Reporting guideline for overviews of reviews of healthcare interventions: the Preferred Reporting Items for Overviews of Reviews (PRIOR) statement

PRIOR Explanation and Elaboration

TITLE

Item 1. Identify the report as an overview of reviews.

Rationale: No agreed upon standardized terminology for authors reporting on overviews of reviews exists. As a result, there is considerable inconsistency in the terms that are used in published overviews (e.g., review of systematic reviews, meta-review, umbrella review) (1-3) as well as across major evidence synthesis centres (e.g., Cochrane (4), JBI (formally Joanna Briggs Institute) (5)). Several authors have cited the need for consistent terminology to assist in indexing, searching for, and accurately and reliably identifying overviews of reviews (2, 6-8). At the time of protocol development, 'overview of reviews' was the most common label used (2) and had gained widespread acceptance (9), at least in part due to its use by Cochrane (4). Thus, this term was chosen for use within the PRIOR reporting guideline. Including the term 'overview of reviews' in the title will make the document type immediately apparent to readers.

Essential elements

- Use the term 'overview of reviews' in the title to ensure that the study design is easily identifiable.
- Report an informative title that includes the main objective (e.g., effectiveness) and key information about the population(s), intervention(s), and comparator(s) of interest.

Additional elements

- Indicate whether the overview of reviews is an update of an existing overview of reviews, or is being continually updated as a living overview of reviews.

Example: "Comparative effectiveness and safety of pharmacological and non-pharmacological interventions for insomnia: an overview of reviews" (10)

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ABSTRACT

Item 2. Provide a comprehensive and accurate summary of the purpose, methods, and results of the overview of reviews.

Rationale: Well-written abstracts allow readers to quickly understand the objectives, scope, methods, and findings of overviews of reviews, and to decide whether they should read the full report (11). Following the title, the abstract is the most read section of research reports (12), and for some readers may be the only component of the report that is accessible (13). It is therefore critical that the abstract accurately and succinctly conveys an unbiased summary of the main results, and how these were determined (11, 13). The quality of the information provided in abstracts is improved when conveyed in a structured format (i.e., including standard headings under which information is reported) (14, 15); however, reporting of a structured abstract is not common among published overviews of reviews (3). Until evidence- and consensus-based guidance for overview of reviews abstracts is developed, PRIO for abstracts (13) and PRISMA 2020 guidance for abstracts (16) may provide useful frameworks for authors.

Essential elements

- Until overview of reviews-specific guidance is developed, abstracts should be reported according to PRIO for abstracts (17) and PRISMA 2020 for abstracts (16).

Example:

"**Background**
Overviews are a new approach to summarising evidence and synthesising results from related systematic reviews.

Objectives
To conduct an overview of Cochrane systematic reviews to provide a contemporary review of the evidence for delivery of cardiac rehabilitation, to identify opportunities for merging or splitting existing Cochrane reviews, and to identify current evidence gaps to inform new cardiac rehabilitation systematic review titles.

Methods
We searched The Cochrane Database of Systematic Reviews (2014, Issue 10) to identify systematic reviews that addressed the objectives of this overview. We assessed the quality of included reviews using the Revised Assessment of Multiple Systematic Reviews (R-AMSTAR) measurement tool and the quality of the evidence for reported outcomes using the GRADE framework. The focus of the data presentation was descriptive with detailed tabular presentations of review level and trial level characteristics and results.

Main results
We found six Cochrane systematic reviews and judged them to be of high methodological quality. They included 148 randomised controlled trials (RCTs) in 98,093 participants. Compared with usual care alone, the addition of exercise-based cardiac rehabilitation in low-risk people after myocardial infarction or percutaneous coronary intervention or with heart failure appeared to have no impact on mortality, but did reduce hospital admissions and improved health-related quality of life. Psychological- and education-based interventions alone appeared to have little or no impact on mortality or morbidity but may have improved health-related quality of life. Home- and centre-based programmes were equally effective in improving quality of life outcomes at similar healthcare costs. Selected interventions can increase the uptake of cardiac rehabilitation programmes whilst there is currently only weak evidence to support interventions that improve adherence to cardiac rehabilitation programmes. The quality of the primary RCTs in the included systematic reviews was variable, and limitations in the methodological quality of the RCTs led to downgrading of the quality of the evidence, which varied widely by review and by outcome.

Authors' conclusions

Exercise-based cardiac rehabilitation is an effective and safe therapy to be used in the management of clinically stable people following myocardial infarction or percutaneous coronary intervention or who have heart failure. Future RCTs of cardiac rehabilitation need to improve their reporting methods and reflect the real world practice better including the recruitment of higher risk people and consideration of contemporary models of cardiac rehabilitation delivery, and identify effective interventions for enhancing adherence to rehabilitation." (18)

RATIONALE

Item 3. Describe the rationale for conducting the overview of reviews in the context of existing knowledge.

Rationale: After reading the introduction, the reader should be able to understand the reason(s) why the overview of reviews was undertaken and what it adds to the existing body of knowledge. It is good practice for authors to begin by describing the problem that the overview of reviews plans to address and the existing knowledge on the topic (19). Authors should describe limitations in the existing literature and explain how the overview of reviews will improve upon what already exists (19). In a descriptive analysis of overviews of reviews published from 2015 to 2017, Lunny *et al.* found that only 60% fully reported a clinical rationale for the work (20).

It is essential that authors describe why an overview of reviews format is the best fit for the research question and the nature of the available evidence (i.e., systematic reviews) (4, 21). When justifying the overview of reviews format, authors will require some knowledge about the nature and amount of existing systematic reviews, potentially by running a preliminary search (1, 4, 21-25). Important considerations include the up-to-datedness of existing systematic reviews; sufficient homogeneity in populations, comparators, and/or outcome measures; the amount and type of outcome data presented; and sufficiently low risk of bias (or adequate methodological quality) across the available systematic reviews (1, 4, 21-25). Additional guidance on choosing between an overview of reviews and systematic review can be found in Chapter V of the Cochrane Handbook (4). The online tool, "What Review is Right for You?" (https://whatreviewisrightforyou.knowledgetranslation.net/) can also help inform whether an overview of reviews is appropriate.

Essential elements

- Describe the problem that the overview of reviews plans to address.
- Describe the existing knowledge on the topic, its limitations, and how the overview of reviews will improve upon what already exists.
- Describe why an overview of reviews is an appropriate methodology for addressing the research question(s).

Additional elements

- Indicate whether the overview of reviews is an update of an existing overview of reviews or is being continually updated as a 'living' overview of reviews.
- If applicable, cite the existing overview of reviews that is being updated.

Example: "The care of children with asthma is based upon escalation of treatment in response to disease severity: mild disease receives less intensive treatment than severe disease. Broadly speaking, interventions take the form of inhaled bronchodilators, parenteral (intravenous or subcutaneous) pharmacotherapy, and mechanical efforts to reduce the work of breathing. With increasing 'level of treatment' come risks of increasing costs, patient discomfort, potential for complications, and requirement for monitoring and/or transfer to intensive care units. […] Variation in the management of acute severe asthma in children is considerable and may be due to considerations around efficacy, safety, cost, clinical experience, and individual practitioner preference. […] With a large number of treatment options and wide variation in self-reported and actual practice, it is important to have a single comprehensive and user-friendly document that provides the best available evidence upon which to base clinical decisions. […] This overview will document the efficacy of second-line interventions from systematic reviews and will provide information about toxicity and adverse effects. Potential additional benefits of this overview will include a clear foundation upon which further research can be based and an understanding of reported outcome measures, which may be used to assist in development of a set of core outcome measures for future clinical trials. Currently, the Cochrane Airways Group has prepared approximately 50 published reviews on the effectiveness of various interventions for acute asthma. These include 43 reviews on pharmacotherapy and another seven reviews on non-

pharmacotherapy interventions. Given the large number of potentially relevant reviews and the likely heterogeneity in eligibility criteria and study outcomes, we have chosen to utilize an overview design rather than a network meta-analysis as the first step in assessing the literature." (26)

OBJECTIVES

Item 4. Provide an explicit statement of the objective(s) or question(s) addressed by the overview of reviews.

Rationale: Precisely worded questions allow readers to quickly understand the purpose and scope of the intended overview of reviews and assess its relevance (27, 28). However, in an assessment of the completeness of reporting in overviews of reviews published from 2015 to 2017, Lunny *et al.* found that just 56% included a statement of the question(s) or objective(s) that addressed all PICOT (population, intervention, comparator, outcomes, time frame) elements (29). Authors should take the time to formulate clear questions as these set the basis for the methods used in the overview of reviews (e.g., search, selection, data extraction, analysis) (28). The PICOT approach to writing objective statements is now widely endorsed (28, 30, 31). Adherence to this framework ensures that the population, interventions, comparators, outcomes, and time frame of interest are clearly articulated.

Essential elements

- Report the objective(s) or question(s) addressed by the overview of reviews, including the population(s), intervention(s), comparator(s), outcome(s) (at minimum the primary outcome), setting(s), and time frame(s) of interest.

Additional elements

- Report additional outcomes of interest, if not already stated.
- Specify the intended user(s) of the overview of reviews.

Example: "This [overview of reviews] aimed to determine the clinical effectiveness of self-management interventions for adults with chronic obstructive pulmonary disease. The outcomes of interest are health-related quality of life (HRQoL), health care utilization and mortality." (32)

ELIGIBILITY CRITERIA

Item 5a. Specify the inclusion and exclusion criteria for the overview of reviews. If supplemental primary studies were included, this should be stated, with a rationale.

Rationale: The scope of an overview of reviews is often broad (4, 5, 33) and needs to be tailored to match that of the available systematic reviews (e.g., by population, intervention, or methodological characteristics) (34). Information regarding the eligibility criteria for the inclusion of systematic reviews in overviews of reviews is needed if readers are to appraise their validity, applicability, and comprehensiveness. The eligibility criteria and restrictions to scope should be reasonably justified. To date, the reporting of eligibility criteria in overviews of reviews has been suboptimal (2, 6, 29).

There is conflicting guidance on the inclusion of supplemental primary studies in overviews of reviews (that is, studies that are not contained in any included systematic review) (34). How these may be appropriately incorporated into overviews of reviews is not agreed upon (34). Guidance from Cochrane (4) and the JBI (formally Joanna Briggs Institute) (5), among others (1, 35), cautions against the incorporation of supplemental primary studies in overviews of reviews, and suggests that authors who wish to include supplemental primary studies re-assess the appropriateness of the overview of reviews methodology. Others suggest that supplemental primary studies may be included when pre-specified eligibility criteria are met: e.g., a systematic review is not up-to-date; a systematic review is inconclusive and new studies may change its results; the included systematic reviews provide incomplete coverage in relation to the scope of the overview of reviews; and/or there are concerns about the methods used to identify and select studies in systematic reviews (20, 25, 35). Authors who consider including supplemental primary studies should provide a rationale, and criteria for their inclusion. To date, such reporting has been suboptimal (29).

Essential elements

- Define the scope of the overview of reviews; this includes the population(s), intervention(s), comparator(s), primary outcome(s), setting(s), and time frame(s) of interest within eligible systematic reviews.
- Report any restrictions based on report characteristics, including language, publication status, and year indexed or published.
- If supplemental primary studies are included, justify the decision to include these within the overview of reviews
- If supplemental primary studies are included, define the study design(s), population(s), intervention(s), comparator(s), primary outcome(s), setting(s), and time frame(s) of interest.

Additional elements

- Justify notable restrictions to systematic review and/or supplemental primary study eligibility.

Example: "[below are] our eligibility criteria. We included SRs [systematic reviews] that assessed SOT's [systemic oncological treatments] impact in esophageal or gastric cancer patients at high risk of dying in the short or medium term. We searched for the following outcomes: 1) overall survival (OS); 2) progression-free survival (PFS); 3) functional status (FS); 4) toxicity; 5) symptoms related to the disease; 6) QoL [quality of life]; 7) admissions to hospital or long-term center, or emergency consultations; 8) quality of death (admission to the hospital at the end-of-life; palliative care provided during the last year; place of death). We considered the following as primary outcomes: OS, QoL, FS, and toxicity.

Patients

- Adults 18 years of age or older
- Esophageal or gastric cancer, primary or recurrent, in stage III or IV (advanced) or metastatic

Interventions

- Any chemotherapy, either monotherapy or in combination, or another oncological treatment (biological, targeted therapy or immunotherapy), whether individual or combined, with or without supportive care

Comparators

- Any supportive treatment, usual treatment or best supportive care

Outcomes

- Clinical outcomes: survival; progression-free survival; functional status; toxicity
- Patient-centered outcomes: symptoms related to disease; quality of life; admissions to hospital or long-term centre, or emergency consultations; quality of death (admission to hospital at end-of-life; palliative care provided during the last year; place of death)

Timing

- Studies published from 2008 onwards

Setting and study design

- Systematic reviews that assessed the impact of systemic oncological treatments in esophageal and gastric cancers at high risk of dying in the short or medium term"

(reproduced from Figure 1 in Santero et al., 2021) (36)

ELIGIBILITY CRITERIA

Item 5b. Specify the definition of 'systematic review' as used in the inclusion criteria for the overview of reviews.

Rationale: Many publications described as 'systematic reviews' are not conducted following systematic approaches and/or are poorly reported (37). As systematic reviews are the unit of analysis in overviews of reviews, but the use of the term 'systematic review' varies, authors of overviews of reviews must explicitly define the criteria used to determine if a publication was a systematic review (4). At present, very few published overviews of reviews include an explicit systematic review definition (38). While the definition used for eligibility should be explicit, enabling replication of selection decisions, it is common not to use all defining features of a systematic review (i.e. a definition that includes all features of a gold standard systematic review). Doing so can lead to unintentional exclusion of relevant reviews.

Essential elements

- Explicitly define both the methodological and reporting characteristics required for reports to be considered systematic reviews.

Example: "We defined systematic reviews as peer-reviewed studies with a clearly reported research question, systematic search of at least two databases and systematic data synthesis, replicating the eligibility criteria used in other overviews of SRs. […] We also excluded reviews with only one author and those that searched only one database because such reviews do not have elementary characteristics of systematic methodology." (39)

INFORMATION SOURCES

Item 6. Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify systematic reviews and supplemental primary studies (if included). Specify the date that each source was last searched or consulted.

Rationale. To ensure comprehensiveness and reduce the risk of selection bias, author teams should undertake thorough and reproducible searches of multiple sources to identify as many relevant systematic reviews as possible within resource limits (40). It is recommended that authors search at least two bibliographic databases (e.g., Medline, Embase) and systematic review databases (e.g., Epistemonikos, CDSR) (4, 5, 24, 32, 34, 35, 41, 42). One investigation found that searching Medline, Embase and Epistemonikos identified just over 99% of systematic reviews [43].

In addition, it may be prudent to search subject-specific databases (e.g., LILACS, CINAHL, AMED) for systematic reviews on certain topics (4). It has been recommended that overview of reviews teams should also contact content experts and conduct hand searches of relevant sources (4, 34), and search for registered systematic reviews (e.g., via PROSPERO).

To date, the reporting of search methods in overviews of reviews has been sub-optimal (2, 43). In a descriptive analysis of overviews of reviews published from 2012 to 2016, Pieper *et al.* (unpublished data) found that 26% failed to fully report the databases searched and years of coverage (43). Complete documentation of the information sources (including the database name, date range searched, and search platform or provider for electronic databases) helps readers to assess comprehensiveness, enhances reproducibility, and can inform search updates (40).

Essential elements

- **Bibliographic databases:** specify for each the name (e.g., Medline, Embase), the interface or platform through which the database was searched (e.g., Ovid, EBSCOhost), the dates of coverage, and date searched.
- **Registers or online repositories**: specify for each the name (e.g., PROSPERO), date restrictions applied, and date searched.
- **Websites, search engines, or any other online sources**: specify the name of each source (e.g., Google Scholar), URL, date restrictions applied, number of pages or search results reviewed and whether they were sorted by relevance or date (if applicable), and date searched. Report web sources within the main text (e.g., Google Scholar [https://scholar.google.com/]), or cite them in the reference list or a supplementary file.
- **Organizations**: if contacted, specify the name of each source and date contacted.
- **Content experts or other individuals:** if contacted, specify the types of individuals, contact method (e.g., email, videoconference), and date contacted.
- **Reference lists:** specify the types of documents examined (e.g., included systematic reviews or supplemental primary studies; systematic reviews of similar topics).
- **Any other sources (e.g., conference proceedings, hand search of journals):** specify the name of each source and other pertinent information (e.g., web address for online conference proceedings and dates of the conference).

Additional elements

- Report who was involved in selecting the information sources (e.g., information specialist).
- If supplemental primary studies are included, reporting should adhere to the guidance outlined in the PRISMA 2020 statement [16].

Example: "The search strategy involved searching the following electronic databases: MEDLINE (Pubmed), EMBASE, Cochrane Library, CINAHL, PsycINFO, Campbell Systematic Reviews, Database of Abstracts of Reviews of Effects, Epistemonikos, Joanna Briggs Institute Database of Systematic Reviews and implementation Reports and International prospective register of systematic reviews, from inception until December 2017. […] Further, we hand-

searched key Governmental and organizational websites (such as: Evidence for Policy and Practice Information and Co-ordinating Centre, National Institute for health and Care Excellence, The Community Guide) and the reference lists of included studies." (44)

SEARCH STRATEGY

Item 7. Present the full search strategies for all databases, registers and websites, such that they could be reproduced. Describe any search filters and limits applied.

Rationale. As in systematic reviews, providing the full details of the search strategy will improve transparency and allow readers to assess an overview of reviews' comprehensiveness and completeness (16). Moreover, documentation of the full electronic search strategy in all databases and grey literature sources allows for it to be reproduced, and is informative for search updates (40). If the overview of reviews aims to answer more than one research question, the search strategy should be provided in all databases and grey literature sources for each question. To date, the transparent reporting of search strategies in published overviews of reviews has been suboptimal (29).

Among a sample of 50 overviews of reviews published from 2015 to 2017, few reported using a search filter for the retrieval of systematic reviews (29). To improve the sensitivity of the search it has been recommended that searches be restricted when possible, to capture systematic reviews while minimizing the capture of other study types (4, 5, 35, 41). This may be accomplished by using systematic review-specific Medical Subject Headings (MeSH) and search terms, and/or validated systematic review search filters (4, 5, 35, 41). Any additional means to improve the specificity of the search should be reported, and their limitations (e.g., certain indexers may not complete all fields available in search engines). When overview of reviews teams decide to conduct a search for supplemental primary studies, they should report their methods in sufficient detail such that they may be reproduced, akin to the search for systematic reviews.

Essential elements

- Provide the full line-by-line search strategy in each database, such that it could be repeated. This may be included as a supplementary file, or accessible via a source external to the published report (e.g., institutional repository). When the search documentation is external to the published report, the location should be cited and publicly available.
- If the overview of reviews aims to answer multiple research questions, include the strategy for each question, as applicable.
- Describe any search limits applied, including limits based on date, language, or study design, among others. Justify any limits with reference to the eligibility criteria.
- If published approaches were used, including search filters, these should be cited. If published approaches were modified, all changes should be described.
- If searches for supplemental primary studies are undertaken, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Additional elements

- Report who was involved in developing and implementing the search strategies, and the date that the search was developed.
- If the search strategy was peer reviewed, report the credentials of the peer reviewer (e.g., research librarian) and how the peer review was done (e.g., using PRESS (45) or another checklist).
- If tools were used to optimize and automatically refine the search query (e.g., 2Dsearch, searchrefiner) and/or to translate search queries from one electronic database to another (e.g., SR-Accelerator, Medline Transpose) these should be reported.

Example: "A comprehensive search of the following electronic databases was conducted by an information specialist (RF) between March and May 2014: Cochrane Database of Systematic Reviews (CDSR) via Cochrane Library (from 2005), MEDLINE via Ovid (from 1946), EMBASE via Ovid (from 1980), Database of Abstracts of Reviews of Effects (DARE) (2nd quarter 2014), the Health Technology Assessment database (2nd quarter 2014) via Cochrane Library, and

the Cumulative Index to Nursing and Allied Health Literature (CINAHL) Database via EBSCOhost (from 1937). Searches used validated child and SR filters, as appropriate. Searches were restricted to published English-language documents from 1990 to the present. We reviewed reference lists of relevant SRs to identify additional SRs. Update searches were conducted in the CDSR and Ovid MEDLINE in November 2015 (Appendix S1)." (46)

SELECTION PROCESS

Item 8a. Describe the methods used to decide whether a systematic review or supplemental primary study (if included) met the inclusion criteria of the overview of reviews.

Rationale. Agreement is lacking on the best strategy to select systematic reviews for inclusion in overviews of reviews (20, 34). It has been suggested that at all stages, either: 1) two reviewers should independently (and in duplicate) select eligible records and agree on which to include, or 2) two independent reviewers should achieve good agreement (≥80%) on the selection of a sample of eligible records before selection is completed by a single reviewer (47, 48). To date, the reporting of the selection of records in published overviews of reviews has been suboptimal (2, 6, 29). Given the array of potential approaches, thorough reporting of the process will help readers to judge the comprehensiveness, completeness, and validity of the overview of reviews. The approach to resolving discrepancies should also be described (47, 48).

If overview of reviews authors choose to leverage automation tools in the screening process, this should be documented as it will factor into readers' judgments about the overview of reviews' credibility. Since automated or semi-automated methods are not yet widely accepted (49), authors should justify their choice and transparently report procedures that were used (e.g., natural language processing algorithm), as well as the strengths and limitations of the methodology.

Essential elements

- Report the number of reviewers who screened each record retrieved at the title-abstract and full text stages; whether they worked independently and/or in duplicate; and any processes that were in place to achieve agreement (e.g., consensus meetings; third-party reviewer).
- Indicate whether standard forms were used. Describe if any pilot testing of the selection form(s) and process occurred.
- If automation tools were used in the selection process, the software should be named and cited and the methods used to train (if relevant) and integrate the tools into selection (e.g., prioritization, semi-automation) should be described such that they could be repeated. Relevant internal and/or external validations of the tool should be reported and cited.
- If crowdsourcing was used during the selection process, describe how the crowd was selected and trained, how they were integrated into the selection process, and name and cite any software platform used.
- If supplemental primary studies are included, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Additional elements

- Name and cite any software used to manage and track the flow of records through the selection process.
- If pilot testing occurred, report the level of agreement achieved during the pilot testing phase.
- If any reports needed to be translated to determine their eligibility, indicate how and by whom (e.g., first-language speaker) this was done.
- If the authors of any reports were contacted to confirm the availability of data or materials, report how this was done, and the number of responses received.

Example: "Calibration exercises were completed with the review team prior to level 1 (title/abstract) and level 2 (full-text) screening, […] to ensure reliability of the processes and revise forms as needed. Only one round of calibration using 25 citations was required prior to level 1 screening (≥ 75% agreement), […], while two rounds of calibration (≥ 75% agreement) were required prior to level 2 screening (15 and 25 articles, respectively). Level 1 and 2 screening was completed in duplicate by pairs of reviewers working independently and any discrepancies were resolved by a third reviewer, […]. Screening was completed using synthesiSR, proprietary online software developed by the

Knowledge Translation Program of St. Michael's Hospital [Knowledge Translation Program. Synthesi.SR Toronto, Ontario: Li Ka Shing Knowledge Institute, St. Michael's Hospital; 2014." (10)

SELECTION PROCESS

Item 8b. Describe how overlap in the populations, interventions, comparators, and/or outcomes of systematic reviews was identified and managed during study selection.

Rationale. Overview of reviews authors are likely to identify two or more systematic reviews that investigate the same intervention and include at least some (but not necessarily all) of the same primary studies (4). Despite the existence of often substantial primary study overlap, almost half (47%) of published overviews of reviews do not mention the overlap (50) and only 28% describe how this was managed at the selection stage (29).

When faced with multiple 'overlapping' systematic reviews (i.e., those which contain some or all of the same studies for a given comparison-outcome), authors may choose from among multiple approaches to dealing with the overlaps, each of which has the potential to introduce bias (51, 52). As such, authors should be explicit as to which approach was used and why. Authors can use a decision algorithm such as that developed by Pollock *et al.* to assist in taking the best approach (i.e., including all or some of the overlapping systematic reviews) for their overview of reviews (52).

Essential elements

- Report on the eligibility of overlapping systematic reviews (i.e., those that investigate the same intervention and include at least some of the same primary studies) during selection.
- If only some overlapping systematic reviews are included, describe and justify the process for prioritizing systematic reviews for inclusion in detail (e.g., tool used to assess quality or risk of bias, how 'comprehensiveness' or 'relevance' were defined).

Example: "We sorted all included reviews by population and intervention comparisons (the PICOs). In cases were more than one review addressed the same comparison for the same population, we included the review with the newest search date (and completeness of this search by considering the included primary studies) and the best quality. In considering overlap, the first author (ISM) extracted this information from the reviews, and the second author (AA) double-checked the information. Further, we assessed the methodological quality of the included reviews based on a checklist for systematic reviews (AMSTAR: A MeaSurement Tool to Assess systematic Reviews). Two people (ISM, IB) considered each publication independently and decided on the quality through discussions until consensus. The final decision on which reviews to include was done through agreement between two of the authors (ISM and AA)." (53)

DATA COLLECTION PROCESS

Item 9a. Describe the methods used to collect data from reports.

Rationale. Given that data extraction errors are prevalent (54) and have the potential to affect the results of overviews of reviews (55), authors should report the methods used to mitigate errors in the data extraction process. Transparent reporting of the data extraction process allows readers to judge the trustworthiness and completeness of the presented findings. Descriptive analyses by Hartling *et al.* and Pieper *et al.* (unpublished data) showed that the methods to undertake data extraction were described in only about two-thirds of published overviews of reviews (2, 43).

Guidance is relatively sparse on the best approach to extracting data from the included systematic reviews (20, 34). Suggested approaches include duplicate data extraction, extraction by a single reviewer (after a pilot phase where a high level of agreement has been reached), or extraction by a single reviewer with verification by another (47, 48, 56). Regardless of the data extraction method selected, piloting the process with a standardized form is recommended (5, 54, 57). Any training processes that have been undertaken should be described. If two (or more) reviewers are involved, the method used to handle disagreements should be stated.

To judge the credibility of the overviews of reviews readers need to know if and how automation tools were used in the data extraction process. Overview of reviews authors who choose to use tools to automate or semi-automate parts of the data extraction process should thus report the tool, its validity, and how it was used.

Essential elements

- Report how many reviewers collected data from each report; whether they worked independently; and any processes that were in place to mitigate errors (e.g., independent verification) and/or achieve agreement (e.g., consensus meetings; third-party reviewer).
- Indicate whether standard forms were used. Describe whether any pilot testing of the data collection form(s) and process occurred.
- Name and cite any software used to assist with data collection from the reports.
- Name and cite any software used to extract data from figures.
- If automation tools were used in the data collection process, name and cite the software, and describe the methods used to train (if relevant) and integrate the tools into data collection, such that they could be repeated. Report and cite relevant internal and/or external validations of the tool.
- If crowdsourcing was used during the data extraction process, describe how the crowd was selected and trained, how they were integrated into the data extraction process, and name and cite any software platform used.
- If supplemental primary studies are included, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Additional elements

- If pilot testing occurred, report the level of agreement achieved during the pilot testing phase.
- If any reports needed to be translated to enable data collection, indicate how and by whom this was done.
- If the authors of any reports were contacted to obtain or confirm relevant data, report how this was done.

Example: "**Data extraction and management**: Two of the overview authors independently extracted data from each systematic review, using an electronic form which we designed and piloted. We resolved disagreements by consensus or by discussion with a third overview author." (58)

DATA COLLECTION PROCESS

Item 9b. If applicable, describe the methods used to identify and manage primary study overlap at the level of the comparison and outcome during data collection. For each outcome, specify the method used to illustrate and/or quantify the degree of primary study overlap across systematic reviews.

Rationale. Depending on the purpose of the overview of reviews, it may be appropriate to collect data from all systematic reviews with overlapping data, or only one of the systematic reviews based on the selection criteria (i.e., in the case of a pooled analysis) (4, 52). Because the appropriateness of the approach will depend on the purpose of the overview of reviews and the scope of the included systematic reviews, authors should justify their choice about how data from overlapping systematic reviews will be included. In a descriptive analysis by Lunny *et al.*, among a sample of overviews of reviews published from 2015 to 2017, only 26% reported methods for handling overlapping information across systematic reviews (29).

If a primary study result is reported multiple times within a pooled analysis (i.e., double-counting), it overstates its sample size and number of events, falsely leading to greater precision in the analysis (59). Suggested methods to manage overlap at the data extraction step in the conduct of an overview of reviews include: a) extract primary study data from all reviews (and manage overlap at other stages), or b) extract primary study data from only one (or more) review using pre-specified eligibility criteria. If overlap is not addressed at the data extraction step, overview of reviews authors are advised to quantify and assess the influence of overlap at the synthesis stage.

Regardless of the selected approach to dealing with overlap, authors should at minimum construct a citation matrix (table) to present the extent of overlap across systematic reviews (4, 29, 50, 59). An outcome matrix and/or other graphical displays may also be relevant (59, 60). Visual investigation of citation and outcome matrices can be used to determine if low primary study overlap is related to temporal gaps in search time frames, gaps in research topics, or how studies are clustered (59). Authors may also find it useful to calculate and report the corrected covered area (CCA) and/or percent overlap (50). Pieper *et al.* provide detailed instructions on how to calculate these metrics (50).

Essential elements

- Describe the process used to identify and illustrate the degree of primary study overlap across systematic reviews at the citation and outcome levels.
- Justify the approach used to deal with overlapping systematic reviews at the data extraction phase (e.g., extract all data, extract data only from non-overlapping reviews).

Example: "Overlap of included studies was assessed using the corrected covered area (CCA). CCA calculations followed Pieper et al's protocol according to $CCA = \frac{N-r}{rc-r}$, where N is the number of included publications (including double counting), r is the number of primary publications, and c is the number of reviews. Pre-determined overlap thresholds were used for interpretation of overlap (0–5%—slight, 6–10%—moderate, 11–15%—high, >15%—very high). For each outcome, a citation matrix and pairwise CCA tables were created in addition to the outcome level CCA calculations to address overlap. Overlap is presented visually as per recommendations from Pérez-Bracchiglione et al. at the 2019 Cochrane Colloquium." (61)

DATA COLLECTION PROCESS

Item 9c. If applicable, specify the methods used to manage discrepant data across systematic reviews during data collection.

Rationale. Authors of overviews of reviews are likely to encounter discrepant data, that is, data from the same primary study that is reported differently across various systematic reviews. Some of the reasons for discrepant data reported across reviews include: errors in data extraction, data are extracted from different sources for the same primary study (e.g. different reports, unpublished data), data retrieved/not retrieved by contacting primary study authors, different results are selected for the same comparison/outcome. Because the inclusion of incorrect data from systematic reviews can introduce bias (51), it is important that authors explain the procedures used to identify discrepant data and the process undertaken to correct the data (4). Among a sample of overviews of reviews published from 2015 to 2017, Lunny *et al.* found that just 6% reported methods for handling discrepant data (29).

Suggested methods to deal with discrepancies vary in rigour and resource-intensiveness, and include: a) extracting all data and recording discrepancies; b) extracting data from only one systematic review based on *a priori* decision rules; or c) reconciling discrepancies by contacting authors, retrieving the data from the original primary studies, or searching systematic review or trial registry entries for the required data (18). Because the chosen methodology has the potential to impact the findings of the overview of reviews, authors should indicate the approach that was used and justify their choice.

Essential elements

- Report and justify the processes used to identify and resolve discrepant data for the same primary studies across systematic reviews.

Example: "If we identified discrepant data across systematic reviews, we planned to extract data from all included reviews and reconcile the discrepancies by contacting the authors of included reviews, retrieving primary studies from the included reviews, and searching relevant trial registries. We planned to discuss potential discrepancies in data in the Results section. We identified no discrepant data." (26)

DATA ITEMS

Item 10. List and define all variables and outcomes for which data were sought. Describe any assumptions made and/or measures taken to identify and clarify missing or unclear information.

Rationale. Authors of overviews of reviews should consider and list variables that will allow readers to clearly ascertain the scope and characteristics of the included systematic reviews, as well as the characteristics of the primary studies included within each review. This allows readers to assess the relevance of the included systematic reviews to their needs, and the extent and nature of the relevant primary literature. In a review of overviews of reviews published from 2015 to 2017, Lunny *et al.* found that just 60% fully reported the data extracted about the characteristics of the included systematic reviews (29). Variables about the included systematic reviews may include: bibliographic information (e.g., title, authors, year of publication); elements of the review question(s) (e.g., population, interventions, comparators, outcomes); and review methods (e.g., search strategy, date of search or last update, statistical methods) (4). Variables describing the primary studies identified as relevant to each systematic review may include: years of publication, countries where studies were conducted, funding sources, study designs, numbers of studies and participants, characteristics of participants, characteristics of interventions and comparators, and outcomes (4).

Authors of overviews of reviews may specify which outcomes are considered primary and secondary; this allows for more transparent conclusions to be drawn. These should follow from the objective(s) and/or question(s) addressed by the overview of reviews (see item 4). The time frame(s) of interest should also be specified for each outcome. Overview of reviews authors may select outcomes and time points that are reported in a similar fashion across the included systematic reviews to provide more consistency in presenting data/results across systematic reviews. Where information on the overview of reviews' pre-specified outcomes and time points is not reported in the systematic reviews, most guidance documents recommend simply indicating that the information is missing (34). A more resource-intensive approach that will improve the completeness of the findings (and avoid risk of bias due to missing information) is to contact systematic review authors for the data, or to extract the data from the primary studies anew (34).

Essential elements

- Specify all variables (e.g., systematic review characteristics, funding sources, interventions) for which data were sought.
- List and define the outcome domains and time frames of measurement for which data were sought.
- Specify whether all results that were compatible with each outcome domain in each systematic review were sought, and if not, what process was used to select results within eligible domains.
- Describe any assumptions made about any missing or unclear information from the systematic reviews and/or measures taken to identify or clarify missing or unclear information (e.g., reviewing primary study reports; contacting authors).

Example:
"When information from the review was missing, we accessed the published papers of the individual study and contacted the systematic review authors for further details. We extracted and tabulated information for the following.

- Review title and authors.
- Search date: date of search conducted by review (we considered less than two years ago to be current).
- The number of trials in the review, number of women and their infants, and their characteristics.
- Risk of bias of the included trials (as reported by the review authors; see 'Risk of bias of included studies within reviews' below, under Assessment of methodological quality of included reviews).
- Interventions and comparisons relevant to this overview.

- The prespecified outcome (GDM) relevant to this overview.

Any other characteristics required to assess and report on review quality […]" (58)

RISK OF BIAS ASSESSMENT

Item 11a. Describe the methods used to *assess* risk of bias or methodological quality of the included systematic reviews.

Rationale. An assessment of the risk of bias or methodological quality of the included systematic reviews will allow for an informed interpretation of the evidence presented. A valid tool should be used to guide the assessment (34). Recent guidance suggests that AMSTAR 2 (47) can be used to assess the methodological quality of systematic reviews, while ROBIS (48) can be used to assess risk of bias (4, 5, 24, 62). Studies comparing both tools can assist overview authors to make a choice between them (63-67). Because judgments of risk of bias or methodological quality may vary by outcome, authors should indicate the outcome(s) that they have assessed. Depending on the context, authors may choose to use a tool in its entirety or parts of a tool that are most relevant to the systematic reviews that are included. For transparency, authors should specify the domains, components, and/or items that have been used to guide their assessment. If a judgment of the *overall* methodological quality or risk of bias of the systematic review has been undertaken, authors should indicate how this was done such that readers can appraise the appropriateness of the judgment. Guidance on judging the overall risk of bias or methodological quality are available for AMSTAR 2 (47) and ROBIS (48).

Available guidance indicates that it is highly desirable that assessments be undertaken by two independent reviewers, with a process in place for reaching consensus (4, 5, 34). This reduces the potential of a single reviewer's opinion to bias the assessments and also the possibility of errors. Authors of overviews of reviews should report the methods used to assess risk of bias or methodological quality, including how many reviewers were involved, whether any piloting was undertaken and/or if decision rules were developed (and what they were), and the process for resolving discrepancies so that readers can judge the appropriateness and trustworthiness of the findings. To date, reporting of the process to assess risk of bias or methodological quality in published overviews of reviews has been suboptimal (29, 43).

Essential elements:

- Specify the tool(s) (and version) used to assess risk of bias or methodological quality of the systematic reviews included in the overview of reviews.
- Indicate the outcome(s) for which methodological quality or risk of bias have been assessed.
- Specify the domains/components/items of the risk of bias or methodological quality assessment or quality appraisal tool used.
- Report whether a judgment was made about the overall risk of bias or methodological quality of each included systematic review, and if so, what criteria were used for the overall judgment.
- Report how many reviewers assessed the risk of bias or methodological quality of each systematic review; whether they worked independently; and any processes that were in place to achieve agreement (e.g., consensus meetings; third-party reviewer).
- Describe whether any pilot testing of the risk of bias or methodological quality tool occurred.
- Report any decision rules that were developed.
- If automation tools were used for risk of bias or methodological quality assessment, name and cite the software, and indicate the methods used to train (if relevant) and integrate the tools into data collection, such that it could be repeated. Relevant internal and/or external validations of the tool should be reported and cited.

Additional elements:

- If pilot testing occurred, report the level of agreement achieved during the pilot testing phase.
- If any reports needed to be translated to enable risk of bias or methodological quality assessments, indicate how and by whom this was done.
- If the authors of any reports were contacted to obtain or confirm relevant information, report how this was done.

Example: "Two overview authors independently assessed the risk of bias of included systematic reviews using the Risk of Bias in Systematic Reviews (ROBIS) tool. The ROBIS tool (see Appendix 3) consists of three phases: assessment of relevance of the systematic review to the study question, identification of potential concerns regarding the review process, and a judgement of risk of bias. We planned to report in a table assessment for individual ROBIS items or domains (along with the rationale for judgements for each assessment).

We defined a high-quality systematic review with meta-analysis as one that has low risk of bias judgements for the first three domains of the ROBIS tool, namely, specification of study eligibility (domain 1), methods used to identify and/or select studies (domain 2), and methods used to collect data and appraise studies (domain 3). […] We planned to use the risk of bias assessment to conduct sensitivity analyses, but we did not exclude reviews on the basis of the risk of bias assessment. We planned to present a summary of this information according to guidelines provided in the *Cochrane Handbook for Systematic Reviews of Interventions*." (68)

RISK OF BIAS ASSESSMENT

Item 11b. Describe the methods used to *collect* data on (from the systematic reviews) and/or *assess* the risk of bias of the primary studies included in the systematic reviews. Provide a justification for instances where flawed, incomplete, or missing assessments are identified but not re-assessed.

Rationale. Readers need accurate and reliable information about the risk of bias in the systematic reviews' included studies to ascertain the trustworthiness of an overview of reviews' findings. To date, fewer than half of published overviews of reviews have extracted this information from the included systematic reviews (6, 29). It is generally recommended that authors collect risk of bias assessments from the included systematic reviews directly; however, when these are missing (e.g., not done or only partly done), flawed (e.g., using problematic tools), or discordant (e.g., different assessments for the same primary study across systematic reviews), overview of reviews authors may choose to independently assess risk of bias for all primary studies anew, or supplement existing risk of bias assessments as necessary (4, 5, 34, 35, 69). For full transparency, authors should explicitly state how data on risk of bias in the primary studies was collected, any methods used to ascertain the accuracy and consistency of assessments, and how they dealt with missing, flawed, or discordant data. When overview of reviews authors decide to conduct their own assessments, information on how they were conducted and the tools that were used should be provided.

Major evidence synthesis organizations (4, 5) recommend that data (including risk of bias assessments) be extracted from the included systematic reviews independently by two reviewers, along with consensus. Extraction by a single reviewer with verification by a second is another option. Because the chosen methodology has the potential to impact the findings of the overview or reviews, authors should indicate the approach that was used.

Essential elements:

- If choosing to *collect* data on risk of bias assessments directly from the included systematic reviews (rather than assessing risk of bias anew), adhere to the reporting criteria for data extraction (item 9a).
- Report the processes used to identify and manage flawed, incomplete, missing, and/or discrepant risk of bias assessments for the primary studies across systematic reviews.
- If risk of bias is *assessed* anew by the overview of reviews authors, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).
- Provide justification if new assessments are not undertaken when those in the systematic reviews are flawed, incomplete, or missing.

Example:

"Where risk of bias had already been assessed for the studies in reviews included in the CNMA [component network meta-analysis], we checked that this was performed consistently in accordance with Cochrane Tobacco Addiction Group guidance for assessing each domain. Where this had been done, we used these 'Risk of bias' assessments and did not re-evaluate. Where it appeared that the risk of bias guidance had not been consistently applied, or where specific domains had not been evaluated for specific reviews, two authors independently assessed risk of bias as part of the data extraction process, with discrepancies resolved by discussion or referral to a third author, where necessary.

For studies that required further assessment, we used the Cochrane 'Risk of bias' tool v1 for the following domains: random sequence generation, allocation concealment, blinding of outcome measure, attrition, and other bias. Random sequence generation, allocation concealment, and other bias were assessed based on standard methods set out in the *Cochrane Handbook for Systematic Reviews of Interventions*. Following standard Cochrane Tobacco Addiction Group methods for reviews of behavioural interventions where blinding is not possible, we did not assess performance bias, and assessed detection bias in the following way.

- We judged studies to be at low risk of bias when the following conditions were all met: numbers lost to follow-up were clearly reported for each group (not just overall, unless the overall percentage lost was less than 10%); the overall number of participants lost was not greater than 50%; and the difference in percentage followed up between groups was not greater than 20%. We also considered results at low risk of attrition bias if the authors reported sensitivity analyses that indicated the overall direction of effect was not sensitive to different imputation methods for loss to follow-up.
- We judged studies to be at high risk of bias when the above thresholds were not met, or in the case of cluster-randomised trials, where entire clusters were not followed up.
- We judged studies at unclear risk when the number lost to follow-up in each group was not clear, and authors did not report sensitivity analyses based on loss to follow-up.

We judged studies at low risk of bias overall if judged to be of low risk for all domains. We considered them at high risk of bias overall if they were judged to be at high risk of bias in one or more domains. We considered all other studies at unclear risk of bias overall. We presented the results of the risk of bias assessment in a 'Risk of bias' summary figure." (70)

RISK OF BIAS ASSESSMENT

11c. Describe the methods used to *assess* the risk of bias of supplemental primary studies (if included).

Rationale. Readers need accurate and reliable information about the risk of bias in any included supplemental primary studies to ascertain the trustworthiness of an overview of reviews' findings. Authors of overviews of reviews who choose to include supplemental primary studies should describe the methods used, following the guidance provided in the PRISMA 2020 statement.

Essential elements:

- If supplemental primary studies are included, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Example: "We used the Cochrane Collaboration's risk-of-bias tool to evaluate the methodological quality* of the RCTs (8). Two reviewers working independently assessed the risk of bias for random-sequence generation; allocation concealment; blinding of patients, caregivers, or outcome assessors; incomplete outcome data; selective reporting; and other biases (funding source and nature). Disagreements were resolved by discussion or arbitrated by a third reviewer. We summarized the risk of bias for all domains to produce an overall risk of bias for every trial (8). Risk of bias was considered to be high if there was concern for bias in any key domain (allocation concealment or blinding of patients), low if risk of bias was low for all key domains, and unclear in all other cases. We chose a priori to consider allocation concealment and blinding as key quality domains because of their relative importance for preventing selection bias and bias in the assessment of subjective outcomes, such as pain." (71)

* the term "risk of bias" is preferred in the context of randomized controlled trials

SYNTHESIS METHODS

Item 12a. Describe the methods used to summarize or synthesize results (including methods used to tabulate or visually display results) and provide a rationale for the choice(s).

Rationale. There are two main approaches to synthesis in overviews of reviews. Authors of overviews of reviews may: 1) summarize outcome data as they are presented in the included systematic reviews, or 2) re-analyze data from the included systematic reviews using standard meta-analytic techniques (4, 5, 35, 69). A justification for the chosen approach should be provided, and authors should clearly state whether or not they re-analyzed data. In a sample of overviews of reviews published from 2015 to 2017, Lunny *et al.* found that only 26% reported whether they performed a statistical synthesis (29). Common reasons for re-analyzing data include: to use a new or more appropriate synthesis method other than that used in the original systematic reviews; to use a different summary measure or make summary measures consistent across systematic reviews; concerns about the trustworthiness of the analyses in existing systematic reviews; or to incorporate supplemental primary studies (69).

Overview of reviews authors may choose to use only a subset of the data available in the included systematic reviews (e.g., data pertaining to children in a systematic review that includes a broader population). Authors should indicate how this was accomplished. For example, by using only a subset of the originally included primary studies, or re-examining included primary studies. Authors should anticipate that they will need to reformat available data if discrepant measures are provided across systematic reviews, and provide details on how they calculated or estimated the necessary outcome measures if they were not available as desired. For example, authors might need to combine two or more groups (or arms of a study), manipulate scales, or estimate or impute standard deviations when these are not available (72). When multiple summary measures were used (e.g., because data needed to convert all studies to one measure are not available), this should be clearly delineated. Finally, authors should state the software used to run the analysis, the approach used (e.g., random or fixed effects), and the summary effect measures.

Essential elements:

- Identify and justify the type of synthesis used (e.g., summary, re-analysis); if re-analysis occurred, this should be clearly stated.
- Describe the process used to decide which systematic reviews and supplemental primary studies (if included) were eligible for each synthesis.
- If only a subset of the data within the included systematic reviews was used, indicate how this was accomplished.
- Report any methods required to prepare the data collected from systematic reviews and supplemental primary studies (if included) for presentation of the summary or synthesis, such as handling of missing summary statistics, or data conversions.
- Report the chosen approach (e.g., tables, graphs, forest plots) used to display results of individual systematic reviews and supplemental primary studies (if included) in the summary or synthesis.
- If statistical synthesis methods were used, reference the software, packages, and version numbers used to implement the synthesis methods.
- If performing a re-analysis via meta-analysis, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Example: "We presented data as a narrative synthesis* supported by tables of statistical outcomes reported in the original reviews. The comparisons presented were determined by data in the included reviews. Although we had planned to update Cochrane reviews with new studies identified for inclusion, we did not do this because the scope of a number of the reviews requires modification before they are updated.

Reporting guideline for overviews of reviews of healthcare interventions: the Preferred Reporting Items for Overviews of Reviews (PRIOR) statement

In order to reflect and prioritise clinical decision-making in the overview, we summarised the evidence using an evidence map, incorporating Cochrane reviews and RCTs not yet included in the reviews (Table 1). These were set in the context of practice recommendations using the BTS [British Thoracic Society] guidelines for bronchiectasis.

We grouped data by intervention and outcome against the following framework: pharmacological interventions (antibiotics, vaccines, bronchodilators, anti-inflammatories, bronchodilators and anti-inflammatories combinations, mucous clearance agents); and non-pharmacological interventions (physiotherapy, disease management and education, surgery, other interventions).

We tabulated the evidence separately (post-hoc) for each of our planned outcomes and classified them by consensus taking into account the BTS/Scottish Intercollegiate Guidelines Network (SIGN) bronchiectasis guidelines. The following classifications are listed in the tables under 'Evaluation':

- no evidence of benefit - no statistically significant or clinically relevant effect;
- evidence of statistical benefit - statistically significantly effect in favour of intervention;
- evidence of statistical benefit but not clinically relevant change - as above but magnitude of effect below published threshold of minimum clinically important difference (MCID) for the outcome, where available (MCID listed in table footnote);
- evidence of clinically relevant benefit - as point 2. above and mean effect of MCID or greater;
- evidence of harm - statistically significant effect in favour of control;
- unclear - conflicting evidence of effects." (73)

* Cochrane currently recommends not using this term: "Authors should report the specific methods used in lieu of meta-analysis (including approaches used for presentation and visual display), rather than stating that they have conducted a 'narrative synthesis' or 'narrative summary' without elaboration" (74).

SYNTHESIS METHODS

Item 12b. Describe any methods used to explore possible causes of heterogeneity among results.

Rationale. Authors need to describe any methods used to explore heterogeneity in the results across systematic reviews and supplemental primary studies, such that authors can judge the credibility of their findings. When overview of reviews authors choose to report the subgroup analyses as presented in individual systematic reviews, they need to specify which analyses they extracted and reported on. A common challenge is that not all included systematic reviews will report the same subgroup analyses of interest. In this case, the methods used to deal with these differences should be specified, and the differences across systematic reviews should be described.

If a re-analysis of outcome data is undertaken, authors should describe the methods for subgroup analyses or other techniques used to investigate heterogeneity (e.g., meta-regression), including whether they were pre-specified. Because they are observational and not based on randomized comparisons, the findings from multiple subgroup analyses can be misleading (75). Nevertheless, subgroup analyses can add value by providing informative insights into treatment effects that could not be obtained otherwise (76). Subgroup analyses that are part of a small number of pre-specified analyses are more reliable than one of numerous post-hoc analyses (75). For this reason, authors should specify whether the subgroup analyses were planned *a priori* so that readers can judge the credibility of the findings.

Essential elements:

- Describe any methods used to explore heterogeneity in the results across systematic reviews and supplemental primary studies (if included), e.g., structuring tables to examine variation in results across systematic reviews and supplemental primary studies.
- Specify the methods used to deal with differences in available subgroup analyses across the included systematic reviews.
- If a re-analysis of outcome data is undertaken, reporting should adhere to the guidance outlined in the PRISMA statement (16).

Example: "Assessment of non-statistical heterogeneity: We planned to determine whether there is clinical heterogeneity between systematic reviews (i.e., differences in severity of asthma or differences in treatment administered before enrolment) by assessing the inclusion criteria of each systematic review. We also planned to assess clinical heterogeneity within each systematic review that will contribute to the certainty of evidence assessment of each review. We planned to identify commonly used outcomes and to categorise them in a taxonomy by creating a list of all outcomes and discussing their categorisation among the review author group until consensus was reached. This taxonomy will inform recommendations for a core set of outcome measures, which may be applicable in future RCTs.

Subgroup analysis: Given the pathophysiological differences between preschoolers and older children, we intended to subgroup studies of children from birth to five years of age and children aged six to 18 years (or younger and older children as defined by review authors) and to provide separate summary tables within the overview. Finally, we planned to group studies occurring in the ED/outpatient setting separately from those occurring in the inpatient setting (ward or intensive care unit). We planned to extract summary event data for each treatment/placebo group from the included reviews for all subgroup analyses." (26)

SYNTHESIS METHODS

Item 12c. Describe any sensitivity analyses conducted to assess the robustness of the synthesized results.

Rationale. When overview of reviews authors choose to report the analyses as presented in individual systematic reviews, they should specify any measures that were taken to verify the robustness of the included systematic reviews. This would ideally include a presentation of relevant sensitivity analyses that were reported in these systematic reviews.

When overview of reviews authors choose to re-analyze outcome data from the included systematic reviews, they should acknowledge any decision points in the systematic review process (e.g., searching for studies, eligibility criteria, analysis methods) that may warrant sensitivity analyses to better understand the influence of these decisions on the finding of the overview of reviews (75). Although not all sensitivity analyses can be planned in advance, overview of reviews authors should report on which sensitivity analyses were planned *a priori*. Overview of reviews authors should also specify which steps they plan to take if sensitivity analyses demonstrate that decisions made during the systematic review process greatly influence the overview of reviews' findings. This may include contacting authors to obtain additional unpublished information, altering planned analysis methods, or presenting the findings with the caveat that they should be interpreted cautiously (75).

Essential elements:

- If a re-analysis of outcome data is undertaken, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Example: "Heterogeneity was assessed using the I^2 statistic, and the following values were used for interpretation: low (0–40%); moderate (30–60%); substantial (50–90%) and considerable (75–100%); the corresponding p-values were also considered. Sensitivity analyses were conducted by deleting each study from the model, and the pooled analyses were recalculated without each study to assess its influence on the overall SMD or RR." (77)

REPORTING BIAS ASSESSMENT

Item 13. Describe the methods used to *collect* data on (from the systematic reviews) and/or *assess* the risk of bias due to missing results in a summary or synthesis (arising from reporting biases at the levels of the systematic reviews, primary studies, and supplemental primary studies, if included).

Rationale. Bias due to missing results can arise if the available (e.g., reported) results differ systematically from results that are missing (16). This can arise due to reporting biases such as selective non-publication or selective non-reporting of results (16). Although a variety of tools exist, these are limited with respect to scope, measurement properties, and guidance for reaching consensus on risk of bias judgments (78). The ROB-ME tool (79) aims to address the limitations of currently available tools.

Authors of overviews of reviews should consider the risk of bias due to missing results in a summary or synthesis. In doing so, authors should consider bias arising from missing data at the level of the included systematic reviews and their included studies, as well as arising from supplemental primary studies (if included).

Authors should report any methods that they used to assess risk of bias due to missing results and/or collect this information from the included systematic reviews. The methods should be reported in enough detail that they could be repeated. An important caveat is that this is a new item in the PRISMA 2020 statement (16); therefore, this may not be addressed in systematic reviews published earlier or those that have followed earlier guidance.

Essential elements:

- Describe any methods used to collect (from the systematic reviews) data on and/or assess the risk of bias due to missing results in a summary or synthesis, including bias arising from missing data at the level of the included systematic reviews, their included primary studies, and supplemental primary studies (if included).

Example: "We planned to address data missing from an included systematic review or variation in information reported across reviews by retrieving and examining the full reports of RCTs included in the systematic reviews; contacting systematic review authors for missing information or clarification; searching systematic review protocols; and/or searching registries of systematic reviews or clinical trials for further information. If this occurred, we planned to include discussion on potential discrepancies with information provided in the original reviews." (68)

Example: "For each outcome, heterogeneity was evaluated with the I^2 and publication bias was estimated with the Egger's statistical test. Due to the plethora of primary studies included in each meta-analysis, all relevant measures were presented as they were reported in each study without reviewing the corresponding primary studies. All analyses were undertaken using Microsoft Excel (Version 16.42) and R statistical software (version 3.6.3)." (80)

CERTAINTY ASSESSMENT

Item 14. Describe the methods used to *collect* data on (from the systematic reviews) and/or *assess* certainty (or confidence) in the body of evidence for an outcome.

Rationale. Presenting an assessment of certainty (or confidence) in the body of evidence for each pre-defined outcome of interest enables appropriate interpretation of results. To date, the reporting of the methods used to present certainty assessments in overviews of reviews has been suboptimal (2, 29). When available and appropriate, certainty of evidence assessments may be extracted from the included systematic reviews (4, 35). Challenges may arise when assessments of certainty of evidence are unavailable for some or all outcomes, are incomplete (e.g., explanations for rating down are missing) or different decision rules (e.g., thresholds) or systems are used for rating the certainty of evidence (4). When a new meta-analysis is undertaken for the overview of reviews, the certainty of evidence may change, requiring a new assessment (4).

The GRADE approach is commonly used in systematic reviews to assess certainty of evidence, and major evidence synthesis organizations suggest that it also be used in overviews of reviews (4, 5). Because GRADE methods for overviews of reviews are in development (81), authors should describe how the methods were applied so that readers can verify the approach. Authors should specify: 1) whether the assessments were extracted from the included systematic reviews (and what was extracted – individual domains or the overall assessment) or determined anew; 2) the system used (e.g., GRADE) and domains assessed (e.g., risk of bias, imprecision, indirectness, inconsistency, publication bias); 3) the criteria used to assess each domain or reference to guidance describing the criteria; 4) any modifications to the standard approach; 5) the number of reviewers involved, whether any piloting occurred and/or decision rules were developed; and 6) whether there was a process in place to achieve consensus.

Essential elements:

- Report any methods used to collect information reported in the included systematic reviews about the certainty (or confidence) in the body of evidence for each predefined outcome. Authors should adhere to the reporting criteria for data extraction and indicate what was extracted (e.g., individual domains, overall assessment) (item 9a).
- When the certainty (or confidence) in the body of evidence for an outcome differs between systematic reviews, report the approach (or decision rules) used to select one assessment or reconcile the different assessments.
- When the certainty (or confidence) in the body of evidence for an outcome is assessed anew, reporting should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Example*: "We used the GRADE approach for assessing the overall strength of the evidence for each primary outcome. We had planned to extract the grading from each eligible Cochrane Review. Since only two of the reviews had conducted grading, we graded the body of evidence for each comparison in terms of short-term trials (follow-up duration of one week or shorter), medium-term trials (follow-up duration longer than one week and up to six months), and long-term trials (follow-up duration longer than six months). We based our assessments on the information provided in the review, but when needed, we confirmed the data by checking the original trial reports. Two review authors evaluated the quality of the body of evidence and resolved their differences through discussion. The quality of the body of evidence was based on trial design, directness of the evidence, consistency of results, precision of results, and probability of publication bias. We classified the strength of the evidence as:

- high quality - where we are very confident that the true effect lies close to that of the estimate of the effect;
- moderate quality - where we are moderately confident in the effect estimate, such that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different;
- low quality - where our confidence in the effect estimate is limited and the true effect may be substantially different from the estimate of the effect;

- very low quality - where we have very little confidence in the effect estimate and the true effect is likely to be substantially different from the estimate of the effect." (82)

*Some of the terminology used in this example has been superseded (e.g. quality is now referred to as 'certainty' or 'confidence') and other terms are not standard GRADE terms (e.g. GRADE refers to 'certainty' of the evidence not 'strength' of the evidence).

SYSTEMATIC REVIEW AND SUPPLEMENTAL PRIMARY STUDY SELECTION

Item 15a. Describe the results of the search and selection process, including the number of records screened, assessed for eligibility, and included in the overview of reviews, ideally with a flow diagram.

Rationale. It can be helpful for readers to know where records were identified and how they were selected so that they can judge the credibility of the overview of reviews' findings. Depending on where the majority of the included systematic reviews were identified, the findings could be subject to bias (e.g., records identified via reference lists or content experts can be prone to citation or publication bias) (83). For full transparency, overview of reviews authors should report the number of unique records retrieved via the electronic database searches, hand searches of various sources, reference lists, contacting experts, and any other sources. They should also report the number of unique records screened by title and abstract, the number screened by full text, the number excluded following full text review and the primary reason for exclusion, and the number included in the overview of reviews.

Sometimes, after identifying all relevant systematic reviews, important gaps in coverage remain and authors may choose to also include supplemental primary studies (4, 20, 25, 35). When this is the case, authors should report both on the selection of relevant systematic reviews and of supplemental primary studies. Authors may wish to report these within the same flow diagram, or within separate flow diagrams (i.e., one for systematic reviews and one for supplemental primary studies).

Essential elements:

- Report, ideally with a flow diagram, the number of records identified (by the searches); records excluded before screening; records screened; records excluded after screening titles and abstracts; potentially eligible reports retrieved for full text inspection; potentially eligible reports that could not be retrieved; retrieved reports that were excluded, with the primary reason for exclusion; the number of systematic reviews (and supplemental primary studies, if applicable) included in the overview of reviews.
- If supplemental primary studies are included, reporting of the selection process should adhere to the guidance outlined in the PRISMA statement (16). The same or a separate flow diagram may be used.

Example: "The electronic searches yielded 7474 records after removing duplicates and searching other sources. After screening titles and abstracts, we excluded 7386 irrelevant studies. We retrieved and scrutinized 106 reviews, of which we excluded 93 for reasons including results not being separately reported for adolescents, inclusion of studies of adolescents who were exclusively obese, or ineligible review methods (see Table S2). We judged 13 reviews as eligible for inclusion in this overview of reviews. See Figure 1 for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) study flow chart. In total, 108 primary studies were included in the 13 reviews, 76 were included in only 1 review, 24 studies were included in 2–3 reviews, and 4 primary studies published between 2006 and 2014 were included in 4–6 reviews. In one review, all of the four included primary studies overlapped with studies included in another review, but these reviews reported on different outcomes (see Table S4 for the details)."

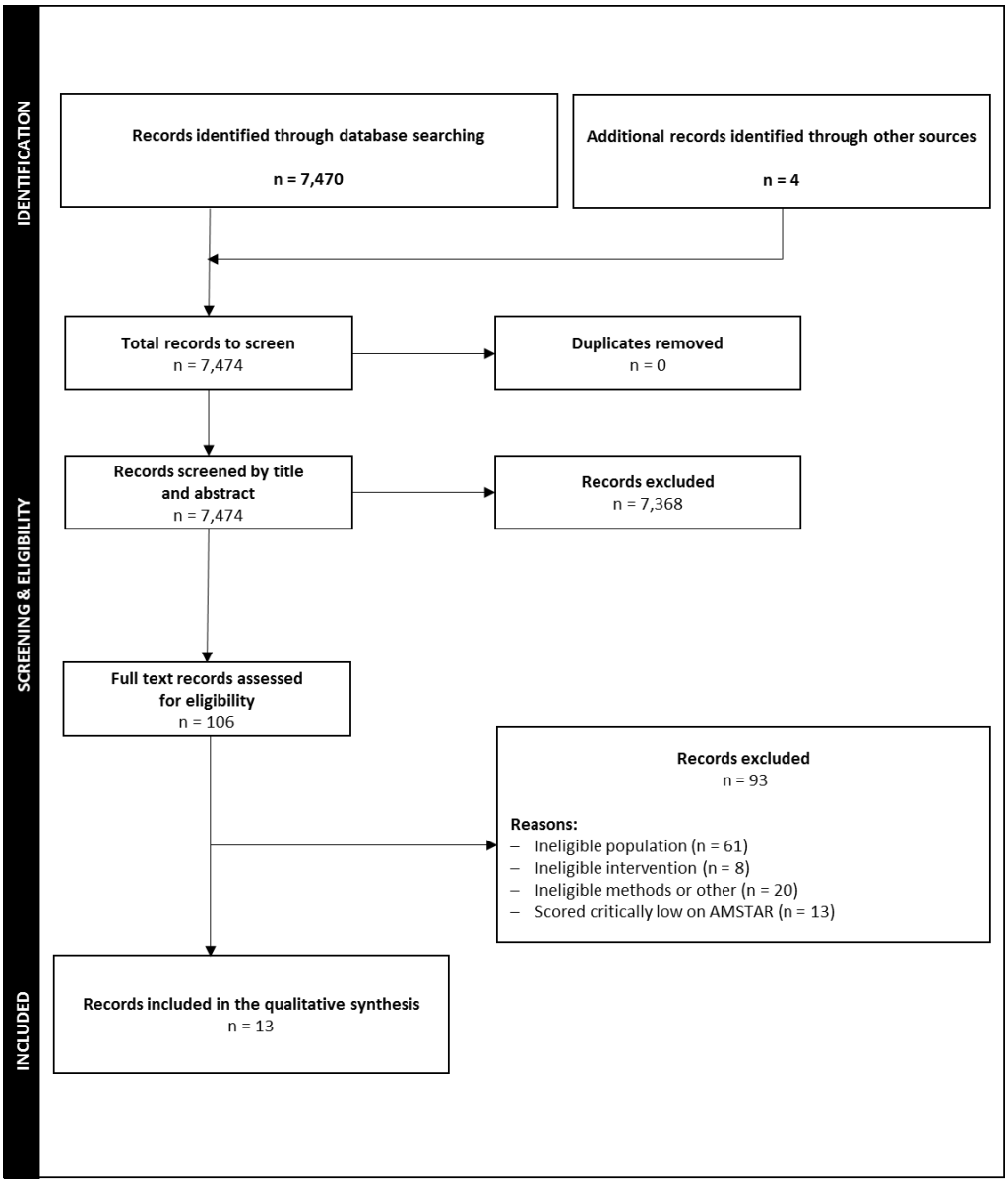

Figure 1. PRISMA Flow Diagram (reproduced and modified from Flodgren et al. 2020)" (84)

SYSTEMATIC REVIEW AND SUPPLEMENTAL PRIMARY STUDY SELECTION

Item 15b. Provide a list of studies that might appear to meet the inclusion criteria, but were excluded, with the main reasons for exclusion.

Rationale. Although the majority of overviews of reviews provide a list of the included systematic reviews, few provide a list of those that were excluded (2). A list of the systematic reviews excluded following full text screening (as well as supplemental primary studies, if included), including a citation and the primary reason for their exclusion, helps readers to judge the comprehensiveness, completeness, and validity of the overview of reviews. The list of excluded records should cite the systematic reviews (and supplemental primary studies, if included) that appear to meet the inclusion criteria, and that readers may expect to be included, but are in reality not relevant (40). It is also useful to list: a) systematic reviews that were eligible according to the inclusion criteria but were ultimately excluded during selection due to the same (or similar) PICOs (Population, Intervention, Comparator, Intervention); and b) potentially relevant systematic reviews that could be considered for inclusion in future updates of the overview of reviews (e.g., those where the full text was not accessible by the overview of review authors, or those where no data were reported for the outcomes of interest).

Essential elements:

- Cite the retrieved reports that were excluded following full text review, including the reason for their exclusion. The list can be supplied in a supplementary file, made available in a publicly accessible repository, or made available from the corresponding author.

Example: "After full-text screening, 39 systematic reviews were excluded because the inclusion criteria were not fully met (references and reasons are provided in Supplemental Digital Content 2 [link]" (85)

CHARACTERISTICS OF SYSTEMATIC REVIEWS AND SUPPLEMENTAL PRIMARY STUDIES

Item 16. Cite each included systematic review and supplemental primary study (if included) and present its characteristics.

Rationale. Similar to systematic reviews, readers of overviews of reviews require some knowledge of the included systematic reviews and supplemental primary studies (if included) in order to make judgments about the validity and applicability of the findings (16). For each included systematic review, overview of reviews authors should report, at minimum, information about the: 1) systematic review and supplemental primary study, if included (title, first author, year of publication, numbers and types of included studies and participants); 2) search details (number of databases searched, names of databases searched, date ranges of databases searched, language and publication restrictions [if applied]); 3) population (participant characteristics, i.e., age, sex, ethnicity, stage of disease, co-morbidities, definition of disorder, setting); 4) interventions (type, dose, intensity, frequency, duration); 5) comparators (type, dose, intensity, frequency, duration); and 6) primary and secondary outcomes (4, 5, 35). Each study should be cited. In a descriptive analysis of overviews of reviews published from 2000 to 2011, 21% did not include a description of the characteristics of the included systematic reviews (2).

Characteristics of each included systematic review and supplemental primary study (if included) can be presented in table format, and the characteristics should be summarized descriptively in the text. Enough information should be presented for readers to make their own judgments regarding the relevance of the included systematic reviews and supplemental primary studies (if included) (4, 16, 35). Since tables have the potential to become large, publication as an online supplement is acceptable.

Essential elements:

- Cite each included systematic review.
- Descriptively and/or in a table(s), report the basic characteristics of each included systematic review, including: a) descriptive characteristics of the systematic review (e.g., title, first author, year of publication, number and design of studies and participants); b) search details (e.g., number of databases searched, names of databases searched, data ranges of databases searched, language and publication restrictions [if applied]); c) population (e.g., participant characteristics (e.g., age, sex, ethnicity, stage of disease, co-morbidities, definition of disorder, and setting, as applicable); d) interventions (e.g., type, dose, intensity, frequency, and duration, as applicable); comparators (e.g., type, dose, intensity, frequency, and duration, as applicable); e) outcomes of interest.
- Summarize the characteristics of the included systematic reviews within the text.
- If supplemental primary studies are included, reporting of the study characteristics should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Example: "Table 1 shows the characteristics of the 10 included studies. Studies were published between 2012 and 2020. The studies were from China (n = 2), Germany (n = 2), Denmark (n = 2), United States (n = 1), Singapore (n = 1), and Spain (n = 1). All studies included used more than two databases for their systematic searches, with Medline, Pubmed, PsycInfo, Cumulative Index to Nursing, and Allied Health Literature (CINAHL), and Cochrane Central Register of Controlled Trials being the most common. Most of the studies were focused on cancer patients/survivors with several cancer types (n = 4), with the majority addressing specifically breast cancer patients and survivors (n = 6). All studies addressed MBIs [mindfulness based interventions] as the main goal, namely MBSR/MBCT/MBCR [Mindfulness-Based Stress Reduction/Mindfulness-Based Cognitive Therapy/Mindfulness-Based Cancer Recovery]. From the 10 studies included, 2 explored both the effect of mindfulness on psychological and biological outcomes. The most common outcomes were anxiety, depression, and stress. The inclusion criteria for participants' age ranged from 18 to 75, with most studies reporting a mean age around 55 years old. The majority of studies included participants with any cancer stage and any treatment status or adjuvant treatment, with only one excluding

metastatic cancer. The follow-up times ranged between 2 and 24 months, being the most common 6-month follow-up." (86)

Table 1. Characteristics of included studies (reproduced and modified from Pedro et al., 2021) (86)

Author, Year Country	**Design**	**Databases searched**	**Eligibility criteria**	**Search period**	**Sample characteristics**	**Interventions addressed**	**Control group**	**Primary outcome**	**N studies**	**Follow-up**
Calero, 2018 Spain	Systematic review	Pubmed, CINAHL, PsycINFO	Randomized controlled trials with follow-up	January 2011 to October 2017	1839 women survivors of BC stage 0-III; age 18-59 years	MBCT, MBSR, MBCR	UC	Psychological	10 (14 reports)	3 to 12 months
Cilessen, 2019 Denmark	Systematic review and meta-analysis	Pubmed, Web of Science, PsycINFO	Randomized controlled trials	Inception to 10 October 2018	3274 cancer patients and survivors (any cancer, all stages); age 46-71 years	MBCT, MBSR, MBCR	WL	Stress, anxiety, depression	29 (38 reports)	Mean follow-up 6 months
…	…	…	…	…	…	…	…	…	…	…

PRIMARY STUDY OVERLAP

Item 17. Describe the extent of primary study overlap across the included systematic reviews.

Rationale. When multiple systematic reviews with overlapping primary studies are included, authors must decide whether to report the results from all systematic reviews or only a subset (69). Both methods may result in biases (4). Presenting the results of all systematic reviews regardless of overlap means that the results of singular primary studies will contribute more than once to the findings. Presenting only a subset of systematic reviews may result in the loss of important data via the exclusion of studies that are not overlapping within the selected systematic reviews' results (69). To date, about half of published overviews of reviews fail to mention the issue of primary study overlap (50).

Poor reporting of overlap in primary studies hinders readers' ability to interpret overview of reviews' findings. Thus, overview of reviews authors should: 1) be fully transparent as to the presence and degree of overlap across systematic reviews; 2) discuss how the overlap could have contributed to imprecision in the findings; and 3) when possible, include a visual representation of the nature and degree of overlap at the outcome level. Some options have been used to quantify or otherwise represent overlap. The corrected covered area is a statistical measure of the degree (percentage) of overlap in overview of reviews (50). Another approach is to provide a visual representation of overlap, using a citation matrix (50) or other graphical display (60), but to date these have been reported in less than 20% of published overviews of reviews (29). Citation matrices can be bulky, so it may not always be feasible to include them within published reports. Where possible, they should be included as online supplementary material.

Essential elements:

- Report the results of assessments of the nature and extent of overlap across the included systematic reviews (e.g., citation matrix or other graphical display, corrected covered area). Ideally, this should be reported by comparison-outcome to adequately assess the impact of overlap on the precision of a given result.
- Indicate the extent to which the overlap may have contributed to imprecision in the results of the overview of reviews.

Additional elements:

- Include a visual representation of the nature and degree of overlap (e.g., table, citation matrix, or graphical display).
- Present the nature and extent of overlap individually for each comparison-outcome.

Example: "Mortality was reported in twenty reviews, with data included from 63 primary studies (S3 Table). Overlap of included primary studies across the set of twenty reviews was high, with a CCA of 10.4% (Fig 3)." (61)

Reviews (Author, n included trials, u unique trials)	**Included randomized controlled trials**															
	Bao 2017	Fan 2017	Shabaan 2018	Zhao 2015	Cutro 2013	Dow 2013	Ye 2012	Roberts 2012	Patel 2010	Hughes 2010	Lau 2009	Lorente 2009	Cousson 2008	Jones 2007	Wang 2007	Lee 2006
Rhodes 2018 (n = 10; u = 2)	✓			✓	✓	✓	✓			✓	✓	✓	✓		✓	
Vardakes 2018 (n = 9; u = 0)	✓	✓	✓		✓		✓	✓		✓	✓				✓	
Roberts 2015 (n = 6; u = 0)					✓		✓	✓		✓		✓				✓
Burgess 2014 (n = 9; u = 1)					✓		✓	✓	✓	✓		✓	✓	✓		✓
Jacobs 2012 (n = 5, u = 0)							✓	✓			✓		✓			✓
Johnson 2010 (n = 6, u = 0)										✓	✓		✓	✓	✓	✓
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…

Black = primary studies published after systematic review and therefore not possible for inclusion

✓ = included in the systematic review

Figure 3. Citations matrix for reviews reporting mortality of prolonged infusions versus intermittent infusions of beta-lactams (reproduced and modified from Thabet et al., 2021; data in this reproduction are fabricated) (61)

RISK OF BIAS IN SYSTEMATIC REVIEWS

Item 18a. Present assessments of risk of bias or methodological quality for each included systematic review.

Rationale. Knowledge of the domain-level and overall risk of bias (or methodological quality, depending on the tool used) across included systematic reviews helps readers judge the validity of the overview of reviews' findings. Authors should thus provide the results of assessments of risk of bias and/or methodological quality for each item and/or domain for each systematic review (4). For each item and/or domain, a brief rationale for the rating should be provided. Authors may wish to provide an overall rating of risk of bias and/or methodological quality for each individual systematic review, where applicable (47, 48). Of overviews of reviews of healthcare interventions published from 2000 to 2011, less than 40% reported on assessments of risk of bias for the included systematic reviews (2).

The risk of bias and/or methodological quality assessments are often best presented in a table or figure; however, authors may also choose to describe them in the text (69). Either way, the assessments of domain- or item-specific and overall risk of bias must be available to readers for each individual systematic review (4). If necessary, these can be included as online supplementary material. Along with the individual assessments, authors may wish to provide a summary of the risk of bias and/or methodological quality assessments across included systematic reviews (e.g., "25% of systematic reviews did not report an a priori protocol"). This can help readers understand the extent of risk of bias and/or methodological quality concerns across included systematic reviews.

Essential elements:

- In table(s) or figure(s), report for each systematic review the risk of bias or methodological quality in each domain/component/item assessed and overall risk of bias or methodological quality.
- Provide a justification for each assessment (for each domain and overall), e.g., a quote from the systematic review report.

Additional elements:

- Provide a summary of the risk of bias and/or methodological quality assessments across included systematic reviews.

Example: "AMSTAR 2 ratings for the included reviews are summarised in S5 AMSTAR2 judgements. Of the 33 included reviews, the majority had an overall AMSTAR 2 rating of low (15 reviews) or critically low (five reviews) confidence in review results because of at least one critical weakness. Nine reviews were rated moderate and four rated high.

Of the critical domains, 18/33 reviews had accessible protocols. An additional 14 reviews reported a protocol publication date with or without discussion of protocol deviations which also suggests an a priori protocol was followed. All reviews used a comprehensive literature search strategy, but some reviews only partially adhered to this standard because the authors did not report searching the reference lists of included studies or did not consult content experts in the field, or both. All review authors provided a list of excluded studies with justifications for exclusions, and most reviews reported an appropriate method for statistical combination of results when meta-analyses were performed. Thirteen reviews reported satisfactory techniques for assessing risk of bias in individual studies. This standard was partially met by an additional 15 review authors who did not assess for selective reporting. Thirty-one reviews discussed the impact of risk of bias in individual studies, but only 14 reviews adequately investigated and discussed the impact of publication bias on review findings.

Of the non-critical domains, the majority of reviews included the components of PICO in their research questions and inclusion criteria, although only one review provided an explanation for their selection of study designs (which in most cases was solely randomised controlled trials). Most reviews performed study selection and extraction in duplicate, but six reviews provided inadequate descriptions of the study settings, population or comparator (or both) groups of

included studies. When meta-analysis was conducted, most review authors investigated the potential impact of risk of bias in individual studies on results and satisfactorily explained any heterogeneity observed. Thirty of the 33 reviews reported on sources of conflict of interest and adequately discussed how this was managed, when necessary." (70)

S5: AMSTAR-2 Judgements (reproduced and modified from Hartmann-Boyce et al., 2020 (70))

Review ID and title	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**	**Q12**	**Q13**	**Q14**	**Q15**	**Q16**	**Overall**
Barnes 2019 Hypnotherapy for smoking cessation	**Y**	**PY**	**N**	**PY**	**Y**	**Y**	**Y**	**Y**	**Y**	**Y**	**Y**	**Y**	**Y**	**N**	**Y**	**Y**	Moderate
	Critical weaknesses: Q2 – protocol not accessible but protocol publication data provided and differences between protocol and review discussed; Q4 – search strategy did not search reference lists of included studies and grey literature; context experts were consulted. Non-critical weaknesses: Q3 – no explanation for selection of study designs; Q14 – while there was heterogeneity, it was either explained through subgroup analysis or observed in a less-relevant minor comparator (there was moderate heterogeneity in comparison 5.1 and not discussed).																
Behbod 2018 Family and carer smoking control programmes for reducing children's exposure to environmental tobacco smoke	**N**	**PY**	**N**	**Y**	**Y**	**Y**	**Y**	**Y**	**PY**	**N**	**NMA**	**NMA**	**Y**	**Y**	**NMA**	**Y**	Moderate
	Critical weaknesses: none; Q2 – protocol not accessible but protocol publication data provided and differences between protocol and review discussed; Q9 – selective reporting in studies was not assessed. Non-critical weaknesses: Q1 – research questions and inclusion criteria did not describe comparator group; Q3 – no explanation for selection of study designs; Q10 – sources of funding not reported for all included studies.																
…	…		…	…	…	…	…	…	…	…	…	…	…	…	…	…	…

N = no; NMA = network meta-analysis; PN = probably no; PY = probably yes; Y = yes

RISK OF BIAS IN PRIMARY STUDIES

18b. Present assessments (*collected* from systematic reviews or *assessed* anew) of the risk of bias of the primary studies included in the systematic reviews.

18c. Present assessments of the risk of bias of supplemental primary studies (if included).

Rationale. Knowledge of the domain-level and overall risk of bias across included primary studies (within systematic reviews) and supplemental primary studies (if included) helps readers to judge the validity of the overview of reviews' findings. To the extent that is feasible, authors should report, for each outcome, the results of an assessment of each risk of bias domain (randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result) and the overall risk of bias (4, 87). To date, the reporting of the risk of bias in the primary studies among published overviews has been inadequate (2). Authors should provide the same details for supplemental primary studies (if included).

There is no consensus as to how to deal with discordant assessments or assessments from different risk of bias tools across systematic reviews (34). No matter the method used to deal with these issues, it should be clear which assessments were extracted directly from the included systematic reviews and which were assessed anew (fully or partially).

Authors may choose to describe the results of risk of bias assessments either in a table or figure, or in the text. If necessary, these can be included as online supplementary material.

Essential elements:

- In a table(s) or figure(s), report for each primary study the risk of bias in each domain/component/item (if available) and overall risk of bias.
- Indicate which assessments were extracted directly from one or more systematic review reports, and any limitations to the existing reports.
- Indicate which assessments were undertaken anew, including whether the assessments were undertaken partially or in full. For assessments that were undertaken partially, indicate which domains/components/items were re-assessed.
- If supplemental primary studies are included, reporting of risk of bias assessments should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Additional elements:

- Provide a summary of the risk of bias across primary studies contained within the included systematic reviews, and supplemental primary studies (if included).

Example: "Risk of bias ratings for the studies eligible for the CNMA [component network meta-analysis] can be found in **S2 Details of included studies**. Reasons for these judgements as they apply to individual studies can be found in the primary reviews from which the studies were identified. A subset of studies was listed in included reviews but did not have full risk of bias assessments; reasons for risk of bias judgements for these studies can be found in **S3 Additional characteristics of previously excluded studies** and in **S6 Additional risk of bias domains** for the two reviews, which did not originally assess all core domains as set out above. Overall, 50/312 included studies were judged at low risk of bias (low risk across all domains), 125 were judged at high risk of bias (high risk in at least one domain), and 137 were judged at unclear risk of bias. A summary of the risk of bias judgements for individual domains can be found in Figure 4. Most studies were at unclear risk of selection bias due to inadequate reporting of methods for random sequence generation or allocation concealment (or both). The domain contributing the most 'high risk' judgements was blinding of outcome assessment; in 72 studies, detection bias was a potential issue to differential amounts of support between study arms and self-reported outcome measures, introducing the risk of differential misreport, though the majority of studies were still at low risk in this domain (216/312 studies). The majority of studies (221/312) were also at low risk of attrition bias, 55 did not provide sufficient information with which to judge, and 36 were at high risk due to substantial attrition overall or substantial differences in attrition rates by study arm. We only assessed 'other risk of bias' when we suspected it to be present." (70)

S2 Details of included studies (reproduced and modified from Hartmann-Boyce et al., 2020; some data in this reproduction are fabricated (70))

		Risk of bias				
Primary review	**Study ID**	**Random sequence generation**	**Allocation concealment**	**Blinding of outcome measure**	**Attrition**	**Other bias**
Lancaster 2017	Aleixandre 1998a	Low	Unclear	High	Low	Low
Lancaster 2017	Aleixandre 1998b	Low	Unclear	High	Low	Low
Fanshawe 2019	Alessi 2017a	Unclear	Unclear	Low	Unclear	Low
Fanshawe 2019	Alessi 2017b	Unclear	Unclear	Low	Unclear	Low
Hartmann-Boyce 2019	Alterman 2001	Low	Unclear	Low	Low	Low
…	…	…	…	…	…	…

S3 Additional characteristics of previously excluded studies (reproduced and modified from Hartmann-Boyce et al., 2020 (70))

Study ID **Country**	**Funding**	**Declarations of interest**	**Random sequence generation**		**Allocation concealment**		**Blinding of outcome measure**		**Attrition**	
			Judgment	**Reason**	**Judgment**	**Reason**	**Judgment**	**Reason**	**Judgment**	**Reason**
Ashraf 2009 Denmark	Government grant	PT serves on an advisory board for Pfizer; MD serves on an advisory board for Pfizer and Merck	Low	Quote: "Participants were randomised by a computer program."	Unclear	Not reported	Low	Abstinence biochemically validated	Low	Attrition similar between study arms
…	…	…	…	…	…	…	…	…	…	…

S6 Additional risk of bias domains (reproduced and modified from Hartmann-Boyce et al., 2020 (70))

Review name	Study ID	RoB domain	Judgment	Reason for judgment
Rice 2017	Kim 2003	Blinding of outcome measure	High	Self-report only and different amounts of contact
	Lancaster 1999	Blinding of outcome measure	Low	Biochemical validation
	…	…	…	…
Stead 2013	Demers 1990	Blinding of outcome measure	High	No biochemical validation
	Fagerström 1984	Blinding of outcome measure	Low	Biochemical validation
	…	…	…	…
…	…	…	…	…

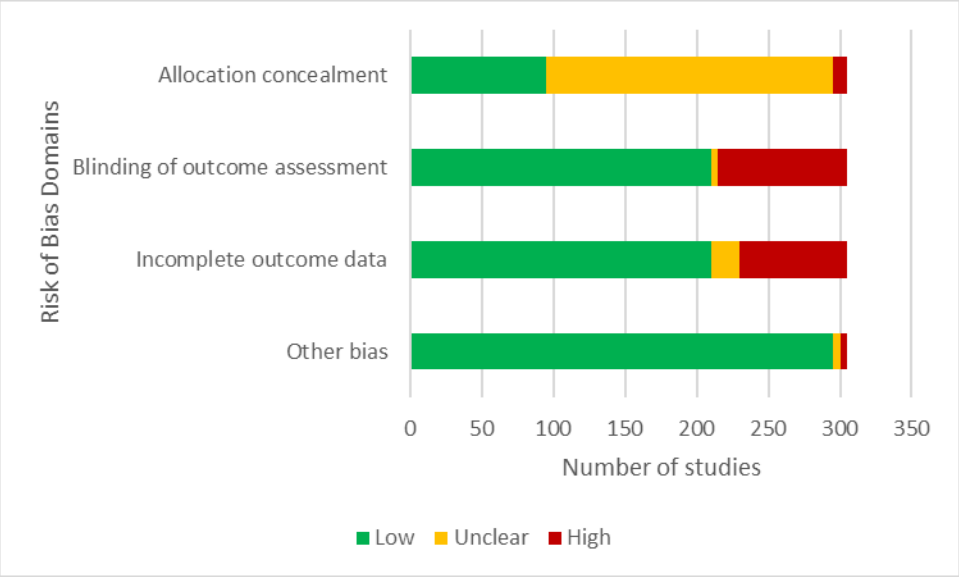

Figure 4. Risk of bias judgements for studies included in the network meta-analysis by domain (reproduced and modified from Hartmann-Boyce et al., 2020; data in this reproduction are fabricated (70))

SUMMARY OR SYNTHESIS OF RESULTS

Item 19a. For all outcomes, summarize the evidence from the systematic reviews and supplemental primary studies (if included). If meta-analyses were done, present for each the summary estimate and its precision, the direction of the effect, and measures of statistical heterogeneity.

Rationale. Authors may choose to present a descriptive summary of the included systematic reviews or to re-synthesize their findings (34). Authors should include all pre-defined outcomes when presenting results for the systematic reviews, including both benefits and harms. Contributing systematic reviews may frequently omit the outcomes sought by overview of reviews authors or include outcomes that are not of interest to overview of reviews authors.

When presenting the results of the included systematic reviews descriptively (and/or in a table(s) or figure(s)), authors may present each outcome measure in turn across systematic reviews, or present the outcomes from each systematic review in turn (4). The latter approach is preferred if the primary studies in the systematic reviews do not meet the transitivity assumption (4). Presenting a matrix of interventions versus outcomes, including a summary of how many primary studies and participants contributed data to each outcome, may help readers visualize which data were synthesized (4). If authors choose to re-synthesize the systematic review findings, the evidence should also be presented descriptively and, ideally, using table(s) and/or figure(s) (4, 5, 35).

Authors should take measures to reduce the risk that readers will make informal indirect comparisons across systematic reviews. It should be cautioned that indirect comparisons within overviews of reviews is discouraged because the transitivity assumption is usually difficult or impossible to assess using the data provided in individual systematic reviews (4, 5). Authors may wish to provide a clear explanation of the dangers associated with informal indirect comparisons within the main text and the table(s) and/or figure(s) (4).

Essential elements:

- Present the results of each summary or synthesis descriptively, and if appropriate, accompanied by tables and/or figures. Include all pre-defined outcomes, including both benefits and harms. If outcomes were added post-hoc, identify these as such.
- If authors summarize the evidence: Summarize the findings of the included systematic reviews, and if included, supplemental primary studies. Consider presenting the results of individual systematic reviews and supplemental primary studies (if included), in turn within a table.
- If authors summarize the evidence: Avoid informal indirect comparisons (e.g., across systematic reviews) and provide a clear explanation of the risks associated with informal indirect comparisons within the main text and/or as footnotes to table(s) and/or figure(s).
- If authors synthesize the evidence: If meta-analyses were done, reporting of the results of each synthesis should adhere to the guidance outlined in the PRISMA 2020 statement (16).

Additional elements:

- Present a matrix of interventions versus outcomes, including a summary of how many primary studies and participants contributed data to each outcome, to help readers visualize which data were summarized or synthesized.

Example:
"Effect of interventions
Outcomes varied considerably between systematic reviews, and similar outcomes were measured via different methods at different points in time. […]. A series of tables is presented, including data for each outcome from the included systematic review […]. These tables present odds or risk ratios and also absolute event rates per thousand in

each group. We summarise below information from reviews that contribute data to each outcome, including the certainty of evidence assessment we performed on each included systematic review with meta-analysis. Comparisons are between treatment and placebo unless otherwise stated.

Common themes in recommendations for future research from the included reviews were the need for adequately powered and methodologically sound RCTs, an agreed core outcome set for acute asthma in children, reliable assessment of baseline severity and response to treatment, and the need to perform subgroup analyses in preschool and school-aged children, and for varying degrees of asthma severity.

[…].

Primary outcome: length of stay
Two reviews included ED treatment time as an outcome measure, and six reviews included hospital length of stay (Table 7). Comparisons ranged from single RCTs with as few as 29 participants to three RCTs with a total of 327 participants.

Inhaled treatment
Two reviews reported low-certainty evidence for the effects of inhaled treatment on length of stay. The review comparing continuous versus intermittent nebulisation showed an unclear difference in ED treatment time between the two groups (mean difference (MD) -1.00 hours; 95% confidence interval (CI) -13.50 to 11.50 hours; 70 participants; 1 trial).

A review examining the effects of adding inhaled anticholinergics to short acting beta$_2$-agonists (SABAs) found an unclear difference in hospital length of stay (MD -0.28 hours; 95% CI -5.07 to 4.52 hours; 327 participants; 3 trials).

[…].” (68)

Table 7. Length of stay measures (reproduced and modified from Craig et al., 2020) (68)

Intervention/comparison	Outcome	Results: treatment effect (95% CI)	Number of participants (studies)	Certainty of evidence (GRADE)	Comments: overview authors' assessment of the certainty of evidence
ED treatment time					
Continuous vs intermitted nebulization: moderate to severe (Camargo 2003)	ED treatment time (units not specified)	MD -1.00 (-13.50 to 11.50)	70 (1)	Low	Certainty downgraded due to serious imprecision and serious risk of bias of the single study; unclear sequence generation, no allocation concealment (single-blind study)
IV magnesium sulfate (Griffiths 2016)	ED treatment time (minutes)	MD 5.00 (-24.40 to 34.40)	27 (1)	Moderate	Certainty downgraded due to serious imprecision
Hospital length of stay					
Antibiotics vs placebo (Normansell 2018)	Length of hospital stay (days)	MD -0.10 (-0.53 to 0.33)	43 (1)	Very low	Certainty downgraded due to serious imprecision, risk of bias in a single study, imprecision (all children with status asthmaticus)
Addition of IV SABA to inhaled SABA (Travers 2012a)	PICU length of stay (hours)	MD -12.95 (-38.74 to 12.84)	46 (1)	Moderate	Certainty downgraded due to serious imprecision
…	…	…	…	…	…

CI = confidence interval; ED = emergency department; IV = intravenous; MD = mean difference; PICU = pediatric intensive care unit; SABA = short-acting beta agonists

SUMMARY OR SYNTHESIS OF RESULTS

Item 19b. If meta-analyses were done, present results of all investigations of possible causes of heterogeneity.

Rationale. Authors should report the outcomes of any planned or post-hoc additional analyses used to explore heterogeneity in their findings (e.g., subgroup analyses, meta-regression). When interpreting the findings of subgroup analyses, authors should keep in mind that these comparisons are observational (75). Authors should report whether the subgroup analyses were planned, and may wish to remind readers how the findings of subgroup analyses may be affected by biases (e.g., residual confounding). Moreover, when the magnitude of difference between subgroups will not result in different recommendations for different population groups, authors may consider presenting the overall analysis results to avoid misinterpretation (75).

For analyses to compare subgroups of primary studies, authors should report the magnitudes of effect for the subgroups, including confidence intervals, and comparisons should be made informally (75). Authors should avoid comparing statistical significance of effects between subgroups as a means to explain heterogeneity, as this can be extremely misleading (75). To avoid reporting bias, authors should follow the subgroup analysis plan specified in the protocol without omitting pre-planned analyses or placing specific emphasis on any particular result (75). Should the authors deem post-hoc analyses to be sensible and informative, a rationale should be provided and the results should be reported regardless of outcome (75).

Essential elements:

- Report the results of any planned or post-hoc subgroup analyses that may provide an indication of the robustness of the overview of reviews' findings, adhering to the guidance outlined in the PRISMA 2020 statement (16).

Example: "There was no significant difference in risk of mortality between participants who received HCQ [hydroxychloroquine] with or without Azithromycin and those on standard care (RR 1.07, 95%CI 0.97 – 1.19; Fig 4), which was consistent across studies (I2 =0%). The Doi plot […] showed minor asymmetry. As Horby et al. had the most weight in the meta-analysis, we carried out a sensitivity analysis without this study and the effect of HCQ with or without Azithromycin on all-cause mortality remained non-significant (RR 1.02, 95%CI 0.19 -5.64)." (88)

SUMMARY OR SYNTHESIS OF RESULTS

Item 19c. If meta-analyses were done, present results of all sensitivity analyses conducted to assess the robustness of synthesized results.

Rationale. Authors should report the outcomes of any planned or post-hoc sensitivity analyses that may provide an indication of the robustness of the overview of reviews' findings. Throughout the conduct of an overview of reviews, authors will need to make somewhat arbitrary decisions about study eligibility, the types of data to be analyzed, and what to do about missing data (48, 75). Authors may also perform sensitivity analyses to better understand how primary studies at high risk of bias may be affecting the findings. Sensitivity analyses can help authors and readers to better understand how these decisions may have impacted the findings (48, 75). The results of sensitivity analyses may best be reported in a table (either in the manuscript or a supplementary file) (75).

Essential elements:

- Report the results of any planned or post-hoc sensitivity analyses that may provide an indication of the robustness of the overview of reviews' findings adhering to the guidance outlined in the PRISMA 2020 statement (16).

Example: "Updated meta-analysis of experimental studies: Five experimental studies, 4 RCTs and the single quasi-experimental study, assessed virological cure, with a total of 277 participants, of which 147 were in the intervention group. In pooled analyses, HCQ [hydroxychloroquine] with or without Azithromycin appeared to improve virological cure although there was little evidence against the model hypothesis at this sample size (OR 1.46, 95%CI 0.48–4.48, I^2 = 39.6%) (Fig. 5B). The Doi plot showed major asymmetry indicative of publication bias (Supplementary Fig. 3C). Removal of the quasi-experimental study, Gautret et al., 2020, did not alter the results of the pooled analysis (RR 1.02 95%CI 0.91–1.14, I^2 = 0%)." (89)

REPORTING BIASES

Item 20. Present assessments (*collected* from systematic reviews and/or *assessed* anew) of the risk of bias due to missing results in a summary or synthesis (arising from reporting biases at the levels of the systematic reviews, primary studies, and supplemental primary studies, if included) for each summary or synthesis assessed.

Rationale. Overview of reviews authors should report (or summarize) assessments for publication bias (e.g., funnel plots, statistical tests) and missing primary studies, analyses, or results (e.g., ROB-ME) (79) completed by systematic review authors for each outcome presented in the overview of reviews. This allows the reader to assess the validity of results and any potential for bias arising from selective publication or selective reporting of results. Risk of bias due to publication or reporting biases may also be reported by overview of reviews authors within certainty of evidence assessments (e.g., GRADE) conducted by systematic review or overview of reviews authors. If systematic review authors did not assess for publication or reporting biases, this should be noted with rationale if provided. If overview of reviews authors have re-analyzed data, they should present results of any assessments for publication or reporting biases, or provide a rationale if not done. They should also conduct and report certainty of evidence (e.g., GRADE) assessments (90) with publication or reporting biases as one of the domains. Finally, overview of reviews authors should assess and report whether systematic review authors reported on the outcomes pre-specified in protocols or registers, as well as any rationale for changes provided by the systematic review authors. This allows the reader to assess whether there were changes to what outcomes were reported, the reasons for the changes, and whether these may be related to selective reporting at the systematic review or primary study level.

Essential elements:

- Present or summarize results of assessments for publication and reporting biases completed by systematic review authors for each outcome.
- If data were re-analyzed, report results of assessments for publication and reporting biases for each outcome.
- Present certainty of the evidence (e.g., GRADE) assessments including publication/reporting bias as a domain for each outcome.

Example: "All of the reviews reported on their pre-defined analyses and used appropriate methods. […]. The trials were considered to have an unclear to high risk of bias since, with a few exceptions, they did not report sufficient details about methodology to assess trial quality*. One of the trials blinded the outcome assessors. Three trials had a high loss to follow-up. Four trials had a high risk of reporting bias and two trials were published only as conference abstracts. We graded the evidence as very low because of the high risk of bias and the strong suspicion of publication bias." (82)

Summary of results and quality of evidence (GRADE): FEV1 (reproduced and modified from Wilson et al., 2019 (82))

Comparison (intervention vs. control)	**Follow-up**	**Mean difference (95% CI)**	**N participants (trials)**	**Quality of evidence (GRADE)**	**Comments**
Conventional chest physiotherapy vs. PEP therapy	>1 week ≤6 months	-0.65% predicted (95% CI, 5.66% to 4.36% predicted)	18 participants (1 cross-over RCT)	Very low	Based on single cross-over RCT of unclear risk of bias; results were imprecise and could be subject to **publication bias**
	>6 months	Range in MD, -8.26% to 0.65% predicted	102 participants (2 RCTs)	Very low	Based on two RCTs with unclear risk of bias; results were inconsistent and imprecise
Conventional chest physiotherapy vs. active cycle of breathing technique	>6 months	2.8% predicted (95% CI, 0.39% to 5.99% predicted)	63 participants (1 RCT)	Low	Based on a single RCT with an unclear risk of bias and imprecise results
	>1 week ≤6 months	1.29% predicted (95% CI, -4.07 to 6.65% predicted)	18 participants (1 cross-over RCT)	Very low	Based on a single cross-over RCT of unclear risk of bias; results were imprecise and could be subject to **publication bias**

CI = confidence interval; MD = mean difference; RCT = randomized controlled trial

* Authors recommend consistent use of "risk of bias" vs. "methodological quality".

CERTAINTY OF EVIDENCE

Item 21. Present assessments (*collected* or *assessed* anew) of certainty (or confidence) in the body of evidence for each outcome.

Rationale. Overview of reviews authors should report the certainty of evidence for each clinically important outcome and comparison, to support the interpretation of results (4).

When possible, authors should collect and report on certainty of evidence assessments from included systematic reviews (4). Issues may arise if an assessment of certainty of evidence is missing for some or all outcomes, there are concerns that the reported assessments are not trustworthy or are inappropriate for the overview of reviews, different decision rules (e.g., thresholds) or systems are used to assess the certainty of evidence across systematic reviews, or assessments are presented without explanation of rating decisions. Moreover, when authors of overviews of reviews re-extract or re-analyze outcome data, the reported certainty of evidence assessments may no longer apply. In this case, authors should report on their own assessments. When authors perform their own assessments, justifications for decisions to rate down the certainty should be reported for each outcome. Ideally, certainty of evidence assessments for each outcome should be presented in a summary of findings table facilitating use by decision-makers (91).

Essential elements:

- Report the overall certainty of evidence for each important outcome (4, 8) and provide justification for the certainty of evidence judgments, i.e., reasons for rating up or down.
- Include the certainty of evidence wherever results are reported (i.e., abstract, evidence summary tables, results, conclusions).

Additional elements:

- Present the certainty of evidence assessments and judgments for each domain in evidence summary tables (e.g., GRADE Summary of Findings tables (92)).

Example: "NSAIDs (mefenamic acid) compared with another NSAID (naproxen): Bofill Rodriguez 2019a reported there was no clear difference in mean menstrual blood loss, measured by the alkaline haematin method, when comparing mefenamic acid with naproxen (MD 21mL per cycle, 95% CI –6 to 48 mL per cycle; 2 RCTs, 61 women; low-certainty evidence; Table 3)." (93)

Table 3. NSAIDs compared with another intervention, placebo, or no treatment (reproduced and modified from Bofill Rodriguez et al., 2020 (93))

Intervention	Comparator	Outcomes	Anticipated absolute effects (95% CI)		Relative risk (95% CI)	N women (trials)	Certainty of evidence (GRADE)	Comments
			Risk with comparator	Risk with NSAIDs				
NSAIDs	Placebo	Menstrual bleeding (alkaline haematin method)	Menstrual blood loss was lower with NSAIDS than with placebo (MD -124 mL per cycle (95% CI, -186 to -62 mL per cycle))			11 women (1 RCT)	Low[a]	Mefenamic acid
		Menstrual bleeding improvement (self-reported)	200 per 1000 women reported improvements in menstrual bleeding with	766 women (range, 578 to 887) reported improvements in menstrual	RR 4.25 (2.26 to 8.01)	80 women (1 RCT)	Low[b,c]	

			placebo or no treatment	bleeding with NSAIDs				

CI = confidence interval; MD = mean difference; NSAIDs = non-steroidal anti-inflammatory drugs; RCT = randomized controlled trial; RR = relative risk

[a]Downgraded two levels for imprecision.

[b]Downgraded one level for serious risk of bias.

[c]Downgraded one level for imprecision.

DISCUSSION

Item 22a. Summarize the main findings, including any discrepancies in findings across the included systematic reviews and supplemental primary studies (if included).

Rationale. Overview of reviews authors should provide a concise, balanced summary of their findings, in light of the quality of the included systematic reviews, primary studies, and supplemental primary studies (if included) and the methods used to analyze the data (4, 5, 35). The results for all pre-defined, clinically important outcomes should be mentioned, regardless of the direction or statistical or clinical significance of the findings. The certainty of evidence for each outcome should be mentioned (4), and authors should address any discrepancies in findings across the included systematic reviews and supplemental primary studies (if included). Authors should ideally focus on the findings with the highest certainty of evidence, and take caution not to rely solely on statistical significance when interpreting their findings (94). The incorrect interpretation of statistically non-significant results as "no difference" between interventions or "no effect" of an intervention is pervasive in primary research (94). Rather, authors should focus their interpretations on clinical importance and relevance (4, 94). Authors may also wish to urge readers against making inappropriate informal indirect comparisons (4). When applicable, key research gaps should be discussed, including mention of where additional primary studies are warranted. Authors should also mention whether more research is likely to change the results of the overview of reviews (34).

Essential elements:

- Provide a concise, balanced summary of the findings of the overview of reviews. In doing so:
    - Focus on the findings with the highest certainty of evidence, and take caution not to rely solely on statistical significance.
    - Focus interpretations on clinical importance and relevance.
    - Avoid informal indirect comparisons.

Example: "This comprehensive overview of reviews included 64 systematic reviews representing 358 unique primary studies and found consistent evidence of effectiveness for both pharmacological and non-pharmacological interventions based on data from moderate to high quality SR + MAs [systematic reviews with meta-analysis]. There was evidence of effectiveness across multiple outcomes reported in more than one high- or moderate quality SR + MA for zolpidem, suvorexant, doxepin, and melatonin, and evidence of effectiveness across multiple outcomes reported in one high-quality SR + MA for temazepam, triazolam, zopiclone, and trazodone. Additionally, the evidence for these interventions included reviews rated as having a high (melatonin) or medium (temazepam, triazolam, zolpidem, zopiclone, suvorexant, doxepin, and trazodone) strength of evidence based on GRADE. However, there was very little harms data available for these interventions. There was little to no evidence of effectiveness or no high- or moderate quality evidence available for flurazepam, quetiapine, or diphenhydramine. Moreover, most interventions were studied in the short term ($\leq$ 12 weeks) and the primary studies included in the reviews tended to have small sample sizes. The lack of harms data and small study sizes are concerning given that a large proportion of the general population are on these medications. Likewise, there was evidence of effectiveness across multiple outcomes reported in multiple high- or moderate quality SR + MAs for CBT [cognitive behavioral therapy] and reported in one high-quality SR + MA for BT [behavioral therapy]; there were no high-quality SR + MAs that examined mindfulness-based or combination therapies. The evidence for these interventions also included reviews rated as a high (CBT) or medium (CBT and behavioral therapy) strength of evidence based on GRADE. The studies that examined CBT and BT were often conducted in the short term, and only one SR + MA examined the effect of online versus in-person CBT, which is an important question for future research given the cost of and difficulties accessing in-person CBT." (10)

DISCUSSION

Item 22b. Provide a general interpretation of the results in the context of other evidence.

Rationale. Like systematic reviews (16), overviews of reviews have a great potential for guiding future research and clinical practice. To help readers accurately interpret the implications of an overview of reviews' findings, authors should discuss implications for future research and practice. A descriptive analysis of overview of reviews published up to 2010 found that 24% did not include a conclusion or discussion of implications for research and practice (3).

Authors should refrain from making specific recommendations for practice, as these are often dependent on particular circumstances and values that are not necessarily well-known to overview of reviews authors (95). Although little evidence exists regarding the accuracy of conclusions reported in published overviews of reviews, a descriptive analysis of systematic reviews published in 2014 found that 40% had potentially misleading conclusions (96). Indeed, a common mistake of systematic review authors is coming to conclusions that go beyond the available evidence (95). This can be problematic if readers rely on the conclusions to inform decision-making, potentially implementing interventions that are ineffective or harmful. Thus, overview of reviews authors should make efforts to draw cautious conclusions in light of the limitations of the evidence from the included systematic reviews, primary studies, and supplemental primary studies (if included) (96).

Essential elements:

- Draw conclusions in light of limitations of the evidence from the included systematic reviews, primary studies, and supplemental primary studies (if included).

Example: "Based on the results of this overview, clinicians and patients with insomnia can consider cognitive behavioral therapy as a first-line intervention due to its consistent evidence of effectiveness and a high strength of evidence across multiple outcomes and because it is likely associated with few or no serious harms, though there is insufficient evidence to properly evaluate the benefit to harm ratio for this intervention. If cognitive behavioral therapy is not effective, then other behavioral interventions can be considered or short courses of melatonin, zolpidem, suvorexant, or doxepin can be added to non-pharmacological therapy. However, these agents have only been tested in short-term studies, and there is little evidence for their effectiveness or safety beyond 16 weeks of treatment." (10)

DISCUSSION

Item 22c. Discuss any limitations of the evidence from systematic reviews, their primary studies, and supplemental primary studies (if included) included in the overview of reviews. Discuss any limitations of the overview of reviews methods used.

Rationale. There are unique limitations to conducting overviews of reviews that authors should mention within the discussion (34). These may include factors that are within the authors' control and others that are outside of their control. Potential limitations to consider include: 1) whether all relevant systematic reviews were identified and included in the overview of reviews; 2) whether there were gaps in coverage or methodological limitations in the existing systematic reviews; 3) whether all relevant data could be obtained or if data were missing; and 4) whether the methods used to conduct the overview of reviews could have introduced bias (e.g., search, study selection, data collection and analysis) (4, 34, 35). Apart from listing the limitations, authors should discuss their potential implications on the findings of the overview of reviews.

Essential elements:

- Report and discuss limitations, considering:
  - whether all relevant systematic reviews were identified and included in the overview of reviews;
  - whether there were gaps in coverage or methodological limitations in the existing systematic reviews;
  - whether all relevant data could be obtained or if data were missing;
  - whether methods used to conduct the overview of reviewers could have introduced bias (e.g., search, selection, data collection and analysis).

Example: "There are limitations to the currently available evidence: Although our quality assessment of the included SRs found there was a low level of concern regarding the identification and the selection of primary studies, the overviews methodology might not have captured all relevant primary studies if they were not included in SRs. The overviews methodology also did not allow for direct comparisons of primary studies included in the SRs. Instead, this report relied on the quality assessments, interpretations, and conclusions of the authors of the SRs and might not have captured the heterogeneity in methods and assumptions across the included SRs. Further, most of the included primary studies were non-randomized controlled studies of poor quality that recruited participants over 10 years and at different times for different interventions and did not necessarily adjust for potential confounding. Some SRs had discrepancies in the data they extracted from, or quality they assessed of, the same studies. Discrepancies in the data were cross-checked against each other among the relevant SRs and corrected in cases where wrongful information was reported. Data extracted from the SRs and the included primary studies were not cross-checked for accuracy or missing information, except in cases of discrepancies. Only three of the included SRs conducted subgroup analyses of interest, and none of the included SRs reported on loss to follow-up. Therefore, in addition to the current evidence being of poor quality, the findings of this overview had limitations from the shortcomings associated with the overviews methodology and therefore need to be interpreted with caution." (97)

DISCUSSION

Item 22d. Discuss implications for practice, policy, and future research (both systematic reviews and primary research). Consider the relevance of findings to end users of the overview of reviews, e.g., healthcare providers, policymakers, patients, among others.

Rationale. Overview of reviews authors should comment on the circumstances under which the overview of reviews' conclusions can be applied (98). Despite overview of reviews often having a broader scope than systematic reviews, it can be difficult for readers to readily assess applicability of the findings to their particular context. Providing explicit commentary on the specific patients and settings in which the overview of reviews' conclusions may be applied will enhance its usability for clinical decision-making (98-100). Overview of reviews authors should report and discuss factors that limit and strengthen the applicability of their findings to at least one main population of interest (100). Threats to applicability that may be discussed can include populations, settings, interventions, comparators, and outcomes that differ from those of primary interest (99, 100). The reporting of applicability in overviews of reviews is not yet established, but in a sample of 163 Cochrane systematic reviews, Missiou *et al.* found that only about 25% commented on the potential application of the findings to clinical practice (101). Reporting on the factors that limit or strengthen the applicability of the findings transparently will allow readers to readily understand how they may be applied to their particular context.

Essential elements:

- Discuss implications for practice, policy, and future research.

Example: "Implications for practice: This overview provides the most up-to-date evidence on prevention of surgical site infections from currently published Cochrane Reviews. Generally, we found insufficient or low-certainty evidence for most interventions. It is important to note that one review with high-certainty evidence showed harms associated with the use of adhesive drapes; and another review also with high-certainty evidence showed benefit when using prophylactic intravenous antibiotics administered before caesarean incision. As there remains uncertainty on the use of a number of prophylactic surgical site infection prevention options, health professionals are likely to follow local and national guidelines until more information becomes available.

Implications for research: The individual reviews and this overview have highlighted the lack of good evidence for intraoperative interventions for surgical site infection prevention. Included reviews in this category focused on interventions administered during the procedure (e.g. prophylactic antibiotics, patient warming) and methods to reduce bacterial contamination (e.g. glove changes, incise drapes). Just a few interventions altered the surgical approach itself (e.g. closure methods, the use of electrosurgical incisions). It is possible that different surgical techniques may influence surgical site infection and this may be an area in need of more research. Most of the trials and the participants included in them did not contribute to any reliable assessment of efficacy or harm, which may lead to research waste. Robust randomised controlled trials with good internal validity from use of appropriate methods of randomisation, blinding and analysis are required. Studies also need to have carefully considered sample size calculations and recruitment strategies to ensure that they are not underpowered. It is also important that the outcomes that are important to patients and health professionals are measured. Future studies should use appropriate outcome measures that are consistent, reliable, have internal and external validity, and are sensitive to change in what is being measured. Consistent use of outcomes and related definitions would maximise the value of data from across multiple studies. Improving measurement of SSI [surgical site infection], especially after hospital discharge, is warranted to improve data collection in this phase using validated patient-reported outcome (PRO) measures or methods for wound photography, or both, to complement these. A core outcome set focused on surgical wounds may be considered by developing and applying agreed, standardised sets of outcomes in this area. Trials should also collect quality-of-life data and consider incorporating cost-effectiveness analysis. Whilst adverse events

should be collected as part of a trial, additional data on mortality and other rare events might be better collected as part of observational, prospective studies - perhaps using routinely collected data if possible. Crucially it is important to understand the risk of death as a function of surgical site infection severity and these data are unlikely to be obtained from trials. This research also highlights the need for review authors to update existing reviews to ensure that new studies are incorporated into existing reviews so that Cochrane Reviews remain contemporary and relevant." (102)

REGISTRATION AND PROTOCOL

Item 23a. Provide registration information for the overview of reviews, including register name and registration number, or state that the overview of reviews was not registered.

Rationale. Stating where the overview of reviews was registered (e.g., PROSPERO, Open Science Framework, university repository) and the registration number or digital object identifier (DOI) for the register entry facilitates identification of the overview of reviews in the register. Akin to systematic reviews, such transparency reduces unplanned duplication of effort, and allows readers to compare what was pre-specified with what was eventually reported in the overview of reviews and decide if any deviations may have introduced bias (103). Reporting registration information also facilitates linking of publications related to the same overview of reviews (e.g., journal publication or conference presentation). Registration also enables meta-researchers to examine potential publication bias.

Essential elements:

- Indicate whether the overview of reviews was registered.
- If the overview of reviews was registered, provide registration information, including register name and registration number.

Example: "This protocol has been registered within the International Prospective Register of Systematic Reviews (PROSPERO) database (registration ID: CRD42020186003)." (104)

REGISTRATION AND PROTOCOL

Item 23b. Indicate where the overview of reviews protocol can be accessed, or state that a protocol was not prepared.

Rationale. In addition to registering an overview of reviews, authors may prepare a more detailed protocol. It is possible that the overview of reviews protocol includes information about the methods that is not provided in the registration or in the final report (e.g., preprint, publication) of the overview of reviews. Providing a citation, digital object identifier (DOI), or some other electronic link to the overview of reviews protocol allows readers to locate the protocol more easily. Comparison of the methods pre-specified in the overview of reviews protocol with what was eventually done (i.e., the completed overview of reviews) allows readers to assess whether any deviations may have introduced bias. Where there is no information leading to the protocol, reporting biases cannot be ruled out. While it is not considered as best publication practice, if the overview of reviews protocol was not made available (i.e., published or deposited in a public repository), or uploaded as a supplementary file to the overview of reviews final report, we recommend providing the contact details of the author responsible for the protocol (i.e., the guarantor).

Essential elements:

- Indicate whether there was an *a priori* protocol for the overview of reviews.
- If there was a protocol, indicate where the protocol can be accessed.

Example: "[the protocol] is registered on the International Prospective Register of Systematic Reviews (PROSPERO no. CRD42017080014; http://www.crd.york.ac.uk/prospero)." (105)

PROTOCOL AND REGISTRATION

23c. Describe and explain any amendments to information provided at registration or in the protocol. Indicate the stage of the overview of reviews at which amendments were made.

Rationale. Inconsistencies between protocols and published primary studies as well as systematic reviews are prevalent (106-108); however, few authors report protocol deviations in their published systematic reviews (106). Although we are unaware of data specific to overviews of reviews, extrapolating from reports of primary research and systematic reviews, it is likely that similar reporting shortcomings exist. Deviations from the planned protocol can occur for legitimate reasons. When modifications to research protocols are unexplained, however, it may be difficult for readers to judge whether and to what extent bias may have been introduced. Readers can more readily assess the impact of protocol deviations when authors explicitly document and provide justification for changes and their timing in the overview of reviews process (34, 35). Protocol deviations can also be tracked in the overview of reviews registration record (e.g., PROSPERO).

Essential elements:

- Describe and explain amendments to the registration or protocol.
- Indicate the stage of the overview of reviews at which amendments were made (this information could be provided in the results, discussion, appendix, or supplementary files).

Example from a published overview of reviews: "**Differences between protocol and review:** […] We identified several reviews that included mixed populations (e.g. men and women), which we could not allocate to one of the prespecified age groups. Therefore, we created a new category, 'mixed populations', as a type of participants. We included reviews with other trial designs if the results for RCTs were reported separately. We excluded reviews where our primary or secondary outcomes were not included or prespecified. This became necessary because we already included a high number of systematic reviews. Including reviews without our primary or secondary outcomes would have increased the number of included reviews dramatically, making our overview review confusing, unclear and difficult to convey to the reader which interventions prevent or control anaemia. We searched the final issue of DARE in 2018, after which no new content was added to this database. The POPLINE website was retired on 1 September 2019 so was no longer available for the top-up search. We assessed risk of bias using AMSTAR, however, we did not show the overall rating scores." (109)

Example of version history from a PROSPERO Record: "**Revision note:** Following initial screening of the searches it became apparent that there was a large volume of reviews with substantial overlap but with mixed quality. In light of this we made two post hoc amendments to our inclusion criteria. To be considered a systematic review we added the following minimum criteria to the existing one: • The characteristics of the included studies must be summarised in tabulated format (AMSTAR Item 6) • The scientific quality/ risk of bias of the included studies must assessed and documented (AMSTAR item 7). We considered that this approach would only reduce the number of low quality reviews, which present serious challenges to interpretation. In addition we reviewed all eligible reviews for redundancy. We identified reviews that were essentially redundant on the basis that the review was superseded by a more up-to-date review that included the same participants, intervention type and outcomes. That is, where the review does not offer additional relevant information provided by more recent reviews." (110)

SUPPORT

Item 24. Describe sources of financial or non-financial support for the overview of reviews, and the role of the funders or sponsors in the overview of reviews.

Rationale. Authors must report all sources of financial support received to conduct the overview of reviews and the specific role of the supporters in the work. Financial supporters may be involved in various aspects of an overview of reviews, for example, providing salary support for the investigator(s), developing the research question(s), selecting the studies, collecting and analyzing the data, and revising the final report. Further, overview of reviews authors may receive non-financial sources of support, including services such as in kind translation, librarian or statistical support, or access to a commercial database. The involvement of financial supporters in the research, especially industry funders, can result in bias, especially if they have an interest in obtaining a particular result (111). The reporting of the sources of financial and non-financial support and their role in the research improves transparency and allows readers to judge the credibility of the findings; however, both Hartling et al. (2012) (2) and Pieper et al. (2012) (6) found that in half (49% to 58%) of published overviews of reviews sources of financial support were not reported.

Essential elements:

- Describe sources of financial or non-financial support for the overview of reviews, including the relevant grant number for each funder. If there was no specific financial or non-financial support for the work, this should be stated.
- Describe the specific role of the funders and/or sponsors in the overview of reviews. If the funders and/or sponsors had no role in the work, this should be stated.

Example: "This work was supported by the Association of Danish Physiotherapists and by The Oak Foundation. The Parker Institute, Bispebjerg and Frederiksberg Hospital is supported by a core grant from the Oak Foundation (OCAY-13-309). The funders had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the article for publication." (112)

COMPETING INTERESTS

Item 25. Declare any competing interests of the overview of reviews' authors.

Rationale. The International Committee of Medical Journal Editors (ICMJE) asserts that, *"Public trust in the scientific process and the credibility of published articles depend in part on how transparently conflicts of interest are handled during the planning, implementation, writing, peer review, editing, and publication of scientific work. […]. Purposeful failure to disclose conflicts of interest is a form of misconduct […]."* (113) Conflicts of interest can bias overview of reviews authors' professional judgments, with the potential to influence all stages of the overview of reviews process (114). Included systematic reviews with financial conflicts of interest are more likely to report favourable conclusions (115), and industry sponsorship can influence the results and/or conclusions of primary studies and systematic reviews, generally towards the findings being more favourable (116, 117).

Among a sample of overviews of reviews published between 2012 and 2016 (Pieper *et al.*, unpublished data), 18% failed to report on conflicts of interest (43). Moreover, Lunny *et al.* found that among a sample of 50 overviews of reviews published from 2015 to 2017, only one (2%) reported a process for managing conflicts of interest when an overview of reviews' author was also an author on an included systematic review or primary study (29). Given the potential ramifications of conflicts of interest on the conduct and reporting of overviews of reviews, the inclusion of a statement disclosing conflicts of interest will help readers judge the credibility of the findings. Overview of reviews authors may refer to the International Committee of Medical Journal Editors (ICMJE) recommendations (113) as a guide to the relationships and activities that must be reported.

Essential elements:

- Report any of the authors' relationships or activities that readers could consider pertinent, or to have influenced the overview of review. This includes authorship on the included systematic reviews, their primary studies, and any supplemental primary studies (if included).
- Indicate whether the authors had access to raw data from the included systematic reviews and/or primary studies, including the nature and extent of access.
- If any authors had competing interests, describe how they were managed in the context of the overview of reviews.

Example: "JD is funded as part of the NIHR Cochrane Programme Grant Project: 13/89/08 - High Priority Cochrane Reviews in Wound Prevention and Treatment. She was also an author on one of the included studies. All her work for the review regarding this study was closely checked and she did not extract the study data." (118)

AUTHOR INFORMATION

Item 26a. Provide contact information for the corresponding author.

Rationale. A valid e-mail address for the corresponding author ensures that readers who have questions or those who may wish to update the overview of reviews can contact the authors.

Essential elements:

- Provide a valid e-mail address for the corresponding author.

Example:	Correspondence to: author@university.com.

AUTHOR INFORMATION

Item 26b. Describe the contributions of individual authors and identify the guarantor of the overview of reviews.

Rationale. Because multiple factors might be considered when deciding the list of authors for an overview of reviews, the order in which the authors are presented is not necessarily informative as to each author's contributions (119, 120). Contributor statements help to prevent erroneous assumptions based on author order (120), and allow readers to assign credit and responsibility for various aspects of the work. Some journals now ask for one author on a paper to be listed as a guarantor who accepts official responsibility for the overall integrity of the manuscript (including ethics, data handling, reporting of results, and study conduct); the guarantor is often the corresponding author. All authors must read and accept responsibility for the final manuscript (121). Relatively few journals provide explicit guidance for author contribution statements (122), although general guidance does exist (123). To promote responsible authorship, some high-tier medical journals require or encourage that research teams disclose the contributions of the co-authors (124). Authors are generally expected to have made substantial contributions to the project and to meet established norms, e.g., the criteria outlined by the International Committee of Medical Journal Editors (ICMJE) (113) or CRediT criteria (125).

Essential elements:

- Describe the contributions of individual authors.
- Identify the guarantor of the overview of reviews.

Example: "MCM-C and FJB-R contributed to the protocol design. MCM-C was the major contributor in writing the manuscript. FJB-R critically revised the content and contributed to the manuscript. All authors gave their final approval of the version to be published." (126)

AVAILABILITY OF DATA AND OTHER MATERIALS

Item 27. Report which of the following are available, where they can be found, and under which conditions they may be accessed: template data collection forms; data collected from included systematic reviews and supplemental primary studies; analytic code; any other materials used in the overview of reviews.

Rationale. Sharing research data can help to enhance transparency and facilitates the reproducibility of the overview of reviews. Making the data used within an overview of reviews publicly available can maximize their value, by facilitating future updates and the exploration of related research questions (127-129). Data sharing is resource-efficient, and may help to improve the quality of future overviews of reviews (128, 129). Support for sharing research data is growing among research participants (130), funders (131), and journal editors (132), and it is recognized that this sharing will promote innovation and collaboration among researchers (129, 133).

Essential elements:

- State the availability of data and other materials used in the overview of reviews.
- If any data or other materials may be available upon request, provide the contact details of the author or other individual responsible for sharing the materials and describe the circumstances under which such materials will be shared.

Example: "The data underlying this article will be shared on reasonable request to the corresponding author." (134)

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