University of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

Guidance notes for registering a systematic review protocol with PROSPERO

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www.crd.york.ac.uk/prospero

Contents

Registering a review on PROSPERO

PROSPERO is an international database of prospectively registered systematic reviews in health and social care. Key features from the review protocol are recorded and maintained as a permanent record in PROSPERO. The aim is to provide a comprehensive listing of systematic reviews registered at inception, to help avoid unplanned duplication. By promoting transparency in the process and enabling comparison of reported review findings with what was planned in the protocol PROSPERO also aims to minimise the risk of bias in systematic review.

PROSPERO has been developed and is managed by the Centre for Reviews and Dissemination (CRD) at the University of York and is funded by the UK's National Institute for Health Research (NIHR).

What does registration on PROSPERO involve?

Registration in PROSPERO involves the prospective submission and publication of key information about the design and conduct of a systematic review.

Registration on PROSPERO is free of charge. In return, registrants are accountable for the accuracy and updating of information submitted.

Inclusion criteria

PROSPERO includes details of any ongoing systematic review that has a health related outcome in the broadest sense. Reviews may be of interventions, diagnosis, service delivery, prognostic factors, risk factors, genetic associations, and epidemiological reviews relevant to health and social care, welfare, public health, education, crime, justice, and international development, as long as there is a health related outcome. Systematic review protocols registered on PROSPERO can include studies of any design. Work is underway to facilitate the inclusion of reviews of pre-clinical studies.

Reviews of methodological issues need to contain at least one outcome of direct patient or clinical relevance in order to be included in PROSPERO. The review may also contain a substantial component of methodological review, but this latter component alone is not sufficient for inclusion. For example: a comparison of tools for the diagnosis of a condition may look at how these are reported but as long as an element of assessment of the value of the tools was included and a clinician could use the results to choose the appropriate tool in a given circumstance, it would be included in PROSPERO. Simply looking at the reporting of and/or use of outcomes in research would not be included.

Systematic reviews of reviews will be accepted for registration as long as they meet all the standard PROSPERO eligibility criteria and the registration form includes complete systematic review methodology details.

Ideally reviews should be registered before screening against eligibility criteria commences. However, reviews are currently accepted for registration as long as they have not progressed beyond the completion of data extraction.

Scoping reviews and literature reviews are not eligible for inclusion in PROSPERO.

New Cochrane protocols are automatically uploaded. To avoid duplication of records, Cochrane protocols **should not** be registered separately with PROSPERO.

Submissions must be in English for practical reasons, but search strategies and protocols attached to a record may be in any language.

If you are in any doubt about the eligibility of your review, including the stage of progress please contact crd-register@york.ac.uk for advice.

Accessing and navigating the registration form

Obtain a username and password by following the 'Join' link in the top right hand corner of the PROSPERO website.

Once you have joined, you can 'Sign in' and then you will be able to select 'Register a review' in the left hand column. This opens a page that encourages you to check that your review will meet the inclusion criteria, if you are sure it does, click on 'Register a review'.

The 'Register a review' option opens a four page electronic registration form which has 22 required fields and 18 optional fields. 'Required' fields, marked with a red asterisk, must be completed before the Submit button can be accessed. You may save and exit the form at any time, and return at a later date to add or edit information by signing in and going to 'My PROSPERO records'.

Each page of the form has a: 'Save' button, changes are automatically saved when a field is exited, but the save button can be used at any time; a 'Validate this page' button, which will highlight any 'Required' fields that still need to be completed; and a 'Print' button, which will print a copy of the current page only. To print a copy of the whole form, use the 'Print review' button on the left hand side of the screen, next to the 'Submit' button.

The fields can be completed by cutting and pasting information from your protocol, or you can use the form to help develop your protocol. The form can be saved as a pdf or word processing document if you want to share with others working on the review before submitting.

Providing access to a protocol is not a substitute for entering data into the required fields. Most registrants complete the form in 60 minutes or less.

Brief guidance about the information required in each field is given in the form and more detailed information, with examples, is given below and can be accessed in the form itself by clicking on the 'more…' link next to each field.

When you are ready, the form can be sent to the PROSPERO administrators by clicking on Submit.

What happens after submitting a form

Access to your record is suspended during the administrative process. Receipt of submission is acknowledged in an automated email sent to the named contact.

Application forms are checked against the eligibility criteria for PROSPERO and for clarity of content before being approved and published on the register, returned to you for clarification or rejected. You should receive notification within five working days. If you do not, please contact crd-register@york.ac.uk

Once published on the register, the record will again become accessible for editing.

Making changes, amendments and updating a published record

Changes, amendments and updates can be made by signing in, going to My PROSPERO records and opening the form. Once the changes have been made, click the Submit button. You will be asked to give brief details of the changes made. The information entered here will appear in the public record and should inform users of the database of the nature of the changes made (e.g. removed one of the outcome measures; changed the anticipated completion date).

All submitted edits and changes to a PROSPERO record will be recorded, dated and be made available within the record audit trail. The most recent version will appear with previous versions accessible from dated links on the right hand side of the screen, with the revision notes.

What to do after completing a review and after publishing the findings

Records remain permanently on PROSPERO. Once the review is completed this information should be recorded in the record together with the anticipated publication date. The bibliographic reference and electronic links to publications should be added to the record by the authors. In the absence of a publication, details of availability of the review's unpublished results, or reasons for the termination of the review, should be documented. Reminder emails with detailed instructions on what to do, are sent on the anticipated completion and the anticipated publication dates.
Links to critical abstracts in the Database of Abstracts of Reviews of Effects (DARE) were added to records as appropriate.

Registering an update of a completed review

If you decide to update a completed review that has a PROSPERO record, you can access this by signing in and going to My PROSPERO records. You can make changes to the protocol and submit it as an update and it will be processed as for a new review. It is important to decide if you are updating a review, or in fact because of changes to the protocol, are doing a new review. The following definitions have been provided to help you decide.

What is an update of a review?

Updating a systematic review is a discrete event during which efforts are made to

identify and incorporate new evidence into a previously completed systematic review An ‘update’ may be any modified version of a review that includes the findings of a more recent search than the previously completed version of the review. It can still be considered an update even if the new search reveals no additional studies. Any newly identified studies should be assessed and, if appropriate, incorporated into the updated review. An update might also be an opportunity to conduct new analyses or add additional information to the review.

What constitutes a new review rather than an update?

It can be difficult to decide whether an update to a review is in fact a new review. There is little published guidance on this. PROSPERO adopts a pragmatic approach. If changes to the review questions or methods are so substantial that they require major changes to the original protocol, this should be regarded as a new review rather than an update. Examples that would constitute a new review:

- addition of new treatment comparisons e.g. direct comparison of different drugs, when the old review included only comparisons of drug with placebo;
- substantial changes to the population being studied e.g. adding adults to a review that was previously restricted to children;
- exclusion criteria in the old review become inclusion criteria in the new review;
- introduction of new analysis techniques e.g. a switch from aggregate data meta-analyses to individual participant meta-analyses.

If in doubt, a new record for a new review should be created. This will minimise the complexity of the editing to the original record in PROSPERO and make it easier for users to distinguish between the original review and the later version. Links between the new and original review can be added in the registration form.

Guide to completing the registration fields

The following guidance notes follow the format of the registration form, which has four sections. The guidance includes a description and example of what is required for each of the fields within each section.

SPECIAL NOTES:
We accept information in good faith and rely upon the integrity of researchers to ensure the validity of <u>all</u> the data presented in PROSPERO records. Action will be taken if inaccuracies in data, particularly stage of review and anticipated completion date, are identified at any time.

PROSPERO records need to be fully searchable so the information requested needs to be in the fields, even if access to a protocol is given in Field 34. The records are permanent but links are not. Not everyone has internet speeds to enable them to download attachments; not everyone has access to pay per view journals where protocols may be published. We therefore do not accept submissions that refer the reader to the protocol without providing the basic information in the fields.

Review title and timescale

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 postoperative 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 original 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 2013

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.

Example:

The review has not yet started [ ]

	Started	Completed
Preliminary searches	☑	☑
Piloting of the study selection process	☑	☐
Formal screening of search results against eligibility criteria	☐	☐
Data extraction	☐	☐
Risk of bias (quality) assessment	☐	☐
Data analysis	☐	☐

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

Review team details

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 joining 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

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

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 dialing code. (N.B. This field is automatically populated from the named contact's joining details.)

This telephone 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)

11. Review team members' and their organisational affiliations

Give the title, first name, last name and the organisational affiliations of each member of the review team. 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.

13. Conflicts of interest *

List any conditions that could lead to actual or perceived undue influence on judgments 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.

14. Collaborators

Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

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

Review methods

15. Review Question(s) *

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. Complete a separate box for each question.

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

16. Searches *

Give details of the sources to be searched, search dates (from and to), and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.

List all sources that will be used to identify studies for the review. Sources include (but are not limited to) bibliographic databases, reference lists of eligible studies and review articles, key journals, trials registers, conference proceedings, Internet resources and contact with experts and manufacturers.

Example: We will search the following electronic bibliographic databases: MEDLINE, EMBASE, PsycINFO, Global Health, The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register), Health Technology Assessment Database, and Web of Science (science and social science citation index).

The search strategy will include only terms relating to or describing the intervention. The terms will be combined with the Cochrane MEDLINE filter for controlled trials of interventions. The search strategy for MEDLINE is available in the published protocol. The search terms will be adapted for use with other bibliographic databases in combination with database-specific filters for controlled trials, where these are available.

There will be no language restrictions. Studies published between January 1990 and the date the searches are run will be sought. The searches will be re-run just before the final analyses and further studies retrieved for inclusion.[2]

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

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 crossborder 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 initially *

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. Primary 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 measurements 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.

25. Secondary outcomes *

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.

26. Data extraction (selection and coding)

Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.

Other relevant details could include whether study selection and/or data extraction will be blinded (researchers unaware of author/journal details) and whether and how authors of eligible studies will be contacted to provide missing or additional data.

For reviews of individual participant data, this field should include the data to be sought and how this will be collected.

A description of any other manipulation or transformation of the extracted data that is planned may be included.

Example: Titles and/or abstracts of studies retrieved using the search strategy and those

from additional sources will be screened independently by two review authors to identify studies that potentially meet the inclusion criteria outlined above. The full text of these potentially eligible studies will be retrieved and independently assessed for eligibility by two review team members. Any disagreement between them over the eligibility of particular studies will be resolved through discussion with a third reviewer.

A standardised, pre-piloted form will be used to extract data from the included studies for assessment of study quality and evidence synthesis. Extracted information will include: study setting; study population and participant demographics and baseline characteristics; details of the intervention and control conditions; study methodology; recruitment and study completion rates; outcomes and times of measurement; indicators of acceptability to users; suggested mechanisms of intervention action; information for assessment of the risk of bias. Two review authors will extract data independently, discrepancies will be identified and resolved through discussion (with a third author where necessary). Missing data will be requested from study authors.

Example for IPD: Those responsible for the included studies will be asked to supply line by line individual participant data comprising: de-identified patient reference; allocated treatment, date of randomisation; date of birth, gender, tumour stage, tumour histology, survival status, date of last follow up or death.

27. Risk of bias (quality) assessment *

State whether and how risk of bias will be assessed (including the number of researchers involved and how discrepancies will be resolved), how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.

The criteria to be used to assess internal validity (risk of bias) of included studies should be listed. These may be different for different study designs. If a standard scale or checklist is to be used (e.g. Cochrane risk of bias tool, QUADAS, Jadad score, or PEDro scale), this should be specified.

Use of the findings of the quality assessment in the synthesis could include, for example, pre-planned sensitivity analyses to test the effect of removing poor-quality studies.

For reviews using individual participant data, this should briefly describe how data will be checked and validated.

For reviews of qualitative studies give details of how quality or trustworthiness will be assessed or judged (e.g. use of checklist such as Hawker). It is acceptable to add that ‘Risk of bias assessment is not applicable.’

Example: Two review authors will independently assess the risk of bias in included studies by considering the following characteristics:

Randomisation sequence generation: was the allocation sequence adequately generated? Treatment allocation concealment: was the allocated treatment adequately concealed from study participants and clinicians and other healthcare or research staff at the enrolment stage?

Blinding: were the personnel assessing outcomes and analysing data sufficiently blinded to the intervention allocation throughout the trial?

Completeness of outcome data: were participant exclusions, attrition and incomplete outcome data adequately addressed in the published report?

Selective outcome reporting: is there evidence of selective outcome reporting and might this have affected the study results?

Other sources of bias: was the trial apparently free of any other problems that could produce a high risk of bias?

Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.

Example for IPD: Data supplied for included RCTs will be checked for: missing data; internal data consistency; randomisation integrity (balance of patient characteristics at randomisation, pattern of randomisation); follow-up and censoring pattern. Summary tables will be checked with the trial protocol and latest trial report or publication. Any discrepancies or unusual patterns will be checked with the study investigator. A final copy of the form from each trial will be returned to the appropriate trial investigator for verification.

28. Strategy for data synthesis *

Give the planned general approach to synthesis, e.g. whether aggregate or individual participant data will be used and whether a quantitative or narrative (descriptive) synthesis is planned. It is acceptable to state that a quantitative synthesis will be used if the included studies are sufficiently homogenous.

Where appropriate, the planned analytical approaches (e.g. Bayesian or frequentist (classical), fixed or random effects; categorising studies within a narrative synthesis) should be outlined. Whether and how statistical heterogeneity will be explored and how any observed heterogeneity will impact on or modify the planned approach to analysis should be stated, along with any planned sensitivity analyses.

Example: We will provide a narrative synthesis of the findings from the included studies, structured around the type of intervention, target population characteristics, type of outcome and intervention content. We will provide summaries of intervention effects for each study by calculating risk ratios (for dichotomous outcomes) or standardised mean differences (for continuous outcomes).

We anticipate that there will be limited scope for meta-analysis because of the range of different outcomes measured across the small number of existing trials. However, where studies have used the same type of intervention and comparator, with the same outcome measure, we will pool the results using a random-effects meta-analysis, with standardised mean differences for continuous outcomes and risk ratios for binary outcomes, and calculate 95% confidence intervals and two sided P values for each outcome. In studies where the effects of clustering have not been taken into account, we will adjust the standard deviations for the design effect. Heterogeneity will be assessed using both the Chi-squared test and the I-squared statistic. We will consider

an I-squared value greater than 50% indicative of substantial heterogeneity. We will conduct sensitivity analyses based on study quality. We will use stratified meta-analyses to explore heterogeneity in effect estimates according to: study quality; study populations; the logistics of intervention provision; and intervention content. We will also assess evidence of publication bias.

Example for IPD: Individual data from all randomised participants will be included in the analyses, which will be performed on an intention to treat basis. A two-stage approach to synthesis will be used. For time to event outcomes, the individual times to event will be used in the stratified (by trial) logrank test to produce hazard ratio estimates of the effect of treatment for individual trials. These hazard ratios will then be combined across studies using a fixed effect model to give combined hazard ratios. For dichotomous outcomes, the number of events and the number of patients will be used to calculate Peto odds ratio estimates of treatment effect. These will be generated for individual trials and then combined across trials using a fixed effect model. For all outcomes, trial results will also be combined using a random effects model to test robustness to model choice.

29. Analysis of subgroups or subsets *

Give details of any plans for the separate presentation, exploration or analysis of different types of participants (e.g. by age, disease status, ethnicity, socioeconomic status, presence or absence or co-morbidities); different types of intervention (e.g. drug dose, presence or absence of particular components of intervention); different settings (e.g. country, acute or primary care sector, professional or family care); or different types of study (e.g. randomised or non-randomised).

The approach to be taken should be stated, e.g. whether subgroup analyses, meta-regression or modelling of covariates is planned and, where appropriate, details of categorisation (e.g. BMI <25, 25-30,>30) should be given.

Where it is not possible or appropriate to specify subgroups or subsets in advance, for example in a qualitative synthesis, please make a statement to this effect.

Examples:

If the necessary data are available, subgroup analyses will be done for people with stage I and stage II disease separately. Within each stage, and overall, we also plan to do a subgroup analysis by age (<20, 20-30, 30-40, >40 years).

This is a qualitative synthesis and while subgroup analyses may be undertaken it is not possible to specify the groups in advance.

General information

30. Type of review and method of review *

Select the type of review and methods from the drop down lists. You may select more than one category by holding down the control key:

Type of review

- Diagnostic
- Epidemiologic (may include aetiological or observational reviews; and reviews looking at risk or prevalence).
- Intervention (may include treatments, other health technologies, adverse effects, etc.)
- Prevention
- Prognostic
- Service Delivery (may include practice, management, education, etc.)
- Systematic review
- Methodology
- Meta-analysis
- Individual patient data (IPD) meta-analysis
- Prospective meta-analysis
- Network meta-analysis
- Review of reviews
- Qualitative synthesis
- Cost effectiveness
- Other (please specify in the free text box)

Health area of review

- Alcohol/substance misuse/abuse
- Blood and immune system
- Cancer
- Cardiovascular
- Child health
- Complementary therapies
- Crime and justice
- Dental
- Digestive system
- Ear, nose and throat
- Education
- Endocrine and metabolic disorders
- Eye disorders
- General interest
- Genetics
- Health inequalities/health equity
- Infections and infestations
- International development
- Mental health and behavioural conditions
- Musculoskeletal
- Neurological
- Nursing
- Obstetrics and gynaecology
- Oral health
- Palliative care
- Perioperative care
- Physiotherapy
- Pregnancy and childbirth

- Public health (including social determinants of health)
- Rehabilitation
- Service delivery
- Skin disorders
- Social care
- Tropical medicine

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.

31. Language

Select the language(s) in which the review is being written and will be made available, from the drop down list. To select multiple languages, select a language and hold down the control (CTRL) key and click another language.

The entry will default to English if no other selection is made. For languages other than English, registrants are asked to indicate whether a summary or abstract will be made available in English.

Example: English, French.

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. To select multiple countries, select a country and hold down the control (CTRL) key and click another country.

Example: England, Canada.

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.

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

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.

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 drop down list to indicate the current status of the review:

Ongoing
Completed, but not published: *(Please provide anticipated publication date)*
Completed and published
Completed, published and being updated
Abandoned *(Please provide a brief reason)*

Example: Abandoned: This review has been abandoned as we have been unable

to secure adequate funding to proceed.

39. 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 unpublished 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

References

1. International Committee of Medical Journal Editors. *Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Ethical Considerations in the Conduct and Reporting of Research: Conflicts of Interest*
www.icmje.org/ethical_4conflicts.html

2. 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
www.biomedcentral.com/1756- 0500/3/250

3. Main C, Thomas S, Ogilvie D, Stirk L, Petticrew M, Whitehead M, Sowden A. Population tobacco control interventions and their effects on social inequalities in smoking: placing an equity lens on existing systematic reviews. *BMC Public Health*. 2008; 8: 178. doi: 10.1186/1471-2458-8-178

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PROSPERO
Centre for Reviews and Dissemination
University of York
York, UK
YO10 5DD
t: +44 (0)1904 321040
f: +44 (0)1904 321041
e: crd-register@york.ac.uk
www.crd.york.ac.uk/PROSPERO