Abstract

The abstract cannot be longer than 1000 words (word count: 1011)

1. Rationale
    A. **Default text in this template will not be published at protocol stage if it appears in a deactivated section (greyed out on left-hand menu). Please leave this text in place as it will help you to write your review. Use the Submission preview at the bottom of the left-hand menu to preview content to be published.**
    B. **Abstract word limit: 700 to 1000 words**
    C. Provide a brief description of the evidence base you are interested in, what is currently unknown or uncertain, and why it is important to resolve this uncertainty with this systematic review.
    D. Two or three sentences maximum.
2. Objectives
    A. PRISMA 2020 for Abstracts guidance #2: Provide an explicit statement of the main objective(s) or question(s) the review addresses.
    B. Refer to the population(s), health conditions, and intervention comparison(s). The objective(s) in the Abstract should include the primary objectives in the Review exactly, and may include secondary objectives, such as those that are important for making healthcare decisions or relate to outcomes in the Summary of Findings table(s).
3. Search methods
    A. PRISMA 2020 for Abstracts guidance #4: Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched (month and year).
    B. Recommended format:
        i. *We used CENTRAL, MEDLINE, xx other databases and xx trials registers, together with reference checking, citation searching and contact with study authors to identify studies that are included in the review. The latest search date was x/xx.* [Add key limitations, if present].
4. Eligibility criteria
    A. PRISMA 2020 for Abstracts guidance #3: Specify the inclusion and exclusion criteria for the review.
    B. Recommended formats:
        i. *We included [study design] in [participants] comparing [intervention/s] with*

[comparator/s]. We excluded studies [characteristics].

We included [study design] in [participants] comparing [an intervention] with [each of x comparators: comparator 1, comparator 2, comparator 3 …..comparator x]. We excluded studies [characteristics].

5. Outcomes
   A. List the main outcomes (those planned for inclusion in your summary of findings table(s)).
   B. Recommended format:
      i. *Our outcomes were [1, 2, 3, 4, 5, adverse effects].*
   C. Ideally, this list should include time points and measurement scales, if relevant. This list should be succinct and easily readable (separated with commas or semicolons). To keep this section succinct, authors may need to provide just an overview of the outcome domains (with time points for measurement, scales, and outcome descriptions removed).
6. Risk of bias
   A. PRISMA 2020 for Abstracts guidance #5: Specify the methods used to assess risk of bias in the included studies.
   B. Recommended format:
      i. *We used xx tool to assess bias in the [study design].*
7. Synthesis methods
   A. PRISMA 2020 for Abstracts guidance #6: Specify the methods used to present and synthesize results.
   B. Recommended format:
      i. *We synthesized results for each outcome using meta-analysis where possible* (state the statistical and analysis models used). *Where this was not possible due to the nature of the data, we synthesized results using* (state the synthesis without meta-analysis (SWiM) methods used). *We used GRADE to assess certainty of evidence for each outcome.*
8. Included studies
   A. PRISMA 2020 for Abstracts guidance #7: Give the total number of included studies and participants and summarize relevant characteristics of studies.
   B. Relevant characteristics may include important information about the applicability of the included studies, for example, if the review aimed to recruit all age groups but only included studies with adolescents.
   C. Recommended format:
      i. *We included a total of [number] studies with [number] participants.*
9. Synthesis of results

A. PRISMA 2020 for Abstracts guidance #8: Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).
B. Use of subheadings in this section is recommended, for example, by comparison, or outcome, or intervention.
C. The standard format for reporting the results of meta-analysis includes an indication of the summary measure, point estimate and confidence interval, for example, odds ratio 0.75 (95% confidence interval 0.62 to 0.89).
D. Reporting of adverse effects requires special attention dependent on whether study authors prespecified it as an outcome and whether it was reported.
E. **Recommended**: Insert dynamic analysis results when reporting in the text > if you update the analysis at a later date, e.g., to add or remove studies or change the statistical setting, it will automatically update the analysis result in the text.
F. PRISMA 2020 for Abstracts guidance #9: Provide a brief summary of the certainty or limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).

10. Authors' conclusions
    A. PRISMA 2020 for Abstracts guidance #10: Provide a general interpretation of the results and important implications.
    B. State the key conclusions and implications for practice or research, or both, including the magnitude and direction of effects, together with an indication of the certainty of the evidence. Avoid giving recommendations for practice.
    C. Recommended formats:
        i. *[Intervention X] probably reduces/increases the risk of [outcome A] at [time point] by a clinically significant amount.*
        There may be little to no difference between [Intervention X] and [Intervention Y].
        The available data are of very low certainty, and so we are not able to draw conclusions about the effects of [Intervention X].
        No studies evaluated [outcome A].
        No data are available relating to [outcome A].
        We found no [useable data] for[outcome A].
        There are inadequate data [to allow us] to draw conclusions about the effects of [Intervention X] compared to [Intervention Y] on [outcome A].
        For adverse effects: It was not clear if adverse effects were monitored and reported in

the included studies.

11. Funding
    A. PRISMA 2020 for Abstracts guidance #11: Specify the primary source of funding for the review.
    B. Recommended formats:
        i. *This Cochrane review was funded (in part) by XXX.*
        This Cochrane review had no dedicated funding.
12. Registration
    A. PRISMA 2020 for Abstracts guidance #12: Provide the register name, registration number and /or DOI to the published protocol.
    B. Recommended formats:
        i. *Registration: [Register name], [Registration number] via DOIXXX.*
        Protocol [and previous versions] available via DOIXXX, [DOIXXX and DOIXXX].
        Applicable to Protocols only: Not registered

Plain language summary

: Write the main review question here, in plain language.

: Read, and cite when applicable, Guidance for writing a Cochrane Plain language summary (III.S2 Supplementary material of the *Cochrane Handbook for Systematic Reviews of Interventions*).

1. **Word limit:** 400 to 850 words, including the title
2. **Title:** Write the main review question above in plain language. Examples of text you could use:
    A. *What are the benefits and risks of intervention for [treating] condition?*
    Intervention a or intervention b: which works better to treat condition?
3. **Key messages**
    A. Add at least 2 and no more than 3 bullet points that summarize the main findings and implications of the review.
    B. Explain any technical terms that appear in the key messages. The key messages will likely be read first, and they might be the only part of the summary that some people read. Do not use any terms that your readers might not understand. Even if you explain those technical terms later in the summary, you should also explain them in the key messages.
    C. Do not make any recommendations about whether or not a treatment should be used.

4. **Tailored heading: for example, What is epilepsy?**
    A. Replace the heading for this section with heading(s) tailored to the review. Briefly explain what the review is about and why it is important. Make sure that you: avoid acronyms and abbreviations (or introduce and explain them if you need to use them); and define any technical terms you use.
    B. Example of text you could use:
    C. *What is [condition]?*
    D. *Condition is a [common/rare] condition that affects relevant part of the body. It is caused by [brief explanation of cause]. People with condition [can] experience symptoms.*
5. **Optional tailored heading: for example, How is epilepsy treated?**
    A. Add another section to explain something else if necessary. For example:
    B. *How is [condition] treated?*
    C. *Treatments for [condition] include: [intervention a] and [intervention b].*
6. **What did we want to find out?**
    A. Briefly explain the review aims. Example of text you could use:
    B. *We wanted to find out if intervention a was better than intervention b to improve: outcome 1 and outcome 2.*
    C. *We also wanted to find out if intervention a was associated with any unwanted effects.*
7. **What did we do?**
    A. Briefly mention the review methods (for example, that the review involved searching for studies with specific characteristics, summarising their results and evaluating the evidence). Example of text you could use:
        i. *We searched for studies that looked at/investigated/examined intervention a compared with intervention b in population.*
        ii. *We compared and summarized the results of the studies and rated our confidence in the evidence, based on factors such as study methods and sizes.*
8. **What did we find?**
    A. Write about the main characteristics of the studies that were included in the review. Example of text you could use to report study characteristics:
        i. *We found X number of studies that involved XX number of people with condition and lasted for study duration.*
    B. Also write about the main results of the review (those presented in the summary of findings table(s) and the Abstract). Reminder: do not report summary statistics and confidence intervals or use 'low-/moderate-/high-certainty evidence'.
9. **Optional heading: Main results**

    A. Add another heading to present your results if you need to.
10. **What are the limitations of the evidence?**
    A. Mention the main limitations of the evidence.
    B. Reminder: do not use technical phrases like 'risk of bias' or 'low-certainty evidence'. See full guidance for ways to express the limitations of the evidence in plain language.
11. **How up to date is this evidence?**
    A. State the month and year when studies were searched for. Example of text you could use:
        i. *[This review updates our previous review.] The evidence is up-to-date to month and year of search.*

Summary of findings tables

: use GRADEpro GDT or RevMan

Background

: Why use this template? Submissions that follow this template will have a better chance of being accepted for publication. Please also refer to Cochrane's author guidelines. Reviews and updates should be concise (recommended word limit is 10,000 words).

: This template will help you **focus your review** and **report your findings concisely**. Cochrane recommends you follow this general guidance.

- **Focus on a manageable scope.** Decide how to address the review objectives as early in the process as possible. Your findings should be easy for you to summarize and easy for users of Cochrane evidence to read. If you need to include multiple interventions or comparators outside a network meta-analysis in a series of pairwise meta-analyses, please consider whether you should split this review into more than one review.
- **Include the smallest number of comparisons** that address the main objectives (most often this is one, but it can be more than one).
- **Include up to seven outcomes** within each comparison (these are your outcomes that are critical or important to users of the review).
- For reviews based on pairwise meta-analyses, there should be **one summary of findings**

table for each relevant comparison that includes your (up to) seven critical and important outcomes for that comparison. Reviews that include a network meta-analysis may need to include one summary of findings table for each outcome.

- Focus on comparisons and outcomes that users will find most useful in decision making. **You must be able to summarize all of the comparisons in the Abstract** (word limit approximately 700 to 1000 words).

1. How to use this template?
   A. This is a standard template for Cochrane intervention reviews that include randomized controlled trials (RCTs) and quasi-RCTs.
   B. You may see this template within your review, or open it as a practice review. The template includes essential guidance for authors within each section on the left-hand menu.
2. Within your review
   A. Writing your protocol
      i. If text appears in the deactivated sections of this template (greyed out on the left-hand menu; Abstract, Plain language summary, Summary of findings, Results, Discussion, Authors' conclusions), it will not be published at protocol stage. Leave this text in place as it will help you to write your review.
      ii. Replace default text in activated sections (Background, Objectives, Methods) with your own work, following the guidance given. Use the **future tense** when planning your protocol methods.
      iii. Use the Submission preview at the bottom of the left-hand menu to preview content to be published.
   B. Writing your review
      i. Replace default text in all sections with your own work, following the guidance given.
      ii. Update your protocol methods and change the future tense to the **past tense** when reporting your review.
   C. Practice review
      i. View the template side by side with your review to ensure you have followed our essential guidance. How can I do this?
   D. Study centric data
      i. This template has **study centric data management** enabled. Using this feature allows

you to:

1. **plan** your review criteria: start your study centric data management at protocol stage by setting up your review criteria and analyses in Review Manager (RevMan) [7]
2. **prepare** your templates: create data extraction templates to match your chosen criteria
3. **populate** your analyses: import your study data files into RevMan and your analyses will automatically be populated in your review.

ii. This means that you should start your protocol by defining your review criteria.

E. Review criteria

i. Before completing the Review criteria section, you should plan the syntheses that you will conduct. As an example, in a review of exercise interventions for depression, the criteria for the review might be as follows.

1. Population: people at risk of depression
2. Intervention: exercise
3. Comparator: usual care
4. Outcomes: various mental health and quality of life outcomes

ii. You will need to plan various syntheses to answer this question, including (for example) examining particular types of exercise for particular outcomes.

iii. A synthesis PICO might be this.

1. Population: people at risk of depression
2. Intervention: yoga
3. Comparator: usual care
4. Outcome: depression as measured by a validated scale

iv. You should enter these PICO elements in this section, so that analyses can be created in the full review. There is more information in Chapter III of the *Cochrane Handbook for Systematic Reviews of Interventions* [10]. You can also refer to the InSynQ checklist, which provides guidance for developing review and synthesis PICOs.

3. Description of the condition

A. Briefly describe the condition or problem being addressed, and who is affected.

B. Recommended: one short paragraph maximum.

4. Description of the intervention and how it might work
   A. Read, and cite when applicable, Chapter 2 [33], and Chapter 17 [39], of the *Cochrane Handbook for Systematic Reviews of Interventions*.
   B. If the review examines the effects of interventions, briefly describe how the intervention(s) examined might work.
   C. Recommended: one or two short paragraphs maximum.
   D. If there is complexity in the intervention or context of its delivery, or both (such as multi-component interventions, interventions targeting the population and individual level, or equity considerations), consider presenting a logic model (sometimes referred to as a conceptual framework or theory of change) as an additional supplementary material to visually display the hypothesized relationship between intervention components and outcomes.
5. Why it is important to do this review
   A. PRISMA 2020 guidance #3: Describe the rationale for the review in the context of existing knowledge and its uncertainties [6].
   B. Explain clearly why the questions addressed by the review are important. This is an opportunity to draw on recent priority setting or guideline development processes, or to explain a particular uncertainty, debate or controversy in the field of interest relating to the evidence base or the intervention.
   C. If other systematic reviews that address the same (or a largely similar) question are available, explain why the current review was considered necessary (for example, previous reviews are out of date or have discordant results; new review methods are available to address the review question; existing reviews are methodologically flawed; or the current review was commissioned to inform a guideline or policy for a particular organization).
   D. If the review is an update of a systematic review, indicate this and cite the previous review.
   E. Example text:
      i. *This is an update of a Cochrane review first published in XXX, and previously updated in XXX.*

Objectives

1. **Cochrane conduct standards:** Setting the research question to inform the scope of the

review [48]

2. Read, and cite when applicable, Chapter III [10], and Chapter 2 [33], of the *Cochrane Handbook for Systematic Reviews of Interventions*. For economic evidence, see Chapter 20 [16], and for qualitative evidence, see Chapter 21 [17].
3. PRISMA 2020 guidance #4: Provide an explicit statement of all objective(s) or question(s) the review addresses.
4. Use the Population, Intervention, Comparator, Outcome (PICO) framework or one of its variants to state the comparisons you will make.
5. Authors should include the smallest number of comparisons that will address the review's objective(s); most often this is one, but it can be more than one. If a review includes more than one comparison, authors may wish to list them in order of priority (justifying the order for priority). Please note, **you must be able to summarize all the comparisons in the Abstract, so ensure you keep the scope manageable (word limit 700 to 1000 words).**
6. Recommended formats:
   A. Standard*: To evaluate the benefits and harms of [intervention] for [health issue/problem] in [population] comparing [comparisons]*
      Head-to-head comparison*: To evaluate the benefits and harms of [intervention] versus [comparator] for [health issue/problem] in [population]*
      Multiple comparisons*: To evaluate the relative benefits and harms of [multiple interventions] for [health issue/problem] in [population]*
7. Some comparisons may have secondary objectives, such as if the review aims to consider equity, or economic or qualitative evidence. Ensure this is stated explicitly, ideally using a separate 'Secondary objectives' subheading.

Methods

1. **Cochrane conduct standards:** Setting eligibility criteria for including studies in the review [48]
   A. Read, and cite when applicable, Chapter III of the *Cochrane Handbook for Systematic Reviews of Interventions* [10].
   B. PRISMA 2020 guidance #24c: Describe and explain any amendments to information provided at registration, in the protocol or the last update. Note: (a) the amendment itself and (b) the reason for the amendment. This includes post-hoc decisions about eligibility criteria or the addition of subgroup analyses). Report aspects of the protocol that were not implemented (e.g. because no studies, or few studies, were found) [6]. If more than a

few sentences are needed to detail the deviations, use an additional supplementary material. Alternatively, if there were no deviations to information provided at registration, in the protocol or the last update, please state this.

C. State which conduct and reporting guidelines were adhered to.

D. Example text:

i. **Protocol:** *We will follow the Methodological expectations for Cochrane intervention reviews (MECIR) when conducting the review [add citation for MECIR, see* [48]*], and PRISMA 2020 for the reporting [add citation for PRISMA, see* [6]*].*

Review: *We followed the Methodological expectations for Cochrane intervention reviews (MECIR) when conducting the review [add citation for MECIR, see* [48]*], and PRISMA 2020 for the reporting [add citation for PRISMA, see* [6]*].*

2. Criteria for considering studies for this review

A. **Cochrane conduct standards:** Setting eligibility criteria for including studies in the review [48]

B. Read, and cite when applicable, Chapter III [10] and Chapter 3 [28] of the *Cochrane Handbook for Systematic Reviews of Interventions*.

C. PRISMA 2020 guidance #5: Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses, for types of studies, participants, interventions and outcome measures, using the following subsections [6].

3. Types of studies

A. Specify all characteristics, related to the types of studies, that you will use to decide whether a study is eligible for inclusion or exclusion in the review, which should focus on study design(s) features, not labels, as well as other characteristics, such as setting(s). Also, specify report characteristics eligible for inclusion or exclusion in the review, such as year of dissemination, language, and report status (for example, whether reports such as unpublished manuscripts and conference abstracts are eligible for inclusion).

B. State explicitly whether cross-over, cluster-RCTs or quasi-RCTs will be eligible and justify the decisions.

C. Provide rationales for any notable restrictions to study eligibility. For example, review authors might explain that the review is restricted to studies published from 2000 onward because the device was first available in that year.

4. Types of participants

A. See InSynQ checklist.

B. Specify all characteristics related to the participants that you will use to decide whether a study is eligible for inclusion or exclusion in the review, such as location, setting, diagnosis

or definition of condition, and demographic factors. Also, how you will address studies,will including subsets of relevant participants. Define in advance how you will handle studies that include only a subset of relevant participants (e.g. contact study authors to obtain data, include if more than X% of participants are eligible). Justify and describe restrictions to study populations here. Define an age cut-off for adults/children/infants.

C. Provide rationales for any notable restrictions to study eligibility.

D. Specify **population groups** to be used in different syntheses in enough detail for them to be replicated, which should reflect the comparison(s) specified in the objectives (see Objectives).

E. Example text:

i. We will measure each outcome by under-five mortality rates per country, taken from the UNICEF report on levels and trends in child mortality (UNICEF 2019), as follows:
low-mortality countries: those in the lowest quartile of under-five child mortality rates
medium-mortality countries: those in the second quartile of under-five child mortality rates
high-mortality countries: those in the highest two quartiles of under-five child mortality rates.
Example modified from Bergman H, Henschke N, Hungerford D, Pitan F, Ndwandwe D, Cunliffe N, et al. Vaccines for preventing rotavirus diarrhoea: vaccines in use. Cochrane Database of Systematic Reviews 2021, Issue 11.Art. No.: CD008521. DOI: 10.1002/14651858.CD008521.pub6

5. Types of interventions

A. See InSynQ checklist.

B. Study centric data management **allows authors to specify their interventions and intervention groupings within RevMan under the Review criteria tab. This informs your data extraction form, facilitates data extraction and enables authors to automatically populate their meta-analyses. More details about** setting up the review criteria in RevMan is available in the Knowledge Base.

C. Specify all characteristics related to the intervention and comparator(s) that you will use to decide whether a study is eligible for inclusion or exclusion in the review, such as criteria for interventions and comparators, including any criteria for delivery, dose, duration, intensity, co-interventions and characteristics of complex interventions, as well as other characteristics, such as minimum duration of follow-up. Pay attention to active comparator interventions (e.g. a different variant of the same intervention, a different drug or a different type of therapy).

D. Provide rationales for any notable restrictions to study eligibility.

E. Specify **intervention groups** that you will use in each synthesis in enough detail for them to be replicated, which should reflect the comparison(s) specified in the objectives (see Objectives). If you plan more than one comparison, define each one, preferably as a list, in a box, or in a table. See example Table 6.

F. Example text:

i. We will base comparisons on the interventions grouped as follows:
antibiotics: xibornol, Aureomycin, tetracycline, co-amoxiclav, co-trimoxazol, penicillin V;
placebo.

ii. We will base comparisons on the interventions grouped as follows:
broad-spectrum antibiotics: tetracycline, co-amoxiclav, co-trimoxazol;
narrow-spectrum antibiotics: penicillin V, xibornolics, Aureomycin; |
lacebo.

6. Outcome measures

A. **Cochrane conduct standards:** Selecting outcomes to be addressed for studies included in the review [48]

B. Read, and cite when applicable, Chapter III [10], and Chapter 3 [28], of the *Cochrane Handbook for Systematic Reviews of Interventions,* and see InSynQ checklist.

C. PRISMA 2020 guidance #10a (part): List and define all outcomes for which data were sought [6].

7. Critical outcomes

A. **These outcomes are critical to users of the review**, such as healthcare consumers (patient-important outcomes), health professionals and policymakers. Cochrane recommends the use of core outcomes sets, such as those available via the COMET Initiative [29]. Reviews should have up to seven critical and important outcomes for each comparison. They will be the basis of the review's conclusions.

B. For each outcome, list the measurement tools (for example, 36-item Short Form (SF-36)) that you will use within each outcome domain (for example, quality of life). List a hierarchy of appropriate outcome measurements if you anticipate that studies may include more than one in each domain. List the time points that you will use, including your primary time point of interest. Provide the rationale for the labelling.

C. Example text: *A recent core outcome set identified the outcomes labelled critical as being the most important to patients*.

D. It is preferable to avoid composite outcomes (such as major adverse events) that may double-count participants who had more than one event. The most important types of event should be reflected as separate outcomes.

E. If the review aims to consider equity, economic or qualitative evidence, ensure you include them in the outcomes.

F. Specify **outcome groups** that you will use in each synthesis in enough detail for them to be replicated, which should reflect the comparison(s) specified in the objectives (see Objectives). If more than one comparison is planned, define each one, preferably as a list, in a box, or in a table. See example Table 7.

G. Example text:

i. We will group outcomes into three sets of time points.

T1: short term/immediate postintervention (defined as 0 to 1 month postintervention) to detect illness recovery/symptom reduction of the intervention.

T2: intermediate term (defined as 1 to 6 months postintervention) to detect sustained illness recovery/symptom reduction

T3: longer term (defined as 7 to 24 months postintervention) as a measure of medium- to long-term avoidance of recurrence and chronicity. We performed subgroup analyses for one- to two-year outcomes if available.

If an outcome is reported more than once during any of the above time points, we will use the latest time point within that category (e.g. if there is a measure at three months and at six months, we will use the results at six months for T2) or the time point that correlated best with other studies compared within each outcome.

Example modified from van Ginneken N, Chin WY, Lim YC, Ussif A, Singh R, Shahmalak U, et al. Primary-level worker interventions for the care of people living with mental disorders and distress in low- and middle-income countries. Cochrane Database of Systematic Reviews 2021, Issue 8. Art. No.: CD009149. DOI: 10.1002/14651858.CD009149.pub3

8. Important outcomes

A. **These outcomes are important to users of the review.**

B. Reporting guidance is the same as for Critical outcomes above.

9. Search methods for identification of studies

A. **Cochrane conduct standards:** Planning the review methods at protocol stage **and** Searching for studies [48]

B. Read, and cite when applicable, Chapter III [10], and Chapter 4 [13], of the *Cochrane*

Handbook for Systematic Reviews of Interventions, as well as Chapter 16 for equity [14], Chapter 19 for adverse effects [15], Chapter 20 for economic evidence [16], and Chapter 21 for qualitative evidence [17].

C. Please note, review authors who have direct involvement in the conduct, analysis, and publication of a study that could be included in the review, cannot make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of that study. See Cochrane's editorial policy on conflicts of interest for more information.

10. Electronic searches

A. PRISMA 2020 guidance #6 (part): Specify all databases, registers, websites, other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted [6].

B. At the point of publication, searches should not be more than 12 months old. If this time frame is exceeded, rerun or update searches for all relevant sources, screen the results for potentially eligible studies and update the review accordingly.

C. For bibliographic databases, specify:

i. the name of each database (such as MEDLINE, CINAHL);

ii. the interface or platform through which each database will be searched (such as Ovid, EBSCOhost); and

iii. the dates of coverage for each database (where this information is provided).

D. State that your preliminary search strategy (e.g. MEDLINE (Ovid)) will be adapted for use in other electronic bibliographic databases. See the Cochrane Style Manual section on reporting database names and coverage dates (search methods).

E. For study registers (such as ClinicalTrials.gov), regulatory databases (such as Drugs@FDA), and other online repositories (such as SIDER Side Effect Resource), specify the name of each source and any date restrictions that were applied.

F. For websites, search engines, or other online sources, specify the name and URL (uniform resource locator) of each source.

G. Include an explicit statement that your search was designed to identify post-publication amendments, such as retractions.

H. If the review aims to consider adverse effects, equity, economic or qualitative evidence, describe search methods for identifying such studies.

I. PRISMA 2020 guidance #7: Present the full search strategies for all databases, registers,

and websites, including any filters (with citations and detailing adaptions, if applicable) and limits (such as date or language) used [6].

J. **!! Go to Search strategies -> Include the full line-by-line search strategies for each database (and other sources, if applicable) in this** Supplementary material 1 **!!** Include search strings, database names, access platforms, search fields and other limitations or settings, and link to this supplementary material from this section.

   i. If you plan to use natural language processing or text frequency analysis tools to identify or refine keywords, synonyms, or subject indexing terms to use in the search strategy, specify which tool(s) you will use.

   ii. If you plan to use a tool to automatically translate search strings for one database to another, specify the tool you will use.

   iii. If the search strategy will be validated - for example, by evaluating whether it could identify a set of clearly eligible studies - report the validation process you will use and specify which studies you will include in the validation set.

   iv. If the search strategy will be peer-reviewed, report the peer review process and specify any tool that will be used, such as the Peer Review of Electronic Search Strategies (PRESS) checklist [43].

K. Indicate when you will adapt or reuse search strategies from other literature reviews for a substantive part or all of the search, citing the previous review(s), such as for Cochrane review updates. If applicable, report the methods that you will use to update the search(es) (e.g. rerunning searches, email alerts).

11. Searching other resources

A. PRISMA 2020 guidance #6 (part): Specify all organisations, reference lists, and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted [6].

B. If you plan to:

   i. contact organizations or manufacturers to identify studies, specify the name of each source;

   ii. contact individuals to identify studies, specify the types of individuals contacted (such as authors of studies included in the review or researchers with expertise in the area);

   iii. examine reference lists, specify the types of references examined (such as references cited in study reports included in the systematic review, or references cited in

systematic review reports on the same or a similar topic);

iv. conduct cited or citing reference searches (also called backwards and forward citation searching), specify the bibliographic details of the reports to which you will apply citation searching, and the citation index or platform you will use (such as Web of Science) - for the review, specify the date you did the citation searching;

v. consult journals or conference proceedings, specify the names of each source, the dates you will cover and how you will search (such as handsearching or browsing online).

12. Data collection and analysis
    A. **Cochrane conduct standards:** Selecting studies to include in the review [48]
    B. Read, and cite when applicable, Chapter III of the *Cochrane Handbook for Systematic Reviews of Interventions* [10].
13. Selection of studies
    A. Read, and cite when applicable, Chapter 4 of the *Cochrane Handbook for Systematic Reviews of Interventions* [13].
    B. PRISMA 2020 guidance #8: Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record (title/abstract) and each report retrieved, with their initials, state that they worked independently (that is, were unaware of each other's decisions), and any processes used to resolve disagreements between screeners (for example, referral to a third reviewer or by consensus). If applicable, specify details of crowdsourcing or automation tools used in the process [6].
    C. State your process for identification and recording reasons for exclusion of the ineligible studies (e.g. if you plan to use a hierarchy of exclusion reasons for exclusion, which can be useful for certain reviews).
    D. If you plan to use Cochrane Crowd or Screen4Me service, see the guidance on how to report it, which includes recommended references and template text and figures.
    E. Report any processes you will use to obtain or confirm relevant information from study investigators.
    F. If abstracts or articles require translation into another language to determine their eligibility, report how you will translate them (for example, by asking a native speaker or by using software programs).
    G. State how you plan to manage the results of your search (e.g. using software such as Rayyan [19], Covidence [18], Endnote [20], etc.).

H. Please note, review authors who have direct involvement in the conduct, analysis, and publication of a study that could be included in the review, cannot make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of that study. See Cochrane's editorial policy on conflicts of interest for more information.

14. Data extraction and management
    A. Read, and cite when applicable, Chapter 5 [21], and Chapter 9 [22], of the *Cochrane Handbook for Systematic Reviews of Interventions*.
    B. Study centric data management **in RevMan allows authors to import their study data directly into RevMan. To facilitate the import, it is recommended that Cochrane authors use the study data import files to inform their data extraction forms or use Covidence. More details about** populating study data in RevMan are available in the Knowledge Base.
    C. PRISMA 2020 guidance #9: Specify the methods used to collect data from reports, including how many reviewers collected data from each report (and their initials), that they worked independently, how disagreements were resolved, any processes for obtaining or confirming data from study investigators, and if applicable, specify details of crowdsourcing or automation tools used in the process [6].
    D. PRISMA 2020 guidance #10a: List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.
    E. PRISMA 2020 guidance #10b: List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information, for example, in a study that includes "children and adolescents," for which the investigators did not specify the age range, authors might assume that the oldest participants would be 18 years, based on what was observed in similar studies included in the review, and should report that assumption. Please note, this information does not need to be listed here as with the use of RevMan, compliance will be automatic within the characteristics of studies Supplementary material.
    F. Cite any tools or data collection forms that you will use to collect data or to inform the data items to collect (such as the Tool for Addressing Conflicts of Interest in Trials (TACIT) [44], or a tool for recording intervention details). Pilot any data collection forms, and state that you piloted them, along with the number of studies in the pilot.

G. Describe the data collection process for any reports that require translation.

H. State how you will convert data found in studies to a format appropriate for meta-analysis following methods described in Chapter 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* [4].

15. Risk of bias assessment in included studies

A. **Cochrane conduct standards:** Planning the review methods at protocol stage **and** Assessing risk of bias in included studies [48]

B. Read, and cite when applicable, Chapter 7 [23] and Chapter 8 [24], of the *Cochrane Handbook for Systematic Reviews of Interventions*, as well as Chapter 23 for variants of trials (cluster and cross-over trials) [25], and Chapter 25 for non-randomized studies of interventions [26].

C. PRISMA 2020 guidance #11: Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study (and their initials), that they worked independently, and any processes used to resolve disagreements between assessors [6].

D. For each study design included in the review (RCT, cluster-RCT, cross-over trial or non-randomized studies of interventions), specify and cite the methods and tool(s) you will use to assess risk of bias in the included studies, with the risk of bias judgements and support for those judgements across the series of domains of bias.

E. Cochrane reviews assess the risk of bias of included studies to judge the possible impact of bias on the results of outcomes in the summary of findings table. For randomized trials, the RoB 2 tool is the preferred tool [24], though authors can use the original risk of bias tool, RoB 1 (use chapter 8 in Version 5.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* if using the original tool [34]). Extensions of RoB 2 are available for cluster and cross-over trials [25].

F. **Authors can switch this review to RoB 2 in RevMan via the Dashboard (see *Enable advanced features → Risk of bias 2*)**

G. Report whether you will make an overall judgement to summarize risk of bias across domains/components/items. If so, state the rules that you will use to reach an overall judgement.

H. For RoB 2, state whether you are interested in quantifying the effect of assignment to the interventions at baseline, regardless of whether the interventions are received as intended (the 'intention-to-treat effect'); or the effect of adhering to the interventions as specified in the trial protocol (the 'per-protocol effect').

I. List the outcomes (including measure(s) and time point(s)) for which you will assess results

for risk of bias.

J. For non-randomized studies of interventions, if you adapt an existing tool to assess risk of bias in studies (such as omitting or modifying items), specify the adaptations.

K. Report any processes you will use to obtain or confirm relevant information from study authors.

L. Please note, review authors who have direct involvement in the conduct, analysis, and publication of a study that could be included in the review, cannot make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of that study. See Cochrane's editorial policy on conflicts of interest for more information.

16. Measures of treatment effect

A. **Cochrane conduct standards:** Planning the review methods at protocol stage**,** Collecting data from included studies **and** Synthesising the results of included studies [48]

B. Read, and cite when applicable, Chapter 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* [4].

C. PRISMA 2020 guidance #12: Specify for each outcome or type of outcome (such as binary, continuous) the effect measure(s) (such as risk ratio, mean difference) used in the synthesis or presentation of results [6].

D. State any thresholds or ranges you will use to interpret the size of effect (such as minimally important difference; ranges for no or trivial, small, moderate, and large effects) and the rationale for these thresholds.

E. If you plan to re-express synthesized results to a different effect measure, report the methods you will use (such as meta-analysing risk ratios and computing an absolute risk reduction based on an assumed comparator risk).

F. If relevant, provide justification for the choice of effect measure. For example, you may have chosen a standardized mean difference because you will use multiple instruments or scales across studies to measure the same outcome domain (such as different instruments to assess depression).

17. Unit of analysis issues

A. **Cochrane conduct standards:** Synthesising the results of included studies [48]

B. Read, and cite when applicable, Chapter 6 [4], and Chapter 11 [30], of the *Cochrane Handbook for Systematic Reviews of Interventions*.

C. Specify any methods you plan to use to address unit of analysis issues in studies included in the review with relevant design issues, such as RCTs with three or more arms or RCTs with repeated outcome measurement at different time points. This includes clustering,

matching or other non-standard design features of the included studies, and should consider the impact on the meta-analysis (consider methods that will avoid double-counting). Study designs to be considered include cluster-randomized trials, cross-over trials, repeated observation on participants, events that may re-occur, multiple treatment attempts, randomization of body parts, and multiple intervention groups. For RCTs with parallel design and only two arms (intervention 1 versus control or intervention 1 versus intervention 2), you do not need to consider unit of analysis issues, but you may encounter studies with three or more intervention arms of interest.

18. Dealing with missing data
    A. **Cochrane conduct standards:** Collecting data from included studies **and** Synthesising the results of included studies
    B. Read, and cite when applicable, Chapter 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* [4].
    C. PRISMA 2020 guidance #13b: Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, e.g. last observation carried forward, or assumptions of particular values such as worst-case or best-case scenarios, or data conversions [6].
19. Reporting bias assessment
    A. **Cochrane conduct standards:** Synthesising the results of included studies [48]
    B. Read, and cite when applicable, Chapter 13 of the *Cochrane Handbook for Systematic Reviews of Interventions* [31].
    C. PRISMA 2020 guidance #14: Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases) [6].
    D. State whether or not you will assess risk of bias due to missing results in a synthesis (arising from reporting biases). If you will, specify the methods you will use (tool, graphical, statistical, or other).
    E. If you plan to assess risk of bias due to missing results using an existing tool, specify the process you will use to reach a judgement of overall risk of bias and whether you will make any adaptations (such as omitting or modifying items).
    F. Report how many review authors, (add their initials), will assess risk of bias due to missing results in a synthesis, whether multiple review authors will work independently, and any processes you will use to resolve disagreements between them.
    G. Report any processes you will use to obtain or confirm relevant information from study authors.
    H. If you plan to use an automation tool to assess risk of bias due to missing results, report

how you will use the tool, how it will be trained, and details of its performance and internal validation.

20. Synthesis methods
    A. **Cochrane conduct standards:** Planning the review methods at protocol stage **and** Synthesising the results of included studies [48]
    B. Read, and cite when applicable, Chapter 10 [11], and Chapter 12 [32], of the *Cochrane Handbook for Systematic Reviews of Interventions.*
    C. The concept of data synthesis for systematic reviews includes both meta-analysis and synthesis without meta-analysis (SWiM). Both should be addressed in this section.
    D. **Cochrane authors should aim for the smallest number of comparisons** that address the main objectives (most often this is one, but it can be more than one).
    E. PRISMA 2020 guidance #13a: Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis) [6].
    F. Syntheses should only occur if participants, interventions, comparisons and outcomes are judged to be sufficiently similar to ensure an answer that is clinically meaningful; therefore use the population, intervention and outcome groupings as defined above (in Types of studies; Types of participants; Types of interventions; Outcome measures) to justify your planned synthesis and facilitate clear decisions on which studies are eligible for each synthesis.
    G. Example text:
        i. We will include studies of self-management interventions delivered in any form (e.g. Internet, mobile device, face-toface, paper) with the following comparisons.
        Self-management versus usual care
        Self-management versus an alternate form of self-management (e.g. paper-based booklet versus mobile app).
        For comparisons between different types of self-management programmes we will include co-interventions, including types of exercise interventions, provided that they were evenly distributed between groups.

        Example modified from Kelly C, Grundy S, Lynes D, Evans DJ, Gudur S, Milan SJ, et al. Self-management for bronchiectasis. Cochrane Database of Systematic Reviews 2018, Issue 2 Art. No.: CD012528. DOI: 10.1002/14651858.CD012528.pub2.
    H. PRISMA 2020 guidance #13c: Describe any methods used to tabulate or visually display results of individual studies and syntheses [6].

I. If you plan to order or group studies within tables or graphs based on study characteristics (such as by size of the study effect, year of publication), report the basis for the chosen ordering or grouping.

J. If you plan to use non-standard graphs, report the rationale for selecting the chosen graph.

K. PRISMA 2020 guidance #13d: Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity (variability in the numerical effect estimates resulting from clinical and methodological diversity), and software package(s) used [6].

L. Where you plan to combine data in statistical software external to RevMan, reference the software, packages, and version numbers used to implement synthesis methods (such as metan in Stata 16 [41], metafor (version 2.1-0) [42]).

M. If it is not possible to conduct a meta-analysis, describe and justify the synthesis methods or summary approach you will use (such as combining P values because no or minimal information beyond P values and direction of effect is reported in the studies).

N. Specify the meta-analysis model you will use (fixed-effect or random-effects), provide the rationale for the selected model, and state the method you will use (such as Mantel-Haenszel, inverse-variance). Review authors should not base their choice of model on the presence of heterogeneity according to particular threshold values of the I^2 statistic [37].

O. If you plan to use a random-effects meta-analysis model, specify the between-study (heterogeneity) variance estimator you will use (such as DerSimonian and Laird [45], restricted maximum likelihood (REML) [46]). Best practice is generally using the same method for estimating heterogeneity (e.g., either REML, recommended and default in RevMan, or DL) throughout a review. In the unlikely event that your prespecified estimator fails for one of the analyses, you should select the alternative for that analysis only.
Specify the method you will use to calculate the confidence interval for the summary effect (such as Wald-type confidence interval, Hartung-Knapp-Sidik-Jonkman [4]).
The *Cochrane Handbook for Systematic Reviews of Interventions* explains which methods are recommended in different situations – see section 10.10.4.4 [11].

P. Specify other details about the methods you will use, such as the method for calculating confidence limits for the heterogeneity variance and whether you will include a prediction interval [11].

Q. If you plan to use a Bayesian approach to meta-analysis, describe the prior distributions about quantities of interest (such as intervention effect being analysed, amount of

heterogeneity in results across studies).

R. If you plan to include multiple effect estimates from a study in a meta-analysis (as may arise, for example, when a study reports multiple outcomes eligible for inclusion in a particular meta-analysis), describe the method(s) you plan to use to model or account for the statistical dependency (such as multivariate meta-analysis, multilevel models, or robust variance estimation).

S. Describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity (such as visual inspection of results, a formal statistical test for heterogeneity, heterogeneity variance (τ2), inconsistency (such as I^2 statistic [37]), and prediction intervals), and software package(s) you plan to use to perform meta-analysis.

21. Investigation of heterogeneity and subgroup analysis

A. **Cochrane conduct standards:** Synthesising the results of included studies [48]

B. Read, and cite when applicable, Chapter 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* [11].

C. PRISMA 2020 guidance #13e: Describe any methods used to explore possible causes of heterogeneity amongst study results (e.g. subgroup analysis, meta-regression) [6].

D. Use this section to describe any approach you will use to investigate clinical diversity (participants, interventions, etc., within or between the included studies) and methodological diversity (study design, outcome measurement tools used, etc.).

E. Generally, reviews will consider three to five subgroup analyses, if applicable. If you plan to perform subgroup analysis or meta-regression, specify for each:

i. the rationale (why do you think this is an effect modifier);

ii. which factors you will explore, levels of those factors, and which direction of effect modification is expected and why (where possible);

iii. whether you will conduct analyses using study-level variables (where each study is included in one subgroup only), within-study contrasts (where data on subsets of participants within a study are available, allowing the study to be included in more than one subgroup), or some combination of the above;

iv. how you will compare subgroup effects (such as statistical test for interaction for subgroup analyses).

F. If you are unable to implement subgroup analysis because there are insufficient studies (the general rule is you need at least 10 studies for a meaningful analysis) or insufficient information available about them, report this here.

G. If you plan to use other methods to explore heterogeneity because data are not amenable to meta-analysis of effect estimates, describe the methods you will use (such as structuring tables to examine variation in results across studies based on subpopulation, key intervention components, or contextual factors) along with the factors and levels.

H. Examples include:

i. We will perform subgroup analyses, if possible, using the country under-five mortality rates as a stratifying variable (detailed in Types of participants).

From the *Types of participants* section:

We will stratify each outcome by under-five mortality rates per country, taken from the UNICEF report on levels and trends in child mortality (UNICEF 2019), as follows:
low-mortality countries: those in the lowest quartile of under-five child mortality rates
medium-mortality countries: those in the second quartile of under-five child mortality rates
high-mortality countries: those in the highest two quartiles of under-five child mortality rates.

Example modified from Bergman H, Henschke N, Hungerford D, Pitan F, Ndwandwe D, Cunliffe N, et al. Vaccines for preventing rotavirus diarrhoea: vaccines in use. Cochrane Database of Systematic Reviews 2021, Issue 11. Art. No.: CD008521. DOI: 10.1002/14651858.CD008521.pub6

ii. To ensure that we will capture all relevant study types, we will consider a broad range of empirical studies of any size that provide a quantitative measure of impact, including experimental and quasi-experimental studies, observational studies, and mathematical modelling studies. Given that empirical and observational studies provide a measured estimate of effect whereas modelling studies predict such an effect, we will treat these as two separate bodies of evidence in the synthesis.

Example modified from Burns J, Movsisyan A, Stratil JM, Biallas RL, Coenen M, Emmert-Fees KM, et al. International travel-related control measures to contain the COVID-19 pandemic: a rapid review. Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013717. DOI: 10.1002/14651858.CD013717.pub2

22. Equity-related assessment

A. Read, and cite when applicable, Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* [14].

B. State whether or not you will consider equity-related assessments. If the review will not consider health inequity, state "We will not investigate health inequity in this review" and explain why.

C. If the review will consider health inequity:

   i. define which populations experience it with respect to the condition, problem or intervention being assessed. A framework, such as PROGRESS-Plus [47], might help identify the populations to consider in a systematic way, as well as different settings like high-income, low- and middle-income countries. If appropriate, include a logic model as an additional supplementary material dedicated to equity methods;

   ii. specify what methods will be used to identify and appraise evidence related to equity and specific populations. Define how you are going to extract information to inform the Characteristics of included studies and Results sections. In an additional supplementary material dedicated to equity methods, describe whether there are differences in the lived experiences of these populations (e.g. racism, ageism, stigma, acceptability, other underlying determinants of health); explain the rationale for methodological decisions related to specific populations (e.g. inclusion/exclusion criteria, subgroup analyses, choice of outcomes); and the choice of databases to locate studies including some of our populations of interest.

   iii. if you are planning separate comparisons or want to assess different baseline risks for specific population characteristics, report how your will address this in the summary of findings table(s). For example, separate summary of findings tables for (needs justification) or separate rows for differences in risk of events.

D. *The* PRO EDI initiative *provides guidance on equity, diversity and inclusion in evidence synthesis. Please note, PRO EDI is not formally endorsed by Cochrane yet as it is still in development but may be a helpful resource for authors; if you use it, please cite it.*

23. Sensitivity analysis

A. **Cochrane conduct standards:** Synthesising the results of included studies [48]

B. Read, and cite when applicable, Chapter 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* [11].

C. PRISMA 2020 guidance #13f: Describe any sensitivity analyses conducted to assess robustness of the synthesized results [6].

D. If you plan to perform sensitivity analyses, provide details of each analysis (such as removal of studies at high risk of bias, impact of notable assumptions, imputed data,

borderline decisions, or use of an alternative meta-analysis model).

E. If you plan to consider risk of bias in a sensitivity analysis, it is recommended to use overall risk of bias, if applicable. Primary analyses can be restricted to studies judged at an overall low risk of bias or low risk of bias and some concerns.

F. Unlike subgroup analysis, there is no formal statistical test that can be used for sensitivity analysis, so review authors must make informal comparisons between the different ways of estimating the effect under different assumptions. Comparing changes in P values to judge whether there is a difference between the meta-analysis and sensitivity analysis is not appropriate.

24. Certainty of the evidence assessment

A. **Cochrane conduct standards:** Planning the review methods at protocol stage **and** Assessing the quality of evidence and summarising the findings [48]

B. Read, and cite, when applicable, Chapter 14 of the *Cochrane Handbook for Systematic Reviews of Interventions* [8].

C. PRISMA 2020 guidance #15: Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome [6].

D. Cochrane reviews assess the certainty of the evidence for each outcome in the summary of findings table. Cochrane reviews should have one summary of findings table for each comparison that includes up to seven critical and important outcomes for the comparison.

E. The preferred system for assessing the certainty of the evidence for Cochrane reviews of interventions is the GRADE approach. Report the factors you will consider (risk of bias, consistency of effect, imprecision, indirectness and publication bias) and the criteria you will use to assess each factor when assessing certainty in the body of evidence.

F. Describe the decision rules you will use to arrive at an overall judgement of the level of certainty (such as high, moderate, low, very low), together with the intended interpretation (or definition) of each level of certainty.

G. If applicable, report any review-specific considerations for assessing certainty, such as thresholds you will use to assess imprecision and ranges of magnitude of effect that might be considered trivial, moderate or large, and the rationale for these thresholds and ranges.

H. Report the number and initials of the review authors who will assess the certainty of evidence, that they will work independently, and any processes used to resolve disagreements between them.

I. If you plan to use an automation tool to support the assessment of certainty, report how

you will use it, how it was trained, and details of its performance and internal validation.

J. In this section, authors often cite:

   i. *Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach* [38]

   ii. GRADEpro GDT [2]

   iii. Chapter 14 of the C*ochrane Handbook for Systematic Reviews of Interventions*, Completing 'Summary of findings' tables and grading the certainty of the evidence [8]

K. Please note, review authors who have direct involvement in the conduct, analysis, and publication of a study that could be included in the review, cannot make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of that study. See Cochrane's editorial policy on conflicts of interest for more information.

25. Consumer involvement

A. State whether or not consumers or other people will be involved in the review. This may include researchers, patients and members of the public, or other professionals, such as policy makers or commissioners.

B. If consumers or others will be involved, review authors should report on their methods for involving them. This includes:

   i. the level of involvement of the people involved;

   ii. the general approach to involvement;

   iii. the roles of the people who will be involved;

   iv. the stage in the review process at which they will be involved; and

   v. any formal research methods or techniques which are to be used.

C. A template supplementary material for reporting consumer involvement is available. See Supplementary material 3.

D. *The ACTIVE framework provides guidance on consumer and stakeholder involvement in systematic reviews [49]; if you use it, please cite it.*

E. If you will not involve consumers, state this with a rationale as to why, along with any details that may be relevant.

F. Example text:

   i. *We will not involve consumers in this review due to limited resources, although we*

will use core outcome sets for the review's outcomes, which have been developed with consumer involvement.

Results

1. Description of studies
    A. Read, and cite when applicable, Chapter III of the *Cochrane Handbook for Systematic Reviews of Interventions* [10].
2. Results of the search
    A. Also see Chapter 4 [13], and Chapter 5 [21], of the *Cochrane Handbook for Systematic Reviews of Interventions*.
    B. PRISMA 2020 guidance #16a: Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram [6].
    C. Report, ideally using a PRISMA flow diagram, the number of: records identified; records excluded before screening (for example, because they were duplicates or deemed ineligible by machine classifiers); records screened; records excluded after screening titles or titles and abstracts; reports retrieved for detailed evaluation; potentially eligible reports that were not retrievable; retrieved reports that did not meet inclusion criteria and the primary reasons for exclusion (such as ineligible study design, ineligible population); and the number of studies and reports included in the review [6]. If applicable, authors should also report the number of ongoing studies and associated reports identified.
    D. If the review is an update of a previous review, report results of the search and selection process for the current review and specify the number of studies included in the previous review. An additional box could be added to the flow diagram indicating the number of studies included in the previous review.
    E. If applicable, indicate in the PRISMA flow diagram how many records were excluded by a human and how many by automation tools [6].
    F. If a review identifies no eligible studies, restrict the Results section to a description of the flow of studies and any brief comments about reasons for exclusion of studies.
3. Included studies
    A. Read, and cite when applicable, Chapter 5 of the *Cochrane Handbook for Systematic Reviews of Interventions* [21].
    B. PRISMA 2020 guidance #17: Cite each included study and present its characteristics [6].

C. Summarize the characteristics of the included studies. This should give an overview of the setting of the studies, who was recruited, the comparator interventions delivered, and the outcomes measured. Do not describe each study individually. Instead, link to the Characteristics of included studies (Supplementary material 2), which includes the full details of included studies and all reports of each study.

D. **Please check your Characteristics of included studies supplementary material to ensure that you have used quotation marks around any text copied directly from study reports (see also** Cochrane's plagiarism policy**).**

E. Key characteristics of each study that are particularly important for understanding the results of the review should be presented in an overview of synthesis and included studies table (see guidance).

F. **!! Go to Tables > Add table** to **create your overview of synthesis and included studies table !!** Consider a format that will facilitate comparison of characteristics across the studies, including to which review outcomes each study contributes results. See examples in Table 1; Table 2; Table 3; Table 4; and Table 5.

G. **All included studies must be referenced, ideally in the overview of synthesis and included studies table** or alternatively, in this section.

H. Consider presenting an additional table that summarizes the intervention details for each study, particularly for complicated or complex interventions.

I. If applicable, link to the Characteristics of studies awaiting classification supplementary material. It includes studies that have been identified as potentially eligible but have not yet been incorporated into the review, along with the reason that they have not yet been incorporated. This supplementary material also includes all reports of each study.

J. If applicable, link to the Characteristics of ongoing studies supplementary material. It includes studies that have been identified as potentially eligible, along with any details that are known about the study, and cite all reports of each study.

4. Excluded studies

A. Read, and cite when applicable, Section III.3.4.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* [10].

B. PRISMA 2020 guidance #16b: Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded [6].

C. Link to the Characteristics of excluded studies supplementary material, which gives reasons for exclusion. The list of excluded studies should be as brief as possible, and should include studies that fulfil eligibility criteria for the review but have associated retractions. It should not list all the reports that were identified by an extensive search. It

should not list studies that obviously do not fulfil the eligibility criteria for the review.

5. Risk of bias in included studies
   A. **Cochrane conduct standards:** Assessing risk of bias in included studies [48]
   B. Read, and cite when applicable, Chapter III [10], Chapter 7 [23], and Chapter 8 [24], of the *Cochrane Handbook for Systematic Reviews of Interventions*.
   C. PRISMA 2020 guidance #18: Present assessments of risk of bias for each outcome or result from each study [6].
   D. Provide a brief overview of the risk of bias assessments. For example, any overall comments or important differences, or if risk of bias assessments are very similar or very different for certain outcomes in the review, and why that might be.
      i. For RoB 2 link to the Risk of bias supplementary material.
      ii. For RoB 1 (the original risk of bias tool for RCTs) link to the Characteristics of included studies supplementary material (Supplementary material 2).
      iii. For tools that assess non-randomized studies of interventions, link to an additional supplementary material that includes the risk of bias judgements and support for judgements.
   E. If applicable, state how to access detailed risk of bias assessment data (with consensus responses to the signalling questions).
6. Synthesis of results
   A. **Cochrane conduct standards:** Synthesising the results of included studies [48]
   B. Read, and cite when applicable, Chapter III [10], Chapter 10 [11], Chapter 12 [32], Chapter 14 [8], and Chapter 15 [40], of the C*ochrane Handbook for Systematic Reviews of Interventions*.
   C. Present a summary of findings table.
   D. For reviews based on pairwise meta-analyses, there should be one summary of findings table for each relevant comparison that includes up to seven outcomes for that comparison. While there is no upper limit on the number of comparisons or summary of findings tables in a Cochrane review, it is advisable to focus on comparisons and outcomes that users will find most useful in decision making. Please note, **you must be able to summarize all the comparisons in the Abstract (700 to 1000 words) so ensure you keep the scope manageable**. Reviews that include a network meta-analysis may need to include one summary of findings table for each outcome.
   E. A summary of findings table should include results for one clearly defined population

group (with few exceptions); indicate the intervention and the comparison intervention; include seven or fewer outcomes; describe the outcomes (e.g. scale, scores, follow-up); indicate the number of participants and studies for each outcome; present at least one baseline risk for each dichotomous outcome (e.g. study population or median/medium risk) and baseline scores for continuous outcomes (if appropriate); summarize the intervention effect (if appropriate); and include a measure of the certainty of the body of evidence for each outcome.

F. Link to the Analyses supplementary material, which includes all comparisons and forest plots for all syntheses, including subgroup and sensitivity analyses.

G. Subheadings using critical and important outcomes are recommended in this section. For each outcome, cover the following, when applicable.

H. PRISMA 2020 guidance #19: For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots [6].

I. Ensure that key findings are interpretable, or are re-expressed in an interpretable way. Absolute effects are usually easier to understand than relative effects (e.g. assumed and corresponding risks, number needed to treat for an additional beneficial outcome (NNTBs), group means). However, they may need to be accompanied by information about assumed baseline risks. Confidence intervals should be presented for NNTBs and similar summary measures. Re-expressing relative effects as absolute effects often requires the specification of assumed (e.g. untreated) risks, and the source of these should be provided. Results expressed as standardized mean differences reflect the number of standard deviations' difference between mean responses. This is not intuitive to many readers who may be more familiar with specific scales (where possible, use units that are more naturally understood). Ideally, minimally important effect sizes should be specified in the protocol.

J. PRISMA 2020 guidance #20a: For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies [6].

K. Within the forest plots, display risk of bias judgements next to the study results, so that the limitations of studies contributing to a particular meta-analysis are evident.

L. If data were not amenable to meta-analysis, use other figures or a table to facilitate comparison of the limitations of studies.

M. PRISMA 2020 guidance #20b: Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing

groups, describe the direction of the effect.

N. Syntheses that help the review address its objectives and support its conclusions should be added as Figures or Tables, such as forest plot figures or tables when data were not amenable to meta-analysis. The results of these syntheses should be found among those reported in summary of findings tables. It may be necessary to omit certain results as Figures where there are multiple summary of findings tables. To reference any other syntheses, link to the Analyses supplementary material.

O. **!!** Insert dynamic analysis results **when reporting in the text** > if you update the analysis at a later date, e.g., to add or remove studies or change the statistical setting, it will automatically update the analysis result in the text.

P. PRISMA 2020 guidance #20c: Present results of all investigations of possible causes of heterogeneity among study results [6].

Q. Investigations of heterogeneity that help the review address its objectives and support its conclusions can be described in the text or, if necessary, added as Figures, such as forest plot figures. To reference any other investigations of heterogeneity, link to the Analyses supplementary material.

R. PRISMA 2020 guidance #20d: Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results [6].

S. Sensitivity analyses that help the review address its objectives and support its conclusions can be described in the text or, if necessary, added as Figures, e.g. forest plot figures. To reference any other sensitivity analyses, link to the Analyses supplementary material.

T. PRISMA 2020 guidance #22: Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed [6].

7. Equity assessment

A. Read, and cite when applicable, Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* [14].

B. **If the review does not consider health inequity, leave this section blank and it will not publish.**

C. If the review does consider health inequity, provide a brief overview of the assessments, for example, any overall comments or important differences and why that might be, or gaps in the evidence base.

D. Link to an additional supplementary material (template available in Supplementary material 4) that describes the characteristics of the populations you expected to see and what was represented in your included studies. Summarize these population details across included studies, including whether there are differences in baseline risk or prevalence of

the problem or condition.

8. Reporting biases
    A. PRISMA 2020 guidance #21: Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed [6].
    B. If not applicable for the review, leave this section empty, and it will not be published.

Discussion

1. Summary of main results
    A. Provide a concise narrative description of results for the main outcomes of the review. This should not simply repeat numerical results provided elsewhere. If the review has a number of comparisons, this section should focus on those that are most prominent in the review, and that address the main review objectives. Avoid repeating all the results of the synthesis.
2. Limitations of the evidence included in the review
    A. PRISMA 2020 guidance #23b: Discuss any limitations of the evidence included in the review [6].
    B. Present an assessment of how well the evidence identified in the review addressed the review question. It should indicate whether the studies identified were sufficient to address all the objectives of the review, and whether all relevant types of participants, interventions and outcomes have been investigated. Information presented under Description of studies will be useful to draw on in writing this part of the discussion.
    C. This section should summarize the considerations that led to downgrading or upgrading the certainty of the evidence in the implementation of GRADE. This information can be based on explanations for downgrading decisions alongside the summary of findings tables in the review.
    D. If the review considered health inequity, discuss how population characteristics or settings may affect the applicability of the review. Refer to the equity results supplementary material (for example Supplementary material 4) and consider whether the representation of people in the included studies affect the generalisability of the review's findings based on what people you expected to see. Consider whether there may be differences in the effectiveness of the intervention, the baseline risk, and whether there are differences in

the importance of some outcomes.

3. Limitations of the review processes
    A. Read, and cite when applicable, Chapter 13 of the *Cochrane Handbook for Systematic Reviews of Interventions* [31].
    B. PRISMA 2020 guidance #23c: Discuss any limitations of the review processes used [6].
    C. Discuss any limitations of the review processes used and comment on the potential impact of each limitation, such as incomplete identification of studies, completeness of data collection processes, any completed studies that have been identified as potentially eligible but have not been incorporated into the review (see item above), assumptions made regarding classification of interventions, outcomes or subgroups, and methods used to account for missing results in specific syntheses.
    D. In particular, if the review methods do not allow for detection of serious or rare adverse events, or either, the review authors must explicitly state this as a limitation.
4. Agreements and disagreements with other studies or reviews
    A. PRISMA 2020 guidance #23a: Provide a general interpretation of the results in the context of other evidence [6].

Authors' conclusion

: Read, and cite when applicable, Chapter III [10], and Chapter 15 [40], of the *Cochrane Handbook for Systematic Reviews of Interventions*.

1. Implications for practice
    A. PRISMA 2020 guidance #23d (part): Discuss implications of the results for practice and policy [6].
    B. Avoid making recommendations for practice.
    C. Review authors should provide a general interpretation of the evidence so that it can inform healthcare or policy decisions. The implications for practice should be as practical and unambiguous as possible, should be supported by the data presented in the review and should not be based on additional data that were not systematically compiled and evaluated as part of the review. It may help readers if review authors identify factors that are likely to be relevant to their decision making, such as the relative value of the likely benefits and harms of the intervention, participants at different levels of risk, or resource issues.
    D. Avoid using abbreviations and acronyms as this is a standalone section.

2. Equity-related implications for practice
    A. If the review considered equity, discuss the equity-related implications for practice and policy. Otherwise, leave this section empty and it will not be published.
3. Implications for research
    A. PRISMA 2020 guidance #23d (part): Discuss implications of the results for future research [6].
    B. Make explicit recommendations for future research that offer constructive guidance on addressing the remaining uncertainties identified by the review. Draw on important gaps in the limitations of the evidence noted in the Discussion and any downgrading decisions in rating the certainty of evidence. This could include avoidable sources of bias or larger studies. Include references to ongoing studies that have been identified as potentially eligible. Recommendations for initiating new studies should be made in the light of what is already known about ongoing or recently completed studies. Structure these recommendations to address the nature of evidence required, including population, intervention comparison, outcome, and type of study.
    C. Avoid using abbreviations and acronyms as this is a standalone section.
4. Equity-related implications for research
    A. If the review considered equity, discuss the equity-related implications for research. Otherwise, leave this section empty and it will not be published.

Acknowledgements

1. Review authors should acknowledge the contribution of people not listed as authors of the review and any contributions to searching, data collection, study appraisal or statistical analysis performed by people not listed as review authors. See Cochrane's editorial policy on authorship for the different criteria for authors against those who are acknowledged.
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4. Example format:

A. *Cochrane [GROUP/UNIT NAME] supported the authors in the development of this review. We are grateful to all authors who developed the protocol for this review [9], and contributed to previous review versions in 2010 [7], and 2016 [8]. X helped develop the original protocol and contributed in the interpretation, write-up and sign-off of the 2010 and 2016 reviews; Y co-led the 2016 update including sift and study selection, data extraction, syntheses, risk of bias assessment and write-up; Z, V and U were all authors for the 2010 version and their contributions are described in the publication. We are very grateful to the study authors A, B, C and D, who kindly responded to requests for additional information for the previous version and this review update.*

B. *The following people conducted the editorial process for this review: [NAME, AFFILIATION] (Sign-off Editor); [NAME, AFFILIATION] (Managing Editor); [NAME, AFFILIATION] (Editorial Assistant); [NAME, AFFILIATION] (clinical/content peer review)*, [NAME, AFFILIATION] (consumer peer review), [NAME, AFFILIATION] (methods peer review), [NAME, AFFILIATION] (search peer review). [NUMBER] of additional peer reviewers provided [CLINICAL/CONTENT/CONSUMER/METHODS/SEARCH] peer review but chose not to be publicly acknowledged. [NAME, AFFILIATION] copyedited the [ARTICLE TYPE] during the production process.*

Contributions of authors

1. The contributions of each review author to both the current review and previous versions should be described. It is helpful to specify which authors were involved in each of the following tasks: conception of the review; design of the review; co-ordination of the review; search and selection of studies for inclusion in the review; collection of data for the review; assessment of the risk of bias in the included studies; analysis of data; assessment of the certainty in the body of evidence; interpretation of data, and; writing of the review.
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2. Example format:
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3. *Some authors involved in previous published versions of this review in YEAR and YEAR are no longer included on the author byline: NAME, NAME and NAME. Some of the content retained in this review reflects their contributions.*

Declarations of interest

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