Performing the review (C24-75)

Searching for studies (C24-38)

Searching for studies

Cochrane Training resource: searching for studies

Cochrane Interactive Learning (CIL): module 3 - searching for studies

	Standard	Rationale and elaboration	Resources
C24	*Searching general bibliographic databases and CENTRAL*	***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*.	Cochrane Training resource: Register of Studies and RevMan
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, PsycINFO 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 Cochrane Training resource: searching for adverse effects
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	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

	sources such as reports, dissertations, theses, databases and databases of conference abstracts.		
C29	*Searching within other reviews*	***Highly desirable***	
	Search within previous reviews on the same topic.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible.	See *Handbook* 6.2.2.5
C30	*Searching reference lists*	***Mandatory***	
	Check reference lists in included studies and any relevant systematic reviews identified.	Searches for studies should be as extensive as possible in order to reduce the risk of publication bias and to identify as much relevant evidence as possible.	See *Handbook* 6.2.2.5
C31	*Searching by contacting relevant individuals and 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	Inappropriate or inadequate search strategies may fail to identify records that are included in bibliographic databases. Search	See *Handbook* 6.4.11,

	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.	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.	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 (C39-42)

Selecting studies to include in the review

Cochrane Training resources: selecting studies and Covidence webinar (online tool for review production)

Cochrane Interactive Learning (CIL): module 4 - selecting studies and collecting data

	Standard	Rationale and elaboration	Resources
C39	*Making inclusion decisions*	***Mandatory***	
	Use (at least) two people working independently to determine whether each study meets the eligibility	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	See *Handbook* 7.2.4

	criteria, and define in advance the process for resolving disagreements.	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.	
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 be able to complete a flow diagram and a table of 'Characteristics of excluded studies'.	A PRISMA type flow diagram 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 (C43-51)

Collecting data from included studies

Cochrane Training resources: collecting data and Covidence webinar (online tool for review production)

Cochrane Interactive Learning (CIL): module 4 - selecting studies and collecting data

	Standard	Rationale and elaboration	Resources

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 Cochrane Training resources: dichotomous outcomes and continuous outcomes
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 Cochrane Training resource: non-standard data and study design
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.	Cochrane Training resource: common errors

Assessing risk of bias in included studies (C52-60)

Assessing risk of bias in included studies

Cochrane Training resources: assessing RoB and RoB 2.0 webinar

Cochrane Interactive Learning (CIL): module 5 - introduction to study quality and risk of bias

	Standard	Rationale and elaboration	Resources
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	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

	resolving disagreements.		
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	*Ensuring results of outcomes included in 'Summary of findings' tables are assessed for risk of bias.*	***Highly desirable***	
	Ensure that assessments of risk of bias cover the outcomes included in the 'Summary of findings' table.	It may not be feasible to assess the risk of bias in every single result available across the included studies, particularly if a large number of studies and results are available. Review author should strive to assess risk of bias in the results of outcomes that are most important to patients. Such outcomes will typically be included in 'Summary of findings' tables, which present the findings of seven or fewer patient-important outcomes.	See *Handbook* 8.5.1, 8.11.2, 8.12.2
C57	*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 certainty of the body of evidence.	See *Handbook* 8.5.1, 8.13.2
C58	*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 results. This is useful in determining the strength of conclusions and how future research should be designed and conducted.	See *Handbook* 8.7
C59	*Incorporating assessments of risk of bias.*	***Mandatory***	
	If randomized trials have been assessed using one or more tools in addition to the RoB 2 tool, use the RoB 2 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 RoB 2 tool should take precedence when two or more tools are used for assessing risk of bias in randomized trials. The RoB 2 tool also feeds directly into the GRADE approach for assessing the certainty of the body of evidence.	See *Handbook* 8.8.1
C60	*Addressing conflicts of interest in included trials.*	***Highly desirable***	
	Address conflict of interests in included trials, and reflect on possible impact on: a) differences in study	Review authors should consider assessing whether they judge a trial to be of "notable concern of conflicts of interest". This assessment is useful for exploration of possible heterogeneity	See *Handbook* 8.8.1

	design; b) risk of bias in trial result, and c) risk of bias in synthesis result	between trials (e.g. in a subgroup analysis), and for reflection on relevant mechanisms for how conflict of interest may have biased trial results and synthesis results. Concerns about conflicts of interest can be reported in the 'Characteristics of included studies' table.	

Synthesizing the results of included studies (C61-73)

Synthesizing the results of included studies

Cochrane Interactive Learning (CIL): module 6 - analysing the data

	Standard	Rationale and elaboration	Resources
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 Cochrane Training resource: analysing continuous outcomes
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 Cochrane Training resources: intro to meta-analysis and exploring heterogeneity
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 Cochrane Training resource: exploring heterogeneity
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 Cochrane Training resources: assessing RoB included studies and RoB 2.0 webinar
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 Cochrane Training resource: analysing continuous outcomes
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 Cochrane Training resource: analysing non-standard data & study designs
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 Cochrane Training resources: exploring heterogeneity and common interpretation errors
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 Cochrane Training resources: exploring heterogeneity and common interpretation errors
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 Cochrane Training resource: exploring heterogeneity
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 Cochrane Training resource: non-standard study designs
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	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 Cochrane Training resource: exploring

	and studies at high risk of bias.		heterogeneity
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 Cochrane Training resource: common interpretation errors CIL: module 7 - interpreting the findings
C73	*Investigating risk of bias due to missing results*	***Highly desirable***	
	Consider the potential impact of non-reporting biases on the results of the review or the meta-analyses it contains.	There is overwhelming evidence of non-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 Cochrane Training resources: small study effects & reporting biases CIL: module 7 - interpreting the findings

Assessing the quality of evidence and summarizing the findings (C74-75)

Assessing the quality of evidence and summarizing the findings

Cochrane Training resource: GRADE approach to evaluating evidence quality

Cochrane Interactive Learning: module 7 - interpreting the findings

	Standard	Rationale and elaboration	Resources
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 Common issues in Summary of Findings tables. Planning GRADE and Summary of Findings tables. Incorporating GRADE in Cochrane Reviews.
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

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