

Systematic review

Please complete all mandatory fields below (marked with an asterisk *) and as many of the non-mandatory fields as you can then click *Submit* to submit your registration. You don't need to complete everything in one go, this record will appear in your *My PROSPERO* section of the web site and you can continue to edit it until you are ready to submit. Click *Show help* below or click on the icon to see guidance on completing each section.

1. * Review title.

Give the working title of the review, for example the one used for obtaining funding. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.

Acronyms may be included in titles, but should not be used alone without expansion unless they are regarded as more usual than the expansion (e.g. HIV).

The title in this field must be in English. If the original title is in a different language the English version must be entered here, with the non-English version entered into the field labeled "Original Language Title".

If the final title of the review differs, this can be displayed in the Publication of Final Report Field.

Example: Systematic review and meta-analysis of recurrence and survival following pre- versus post-operative radiation in localized, resectable soft-tissue sarcoma.

2. Original language title.

For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

Example: Revisión sistemática y meta-análisis de la recurrencia y la supervivencia tras la fase de radiación en comparación con post-operatorio en el sarcoma localizados resecables de tejido blando.

3. * Anticipated or actual start date.

Give the date when the systematic review commenced, or is expected to commence.

For the purposes of PROSPERO, the date of commencement for the systematic review can be defined as any point after completion of a protocol but before formal screening of the identified studies against the eligibility criteria begins.

A protocol can be deemed complete when it is approved by a funder or the person commissioning the review; when peer review is complete; when the protocol is published or when the authors decide that it is complete and they do not anticipate any major revisions to the design of the systematic review.

This field may be edited at any time. All edits to published records will appear in the record audit trail. A brief explanation of the reason for changes should be given in the Revision Notes facility.

Example: 01 June 2011

4. * Anticipated completion date.

Give the date by which the review is expected to be completed. In the absence of an agreed contractual date, a realistic anticipated date for completion should be set. It can be modified should the schedule change. When this date is reached, the named contact will receive an automated email to ask them to provide an update on progress.

This field may be edited at any time. All edits will appear in the record audit trail. A brief explanation of the reason for changes should be given in the Revision Notes facility.

Example: 01 June 2011

5. * Stage of review at time of this submission.

Indicate the stage of progress of the review by ticking the relevant Started and Completed boxes. Additional information may be added in the free text box provided.

Please note: Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. Should evidence of incorrect status and/or completion date being supplied at the time of submission come to light, the content of the PROSPERO record will be removed leaving only the title and named contact details and a statement that inaccuracies in the stage of the review date had been identified.

This field should be updated when any amendments are made to a published record and on completion and publication of the review. If this field was pre-populated from the initial screening questions then you are not able to edit it until the record is published.

The review has not yet started: Yes

Review stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here (e.g. Funded proposal, protocol not yet finalised).

6. * Named contact.

The named contact acts as the guarantor for the accuracy of the information presented in the register record. This should be the lead reviewer or a representative of the review team. This person is also responsible for submitting details of any amendments while the review is ongoing and publication details after the review is completed. The named contact is the person to whom users of PROSPERO would send questions or comments.

This field is automatically populated from the named contact's signing in details. The named contact's name will be displayed in the public record.

Example: Dr Joseph Bloggs

N.B. To change the named contact for a published record, send details of the existing and new contact to crd-register@york.ac.uk

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:

7. * Named contact email.

Give the electronic mail address of the named contact. This may be a generic email address to which the named contact has access.

This field is automatically populated from the named contact's joining details, but can be changed if required. The email address supplied here will be displayed in the public record.

Examples: joseph.bloggs@city.ac.uk or research.secretary@city.ac.uk

8. Named contact address

PLEASE NOTE this information will be published in the PROSPERO record so please do not enter private information

Give the full postal address for the named contact. (N.B. This field is automatically populated from the named contact's joining details.)

This address will be displayed in the public record. If you do not wish it to appear in the public record delete the content of this field.

Example: Alcuin B Block, University of York, York, YO10 5DD, UK

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code. (N.B. This field is automatically populated from the named contact's joining details.)

This number will be displayed in the public record. If you do not wish it to appear in the public record delete the content of this field.

Example: +44 (0)10904 321040

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Example: Andalusian Agency for Health Technology Assessment (AETSA)

Organisation web address:

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong. **NOTE: email and country are now mandatory fields for each person.** Affiliation refers to groups or organisations to which review team members belong.

Review team members will be listed 'manuscript' style in the order entered in this list. The named contact will be automatically added to this field, but can be deleted if not a member of the review team. To place the named contact somewhere other than first in order, delete the automatic entry and enter members' details in the required order.

Membership of the review team and details of affiliations can be updated at any time. All edits will appear in the record audit trail.

Example: Mr Joseph Bloggs, Centre for Reviews and Dissemination, University of York, UK. Dr Jane Smith, Department of Health Sciences, University of York, UK. Prof. Steven Jones, Centre for Health Statistics, Medical Research Centre, Canada.

12. * Funding sources/sponsors.

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Include any unique identification numbers assigned to the review by the individuals or bodies listed.

Examples: NIHR HTA Programme (Project ref 09/13/02). The Terry Fox New Frontiers Program in Cancer (Ref 201006TFL). Funding provided by Amgen, Merck, Roche, and Sanofi-aventis.

Grant number(s)

13. * Conflicts of interest.

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review. The conflicts of interest listed should cover the review team as a whole, as well as individuals in the team.

Conflicts of interest arise when a team member or the team as a whole (e.g. because of the team's institution) has financial or personal relationships that may inappropriately influence (bias) their actions (such relationships are also known as dual commitments, competing interests, or competing loyalties). These relationships vary from being negligible to having great potential for influencing judgment. Not all relationships represent true conflict of interest.

On the other hand, the potential for conflict of interest can exist regardless of whether a person believes that the relationship affects his or her scientific judgment. Financial relationships (such as employment, consultancies, stock ownership, honoraria, and paid expert testimony) are the most easily identifiable conflicts of interest and the most likely to undermine the credibility of the review.

However, conflicts can occur for other reasons, such as personal relationships, academic competition, and intellectual passion. For the purposes of disclosure, the term "competing interest" should be considered synonymous with conflict of interest.¹

Example: The lead reviewer (JB) has given talks on this topic at workshops, seminars, and conferences for which travel and accommodation has been paid for by the organisers. The other authors declare that they have no known conflicts of interest.

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country are now mandatory fields for each person.**

Example: Dr Eric Porter, Oncologist, University Hospital, Brighton, UK. Clinical advisor.

15. * Review question.

State the question(s) to be addressed by the review, clearly and precisely. Review questions may be specific or broad. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS where relevant.

Example: How does pre-operative chemotherapy impact on survival of early stage non-small cell lung cancer compared to surgery alone?

16. * Searches.

State the sources that will be searched. Give the search dates, and any restrictions (e.g. language or publication period). Do NOT enter the full search strategy (it may be provided as a link or attachment.)

The search strategy reported in systematic review protocols should:

- Name all sources that will be used to identify studies for the systematic review.

Sources include (but are not limited to) bibliographic databases, reference lists of eligible studies and review articles, key journals, conference proceedings, trials registers, Internet resources and contact with study investigators, experts and manufacturers.

Systematic reviews typically use more than one database. Examples of electronic bibliographic databases include MEDLINE, EMBASE, PsycINFO. Other database sources include The Cochrane Library, Health Technology Assessment Database, and Web of Science.

- Search dates (from and to)
- Restrictions on the search including language and publication period
- Whether searches will be re-run prior to the final analysis

It is considered good practice for searches to be re-run just before the final analyses and any further studies identified, retrieved for inclusion.

- Whether unpublished studies will be sought

17. URL to search strategy.

Give a link to the search strategy or an example of a search strategy for a specific database if available (including the keywords that will be used in the search strategies).

Alternatively, an electronic file could be supplied which will be linked to from the Register record. This will be made publicly available from the published record immediately, or it can be held in confidence until the review has been completed, at which time it will be made publicly available.

Example: <http://www.biomedcentral.com/1756-0500/3/250>

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Examples: Type 2 diabetes. Physical activity in children.

19. * Participants/population.

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

Example:

Inclusion: Adults with schizophrenia (as diagnosed using any recognised diagnostic criteria).

Exclusion: Adolescents (under 18 years of age) and elderly people (over 70).

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed. This is particularly important for reviews of complex interventions (interventions involving the interaction of several elements). If appropriate, an operational definition describing the content and delivery of the intervention should be given.

Ideally, an intervention should be reported in enough detail that others could reproduce it or assess its applicability to their own setting. The preferred format includes details of both inclusion and exclusion criteria.

For reviews of qualitative studies give details of the focus of the review.

Example: Population-level tobacco control interventions are defined as those applied to populations, groups, areas, jurisdictions or institutions with the aim of changing the social, physical, economic or legislative environment to make them less conducive to smoking. These are approaches that mainly rely on state or institutional control, either of a link in the supply chain or of smokers' behaviour in the presence of others.

Examples include tobacco crop substitution or diversification, removing subsidies on tobacco production, restricting trade in tobacco products, measures to prevent smuggling, measures to reduce illicit cross-border shopping, restricting advertising of tobacco products, restrictions on selling tobacco products to minors, mandatory health warning labels on

tobacco products, increasing the price of tobacco products, restricting access to cigarette vending machines, restricting smoking in the workplace, and restricting smoking in public places. Such approaches could also form part of wider, multifaceted interventions in schools, workplaces or communities.³

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Control or comparison interventions should be described in as much detail as the intervention being reviewed. If the comparator is 'treatment as usual' or 'standard care', this should be described, with attention being paid to whether it is 'standard care' at the time that an eligible study was done, or at the time the review is done.

Systematic reviews of qualitative studies rarely have a comparator or control; stating 'Not applicable' is therefore acceptable.

Examples: Placebo. A group of hospital in-patients who were not exposed to the infectious agent.

22. * Types of study to be included.

Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria.

If different study designs are needed for different parts of the review, this should be made clear. Where qualitative evidence will be incorporated in or alongside a review of quantitative data, this should be stated.

Example: We will include randomised trials to assess the beneficial effects of the treatments, and will supplement these with observational studies (including cohort and case-control studies) for the assessment of harms.

23. Context.

Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

Include relevant details if these form part of the review's eligibility criteria but are not reported elsewhere in the PROSPERO record.

Examples: Studies in hospital accident and emergency departments. Research in low- and middle-income countries only will be included.

24. * Main outcome(s).

Give the pre-specified primary (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

For systematic reviews of qualitative studies give details of what the review aims to achieve.

Examples: Change in depression score from baseline to the last available follow-up, measured using the Beck Depression Inventory. Five year progression-free survival (measured from randomisation). Establishing the barriers and facilitators to smoking cessation in pregnancy.

* Measures of effect

25. * Additional outcome(s).

List the pre-specified secondary (additional) outcomes of the review, with a similar level of detail to that required for primary outcomes. Where there are no secondary outcomes please state 'None' or 'Not applicable' as appropriate to the review

Example: Apgar scores for the baby at 1 and 5 minutes after birth.

* Measures of effect

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Data extraction methods reported in systematic review protocols should include:

Study selection

- The number of reviewers applying eligibility criteria and selecting studies for inclusion in the systematic review (good practice suggests more than one individual) and how this will be done (e.g. whether two people will independently screen records for inclusion or whether one will screen and another check decisions) and whether researchers will be blinded to each other's' decisions.
- How disagreements between individual judgements will be resolved
- The software system or mechanism for recording decisions

Data extraction

- List which data will be extracted from study documents, including information about study design and methodology, participant demographics and baseline characteristics, numbers of events or measures of effect (where applicable). Alternatively, state how this information will be obtained from study investigators.
- The number of people extracting or checking received data (good practice suggests more than one individual) and how this will be done (e.g. whether two people will independently extract data or whether one will extract data and another person check the extracted data).
- How disagreements between individual judgements will be resolved
- How missing data will be handled including whether study investigators will be contacted for unreported data or additional details.
- The means of recording data (e.g. in an excel spreadsheet, in a software system such as Eppi Reviewer)
- Another relevant detail that should be included is the software or tool, if any, that will be used for data extraction and management. An example of such a software tool is the Systematic Review Data Repository-Plus

27. * Risk of bias (quality) assessment.

Describe the method of assessing risk of bias or quality assessment. State which characteristics of the studies will be assessed and any formal risk of bias tools that will be used.

Methods for assessing risk of bias reported in systematic review protocols should include:

- Which characteristics will be assessed (e.g. methods of randomisation, treatment allocation, blinding).
- Whether assessment will be done at study or outcome level
- The criteria used to assess internal validity, if formal a risk of bias assessment is planned (e.g. the Cochrane risk of bias tool, ROBINS, QUADAS).
- How the results of the assessment will inform data synthesis (where applicable).
- The number of reviewers that will be involved in the quality assessment
- How disagreements between reviewers judgements will be resolved

28. * Strategy for data synthesis.

Provide details of the planned synthesis including a rationale for the methods selected. This **must not be generic text** but should be **specific to your review** and describe how the proposed analysis will be applied to your data.

Data synthesis methods reported in systematic review protocols should be specific about how they apply to the review and data in question and include:

- Criteria under which the data will be synthesised (e.g. the minimum number of studies or level of consistency required for synthesis)
- Which data will be synthesised including outcomes and summary effect measures (e.g. risk ratios for progression free survival at 2 years)
- The formal method of combining individual study data including, as applicable, information about statistical models that will be fitted (e.g. risk ratios for individual studies will be combined using a random effects meta-analysis) or methods of synthesising qualitative data.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

Planned 'subgroup' analysis or investigation of potential effect modifiers in reported in systematic review protocols should include:

- The rationale for the investigation (why are differences anticipated, or why is it important to look separately at different types of study or individual)
- Clear definitions of which types of study or individual will be included in each group (e.g. study design such as randomised/ non-randomised trial, intervention type such as high dose/low dose drug, setting such as hospital/ home care, participant characteristics such as male/female, stage III/stage IV tumour, <18 years/ ≥18 years)
- Details of the planned analytic approach (e.g. meta-regression, tests of interaction between groups, logistic regression using individual-level data). Where applicable this should include details of statistical models to be used.

30. * Type and method of review.

Select the type of review and the review method from the lists below. Select the health area(s) of interest for your review.

N.B. The information required here relates to the topic and outcome of the systematic review rather than the methods to be used. It is used to facilitate accurate searching of the database.

Type of review

Cost effectiveness	No
Diagnostic	No
Epidemiologic	No
Individual patient data (IPD) meta-analysis	No
Intervention	No
Meta-analysis	No
Methodology	No
Narrative synthesis	No
Network meta-analysis	No
Pre-clinical	No
Prevention	No
Prognostic	No

Prospective meta-analysis (PMA)	No
Review of reviews	No
Service delivery	No
Synthesis of qualitative studies	No
Systematic review	No
Other	No
Health area of the review	
Alcohol/substance misuse/abuse	No
Blood and immune system	No
Cancer	No
Cardiovascular	No
Care of the elderly	No
Child health	No
Complementary therapies	No
Crime and justice	No
Dental	No
Digestive system	No
Ear, nose and throat	No
Education	No
Endocrine and metabolic disorders	No
Eye disorders	No
General interest	No
Genetics	No
Health inequalities/health equity	No
Infections and infestations	No
International development	No
Mental health and behavioural conditions	No
Musculoskeletal	No
Neurological	No

Nursing	No
Obstetrics and gynaecology	No
Oral health	No
Palliative care	No
Perioperative care	No
Physiotherapy	No
Pregnancy and childbirth	No
Public health (including social determinants of health)	No
Rehabilitation	No
Respiratory disorders	No
Service delivery	No
Skin disorders	No
Social care	No
Surgery	No
Tropical Medicine	No
Urological	No
Wounds, injuries and accidents	No
Violence and abuse	No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved.

England

33. Other registration details.

Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. (N.B. Registration details for Cochrane protocols will be automatically entered). If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

Example: The title for this review and the review protocol are recorded in the Campbell Library as Project 27

34. Reference and/or URL for published protocol.

Give the citation and link for the published protocol, if there is one. This may be to an external site such as a journal or organisational website. Alternatively an unpublished protocol may be deposited with CRD in pdf format. A link to this will be automatically added.

Example: Free C, Phillips G, Felix L, Galli L, Patel V, Edwards P. The effectiveness of M-health technologies for improving health and health services: a systematic review protocol. BMC Research Notes 2010, 3:250 doi:10.1186/1756-0500-3-250 <http://www.biomedcentral.com/1756-0500/3/250>.

No I do not make this file publicly available until the review is complete

35. Dissemination plans.

Give brief details of plans for communicating essential messages from the review to the appropriate audiences. Any knowledge transfer or implementation activities beyond publication of the final report that are planned should be included.

Example: In addition to producing a report for the funders of this review, which will be made available free of charge on their website, a paper will be submitted to a leading journal in this field. Furthermore, should the findings of the review warrant a change in practice, a one page summary report will be prepared and sent to lead clinicians and healthcare professionals in the National Health Service.

Do you intend to publish the review on completion?

No

36. Keywords.

Give words or phrases that best describe the review. Keywords will help users find the review in the Register (the words do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

The addition of keywords is particularly important for non-effectiveness reviews. These records are likely to contain fewer relevant terms in other fields such as comparators and outcomes.

Information specialists at the Centre for Reviews and Dissemination (CRD) will assign MeSH terms, which will appear in the public record.

Example: Systematic review; meta-analysis; recurrence; survival; radiation; resectable; soft-tissue; sarcoma.

37. Details of any existing review of the same topic by the same authors.

Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

Example: This review is an update of our earlier systematic review and economic model and is being undertaken in the light of the publication of significant new research which will assist in developing our model. The citation for the existing review is Fayter D, Nixon J, Hartley S, Rithalia A, Butler G, Rudolf M, Glasziou P, Bland M, Stirk L, Westwood M. A systematic review of the routine monitoring of growth in children of primary school age to identify growth-related conditions. *Health Technol Assess.* 2007;11(22):1-87.

38. * Current review status.

Review status should be updated when the review is completed and when it is published.

Select from the list below to indicate the current status of the review.

Use the free text box to provide an explanation of the status of the review.

Example: Discontinued: This review has been abandoned as we have been unable to secure adequate funding to proceed.

Review_Ongoing

39. Any additional information.

Provide any other information the review team feel is relevant to the registration of the review.

Example: This review is being undertaken as part of the planning for a randomised trial to compare all different types of radiotherapy for localised, resectable soft-tissue sarcoma.

40. Details of final report/publication(s).

This field should be left empty until details of the completed review are available.

Give the full citation for the final report or publication of the systematic review, including the URL where available.

This field may also be used to record the availability of an un-published final report, summary results etc.

Example: Toulis KA, Goulis DG, Venetis CA, Kolibianakis EM, Negro R, Tarlatzis BC, Papadimas I. Risk of spontaneous miscarriage in euthyroid women with thyroid autoimmunity undergoing IVF: a meta-analysis. Eur J Endocrinol. 2010 Apr;162(4):643- 52. Epub 2009 Dec 2. <http://eje-online.org/cgi/content/full/162/4/643>