Non-Interventional, Reproducible, and Open (NIRO) Systematic Reviews

This document provides guidance on the preparation of a systematic review protocol intended for pre-registration (Part A). Further instructions facilitate the completion of the systematic review write-up (Part B).

This guide is designed specifically for non-interventional systematic reviews.

It does not aim to cover the details of performing a meta-analysis as part of the systematic review as this component is comprehensively detailed elsewhere in the literature. This framework can still be used for systematic reviews that do incorporate a meta-analysis.

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Part A
Preparing the Protocol for Pre-Registration

PRE-REGISTRATION GUIDANCE

Why should you pre-register your protocol?
Pre-registration is becoming the new standard practice among many disciplines. Pre-registering your systematic review protocol constrains biases and questionable research practices (such as selective reporting) that can undermine robust research synthesis. When the protocol is made public, it enhances the discoverability of your work and helps others to evaluate the quality of your review.

When should you pre-register your protocol?
You must pre-register your protocol before conducting the final search. Initial scoping searches which may inform your final search strategy can be conducted before pre-registration.

Where can you pre-register your protocol?
It is your decision to choose the platform to pre-register your protocol. The most commonly used open-source platforms include:
Prospective Register of Systematic Reviews (PROSPERO) - a platform designed for pre-registering systematic reviews.
Open Science Framework (OSF) - a platform which hosts research materials including pre-registrations, pre-prints, data and supplementary materials.

What if you need to make changes after the protocol has been pre-registered?
Any changes that need to be made after pre-registration (for example, you decided to change the data management software) must be reported and justified in the Transparency section of your review. If you realise that the initial protocol needs significant changes you should consider updating your pre-registration. All versions of your pre-registration should be linked and refer back to the original pre-registration.

SYSTEMATIC REVIEW PROTOCOL GUIDELINES

*All items with an asterisk * are required, and the remaining items are recommended for good scientific practice.*

Title
1. * **Provide a working title for your study.** The title must include key information that is informative to the reader. It does not have to be the same as the title of the paper.

Description and Aims
2. * **Provide a brief description of your review topic, including background, purpose and rationale of the review, and overriding research questions.** Your exact research question(s) should be given in the next section. In writing your description, consider why the review is needed and how it contributes to knowledge in the wider research area of interest. Reasons can include: ● The literature requires synthesis and no previous or ongoing systematic reviews exist. Specify how this was checked (e.g. scoping search, consultation with researchers in the field, etc.). ● An update to previous systematic reviews is needed (e.g. significant time since the last relevant review, a significant new body of work is available, theoretical reasons to examine new measures related to the topic, etc.) ● Previous review(s) was/were flawed (e.g. no quality assessment, bias in exclusion/inclusion criteria, etc.)

Research Question
3. * **What is the primary review question? The review question must be clearly defined and include the following:** ● The primary outcome measure of interest (the dependent variable; DV) ● The primary independent variables (IVs) of interest ● The population/participants of interest (e.g., undergraduate students, participants with a specific diagnosis, school-age children etc.) ● (optional) Study design(s) of interest, for example: i. observational - measured variables at one time-point

ii. cross-sectional - measured variables with different individuals at different ages/timepoints
iii. longitudinal - same individuals followed over time; could be prospective or retrospective
iv. experimental - examining effect of specific manipulation

- (optional) Any covariates of interest or variables you want to control for (e.g. participant age)

4. **Clearly define secondary review questions, if any.**
Secondary questions can supplement the primary review question by investigating the effect of interest in more detail (e.g., by considering other relevant methodological aspects, outcome measures, or any additional variables. These questions can be more exploratory (i.e. the researcher might not know what effects can be expected), but they must be defined in as much detail as possible.

5. * **Clearly state any hypothesis/hypotheses.**
If applicable, specify the expected direction of the effects for one-tailed hypotheses. If you have no hypothesis and you are planning an explorative review, explain what your expectations are or state that you have no expectations with regards to the findings.

Search Strategy

6. * **Supply at least one full search strategy for at least one database, with enough information so that it can be repeated. This can be copied directly from your search interface. In addition, you must include the following:**
    - A justification of the keywords (search terms), for example, consulting experts; use of technological aids; such as the R package litsearchr; based on previous systematic reviews.
    - Exact search strings including boolean operators (e.g. AND, OR, NOT), the order of parentheses, truncation and wildcard symbols (e.g. *, #, ?).
    - List all fields used when performing the search e.g. Author, Title, Abstract, Keywords
    - List all limits applied to the search. You should specify:
        i. Whether you only searched full text articles
        ii. Whether you only searched peer reviewed articles
        iii. The language(s) of the searched publications and provide details of any translations and interpretations.
        iv. The dates of publications included in the search (e.g. Jan 1990-Oct 2019)

      Provide justification for using these limits and how they may impact the review outcomes.

7. * **State the database(s) and the interface (including the URL) used to find the records to include in your systematic review. List all additional sources which will be searched. You may consider:**
    - Additional databases including URLs of the interfaces used and justifications. Note that the same platform (e.g. Web of Science) may search different databases depending on Institutional subscription, so you need to specify the actual databases. State whether you used open access engines (recommended), pay-to-access engines accessed via your institution, or both. Justify how the databases were selected (e.g. consultation with librarian, based on previous reviews, etc.)
    - Searching reference lists in order to find more relevant articles. Specify which reference lists, for example you may choose to search all reference lists in the papers that passed screening at the full text stage or reference lists of previous reviews and meta-analyses on a similar topic.
    - Searching the key journals in the relevant field.
    - Tracing forward citations i.e. checking where each paper has been cited since its publication. You should specify if you decide to do author tracing i.e. checking the list of publications by a list of authors who contribute to the topic under investigation.
    - A strategy for identifying and removing retracted papers.

8. * **List all grey literature searches (i.e. work from non-commercial or non-academic publishing outlets). State databases, platforms and sources you will consider, for example:**
    - Dissertations and theses
    - Pre-prints (e.g. subject-specific arXivs or university repositories)
    - Government reports
    - Conference presentations, posters, and/or abstracts
    - Unpublished manuscripts
    - Other (specify any field-specific materials you aim to include)

    If you do not plan to search grey literature, explain why.

9. * **Will you attempt to contact study authors to find unpublished/inaccessible papers or additional materials not included in the original publication?**
    If not, why? Prepare a protocol to guide and report this process and attach it to the pre-registration. Make sure the protocol details:
    - What information, specifically, you need from each paper
    - Which authors will you contact (e.g. first and senior authors? All authors?)
    - How many times will you attempt to contact the author(s)
    - A cut-off date that you would need responses by (e.g. one week, two weeks?
    - How will you proceed if you get no response?
    - You can also consider sharing email templates or contact forms that you will send to the authors when requesting further information.

N.B. If requesting unpublished materials, you should ask the authors for permission to share these within your systematic review supplementary materials to ensure better reproducibility.

10. **Explain how your search strategy is adequate to investigate the primary review question.**
    You can draw on the results from your scoping searches and comment on the feasibility of obtaining enough papers on the chosen topic (e.g. did you find all the papers you already knew about? Did you find additional relevant papers that you had missed? Have you included a broad enough range of keywords to find additional missing papers?)

11. * **Do you plan to repeat your search? If so when?**
    It is good practice to update the search at least every two years if you are not yet ready to publish your review. If you plan to update the search before completing the review, please specify how the update will be conducted (e.g., the search strategy will be rerun, you will request email alerts of related articles published since last search).

Screening

12. * **What software/applications will be used to store and manage the data throughout the review process?**
    For example, exporting .bib/.ris files from search platforms into reference manager software such as Zotero, Endnote, or Mendeley, applications such as Covidence or Rayyan, or a spreadsheet or other manual method. Indicate whether the same platform will be used to screen for duplicates and to deliver your final set of records to your co-reviewers.

13. * **State whether you are planning to design screening manuals for your co-reviewers.**
    These should include detailed instructions on the screening process to facilitate the standardisation of this process across all co-reviewers. This should be attached to the pre-registration document.

14. * **Clearly define the inclusion/exclusion criteria of the studies. Use the following for guidance:**
    - The main effect of interest (dependent variable) described in a standardised form (e.g. percentage of accurate trials to reflect task

performance, overall score on a self-perception questionnaire etc.) and whether this is within-groups, between-groups, or both
- The independent variable(s) described in a standardised form (e.g. task difficulty reflected by different trial types, participant anxiety levels reflected by a total sum of questionnaire scores)
- Detailed description of participant groups of interest to match the aims (e.g. population of adults with social anxiety defined as a score of 50 or more on the Liebowitz Social Anxiety Scale, elderly adults over 80 years old in the general population) including details of any other relevant participant characteristics especially in the case of clinical groups (e.g. diagnostic information)
- Study design (e.g. observational (measured variables at one time-point), cross-sectional (measured variables with different individuals at different ages/timepoints), longitudinal (same individuals followed over time; could be prospective or retrospective) experimental (examining effect of specific manipulation)
- Method of data collection (e.g. lab experiment, questionnaires, any specific requirements to assure that the method is comparable across the included studies)

15. **Justify your decisions above in accordance to your research question.**
Explain how these decisions help to address your research question in an objective way. It is important to consider what factors may impact the outcomes of the review and how/whether you should control for these.

16. * **How many reviewers will screen the titles and abstracts of each search result?**
Specify whether the titles and abstracts will be reviewed simultaneously or in stages, whether and how you will 'blind' these decisions, and whether all titles and abstracts will be screened by the same reviewers.

N.B. In order to increase reliability more than one reviewer should contribute to this process. There should be enough overlap in the number of items screened by each reviewer to calculate consistency in decision-making.

17. * **How many reviewers will screen the full text of the records selected for inclusion at the title and abstract screening stage?**
Describe how the reliability of the decisions will be assessed regardless of whether one or more reviewers perform the screening.

N.B. In order to avoid bias more than one reviewer should contribute to this process and there should be enough overlap between the items that each reviewer screens to calculate consistency in decision-making.

18. * **How will any disagreement between co-reviewers' screening-decisions be resolved at both stages of the screening process?**
    For example, resolution by discussion, resolution by a third reviewer who may or may not specialise in the investigated topic.

Data Extraction

19. * **Specify the data that you plan to extract from the studies, which may include:**
    - Participant groups/sample size and characteristics (e.g. adult, children, clinical)
    - Study design
    - Methods of IV and DV collection
    - Covariates
    - Results (e.g. mean, SD, effect sizes, statistical test used, p-values, Bayes factors)
    - Any specific limitations or other notes about the study

20. **Provide justification for the proposed data extraction in relation to your research question.**

21. **Create and provide the data extraction forms including all information to be extracted from each study.**
    You can add it as a supplementary file within the pre-registration.

22. * **How many reviewers will extract data ?**
    Describe how reliability of the decisions will be assessed if only one reviewer will be involved.

    N.B. In order to increase reliability, more than one reviewer should contribute to this process and there should be enough overlap between the data that each reviewer extracts to calculate consistency in decision-making.
    Alternatively, if you are planning to use a data mining software, describe in detail how you will extract this information, whether you have piloted this process, and how reliable it is (e.g. sensitivity and specificity ratings for your search criteria).

Risk of Bias (RoB) and Quality Assessment (QA)

23. * State how you will assess the risk of bias and/or methodological quality within the included studies.

You should aim to assess the methodological quality of the papers included in the systematic review, as well as the reporting quality. It is good practice to use an existing, validated tool. Provide all the details about the tool used and why this tool was selected. If there is no validated tool available that is appropriate to assess the studies included in your review, clearly explain any alternative methods of quality assessment (e.g., power analysis) or if you intend to adapt an existing tool. If you intend to adapt an existing tool, clearly state and justify what changes you made to the tool and why these changes were made. You should also state whether any validation of the adapted tool will be undertaken.

24. * How many reviewers will assess the risk of bias and/or methodological quality of each study?

To avoid bias, more than one reviewer should assess RoB and QA. Each reviewer should do so independently, and discrepancies should be resolved by consensus or by an additional reviewer. If only one reviewer will conduct the RoB and QA assessment, describe how you intend to avoid bias and ensure reliability.

Synthesis

25. * How many reviewers will synthesise the results?

Describe how the reliability of the decisions will be assessed if only one reviewer will be involved.

N.B. In order to avoid bias more than one reviewer should contribute to this process.

26. * How will the results be synthesised?

Narrative/qualitative synthesis? Is there a planned meta-analysis? If you are combining methods (e.g. qualitative synthesis and meta-analysis), describe how this division will be made. If you will meta-analyse groups of studies based on a given characteristic together (e.g. studies in low-income vs high-income settings), provide specific detail on how studies will be grouped and what is your minimal threshold for the number of studies available to allow for a meta-analysis.

27. * How will you assess the methodological heterogeneity of the studies included in the review?

28. * **How are you planning to weigh the evidence of the included studies based on their risk of bias rating?**
Will only include studies with high methodological quality? Will you compare the results from studies with high and low methodological quality?

Transparency

29. * **Provide a clear statement clarifying which point in the review you are at the time of submitting this pre-registration (include all that apply)**
    - None of the below
    - Scoping searches completed
    - Final database search completed and results exported/download into review management software/spreadsheet
    - Grey literature search completed
    - Reference lists and/or forward citation search completed
    - Screening of titles and abstracts begun
    - Any other later stage with justification for why the pre-registration was not completed earlier

30. * **Have you made any changes or have you updated the protocol since the first pre-registration?**
Include details, justifications, and dates of any changes.

31. * **Declare if you or any of the review co-authors are an author of one of the studies that will likely be included in the review (based on your search strategy).**
Describe the process for protecting against bias when reviewing articles authored by a member of the review team at all stages of the review process.

32. * **Pre-register the protocol on a designated online platform with a link protected from expiration or deactivation.**
The pre-registered protocol can be uploaded under an embargo until you are ready to share it, such as during the peer-review process, or at the point of publication. It is good practice to make your protocol public and accessible at the point of publication (if not before).

Part B

Writing the Review

This section will guide the write-up of the systematic review following the completion of a pre-registered protocol.

In this section, all items are required.

NB: If you have not previously followed the accompanying pre-registration protocol guidelines, or did not pre-register your study, include all relevant information as much as possible from the items in Section A into the final review.

Title

1. **The title must include key information that is accessible to the reader.** The title should be a specific and informative description of the planned systematic review. As a minimum, the title must identify the project as a systematic review (and/or meta-analysis, when applicable) to enhance discoverability. The title should include key information about the review (e.g., effect of interest, independent variables of interest, outcomes, and study design).

Introduction

Introduction Statements

2. **Include the following items** (these items should have been specified in your pre-registration protocol already):
    - Why is the review needed? What is your rationale?
    - Aims and research questions
    - Hypotheses (if applicable) including the direction of expected effects if one-tailed

Method

Pre-registration Protocol

3. **State whether a pre-registered protocol exists for the review.**
   If a pre-registered protocol exists:
   - Advise how to access the protocol. Provide a link or the name of the database and any registration numbers.

   If a pre-registered protocol does not exist:
   - Explain the reason why and how the absence of a pre-registered protocol might affect the quality of this review?

4. **Include one of the following transparency statements:**
   - A declaration that there were no deviations from the final pre-registered protocol.
   - A "Deviations from the pre-registered protocol" section with deviations explicitly described and full justification for any changes or aspects that were not implemented. If lengthy explanation is required, expand this in the supplementary materials.

Search strategy

5. **Include one full search strategy string used in at least one database (e.g. as an appendix). This is necessary to ensure transparency and reproducibility by another researcher.**
   Include the following details:
   - Justification of the keywords selected (consulting experts, technological aids such as the R package litsearchr, based on previous systematic reviews)
   - Exact search strings including boolean operators (e.g. AND, OR, NOT), the order of parentheses, truncation and wildcard symbols (e.g. *, #, ?).
   - List all fields used when performing the search e.g. Author, Title, Abstract, Keywords
   - All limits used when performing the search. You should specify:
     i. Whether you only searched full text articles
     ii. Whether you only searched peer reviewed articles
     iii. The language(s) of the searched publications and provide details of any translations and interpretations.
     iv. The dates of publications included in the search (e.g. Jan 1990-Oct 2019)

     Provide justification for using these limits and how they may impact the review outcomes.

6. * **List all additional sources used to obtain the records for your review. These are some of the options:**
    - Additional databases
    - Searching reference lists in order to find more relevant articles. Specify which reference lists; for example you may have searched reference lists in the papers that passed screening at the full text stage or reference lists of previous reviews and meta-analyses on a similar topic.
    - Searching the key journals in the relevant field.
    - Tracing forward citations i.e. checking where each paper has been cited since its publication. You should specify if you do author tracing i.e. checking the list of publications by a list of authors who contribute to the topic under investigation.

7. * **List all grey literature searches (i.e. work from non-commercial or non-academic publishing outlets), State databases, platforms and sources you will consider, for example:**
    - Dissertations and theses
    - Pre-prints (e.g. subject-specific arXivs or university repositories)
    - Government reports
    - Conference presentations, posters, and/or abstracts
    - Unpublished manuscripts
    - Other (specify any field-specific materials you aim to include)

    If you do not plan to search grey literature, explain why.

8. **State the date(s) that the search was performed including the dates of search updates if applicable.**

9. **Give a summary of your attempts to obtain unpublished/inaccessible papers or additional materials and whether this was successful.**
    What impact will it have on the results of the systematic review (e.g. if it was not possible to obtain unpublished papers with non-significant results)?

Screening

10. **State the software, applications, and/or methods that were used for storing and managing the data throughout the review process.**

11. **State the level of agreement (e.g. reliability metrics, consistency) between the reviewers during the screening process for:**
    - Titles and abstracts
    - Full texts

12. **How did you resolve any discrepancies between reviewers where appropriate?**
    You should describe the general strategies of resolving discrepancies. In addition, within your supplementary materials, you should provide a decision log with all reviewer decisions, notes, and outcomes of discussions for each of the results from the initial search.

13. **Provide a full list or a table of studies that were excluded during the screening process together with reasons and explanations for the exclusion (this could be included as supplementary materials).**
    You should specify how many records were excluded when screening titles and abstracts, how many were excluded when screening the full text and at any other point during the process if applicable.

Data Extraction

14. **State the level of agreement between the reviewers for data extraction.**
    This should be included in a decision log along with the method by which consensus was achieved in the event of disagreement.

15. **Provide the details of any missing data and how it was dealt with.**
    For example, did you attempt to contact the authors of the studies to gain more information? Did you exclude the studies with incomplete information?

Results

Risk of Bias (RoB) and Quality Assessment (QA)

16. **Provide full details of the RoB/QA assessments for each study (this could be included as supplementary materials).**
    You could think about representing this visually for clarity. Make sure to address the quality of methods and the quality of reporting separately for each study. You should be transparent about the tools you used to guide your risk and quality assessments and describe any adaptations that were needed. If you adapted an existing tool, describe why the adaptations were needed and when adaptations were made (i.e., whether changes to the tool were made before or after the data extraction). You should also explain whether your approach for RoB/QA was validated.

17. Summarise the impact and outcomes of the RoB/QA process.
Would you evaluate the literature as of high or low quality?

18. State the level of agreement (e.g. reliability metrics, consistency) between the reviewers when assessing RoB/QA.

19. How have you assessed publication bias among the studies included in the review?
Specify the methods used.

Extracted Results

20. Report the number of studies found in the search. Specify the date of the search.
You should specify the number of studies:

- found using each search method e.g. database searches, grey literature searchers, contacting authors
- removed as duplicates
- removed after titles and abstracts were screened
- removed after the full texts were screened
- removed for other reasons with clear justifications
- included in the final synthesis (qualitative and/or quantitative)

N.B. You can present this in the form of a PRISMA flowchart, or describe in text.

21. Present the data extracted from each study in a table.
This should include data for each individual study, rather than summaries of groups of studies. The table should include the items that were identified for extraction in the pre-registration protocol. It should also include a score/rating (if applicable) or a summary from the RoB/QA and the source (e.g. found in a peer-reviewed article, obtained by contacting the author etc.).

Synthesis

22. Describe the methodological heterogeneity of the studies included in the review (e.g. how comparable are the methods used?).

23. How have the methodological heterogeneity and quality assessment outcomes affected the synthesis of the results?
Refer to your pre-registration protocol if needed to emphasise whether the results

were weighed based on the methodological quality (as determined by RoB/QA scores).

24. **Provide a descriptive summary of findings for all planned analyses and effects of interest (these should have been pre-registered).**
    These summaries should be aligned with the research questions and any relevant hypotheses. Make sure to clearly present the results in relation to the primary and secondary research questions.

25. **You should present any exploratory analyses separately.**
    Exploratory analyses are those conducted in addition to the planned analysis. These normally emerge during the process of analysing data to answer your pre-planned research question(s). This may happen if you observed something interesting in your data that you had not taken into consideration before. You must make it clear that these exploratory observations are separate from the pre-planned analyses.

Discussion

26. **Summarise the main conclusions of your review with regards to the main research question(s).**

27. **Within this summary consider the overall direction of the effect in the context of the quality of the included studies and the strength of the body of evidence.**
    Present a balanced view of the obtained data. It is important that your conclusions do not overemphasise what is evident in your data.

28. **Present conclusions from exploratory analyses separately to confirmatory analyses and explain how these may impact the field and the future direction of research.**

29. **Discuss the problems, gaps and limitations within the reviewed literature. Provide future research recommendations.**

30. **Discuss any strengths and limitations regarding the process of conducting this systematic review which may have an effect on the overall outcome (e.g. incomplete detection of relevant studies).**

Transparency

31. **Keep a record of your decision processes throughout the different stages of the review and upload the records as open data/supplementary materials for transparency**.
    For example, for each paper in the original search, log whether they were included/excluded at each stage by each reviewer (removed as a duplicate, removed at the screening of titles and abstracts/screening of full text), how any discrepancies were resolved, and any additional information that contributed to each decision where appropriate. Similar can be done for data extraction and RoB/QA.

32. **State the name and version number of all software and any packages, if applicable.**
    For example, `revtools v0.4.0` with `RStudio v3.6`.
    Analysis scripts should be made available (e.g. on the Open Science Framework or Github) alongside the data where possible and should include a persistent identifier, such as a Digital Object Identifier (DOI). The scripts should be reproducible, meaning that they should include enough instructions for other researchers to computationally reproduce the outcomes.

33. **Declare your funding and any conflicts of interest including whether you authored any of the papers that were included in the review.**
    Make a clear statement where there are no conflicts of interest.

34. **Declare any non-financial support you have received for this systematic review project.**

35. **Provide details about the contribution of each author to the completion of the review.**