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# Undertaking and writing up a systematic review: a step by step guide

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## Abstract

Undertaking a systematic review is a challenging but ultimately rewarding exercise that helps to better inform medical practice through the synthesis of the best evidence in the literature for any given topic. One of the appeals of undertaking a systematic review is that there is not normally a requirement for ethical approval, funding or collecting new patient data. However, it must not be assumed that this means it will be an easy thing to do. A 12-step approach is proposed here, with a suggested template for manuscript writing. These can be used as a basic framework for the undertaking and writing of a systematic review. It is suggested that these be used in conjunction with expert advice and utilisation of other online and library services.

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## Introduction

A systematic review (SR) of high quality randomised controlled trials is the highest level of evidence within medical literature[1, 2]. The aim of a SR is to summarise the evidence for a particular research question by synthesising all the available evidence that addresses it. In this way, individual studies are brought together as if they are really part of one bigger study. The Cochrane Library is a well-established resource that utilises the SR as a means to provide evidence for informed decisions and better health[3].

Undertaking SRs may be an appealing to researchers because they provide a mechanism to establish best evidence for topics without ordinarily requiring ethical approval, collection of new patient data or funding. It might be tempting therefore, for early-career researchers to assume that a SR will be easier to complete than original research. However, SRs can be laborious, time-consuming and difficult, and should not be started without researchers being armed with the understanding of what this will entail. The aim of the current article is to guide the researcher in a step-by-step manner through the process, highlighting the considerations that need to be made along the way. This basic '12-step' framework should be supplemented by expert help and advice by a senior co-author, as well as further reading and instruction found at the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) website[4], the Cochrane Handbook[5] and related publications[6].

## Step 1. Establish the research question

The most important first step in undertaking a SR is establishing the research question. These are ordinarily constructed using the 'PICO' model, with a particular patient population, intervention, control/comparison and outcome. It is recommended that researchers write down their research question in a way that incorporates all four of these domains so that they can plan their SR. It should be a full sentence with a question mark at the end; something that sounds simple but sometimes takes some time to formulate.

### Step 2. Assemble a team

A SR cannot be undertaken alone, since co-authors are required to corroborate the searches, data collection and assessment of studies. This is often done by two main researchers, with a third used to settle any disagreements or discrepancies. It is highly recommended that at least one of the authors be experienced in conducting and writing up SRs, since their expertise will be required throughout the process. It is also recommended that authorship (who is an author, and the order of the authorship) is established at the outset, according to the recommendations by the International Committee of Medical Journal Editors[7], and that all authors are content with their roles within the working group.

### Step 3. Scoping search

Before embarking on a more 'formal' search for studies, the team should first undertake a scoping search. This is where the authors use online and library resources to determine whether their SR will be original and feasible. If several similar studies are found that address the SR research question then a SR is likely to be feasible. The authors should also search to determine whether other researchers are already doing the same project or have already published it. The International Prospective Register of Systematic Reviews (PROSPERO)[8] is a resource that can be searched to determine originality. At this stage, the research question can be modified or adapted according to what has already been done, or what might be most original.

### Step 4. Protocol and registration

If it appears that the research question is both original and feasible to answer from the scoping search, it is a good idea to write a protocol and register the SR. The prospective registration of the SR allows the readers and reviewers of the final SR to be able to look at the protocol and SR side-by-side, which proves that the latter was not adjusted during post-hoc analysis. Furthermore, registration lets other researchers know that the topic is being worked on, and limits redundancy of effort. Importantly, a registered protocol also facilitates easier collaboration between researchers since the methodology is clear from the outset. Researchers that are tempted to miss this step may find themselves in difficulty later in the process due to errors in communication or understanding.

### Step 5. Formal search

At this stage a formal, systematic search can be conducted by the authors, with or without the assistance of library services. This is a comprehensive search of all available literature, using search inclusion and exclusion criteria, and terms appropriate for all the domains in the PICO statement. This search should yield all the studies that were discovered during the scoping search, as well as other relevant studies not initially picked up at that stage. It should also find lots of studies that are *not* relevant to the SR. The authors then need to look through these in a systematic way to identify the studies that are relevant for the SR. Firstly by looking at titles and abstracts, then full texts. All records should be kept of the number of studies identified at each stage, and authors should construct a PRISMA flow diagram[4]. This will usually be the first figure (i.e. Figure 1) in the resulting manuscript.

### Step 6. Collect all included studies

The result of the formal search should be a collection of full texts for studies that will be included in the SR. It is essential to have the full texts (rather than just the abstracts), and this can be achieved by a combination of online (e.g Athens[9] or Institutional access) or library services.

### Step 7. Data extraction

Data now must be extracted from individual included studies into a spreadsheet, with a row for each included study. This is most commonly done using software such as Microsoft Excel (Microsoft Office, Redmond, USA) or equivalent data capture tools. Each column should be a domain within the study such as author, year, type of study, country of origin, number of patients, demographic details, as well as other parts of the PICO such as interventions, comparators/controls and outcomes. Authors can chose to have as many columns as they wish. These will eventually be synthesised and reported in the SR results, tables and figures. More than one author should check the data extraction for errors.

### Step 8. Quality and risk of bias assessments

There will need to be some assessments of the quality of evidence and risk of bias for individual studies. These assessments are usually made using tools specifically designed for this purpose according to the types of studies[10-13]. These assessments are normally displayed as tables in the SR, either within the main body or as supplementary material.

### Step 9. Data synthesis

Data that has been extracted now needs to be synthesised (i.e as if each study is part of one larger study). If outcomes are comparable between studies, then meta-analysis may be feasible. This is a quantitative assessment of outcome effects according to interventions versus controls. Statistical software is required for this stage and may yield some forest plots. Researchers must learn the techniques to undertake such analyses.

### Step 10. Writing up

When writing up a manuscript for a SR, there are certain sections that are required, and the best resource to determine the manuscript contents is the PRISMA checklist[4]. Many journals will also require that this checklist is submitted as a supplementary file to ensure that it has been completed according to best practice. The Introduction and Methods sections will normally be mostly written as the protocol, and just needs to be adapted into manuscript format. The Introduction should include paragraphs such as the background (what is the research topic and why important?), what is already known, what is the gap in the literature, and the aim of the SR (include PICO statement). The Results section would normally be orders as: "Search results" (Figure 1 is the PRISMA); "Study characteristics" (including a Table); "Patient characteristics"; "Quality assessment"; "Risk of bias assessment; "Outcomes". If no meta-analysis is possible, extracted data can still be synthesised in a narrative manner. It is important that the Methods and Results sections match each other neatly. In the Discussion section, the first paragraph should summarise the main findings, and then subsequent paragraphs should frame these findings within the current literature.

There should also be a 'Limitations' paragraph that describes both the limitations in evidence within the SR and also the limitations of the SR itself. A basic template for a SR manuscript is included as Supplementary file 1.

### Step 11. Submission and peer reviewing process

At this stage authors will need to format the manuscript according to the author guidelines for the journal of choice. These are usually listed on the journal websites. Failure to have the correct format may lead to the manuscript being sent back to the authors for editing. Authors should also check that they have included the PRISMA checklist, which can be submitted as a supplementary file. It is almost certain that the first round of reviews will request some clarifications or revisions, and therefore the authors will need to re-submit a revised manuscript. At this stage the authors should cut and paste the reviewer comments onto a new document and annotate responses underneath each comment. If there are revisions made in the manuscript, these should be indicated in the responses, and saved as 'tracked changes' in the main manuscript. This document can be submitted to the journal along with the revised manuscript as 'responses to reviewer comments'. Responses to reviewers should be comprehensive, whilst also being professional, polite, and respectful.

### Step 12. Dissemination

As well as working towards publication of the SR in a peer-reviewed journal, researchers may also wish to submit their work to conferences in abstract form. These are usually judged by a committee and the authors will be offered either an oral or poster presentation to deliver at the conference. This is an important part of dissemination of the work, which may lead to further discussion, collaboration and further research proposals.

### Conclusion

SRs are important pieces of research that synthesise the evidence in the literature and lead towards better informed care for patients. Undertaking a SR requires a team approach, and must follow a comprehensive, step-wise strategy so that the research and writing elements are conducted appropriately and in a manner that will lead to publication and dissemination.

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