategies to be developed. 2. Additional sources might need to be searched (e.g. trials registers) if not searched for the last published version of the review. Consideration should also be given to the importance of searching data repositories and information available from regulatory agencies. 3. The update search (for unchanged eligibility criteria) will normally be limited to material added or indexed after the date of the previous search. The yield of the previous searches may be useful to decide whether the full search is repeated or whether only a subset of sources should be searched for the update. 4. The original database search strategies may need to be modified, for example by adding search terms, adding new database subject

	headings, or by removing unhelpful search terms that identified many irrelevant studies in the original search. *MECIR update standards U6 and UR3* See *Handbook* 3.3.3
U5 Reconsidering data collection and analysis methods	**Mandatory**
Consider whether methods for data collection and analysis (including a GRADE assessment) need to be amended in the light of recent methodological developments.	Decide if changes are required to make better use of existing data or to incorporate new data by referring to the current version of the *Handbook*. Recent developments in 'Risk of bias' assessment, statistical methods or narrative synthesis approaches may lead to more inclusive or more robust synthesis of the evidence. The GRADE assessment will require evaluation of risk of bias, inconsistency, imprecision, indirectness and publication bias. See *MECIR update standard U11* If a 'Summary of findings' table is not included in the current version, decide on the main outcomes and comparisons to be included and ensure that the relevant data have been (or will be) collected. See *MECIR update standard UR5* *MECIR update standards U9-U10*

Conduct standards specific to updates

Standard	Rationale and elaboration
U6 Searching	**Mandatory**
Undertake a new search.	An updated review must include an update search for new (or additional) studies. For issues to consider in planning the search, see *MECIR update standard U4.* The most recent search must be no more than 12 months (preferably six months) from the intended publication date, and the results screened for potentially eligible studies. See *MECIR conduct standard C37:* 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.
U7 Including new studies	**Mandatory**
Implement conduct standards for study selection and data collection for any newly identified studies (with updated criteria or methods as determined above).	*MECIR conduct standards C39-C51*

U8 Reconsider previously identified studies	Mandatory
Consider studies previously identified as included, awaiting classification, ongoing and excluded, and collect additional information from them if necessary.	Ensure appropriate methodology is followed to select included studies and collect information from them. It will be necessary to establish whether any studies previously identified as ongoing have now been completed. Ensure that reasons for excluding studies are consistent with current eligibility criteria and methodological standards. A redesign of the data collection form may be required if review questions or objectives have been modified.
U9 Assessing risk of bias	**Mandatory**
Ensure all studies are consistently assessed for risk of bias.	The updated review must include a 'Risk of bias' assessment of all new and previously included studies. For randomized trials, they must be assessed using a currently accepted version of the Cochrane 'Risk of bias' tool. The separation of performance bias and detection bias in the evaluation of blinding is highly desirable. *MECIR conduct standards C52-C61*
U10 Synthesizing results	**Mandatory**
Implement review synthesis methods (possibly revised for the update) according to conduct standards for synthesis, across all included studies.	*MECIR conduct standards C62-C74*
U11 Assessing quality of the evidence	**Mandatory**
Assess quality of evidence using GRADE considerations of risk of bias, inconsistency, imprecision, indirectness and publication bias.	This must be applied to the full body of evidence for the key outcomes included in the updated review. The most convenient way to present GRADE assessments is in a 'Summary of findings' table. *MECIR conduct standards C74-C75 and MECIR reporting standard R97*

Reporting standards specific to updates

Standard	Rationale and elaboration
UR1 Background	**Mandatory**
Review and update background as necessary to reflect changes over time.	Examples of changes that should be addressed include updated estimates of disease burden, new understanding of how people are affected by the disease or condition, new insights into mechanisms of action, or changes in policy or practice. Up-to-date references should be supplied to support this information.
UR2 Changes to scope	**Mandatory**
Explain any changes to questions, objectives or eligibility criteria.	Motivations to amend review questions and objectives for the update (such as addition of new interventions, or concerns over adverse effects) should be explained in the Background, and changes to eligibility criteria should be explained, dated and justified as 'Differences between the protocol and the review'.

UR3	Search for studies	Mandatory
Describe the update search.	Describe which sources of information were searched for the update, and how. If any of the sources originally searched were not searched for the update, this should be explained and justified. There are at least four possibilities for providing information about search methods in an updated review: 1. An *integrated* approach is to describe all searches together, which may be most feasible if the same search was repeated. 2. An *incremental* approach is to add information at each update to describe explicitly which searches were done for the update, retaining all information about previous searches. 3. A *replacement* approach is to describe only the searches done for the update, using the previous review as one source of studies. 4. A *hybrid* approach is to describe only the searches done for the update in the main text, using Appendices to provide information about previous searches.	

UR4	Flow of studies	Mandatory
Record the flow of studies.	Provide information on the flow of studies into the updated review, ideally using a PRISMA flow diagram. There are two broad options for providing information about how studies were identified that are included in the updated version of the review: 1. The results of previous searches can be retained in the review and supplemented with information about studies identified in the update. 2. Alternatively, only information about searches in the current update can be presented, with the previous version of the review serving as one particular source of studies. Either approach is acceptable. If taking the latter approach, the flow diagram should show one box for the number of studies included in the original review or previous update and an additional box for the new studies retrieved for the current update. If multiple searches have been conducted for the current update, the results of all the searches should be added together.	

UR5	'Summary of findings' tables	Highly desirable
Present a 'Summary of findings' table according to recommendations described in Chapter 11 of the *Handbook* (version 5 or later). Specifically, include results for one clearly defined population group (with few exceptions).	Efforts should be made to incorporate information presented in 'Summary of findings' tables (such as absolute effects, GRADE quality ratings and downgrading decisions) in other parts of the review including the Abstract, Plain language summary, Effects of interventions, Discussion and Authors' conclusions.	

UR6	Integrating findings	Mandatory
Present findings integrated across new and previously included studies and not just for the new studies (in the main text, Abstract, 'Summary of findings' tables and Plain language summary).	The main findings should be presented for the totality of evidence: it is not helpful to a new reader to be told about incremental updates to the evidence base. However, the impact of new evidence on review findings may be useful to draw on when interpreting the results.	

UR7 What's new?	**Mandatory**
Explain what's new.	It is important that changes are explained to inform returning readers about what's new. This should be achieved in several ways. A comment should be inserted to explain that the review is an update of a previously published review. This might be placed at the beginning or end of the Background or the start of the section 'Search methods for identification of studies'. It can be helpful to explain also whether the article describes the first, second, third and so on update of the review. Changes in review questions, eligibility criteria and methods should be reported in the section 'Differences between protocol and review', making it clear that they are changes since the previous version. Changes in findings must be reported and dated in the 'What's new' section. This should include the numbers of new studies and participants in those studies; and the nature of any changes in assessments of the quality of the evidence (e.g. using GRADE) and in the clinical implications of the findings. For particularly notable changes it is useful to comment on these within the text of the review.

Explanatory note

The practice of arbitrarily updating all reviews is now replaced by a review-by-review appraisal that assesses whether the review will include new data, new methods, new analyses or corrections to the previous review (Garner 2016). The update will address a similar PICO, however, it may necessitate modifications to accommodate developments in the topic area (Garner 2016).

Garner P, Hopewell S, Chandler J, MacLehose H, Akl E, Beyene J, et al. When to update systematic reviews and how to do it: consensus and checklist. *BMJ* 2016;354:i3507.