The PRISMA 2020 statement: an updated guideline for reporting systematic reviews

Matthew J Page,[1] Joanne E McKenzie,[1] Patrick M Bossuyt,[2] Isabelle Boutron,[3] Tammy C Hoffmann,[4] Cynthia D Mulrow,[5] Larissa Shamseer,[6] Jennifer M Tetzlaff,[7] Elie A Akl,[8] Sue E Brennan,[1] Roger Chou,[9] Julie Glanville,[10] Jeremy M Grimshaw,[11] Asbjørn Hróbjartsson,[12] Manoj M Lalu,[13] Tianjing Li,[14] Elizabeth W Loder,[15] Evan Mayo-Wilson,[16] Steve McDonald,[1] Luke A McGuinness,[17] Lesley A Stewart,[18] James Thomas,[19] Andrea C Tricco,[20] Vivian A Welch,[21] Penny Whiting,[17] David Moher[22]

For numbered affiliations see end of the article.

Correspondence to: M J Page
matthew.page@monash.edu
(ORCID 0000-0002-4242-7526)

Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2021;372:n71
http://dx.doi.org/10.1136/bmj.n71

Accepted: 4 January 2021

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement, published in 2009, was designed to help systematic reviewers transparently report why the review was done, what the authors did, and what they found. Over the past decade, advances in systematic review methodology and terminology have necessitated an update to the guideline. The PRISMA 2020 statement replaces the 2009 statement and includes new reporting guidance that reflects advances in methods to identify, select, appraise, and synthesise studies. The structure and presentation of the items have been modified to facilitate implementation. In this article, we present the PRISMA 2020 27-item checklist, an expanded checklist that details reporting recommendations for each item, the PRISMA 2020 abstract checklist, and the revised flow diagrams for original and updated reviews.

SUMMARY POINTS

To ensure a systematic review is valuable to users, authors should prepare a transparent, complete, and accurate account of why the review was done, what they did, and what they found

The PRISMA 2020 statement provides updated reporting guidance for systematic reviews that reflects advances in methods to identify, select, appraise, and synthesise studies

The PRISMA 2020 statement consists of a 27-item checklist, an expanded checklist that details reporting recommendations for each item, the PRISMA 2020 abstract checklist, and revised flow diagrams for original and updated reviews

We anticipate that the PRISMA 2020 statement will benefit authors, editors, and peer reviewers of systematic reviews, and different users of reviews, including guideline developers, policy makers, healthcare providers, patients, and other stakeholders

Systematic reviews serve many critical roles. They can provide syntheses of the state of knowledge in a field, from which future research priorities can be identified; they can address questions that otherwise could not be answered by individual studies; they can identify problems in primary research that should be rectified in future studies; and they can generate or evaluate theories about how or why phenomena occur. Systematic reviews therefore generate various types of knowledge for different users of reviews (such as patients, healthcare providers, researchers, and policy makers).[1 2] To ensure a systematic review is valuable to users, authors should prepare a transparent, complete, and accurate account of why the review was done, what they did (such as how studies were identified and selected) and what they found (such as characteristics of contributing studies and results of meta-analyses). Up-to-date reporting guidance facilitates authors achieving this.[3]

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement published in 2009 (hereafter referred to as PRISMA 2009)[4-10] is a reporting guideline designed to address poor reporting of systematic reviews.[11] The PRISMA 2009 statement comprised a checklist of 27 items recommended for reporting in systematic reviews and an "explanation and elaboration" paper[12-16] providing additional reporting guidance for each item, along with exemplars of reporting. The recommendations have been widely endorsed and adopted, as evidenced by its co-publication in multiple journals, citation in over 60 000 reports (Scopus, August 2020), endorsement from almost 200 journals and systematic review organisations, and adoption in various disciplines. Evidence from observational studies suggests that use of the PRISMA 2009 statement is associated with more complete reporting of systematic reviews,[17-20] although more could be done to improve adherence to the guideline.[21]

Many innovations in the conduct of systematic reviews have occurred since publication of the PRISMA 2009 statement. For example, technological advances have enabled the use of natural language processing and machine learning to identify relevant evidence,[22-24] methods have been proposed to

synthesise and present findings when meta-analysis is not possible or appropriate,[25-27] and new methods have been developed to assess the risk of bias in results of included studies.[28 29] Evidence on sources of bias in systematic reviews has accrued, culminating in the development of new tools to appraise the conduct of systematic reviews.[30 31] Terminology used to describe particular review processes has also evolved, as in the shift from assessing "quality" to assessing "certainty" in the body of evidence.[32] In addition, the publishing landscape has transformed, with multiple avenues now available for registering and disseminating systematic review protocols,[33 34] disseminating reports of systematic reviews, and sharing data and materials, such as preprint servers and publicly accessible repositories. To capture these advances in the reporting of systematic reviews necessitated an update to the PRISMA 2009 statement.

Development of PRISMA 2020

A complete description of the methods used to develop PRISMA 2020 is available elsewhere.[35] We identified PRISMA 2009 items that were often reported incompletely by examining the results of studies investigating the transparency of reporting of published reviews.[17 21 36 37] We identified possible modifications to the PRISMA 2009 statement by reviewing 60 documents providing reporting guidance for systematic reviews (including reporting guidelines, handbooks, tools, and meta-research studies).[38] These reviews of the literature were used to inform the content of a survey with suggested possible modifications to the 27 items in PRISMA 2009 and possible additional items. Respondents were asked whether they believed we should keep each PRISMA 2009 item as is, modify it, or remove it, and whether we should add each additional item. Systematic review methodologists and journal editors were invited to complete the online survey (110 of 220 invited responded). We discussed proposed content and wording of the PRISMA 2020 statement, as informed by the review and survey results, at a 21-member, two-day, in-person meeting in September 2018 in Edinburgh, Scotland. Throughout 2019 and 2020, we circulated an initial draft and five revisions of the checklist and explanation and elaboration paper to co-authors for feedback. In April 2020, we invited 22 systematic reviewers who had expressed interest in providing feedback on the PRISMA 2020 checklist to share their views (via an online survey) on the layout and terminology used in a preliminary version of the checklist. Feedback was received from 15 individuals and considered by the first author, and any revisions deemed necessary were incorporated before the final version was approved and endorsed by all co-authors.

The PRISMA 2020 statement

Scope of the guideline

The PRISMA 2020 statement has been designed primarily for systematic reviews of studies that evaluate the effects of health interventions, irrespective of the design of the included studies. However, the checklist items are applicable to reports of systematic reviews evaluating other interventions (such as social or educational interventions), and many items are applicable to systematic reviews with objectives other than evaluating interventions (such as evaluating aetiology, prevalence, or prognosis). PRISMA 2020 is intended for use in systematic reviews that include synthesis (such as pairwise meta-analysis or other statistical synthesis methods) or do not include synthesis (for example, because only one eligible study is identified). The PRISMA 2020 items are relevant for mixed-methods systematic reviews (which include quantitative and qualitative studies), but reporting guidelines addressing the presentation and synthesis of qualitative data should also be consulted.[39 40] PRISMA 2020 can be used for original systematic reviews, updated systematic reviews, or continually updated ("living") systematic reviews. However, for updated and living systematic reviews, there may be some additional considerations that need to be addressed. Where there is relevant content from other reporting guidelines, we reference these guidelines within the items in the explanation and elaboration paper[41] (such as PRISMA-Search[42] in items 6 and 7, Synthesis without meta-analysis (SWiM) reporting guideline[27] in item 13d). Box 1 includes a glossary of terms used throughout the PRISMA 2020 statement.

PRISMA 2020 is not intended to guide systematic review conduct, for which comprehensive resources are available.[43-46] However, familiarity with PRISMA 2020 is useful when planning and conducting systematic reviews to ensure that all recommended information is captured. PRISMA 2020 should not be used to assess the conduct or methodological quality of systematic reviews; other tools exist for this purpose.[30 31] Furthermore, PRISMA 2020 is not intended to inform the reporting of systematic review protocols, for which a separate statement is available (PRISMA for Protocols (PRISMA-P) 2015 statement[47 48]). Finally, extensions to the PRISMA 2009 statement have been developed to guide reporting of network meta-analyses,[49] meta-analyses of individual participant data,[50] systematic reviews of harms,[51] systematic reviews of diagnostic test accuracy studies,[52] and scoping reviews[53]; for these types of reviews we recommend authors report their review in accordance with the recommendations in PRISMA 2020 along with the guidance specific to the extension.

How to use PRISMA 2020

The PRISMA 2020 statement (including the checklists, explanation and elaboration, and flow diagram) replaces the PRISMA 2009 statement, which should no longer be used. Box 2 summarises noteworthy changes from the PRISMA 2009 statement. The PRISMA 2020 checklist includes seven sections with 27 items, some of which include sub-items (table 1). A checklist for journal and conference abstracts for systematic reviews is included in PRISMA 2020. This abstract checklist is an update of the 2013 PRISMA for Abstracts statement,[54] reflecting new and modified

Box 1: Glossary of terms

- *Systematic review*—A review that uses explicit, systematic methods to collate and synthesise findings of studies that address a clearly formulated question[43]
- *Statistical synthesis*—The combination of quantitative results of two or more studies. This encompasses meta-analysis of effect estimates (described below) and other methods, such as combining P values, calculating the range and distribution of observed effects, and vote counting based on the direction of effect (see McKenzie and Brennan[25] for a description of each method)
- *Meta-analysis of effect estimates*—A statistical technique used to synthesise results when study effect estimates and their variances are available, yielding a quantitative summary of results[25]
- *Outcome*—An event or measurement collected for participants in a study (such as quality of life, mortality)
- *Result*—The combination of a point estimate (such as a mean difference, risk ratio, or proportion) and a measure of its precision (such as a confidence/credible interval) for a particular outcome
- *Report*—A document (paper or electronic) supplying information about a particular study. It could be a journal article, preprint, conference abstract, study register entry, clinical study report, dissertation, unpublished manuscript, government report, or any other document providing relevant information
- *Record*—The title or abstract (or both) of a report indexed in a database or website (such as a title or abstract for an article indexed in Medline). Records that refer to the same report (such as the same journal article) are "duplicates"; however, records that refer to reports that are merely similar (such as a similar abstract submitted to two different conferences) should be considered unique.
- *Study*—An investigation, such as a clinical trial, that includes a defined group of participants and one or more interventions and outcomes. A "study" might have multiple reports. For example, reports could include the protocol, statistical analysis plan, baseline characteristics, results for the primary outcome, results for harms, results for secondary outcomes, and results for additional mediator and moderator analyses

content in PRISMA 2020 (table 2). A template PRISMA flow diagram is provided, which can be modified depending on whether the systematic review is original or updated (fig 1).

We recommend authors refer to PRISMA 2020 early in the writing process, because prospective consideration of the items may help to ensure that all the items are addressed. To help keep track of which items have been reported, the PRISMA statement website (http://www.prisma-statement.org/) includes fillable templates of the checklists to download and complete (also available in the data supplement on bmj.com). We have also created a web application that allows users to complete the checklist via a user-friendly interface[58] (available at https://prisma.shinyapps.io/checklist/ and adapted from the Transparency Checklist app[59]). The completed checklist can be exported to Word or PDF. Editable templates of the flow diagram can also be downloaded from the PRISMA statement website.

We have prepared an updated explanation and elaboration paper, in which we explain why reporting of each item is recommended and present bullet points that detail the reporting recommendations (which we

Box 2: Noteworthy changes to the PRISMA 2009 statement

- Inclusion of the abstract reporting checklist within PRISMA 2020 (see item #2 and table 2).
- Movement of the 'Protocol and registration' item from the start of the Methods section of the checklist to a new Other section, with addition of a sub-item recommending authors describe amendments to information provided at registration or in the protocol (see item #24a-24c).
- Modification of the 'Search' item to recommend authors present full search strategies for *all* databases, registers and websites searched, not just at least one database (see item #7).
- Modification of the 'Study selection' item in the Methods section to emphasise the reporting of how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process (see item #8).
- Addition of a sub-item to the 'Data items' item recommending authors report how outcomes were defined, which results were sought, and methods for selecting a subset of results from included studies (see item #10a).
- Splitting of the 'Synthesis of results' item in the Methods section into six sub-items recommending authors describe: the processes used to decide which studies were eligible for each synthesis; any methods required to prepare the data for synthesis; any methods used to tabulate or visually display results of individual studies and syntheses; any methods used to synthesise results; any methods used to explore possible causes of heterogeneity among study results (such as subgroup analysis, meta-regression); and any sensitivity analyses used to assess robustness of the synthesised results (see item #13a-13f).
- Addition of a sub-item to the 'Study selection' item in the Results section recommending authors cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded (see item #16b).
- Splitting of the 'Synthesis of results' item in the Results section into four sub-items recommending authors: briefly summarise the characteristics and risk of bias among studies contributing to the synthesis; present results of all statistical syntheses conducted; present results of any investigations of possible causes of heterogeneity among study results; and present results of any sensitivity analyses (see item #20a-20d).
- Addition of new items recommending authors report methods for and results of an assessment of certainty (or confidence) in the body of evidence for an outcome (see items #15 and #22).
- Addition of a new item recommending authors declare any competing interests (see item #26).
- Addition of a new item recommending authors indicate whether data, analytic code and other materials used in the review are publicly available and if so, where they can be found (see item #27).

Table 1 | PRISMA 2020 item checklist

Section and topic	Item #	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist (table 2).	
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	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.	
	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.	
Study risk of bias assessment	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 whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	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 (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesise 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, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesised results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
Results			
Study selection	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 (see fig 1).	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	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.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	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.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesised results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
Other information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code, and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

Table 2 | PRISMA 2020 for Abstracts checklist*

Section and topic	Item #	Checklist item
Title		
Title	1	Identify the report as a systematic review.
Background		
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.
Methods		
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.
Synthesis of results	6	Specify the methods used to present and synthesise results.
Results		
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.
Synthesis of results	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).
Discussion		
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).
Interpretation	10	Provide a general interpretation of the results and important implications.
Other		
Funding	11	Specify the primary source of funding for the review.
Registration	12	Provide the register name and registration number.

*This abstract checklist retains the same items as those included in the PRISMA for Abstracts statement published in 2013,[54] but has been revised to make the wording consistent with the PRISMA 2020 statement and includes a new item recommending authors specify the methods used to present and synthesise results (item #6).

refer to as elements).[41] The bullet-point structure is new to PRISMA 2020 and has been adopted to facilitate implementation of the guidance.[60 61] An expanded checklist, which comprises an abridged version of the elements presented in the explanation and elaboration paper, with references and some examples removed, is available in the data supplement on bmj.com. Consulting the explanation and elaboration paper is recommended if further clarity or information is required.

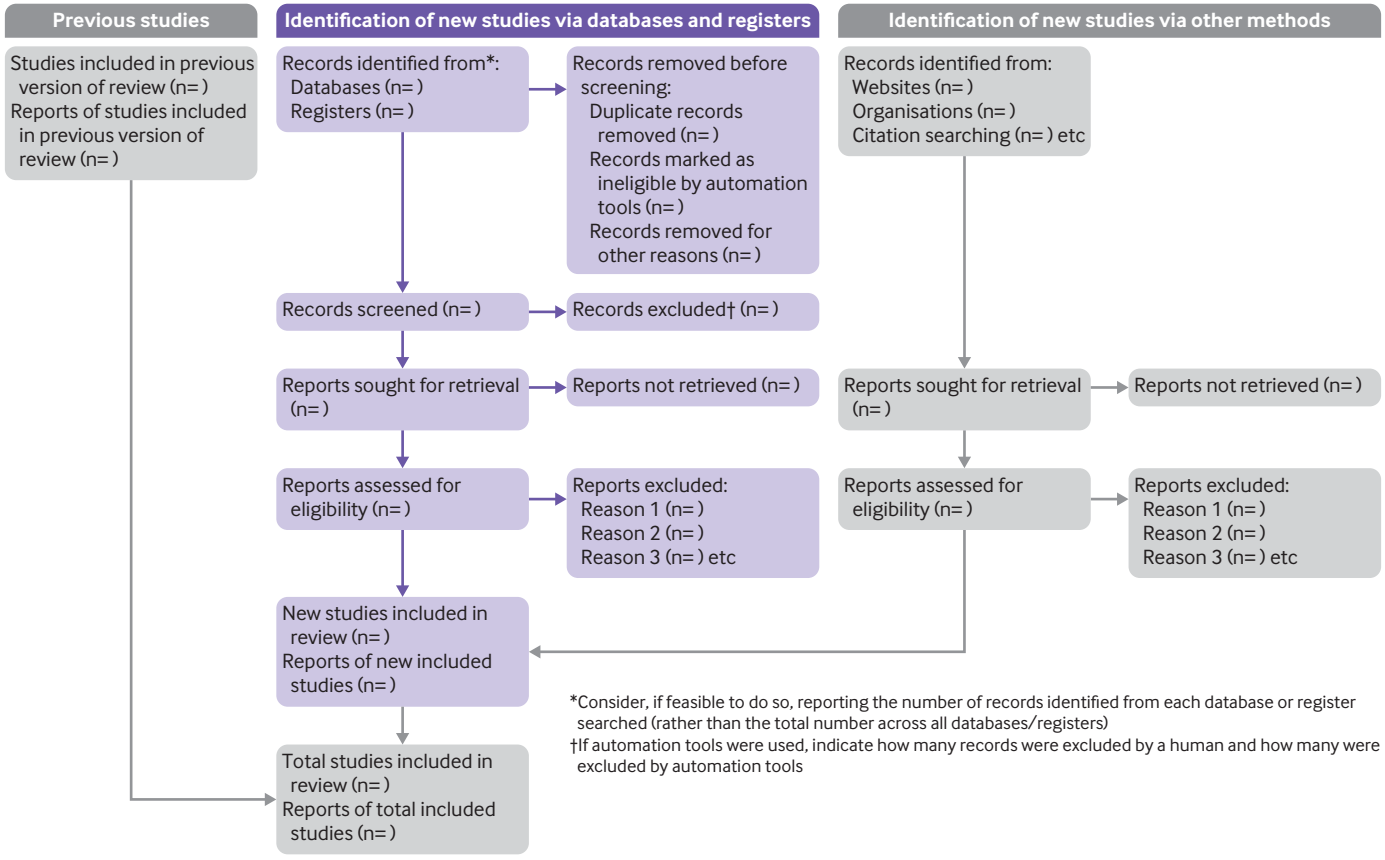


Fig 1 | PRISMA 2020 flow diagram template for systematic reviews. The new design is adapted from flow diagrams proposed by Boers,[55] Mayo-Wilson et al.[56] and Stovold et al.[57] The boxes in grey should only be completed if applicable; otherwise they should be removed from the flow diagram. Note that a "report" could be a journal article, preprint, conference abstract, study register entry, clinical study report, dissertation, unpublished manuscript, government report or any other document providing relevant information.

Journals and publishers might impose word and section limits, and limits on the number of tables and figures allowed in the main report. In such cases, if the relevant information for some items already appears in a publicly accessible review protocol, referring to the protocol may suffice. Alternatively, placing detailed descriptions of the methods used or additional results (such as for less critical outcomes) in supplementary files is recommended. Ideally, supplementary files should be deposited to a general-purpose or institutional open-access repository that provides free and permanent access to the material (such as Open Science Framework, Dryad, figshare). A reference or link to the additional information should be included in the main report. Finally, although PRISMA 2020 provides a template for where information might be located, the suggested location should not be seen as prescriptive; the guiding principle is to ensure the information is reported.

Discussion

Use of PRISMA 2020 has the potential to benefit many stakeholders. Complete reporting allows readers to assess the appropriateness of the methods, and therefore the trustworthiness of the findings. Presenting and summarising characteristics of studies contributing to a synthesis allows healthcare providers and policy makers to evaluate the applicability of the findings to their setting. Describing the certainty in the body of evidence for an outcome and the implications of findings should help policy makers, managers, and other decision makers formulate appropriate recommendations for practice or policy. Complete reporting of all PRISMA 2020 items also facilitates replication and review updates, as well as inclusion of systematic reviews in overviews (of systematic reviews) and guidelines, so teams can leverage work that is already done and decrease research waste.[36 62 63]

We updated the PRISMA 2009 statement by adapting the EQUATOR Network's guidance for developing health research reporting guidelines.[64] We evaluated the reporting completeness of published systematic reviews,[17 21 36 37] reviewed the items included in other documents providing guidance for systematic reviews,[38] surveyed systematic review methodologists and journal editors for their views on how to revise the original PRISMA statement,[35] discussed the findings at an in-person meeting, and prepared this document through an iterative process. Our recommendations are informed by the reviews and survey conducted before the in-person meeting, theoretical considerations about which items facilitate replication and help users assess the risk of bias and applicability of systematic reviews, and co-authors' experience with authoring and using systematic reviews.

Various strategies to increase the use of reporting guidelines and improve reporting have been proposed. They include educators introducing reporting guidelines into graduate curricula to promote good reporting habits of early career scientists[65]; journal editors and regulators endorsing use of reporting guidelines[18]; peer reviewers evaluating adherence to reporting guidelines[61 66]; journals requiring authors to indicate where in their manuscript they have adhered to each reporting item[67]; and authors using online writing tools that prompt complete reporting at the writing stage.[60] Multi-pronged interventions, where more than one of these strategies are combined, may be more effective (such as completion of checklists coupled with editorial checks).[68] However, of 31 interventions proposed to increase adherence to reporting guidelines, the effects of only 11 have been evaluated, mostly in observational studies at high risk of bias due to confounding.[69] It is therefore unclear which strategies should be used. Future research might explore barriers and facilitators to the use of PRISMA 2020 by authors, editors, and peer reviewers, designing interventions that address the identified barriers, and evaluating those interventions using randomised trials. To inform possible revisions to the guideline, it would also be valuable to conduct think-aloud studies[70] to understand how systematic reviewers interpret the items, and reliability studies to identify items where there is varied interpretation of the items.

We encourage readers to submit evidence that informs any of the recommendations in PRISMA 2020 (via the PRISMA statement website: http://www.prisma-statement.org/). To enhance accessibility of PRISMA 2020, several translations of the guideline are under way (see available translations at the PRISMA statement website). We encourage journal editors and publishers to raise awareness of PRISMA 2020 (for example, by referring to it in journal "Instructions to authors"), endorsing its use, advising editors and peer reviewers to evaluate submitted systematic reviews against the PRISMA 2020 checklists, and making changes to journal policies to accommodate the new reporting recommendations. We recommend existing PRISMA extensions[47 49 50 51-53 71 72] be updated to reflect PRISMA 2020 and advise developers of new PRISMA extensions to use PRISMA 2020 as the foundation document.

Conclusion

We anticipate that the PRISMA 2020 statement will benefit authors, editors, and peer reviewers of systematic reviews, and different users of reviews, including guideline developers, policy makers, healthcare providers, patients, and other stakeholders. Ultimately, we hope that uptake of the guideline will lead to more transparent, complete, and accurate reporting of systematic reviews, thus facilitating evidence based decision making.

Author affiliations

[1]School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

[2]Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Amsterdam University Medical Centres, University of Amsterdam, Amsterdam, Netherlands

[3]Université de Paris, Centre of Epidemiology and Statistics (CRESS), Inserm, F 75004 Paris, France

[4]Institute for Evidence-Based Healthcare, Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia

[5]University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA; *Annals of Internal Medicine*

[6]Knowledge Translation Program, Li Ka Shing Knowledge Institute, Toronto, Canada; School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Canada

[7]Evidence Partners, Ottawa, Canada

[8]Clinical Research Institute, American University of Beirut, Beirut, Lebanon; Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

[9]Department of Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, Portland, Oregon, USA

[10]York Health Economics Consortium (YHEC Ltd), University of York, York, UK

[11]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Canada; School of Epidemiology and Public Health, University of Ottawa, Ottawa, Canada; Department of Medicine, University of Ottawa, Ottawa, Canada

[12]Centre for Evidence-Based Medicine Odense (CEBMO) and Cochrane Denmark, Department of Clinical Research, University of Southern Denmark, Odense, Denmark; Open Patient data Exploratory Network (OPEN), Odense University Hospital, Odense, Denmark

[13]Department of Anesthesiology and Pain Medicine, The Ottawa Hospital, Ottawa, Canada; Clinical Epidemiology Program, Blueprint Translational Research Group, Ottawa Hospital Research Institute, Ottawa, Canada; Regenerative Medicine Program, Ottawa Hospital Research Institute, Ottawa, Canada

[14]Department of Ophthalmology, School of Medicine, University of Colorado Denver, Denver, Colorado, United States; Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

[15]Division of Headache, Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; Head of Research, *The BMJ*, London, UK

[16]Department of Epidemiology and Biostatistics, Indiana University School of Public Health-Bloomington, Bloomington, Indiana, USA

[17]Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK

[18]Centre for Reviews and Dissemination, University of York, York, UK

[19]EPPI-Centre, UCL Social Research Institute, University College London, London, UK

[20]Li Ka Shing Knowledge Institute of St. Michael's Hospital, Unity Health Toronto, Toronto, Canada; Epidemiology Division of the Dalla Lana School of Public Health and the Institute of Health Management, Policy, and Evaluation, University of Toronto, Toronto, Canada; Queen's Collaboration for Health Care Quality Joanna Briggs Institute Centre of Excellence, Queen's University, Kingston, Canada

[21]Methods Centre, Bruyère Research Institute, Ottawa, Ontario, Canada; School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Canada

[22]Centre for Journalology, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Canada; School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Canada

We dedicate this paper to the late Douglas G Altman and Alessandro Liberati, whose contributions were fundamental to the development and implementation of the original PRISMA statement.

We thank the following contributors who completed the survey to inform discussions at the development meeting: Xavier Armoiry, Edoardo Aromataris, Ana Patricia Ayala, Ethan M Balk, Virginia Barbour, Elaine Beller, Jesse A Berlin, Lisa Bero, Zhao-Xiang Bian, Jean Joel Bigna, Ferrán Catalá-López, Anna Chaimani, Mike Clarke, Tammy Clifford, Ioana A Cristea, Miranda Cumpston, Sofia Dias, Corinna Dressler, Ivan D Florez, Joel J Gagnier, Chantelle Garritty, Long Ge, Davina Ghersi, Sean Grant, Gordon Guyatt, Neal R Haddaway, Julian PT Higgins, Sally Hopewell, Brian Hutton, Jamie J Kirkham, Jos Kleijnen, Julia Koricheva, Joey SW Kwong, Toby J Lasserson, Julia H Littell, Yoon K Loke, Malcolm R Macleod, Chris G Maher, Ana Marušic, Dimitris Mavridis, Jessie McGowan, Matthew DF McInnes, Philippa Middleton, Karel G Moons, Zachary Munn, Jane Noyes, Barbara Nußbaumer-Streit, Donald L Patrick, Tatiana Pereira-Cenci, Ba' Pham, Bob Phillips, Dawid Pieper, Michelle Pollock, Daniel S Quintana, Drummond Rennie, Melissa L Rethlefsen, Hannah R Rothstein, Maroeska M Rovers, Rebecca Ryan, Georgia Salanti, Ian J Saldanha, Margaret Sampson, Nancy Santesso, Rafael Sarkis-Onofre, Jelena Savović, Christopher H Schmid, Kenneth F Schulz, Guido Schwarzer, Beverley J Shea, Paul G Shekelle, Farhad Shokraneh, Mark Simmonds, Nicole Skoetz, Sharon E Straus, Anneliese Synnot, Emily E Tanner-Smith, Brett D Thombs, Hilary Thomson, Alexander Tsertsvadze, Peter Tugwell, Tari Turner, Lesley Uttley, Jeffrey C Valentine, Matt Vassar, Areti Angeliki Veroniki, Meera Viswanathan, Cole Wayant, Paul Whaley, and Kehu Yang. We thank the following contributors who provided feedback on a preliminary version of the PRISMA 2020 checklist: Jo Abbott, Fionn Büttner, Patricia Correia-Santos, Victoria Freeman, Emily A Hennessy, Rakibul Islam, Amalia (Emily) Karahalios, Kasper Krommes, Andreas Lundh, Dafne Port Nascimento, Davina Robson, Catherine Schenck-Yglesias, Mary M Scott, Sarah Tanveer and Pavel Zhelnov. We thank Abigail H Goben, Melissa L Rethlefsen, Tanja Rombey, Anna Scott, and Farhad Shokraneh for their helpful comments on the preprints of the PRISMA 2020 papers. We thank Edoardo Aromataris, Stephanie Chang, Toby Lasserson and David Schriger for their helpful peer review comments on the PRISMA 2020 papers.

Contributors: JEM and DM are joint senior authors. MJP, JEM, PMB, IB, TCH, CDM, LS, and DM conceived this paper and designed the literature review and survey conducted to inform the guideline content. MJP conducted the literature review, administered the survey and analysed the data for both. MJP prepared all materials for the development meeting. MJP and JEM presented proposals at the development meeting. All authors except for TCH, JMT, EAA, SEB, and LAM attended the development meeting. MJP and JEM took and consolidated notes from the development meeting. MJP and JEM led the drafting and editing of the article. JEM, PMB, IB, TCH, LS, JMT, EAA, SEB, RC, JG, AH, TL, EMW, SM, LAM, LAS, JT, ACT, PW, and DM drafted particular sections of the article. All authors were involved in revising the article critically for important intellectual content. All authors approved the final version of the article. MJP is the guarantor of this work. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: There was no direct funding for this research. MJP is supported by an Australian Research Council Discovery Early Career Researcher Award (DE200101618) and was previously supported by an Australian National Health and Medical Research Council (NHMRC) Early Career Fellowship (1088535) during the conduct of this research. JEM is supported by an Australian NHMRC Career Development Fellowship (1143429). TCH is supported by an Australian NHMRC Senior Research Fellowship (1154607). JMT is supported by Evidence Partners Inc. JMG is supported by a Tier 1 Canada Research Chair in Health Knowledge Transfer and Uptake. MML is supported by The Ottawa Hospital Anaesthesia Alternate Funds Association and a Faculty of Medicine Junior Research Chair. TL is supported by funding from the National Eye Institute (UG1EY020522), National Institutes of Health, United States. LAM is supported by a National Institute for Health Research Doctoral Research Fellowship (DRF-2018-11-ST2-048). ACT is supported by a Tier 2 Canada Research Chair in Knowledge Synthesis. DM is supported in part by a University Research Chair, University of Ottawa. The funders had no role in considering the study design or in the collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication.

Competing interests: All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/conflicts-of-interest/ and declare: EL is head of research for the *BMJ*; MJP is an editorial board member for *PLOS Medicine*; ACT is an associate editor and MJP, TL, EMW, and DM are editorial board members for the *Journal of Clinical Epidemiology*; DM and LAS were editors in chief, LS, JMT, and ACT are associate editors, and JG is an editorial board member for *Systematic Reviews*. None of these authors were involved in the peer review process or decision to publish. TCH has received personal fees from Elsevier outside the submitted work. EMW has received personal fees from the *American Journal for Public Health*, for which he is the editor for systematic reviews. VW is editor in chief of the Campbell Collaboration, which produces systematic reviews, and co-convenor of the Campbell and Cochrane equity methods group. DM is chair of the EQUATOR Network, IB is adjunct director of the French EQUATOR Centre and TCH is co-director of the Australasian EQUATOR Centre, which advocates for the use of reporting guidelines to improve the quality of reporting in research articles. JMT received salary from Evidence Partners, creator of DistillerSR software for systematic reviews; Evidence Partners was not involved in the design or outcomes of the statement, and the views expressed solely represent those of the author.

Provenance and peer review: Not commissioned; externally peer reviewed.

Patient and public involvement: Patients and the public were not involved in this methodological research. We plan to disseminate the research widely, including to community participants in evidence synthesis organisations.

1 Gurevitch J, Koricheva J, Nakagawa S, Stewart G. Meta-analysis and the science of research synthesis. *Nature* 2018;555:175-82. doi:10.1038/nature25753
2 Gough D, Thomas J, Oliver S. Clarifying differences between reviews within evidence ecosystems. *Syst Rev* 2019;8:170. doi:10.1186/s13643-019-1089-2
3 Moher D. Reporting guidelines: doing better for readers. *BMC Med* 2018;16:233. doi:10.1186/s12916-018-1226-0
4 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;151:264-9, W64. doi:10.7326/0003-4819-151-4-200908180-00135
5 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009;339:b2535. doi:10.1136/bmj.b2535
6 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097. doi:10.1371/journal.pmed.1000097
7 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;62:1006-12. doi:10.1016/j.jclinepi.2009.06.005
8 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg* 2010;8:336-41. doi:10.1016/j.ijsu.2010.02.007
9 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *Open Med* 2009;3:e123-30.
10 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Reprint--preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Phys Ther* 2009;89:873-80. doi:10.1093/ptj/89.9.873
11 Moher D, Tetzlaff J, Tricco AC, Sampson M, Altman DG. Epidemiology and reporting characteristics of systematic reviews. *PLoS Med* 2007;4:e78. doi:10.1371/journal.pmed.0040078
12 Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;62:e1-34. doi:10.1016/j.jclinepi.2009.06.006
13 Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700. doi:10.1136/bmj.b2700
14 Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009;151:W65-94. doi:10.7326/0003-4819-151-4-200908180-00136
15 Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100. doi:10.1371/journal.pmed.1000100
16 Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100. doi:10.1371/journal.pmed.1000100
17 Page MJ, Shamseer L, Altman DG, et al. Epidemiology and reporting characteristics of systematic reviews of biomedical research: a cross-sectional study. *PLoS Med* 2016;13:e1002028. doi:10.1371/journal.pmed.1002028
18 Panic N, Leoncini E, de Belvis G, Ricciardi W, Boccia S. Evaluation of the endorsement of the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement on the quality of published systematic review and meta-analyses. *PLoS One* 2013;8:e83138. doi:10.1371/journal.pone.0083138
19 Agha RA, Fowler AJ, Limb C, et al. Impact of the mandatory implementation of reporting guidelines on reporting quality in a surgical journal: A before and after study. *Int J Surg* 2016;30:169-72. doi:10.1016/j.ijsu.2016.04.032
20 Leclercq V, Beaudart C, Ajamieh S, Rabenda V, Tirelli E, Bruyère O. Meta-analyses indexed in PsycINFO had a better completeness of reporting when they mention PRISMA. *J Clin Epidemiol* 2019;115:46-54. doi:10.1016/j.jclinepi.2019.06.014
21 Page MJ, Moher D. Evaluations of the uptake and impact of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Statement and extensions: a scoping review. *Syst Rev* 2017;6:263. doi:10.1186/s13643-017-0663-8
22 O'Mara-Eves A, Thomas J, McNaught J, Miwa M, Ananiadou S. Using text mining for study identification in systematic reviews: a systematic review of current approaches. *Syst Rev* 2015;4:5. doi:10.1186/2046-4053-4-5
23 Marshall IJ, Noel-Storr A, Kuiper J, Thomas J, Wallace BC. Machine learning for identifying randomized controlled trials: an evaluation and practitioner's guide. *Res Synth Methods* 2018;9:602-14. doi:10.1002/jrsm.1287
24 Marshall IJ, Wallace BC. Toward systematic review automation: a practical guide to using machine learning tools in research synthesis. *Syst Rev* 2019;8:163. doi:10.1186/s13643-019-1074-9
25 McKenzie JE, Brennan SE. Synthesizing and presenting findings using other methods. In: Higgins JPT, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions* . Cochrane, 2019. doi:10.1002/9781119536604.ch12 .
26 Higgins JPT, López-López JA, Becker BJ, et al. Synthesising quantitative evidence in systematic reviews of complex health interventions. *BMJ Glob Health* 2019;4(Suppl 1):e000858. doi:10.1136/bmjgh-2018-000858
27 Campbell M, McKenzie JE, Sowden A, et al. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. *BMJ* 2020;368:l6890. doi:10.1136/bmj.l6890
28 Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898. doi:10.1136/bmj.l4898
29 Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919. doi:10.1136/bmj.i4919
30 Whiting P, Savović J, Higgins JP, et al, ROBIS group. ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol* 2016;69:225-34. doi:10.1016/j.jclinepi.2015.06.005
31 Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;358:j4008. doi:10.1136/bmj.j4008
32 Hultcrantz M, Rind D, Akl EA, et al. The GRADE Working Group clarifies the construct of certainty of evidence. *J Clin Epidemiol* 2017;87:4-13. doi:10.1016/j.jclinepi.2017.05.006
33 Booth A, Clarke M, Dooley G, et al. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. *Syst Rev* 2012;1:2. doi:10.1186/2046-4053-1-2
34 Moher D, Stewart L, Shekelle P. Establishing a new journal for systematic review products. *Syst Rev* 2012;1:1. doi:10.1186/2046-4053-1-1
35 Page MJ, McKenzie JE, Bossuyt PM, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. *J Clin Epidemiol* 2021;S0895-4356(21)00040-8. doi:10.1016/j.jclinepi.2021.02.003.
36 Page MJ, Altman DG, Shamseer L, et al. Reproducible research practices are underused in systematic reviews of biomedical interventions. *J Clin Epidemiol* 2018;94:8-18. doi:10.1016/j.jclinepi.2017.10.017
37 Page MJ, Altman DG, McKenzie JE, et al. Flaws in the application and interpretation of statistical analyses in systematic reviews of therapeutic interventions were common: a cross-sectional analysis. *J Clin Epidemiol* 2018;95:7-18. doi:10.1016/j.jclinepi.2017.11.022
38 Page MJ, McKenzie JE, Bossuyt PM, et al. Mapping of reporting guidance for systematic reviews and meta-analyses generated a comprehensive item bank for future reporting guidelines. *J Clin Epidemiol* 2020;118:60-8. doi:10.1016/j.jclinepi.2019.11.010
39 Tong A, Flemming K, McInnes E, Oliver S, Craig J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Med Res Methodol* 2012;12:181. doi:10.1186/1471-2288-12-181
40 France EF, Cunningham M, Ring N, et al. Improving reporting of meta-ethnography: the eMERGe reporting guidance. *BMC Med Res Methodol* 2019;19:25. doi:10.1186/s12874-018-0600-0
41 Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews.*BMJ* 2021;372:n160. doi:10.1136/bmj.n160.
42 Rethlefsen ML, Kirtley S, Waffenschmidt S, et al, PRISMA-S Group. PRISMA-S: an extension to the PRISMA statement for reporting literature searches in systematic reviews. *Syst Rev* 2021;10:39. doi:10.1186/s13643-020-01542-z.
43 Higgins JPT, Thomas J, Chandler J eds. *Cochrane Handbook for Systematic Reviews of Interventions*: Version 6.0. Cochrane, 2019. Available from https://training.cochrane.org/handbook.
44 Dekkers OM, Vandenbroucke JP, Cevallos M, Renehan AG, Altman DG, Egger M. COSMOS-E: Guidance on conducting systematic reviews and meta-analyses of observational studies of etiology. *PLoS Med* 2019;16:e1002742. doi:10.1371/journal.pmed.1002742

45 Cooper H, Hedges LV, Valentine JV, eds. *The Handbook of Research Synthesis and Meta-Analysis*. Russell Sage Foundation, 2019.
46 IOM (Institute of Medicine). *Finding What Works in Health Care: Standards for Systematic Reviews*. The National Academies Press, 2011.
47 Moher D, Shamseer L, Clarke M, et al, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1. doi:10.1186/2046-4053-4-1
48 Shamseer L, Moher D, Clarke M, et al, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;350:g7647. doi:10.1136/bmj.g7647
49 Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med* 2015;162:777-84. doi:10.7326/M14-2385
50 Stewart LA, Clarke M, Rovers M, et al, PRISMA-IPD Development Group. Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data: the PRISMA-IPD Statement. *JAMA* 2015;313:1657-65. doi:10.1001/jama.2015.3656
51 Zorzela L, Loke YK, Ioannidis JP, et al, PRISMAHarms Group. PRISMA harms checklist: improving harms reporting in systematic reviews. *BMJ* 2016;352:i157. doi:10.1136/bmj.i157
52 McInnes MDF, Moher D, Thombs BD, et al, and the PRISMA-DTA Group. Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. *JAMA* 2018;319:388-96. doi:10.1001/jama.2017.19163
53 Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (PRISMA-SCR): Checklist and explanation. *Ann Intern Med* 2018;169:467-73. doi:10.7326/M18-0850
54 Beller EM, Glasziou PP, Altman DG, et al, PRISMA for Abstracts Group. PRISMA for Abstracts: reporting systematic reviews in journal and conference abstracts. *PLoS Med* 2013;10:e1001419. doi:10.1371/journal.pmed.1001419
55 Boers M. Graphics and statistics for cardiology: designing effective tables for presentation and publication. *Heart* 2018;104:192-200. doi:10.1136/heartjnl-2017-311581
56 Mayo-Wilson E, Li T, Fusco N, Dickersin KMUDS investigators. Practical guidance for using multiple data sources in systematic reviews and meta-analyses (with examples from the MUDS study). *Res Synth Methods* 2018;9:2-12. doi:10.1002/jrsm.1277
57 Stovold E, Beecher D, Foxlee R, Noel-Storr A. Study flow diagrams in Cochrane systematic review updates: an adapted PRISMA flow diagram. *Syst Rev* 2014;3:54. doi:10.1186/2046-4053-3-54
58 McGuinness LA. mcguinlu/PRISMA-Checklist: Initial release for manuscript submission (Version v1.0.0).*Zenodo* . doi:10.5281/zenodo.3994319. 2020.
59 Aczel B, Szaszi B, Sarafoglou A, et al. A consensus-based transparency checklist. *Nat Hum Behav* 2020;4:4-6. doi:10.1038/s41562-019-0772-6
60 Barnes C, Boutron I, Giraudeau B, Porcher R, Altman DG, Ravaud P. Impact of an online writing aid tool for writing a randomized trial report: the COBWEB (Consort-based WEB tool) randomized controlled trial. *BMC Med* 2015;13:221. doi:10.1186/s12916-015-0460-y
61 Chauvin A, Ravaud P, Moher D, et al. Accuracy in detecting inadequate research reporting by early career peer reviewers using an online CONSORT-based peer-review tool (COBPeer) versus the usual peer-review process: a cross-sectional diagnostic study. *BMC Med* 2019;17:205. doi:10.1186/s12916-019-1436-0
62 Wayant C, Page MJ, Vassar M. Evaluation of reproducible research practices in oncology systematic reviews with meta-analyses referenced by national comprehensive cancer network guidelines. *JAMA Oncol* 2019;5:1550-5. doi:10.1001/jamaoncol.2019.2564
63 McKenzie JE, Brennan SE. Overviews of systematic reviews: great promise, greater challenge. *Syst Rev* 2017;6:185. doi:10.1186/s13643-017-0582-8
64 Moher D, Schulz KF, Simera I, Altman DG. Guidance for developers of health research reporting guidelines. *PLoS Med* 2010;7:e1000217. doi:10.1371/journal.pmed.1000217
65 Simera I, Moher D, Hirst A, Hoey J, Schulz KF, Altman DG. Transparent and accurate reporting increases reliability, utility, and impact of your research: reporting guidelines and the EQUATOR Network. *BMC Med* 2010;8:24. doi:10.1186/1741-7015-8-24
66 Speich B, Schroter S, Briel M, et al. Impact of a short version of the CONSORT checklist for peer reviewers to improve the reporting of randomised controlled trials published in biomedical journals: study protocol for a randomised controlled trial. *BMJ Open* 2020;10:e035114. doi:10.1136/bmjopen-2019-035114
67 Stevens A, Shamseer L, Weinstein E, et al. Relation of completeness of reporting of health research to journals' endorsement of reporting guidelines: systematic review. *BMJ* 2014;348:g3804. doi:10.1136/bmj.g3804
68 Hair K, Macleod MR, Sena ESIICARus Collaboration. A randomised controlled trial of an Intervention to Improve Compliance with the ARRIVE guidelines (IICARus). *Res Integr Peer Rev* 2019;4:12. doi:10.1186/s41073-019-0069-3
69 Blanco D, Altman D, Moher D, Boutron I, Kirkham JJ, Cobo E. Scoping review on interventions to improve adherence to reporting guidelines in health research. *BMJ Open* 2019;9:e026589. doi:10.1136/bmjopen-2018-026589
70 Charters E. The use of think-aloud methods in qualitative research: an introduction to think-aloud methods. *Brock Education Journal* 2003;12. doi:10.26522/brocked.v12i2.38 .
71 Welch V, Petticrew M, Tugwell P, et al, PRISMA-Equity Bellagio group. PRISMA-Equity 2012 extension: reporting guidelines for systematic reviews with a focus on health equity. *PLoS Med* 2012;9:e1001333. doi:10.1371/journal.pmed.1001333
72 Wang X, Chen Y, Liu Y, et al. Reporting items for systematic reviews and meta-analyses of acupuncture: the PRISMA for acupuncture checklist. *BMC Complement Altern Med* 2019;19:208. doi:10.1186/s12906-019-2624-3

PRISMA 2020 checklist
PRISMA 2020 expanded checklist

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

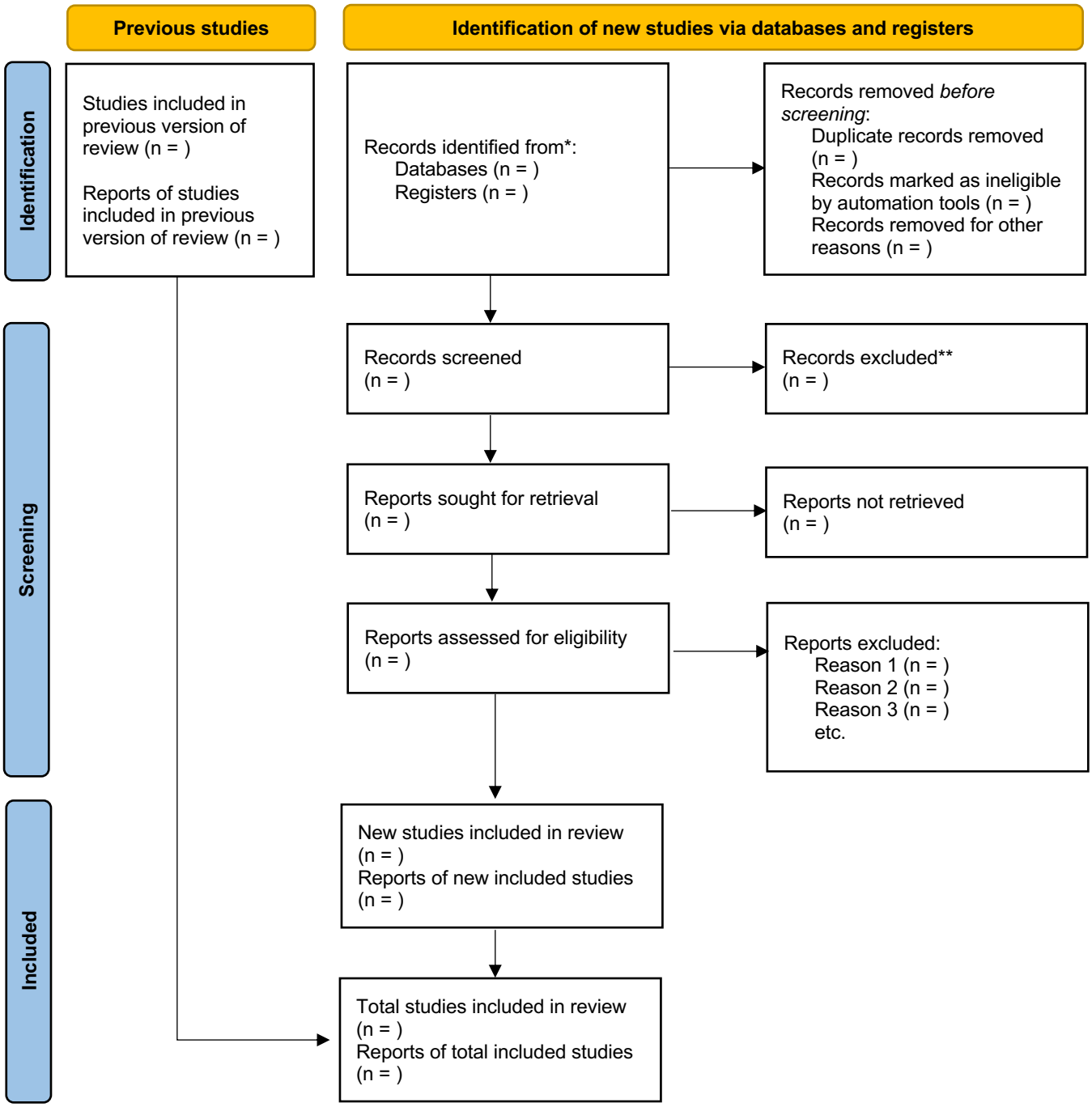
Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

PRISMA 2020 flow diagram for updated systematic reviews which included searches of databases and registers only



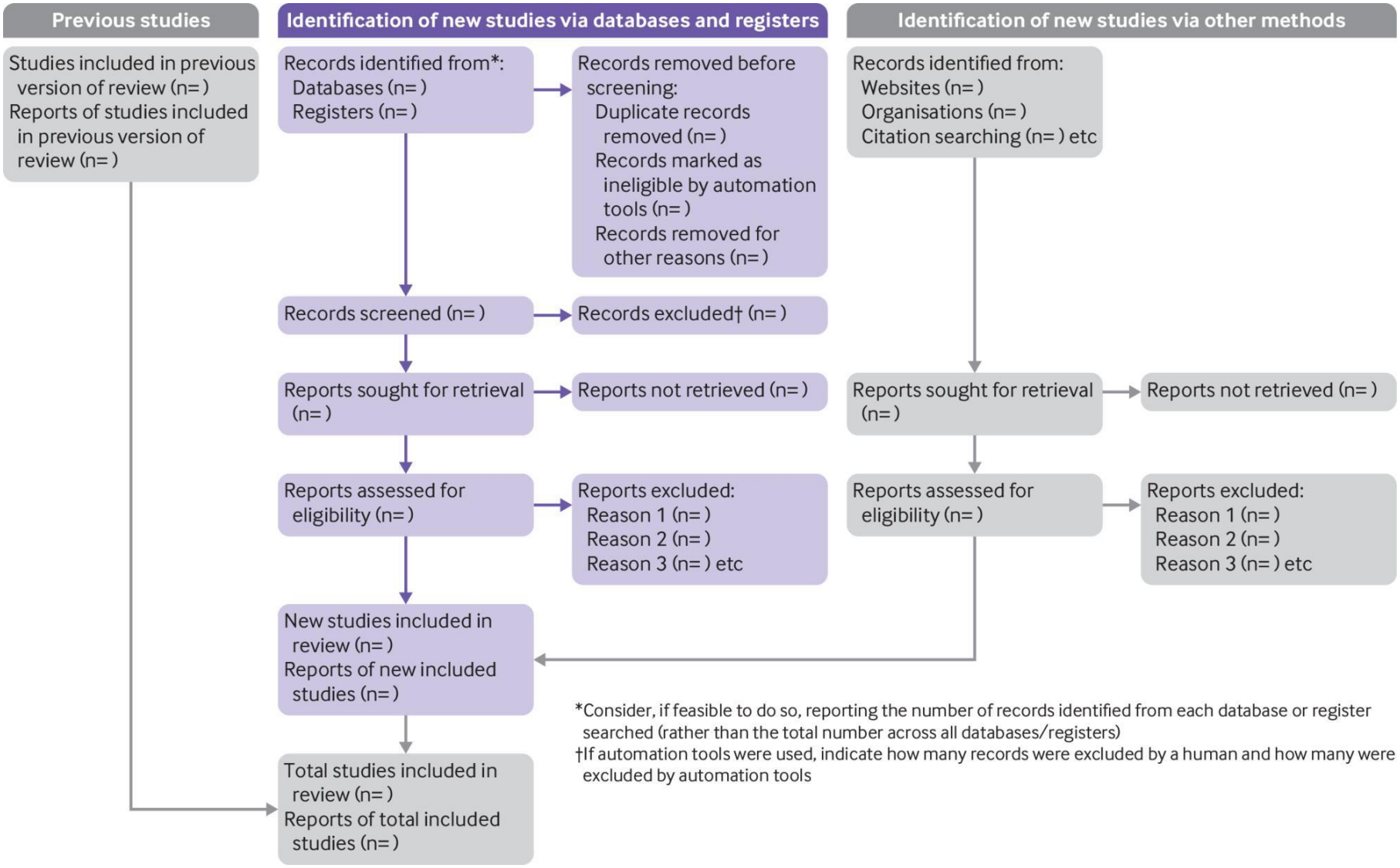
*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

PRISMA 2020 flow diagram template for systematic reviews.



Matthew J Page et al. BMJ 2021;372:bmj.n71

SYSTEMATIC REVIEWS

RESEARCH Open Access

Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement

David Moher[1*], Larissa Shamseer[1], Mike Clarke[2], Davina Ghersi[3], Alessandro Liberati[^], Mark Petticrew[4], Paul Shekelle[5], Lesley A Stewart[6] and PRISMA-P Group

Abstract

Systematic reviews should build on a protocol that describes the rationale, hypothesis, and planned methods of the review; few reviews report whether a protocol exists. Detailed, well-described protocols can facilitate the understanding and appraisal of the review methods, as well as the detection of modifications to methods and selective reporting in completed reviews. We describe the development of a reporting guideline, the Preferred Reporting Items for Systematic reviews and Meta-Analyses for Protocols 2015 (PRISMA-P 2015). PRISMA-P consists of a 17-item checklist intended to facilitate the preparation and reporting of a robust protocol for the systematic review. Funders and those commissioning reviews might consider mandating the use of the checklist to facilitate the submission of relevant protocol information in funding applications. Similarly, peer reviewers and editors can use the guidance to gauge the completeness and transparency of a systematic review protocol submitted for publication in a journal or other medium.

Background

Systematic reviews are the reference standard for synthesizing evidence in health care because of their methodological rigor. They are used to support the development of clinical practice guidelines and inform clinical decision-making. They are becoming increasingly common; in 2010, 11 new reviews were estimated to be published daily [1]. Ideally, systematic reviews are based on pre-defined eligibility criteria and conducted according to a pre-defined methodological approach as outlined in an associated protocol.

The preparation of a protocol is an essential component of the systematic review process; it ensures that a systematic review is carefully planned and that what is planned is explicitly documented before the review starts, thus promoting consistent conduct by the review team, accountability, research integrity, and transparency of the eventual completed review. A protocol may also reduce arbitrariness in decision-making when extracting and using data from primary research, since planning provides an opportunity for the review team to anticipate potential problems. When clearly reported protocols are made available, they enable readers to identify deviations from planned methods in completed reviews and whether they bias the interpretation of a review results and conclusions. Bias related to the selective reporting of outcomes has been characterized as a serious problem in clinical research, including systematic reviews [2-7].

Until recently, systematic review protocols were generally available only through select organizations, such as The Cochrane [8] and Campbell Collaborations and the Joanna Briggs Institute, for which the preparation of a protocol is mandatory. Outside of these organizations, the existence of a protocol is infrequently reported in completed reviews [9,10]. Fewer than half of 300 systematic reviews indexed on MEDLINE in November 2004 (most recent generalizable sample; 2014 update underway) report working from a protocol [10], 80% of which are non-Cochrane affiliated. Of the non-Cochrane therapeutic reviews, only 11% mentioned the existence of a protocol [10]. The majority of reviews in health care are

* Correspondence: dmoher@ohri.ca
[^]Deceased
[1]Ottawa Hospital Research Institute and University of Ottawa, Ottawa, Canada
Full list of author information is available at the end of the article

conducted and published outside of Cochrane, however [10]. The paucity of protocols may be due, in part, to the authors' lack of knowledge about how to write them and what to include. Currently, little succinct guidance is available for those preparing systematic review protocols, although the recent Standards for Systematic Reviews prepared by the Institute of Medicine (IOM) provide some guidance toward addressing this gap [11].

Many groups have called for the widespread preparation and registration of systematic review protocols in order to increase the availability and accessibility of *a priori* methods for systematic reviews [12-14]. Such an effort may reduce the duplication of effort [15] and reduce the publication bias of systematic reviews. This challenge has been taken up by the Centre for Reviews and Dissemination, University of York, which has spearheaded the establishment of an international register—PROSPERO (International Prospective Register of Ongoing Systematic Reviews, http://www.crd.york.ac.uk/prospero) [16,17]. The register, which enables the permanent documentation of 22 mandatory (and 18 optional) items about the *a priori* design and conduct of a review, was launched in February 2011. At the time of writing, >5,000 systematic review protocols from over 70 countries have been registered since its inception. Starting in October 2013, new Cochrane protocols were and continue to be automatically added to PROSPERO.

Along with the improved accessibility of protocols through registration comes the need for strengthened transparency, accuracy, and completeness of the reports of protocols intended for dissemination. A template to aid in the preparation of systematic review protocols, such as a reporting guideline, may help achieve this. Furthermore, such guidance will enable authors to create a clear and complete document of their *a priori* methods, which may facilitate the registration of key information into the PROSPERO database. Building on an established guideline for systematic reviews and meta-analyses of studies evaluating health care interventions —the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA, www.prisma-statement.org) [12,13]—we have developed PRISMA for Protocols (PRISMA-P) 2014. Table 1 summarizes the difference in intentions between PRISMA-P and PROSPERO.

The aim of PRISMA-P 2015 is to improve the quality of systematic review protocols, similar to the impact achieved by other reporting guidelines [18-20]. By helping authors document an *a priori* road map of their systematic review, PRISMA-P also has the potential to improve the conduct of systematic reviews, as has been suggested of other reporting guidelines [21]. This Statement paper summarizes the development of the guideline and presents the PRISMA-P checklist.

Terminology

There is no standard definition for a systematic review and meta-analysis protocol, and we note that some terminology contained within these definitions may carry different meanings for different readers (i.e., 'systematic search'). The terms 'systematic review', 'meta-analysis,' and 'protocol' are defined in Table 2. The former two terms are in accordance with the definitions reported in the PRISMA Statement [13] and are in line with those used by the Agency for Healthcare Research and Quality's Evidence-based Practice Center (EPC) program [22], The Cochrane Collaboration [23], and the 2011 guidance from the Institute of Medicine [11]. The definition provided is a culmination of the terminology used by the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 initiative [24], the PROSPERO register, and the IOM Standards (Table 2).

Scope

The PRISMA-P checklist is intended primarily for the preparation of protocols of systematic reviews and meta-analyses that summarize aggregate data from studies,

Table 1 PROSPERO and PRISMA-P

	Definition and objective
PROSPERO: International Prospective Register of Systematic Reviews	An online portal through which to register the intention to conduct a systematic review, with health-related outcomes, before it is initiated [16]. One of the main goals of PROSPERO is to make the intent of systematic reviews known before they are conducted in order to reduce the unplanned duplication of systematic reviews [15]. In addition, by requiring the documentation of *a priori* methods, the register facilitates increased transparency in the review process by allowing readers of systematic reviews to compare methods, outcomes, and analyses carried out with those planned in advance and judge whether such changes impact the results of a review.
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols	A guideline to help authors prepare protocols for planned systematic reviews and meta-analyses that provides them with a minimum set of items to be included in the protocol. A protocol is intended to provide the rationale for the review and pre-planned methodological and analytic approach, prior to embarking on a review. Investigators should prepare a review protocol in advance of registering it in PROSPERO so that details requiring further consideration may be thought through in advance, avoiding the need for multiple amendments to registration information. PRISMA-P items have been derived largely from the PRISMA checklist and items of the PROSPERO register, in order to facilitate seamless registration.

Table 2 PRISMA-P terminology

Term	Definition
Systematic review	A systematic review attempts to collate all relevant evidences that fits pre-specified eligibility criteria to answer a specific research question. It uses explicit, systematic methods to minimize bias in the identification, selection, synthesis, and summary of studies. When done well, this provides reliable findings from which conclusions can be drawn and decisions made [25,26]. The key characteristics of a systematic review are (a) a clearly stated set of objectives with an explicit, reproducible methodology; (b) a systematic search that attempts to identify all studies that would meet the eligibility criteria; (c) an assessment of the validity of the findings of the included studies (e.g., assessment of risk of bias and confidence in cumulative estimates); and (d) systematic presentation, and synthesis, of the characteristics and findings of the included studies
Meta-analysis	Meta-analysis is the use of statistical techniques to combine and summarize the results of multiple studies; they may or may be contained within a systematic review. By combining data from several studies, meta-analyses can provide more precise estimates of the effects of health care than those derived from the individual studies
Protocol	In the context of systematic reviews and meta-analyses, a protocol is a document that presents an explicit plan for a systematic review. The protocol details the rationale and *a priori* methodological and analytical approach of the review

particularly the evaluations of the effects of interventions. There are many review types that are outside of this scope. As such, given the general lack of protocol guidance for other types of reviews, we encourage reviewers preparing any type of review protocol to make use of PRISMA-P as applicable. Readers can also use the checklist to assess the completeness of the reporting of published protocols. However, it is not recommended to use the checklist as an assessment tool to gauge the appropriateness of the methods of a systematic review protocol; it has not been validated for that purpose.

Development of PRISMA-P 2015

An international steering committee (MC, DG, AL, DM, MP, PS, and LAS) comprising members with wide-ranging experience in systematic review methodology, protocol registry development, and reporting guideline development led the development of PRISMA-P, coordinated by LS. The process proposed by the Enhancing the Quality and Transparency of Health Research (EQUATOR) Network was used to guide PRISMA-P development [27]. The process has 18 step-by-step recommendations grouped into five main stages:

1. Initial steps (determine the need for a reporting guideline);
2. Pre-meeting activities (identify contributors, conduct Delphi exercise, generate a list of potential items, and prepare for face-to-face meeting);
3. Face-to-face consensus meeting (present results of pre-meeting activities and relevant evidence);
4. Post-meeting activities (develop guidance Statement, Explanation and Elaboration document, and a publication strategy);
5. Post-publication activities (encourage uptake of guideline).

The first stage, 'Initial steps,' was described above; details of the remaining four steps are below.

Pre-meeting activities

In developing the PRISMA-P checklist, the steering committee compiled a list of items from various tools relating to the preparation of systematic review protocols for discussion at a consensus meeting of experts. Specifically, we mapped items from a Delphi exercise carried out during the development of PROSPERO [28], PROSPERO register items, PRISMA checklist items [13], SPIRIT 2013 checklist items [29], and items of IOM Standard 2.6 [11] against each other to identify unique and overlapping concepts. Lessons learned from the development of the SPIRIT checklist with respect to the concept and content of research protocols were used to guide discussion and debate at the meeting.

PRISMA-P consensus meeting

Twenty-three international experts attended the PRISMA-P consensus meeting on June 23–24, 2011, in Rockville, MD, USA to gain consensus on and reduce the number of potential PRISMA-P items. Delegates included journal editors, systematic review methodologists (including directors and representatives from international Cochrane Centres, Agency for Healthcare Research and Quality's (AHRQ's) Evidence-based Practice Centres, and the UK National Institute for Health Research), reporting guideline developers, information specialists, biostatisticians, and health research funders. Through group discussion at the meeting, 38 potential checklist items were reduced to 22.

Post-meeting activities

Following the meeting, the steering committee revised the draft 22-item checklist and refined their wording such that they accurately reflected meeting discussions. The draft checklist was also presented to the PROSPERO group, at a scientific meeting of the Cochrane Collaboration, for input and feedback and to AHRQ's Learning Network. After each of these reviews, the steering committee made minor amendments to the items.

The checklist was then circulated to all meeting invitees for critical input.

The PRISMA-P 2015 checklist

The final PRISMA-P 2015 checklist contains 17 numbered items (26 including sub-items) Items are categorized into three main sections: administrative information, introduction, and methods (Table 3).

We made a conscious effort to harmonize the PRISMA-P checklist items with the items of the PRISMA checklist to facilitate authors in transitioning their protocol into a report of a systematic review. Thirteen PRISMA-P sub-items have existing PRISMA counterparts. Where PRISMA wording or content did not sufficiently address protocol reporting, checklist items were modified.

Readers familiar with PRISMA will notice that PRISMA-P does not contain a flow diagram documenting the flow of studies throughout the systematic review process. Such documentation is possible only after a review has been carried out and remains an essential component to include in the report of a completed systematic review or meta-analysis; for further guidance, see the PRISMA Explanation and Elaboration document [12].

We strongly recommend that the present document and the accompanying PRISMA-P 2015 Explanation and Elaboration document [30], which includes examples of good reporting, rationale, and evidence (where available), be read together with the PRISMA-P 2015 checklist.

PRISMA-P 2015 explanation and elaboration

Once the steering committee prepared the PRISMA-P 2015 Statement and checklist, they drafted the content of an Explanation and Elaboration document, with assistance from the larger PRISMA-P group. The explanatory text was derived largely from discussions at the PRISMA-P meeting (recorded at the time) as well as the PRISMA Explanation and Elaboration document [12]. Examples of well-reported PRISMA-P items came from protocols registered in the PROSPERO database, AHRQ's EPC Program, and the Cochrane Database of Systematic Reviews or those published elsewhere. After the entire group had an opportunity to suggest additions, deletions, and changes, the steering committee combined all amendments to create the PRISMA-P 2014 Explanation and Elaboration document [30].

Post-publication activities

The post-publication activities recommended by EQUATOR include seeking and responding to criticism, encouraging the endorsement of and adherence to the guideline from various stakeholders, translating the guideline into other languages, evaluating its impact, ensuring website development, and updating of the guideline. The PRISMA-P 2015 checklist and related publications are freely available on the websites of the PRISMA Group (www.prisma-statement.org) and EQUATOR Network (www.equator-network.org). The PROSPERO register also contains a link to the guidance to encourage registrants to prepare a complete documentation of their protocol if they have not done so already.

We plan to develop an educational webinar about the rationale, usefulness, and potential impact of PRISMA-P, similar to what was done for PRISMA [31]. In addition, the potential for PRISMA-P 2015 to be used as an educational tool for authors, peer reviewers, and editors will be explored. Targeted implementation activities for PRISMA-P will be developed in a systematic manner together with experts in knowledge translation. The PRISMA website and social media (@PRISMAStatement, www.twitter.com/PRISMAStatement) will be used to make announcements about the launch of PRISMA-P and educational initiatives.

Endorsement

We encourage journals publishing systematic review products to modify their 'Instructions for Authors' section to endorse PRISMA-P 2015 and to consider publishing systematic review protocols, if they do not do so already. We plan to communicate with known endorsers of PRISMA (http://prisma-statement.org/endorsers.htm) as well as to other, relevant non-endorsing journals, to ask them to consider extending their support to PRISMA-P.

To help ensure optimal uptake by systematic reviewers, we propose a uniform endorsement policy across organizations and journals involved in the development and publication of systematic review protocols, demonstrated by the adoption of the following statement:

> '*[this organization/journal] requires a completed PRISMA-P 2015 checklist as a condition of submission of systematic review protocols. We recommend that, while completing the PRISMA-P 2015 checklist, you ensure your protocol addresses all items. Taking the time to ensure that your protocol adheres to these basic reporting elements will improve your manuscript and potentially enhance its chances of eventual acceptance.*'

Such a statement could be included in a journal's 'Instructions to Authors,' or for funding agencies and those commissioning systematic reviews, in their Application Guidelines, recommending that applicants developing the proposals of systematic reviews for funding use PRISMA-P 2014. Peer reviewers and scientific committees can also use the checklist to gauge the extent to which protocols include necessary information.

As has been done for previous reporting guidelines [18,32] we plan to evaluate whether and to what degree

Table 3 PRISMA-P 2015 checklist: recommended items to include in a systematic review protocol[a]

Section/topic	Item #	Checklist item
ADMINISTRATIVE INFORMATION		
Title		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number
Authors		
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor/ funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data		
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned

Table 3 PRISMA-P 2015 checklist: recommended items to include in a systematic review protocol[a] *(Continued)*

Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)

PRISMA-P Preferred Reporting Items for Systematic review and Meta-Analysis Protocols.
[a]It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration [30] for important clarification on the items. Amendments to a review protocol should be tracked and dated.

endorsement of PRISMA-P 2015 by journals (and potentially by other organizations) influences the completeness of reported protocols. Such an evaluation will be planned after allowing sufficient time for the wide dissemination of PRISMA-P 2015.

Implementation

The current system of implementing reporting guidelines is not optimal. At present, their primary mechanism of uptake is through endorsement by journals at their discretion, if at all. In journals that do endorse

Table 4 Proposed stakeholders, actions, and potential benefits for supporting adherence to PRISMA-P

Stakeholder	Proposed action	Potential benefits
Funders	Promote or mandate adherence to PRISMA-P or use PRISMA-P as a template for systematic review proposals for grant applications	Improved quality, completeness, and consistency of systematic review proposal submissions
		Standardized protocol content will improve peer review efficiency and investigator understanding of requirements
Systematic review authors/ groups/organizations	Use/adhere to PRISMA-P during protocol development	Improved quality, completeness, and consistency of protocol content
		Enables reviewers to anticipate and avoid future changes to review methods (i.e., outcomes)
		Increased awareness of minimum content for protocol reporting
		Improved completeness of reporting of completed reviews
PROSPERO (and other review registries)	Encourage the development of PRISMA-P-based protocols	Improved quality of registry entries
		Improved consistency across registry entries, protocols, and systematic reviews
Practice guideline developers	Use PRISMA-P to gauge the completeness of protocols and facilitate detection of selective reporting when considering reviews for guideline inclusion	Enables easy comparison across protocols, registry entries, and completed systematic reviews
Policymakers	Advocate use of PRISMA-P by those funding and carrying out systematic reviews	May yield better quality, more complete, and more consistent reviews to inform decision-making
Journal editors	Encourage compliance to PRISMA-P for authors submitting protocols for publication	Improved quality, completeness, and consistency of protocols over those published in journals not endorsing PRISMA-P
	Offer PRISMA-P as a template to assist in protocol writing for publication	Increased efficiency in protocol peer and author understanding of journal requirements
		Improved transparency and interpretation of reviews by readers
Educators	Use PRISMA-P as a training tool	Simplified teaching and grading of protocols
	Encourage adherence in students submitting protocols for coursework	Improved quality, completeness, and consistency of protocol content
Students	Develop protocols for coursework or research using PRISMA-P	Improved understanding of the minimum protocol content
		Well-trained systematic reviewer going into the workforce

guidelines, language describing their support is often vague, leaving authors unclear on what they are supposed to do with a given reporting guideline during the submission process [33]. Furthermore, policies around how journal editors and peer reviewers should ensure and/or enforce adherence to reporting checklists are even less clear, if they exist at all [34]. Other barriers to implementation may include a lack of awareness of the guideline and perceived burden of using a reporting guideline checklist during the editorial process [35].

Some well-known checklists, such as PRISMA, include a column to the right of the main checklists in which users report the page number on which a specific item is reported. This was initially intended to help authors ensure each checklist item is addressed and to aid peer reviewers in locating reported text for each item within a document. However, this system is not optimal. One major problem is that peer reviewers still have to search within a considerable body of text to locate the exact text describing a checklist item. When multiple items are listed separately but reported together or vice versa, this problem is compounded, because exactly which content pertains to each item may remain unclear.

The lack of implementation and adherence to reporting guidelines is systemic; additional authorities encountered early in the research process should promote a clearer message about author adherence to reporting standards if improvements in reporting are to be made. In targeting protocols of systematic reviews, PRISMA-P has a unique opportunity to not only affect the way in which protocols are reported but to also impact the way in which reviews are eventually conducted, perhaps allowing for a more seamless transition into a completely reported systematic review.

To overcome known challenges with reporting guideline uptake [36,37], we are developing a prospective implementation strategy for PRISMA-P 2015 using knowledge translation principles involving theoretically derived interventions [37] which have demonstrated effectiveness in the development of implementation interventions for clinical practice guidelines [38,39]. An initial list of proposed stakeholders who can assist in the implementation of PRISMA-P, along with proposed actions and benefits, is provided in Table 4.

Discussion

Studies comparing trial protocols to final reports have widely documented both the presence and the extent of reporting biases in publications of randomized trials [2,40]. Protocols for systematic reviews are rarely available for such comparisons, with the exception of select organizations. Of 288 reviews with available protocols in a 2006/2007 cohort, 64 (22%) were observed to have at least one discrepant outcome with their completed reviews; only 4 described reasons for the change in the completed review [3]. Discrepant outcomes added or upgraded from secondary to primary at the review stage were more likely to be statistically significant than those outcomes that had not changed. This practice (i.e., including, excluding, or changing outcomes in association with the strength or direction of findings) has the potential to bias the findings of any meta-analysis and the review's conclusions. As review protocols are expected to become increasingly available with the advent of PROSPERO, clear reporting will become essential to facilitate the identification of discrepancies between protocol and review by readers and help them determine whether they need to be cautious in interpreting findings.

Reporting and publishing protocols is an important step in increasing the transparency of the research process and reliability of published papers. For example, some journals require a copy of the protocol as part of the peer review process of randomized trials. As of 1 March 2014, BioMed Central has published 4,158 trial protocols across 66 of its 258 open-access journals, including 1,026 in *Trials. Systematic Reviews*, a BioMed Central journal launched in February 2012, is committed to publishing systematic review products, including protocols [41], and has published 142 protocols since inception (to 8 June 2014).

Journals, granting agencies, and systematic review organizations are encouraged to endorse PRISMA-P 2015 in their 'Instructions to Authors' and guidance for applicants and to implement its use during their peer review process of systematic review proposals. Reviewers are encouraged to use the PRISMA-P checklist and Explanation and Elaboration [30] document to guide them through the documentation of a protocol. Doing so will enhance the completeness of reporting of review protocols, facilitate the assessment of potential in systematic reviews, and hopefully strengthen the methodological quality and reliability of completed systematic reviews.

Competing interests

The PRISMA-P 2015 initiative was supported by the AHRQ, USA (Contract No. HHSA 290 2007 10059 I) and the Canadian Institutes for Health Research (Reference No. 114369). This manuscript does not reflect the opinions of either agency; one author, SC, is an employee of AHRQ. MC, DG, DM, MP, and LAS are members of the Advisory Board for PROSPERO. DGA, SC, MC, JG, MH, JM, and MP are members of the Editorial Board, and DM, PS, and LAS are co-Editors in Chief of *Systematic Reviews*. None of the authors who are editors of *Systematic Reviews* were involved in the handling of this paper or the decision to publish it.

Authors' contributions

DM, LS, MC, DG, AL, MP, PS, and LAS conceived this paper. DM and LS drafted the article, and all authors critically revised it for important intellectual content. All authors approved the final version of this article. DM is the guarantor of this work.

Acknowledgements

The PRISMA-P steering committee would like to thank the following staff from the Ottawa Hospital Research Institute (OHRI): Jodi Peters for her efforts organizing the PRISMA-P consensus meeting, Michael Zhao for his assistance

in preparing documents for the PRISMA-P meeting, Dr. Mohammed Ansari for valuable input and feedback throughout the process, and Justin Thielman for his assistance during the preparation of the PRISMA-P manuscripts.

Dedication

The PRISMA-P 2015 initiative is dedicated to our colleague Alessandro Liberati (1954–2012) who passed away during the time in which PRISMA-P 2015 was under development and whose contributions to this work were invaluable.

PRISMA-P group (listed alphabetically)

Douglas G Altman, DSc, Centre for Statistics in Medicine (CSM), University of Oxford, (Oxford, UK); Alison Booth, Centre for Reviews and Dissemination (CRD), University of York (York, UK); An-Wen Chan, Women's College Research Institute, University of Toronto (Toronto, Canada); Stephanie Chang, Agency for Healthcare Research and Quality (Rockville, USA); Mike Clarke, Queen's University of Belfast (Belfast, Ireland); Tammy Clifford, Canadian Agency for Drugs and Technologies in Health (CADTH) (Ottawa, Canada); Kay Dickersin, Johns Hopkins Bloomberg School of Public Health; Matthias Egger, Institut für Sozial-und Präventivmedizin; Davina Ghersi, National Health and Medical Research Council (Canberra, Australia); Peter C Gøtzsche, Nordic Cochrane Centre (Copenhagen, Denmark); Jeremy M Grimshaw, Canadian Cochrane Centre and OHRI (Ottawa, Canada); Trish Groves, The BMJ (London, UK); Mark Helfand, AHRQ EPC Scientific Resource Center, Portland VA Research Foundation (Portland, USA); Julian Higgins, School of Social and Community Medicine (Bristol, UK); Toby Lasserson, Cochrane Editorial Unit (London, UK); Joseph Lau, Center for Evidence-based Medicine, Brown University (Providence, USA); Alessandro Liberati, University of Modena (Modena, Italy); Kathleen Lohr, Research Triangle Institute-University of North Carolina EPC (Research Triangle Park, USA); Jessie McGowan, University of Ottawa (Ottawa, Canada); David Moher, Clinical Epidemiology Program, OHRI, and University of Ottawa (Ottawa, Canada); Cynthia Mulrow, Annals of Internal Medicine (San Antonio, USA); Melissa Norton, PLoS Medicine (London, UK); Matthew Page, Monash University (Australia); Mark Petticrew, London School of Hygiene and Tropical Medicine (London, UK); Margaret Sampson, Children's Hospital of Eastern Ontario (Ottawa; Canada); Holger Schünemann, McMaster University (Hamilton, Canada); Larissa Shamseer, Clinical Epidemiology Program, OHRI, and University of Ottawa (Ottawa; Canada); Paul Shekelle, Southern California EPC, (Los Angeles, USA); Iveta Simera, CSM, University of Oxford (Oxford, UK); Lesley A Stewart, CRD, University of York (York, UK); William Summerskill, *The Lancet* (London, UK); Jennifer Tetzlaff, Clinical Epidemiology Program, OHRI (Ottawa, Canada); Thomas A Trikalinos, Center for Evidence-based Medicine, Brown University (Providence, USA); David Tovey, The Cochrane Library (London, UK); Lucy Turner, Clinical Epidemiology Program, OHRI (Ottawa Canada); Evelyn Whitlock, Kaiser Permanente Research Affiliates EPC (Portland, USA).

Author details

[1]Ottawa Hospital Research Institute and University of Ottawa, Ottawa, Canada. [2]Queen's University Belfast, Belfast, Ireland. [3]National Health and Medical Research Council, Canberra, Australia. [4]London School of Hygiene and Tropical Medicine, London, UK. [5]Southern California Evidence-based Practice Center, Santa Monica, CA, USA. [6]Centre for Reviews and Dissemination, University of York, York, UK.

Received: 27 August 2014 Accepted: 26 November 2014
Published: 1 January 2015

References

1. Bastian H, Glasziou P, Chalmers I: **Seventy-five trials and eleven systematic reviews a day: how will we ever keep up?** *PLoS Med* 2010, **7**(9):e1000326.
2. Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG: **Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles.** *JAMA* 2004, **291**(20):2457–2465.
3. Kirkham JJ, Altman DG, Williamson PR: **Bias due to changes in specified outcomes during the systematic review process.** *PLoS ONE* 2010, **5**(3):e9810.
4. Kirkham JJ, Dwan KM, Altman DG, Gamble C, Dodd S, Smyth R, Williamson PR: **The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews.** *BMJ* 2010, **340:**c365.
5. Dwan K, Gamble C, Williamson PR, Kirkham JJ, Reporting Bias Group: **Systematic review of the empirical evidence of study publication bias and outcome reporting bias—an updated review.** *PLoS ONE* 2013, **8**(7):e66844.
6. Norris SL, Holmer HK, Ogden LA, Fu R, Abou-Setta AM, Viswanathan MS, McPheeters ML: *Selective Outcome Reporting as a Source of Bias in Reviews of Comparative Effectiveness (Prepared by the Oregon Evidence-Based Practice Center Under Contract no. 290-2007-10057-I).* Rockville: Agency for Healthcare Research and Quality; 2012. Report No.: AHRQ Publication No. 12-EHC110-EF.
7. Page MJ, McKenzie JE, Kirkham J, Dwan K, Kramer S, Green S, Forbes A: **Bias due to selective inclusion and reporting of outcomes and analyses in systematic reviews of randomised trials of healthcare interventions.** *Cochrane Lib* 2014, (10):Art No.:MR000035. doi:10.1002/14651858.MR000035.pub2.
8. Higgins JPT, Green S (Eds): *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0: updated March 2011.* The Cochrane Collaboration; 2011. Available from [www.cochrane-handbook.org]
9. Ma B, Guo J, Qi G, Li H, Peng J, Zhang Y, Ding Y, Yang K: **Epidemiology, quality and reporting characteristics of systematic reviews of traditional Chinese medicine interventions published in Chinese journals.** *PLoS ONE* 2011, **6**(5):e20185.
10. Moher D, Tetzlaff J, Tricco AC, Sampson M, Altman DG: **Epidemiology and reporting characteristics of systematic reviews.** *PLoS Med* 2007, **4**(3):e78.
11. Institute of Medicine. In *Finding What Works in Health Care: Standards for Systematic Reviews.* Edited by Eden J, Levit L, Berg A, Morton S. Washington, DC: The National Academies Press; 2011.
12. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D: **The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration.** *PLoS Med* 2009, **6**(7):e1000100.
13. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement.** *BMJ* 2009, **339:**b2535.
14. Straus S, Moher D: **Registering systematic reviews.** *CMAJ* 2010, **182**(1):13–14.
15. Moher D, Booth A, Stewart L: **How to reduce unnecessary duplication: use PROSPERO.** *BJOG* 2014, **121:**784–786.
16. Booth A, Clarke M, Ghersi D, Moher D, Petticrew M, Stewart L: **An international registry of systematic-review protocols.** *Lancet* 2011, **377**(9760):108–109.
17. Booth A, Clarke M, Dooley G, Ghersi D, Moher D, Petticrew M, Stewart L: **The nuts and bolts of PROSPERO: an international prospective register of systematic reviews.** *Syst Rev* 2012, **1:**2.
18. Turner L, Shamseer L, Altman DG, Schulz KF, Moher D: **Does use of the CONSORT statement impact the completeness of reporting of randomised controlled trials published in medical journals? A Cochrane review.** *Syst Rev* 2012, **1:**60.
19. Smidt N, Rutjes AWS, Van der Windt D, Ostelo R, Bossuyt PM, Reitsma JB, Bouter LM, de Vet HCW: **The quality of diagnostic accuracy studies since the STARD statement: has it improved?** *Neurology* 2006, **67**(5):792–797.
20. Prady SL, Richmond SJ, Morton VM, MacPherson H: **A systematic evaluation of the impact of STRICTA and CONSORT recommendations on quality of reporting for acupuncture trials.** *PLoS ONE* 2008, **3**(2):e1577.
21. Williams HC: **Cars, CONSORT 2010, and clinical practice.** *Trials* 2010, **11:**33.
22. *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*, AHRQ Publication No. 10(14)-EHC063-EF. Rockville: Agency for Healthcare Research and Quality; 2014. Chapters available at: www.effectivehealthcare.ahrq.gov.
23. Green S, Higgins JPT, Alderson P, Clarke M, Mulrow CD, Oxman AD: **1.2.2. What is a systematic review?** In *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0: updated March 2011.* Edited by Higgins JPT, Green S. The Cochrane Collaboration; 2011 [www.cochrane-handbook.org]
24. Chan A, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin JA, Doré C, Parulekar WR, Summerskill WSM, Groves T, Schulz KF, Sox HC, Rockhold FW, Rennie D, Moher D: **SPIRIT 2013 statement: defining standard protocol items for clinical trials.** *Ann Intern Med* 2013, **158**(3):200–207.
25. Antman EM, Lau J, Kupelnick B, Mosteller F, Chalmers TC: **A comparison of results of meta-analyses of randomized control trials and recommendations of clinical experts: treatments for myocardial infarction.** *JAMA* 1992, **268**(2):240–248.

26. Oxman AD, Guyatt GH: **The science of reviewing research.** *Ann N Y Acad Sci* 1993, **703:**125,33. discussion 133–134.
27. Moher D, Schulz KF, Simera I, Altman DG: **Guidance for developers of health research reporting guidelines.** *PLoS Med* 2010, **7**(2):e1000217.
28. Booth A, Clarke M, Ghersi D, Moher D, Petticrew M, Stewart L: **Establishing a minimum dataset for prospective registration of systematic reviews: an international consultation.** *PLoS ONE* 2011, **6**(11):e27319.
29. Chan A, Tetzlaff JM, Gøtzsche PS, Altman DG, Mann H, Berlin JA, Dickersin K, Hróbjartsson A, Schulz KF, Paruleka WR, Krleža-Jerić K, Laupaucis A, Moher D: **SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials.** *BMJ* 2013, **346:**e7586.
30. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, PRISMA-P Group: **Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: *elaboration & explanation*.** *BMJ* 2015, **349:**g7647.
31. Cochrane Canada: **David Moher on crystal clear reporting of systematic reviews and EQUATOR Network**. In 2010 [https://www.youtube.com/watch?v=TVFYenon1Jo]
32. Stevens A, Shamseer L, Weinstein E, Yazdi F, Turner L, Thielman J, Altman DG, Hirst A, Hoey J, Palepu A, Schulz KF, Moher D: **Relation of completeness of reporting of health research to journals' endorsement of reporting guidelines: systematic review.** *BMJ* 2014, **348:**g3804.
33. Hopewell S, Altman DG, Moher D, Schulz KF: **Endorsement of the CONSORT statement by high impact factor medical journals: a survey of journal editors and journal 'Instructions to Authors'.** *Trials* 2008, **9:**20.
34. Hirst A, Altman DG: **Are peer reviewers encouraged to use reporting guidelines? A survey of 116 health research journals.** *PLoS ONE* 2012, **7**(4):e35621.
35. Shamseer L, Weeks L, Turner L, Straus S, Grimshaw J, Moher D: **Identifying barriers to uptake and implementation of the CONSORT statement**. In *The Seventh International Congress on Peer Review and Biomedical Publication: 8–10 Sept 2014: Chicago, USA*.
36. Mills E, Wu P, Gagnier J, Heels-Ansdell D, Montori VM: **An analysis of general medical and specialist journals that endorse CONSORT found that reporting was not enforced consistently.** *J Clin Epidemiol* 2005, **58**(7):662–667.
37. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M: **Developing and evaluating complex interventions: the new medical research council guidance.** *BMJ* 2008, **337**(0959–535):a1655.
38. Davies P, Walker AE, Grimshaw JM: **A systematic review of the use of theory in the design of guideline dissemination and implementation strategies and interpretation of the results of rigorous evaluations.** *Implement Sci* 2010, **5:**14.
39. Carlsen B, Glenton C, Pope C: **Thou shalt versus thou shalt not: a meta-synthesis of GPs' attitudes to clinical practice guidelines.** *Br J Gen Pract* 2007, **57**(545):971–978.
40. Dwan K, Altman DG, Cresswell L, Blundell M, Gamble CL, Williamson PR: **Comparison of protocols and registry entries to published reports for randomised controlled trials.** *Cochrane Database Syst Rev* 2011, **1:**MR000031.
41. Moher D, Stewart L, Shekelle P: **Establishing a new journal for systematic review products.** *Syst Rev* 2012, **1:**1.

doi:10.1186/2046-4053-4-1
Cite this article as: Moher *et al.*: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 **4**:1.

BMJ 2014;349:g7647 doi: 10.1136/bmj.g7647 (Published 2 January 2015)

RESEARCH METHODS & REPORTING

Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation

Larissa Shamseer[1], David Moher[1], Mike Clarke[2], Davina Ghersi[3], Alessandro Liberati (deceased)[4], Mark Petticrew[5], Paul Shekelle[6], Lesley A Stewart[7], the PRISMA-P Group

[1]Ottawa Hospital Research Institute and University of Ottawa, Canada; [2]Queen's University Belfast, Ireland; [3]National Health and Medical Research Council, Australia; [4]University of Modena, Italy; [5]London School of Hygiene and Tropical Medicine, UK; [6]Southern California Evidence-based Practice Center, USA; [7]Centre for Reviews and Dissemination, University of York, UK

Dedication: The PRISMA-P 2015 initiative is dedicated to our colleague Alessandro Liberati (1954–2012), who passed away while PRISMA-P 2015 was under development and whose contributions to this work were invaluable.

Abstract

Protocols of systematic reviews and meta-analyses allow for planning and documentation of review methods, act as a guard against arbitrary decision making during review conduct, enable readers to assess for the presence of selective reporting against completed reviews, and, when made publicly available, reduce duplication of efforts and potentially prompt collaboration. Evidence documenting the existence of selective reporting and excessive duplication of reviews on the same or similar topics is accumulating and many calls have been made in support of the documentation and public availability of review protocols. Several efforts have emerged in recent years to rectify these problems, including development of an international register for prospective reviews (PROSPERO) and launch of the first open access journal dedicated to the exclusive publication of systematic review products, including protocols (BioMed Central's *Systematic Reviews*). Furthering these efforts and building on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines, an international group of experts has created a guideline to improve the transparency, accuracy, completeness, and frequency of documented systematic review and meta-analysis protocols—PRISMA-P (for protocols) 2015. The PRISMA-P checklist contains 17 items considered to be essential and minimum components of a systematic review or meta-analysis protocol.

This PRISMA-P 2015 Explanation and Elaboration paper provides readers with a full understanding of and evidence about the necessity of each item as well as a model example from an existing published protocol. This paper should be read together with the PRISMA-P 2015 statement. Systematic review authors and assessors are strongly encouraged to make use of PRISMA-P when drafting and appraising review protocols.

Introduction

Systematic reviews hold a unique place in healthcare. They help form the basis for developing practice guidelines and they provide information on gaps in knowledge, thus informing future research efforts. This information is relevant to stakeholders across the health system. The rigour and trustworthiness of systematic reviews is, in large part, based on the a priori planning and documentation of a methodical approach to conduct (that is, a protocol).

A systematic review protocol is important for several reasons: (1) it allows systematic reviewers to plan carefully and thereby anticipate potential problems; (2) it allows reviewers to explicitly document what is planned before they start their review, enabling others to compare the protocol and the completed review (that is, to identify selective reporting), to replicate review methods if desired, and to judge the validity of planned methods; (3) it prevents arbitrary decision making with respect to inclusion criteria and extraction of data; and (4) it may reduce duplication of efforts and enhance collaboration, when available.

Various international organizations such as the Cochrane and Campbell Collaborations and the Agency for Healthcare Research and Quality (AHRQ) regularly require and publish protocols. However, outside of such organizations, few protocols are published in traditional journals and most reports of completed reviews (89%) do not mention working from a protocol[1] (2014 update under way). Many experts have called for improved documentation and availability of review protocols. In response, experts (some of whom are authors on this document) launched an international, prospective register for systematic review protocols (PROSPERO, www.crd.york.ac.uk/prospero/) through the Centre for Reviews and Dissemination at the University of York (UK) in February 2011, in which more than 5000 systematic review protocols from 69 countries have been registered as of December 2014. In February 2012, the

Correspondence to: L Shamseer lshamseer@ohri.ca

first open access journal to exclusively publish systematic review products including protocols (BioMed Central's *Systematic Reviews*) was launched, in which 142 protocols have been published (June 2014). Outside of select systematic review organizations, little to no general guidance exists for preparing review protocols.

Selective reporting

Arguably one of the most important functions of systematic review protocols is their role as a documentation of planned review methods, outcomes, and analyses that can be compared with completed reviews to detect whether unintended and undocumented changes were made. Bias related to selective reporting of outcomes (that is, when reporting is related to the statistical significance or direction of effect estimate) is a problem in clinical research. This is a well documented phenomenon in clinical trials,[2-7] and similar findings are starting to emerge for systematic reviews (see item 13 for full discussion).[8-10] When reviewers selectively choose which information to include in a report based on the direction and significance of findings, they risk biasing the evidence base on which healthcare decisions and policies are made.

Further to recent efforts to increase the documentation and availability of review protocols, the next logical step is the development of a set of standards that should be included in a review protocol. A well described protocol may facilitate and enhance the detection of undocumented changes to review methodology; it also may allow readers to gauge the potential impact of such changes as well as selective reporting of information on review findings.

To that end, a reporting guideline for systematic review protocols, an extension of the PRISMA (Preferred Items for Reporting Systematic Reviews and Meta-analyses) statement has been developed for protocols (PRISMA-P) and is described in detail in this paper.

Scope of PRISMA-P

PRISMA-P is intended to guide the development of protocols of systematic reviews and meta-analyses evaluating therapeutic efficacy. Even for systematic reviews that are not evaluating efficacy, authors are encouraged to use PRISMA-P because of the lack of existing protocol guidance overall. For the purpose of this guidance, we define a protocol, broadly, as a document written before the start of a systematic review describing the rationale and intended purpose of the review, and the planned methodological and analytical approach (see box 1 for comprehensive definitions).

PRISMA-P is meant to be used primarily by authors preparing systematic review protocols for publication, public consumption, or otherwise. It is also intended for those commissioning and potentially funding reviews as a guide for applicants on what should they should include in their review protocols, and as a tool for peer reviewers to gauge whether a protocol contains essential details. PRISMA-P will also be helpful for journal editors and peer reviewers gauging the adequacy of review protocols for publication. A list of stakeholders to whom we believe PRISMA-P will be useful along with proposed benefits for each group is provided in table 1⇓.

Development of PRISMA-P

The PRISMA-P checklist is based on elements from the PROSPERO register,[11] the PRISMA checklist,[12] SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) checklist items,[13] and Standard 2.6 from the Institute of Medicine's Standards for Systematic Reviews.[14] A detailed description of the steps undertaken during PRISMA-P development can be found in the PRISMA-P Statement paper.[15] The process follows general recommendations of the EQUATOR (Enhancing the Quality and Transparency of health Research) Network on how to develop a reporting guideline, of which one fundamental part is a consensus process.[16] An in-person consensus meeting of international experts was held in June 2011 in Rockville, MD, USA, to develop and refine PRISMA-P checklist items. All related guidance documents have undergone iterative revision within the PRISMA-P Group listed at the end of this document; members of the PRISMA-P Group contributed to the writing and identifying relevant examples in this document.

PRISMA-P checklist

The final PRISMA-P checklist contains 17 numbered items (26 sub-items) that should be described, at minimum, in protocols of systematic reviews and meta-analyses (table 2⇓). The checklist is divided into three main sections: administrative information, introduction, and methods. Readers familiar with PRISMA will observe that wording of the PRISMA-P checklists has, where possible, been harmonized with PRISMA checklist items, at least 13 of which are overlapping with PRISMA-P. We anticipate this will aid authors in transitioning their systematic review protocols prepared in accordance with PRISMA-P into full text, PRISMA-compliant, systematic review reports.

PRISMA-P Elaboration and Explanation

The format of this document follows that of previously established reporting guidelines such as the PRISMA Explanation and Elaboration document[17]; it aims to provide readers with comprehensive explanations and evidence based rationales for each checklist item. Examples of good reporting for each checklist item have been identified from existing systematic review and meta-analysis protocols and are provided throughout this document to enhance reader understanding of items.

Although PRISMA-P focuses on a minimal list of items to consider when preparing a systematic review protocol, we have indicated instances where additional information may be desirable to improve transparency of the planned review process. The recommendations within PRISMA-P may require more words or space than authors are accustomed to. Providing detailed descriptions for some protocol elements (such as item 8, eligibility criteria; item 13, outcomes and prioritisation) will facilitate transparency and future reproducibility, and allow authors to shorten their methods section in a completed systematic review report, if desired, by providing a brief summary of the methods and referring readers to the completed protocol or PROSPERO record. We believe that providing in depth descriptions of planned methodological details for systematic reviews is in line with emerging journal policies aimed at facilitating reproducibility.[18]

Checklist items are numbered as we envision them appearing in a protocol, and reporting them in this sequential order is a suggestion that may facilitate reader comprehension. Authors should amend the order of appearance of checklist items if they deem it to be necessary. Most important is that authors describe each PRISMA-P item somewhere in their protocol.

Box 1: PRISMA-P terminology

Systematic review—A systematic review attempts to collate all relevant evidence that fits pre-specified eligibility criteria to answer a specific research question. It uses explicit, systematic methods to minimize bias in the identification, selection, synthesis, and summary of studies. When done well, this provides reliable findings from which conclusions can be drawn and decisions made.[179 180] The key characteristics of a systematic review are: (*a*) a clearly stated set of objectives with an explicit, reproducible methodology; (*b*) a systematic search that attempts to identify all studies that would meet the eligibility criteria; (*c*) an assessment of the validity of the findings of the included studies (such as assessment of risk of bias and confidence in cumulative estimates); and (*d*) systematic presentation, and synthesis, of the characteristics and findings of the included studies.

Meta-analysis—Meta-analysis is the use of statistical techniques to combine and summarize the results of multiple studies; they may or may not be contained within a systematic review. By combining data from several studies, meta-analyses can provide more precise estimates of the effects of healthcare than those derived from the individual studies.

Systematic review protocol—In the context of systematic reviews and meta-analyses, a protocol is a document that presents an explicit scientific "road map" of a planned, uninitiated systematic review. The protocol details the rational and planned methodological and analytical approach of the review.

One point to note is that, while the development of a protocol abstract is not a listed requirement on the PRISMA-P checklist, authors are urged to consult the PRISMA extension for reporting conference and journal abstracts if so desired.[19] The examples and explanations for each checklist item follow; citations contained within examples have been removed to avoid potential confusion with citations in this article.

Section 1: Administrative information

Title

Item 1a: Identification. Identify the report as a protocol of a systematic review

Example

"Postoperative outcomes following preoperative inspiratory muscle training in patients undergoing open cardiothoracic or upper abdominal surgery: protocol for a systematic review"[20]

Explanation

The knowledge in systematic reviews can be harnessed only if readers can easily identify them. Data indicate that systematic reviews are not always described as such in either the title or abstract; only 50% of systematic reviews included in a November 2004 sample used the terms "systematic review" or "meta-analysis" in their title or abstract.[1] Similar results have been reported elsewhere.[21] When this happens, reviews and meta-analyses may not be indexed in databases appropriately and risk not being found by potential users. This can lead to wasted efforts by systematic reviewers when knowledge they produce cannot be identified, one consequence of which may be unnecessary duplication of efforts by future reviewers.

Authors should title their report as a protocol of a systematic review and planned meta-analysis (the latter, only if known at the protocol stage). The term protocol indicates the existence of a plan for an upcoming, ongoing, or existing systematic review. Identification as a protocol may reduce unnecessary redundancy of systematic review efforts[22] and may also be helpful for readers seeking assistance in the design of future reviews. Although sensitive search strategies have been developed to identify systematic reviews,[23] inclusion of the terms systematic review or, if a meta-analysis is planned, meta-analysis in the title of a protocol may improve identification and retrieval.

We advise authors to use informative titles that make key information easily accessible to readers. Ideally, a title reflecting the PICO approach (participants, interventions, comparators, and outcomes) as well as time frame, setting, and study design, if desired (see Item 7), will provide readers with key information about the scope of the planned review.

Item 1b: Update. If the protocol is for an update of a previous systematic review, identify as such

Example

"The association between proximity to animal-feeding operations and community health: a protocol for updating a systematic review"[24]

Explanation

As explained in item 1a, authors can help to ensure awareness of the existence of a systematic review and review protocol by indicating this information in their title. Similar transparency will help readers identify whether the protocol in question is for conducting a new systematic review or an update of an existing one; ideally, this information should be reported within the title. Updates and, sometimes, expansions of an existing systematic review allow for the consideration of new evidence to bring previously published systematic reviews up to date.[25] Updating systematic reviews and identifying methods and signals for when to do so are increasingly being studied,[26-30] given that out of date systematic review evidence can be harmful,[31] particularly when updates yield changes in the direction of effect of one or more outcomes. Although systematic review updates are not always published as full length articles, they warrant an independent publication, the title of which should reflect its purpose.

Registration

Item 2. If registered, provide the name of the registry (such as PROSPERO) and registration number

Example

"In accordance with the guidelines, our systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 11 July 2011 and was last updated on 19 January, 2012 (registration number CRD42011001410)."[32]

Explanation

Registration of systematic review protocol details is now recognized as desirable in order to promote and maintain transparency in the systematic review process, to assist in minimizing the risk of bias(es), and help to reduce unnecessary duplication of reviews.[33] At the time of publication, only one registry for prospective systematic review registration exists—the PROSPERO register (www.crd.york.ac.uk/prospero/). The PROSPERO register provides review authors with the opportunity to freely register reviews evaluating interventions and strategies to prevent, diagnose, treat, and monitor conditions for which there is a health related outcome.[34 35] Since October

2013, key details from new protocols published in the *Cochrane Library* have been automatically added to PROSPERO on a daily basis. Future plans for PROSPERO include broadening inclusion to all systematic reviews with a health related outcome in the broadest sense (such as reviews of risk factors and genetic associations).

PROSPERO contains 22 mandatory items and 18 optional fields to capture key review attributes. However, it does not capture all information that should be included in a review protocol and does not preclude documentation and publication of a full review protocol. For easy transition from a registry entry into a full review protocol, many PRISMA-P items are based on PROSPERO items.

As with the preparation of a review protocol, the process of review registration forces authors to think through review methods and hopefully avoid future changes which may be associated with reporting biases. Furthermore, the registry entry itself provides readers with a reference to compare against complete reviews, in the absence of an available protocol, to examine for reporting biases. Logically, the planning, conduct, and reporting of reviews should involve efforts to help detect and minimize such bias.[10 36] Registration helps by prospectively recording key features of the planned review when the protocol has been finalized but before any eligibility screening has started, and making this information available publically and freely. This information provides those contemplating commissioning or undertaking a review to identify whether a relevant review is already planned or underway, if not completed. This should help avoid unplanned duplication, ensuring efficient use of resources and offering potential for future collaboration.[37 38] Of 73 randomly selected systematic reviews of randomised trials published in 2010, 49 (67%) had at least one overlapping meta-analysis that did not represent an update (that is, same comparison, type of population or indication, and outcome).[37] This signals a potentially large degree of wasted efforts.

Details and justification of any changes or amendments (see Item 4) made during the review process should be added to the registration record and reported in the final systematic review results report. By registering this information, the opportunity for post hoc manipulation and potential consequent bias are likely minimized. The public record allows comparison of published review results with what was planned so that readers can judge whether any discrepancies are likely to have introduced bias.

Registration information is increasingly being asked for by a number of journals as part of their submission process.[33 39 40] Once reviews are registered on PROSPERO, authors receive a unique identification number that authors should report in a review protocol, and in all publications arising from a review (that is, the protocol and completed review); doing so ensures that they can easily and confidently be identified as related.

Authors

Item 3a: Contact information. Provide name, institutional affiliation, and email address of all protocol authors; provide physical mailing address of corresponding author

Example

"*Corresponding author: Frances C Hillier frances.hillier@durham.ac.uk

Author Affiliations

1 Department of Geography, Wolfson Research Institute, Durham University Queen's Campus, University Boulevard, Stockton-on-Tees, TS17 6BH, UK

2 Obesity Related Behaviours Research Group, School of Medicine and Health, Wolfson Research Institute, Durham University Queen's Campus, University Boulevard, Stockton-on-Tees, TS17 6BH, UK

Email: Clare L Bambra clare.bambra@durham.ac.uk - Frances C Hillier frances.hillier@durham.ac.uk - Helen J Moore helen.moore@durham.ac.uk - Carolyn D Summerbell carolyn.summerbell@durham.ac.uk"[41]

Explanation

Individuals who have made substantive intellectual contributions to the development of the systematic review protocol should provide their names, affiliations, and contact information even if the protocol is not published or intended to be published. Together with contributorship (Item 3b), this information can help identify competing interests and ghost authorship[42] and enhance the recognition and accountability of protocol authors and transparency of the review.[43] Although ghost authorship itself may not necessarily contribute to scientific bias, it may reflect the undisclosed shaping role played by companies or other groups with vested interests in the design or reporting of a study.[42 44-46]

In some instances, because of the nature of a relationship with a funder or sensitivity of the potential data, reviewers may not wish to have their names on a protocol before the systematic review is completed. In these instances, reviewers should provide contact information for the sponsor (host institution or funder) or for an individual assigned to deal with reader queries.

Item 3b: Contributions. Describe contributions of protocol authors and identify the guarantor of the review

Example

"DF is the guarantor. JE, RR and DM drafted the manuscript. All authors contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria. SB developed the search strategy. RR provided statistical expertise. DF provided expertise on venous thromboembolism. SJ contributed to the section on health economics. All authors read, provided feedback and approved the final manuscript."[47]

Explanation

Some journals urge that published articles include descriptions of the contributions of each named author.[43 48] Likewise, in review protocols, together with names and contact information, the role(s) of each author should be clearly described. In biomedical publishing, journals require authors to have contributed to an article in at least the following ways: (1) contributed substantially to the conception and design of the study, the acquisition of data, or the analysis and interpretation; (2) drafted or provided critical revision of the article; and (3) provided final approval of the version to be published.[49]

The guarantor of a research article is the author who assumes the overall responsibility for the scientific integrity of the work as a whole and should be identified as such.[46 49] The term corresponding author typically represents the notion of "guarantor," and is also used to indicate which co-author is responsible for pre- and post-acceptance communication with

the publishing journal and for taking queries to all other co-authors. A guarantor should be able to answer queries about the order of authors on the manuscript and about the research itself.[49] The guarantor is often listed as either the first named or most senior (often last) author.

Amendments

Item 4 If the report represents an amendment of a previously completed or published protocol, identify as such and indicate what changes were made; otherwise state plan for documenting important protocol amendments

Example 1

"In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale."[50]

Example 2

"If we need to amend this protocol, we will give the date of each amendment, describe the change and give the rationale in this section. Changes will not be incorporated into the protocol."[51]

Explanation

Systematic review protocols are typically iterative documents; modifications to protocols before and during the review process are to be expected. Systematic reviewers should give careful consideration to a review's methodological and analytical approach early on to avoid unnecessary changes after protocol development. A study of trials funded by pharmaceutical companies indicate that at least a third of amendments made to original trial protocols could have been prevented if key issues were given more consideration during protocol development[52]; this is likely true for systematic reviews as well. A 2002 study of 66 Cochrane reviews found that 91% of completed reviews had major changes from the protocol.[36] More recently, at least 20% of Cochrane reviews have been found to make post-protocol modifications to review outcomes (that is, addition, removal, or reprioritization), many of which are based on significance of the outcome in the completed review. Making changes to review outcomes, after knowledge of findings from included studies can introduce bias into the review process, mislead readers and possibly affect patient care. Cochrane reviews have since evolved to provide a dedicated section in which authors should report any changes made from the documented protocol.[53] Likewise, inclusion of a table summarizing protocol amendments is a mandatory requirement for reviews produced by AHRQ's Effective Health Care Program (table 3⇓). The PROSPERO register also allows for and tracks amendments of registered protocols.

Although many amendments do not introduce bias, changes from earlier protocol versions or from the registry entry should be transparently identified as such in each documented version of the protocol so that, at minimum, readers can evaluate the potential for bias. For protocols in which no amendments have yet been made, authors should include a description of the process for dealing with and documenting future amendments (that is, who will ultimately be responsible for approving, documenting, and implementing them). An updated protocol should be identified with a new version number and a list of specific amendments that were made to the previous version (see table 3⇓).

Support

Item 5a: Sources. Indicate sources of financial or other support for the review

Example

"This systematic review is funded by the Institute for Neurosciences, Mental Health and Addition, Canadian Institutes of Health Research (funding reference number KSD-115551; Effectiveness of the Screening, Brief Intervention and Referral to Treatment (SBIRT) Model for Reducing Illicit Drug Use: A Systematic Review)."[54]

Explanation

An updated Cochrane review indicates that drug trials funded by the pharmaceutical industry report significantly greater benefits, fewer harms, and more favourable overall conclusions than those with non-industry funding.[55 56] This issue, termed sponsorship bias, has been characterized less frequently in systematic reviews and meta-analyses. Of note, since 2004 the Cochrane Collaboration has prohibited industry support for its reviews.[57] One study indicates that conclusions from company supported reviews (2003, issue 1) recommended a drug not recommended in a matching, non-industry funded Cochrane review, despite both reviews having similar treatment effects; Cochrane reviews also had greater methodological transparency.[58] Another study of 124 meta-analyses found that meta-analyses with financial ties to one pharmaceutical company (n=49) were associated with more favourable conclusions, yet not more favourable results, than those with other financial ties.[59] Another study failed to replicate these findings, but it did find that industry supported meta-analyses have worse methodological quality than meta-analyses supported by non-profit organizations or unsupported meta-analyses.[60]

Review authors should disclose sources of financial and non-financial support for their review, if known at the protocol stage. If a review is not funded at the time the protocol is first registered and made available, the proposed sources of support should be listed and updated once funding is confirmed. Along with Item 5c (role of funder or sponsor), this information will help readers assess whether any competing interests or potential influences are present. As an example, the evaluation of sugar sweetened beverages and weight gain has recently received much attention for their purported association with negative health outcomes. A systematic review of reviews of sugar sweetened beverages and weight gain found that reviews identified as being affiliated with or supported by the food industry were five times more likely to report no positive, significant association with weight gain than non-industry affiliated reviews.[61] This finding highlights a need for authors to disclose their affiliations and sources of funding. Inclusion of the "financial conflicts of interest checklist 2010" with a protocol is recommended to help readers identify potential conflicts to be aware of; many journals have already instituted its use.[62]

Non-financial sources of support that should be disclosed may include the provision of services by an institution or funder, an information specialist who will help to obtain articles, access to a commercial database not otherwise available to reviewers, or in-kind use of software to manage or analyze review data.

Item 5b: Sponsor. Provide name of the review funder and/or sponsor

Example 1

"The Chartered Society of Physiotherapy Charitable Trust funded this research."[63]

Example 2

"The Laboratory of Research and Clinical Applications in Ophthalmology (Aristotle University of Thessaloniki) is the Sponsor, meaning that it has overall control of the data. No funding has been received for this study."[64]

Explanation

The term "sponsor" is most often associated with clinical trials in reference to the individual, company, institution, or organization assuming overall responsibility for the initiation and management of the trial.[65] However, because systematic reviews are often commissioned and funded by large agencies or companies, it is important for protocol authors to name both the sponsor and funder (Item 5a) in the review protocol, if applicable. The sponsor may not necessarily refer to the main funder if, for instance, a funder provides monies to a third party (sponsor) to carry out the research. This may happen, for example, if a company provides funds to a university researcher, whereby the university would become the sponsor of the review. Where relevant, the sponsor should be named in a review protocol.

Item 5c: Role of sponsor and/or funder. Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol

Example

"The Nova Scotia Health Research Foundation (NSHRF) is funding the Chronic LBP IPD Meta-analysis project. This funding will support the collection of the individual participant data by the original investigators, data management and analyses. The NSHRF is not involved in any other aspect of the project, such as the design of the project's protocol and analysis plan, the collection and analyses. The funder will have no input on the interpretation or publication of the study results."[66]

Explanation

When the sponsor or funder (sometimes the same entity) with competing interests has a substantial role in the planning, conduct, or dissemination of a systematic review, there is potential for bias if authors do not manage the interests of all parties appropriately. Although both industry and non-industry reviews are subject to potential bias(es), published reports of reviews with commercial sponsorship tend to describe lower quality methods and more favourable conclusions.[58-60 67] Examples exist of unfavourable reviews being suppressed by commercial sponsors.[68 69]

To provide full transparency into the potential relevance of competing interests, review protocols should explicitly describe the roles (if any) of the sponsor and funders in protocol development, review conduct, data analysis and interpretation, and dissemination of the final report. It is important to specify who will make the final decision about these elements of the systematic review, particularly if disagreements arise. Any restrictions on disseminating the final report of the review should also be documented.

Section 2: Introduction

Rationale

Item 6. Describe the rationale for the review in the context of what is already known

Example

[Review title: Trends in child and adolescent obesity prevalence according to socioeconomic position: protocol for a systematic review]

"It is well recognised that childhood obesity is a significant public health issue, with adverse physical and psychological effects that persist beyond childhood into the adult years. After decades of rapid increase, it appears that childhood obesity prevalence in developed countries is starting to plateau. Reviews of international evidence have shown that the prevalence of obesity in children and adolescents is stabilising in countries including Australia, Japan, France, the UK and US. However, evidence also suggests that such progress may not have been shared among children across all socioeconomic groups.

An international systematic review published in 2010 examined obesity prevalence trends and reported levelling off of the obesity epidemic in recent years. Heterogeneity in obesity trends were reported across socioeconomic strata, with levelling of obesity prevalence less apparent for more disadvantaged socioeconomic groups. However, the authors noted that trends by socioeconomic strata were only explored in a small number of their included studies. Individual studies reporting the impact of socioeconomic position (SEP) on obesity prevalence provided mixed results. Studies from Australia and England reported socioeconomic differences in obesity trends among children and adolescents, while evidence from France did not show a difference. With a specific focus on SEP and childhood obesity, this review will capture additional data, including papers published since 2010, to allow greater understanding of trends in the prevalence of obesity by SEP.

Further investigation is warranted, particularly because of the existing excess burden of obesity in children in a lower SEP. Given the health risks associated with excess weight, and the observed socioeconomic patterning in chronic diseases, if trends in obesity prevalence are not improving at the same rate across socioeconomic groups, this will likely lead to further inequalities across a range of health and wellbeing outcomes. Understanding the differences between subgroups of the population is critical to ensuring policy makers can make informed decisions as to where preventive efforts should be focused. This is particularly important in light of evidence that demonstrates differential effectiveness of a number of obesity prevention interventions according to SEP."[70]

Explanation

Readers need to understand the rationale behind the decision to perform the systematic review and what the results may add to what is already known. Authors should explain the impetus for the systematic review (such as to support clinical guideline development, to address uncertainty or variation in practice in approaches to a specific clinical problem, to support policy development, to provide a more precise estimate of effect, to update a previous review) and briefly summarize how the review builds on and could add to prior knowledge. In the case of a protocol to update an existing review, authors should cite the previous or original review and, in the methods section, point out any planned modifications from the original review in the protocol for the update,[71] perhaps with a section heading "updated methods." Where possible, the primary audience for

the review and the review perspective (that is, patient or clinician decision making, public health, health policy) should be clear.

Ideally, the rationale section should set the context for both the protocol as well as the systematic review. Background detail on the clinical condition should be sufficient to help the reader establish the overall significance of the proposed systematic review for developing new knowledge of interest and to help clarify key decisions or processes undertaken in the research protocol. These might include the specific focus of the population, intervention, comparator(s), and outcome (with emphasis on specific outcomes), settings, study designs, and time frames. As well, the means by which key perspectives represented in the review were obtained (that is, patient or other stakeholder engagement) should be described.

Objectives

Item 7. Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)

Example 1

"The aim of this systematic review is to evaluate the effectiveness and harms of perioperative pregabalin in the management of postoperative pain for the diverse patients undergoing various surgical procedures. To this end, the proposed systematic review will answer the following questions:

1. When compared with standard multimodal analgesia, what are the comparative effectiveness and harms of the co-administration of pregabalin in the perioperative pain management of adult patients?

2. Is there a definitive opioid-sparing advantage of pregabalin (for example, lower risk of nausea, vomiting, somnolence, opioid use, and other opioid-related side effects) when used for perioperative pain management in adults?

3. For questions 1 and 2 above, what clinical and study methodological characteristics explain the heterogeneity in results?"[72]

Example 2

"The objectives of our study are to systematically review the literature for qualitative evidence that explores the factors that influence the decision of individuals aged 50 years or over at average risk for CRC to participate in CRC screening, and how those factors vary by sex, ethnicity and SES. Our secondary aim will be to generate a framework to better understand the perceived benefits and barriers that affect individual decision-making."[73]

Explanation

Among the most crucial pieces of information to include in a review protocol are the question(s) the reviewers plan to investigate, or simply, the review's objectives. Along with the review's rationale (Item 6), this information provides the reader with context and understanding for why the review is being carried out and what the reviewers hope to achieve. Several key components, namely the planned population, intervention, comparator, and outcome (that is, PICO elements) at minimum should form the basis for developing a specific, well designed review question. Additional elements such as setting, study design, and time frame (that is, length of follow-up) may also be included in the review question, but if not, should certainly appear in the review's eligibility criteria (Item 8). Guidance is available to help researchers develop a research question.[74 75]

Reviews may focus on one PICO element more than others given the planned scope of the review; authors should clearly state this emphasis in the protocol.

Section 3: Methods

Eligibility criteria

Item 8. Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review

Example:

"**Eligibility criteria**

"Studies will be selected according to the criteria outlined below.

Study designs

We will include randomized controlled trials (RCTs), including cluster RCTs, controlled (non-randomized) clinical trials (CCTs) or cluster trials, interrupted time series (ITS) studies with at least three data points before and after the intervention, controlled before-after (CBA) studies, prospective and retrospective comparative cohort studies, and case-control or nested case-control studies. Cluster randomized, cluster non-randomized, or CBA studies will be included only if there are at least two intervention sites and two control sites. We will exclude cross-sectional studies, case series, and case reports.

Participants

We will include studies examining the general adult human population or healthy adult humans (18 years or older). We will also include studies on people who are overweight or obese, but will otherwise exclude studies of populations restricted to specific diseases, conditions, or metabolic disorders. We will include studies addressing both adults and children if data provided for adults are reported separately.

Interventions

Of interest are interventions addressing SSB consumption, taking a broad perspective. In addition to direct consumption studies, we would consider interventions that influence consumption, such as those addressing the level of access to SSBs (e.g. university/college policy) and educational interventions addressing consumption as relevant. Non-specific or multi-faceted behavioural, educational, or policy interventions may also be included subject to the level of evidence that exists for the aforementioned interventions/exposures. We will also consider other types of interventions on a case by case basis, subject to what exists in the literature.

In terms of defining an SSB, we view them as akin to a complex intervention because they are composed of several parts. For example, in addition to sugar, some beverages contain caffeine and the by-products of caramel colouring (2-methylimidazole, 4-methylimidazole), which may contribute independently to adverse health outcomes. The scope of the review, therefore, warrants an examination of SSB consumption as a whole, rather than the specific constituents as exposure variables. Otherwise, such evaluations would have necessarily required the inclusion of studies addressing those constituents and in foods and drinks other than SSBs.

We will use the Centers for Disease Control and Prevention (CDC) definition of SSB for drinks that should be included. According to the CDC, SSBs contain added caloric sweeteners, which would include natural sweeteners such as honey and concentrated fruit juice. We have developed a classification

scheme based on the CDC definition for use during the review (see classification scheme for SSBs below). For beverages such as coffee, tea, and homemade lemonade, studies will be included in the review if they explicitly state that sugar was added. We will exclude artificially sweetened (e.g. with aspartame or sucralose) beverages, alcoholic beverages, and 100% fruit or vegetable juices as exposures/interventions.

We will classify SSBs described in studies according to the following broad categories:

- Sodas-caffeinated/non-caffeinated (soft drinks, soda, pop, soda pop)
- Other non-carbonated sweetened beverages (fruitades, fruit drinks, fruit punches, [iced] teas, coffees, non-dairy fruit smoothies)-caffeinated/non-caffeinated
- Fortified sweetened beverages (energy drinks, fortified waters, sports drinks)-caffeinated/non-caffeinated and containing vitamins, amino acids, herbal stimulants, or other ingredients
- Flavored/sweetened milk or milk alternative beverages (dairy, soy, almond, milkshakes, dairy based fruit smoothies)-caffeinated/non-caffeinated

Comparators

Given the broad perspective for interventions of interest, several comparisons will be relevant to include. Some may be more likely to come from observational designs and others from experimental studies.

Direct consumption studies:

1. SSB consumption compared with consumption of non-SSB drink (e.g. 100% fruit juice, artificially sweetened beverage, water)
2. Higher level of SSB consumption versus lower level of SSB consumption for the same drink type (e.g. carbonated cola beverages)
3. Comparisons among different categories of SSBs (e.g. soft drinks compared with fruit drinks; see classification scheme for SSBs) consumed in similar amounts

Interventions that influence consumption:

4. One level of access to SSB compared with another level of access (e.g. university/college policy on beverages in vending machines)
5. Educational intervention to specifically promote lower or no SSB consumption compared with no educational intervention/regular curriculum coverage/general health-focussed intervention
6. Non-specific or multi-faceted educational, behavioural, or policy dietary intervention (may include component of SSB consumption) compared with no intervention
7. Other comparisons involving interventions that address our research question (interventions assessed on a case by case basis, as encountered in the literature)

For comparator groups 2 and 3, we anticipate that volume will be the most feasible to analyse; however, we will extract all measures in which consumption is reported (e.g. volume, caloric intake from sugar) in studies to see what analysis is possible.

For feasibility, category 6 comparisons (non-specific, multi-faceted interventions) will be coded at title/abstract screening and not put through to full text screening. If sparse evidence exists in the other potential comparison types, we will revisit eligibility for comparison 6.

Outcomes

Endpoints important for decision making are of primary interest. If reported on, these will be analysed and graded. If a given clinical endpoint is not reported on, we will analyse and grade their relevant surrogate outcome(s).

- Endpoints important for decision making:
  - Adverse cardiovascular (including cerebrovascular) events
  - Cancer (excluding basal cell and squamous cell carcinoma)
  - Chronic kidney disease
  - Mortality
  - Overweight/obesity
  - Type 2 diabetes
  - Dental caries
  - Quality of life (generic, validated tools only, such as those in Additional file 2)
  - Gout
- Surrogate outcomes:
  - Pre-diabetes
  - Metabolic syndrome
  - Change in cardiovascular disease (CVD) risk
  - Progression of obesity
  - Dyslipidemia
  - Hypertension

As some outcomes may be reported as a composite measure, we will extract all composite and individual outcomes as reported in the studies.

Outcomes will be collected as reported, with the exception of quality of life, which will be collected only if assessed with generic (not disease specific), validated tools. Due to possible variation in disease definitions over time, we will extract definitions of outcomes as reported in individual studies. We will extract outcomes in all data forms (e.g. dichotomous, continuous) as reported in the included studies.

Timing

Studies will be selected for inclusion based on the length of follow-up of outcomes. The following will be used as a guide for all study designs:

- For all decision making endpoint outcomes, studies should have a follow-up time of at least 1 year.
- For all surrogate outcomes, studies should be at least 6 months duration for follow-up.
- For cancer, studies should be at least 1 year duration for follow-up. Some types of cancer may need longer than a 1 year follow-up, but this will be evaluated on a case by case basis.

Setting

There will be no restrictions by type of setting.

Language

We will include articles reported in the English and French languages. A list of possibly relevant titles in other languages will be provided as an appendix."[76]

Explanation

The requirement and ability to pre-specify eligibility criteria (sometimes denoted inclusion or exclusion criteria) that reviewers will use to identify relevant studies for inclusion is a defining feature of a systematic review.[77] Making this information available to readers of protocols, as in completed

reviews, is essential in appraising the validity, applicability, and comprehensiveness of a review.[74] Thus, authors should provide an unambiguous description of planned eligibility criteria for the impending review; such descriptions are a fundamental component upon which later stages of the review process are conducted. For instance, eligibility criteria often influence the terminology used to develop the search strategy and work to prevent the introduction of bias into the study selection process of a systematic review.

As in PRISMA, there are two general categories of eligibility criteria: study characteristics and report characteristics.[17] Authors should describe both. As in the example above, authors can anticipate that these details will require substantial space in the methods section of a review protocol while at the same time facilitating review transparency and future reproducibility.

Study eligibility criteria are the typical PICO elements that form the basis of clinical questions. These include populations, interventions, comparators, outcomes, time frames for follow-up, settings in which the interventions are delivered, and study designs of interest; they also can include other study specific elements, such as specifying a minimum length of follow-up or a minimum sample size for certain types of studies. Authors should state whether they will exclude studies because the studies do not include (or report) specific outcomes; doing so will help readers ascertain whether the eventual review may be biased as a consequence of selective reporting.[4]

Review eligibility criteria are likely to include geographical location, languages of publication, publication status (such as inclusion of unpublished material or abstracts), and years of publication. Inclusion or not of literature in multiple languages,[78 79] unpublished data, or older data can influence the effect estimates in meta-analyses.[80 81] If it is planned to filter out (via search filter, see Item 10) or exclude specific types of records (such as commentaries, letters, editorials, etc) during screening, this should be stated.

Information sources

Item 9. Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage

Example

"Literature search strategies will be developed using medical subject headings (MeSH) and text words related to influenza vaccination. We will search MEDLINE (OVID interface, 1948 onwards), EMBASE (OVID interface, 1980 onwards), and the Cochrane Central Register of Controlled Trials (Wiley interface, current issue). The electronic database search will be supplemented by searching for trial protocols through metaRegister (http://www.controlled-trials.com/mrct/). The literature search will be limited to the English language and human subjects.

To ensure literature saturation, we will scan the reference lists of included studies or relevant reviews identified through the search. We will also search the authors' personal files to make sure that all relevant material has been captured. Finally, we will circulate a bibliography of the included articles to the systematic review team, as well as to influenza experts identified by the team."[82]

Explanation

A systematic review search typically includes a variety of information sources including electronic bibliographic databases (such as Medline, Embase), reference lists, contact with authors of included studies, study registries, and grey literature. Most biomedical topics will include a Medline search, plus additional electronic databases. Searching additional electronic databases helps ensure more complete coverage of the topic by accounting for variability between the indexing in each database. In situations in which identifying all relevant studies through hand searching and database searching is difficult, if any other searching, such as reference lists, is planned to supplement searching, authors should report this.[83] Documentation of the planned information sources should include the name of each source, the date range that was searched (that is, start and end dates, and, for electronic database searches, the search platform or provider such, as Ovid or PubMed). This information will be important to the person developing and conducting the search if an update to the review is carried out. Authors should also report who developed and carried out the search.[83 84]

The Cochrane Collaboration,[85] AHRQ's Effective Health Care Program,[86] and the Institute of Medicine (Standard 3.1),[14] among others, offer guidance on developing a rigorous systematic review search strategy. If these sources are used, authors should report this information.

Search strategy

Item 10. Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

Example

"Both qualitative and quantitative studies will be sought. No study design, date or language limits will be imposed on the search, although only studies in languages other than English that can be translated adequately using Google translate1 will be included, due to resource limits. Medline, EMBASE, PsycINFO, and the CENTRAL trials registry of the Cochrane Collaboration will be searched. The specific search strategies will be created by a Health Sciences Librarian with expertise in systematic review searching. The MEDLINE strategy will be developed with input from the project team, then peer reviewed by a second librarian, not otherwise associated with the project, using the PRESS standard.2 A draft MEDLINE search strategy is included in Appendix 1. After the MEDLINE strategy is finalized, it will be adapted to the syntax and subject headings of the other databases.

As well, the International Clinical Trials Registry Platform Search Portal and ClinicalTrials.gov will be searched for ongoing or recently completed trials, and PROSPERO will be searched for ongoing or recently completed systematic reviews. As relevant studies are identified, reviewers will check for additional relevant cited and citing articles.

"The search will be updated toward the end of the review, after being validated to ensure that the MEDLINE strategy retrieves a high proportion of eligible studies found through any means but indexed in MEDLINE.

…

Appendix 1

Draft MEDLINE search - Ovid interface

1. Infant, Extremely Premature/
2. Infant, Extremely Low Birth Weight/
3. Infant, Very Low Birth Weight/
4. (extreme* adj2 preterm).mp.

5. (extreme* adj2 prematur*).mp.

6. extreme* low birth weight.mp.

7. (low gestational age neonate* or ELGAN*).mp.

8. very preterm.mp.

9. very premature.mp.

10. ELBW.mp.

11. ((limit* adj2 viability) or (margin* adj2 viability)).tw. or (22 week* or 23 week* or 24 week* or 25 week* or 26 week* or (26* adj5 week*) or (27* adj5 week*) or (28* adj5 week*) or (29* adj5 week*) or (30* adj5 week*) or (31* adj5 week*) or 32* week* or (32* adj2 fewer week*) or (32* adj2 less week*)).mp.

12. resuscit*.mp.

13. exp Obstetric Labor, Premature/

14. or/1-13

15. exp Parents/ or parent*.tw. or mother*.tw. or father*.tw.

16. Decision Making/

17. Counseling/

18. Advance Care Planning/ or Advance Directives/

19. (counsel* and decision*).mp.

20. or/16-19

21. (deliver* or predeliver* or prenatal* or antenatal* or perinatal*).mp.

22. 14 and 15 and 20 and 21"[87]

Explanation

The comprehensiveness and completeness of a literature search is extremely important in systematic reviews. High quality searches of information resources are essential components in the efforts toward accuracy and completeness of the evidence base.[88]

At a minimum, authors should provide the transcript of a draft search strategy for one major database (such as Medline) for each search question (if different searches were run for each question). In the documented strategy, it should be evident which indexing terms reviewers selected and what limits (such as language and date restrictions) were (or will be) applied to the search. If authors plan to use any search filters, information about their validity and performance metrics should be provided. Authors should also describe the planned search strategy approach for other databases, including planned modifications to indexing terms, free text terms, and limits, which may vary across databases.

If limits were used to restrict the search to particular study type (that is, trials, human, or clinical studies) or date range, authors should report what these were and how they were achieved. Simply stating, for example, that all publications in the form of letters will be excluded from the search can be problematic given that the publication of randomised trials as "letters to the editor," is a documented problem,[89] and authors may be intending to make an exception for such reports. Authors should report the logical construction of text used to create such limits within the draft search strategy (such as "NOT (letter.pt NOT randomized controlled trial.pt").[90] Doing so can help readers assess the appropriateness of intended limits within a search strategy.

Most searches have constraints—for example, relating to limited time or financial resources, inaccessible or inadequately indexed reports and databases, unavailability of experts with particular language or database searching skills, or review questions for which pertinent evidence is not easy to find. Authors should be straightforward in describing their search constraints.[17]

Authors should also report the approach that was or will be taken in the development of a search strategy, including qualifications of the searcher (such as a health information specialist with systematic review experience), planned databases to be searched (see Item 9), limits to be imposed (to demonstrate alignment with review eligibility criteria), and whether the search was or will be peer reviewed and by whom.[91] Having a search strategy peer reviewed may help to increase its comprehensiveness or decrease yield where search terminology is unnecessarily broad.

The draft search strategy can be presented in the body of the text or as a table. If the protocol is being published in a journal, the journal may advise on this issue (that is, in their instructions to authors). If space is a concern, authors should ask the editor whether it can be included it as a web based appendix or whether an electronic link to where it can be found can be provided in the manuscript.

Providing details of the planned search strategy will allow readers of systematic review protocols to appraise and avoid potential duplication of efforts, as well as possibly enhance the development of their own searches. Including at least one main search strategy can also specifically facilitate updating.

Study records

Item 11a: Data management. Describe the mechanism(s) that will be used to manage records and data throughout the review

Example

"Literature search results will be uploaded to Distiller Systematic Review (DSR) Software, an Internet based software program that facilitates collaboration among reviewers during the study selection process. The team will develop and test screening questions and forms for level 1 and 2 assessments based on the inclusion and exclusion criteria. Citation abstracts and full text articles will be uploaded with screening questions to DSR. Prior to the formal screening process, a calibration exercise will be undertaken to pilot and refine the screening questions. Further, we will provide training to new members of the review team not familiar with the DSR software and the content area prior to the start of the review."[54]

Explanation

Systematic review data management software is becoming increasingly common. Examples of web based software are Distiller SR and Eppi-Reviewer. These web based software management programs are helpful in managing small or large scale datasets by allowing importation of citations and PDFs to be screened and included. They may reduce data entry errors during the data extraction process by allowing direct entry into pre-created data extraction forms and export of data directly into statistical analysis software. They may also facilitate the creation of a PRISMA flow diagram once the screening process is completed. Whether use of such software is planned to manage records in the review should be described in the protocol. Several other tools may be used during the review process to de-duplicate references (such as reference management software) and to extract or manage data (such as electronic software).[92] Reviewers using more traditional forms of data management should also describe their process.

Whatever process is used, it should be described in sufficient detail so that interested readers can replicate the process.

Some studies are published more than once. Duplicate publications may be difficult to ascertain, and their inclusion may introduce bias.[93 94] We ask authors to describe any steps they are proposing to use to avoid double counting and to piece together data from multiple reports of the same study (such as juxtaposing author names, treatment comparisons, sample sizes, or outcomes). We also recommend that authors indicate whether all reports on a study were considered, as inconsistencies may reveal important limitations. For example, a review of multiple publications of drug trials showed that reported study characteristics may differ from report to report, including the description of the design, number of patients analyzed, chosen significance level, and outcomes.[95] See Item 12 (data items) for more information.

Item 11b: Selection process. State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (screening, eligibility, and inclusion in meta-analysis)

Example

"The review authors will independently screen the titles and abstracts yielded by the search against the inclusion criteria. We will obtain full reports for all titles that appear to meet the inclusion criteria or where there is any uncertainty. Review author pairs will then screen the full text reports and decide whether these meet the inclusion criteria. We will seek additional information from study authors where necessary to resolve questions about eligibility. We will resolve disagreement through discussion. We will record the reasons for excluding trials. Neither of the review authors will be blind to the journal titles or to the study authors or institutions."[96]

Explanation

Reviewers will often identify a large number of studies from electronic database searches, and then use pre-defined eligibility criteria (Item 8) to determine which records are relevant and should be included in the review. There is currently no agreed process for how studies should be selected for inclusion in a systematic review. For example, it is unclear whether all records identified by the search should be initially screened for potential inclusion by two independent reviewers, or if only those noted as excluded by one reviewer should be. Protocol authors should therefore describe their specific approach for identifying potentially eligible records (that is, by title and abstract screening) and for selecting studies for final inclusion (that is, by full text screening). Typical methodology for study selection is aimed at enhancing objectivity and preventing mistakes. Often, screening is carried out in duplicate by independent reviewers at each stage of the review to reduce the possibility of excluding relevant reports.[97] The benefit may be greatest for topics where selection or rejection of an article requires difficult judgments.[98]

Authors should report whether one or several persons will be involved in each stage of screening and name those who will be involved, if known. If independent screening is planned, authors should describe the process for dealing with discrepancies (such as third party arbitration or contacting authors of original studies) and whether inter-rater agreement will be calculated.

Item 11c: Data collection process. Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators

Example

"Using standardized forms … and a detailed instruction manual that will be used to inform specific tailoring of an online data abstraction program (DistillerSR), ten teams of reviewers will extract data independently and in duplicate from each eligible study. To ensure consistency across reviewers, we will conduct calibration exercises before starting the review. Data abstracted will include demographic information, methodology, intervention details, and all reported patient-important outcomes. Reviewers will resolve disagreements by discussion, and one of two arbitrators (JWB or GHG) will adjudicate unresolved disagreements. We will contact study authors to resolve any uncertainties."[99]

Explanation

Reviewers should plan and document the approach they plan to use to extract data from included studies in the review along with which data items (Item 12) and types of data. Data extraction forms should be developed a priori and included in the published or otherwise available review protocol as an appendix or as online supplementary materials.

As with screening, data extraction is often carried out in duplicate by independent reviewers or by one reviewer with verification by another in order to reduce bias and reduce errors in data extraction. The planned approach for resolving discrepancies should be stated. Although single data extraction has not been shown to substantially affect treatment effect estimates, reviewers should explicitly indicate whether single extraction will be employed to allow reviewers and readers to be more mindful of the possibility for errors in the completed review.[100]

Data extraction can be complicated, especially with more complex topics, and level of reviewer experience has not been shown to affect extraction error rates.[101 102] As such, additional strategies planned to reduce errors, such as training of reviewers and piloting of extraction forms should be described. In addition, if reviewers plan to make use of data extraction techniques to obtain outcome data not reported in a usable format, such as translating graphically presented data into a usable (that is, numeric) format,[103] they should plan for this during the protocol stage and report details of proposed software and its sensitivity and specificity.

If an individual patient data (IPD) meta-analysis is planned, authors should also tell readers when and how they sought individual patient data from the original researchers.[104] Data extraction for IPD reviews will often involve collection and scrutiny of detailed raw databases; authors should describe their planned approach clearly. The description might include how they attempted to contact researchers, what they asked for (that is, using a reply form with pre-specified data items), and their plan if they are unable to obtain all requested information. For IPD meta-analyses or otherwise, reviewers should also state whether they intend to confirm the accuracy of the extracted information to be included in their review with original researchers, for example, by sending them a copy of the draft review when available.[105]

Data in primary studies may not always be presented in a format that is useful to systematic reviewers. Contacting authors for

missing information about treatments, for example, has been shown to improve the completeness of treatment descriptions by at least 27%.[106] Ideally, authors of primary studies should be urged to report all aspects of their studies more clearly.[107] However, in the absence of complete descriptions of treatments, outcomes, effect estimates, or other important information, reviewers may consider asking authors for this information. Whether reviewers plan to contact authors of included studies and how this will be done (such as a maximum of three email attempts) to obtain missing information should be documented in the protocol.

Knowledge of duplicate, overlapping, or companion studies (that is, multiple reports of a single study) may come to light only during the data extraction process.[94] The inclusion of data from multiple reports as separate studies may lead to biased treatment effects[93] and should be anticipated by reviewers. Methods for identifying and dealing with multiple reports of a single study have been described.[108 109] Authors should present the algorithm they will follow to select data from overlapping reports and the planned approach for solving logical inconsistencies across reports.

Data items

Item 12. List and define all variables for which data will be sought (such as PICO items, funding sources) and any pre-planned data assumptions and simplifications

Example 1

"We will extract the generic and the trade name of the experimental intervention, the type of control used, dosage, frequency and duration of treatment, patient characteristics (average age, gender, mean duration of symptoms, type of joints affected), type of pain or function related outcome extracted, trial design, trial size, duration of follow-up, type and source of financial support and publication status from trial reports. For non-pharmacological interventions, we will extract type, modes of application and intensity, if appropriate. When necessary, means and measures of dispersion will be approximated from figures in the reports. For cross-over trials, we will extract data from the first period only because of possible carry-over effects. Whenever possible, we will use results from an intention to treat analysis. If effect sizes cannot be calculated, we will contact the authors for additional data."[110]

Example 2 (data simplifications)

"It is possible that individual studies may consist of multiple treatment groups, such as different types of depression interventions or different doses of medication. In order to avoid the possibility of introducing bias caused by multiple statistical comparisons with one control group, we will combine the groups from multiple arm studies into a single group."[111]

Explanation

Readers need to know what information review authors plan to obtain from the included studies. Data items and pre-specified time points are essential to document in a review protocol because this information allows readers to refer back to the protocol when the review is complete to determine whether changes occurred. Extraction forms should include definitions of variables, with particular details about the planned outcomes, and their measurement duration and frequency (Item 13).

The selective reporting of information in reviews is a documented concern.[8 36] Providing readers with the opportunity to identify and make their own judgments about selective reporting is crucial.[112] If the review is limited to reporting only those variables that were obtained, rather than those that were deemed important a priori but could not be obtained, bias might be introduced and the reader might be misled. In protocol amendments and completed reviews, authors should clearly outline whether any data items were added after the protocol was developed or after the review began and give the reasons why. Such variables might include aspects of treatments or outcomes identified as important because they recur during the review process (such as important outcome measures that the reviewers initially overlooked). A more complete discussion of selective outcome reporting in systematic reviews and related bias is found in Item 13.

Authors should describe assumptions they intend to make if they encounter missing or unclear information and explain how they plan to deal with such data or lack thereof, in addition to contacting authors (Item 11c). For example, in studies of women aged 50 or older it may be reasonable to assume that none was pregnant even if this is not reported. Ideally, authors should anticipate as many uncertainties as possible before they arise and have a documented, agreed approach for dealing with such data. Likewise, review authors might make assumptions about the route of administration of drugs assessed. However, a more prudent approach is required when dealing with qualitative information. For example, the upper age limit for "children" can vary from 15 years to 21 years, or the level of severity of an outcome (such as an adverse effect) might be poorly described in primary research and mean very different things to different researchers at different times and for different patients.

If simplifications such as combining treatment arms (for multiple treatment trials) or using first period data for cross over trials are planned, these should be described.

Outcomes and prioritisation

Item 13. List and define all outcomes for which data will be sought, including prioritisation of main and additional outcomes, with rationale

Example

"*Primary outcomes*

"The primary outcome will be the number of patients who responded to treatment, defined as a reduction of at least 50% on the Hamilton Depression Rating Scale (HAM-D), the Montgomery-Asberg Depression Rating Scale (MADRS) or any other depression scale, or 'much or very much improved' (score 1 or 2) on the Clinical Global Impression (CGI) Improvement Scale. All response rates will be calculated from the total number of randomised patients. Where more than one criterion is provided, we will use the HAM-D for judging the response and then follow the sequence described above. Despite the problems surrounding scale-derived response cutoffs, dichotomous outcomes can be understood more intuitively by clinicians than the mean values of rating scales and are therefore preferred.

When studies report response rates at various time points of the trial, we have decided a priori to subdivide the treatment indices as follows.

1. Early response, between one and four weeks, the time point closest to two weeks will be given preference.
2. Acute phase treatment response, between six and 12 weeks, the time point given in the original study as the study endpoint will be given preference.

3. Follow-up response, between four and six months, the time point closest to 24 weeks will be given preference.

The acute phase treatment response, that is between six and 12 weeks, was our primary outcome of interest.

Secondary outcomes

1. The number of participants in remission, as defined by either: (a) at 7 or less on the 17-item HAM-D and at 8 or less for all the other longer versions of HAM-D; (b) at 10 or less on the MADRS; (c) 'not ill or borderline mentally ill' (score 1 or 2) on the CGI-Severity; or (d) other criteria as defined by the trial authors. All remission rates will be calculated out of the total number of randomised patients. Where two or more scales are provided, we prefer the first criteria for judging remission.

'Remission' is a state of relative absence of symptoms. This outcome adds to the primary outcome 'response' to treatment. The disadvantage of 'remission' is that its frequency depends on the initial severity of the participants. If they were only relatively mildly ill, many will be classified as in remission while only few will be in the case of high average severity at baseline. Therefore, studies and meta-analyses usually apply response and not remission as the primary outcome.

2. Change scores from baseline or endpoint score at the time point in question (early response, acute phase response, or follow-up response as defined above) on the HAM-D or MADRS, or any other validated depression scale. The results of mean values of depression rating scales can be more sensitive than dichotomous response data. Therefore, they should also be presented even though their interpretation is less intuitive than with dichotomous response data. Change data will be preferred to endpoint data but both will have to be presented separately because we will use the standardised mean difference as an effect size measure for which pooling of endpoint and change data is not appropriate. We prefer change scores to endpoint scores because they, to a certain extent, take into account small baseline imbalances.

3. Social adjustment, social functioning including the Global Assessment of Function scores.

4. Health-related quality of life as measured by validated disease specific and generic scales such as the Short Form (SF)-36 or the Health of the Nation Outcome Scales (HoNOS).

5. Various reasons for dropping out of the studies:

a) due to any reason, as a measure of the overall acceptability of treatment;

b) due to inefficacy of treatment, as a global efficacy measure;

c) due to adverse events, as a global measure of tolerability.

6. Death:

a) natural causes;

b) suicide;

c) suicide attempts.

7. Side-effects:

a) number of participants experiencing at least one side-effect, b) agitation or anxiety, c) blurred vision, d) constipation, e) urination problems, f) delirium, g) diarrhoea, h) dry mouth, i) fits, j) insomnia, k) hypotension, l) nausea, m) sedation or somnolence, n) vomiting, o) vertigo.

We anticipate including the following main outcomes in a summary of findings table using GRADEpro: response to treatment, acceptability of treatment (dropout due to any reason), quality of life, death due to suicide and overall tolerability (dropout due to adverse events)."[113]

Explanation

Systematic reviews must include a description of all outcomes (endpoints) of interest,[74] and by extension the same applies to protocols. Systematic reviews that aim to inform decision making should summarize both benefits and harms of interventions,[114] and specifying what those are during the planning phases of a review is, at minimum, a reminder or a commitment to do so. Review protocols should distinguish between which outcomes are considered the main outcome(s), also known as primary outcome(s), of a review and those that are additional (secondary) outcomes; these may differ from the prioritisation assigned to outcomes in primary studies.

Listing all outcomes for which data will be sought in a review and providing sufficient details and definitions are essential in a review protocol. Some outcomes may warrant additional details in their definitions such as distinctions between surrogate versus clinical, composite versus non-composite, and objective measurement versus subjective assessment. If, for example, a surrogate outcome is specified in lieu of a clinical outcome, a rationale as to why this was done and how the surrogate outcome is an indicator (associated) of a clinically important outcome should be stated. Consider, for example, a systematic review that focuses primarily on whether continuous positive airway pressure treatment reduces symptoms of somnolence and fatigue in patients with obstructive sleep apnoea (an abnormality of breathing patterns during sleep). The outcomes of interest should include instruments measuring symptoms (such as the Epworth Sleepiness Scale)[115] but not necessarily neurophysiological signals such as the frequency of apnoeas (no breathing) or hypopnoeas (reduced breathing), muscle tone, and heart rate variability, which are commonly reported but do not correlate well with symptoms.[116] Authors should do sufficient investigation during the planning stage to ensure that selected outcomes are relevant. Given increasing efforts to involve patients in the selection and assessment of outcomes,[117] reviewers should indicate whether planned outcomes are patient centred, and further, whether they are patient reported, and how such outcomes will be treated.[118]

The reporting of composite outcomes within a completed systematic review has been found to be variable across the abstract, methods, and results sections of the report.[119] Because the various components of a composite outcome have the potential to be combined in different ways, yielding differences in the direction, strength, and significance of an outcome, it is essential in a review protocol to state and define each component of a composite outcome explicitly, and, further, state how components within a composite outcome will be analysed, whether independently, all together, or in specific combinations (Item 15b).

Meta-analyses within systematic reviews are often limited by information available in included study reports. As such, discrete descriptions of the endpoints are not always possible at the protocol stage. The minimum and often only information one can practically specify is a broad description of the "outcome concept"—for example, what is the effect of an intervention on "survival or mortality." Such a description is too generic, and authors will need to refine it when they conduct their systematic review. Examples of more refined descriptions are "mortality at 12 months" or "mortality at 5 years" (for example, as odds ratios from cross tabulated counts of deaths at these follow-up durations) and "survival" (typically hazard ratios from time-to-event analyses). Reviewers should state their plans to refine outcome definitions based on definitions used in included studies.

Careful consideration of outcomes during the planning stages of a review can also improve efficiency in the review process. For example, if authors make a decision to add an outcome(s) at some point during data extraction, they will need to revisit all included papers to extract the additional information; this is a waste of reviewers' time. Minimizing such back and forth economizes time and resources and reduces the likelihood of mistakes.

The main outcome(s) of a review should be distinguished from additional outcomes and specific definitions of each should be provided. The scientific question or the decisional problem that motivates the systematic review typically dictates the main outcome(s) of interest. Thus for systematic reviews that aim to inform healthcare decisions or policy, the main outcomes are likely to be patient relevant outcomes (such as risk of stroke) or validated surrogate outcomes (for example, change in cholesterol levels is a valid surrogate for the risk of cardiovascular events for statin based interventions). In contrast, systematic reviews that aim to summarize the state of the science in the pathophysiology of a disease might appropriately choose biochemical or other measurements as main outcomes. All other outcomes are considered additional and are reviewed to provide complementary information and for completeness.

Listing and defining outcomes in a review protocol, as well as the prioritization of each as a main or additional outcome, will facilitate the ability of future readers of completed reviews to investigate selective reporting. Selective reporting of outcomes—that is, the addition, removal, or change in the priority of review outcomes between the protocol, methods section, and results of a review—is well recognized.[10 120] A 2010 study comparing Cochrane protocols with the completed reviews found that 22% of Cochrane reviews had a discrepancy in at least one outcome measure compared with their protocols, at least 75% of which were attributable to changes in the primary outcome, some after knowledge of review findings.[10] This is described as outcome reporting bias and occurs when the reporting of an outcome is associated with its significance. Whether in a completed review, outcomes are prioritized as main or additional should not be dependent on their prioritization or statistical significance in included studies.

Readers will note that the contents of this item are overlapping with Item 8 (eligibility criteria). Given the importance of outcomes in the review process, issues in the selection of relevant outcomes, and their potential to be manipulated during the review process, we felt that an item specifically dedicated to the reporting of outcomes would greatly facilitate complete and transparent reporting around this item. Readers should also note that complete definition and description of planned review outcomes, as proposed above, will occupy substantial space in a review protocol.

Risk of bias individual studies

Item 14. Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis

Example 1

"To facilitate the assessment of possible risk of bias for each study, we will collect information using the Cochrane Collaboration tool for assessing the risk of bias (Table 8.5.a in the Cochrane Handbook for Systematic Reviews of Interventions), which covers: sequence generation, allocation concealment, blinding, incomplete outcome data (e.g. dropouts and withdrawals) and selective outcome reporting. For each domain in the tool, we will describe the procedures undertaken for each study, including verbatim quotes. A judgement as to the possible risk of bias on each of the six domains will be made from the extracted information, rated as 'high risk' or 'low risk'. If there is insufficient detail reported in the study we will judge the risk of bias as 'unclear' and the original study investigators will be contacted for more information. These judgements will be made independently by two review authors based on the criteria for judging the risk of bias (Table 8.5.c in the Cochrane Handbook Higgins 2011). Disagreements will be resolved first by discussion and then by consulting a third author for arbitration. We will compute graphic representations of potential bias within and across studies using RevMan 5.1 (Review Manager 5.1). We will consider each item in the risk of bias assessment independently without an attempt to collate and assign an overall score."[121]

Example 2

"Included non-randomised studies may or may not have a comparison group. To assess the risk of bias within included … studies, the methodological quality of potential studies will be assessed by using the Newcastle-Ottawa scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. The NOS for case-control and cohort studies will be adapted (Table 1) to meet the specific needs of this systematic review. The cohort scale will be modified for use in case series. Using the NOS, studies will be awarded a maximum of nine points on items related to the selection of the study groups, the comparability of the groups, and the ascertainment of outcome of interest. Using this modified score, case series will be eligible for a maximum of six points. This will be undertaken by two separate reviewers. Where there is disagreement, a third reviewer will be used as an arbitrator."[122]

Explanation

An assessment of the risk of bias (or "quality") of studies included in a review is an important component of any well planned or conducted systematic review. Such an assessment contributes to the evaluation of the overall strength of evidence of the review (Item 17). Established methods for assessing risk of bias in reviews have been documented.[123 124] Descriptions of the planned approach to assessing risk of bias should include the constructs being assessed and a definition for each, reviewer judgment options (high, low, unclear), the number of assessors, experience of assessors (training, piloting, previous risk of bias assessment experience), as well as method(s) of assessment (independent or in duplicate).[125] Whether reviewers are going to be blinded to studies should also be reported,[126 127] as well as whether agreement between reviewers will be evaluated and, if so, how.

Details of planned methods to summarise risk of bias assessments across studies or outcomes should be provided. Although authors may spend a large proportion of time assessing risk of bias in included studies, they are often silent on how the results might influence their review findings.[128 129] Thus, we encourage reviewers to think about this at the development stage and document their plans in the protocol. Authors should also describe how risk of bias assessments will be incorporated into data synthesis (that is, subgroup or sensitivity analyses) and their potential influence on findings of the review (Item 15c)[129] in the protocol.

The likelihood that the treatment effect reported in a systematic review represents the true effect depends on the validity of the

included studies, namely, the internal validity. Certain methodological characteristics of primary studies may be associated with their resulting effect sizes.[129-131] For example, trials describing inadequate methods of allocation concealment or with unclear concealment exaggerate treatment effects on average compared with trials reporting adequately concealed allocation[132] Therefore, authors should not only describe risk of bias methods and constructs to be assessed for each included study, but also describe how results of the assessment contribute to the overall findings of the review.[128] Additionally, authors should provide a rationale if they do not intend to assess risk of bias.

Many methods exist to assess the overall risk of bias in included studies, including scales, checklists, and individual components.[133 134] As summarized in the PRISMA elaboration document,[17] scales that numerically summarize multiple components into a single number are misleading and unhelpful.[135] Rather, authors should specify the methodological components that they plan to assess and how they plan to assess said components. Common markers of validity for randomised trials, in the Cochrane Risk of Bias tool,[123] include appropriate generation of random allocation sequence[136]; concealment of the allocation sequence[132]; blinding of participants, healthcare providers, data collectors, and outcome adjudicators[137 138]; and proportion of patients lost to follow-up.[139] Reviewers may also anticipate assessing other items that do not necessarily indicate bias, such as the impact of early stopping of trials for benefit,[140 141] industry sponsorship,[55 142] single trial centres,[143] and improper analyses or fabrication of primary study data.[144 145] If authors plan such assessments they should explain this information in the protocol.

Authors should give careful consideration to assessments for reviews that expect to include non-parallel group randomised controlled trials and studies of non-randomised design, for which methodological standards are currently under development.[146] The ultimate decision regarding which methodological features should be evaluated requires consideration of the strength of the empirical data, theoretical rationale, and the unique circumstances of the included studies within the context of the review question.

Data synthesis

Item 15a. Describe criteria under which study data will be quantitatively synthesised

Example 1

"If studies are sufficiently homogeneous in terms of design and comparator, we will conduct meta-analyses using a random-effects model."[121]

Explanation

Diversity in study populations, interventions, outcomes, or trial conduct may mean that including some studies in a meta-analysis, or even conducting meta-analyses at all, will be impossible. Authors should describe, with reference to the PICO criteria, the conditions that should be present before they will proceed with statistical synthesis (Item 15b). Thus authors might consider whether to include trials with differing formulations or doses of the experimental treatment, studies using differing versions of a technology (such as a device), studies with different age profiles in the sample population, or studies with different follow-up times.

Item 15b. If data are appropriate for synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)

Example

"**Measures of treatment effect**

• For dichotomous outcomes

Dichotomous data (occurrence of angiographic restenosis, mortality; recurrence of myocardial infarction, heart failure, angina; adverse events and the major adverse cardiac effects) will be determined by using risk ratio (RR) with 95% confidence interval (CI). It has been shown that RR is more intuitive than the odds ratio (OR) and that OR tend to be interpreted as RR by clinicians, which leads to an overestimate of the effect.

• For continuous outcomes

Continuous outcomes will be analysed using weighted mean differences (with 95% CI) or standardized mean differences (95% CI) if different measurement scales are used. Skewed data and non-quantitative data will be presented descriptively.

Unit of analysis issues

The primary analysis will be per individual randomised; however, all included trials will be assessed in order to determine the unit of randomization and whether or not this unit of randomization is consistent with the unit of analysis. Special issues in the analysis of studies with non-standard design, like cluster randomised trials, cross-over trials, and studies with multiple treatment groups, will be addressed. For cluster randomised trials we will extract an interclass correlation co-efficient to modify the results according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions*. For cross-over trials, a major concern is carry-over effect. We will only use the data from the first phase, guided by the Cochrane Heart Group. When a study has more than two treatment groups, we will present the additional treatment arms. Where the additional treatment arms are not relevant, they will not be taken into account. We will also acknowledge heterogeneity in the randomization unit and perform a sensitivity analysis.

Dealing with missing data

When there are missing data, we will attempt to contact the original authors of the study to obtain the relevant missing data. Important numerical data will be carefully evaluated. If missing data cannot be obtained, an imputation method will be used. We will use sensitivity analysis to assess the impact on the overall treatment effects of inclusion of trials which do not report an intention to treat analysis, have high rates of participant attrition, or with other missing data.

Assessment of heterogeneity

We will test the clinical heterogeneity by considering the variability in participant factors among trials (for example age) and trial factors (randomization concealment, blinding of outcome assessment, losses to follow-up, treatment type, co-interventions). Statistical heterogeneity will be tested using the Chi^2 test (significance level: 0.1) and I^2 statistic (0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity). If high levels of heterogeneity among the trials exist (I^2 >=50% or P <0.1) the study design and characteristics in the included

studies will be analysed. We will try to explain the source of heterogeneity by subgroup analysis or sensitivity analysis.

Data synthesis

Each outcome will be combined and calculated using the statistical software RevMan 5.1, according to the statistical guidelines referenced in the current version of the *Cochrane Handbook for Systematic Reviews of Interventions*. The Mantel-Haenszel method will be used for the fixed effect model if tests of heterogeneity are not significant. If statistical heterogeneity is observed (I^2 >=50% or P <0.1), the random effects model will be chosen. If heterogeneity is substantial, we will not perform a meta-analysis; a narrative, qualitative summary will be done."[147]

Explanation

When authors intend to perform meta-analyses, they should specify the effect measure (such as relative risk or mean difference) (Item 13) and the statistical method (such as inverse variance, DerSimonian-Laird, Mantel-Haenszel, Bayesian) to be used and whether they plan to apply a fixed or random effects approach.[148] Although experts debate this topic, fixed effects meta-analyses have been shown to overestimate confidence in treatment effects; thus, reviewers may wish to use this approach conservatively.[149 150] If estimates of heterogeneity are to be used to decide between fixed and random effects approaches, authors should state the threshold of heterogeneity required.[151] If possible, authors should explain the reasons for these choices.

Reviewers should anticipate that data from included studies may not be in a suitable format for analysis or presentation in the review. For that reason, authors may need to take various steps to process the data, even if they do not plan meta-analyses. Authors should describe their plans for data processing, focusing on anticipated problems specific to their review. In trials with more than two intervention groups (for example, receiving similar but non-identical interventions), combining or splitting results across groups may be necessary.[152] If individual patient data (IPD) meta-analyses are planned, reviewers should consult the (forthcoming) PRISMA extension for IPD meta-analyses.[153]

For analyses of dichotomous data (that is, event data), authors should consider how best to handle rare events or when events are absent from some studies. Outcomes reported as measurement scales (such as for depression) may use different scales in different studies; results may need to be adjusted so that all scales are aligned (for example, so that low values represent good health on all scales).

Reviewers should also anticipate that some desired data will not be reported in included studies at all. In particular, standard deviations and standard errors may have to be reconstructed from other statistics such as P values and *t* statistics[154 155]; occasionally they may be imputed from the standard deviations observed in other studies.[156 157] In analyses of time-to-event data, reviewers should anticipate spending more time and caution during data extraction (for example, from Kaplan-Meier survival curves) and report how conversion to a consistent format is planned.[158]

Statistical combination of data from two or more separate studies in a meta-analysis may not always be necessary, feasible, or desirable. Regardless of the decision to combine individual study results, authors should report how they plan to evaluate between-study variability (heterogeneity or inconsistency), such as by using I^2 or Cochran's Q test. The consistency of results across studies may influence the decision whether to combine individual study data in a meta-analysis. If reviewers plan to use statistical estimates of consistency (such as I^2 or Kendall's τ) to determine whether to perform a meta-analysis, they should state this explicitly (Item 15a) and specify the required number.

Finally, the name (and version) of any software planned for completing meta-analyses should be reported.

Item 15c. Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)

Example

"**Subgroup analysis and investigation of heterogeneity**

Subgroup analyses will be used to explore possible sources of heterogeneity, based on the following.

- Patient characteristic (age, sex).
- Types of treatment (western medicine alone, western medicine plus Tong-xin-luo).
- Follow-up period (three, six, and 12 months).
- Type of stent (drug-eluting and non-drug eluting stent).

Sensitivity analysis

Sensitivity analysis will be performed in order to explore the source of heterogeneity as follows.

- Quality components, including full-text publications versus abstracts, preliminary results versus mature results, published versus unpublished data.
- Risk of bias (by omitting studies that are judged to be at high risk of bias)."[147]

Explanation

Investigating possible causes of between-study variability or exploring the robustness of meta-analyses by using subgroup analysis or meta-regression may be desirable. If authors plan such analyses, they should state this and specify the covariates anticipated for the analyses (such as disease type or severity, or treatment dose). For subgroup analyses, authors should describe how they will partition the covariate into subgroups (for example, what will constitute mild or severe disease, low or high treatment dose). Whether they plan a fixed or random effects approach and how they will evaluate residual heterogeneity should also be stated.

If any sensitivity analyses are intended—such as including or excluding small studies, studies with high risk of bias,[159] industry funded studies, or outlier studies—authors should describe their plan for doing so.

Item 15d. If quantitative synthesis is not appropriate, describe the type of summary planned

Example

"A systematic narrative synthesis will be provided with information presented in the text and tables to summarise and explain the characteristics and findings of the included studies. The narrative synthesis will explore the relationship and findings both within and between the included studies, in line with the guidance from the Centre for Reviews and Dissemination."[160]

Explanation

In nearly all cases, reviews will include a qualitative (narrative) synthesis or summary even if meta-analyses or other quantitative analyses have been done. If, in addressing items 15a, 15b, and 15c, authors have concluded that some or all of the expected data will not be suitable for combining quantitatively, they

should explicitly say so in the protocol and provide the rationale for such decisions. Then for item 15d they should describe the way they propose to present results in narrative form.

Established methods for narrative syntheses are available.[161 162] Authors should, to the extent possible at the protocol stage, highlight the order in which they will present information and what they will give in text or (only) in tables. They should describe what priority they will give to information about participant populations (such as overall patient groups before subgroups, subgroups defined by sociodemographics before those defined by coexisting conditions) and about interventions and comparisons of interventions (such as head to head trials before trials with placebo or usual care controls, ultimate health outcomes before intermediate outcomes, patient related outcomes before utilization outcomes, and so forth). For example, authors may say that they will present results in order by key question and, within key questions, in order of main then additional outcomes. In other cases, they might specify that results will be reported first by key questions but then by important comparisons and outcomes within comparisons.

In addition, authors should say whether they plan to report only on studies for which risk of bias was either low or moderate and omit studies with high risk of bias, or whether they expect to retain studies of any level of risk of bias in their analyses. They should note that levels of risk of bias for a given study may differ depending on the outcome of interest, so that some studies may be retained for certain key questions or outcomes but not for others. In some cases, authors might note that they will report on studies at high risk of bias only when they provide the available information or a critical outcome or population of interest.

Authors should describe how they plan to present information by type of study design (for example, report results only for randomised controlled trials, and then supplement the results with information drawn from non-randomised trials or non-experimental studies). In some cases authors may want to stratify how they present information based on key aspects of how studies were conducted (such as whether investigators, patients, and outcome assessors were all masked to intervention). If authors will focus on specific types of outcome measures, such as demonstrably reliable and valid instruments to measure depression or pain, they should report this information.

Regardless of how many quantitative analyses authors expect to present, they should indicate the extent to which they plan to use tables to summarize (*a*) the characteristics of studies (perhaps only those of low or moderate risk of bias) and (*b*) the principal comparisons or outcomes of concern.

In some cases, review authors may plan to do types of analyses other than meta-analyses. These may include cost of illness, cost of treatment, or cost effectiveness analyses, decision modelling analyses, or various types of subgroup analyses (independent of any required by a key question). In all these cases, authors should be as specific as possible about what they will attempt to do.

Meta-bias(es)

Item 16. Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)

Example

"In order to determine whether reporting bias is present, we will determine whether the protocol of the RCT was published before recruitment of patients of the study was started. For studies published after July 1st 2005, we will screen the Clinical Trial Register at the International Clinical Trials Registry Platform of the World Health Organisation (http://apps.who.int/trialssearch). We will evaluate whether selective reporting of outcomes is present (outcome reporting bias). We will compare the fixed effect estimate against the random effects model to assess the possible presence of small sample bias in the published literature (i.e. in which the intervention effect is more beneficial in smaller studies). In the presence of small sample bias, the random effects estimate of the intervention is more beneficial than the fixed effect estimate. The potential for reporting bias will be further explored by funnel plots if ≥10 studies are available."[163]

Explanation

Authors should pre-specify any methods used to explore the possibility that the data identified are biased due to non-study related processes.[164] Such bias may result from non-publication of studies (publication or dissemination bias) and the reporting of a subset of measured outcomes and analyses within studies (outcome reporting bias) (see box 2).

Detecting or correcting for publication bias in a systematic review is difficult. The results of available studies may provide clues that some studies may be missing (such as when smaller studies have systematically different effect estimates than larger studies ("small study effects")).[165] Recommendations regarding appropriate graphical methods (such as funnel plots) and statistical methods (such as Egger's test) to assess small study effects have been proposed.[166] However, publication bias is only one of several possible explanations for small study effects, and the interpretation of such tests can be problematic.[166-168] Authors should report their planned testing strategy to assess publication bias in detail. The risk of publication bias was formally assessed in only 21% of 100 intervention reviews published in 2006, and only 32% considered this type of bias.[169] A review of antidepressant trials found that effect estimates of meta-analyses of only the published trials were 32% larger on average than effect estimates of meta-analyses including published and unpublished trials.[170] The corresponding magnitude of publication bias in antipsychotic trials was smaller (8%).[171]

Several methods to detect selective outcome reporting exist. If a study protocol is available, reviewers can compare outcomes reported in the protocol and the published report.[7 172] Comparing the outcomes reported in the methods and results sections of the published report is an option when a protocol is unavailable.[173] For some trials, reviewers might assume that it is likely that an outcome was measured even if it was not reported, based on knowledge of the clinical area (such as when systolic, but not diastolic, blood pressure is reported).[112] Authors may use the Outcome Reporting Bias in Trials (ORBIT) classification system.[4] A sensitivity analysis to assess the impact of selective reporting on meta-analytic results may also be considered.[174] In eight of 28 Cochrane reviews published in March 2010, authors did not assess outcome reporting bias; in 16 reviews, authors did assess this bias using the published report; and in the remaining reviews, trial protocols were used.[175] In another study, after investigators applied sensitivity analyses to adjust for outcome reporting bias in 81 Cochrane reviews, the treatment effect estimate was reduced by 20% or more in 19 (23%) of the meta-analyses.[4]

Both publication bias and outcome reporting bias may affect meta-analyses, and the effect can be unpredictable. Adding unreported data from both published and unpublished drug trials to 41 meta-analyses caused 46% of the meta-analytic effect

Box 2: Meta-bias caused by selective publication of studies and selective reporting within studies

Systematic reviews aim to synthesise the results of all relevant studies. However, some studies may not be published, and a subset of outcomes and analyses may be incompletely, inadequately, or selectively reported in a published article, based on the results (such as statistical significance, magnitude, or direction of effect). The validity of systematic reviews may be threatened if the outcome data available to reviewers comprise a biased selection of all data that actually exists.[181 182] Such biases are termed meta-biases, meaning that they occur independent of procedural problems during the conduct of a primary study as do typical methodological biases (such as inappropriate method of random sequence generation in randomized trials).[164]

Publication or dissemination bias—Several systematic reviews of empirical studies have found that clinical trials with statistically significant (P<0.05) or positive results are more likely to be published than those with non-significant or negative results.[2 165 183] Investigators' decisions not to submit papers with negative results for publication, rather than editors' rejection of such papers, tend to be the main source of publication bias.[184] However, the decision to write up a study for publication may be influenced by pressure from study sponsors and journal editor.[185] Studies with statistically significant results also tend to be published earlier than studies with non-significant results.[165] If studies are missing from a systematic review for these reasons, exaggerated results may be produced.

Outcome reporting bias—The selective reporting of outcomes due to their significance, magnitude, or direction is termed outcome reporting bias and has been widely documented across the trial literature.[2] Outcomes specified in the protocol may be completely omitted from the published report. When an outcome is measured using multiple scales or at multiple time points, and analysed in various ways (such as intention-to-treat and per-protocol analysis, unadjusted and adjusted for covariates), the choice of which data to present may be influenced by the results. Non-significant results may be partially reported (such as reporting an effect estimate with no measure of variation), resulting in insufficient data to include in a meta-analysis. All of these examples of selectively reported outcome data in primary studies can bias (and sometimes, overestimate) the results of systematic reviews.[2 7 186]

Empirical evidence of selective outcome reporting bias in trials exists. A systematic review of 16 cohorts of clinical trials comparing outcomes reported in trial protocols with the published reports found that at least one primary outcome was omitted, introduced, or changed in 4-50% of reports.[3] In a landmark study, Chan and colleagues found that statistically significant outcomes had higher odds of being fully reported in trial publications compared with non-significant outcomes for efficacy (pooled odds ratio 2.4 (95% confidence interval 1.4 to 4.0)) and safety (pooled odds ratio 4.7 (1.8 to 12)).[164]

estimates to show lower efficacy of the drug, 7% to show identical efficacy, and 46% to show greater efficacy.[176]

Confidence in cumulative estimate

Item 17. Describe how the strength of the body of evidence will be assessed (such as GRADE)

Example

"The quality of evidence for all outcomes will be judged using the Grading of Recommendations Assessment, Development and Evaluation working group methodology. The quality of evidence will be assessed across the domains of risk of bias, consistency, directness, precision and publication bias. Additional domains may be considered where appropriate. Quality will be adjudicated as high (further research is very unlikely to change our confidence in the estimate of effect), moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low (very uncertain about the estimate of effect)."[54]

Explanation

Authors should describe which approach they plan on using to summarize the confidence they have in the resulting body of evidence, ideally using an established and validated approach. The description should include a plan for assessing the risk of bias across studies, inconsistency, imprecision, indirectness, publication bias, and factors that increase the confidence in an effect (such as large effects, dose effect relations, and issues around opposing bias and confounding not explaining an effect or lack thereof) for each outcome that is included in the PICO. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach is increasingly recommended.[168]

If no such assessments are planned, the authors should state this with a rationale for why not. Authors should describe whether and how they assess the directness related only to populations (including applicability) who are included in the evidence that is assessed (such as if they extrapolated and for what reasons), so that users of the systematic review can make these judgments later for other populations.[177 178] Authors should specify whether the assessment of the strength of evidence will include studies that are excluded from meta-analysis (if applicable).

"Strength of evidence" and "quality of evidence" have been previously been used interchangeably.

Discussion

We hope this detailed explanatory paper will become a pedagogical document that the entire systematic review community can use. Similarly, we have strived to ensure that the paper is useful to authors seeking guidance in what to include in a protocol of their systematic review. We recommend that authors use this paper when seeking a more complete explanation of each item included in the PRISMA-P checklist. We developed this protocol extension to PRISMA in the hopes that it will improve the reporting of protocols and also simplify the process of reporting a protocol, and registering it with PROSPERO. The development of the PRISMA-P 2015 checklist borrowed heavily from the mandatory items included in PROSPERO. When authors register their protocol on PROSPERO, much of this information is the same as what is recommended when completely reporting a protocol using the PRISMA-P checklist.

Similarly, the intent of using PRISMA-P is to make reporting completed systematic reviews easier for authors. For example, once reviewers have described the methods in detail in their protocol, they may not need to repeat them when reporting the final systematic review results, particularly if there have been no protocol amendments. Providing explicit details about planned review methods in a protocol is essential for clarity, transparency, and future reproducibility, and is in line with emerging journal policies.[18] Authors may also wish to develop a protocol to expand on information reported in PROSPERO. For journals that require a more detailed methods section in completed review articles, authors can easily cut and paste information already in their protocol, change the tense of the wording, and add any necessary documentation about protocol modifications or post-review changes where relevant (more likely in complex reviews such as network meta-analyses).

Protocols are important and provide readers with information about the rationale, question(s), and methods proposed by the systematic reviewers. They should always be made available in the public domain. However, for a variety of reasons, they are not always reported or published. Systematic reviewers may,

for instance, be unsure of what information should be included in a review protocol—a problem PRISMA-P 2015 aims to solve.

We hope PRISMA-P will help increase the proportion of systematic review protocols being reported and published. Peer reviewers, editors, and other interested readers might also find protocols helpful in their assessment of completed reviews. Comparing protocols with completed reviews enables users to assess possible selective reporting and other possible deviations from the proposed systematic review plan. Investigators completing systematic reviews of systematic reviews (that is, overviews) might also find protocols useful for similar reasons.

We hope that journal editors will encourage authors submitting systematic review protocols for publication to comply with PRISMA-P. We hope funders and sponsors of systematic reviews will do likewise. We also invite readers to let us know what they think of PRISMA-P and ways we can improve it and keep it up to date.

The PRISMA-P steering committee thank the following staff from DM's research group at OHRI: Jodi Peters for her efforts organizing the PRISMA-P consensus meeting; Michael Zhao for his assistance in preparing documents for the PRISMA-P meeting; Mohammed Ansari for valuable input and feedback throughout the process; and Justin Thielman for his assistance collating group comments during preparation of the PRISMA-P manuscripts.

Members of the PRISMA-P group (listed alphabetically): Douglas G Altman, Centre for Statistics in Medicine (CSM), University of Oxford, Oxford, UK; Alison Booth, Centre for Reviews and Dissemination (CRD), University of York, York, UK; An-Wen Chan, Women's College Research Institute, University of Toronto, Toronto, Canada; Stephanie Chang, Agency for Healthcare Research and Quality, Rockville, USA; Mike Clarke, Queen's University of Belfast, Belfast, Ireland; Tammy Clifford, Canadian Agency for Drugs and Technologies in Health (CADTH), Ottawa, Canada; Kay Dickersin, Johns Hopkins Bloomberg School of Public Health; Matthias Egger, Institut für Sozial-und Präventivmedizin; Davina Ghersi, National Health and Medical Research Council, Canberra, Australia; Peter C Gøtzsche, Nordic Cochrane Centre, Copenhagen, Denmark; Jeremy M Grimshaw, Canadian Cochrane Centre and Ottawa Hospital Research Institute (OHRI), Ottawa, Canada; Trish Groves, *The BMJ*, London, UK; Mark Helfand, AHRQ EPC Scientific Resource Center, Portland VA Research Foundation, Portland, USA; Julian Higgins, School of Social and Community Medicine, Bristol, UK; Toby Lasserson, Cochrane Editorial Unit, London, UK; Joseph Lau, Center for Evidence-based Medicine, Brown University, Providence, USA; Alessandro Liberati, University of Modena, Modena, Italy; Kathleen Lohr, Research Triangle Institute-University of North Carolina EPC, Research Triangle Park, USA; Jessie McGowan, University of Ottawa, Ottawa, Canada; David Moher, Clinical Epidemiology Program, OHRI and University of Ottawa, Ottawa, Canada; Cynthia Mulrow, *Annals of Internal Medicine*, San Antonio, USA; Melissa Norton, *PLoS Medicine*, London, UK; Matthew Page, Monash University, Australia; Mark Petticrew, London School of Hygiene and Tropical Medicine, London, UK; Margaret Sampson. Children's Hospital of Eastern Ontario, Ottawa, Canada; Holger Schünemann, McMaster University, Hamilton, Canada; Larissa Shamseer, Clinical Epidemiology Program, OHRI and University of Ottawa, Ottawa, Canada; Paul Shekelle, Southern California EPC, Los Angeles, USA; Iveta Simera, CSM, University of Oxford, Oxford, UK; Lesley A Stewart, CRD, University of York, York, UK; William Summerskill, *The Lancet*, London, UK; Jennifer Tetzlaff, Clinical Epidemiology Program, OHRI, Ottawa, Canada; Thomas A Trikalinos, Center for Evidence-based Medicine, Brown University, Providence, USA; David Tovey, *The Cochrane Library*, London, UK; Lucy Turner, Clinical Epidemiology Program, OHRI, Ottawa, Canada; Evelyn Whitlock, Kaiser Permanente Research Affiliates EPC, Portland, Oregon, USA.

Contributors: DM, LS, MC, DG, AL, MP, PS, and LAS conceived of this paper. DM and LS drafted the article and all authors critically revised it for important intellectual content. All authors approved the final version of this article. DM is the guarantor of this work.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: (1) support from the Agency for Healthcare Research and Quality, USA (Contract No HHSA 290 2007 10059 I) and the Canadian Institutes for Health Research (Reference No 114369) for this work; this manuscript does not reflect the opinions of either agency; one author, SC, is an employee of AHRQ. (2) No financial relationships with any organisations that might have an interest in the submitted work in the previous three years (3) MC, DG, DM, MP, and LAS are members of the Advisory Board for PROSPERO. TG is the deputy editor of *The BMJ* and was not involved in the handling of or the decision to publish this manuscript.

1 Moher D, Tetzlaff J, Tricco AC, Sampson M, Altman DG. Epidemiology and reporting characteristics of systematic reviews. *PLoS Med* 2007;4:e78.
2 Dwan K, Gamble C, Williamson PR, Kirkham JJ. Systematic review of the empirical evidence of study publication bias and outcome reporting bias—An updated review. *PloS One* 2013;8:e66844.
3 Dwan K, Altman DG, Cresswell L, Blundell M, Gamble CL, Williamson PR. Comparison of protocols and registry entries to published reports for randomised controlled trials. *Cochrane Database Syst Rev* 2011;(1):MR000031.
4 Kirkham JJ, Dwan KM, Altman DG, Gamble C, Dodd S, Smyth R, et al. The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews. *BMJ* 2010;340:c365.
5 Dwan K, Altman DG, Arnaiz JA, Bloom J, Chan AW, Cronin E, et al. Systematic review of the empirical evidence of study publication bias and outcome reporting bias. *PLoS One* 2008;3:e3081.
6 Chan AW, Krleza-Jeric K, Schmid I, Altman DG. Outcome reporting bias in randomized trials funded by the canadian institutes of health research. *Can Med Assoc J* 2004;171:735.
7 Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: Comparison of protocols to published articles. *JAMA* 2004;291:2457-65.
8 Page MJ, McKenzie JE, Kirkham J, Dwan K, Kramer S, Green S, et al. *Bias due to selective inclusion and reporting of outcomes and analyses in systematic reviews of randomised trials of healthcare interventions* . Cochrane Library, 2014.
9 Page MJ, McKenzie JE, Forbes A. Many scenarios exist for selective inclusion and reporting of results in randomized trials and systematic reviews. *J Clin Epidemiol* 2013;66:524-37.
10 Kirkham JJ, Altman DG, Williamson PR. Bias due to changes in specified outcomes during the systematic review process. *PLoS One* 2010;5:e9810.
11 Booth A, Clarke M, Ghersi D, Moher D, Petticrew M, Stewart L. Establishing a minimum dataset for prospective registration of systematic reviews: An international consultation. *PLoS One* 2011;6:e27319.
12 Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *BMJ* 2009;339:b2535.
13 Chan A, Tetzlaff JM, Gøtzsche PS, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: Guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
14 Institute of Medicine. *Finding what works in health care: standards for systematic reviews* . National Academies Press, 2011.
15 Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
16 Moher D, Schulz KF, Simera I, Altman DG. Guidance for developers of health research reporting guidelines. *PLoS Med* 2010;7:e1000217.
17 Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100.
18 Enhancing reproducibility. *Nature Methods* 2013;10:367.
19 Beller EM, Glasziou PP, Altman DG, Hopewell S, Bastian H, Chalmers I, et al. PRISMA for abstracts: reporting systematic reviews in journal and conference abstracts. *PLoS Med* 2013;10:e1001419.
20 Mans CM, Reeve JC, Gasparini CA, Elkins MR. Postoperative outcomes following preoperative inspiratory muscle training in patients undergoing open cardiothoracic or upper abdominal surgery: protocol for a systematic review. *Syst Rev* 2012;1:63.
21 Wen J, Ren Y, Wang L, Li Y, Liu Y, Zhou M, et al. The reporting quality of meta-analyses improves: a random sampling study. *J Clin Epidemiol* 2008;61:770.
22 Moher D, Booth A, Stewart L. How to reduce unnecessary duplication: Use PROSPERO. *BJOG* 2014;121:784-6.
23 Montori VM, Wilczynski NL, Morgan D, Haynes RB. Optimal search strategies for retrieving systematic reviews from medline: analytical survey. *BMJ* 2005;330:68.
24 O'Connor AM, Auvermann BW, Higgins JP, Kirychuk SP, Sargeant JM, Von Essen SG, et al. The association between proximity to animal-feeding operations and community health: a protocol for updating a systematic review. *Syst Rev* 2014;3:99.
25 Moher D, Tsertsvadze A. Systematic reviews: When is an update an update? *Lancet* 2006;367:881-3.
26 Shojania KG, Sampson M, Ansari MT, Ji J, Doucette S, Moher D. How quickly do systematic reviews go out of date? A survival analysis. *Ann Intern Med* 2007;147:224-33.
27 Moher D, Tsertsvadze A, Tricco AC, Eccles M, Grimshaw J, Sampson M, et al. A systematic review identified few methods and strategies describing when and how to update systematic reviews. *J Clin Epidemiol* 2007;60:1095.
28 Garritty C, Tsertsvadze A, Tricco AC, Sampson M, Moher D. Updating systematic reviews: an international survey. *PloS One* 2010;5:e9914.
29 Chung M, Newberry SJ, Ansari MT, Yu WW, Wu H, Lee J, et al. Two methods provide similar signals for the need to update systematic reviews. *J Clin Epidemiol* 2012;65:660-8.

30 Ahmadzai N, Newberry SJ, Maglione MA, Tsertsvadze A, Ansari MT, Hempel S, et al. A surveillance system to assess the need for updating systematic reviews. *Syst Rev* 2013;2:1-16.
31 Chalmers I, Enkin M, Keirse MJ. Preparing and updating systematic reviews of randomized controlled trials of health care. *Milbank Q* 1993:411-37.
32 Cancelliere C, Cassidy JD, Côté P, Hincapié CA, Hartvigsen J, Carroll LJ, et al. Protocol for a systematic review of prognosis after mild traumatic brain injury: an update of the WHO collaborating centre task force findings. *Syst Rev* 2012;1:17.
33 Stewart L, Moher D, Shekelle P. Why prospective registration of systematic reviews makes sense. *Syst Rev* 2012;1:7.
34 Booth A, Clarke M, Ghersi D, Moher D, Petticrew M, Stewart L. An international registry of systematic-review protocols. *Lancet* 2011;377:108-9.
35 Booth A, Clarke M, Dooley G, Ghersi D, Moher D, Petticrew M, et al. The nuts and bolts of PROSPERO: An international prospective register of systematic reviews. *Syst Rev* 2012;1:2.
36 Silagy CA, Middleton P, Hopewell S. Publishing protocols of systematic reviews: comparing what was done to what was planned. *JAMA* 2002;287:2831-4.
37 Siontis KC, Hernandez-Boussard T, Ioannidis JP. Overlapping meta-analyses on the same topic: survey of published studies. *BMJ* 2013;347:f4501.
38 Moher D. The problem of duplicate systematic reviews. *BMJ* 2013;347:f5040.
39 The PLoS ME. Best practice in systematic reviews: the importance of protocols and registration. *PLoS Med* 2011;8:e1001009.
40 Chien PFW, Khan KS, Siassakos D. Registration of systematic reviews: PROSPERO. *BJOG* 2012;119:903-5.
41 Bambra C, Hillier F, Moore H, Summerbell C. Tackling inequalities in obesity: a protocol for a systematic review of the effectiveness of public health interventions at reducing socioeconomic inequalities in obesity amongst children. *Syst Rev* 2012;1:16.
42 Mowatt G, Shirran L, Grimshaw JM, Rennie D, Flanagin A, Yank V, et al. Prevalence of honorary and ghost authorship in cochrane reviews. *JAMA* 2002;287:2769-71.
43 Rennie D, Yank V, Emanuel L. When authorship fails. *JAMA* 1997;278:579-85.
44 Sismondo S. Ghost management: How much of the medical literature is shaped behind the scenes by the pharmaceutical industry? *PLoS Med* 2007;4:e286.
45 Ross JS, Hill KP, Egilman DS, Krumholz HM. Guest authorship and ghostwriting in publications related to rofecoxib. *JAMA* 2008;299:1800-12.
46 Smith R. Maintaining the integrity of the scientific record. *BMJ* 2001;323:588.
47 Ensor J, Riley RD, Moore D, Bayliss S, Jowett S, Fitzmaurice DA. Protocol for a systematic review of prognostic models for the recurrence of venous thromboembolism (VTE) following treatment for a first unprovoked VTE. *Syst Rev* 2013;2:91.
48 Smith R. Authorship is dying: long live contributorship. *BMJ* 1997;315:696.
49 Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication. 2010. www.ICMJE.org.
50 AHRQ Agency for Healthcare Research and Quality, Effective Health Care Program. Research protocol–Apr 3, 2014: Treatments for fibromyalgia in adult subgroups. http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=1887#8696.
51 AHRQ Agency for Healthcare Research and Quality, Effective Health Care Program. Research Protocol–Jul 21, 2014: Treatment of non-metastatic muscle-invasive bladder cancer. http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=1940#9004.
52 Getz KA, Zuckerman R, Cropp AB, Hindle AL, Krauss R, Kaitin KI. Measuring the incidence, causes, and repercussions of protocol amendments. *Drug Inf J* 2011;45:265-75.
53 Higgins JPT, Green S, eds. Guide to the contents of a Cochrane protocol and review. In: *The Cochrane handbook for systematic reviews of interventions* . Wiley-Blackwell, 2011.
54 Young M, Stevens A, Porath-Waller A, Pirie T, Garritty C, Skidmore B, et al. Effectiveness of brief interventions as part of the screening, brief intervention and referral to treatment (SBIRT) model for reducing the non-medical use of psychoactive substances: a systematic review protocol. *Syst Rev* 2012;1:22.
55 Lundh A, Sismondo S, Lexchin J, Busuioc OA, Bero L. Industry sponsorship and research outcome. *Cochrane Database Syst Rev* 2012;(12):MR000033.
56 Bero L. Industry sponsorship and research outcome: a cochrane review. *JAMA Intern Med* 2013;173:580-1.
57 Roseman M, Turner EH, Lexchin J, Coyne JC, Bero LA, Thombs BD. Reporting of conflicts of interest from drug trials in Cochrane reviews: cross sectional study. *BMJ* 2012;345:e5155.
58 Jorgensen AW, Hilden J, Gotzsche PC. Cochrane reviews compared with industry supported meta-analyses and other meta-analyses of the same drugs: systematic review. *BMJ* 2006;333:782.
59 Yank V, Rennie D, Bero LA. Financial ties and concordance between results and conclusions in meta-analyses: retrospective cohort study. *BMJ* 2007;335:1202-5.
60 Jorgensen AW, Maric KL, Tendal B, Faurschou A, Gotzsche PC. Industry-supported meta-analyses compared with meta-analyses with non-profit or no support: differences in methodological quality and conclusions. *BMC Med Res Methodol* 2008;8:60.
61 Bes-Rastrollo M, Schulze MB, Ruiz-Canela M, Martinez-Gonzalez MA. Financial conflicts of interest and reporting bias regarding the association between sugar-sweetened beverages and weight gain: A systematic review of systematic reviews. *PLoS Med* 2013;10:e1001578.
62 Rochon PA, Hoey J, Chan A, Ferris LE, Lexchin J, Kalkar SR, et al. Financial conflicts of interest checklist 2010 for clinical research studies. *Open Med* 2010;4:e69.
63 Holden MA, Haywood KL, Potia TA, Gee M, McLean S. Recommendations for exercise adherence measures in musculoskeletal settings: a systematic review and consensus meeting (protocol). *Syst Rev* 2014;3:1-6.
64 Founti P, Topouzis F, Anastasopoulos E, Pappas T, Lambropoulos A, Chatzikyriakidou A, et al. Association of LOXL1 polymorphisms with pseudoexfoliation syndrome and pseudoexfoliative glaucoma: systematic review and meta-analysis. PROSPERO:CRD42014009228. www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014009228.
65 CDISC Clinical Data Interchange Standards Consortium. *CDISC Clinical Research Glossary* . 2011. www.cdisc.org/stuff/contentmgr/files/0/08a36984bc61034baed3b019f3a87139/misc/act1211_011_043_gr_glossary.pdf.
66 Hayden J, Cartwright J, Riley R, vanTulder M. Exercise therapy for chronic low back pain: Protocol for an individual participant data meta-analysis. *Syst Rev* 2012;1:64.
67 Moseley AM, Elkins MR, Herbert RD, Maher CG, Sherrington C. Cochrane reviews used more rigorous methods than non-cochrane reviews: survey of systematic reviews in physiotherapy. *J Clin Epidemiol* 2009;62:1021-30.
68 Psaty BM, Kronmal RA. Reporting mortality findings in trials of rofecoxib for alzheimer disease or cognitive impairment: A case study based on documents from rofecoxib litigation. *JAMA* 2008;299:1813-7.
69 Cohen D. Rosiglitazone: What went wrong? *BMJ* 2010;341:c4848.
70 Chung A, Backholer K, Wong E, Palermo C, Keating C, Peeters A. Trends in child and adolescent obesity prevalence according to socioeconomic position: Protocol for a systematic review. *Syst Rev* 2014;3:1-4.
71 Moher D, Tsertsvadze A, Tricco AC, Eccles MG, J., Sampson M, Barrowman N. A systematic review identified few methods and strategies describing when and how to update systematic reviews. *J Clin Epidemiol* 2007;60:1095.
72 Eipe N, Penning J, Ansari M, Yazdi F, Ahmadzai N. A protocol for a systematic review for perioperative pregabalin use. *Syst Rev* 2012;1:40.
73 Honein-Abouhaidar GN, Kastner M, Vuong V, Perrier L, Rabeneck L, Tinmouth J, et al. Benefits and barriers to participation in colorectal cancer screening: A protocol for a systematic review and synthesis of qualitative studies. *BMJ Open* 2014;4:e004508.
74 Counsell C. Formulating questions and locating primary studies for inclusion in systematic reviews. *Ann Intern Med* 1997;127:380-7.
75 Whitlock EP, Lopez SA, Chang S, Helfand M, Eder M, Floyd N. AHRQ series paper 3: Identifying, selecting, and refining topics for comparative effectiveness systematic reviews: AHRQ and the effective health-care program. *J Clin Epidemiol* 2010;63:491.
76 Hamel C, Stevens A, Singh K, Ansari MT, Myers E, Ziegler P, et al. Do sugar-sweetened beverages cause adverse health outcomes in adults? A systematic review protocol. *Syst Rev* 2014;3:108.
77 Higgins JPT and Green S, eds. *Cochrane handbook for systematic reviews of interventions* . version 5.0.2. Cochrane Collaboration, 2009.
78 Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, et al. GRADE guidelines: 5. rating the quality of evidence-publication bias. *J Clin Epidemiol* 2011;64:1277-82.
79 Adams D, Wu T, Yasui Y, Aung S, Vohra S. Systematic reviews of TCM trials: How does inclusion of Chinese trials affect outcome? *J Evid Based Med* 2012;5:89-97.
80 Hopewell S, McDonald S, Clarke Mike J, Egger M. *Grey literature in meta-analyses of randomized trials of health care interventions* . John Wiley & Sons, 2007.
81 Van Enst WA, Scholten RJPM, Hooft L. Identification of additional trials in prospective trial registers for cochrane systematic reviews. *PloS One* 2012;7:e42812.
82 Tricco A, Chit A, Hallett D, Soobiah C, Meier G, Chen M, et al. Effect of influenza vaccines against mismatched strains: A systematic review protocol. *Syst Rev* 2012;1:35.
83 Horsley T, Dingwall O, Sampson M. Checking reference lists to find additional studies for systematic reviews. *Cochrane Database Syst Rev* 2011;(8):MR000026.
84 Zhang L, Sampson M, McGowan J. Reporting of the role of the expert searcher in cochrane reviews. *Evid Based Libr Inf Pract* 2006;1:3-16.
85 Lefebvre C, Manheimer E, Glanville J, Cochrane Information Retrieval Methods Group. Searching for studies. In: Higgins JPT, Green S, eds. *Cochrane handbook for systematic reviews of interventions* . 5.1.0 ed. Cochrane Collaboration, 2011.
86 Relevo R, Balshem H. Finding evidence for comparing medical interventions. In: *Methods guide for effectiveness and comparative effectiveness reviews* . AHRQ Publication No 10(12)-EHC063-EF. Agency for Healthcare Research and Quality, 2012.
87 Daboval T, Ward N, Sampson M, Kharrat A. Antenatal counseling about the perinatal care plan at the limit of viability: What do parents want? A systematic review protocol. (unpublished).
88 McGowan J, Sampson M, Lefebvre C. An evidence based checklist for the peer review of electronic search strategies (PRESS EBC). *Evid Based Libr Inf Pract* 2010;5:149-54.
89 Deeks JJ, Altman DG. Inadequate reporting of controlled trials as short reports. *Lancet* 1998;352:1908.
90 Iansavichene AE, Sampson M, McGowan J, Ajiferuke ISY. Should systematic reviewers search for randomized, controlled trials published as letters? *Ann Intern Med* 2008;148:714-5.
91 Sampson M, McGowan J, Cogo E, Grimshaw J, Moher D, Lefebvre C. An evidence-based practice guideline for the peer review of electronic search strategies. *J Clin Epidemiol* 2009;62:944-52.
92 Elamin MB, Flynn DN, Bassler D, Briel M, Alonso-Coello P, Karanicolas PJ, et al. Choice of data extraction tools for systematic reviews depends on resources and review complexity. *J Clin Epidemiol* 2009;62:506-10.
93 Tramèr MR, Reynolds DJM, Moore RA, McQuay HJ. Impact of covert duplicate publication on meta-analysis: a case study. *BMJ* 1997;315:635-40.
94 Von Elm E, Poglia G, Walder B, Tramer MR. Different patterns of duplicate publication. *JAMA* 2004;291:974-80.
95 Gøtzsche P. Multiple publication of reports of drug trials. *Eur J Clin Pharmacol* 1989;36:429-32.
96 Macdonald G, McCartan CJ. Centre-based early education interventions for improving school readiness. *Cochrane Database Syst Rev* 2014;(1):CD010913.
97 Edwards P, Clarke M, DiGuiseppi C, Pratap S, Roberts I, Wentz R. Identification of randomized controlled trials in systematic reviews: Accuracy and reliability of screening records. *Stat Med* 2002;21:1635-40.
98 Cooper H, Ribble RG. Influences on the outcome of literature searches for integrative research reviews. *Sci Commun* 1989;10:179-201.
99 Busse JW, Ebrahim S, Connell G, Coomes EA, Bruno P, Malik K, et al. Systematic review and network meta-analysis of interventions for fibromyalgia: A protocol. *Syst Rev* 2013;2:18.
100 Buscemi N, Hartling L, Vandermeer B, Tjosvold L, Klassen TP. Single data extraction generated more errors than double data extraction in systematic reviews. *J Clin Epidemiol* 2006;59:697-703.
101 Horton J, Vandermeer B, Hartling L, Tjosvold L, Klassen TP, Buscemi N. Systematic review data extraction: Cross-sectional study showed that experience did not increase accuracy. *J Clin Epidemiol* 2010;63:289-98.
102 Jones AP, Remmington T, Williamson PR, Ashby D, Smyth RL. High prevalence but low impact of data extraction and reporting errors were found in cochrane systematic reviews. *J Clin Epidemiol* 2005;58:741-2.
103 Shadish WR, Brasil ICC, Illingworth DA, White KD, Galindo R, Nagler ED, et al. Using UnGraph to extract data from image files: Verification of reliability and validity. *Behav Res Methods* 2009;41:177-83.
104 Stewart LA. Practical methodology of meta?analyses (overviews) using updated individual patient data. *Stat Med* 2007;14:2057-79.
105 Clarke M, Hopewell S, Juszczak E, Eisinga A, Kjeldstrom M. Compression stockings for preventing deep vein thrombosis in airline passengers. *Cochrane Database Syst Rev* 2006;(2):CD004002.

106 Glasziou P, Meats E, Heneghan C, Shepperd S. What is missing from descriptions of treatment in trials and reviews? *BMJ* 2008;336:1472.
107 Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *BMC Med* 2010;8:18.
108 Higgins JPT, Deeks JJ. Selecting studies and collecting data. In: Higgins JPT, Green S, eds. *The Cochrane handbook for systematic reviews of interventions* . 5.1.0 ed. Cochrane Collaboration, 2011.
109 Errami M, Sun Z, Long TC, George AC, Garner HR. Deja vu: A database of highly similar citations in the scientific literature. *Nucleic Acids Res* 2009;37(suppl 1):D921-4.
110 Reichenbach S, Rutjes AWS, Nüesch E, Trelle S, Jüni P. Arthroscopic lavage for osteoarthritis of the knee. Cochrane Library. 2008, doi:10.1002/14651858.CD007320.
111 Tully PJ, Baumeister H. Collaborative care for the treatment of comorbid depression and coronary heart disease: A systematic review and meta-analysis protocol. *Syst Rev* 2014;3:127.
112 Dwan K, Gamble C, Kolamunnage-Dona R, Mohammed S, Powell C, Williamson P. Assessing the potential for outcome reporting bias in a review: A tutorial. *Trials* 2010;11:52.
113 Leucht C, Huhn M, Leucht S. Amitriptyline versus placebo for major depressive disorder (protocol). *Cochrane Database Syst Rev* 2011;(5):CD009138.
114 Helfand M, Balshem H. AHRQ series paper 2: Principles for developing guidance: AHRQ and the effective health-care program. *J Clin Epidemiol* 2010;63:484.
115 Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep* 1991;14:540-5.
116 Johns MW. Reliability and factor analysis of the Epworth sleepiness scale. *Sleep* 1992;15:376-81.
117 Selby JV, Beal AC, Frank L. The Patient-Centered Outcomes Research Institute (PCORI) national priorities for research and initial research agenda. *JAMA* 2012;307:1583-4.
118 Methodology Committee of the Patient-Centered Outcomes Research Institute (PCORI). Methodological standards and patient-centeredness in comparative effectiveness research: The PCORI perspective. *JAMA* 2012;307:1636-40.
119 Cordoba G, Schwartz L, Woloshin S, Bae H, Gotzsche PC. Definition, reporting, and interpretation of composite outcomes in clinical trials: systematic review. *BMJ* 2010;341:c3920.
120 Page MJ, McKenzie JE, Forbes A. Many scenarios exist for selective inclusion and reporting of results in randomized trials and systematic reviews. *J Clin Epidemiol* 2013;66:524-37.
121 Hosseini Araghi M, Chen YF, Jagielski A, Mannan Choudhury S, Banerjee D, Thomas GN, et al. Weight loss intervention through lifestyle modification or pharmacotherapy for obstructive sleep apnoea in adults (protocol). *Cochrane Database Syst Rev* 2012;(12):CD010281.
122 Lawley CM, Lain SJ, Algert CS, Ford JB, Figtree GA, Roberts CL. Prosthetic heart valves in pregnancy: A systematic review and meta-analysis protocol. *Syst Rev* 2014;3:8.
123 Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
124 Viswanathan M, Ansari MT, Berkman ND, Chang S, Hartling L, McPheeters M, et al. Assessing the risk of bias of individual studies in systematic reviews of health care interventions. *AHRQ Methods for Effective Health Care* 2012 Mar 08.
125 Hartling L, Hamm MP, Milne A, Vandermeer B, Santaguida PL, Ansari M, et al. Testing the risk of bias tool showed low reliability between individual reviewers and across consensus assessments of reviewer pairs. *J Clin Epidemiol* 2013;66:973-81.
126 Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Control Clin Trials* 1996;17:1-12.
127 Berlin JA. Does blinding of readers affect the results of meta-analyses? *Lancet* 1997;350:185-6.
128 Moja LP, Telaro E, D'Amico R, Moschetti I, Coe L, Liberati A. Assessment of methodological quality of primary studies by systematic reviews: Results of the meta-quality cross sectional study. *BMJ* 2005;330:1053.
129 Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: Meta-epidemiological study. *BMJ* 2008;336:601-5.
130 Savović J, Harris RJ, Wood L, Beynon R, Altman D, Als-Nielsen B, et al. Development of a combined database for meta-epidemiological research. *Res Synth Methods* 2011;2:78.
131 Dechartres A, Boutron I, Trinquart L, Charles P, Ravaud P. Single-center trials show larger treatment effects than multicenter trials: Evidence from a meta-epidemiologic study. *Ann Intern Med* 2011;155:39.
132 Odgaard-Jensen J, Vist G, Timmer A, Kunz R, Akl E, Schünemann H, et al. Randomised controlled trials as a safeguard against biased estimates of treatment effects. *Cochrane Database Syst Rev* 2011;(4):MR000012.
133 Sanderson S, Tatt ID, Higgins JPT. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: A systematic review and annotated bibliography. *Int J Epidemiol* 2007;36:666-76.
134 Dechartres, A. Charles, P. Hopewell, S. Ravaud, P. Altman, D.G. Reviews assessing the quality or the reporting of randomized controlled trials are increasing over time but raised questions about how quality is assessed. *J Clin Epidemiol* 2011;64:136-44.
135 Jüni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999;282:1054-60.
136 Ioannidis JPA, Haidich AB, Pappa M, Pantazis N, Kokori SI, Tektonidou MG, et al. Comparison of evidence of treatment effects in randomized and nonrandomized studies. *JAMA* 2001;286:821-30.
137 Savovic J, Jones HE, Altman DG, Harris RJ, Juni P, Pildal J, et al. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Ann Intern Med* 2012;157:429-38.
138 Hróbjartsson A, Thomsen ASS, Emanuelsson F, Tendal B, Hilden J, Boutron I, et al. Observer bias in randomised clinical trials with binary outcomes: Systematic review of trials with both blinded and non-blinded outcome assessors. *BMJ* 2012;344:e1119.
139 Bell ML, Kenward MG, Fairclough DL, Horton NJ. Differential dropout and bias in randomised controlled trials: When it matters and when it may not. *BMJ* 2013;346:e8668.
140 Guyatt GH, Briel M, Glasziou P, Bassler D, Montori VM. Problems of stopping trials early. *BMJ* 2012;344:e3863.
141 Briel M, Bassler D, Wang AT, Guyatt GH, Montori VM. The dangers of stopping a trial too early. *J Bone Joint Surg* 2012;94(suppl 1):56-60.
142 DeAngelis CD FP. Impugning the integrity of medical science: The adverse effects of industry influence. *JAMA* 2008;299:1833-5.
143 Kahan BC, Morris TP. Analysis of multicentre trials with continuous outcomes: When and how should we account for centre effects? *Stat Med* 2013;32:1136-49.
144 Shephard RJ. Ethics in exercise science research. *Sports Med* 2002;32:169-83.
145 Fanelli D. How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data. *PLoS One* 2009;4:e5738.
146 Higgins J, Ramsay C, Reeves BC, Deeks JJ, Shea B, Valentine JC, et al. Issues relating to study design and risk of bias when including non-randomized studies in systematic reviews on the effects of interventions. *Res Synth Methods* 2012.
147 Mao C, Yang ZY, Chung VCH, Qin Y, Tam W, Kwong JSW, et al. Tong-xin-luo capsule for patients with coronary heart disease after percutaneous coronary intervention. *Cochrane Library* 2012.
148 Villar J, Mackey ME, Carroli G, Donner A. Meta-analyses in systematic reviews of randomized controlled trials in perinatal medicine: Comparison of fixed and random effects models. *Stat Med* 2001;20:3635-47.
149 Hunter JE, Schmidt FL. Fixed effects vs. random effects meta-analysis models: implications for cumulative research knowledge. *Int J Select Assess* 2002;8:275-92.
150 Schmidt FL, Oh IS, Hayes TL. Fixed- versus random-effects models in meta-analysis: model properties and an empirical comparison of differences in results. *Br J Math Stat Psychol* 2009;62:97-128.
151 Higgins J, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-60.
152 Higgins JPT, Deeks JJ, Altman DG. Special topics in statistics. In: Higgins JPT, Green S, eds. *Cochrane handbook for systematic reviews of interventions* . 5.1.0 ed. Cochrane Collaboration, 2011.
153 Stewart LA, Clarke M, Rovers M, Riley RD, Simmonds M, Stewart G, et al. PRISMA-IPD: an extension to the PRISMA statement guidance for reporting systematic review and meta-analysis of individual participant data. (submitted).
154 Thiessen PH, Barrowman N, Garg A. Imputing variance estimates do not alter the conclusions of a meta-analysis with continuous outcomes: A case study of changes in renal function after living kidney donation. *J Clin Epidemiol* 2007;60:228.
155 Stevens JW. A note on dealing with missing standard errors in meta-analyses of continuous outcome measures in WinBUGS. *Pharmaceut Stat* 2011;10:374-8.
156 Wiebe N, Vandermeer B, Platt RW, Klassen TP, Moher D, Barrowman NJ. A systematic review identifies a lack of standardization in methods for handling missing variance data. *J Clin Epidemiol* 2006;59:342-53.
157 Furukawa TA, Barbui C, Cipriani A, Brambilla P, Watanabe N. Imputing missing standard deviations in meta-analyses can provide accurate results. *J Clin Epidemiol* 2006;59:7.
158 Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials* 2007;8:16.
159 Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008;336:601-5.
160 Whitehead PJ, Drummond AE, Walker MF, Parry RH. Interventions to reduce dependency in personal activities of daily living in community-dwelling adults who use homecare services: protocol for a systematic review. *Syst Rev* 2013;2:1-7.
161 Greenhalgh T, Robert G, Macfarlane F, Bate P, Kyriakidou O, Peacock R. Storylines of research in diffusion of innovation: a meta-narrative approach to systematic review. *Soc Sci Med* 2005;61:417-30.
162 Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systematic reviews. a product from the ESRC methods programme. Version 1. ESRC, 2006.
163 Richards BL, Whittle SL, Buchbinder R. Neuromodulators for pain management in rheumatoid arthritis (protocol). *Cochrane Database Syst Rev* 2011;(1):CD008921.
164 Goodman S, Dickersin K. Metabias: A challenge for comparative effectiveness research. *Ann Intern Med* 2011;155:61-2.
165 Song F, Parekh S, Hooper L, Loke Y, Ryder J, Sutton A, et al. *Dissemination and publication of research findings: an updated review of related biases* . Prepress Projects, 2010.
166 Sterne JAC, Sutton AJ, Ioannidis JPA, Terrin N, Jones DR, Lau J, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:302.
167 Terrin N, Schmid CH, Lau J. In an empirical evaluation of the funnel plot, researchers could not visually identify publication bias. *J Clin Epidemiol* 2005;58:894-901.
168 Lau J, Ioannidis J, Terrin N, Schmid CH, Olkin I. The case of the misleading funnel plot. *BMJ* 2006;333:597-600.
169 Parekh-Bhurke S, Kwok CS, Pang C, Hooper L, Loke YK, Ryder JJ, et al. Uptake of methods to deal with publication bias in systematic reviews has increased over time, but there is still much scope for improvement. *J Clin Epidemiol* 2011;64:349-57.
170 Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. Selective publication of antidepressant trials and its influence on apparent efficacy. *N Engl J Med* 2008;358:252-60.
171 Turner EH, Knoepflmacher D, Shapley L. Publication bias in antipsychotic trials: An analysis of efficacy comparing the published literature to the us food and drug administration database. *PLoS Med* 2012;9:e1001189.
172 Williamson P, Gamble C, Altman D, Hutton J. Outcome selection bias in meta-analysis. *Stat Methods Med Res* 2005;14:515-24.
173 Chan AW, Altman DG. Identifying outcome reporting bias in randomised trials on PubMed: review of publications and survey of authors. *BMJ* 2005;330:753.
174 Williamson PR, Gamble C. Application and investigation of a bound for outcome reporting bias. *Trials* 2007;8:9.
175 Tharyan P, Kirubakaran R, Jabez P. The use of trial protocols to assess risk of bias due to selective reporting in cochrane systematic reviews: a cross-sectional survey. 18th Cochrane Colloquium and 10th Campbell Colloquium; Oct 18-22; Keystone, Colorado; 2010.
176 Hart B, Lundh A, Bero L. Effect of reporting bias on meta-analyses of drug trials: reanalysis of meta-analyses. *BMJ* 2012;344:d7202.
177 Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383-94.
178 Guyatt G, Oxman AD, Sultan S, Brozek J, Glasziou P, Alonso-Coello P, et al. GRADE guidelines. 11: Making an overall rating of confidence in effect estimates for a single outcome and for all outcomes. *J Clin Epidemiol* 2013;66:151-7.
179 Antman EM, Lau J, Kupelnick B, Mosteller F, Chalmers TC. A comparison of results of meta-analyses of randomized control trials and recommendations of clinical experts. treatments for myocardial infarction. *JAMA* 1992;268:240-8.
180 Oxman AD, Guyatt GH. The science of reviewing research. *Ann N Y Acad Sci* 1993;703:125.

181 Dickersin K. The existence of publication bias and risk factors for its occurrence. *JAMA* 1990;263:1385-9.
182 Begg CB. Publication bias: A problem in interpreting medical data. *J R Stat Soc A* 1988;151:419-63.
183 Hopewell S, Loudon K, Clarke MJ, Oxman AD, Dickersin K. Publication bias in clinical trials due to statistical significance or direction of trial results. *Cochrane Database Syst Rev* 2009;(1):MR000006.
184 Dickersin K, Chalmers I. Recognizing, investigating and dealing with incomplete and biased reporting of clinical research: from Francis Bacon to the WHO. *J R Soc Med* 2011;104:532-8.
185 Dickersin K. Publication bias: recognizing the problem, understanding its origins and scope, and preventing harm. In: Rothstein HR, Sutton AJ, Borenstein M, eds. *Publication bias in meta-analysis—Prevention, assessment and adjustments* . John Wiley & Sons, 2005:11-33.
186 Williamson PR, Gamble C, Altman DG, Hutton JL. Outcome selection bias in meta-analysis. *Stat Methods Med Res* 2005;14:515-24.

Cite this as: *BMJ* 2015;350:g7647

Tables

Table 1| Proposed stakeholders, actions, and potential benefits for supporting adherence to PRISMA-P

Stakeholder	Proposed action	Potential benefits
Funders	Promote or mandate adherence to PRISMA-P or use PRISMA-P as a template for systematic review proposals for grant applications	Improved quality, completeness, and consistency of systematic review proposals Standardized protocol content will improve peer review efficiency and investigator understanding of requirements
Systematic reviewers, groups, or organizations	Use or adhere to PRISMA-P during protocol development	Improved quality, completeness, and consistency of protocol content Enables reviewers to anticipate and avoid future changes to review methods (that is, outcomes) Increased awareness of minimum content for protocol reporting Improved completeness of reporting of completed reviews
PROSPERO (and other review registries)	Encourage the development of PRISMA-P based protocols	Improved quality of registry entries Improved consistency across registry entries, protocols, and systematic reviews
Practice guideline developers	Use PRISMA-P to gauge the completeness of protocols and facilitate detection of selective reporting when considering reviews for guideline inclusion	Enables easy comparison across protocols, registry entries, and completed systematic reviews
Policymakers	Advocate use of PRISMA-P by those funding and conducting systematic reviews	May yield better quality, more complete, and more consistent reviews to inform decision making
Journal editors	Encourage compliance with PRISMA-P for authors submitting protocols for publication Offer PRISMA-P as a template to assist in protocol writing for publication	Improved quality, completeness, and consistency of protocols over those published in journals not endorsing PRISMA-P Increased efficiency in protocol peer and author understanding of journal requirements Improved transparency of reviews and interpretation by readers
Educators	Use PRISMA-P as a training tool Encourage adherence in students submitting protocols for coursework	Simplified teaching and grading of protocols Improved quality, completeness, and consistency of protocol content
Students	Develop protocols for coursework or research using PRISMA-P	Improved understanding of the minimum protocol content Well trained systematic reviewers entering the workforce

Table 2| PRISMA-P (preferred reporting items for systematic review and meta-analysis protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item
Administrative information		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
Introduction		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
Methods		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

Table 3| **AHRQ process for dealing with protocol amendments. Changes made to the protocol should not be incorporated throughout the various sections of the protocol. Instead, protocol amendments should be noted only in section VII of the protocol, preferably in a tabular format (see example below), and the date of the amendment noted at the top of the protocol (from http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=1724&pageaction=displayproduct)**

Date	Section	Original protocol	Revised protocol	Rationale
This should be the effective date of the change in protocol	Specify where the change would be found in the protocol	Describe language of the original protocol	Describe the change in protocol	Justify why the change will improve the report. If necessary, describe why the change does not introduce bias. Do not use justification such as, "because the AE/TOO/TEP/Peer reviewer told us to do so," but explain what the change hopes to accomplish