How to write a paper – systematic review

Note please see "Advice on how to write a paper" for information on general aspects of manuscript preparation, which should be read before you start to write up your systematic review.

A systematic review is a piece of research – an experiment - in its own right that you do to establish whether a hypothesis is correct or not. Therefore the first step is to prepare a protocol describing the aims and objectives of the experiment and the methods. The protocol will help to keep you on the right track as you go through the literature.

Systematic review methodology can be applied to any type of literature – epidemiological, randomised trials, observational studies, diagnostic tests, etc – the principals are the same although the search strategy, study assessment criteria, data extraction, and statistical analysis methods differ in some cases. Checklists for assessing the quality of papers in each type of review are given on the Equator Network (www.equator-network.org/).

Hypothesis – test a is better than test b; or treatment a is better than treatment b; or animals with feature a have a shorter lifespan than animals with feature b.

Aim – to determine whether, and in what circumstances, treatment a is better than treatment b in acute ischaemic stroke

Objectives – to identify all randomised controlled trials testing treatment A versus B in patients with acute ischaemic stroke; to assess the quality of those trials; to determine the total number of patients included in such trials to date, and their characteristics; to determine whether treatment a works better than conventional treatment; to identify gaps in knowledge where new trials are needed, etc

Method –

- what information are you looking for – the type of study (techniques, what patients, etc) – be very specific and make sure that the type of data that you are looking for will be relevant to your research question and that you have not "drifted" off the topic
- how and where to look – search strategy; time span; what literature databases; what languages; what journals to hand search; searching of reference lists in review articles, etc.
- inclusion and exclusion criteria – what criteria will a paper have to meet for it to be included, and vice versa excluded?
- what information to extract – minimum criteria for inclusion; quality assessment of studies; actual results; raw data and data presented as associations or correlations or odds ratios, etc
- design your data extraction form – do this in sections so that you can do an early evaluation of a paper for key points on which it would either be included or not, so that you do not waste a large amount of time on papers that are unlikely to provide useful data. Sometimes you can decide whether to include a paper very quickly, but often you are faced with a large pile of literature that you have to whittle down as quickly as possible, therefore you have to identify the promising papers quickly and put them to one side for later more detailed evaluation – some will later turn out not to be includable, but at this stage it is better to be over inclusive than to risk missing key papers through overzealous rejection before you have had a chance to go through them in detail.
- primary and other outcomes – primary outcomes, secondary outcomes and subgroup analyses need to be pre-specified (just like for a primary experiment) - older people; people with a particular characteristic, etc.
- how are you going to present the data: summary tables, odds ratios in forest plots, etc
- how to analyse – this will depend on the type of review you are doing but in the case of diagnostic tests is would include sensitivity; specificity; likelihood ratios; receiver-operator characteristic curves; in the case of treatment reviews, it would be odds ratios; in the case of epidemiological or observational studies it might be standardised or weighted or normalised mean difference plus 95% CI.[1,2]

As you are doing the work, you MUST keep an accurate record of all the titles, abstracts and papers that you screened so that you can produce an accurate flow diagram to show how many potentially relevant papers you found at each stage of the search and evaluation process and how many were rejected at each stage.

You MUST also record why you rejected papers, eg because they were about animal studies and you only wanted human data, etc.

To make this part of the process manageable, it is best to record your reasons for rejection or inclusion in a database with a set of standard reasons (eg wrong topic, wrong patients, retrospective not prospective, etc). If you have all this information recorded as you go along, it makes it much easier when you have to go back and check what you did and whether you extracted the data correctly (as you will inevitably have to do) later on.

Writing up a systematic review is best done in a clear structured way so that the (often) large amount of data can be described accurately and succinctly. You must follow a structured approach, otherwise you will miss important data it put it in the wrong order. Note that additional general guidance on writing scientific papers is available from the International Committee of Medical Journal Editors (http://www.icmje.org/manuscript_1prepare.html) and on The Equator Network (www.equator-network.org/) which you are **strongly advised** to consult (in addition to the accompanying document "Advice on how to write a paper").

Title – should accurately reflect the topic of the review

Abstract - Systematic reviews must have a structured abstract – background, methods, results, conclusion, just like any other paper

Introduction – This is the reader's first exposure to the subject matter and so the introduction should summarise the topic area and say why a systematic review was necessary – for example, was there disagreement in the literature, were there gaps in common knowledge that might actually be filled by a thorough summary of the literature, was the size of the effect of a treatment unclear, or was the treatment being used in situations outside evidence from trials?. The introduction should be normally no longer than a couple of pages (ideally shorter) and the briefer the better. If there have been previous review articles or even systematic reviews, say why another one is necessary.

The introduction should end with a sentence which states clearly the aims of the review; be careful not to duplicate statements made elsewhere.

Methods – You must structure your methods in a logical order.

- Criteria for including studies: Describe the studies which you would include, e.g. prospective study in a particular population testing a particular treatment. In this section use subheadings for example who were the patients/subjects/animals; what were the interventions/characteristic sought; what were the outline outcome measures and indicate which were primary or secondary; what were the study characteristics. Here you might mention certain features that the studies had to report such as the sample size, the primary results, whether there was any language restriction or years within in which the studies had to be done and if they had to be published in full or not.
- Identification of studies: Here you would detail your electronic database search including which databases (Medline, EMBASE, ISI Web of Knowledge, Google Scholar, etc), between which years. Provide a list of search terms in an appendix. You would also detail which journals you hand searched and if you screened review articles and other bibliographies.
- Study selection: Here you would describe how you handled all the studies that you identified, removing duplicates, screening for relevance on title then abstract then full text article; whether you wrote to the author for copies of their paper or used inter-library loan and then screening of the full papers that got through all of these eligibility checks.
- Data extraction: Here you would describe what data you extracted from the paper such as description of included patients/subjects/animals, how many had which outcome, what the summary statistics were as given in the paper, whether you read data off graphs if not provided numerically and what you did if serial results were reported, i.e. which one did you choose. Also mention whether you contacted authors about missing data and what you did with the extracted data (e.g. enter into database).

- Quality assessment: Quality assessment criteria have been described for most types of literature and many of these are available on the EQUATOR Network (www.equator-network.org/) which you should consult. There are ten point comparisons for various types of data (see end).
- Data analysis: Here you should describe how you handled the data. What you do with the data may very much depend on what you have been able to extract from the individual papers. In a treatment review it would be typical to calculate odds ratios for each outcome with 95% confidence intervals, P values for the magnitude of effect and perform test of heterogeneity to see if the studies were all giving broadly the same answer or if there was significant variation between the studies. Analysis may also be influenced by the amount of data that you have. You might in an observational study calculate a standardised mean difference or a weighted mean difference or a normalised mean difference. You also need to assess heterogeneity and you would do this for each outcome. You may sort your studies or outcomes into different subtypes to see whether this reduces any heterogeneity for example in a systematic review of a treatment you might sort the studies by dose or by time of administration after onset of disease or time of assessment of outcome, etc. You can then test differences between groups as well as seeing whether heterogeneity within each group has disappeared.

Results – It is also extremely important that you describe the results in a logical order.

- The results of your search: Say how many studies your literature search identified from each database and by other searching methods, how many were duplicates, how many were excluded on the basis of screening of an abstract, how many full text articles were assessed and of them how many were excluded until you arrive at your final number of included papers. Note this is where you would say how many papers were not included because they were published in another language and translation was not available.
- Study range and characteristics: Here you describe how many patients/subjects/animals were included in those included studies including the mean or median and range. Indicate the type of patients/subjects/animals that were included such as an age range or disease severity range. Indicate other key study methodological features such as any variation in outcome measure. If you are doing a treatment review of a particular class of drug you should say how many different individuals drugs within that class were studied in the included papers. Note you need to be careful that the same patients/subjects/animals have not included in multiple publications as this would artificially inflate your systematic review sample size. If in doubt about duplicate publications you need to exclude patients from one of the apparently duplicate publications or only use the number given in the most recent publication from that group. You need to state what the total number of actual individual studies was within the total number of papers identified. Much of the study characteristics can be usefully presented in graphs or tables thus cutting down the amount of text required.
- Study quality and potential sources: Here you would report the median quality score derived from the appropriate quality assessment method and indicate which quality score points were particularly poorly done in the studies. You can also use study quality score to see whether any apparent heterogeneity between studies for outcome results can be explained by inclusion or exclusion of poor quality studies.
- Effect of intervention on outcome: Here you describe the actual results of your meta-analysis or whatever approach was taken to estimate the overall effect across the different studies. For example you would describe odds ratios for each outcome if in a treatment review or mean differences if in an observational study in order of primary outcome, secondary outcome and then subgroup analyses. You'd then also describe exploring any potential reasons for heterogeneity and what that showed. You would also present the results of any funnel plot performed to identify publication bias.

Discussion - As with any other type of paper your discussion needs to follow logical order and start with a simple statement summarising the major finding from your review. For example is the weight of evidence in favour of a treatment having a beneficial effect or not? Do the studies suggest that some particular feature is associated with future risk of a disease? Is one diagnostic test better than another? If you have found that there is simply not enough evidence to arrive a definite conclusion then you should state that.

The second paragraph should describe limitations of the included studies and of your systematic review and hence the reliability of result – robustness, biases, etc. were there specific problems with the data (amount, populations, etc). Were the individual papers full of biases? Etc.

The third paragraph should describe the strengths and weaknesses of your review methods. For example, did you miss out non-english publications? Were there only a handful of papers with a small sample size that you were able to include?

The fourth paragraph should set the results in context of other knowledge on the topic, eg compare your work with previous systematic reviews or current opinions and guidelines

The fifth paragraph should provide conclusions, and then any implications for current practice and particularly for future research. Has the review highlighted gaps in knowledge that future studies should address? Is there enough information on which to base clinical practice?

Acknowledgements You must acknowledge funding agencies and grant numbers, and any people who have helped you but not to the point that they merit authorship.

References: Check the journal requirements first as each journal has particular requirements. The two commonest systems are the Harvard (names) or Vancouver (Numbering) systems are most commonly used. You should use a reference programme like Reference Manager or Endnote for storing, retrieving and sorting references and putting them into your manuscript. To try any other way of referencing a manuscript is a complete waste of time and will just result in errors. Also by the time it comes to writing a thesis or a really large report you will need to have references so that you can easily manipulate them, change the order, etc.

Tables: should be placed on separate pages at the end of the manuscript. Each needs a Legend and any abbreviations should be explained. A good rule of thumb is to consider whether the table would make sense if it were on its own (ie not in the paper). The title and legend should make it very clear what the table is about and any symbols or abbreviations should be explained in footnotes. Please see the International Committee of Medical Journal Editors (http://www.icmje.org/manuscript_1prepare.html) for advice on use of table superscripts.

Figures: should be placed on separate pages at the end of the manuscript. Each needs a Legend and any abbreviations should be explained. A good rule of thumb is to consider whether the figure would make sense if it were on its own (ie not in the paper). You may want to display some information as a bar chart, e.g the proportion of papers meeting each study quality characteristic, or the proportions of patients with particular characteristics in each paper, etc. In a systematic review, it is helpful to display the main results, ie the odds ratios or risk differences or sensitivity and specificity, etc, graphically in a forest plot or equivalent. You may also need to do a funnel plot to text for publication bias. Note journals vary in their figure format requirements. Please see the International Committee of Medical Journal Editors (http://www.icmje.org/manuscript_1prepare.html) for advice on figure preparation and check your target journal's requirements early on.

Appendix – study quality assessment criteria for different types of study.

See ***The Equator Network*** (www.equator-network.org/) : *"Reporting guidelines are statements that provide advice on how to report research methods and findings. Usually in the form of a checklist, flow diagram or explicit text, they specify a minimum set of items required for a clear and transparent account of what was done and what was found in a research study, reflecting in particular issues that might introduce bias into the research.*
Most widely recognised guidelines are based on the available evidence and reflect consensus opinion of experts in a particular field, including research methodologists and journal editors.
Reporting guidelines complement advice on scientific writing, which concentrates on the basic writing principles and styles of research reports and publications, and journals' instructions to authors."

A brief summary of the key reporting checklists by type of study follows. Please also see The Equator Network for general guidance on writing scientific papers, and other specific reporting guidelines not reproduced here, such as MOOSE (Epidemiological studies), CONSORT (for reporting of clinical trials), and for cost effectiveness analyses etc.

Studies evaluating experimental models
Collaborative Approach to Meta-Analysis and Review of Animal Data in Experimental Stroke (CAMARADES)[3]

A ten item checklist for assessing quality of studies in experimental models

1. Publication in a peer-review journal
2. Statement of control of temperature
3. Randomisation to treatment or control
4. Blinded induction of ischaemia
5. Blinded assessment of outcome
6. Avoidance of anaesthetic with marked intrinsic neuroprotective activity
7. Use of animals with hypertension or diabetes
8. Sample size calculation
9. Statement of compliance with regulatory requirements
10. Statement regarding possible conflicts of interest

A single point is awarded for each item that the study meets on the checklist.

Studies evaluating observational cohort, case control and cross-sectional studies

Studies evaluating randomised trials and meta-analyses of randomised trials (STROBE)[4] –

Checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Studies evaluating potential biomarkers for disease prognosis - REMARK Guidelines: described for tumour growth but sensible and useful guide to any study assessing a putative biomarker for disease prognosis.[5]

Guidelines for reporting Industry sponsored medical research – GPP2 Guidelines.[6]

Studies evaluating diagnostic tests

Standards for Reporting of Diagnostic Accuracy (STARD) criteria:[7] www.consort-statement.org/initiatives/newstard.htm

To improve the quality of reporting of diagnostic accuracy studies – 25 criteria on checklist

Section and Topic	Item		On page
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy(recommend MeSH heading 'sensitivity and specificity').	
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	
METHODS			
Participants	3	Describe the study population: The inclusion and exclusion criteria, setting and locations where the data were collected.	
	4	Describe participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the (evaluated) index tests or the (golden) reference standard?	
	5	Describe participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in items 3 and 4? If not, specify how participants were further selected.	
	6	Describe data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	
Test methods	7	Describe the reference standard and its rationale.	
	8	Describe technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	
	9	Describe definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	
	10	Describe the number, training and expertise of the persons executing and reading the index tests and the reference standard.	
	11	Describe whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	
Statistical methods	12	Describe methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	
	13	Describe methods for calculating test reproducibility, if done.	
RESULTS			
Participants	14	Report when study was done, including beginning and ending dates of recruitment.	
	15	Report clinical and demographic characteristics of the study population (e.g. age, sex, spectrum of presenting symptoms, co morbidity, current treatments, recruitment centers).	
	16	Report the number of participants satisfying the criteria for inclusion that did or did not undergo the index tests and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended).	
Test results	17	Report time interval from the index tests to the reference standard, and any treatment administered between.	
	18	Report distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	
	19	Report a cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	

	20	Report any adverse events from performing the index tests or the reference standard.	
Estimates	21	Report estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	
	22	Report how indeterminate results, missing responses and outliers of the index tests were handled.	
	23	Report estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	
	24	Report estimates of test reproducibility, if done.	
DISCUSSION	25	Discuss the clinical applicability of the study findings.	

STARD checklist 20091112 http://www.stard-statement.org/

Source of Bias:	Solution:
• *publication bias*	• *include unpublished trials*
• *language of publication*	• *include all languages*
• *published or individual patient data?*	• *include individual patient data wherever possible*
• *sample size*	• *larger sample = more reliable*
• *methods of included trials*	• *ensure truly randomised, blinded assessment , relevant outcome measures, etc*

A simplified checklist for diagnostic studies:

1. Prospective not retrospective
2. Patient selection consecutive or random
3. Adequate detail of study population (age, sex, clinical presentation, indication for Ix)
4. Adequate detail of imaging technique (sufficient for study to be replicated
5. Inclusion of all Ix, not just the nice images
6. Blinding of image assessment
7. Adequate detail of how images interpreted, eg method of carotid stenosis measurement
8. Adequate data on measurement reproducibility
9. Study powered according to sample size calculation

Quality Assessment of Diagnostic Accuracy Studies (QUADAS) :[8] http://www.biomedcentral.com/1471-2288/3/25
Includes 14 criteria, very similar to the above nine

Randomised trials and meta-analyses of randomised trials

Preferred reporting items for systematic reviews and meta-analyses (PRISMA)[9,10]

Replaces QUORUM for assessing randomised trials – deals with both original papers and systematic reviews of randomised trials.

TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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