

Module 5: Writing your protocol: why we have them, what to put in the Background section, and defining the question

This module discusses why we have protocols and what should go in the first few parts of a protocol.

Learning objectives

- Understand the rationale for having protocols for reviews
- Understand the role of a Background section in a review
- Understand the reasons for breaking down a question into participants, interventions, outcomes and study designs
- Be aware of pitfalls in defining questions
- Be familiar with entering text and references in RevMan and have completed a cover sheet for a review

Relevant sections of the *Cochrane Handbook for Systematic Reviews of Interventions*

- Chapter 2: Preparing a Cochrane review
- Chapter 4: Guide to the contents of a Cochrane protocol and review
- Chapter 5: Defining the review question and developing criteria for including studies

Other relevant material

- [Cochrane Collaboration Style Guide](#) (available under the Help menu in RevMan 5)

Where does this go in a Cochrane review?

- This module covers the parts of a protocol, and review, with the headings Background, Objectives and Selection Criteria.

Why bother with protocols?

People starting reviews are usually keen to get on with finding studies, reading them and trying to make sense of it all. When you feel like this, having to try to write down exactly what you want to do can seem like a good way to kill that enthusiasm. So we must think protocols are important to expect everyone to produce one. Here are the reasons why.

Planning

An even better way to kill enthusiasm than pausing to write a protocol is to start doing something, only to find out you've gone about it the wrong way. Preparing a protocol for your review makes you stop and think about what you're doing. If you get the protocol right, the rest of the review really does follow from it.

Most reviews have a team of people working on them, and the protocol stage is a good opportunity to focus everyone's thoughts on the task in hand, debate areas of uncertainty, and make sure everyone knows just what is involved in doing the systematic review.

Use your protocol as a plan for who is doing what, and when

Once you've written down exactly what you plan to do, the protocol can act as a working document for the reviewers. You can use it to assign tasks to people, identify the resources you'll need, and keep track of progress by setting target dates for parts of the review.

Protocols can be useful in applying for funding

People also use protocols to apply for funding – the information required for a grant application is often similar to what you will put in the protocol.

Tell everyone else what you're doing

Within the Cochrane Collaboration, protocols for reviews go through some form of peer review (the exact arrangements vary between review groups). Some people also send their protocols to others they know are interested in the review question, as they may have helpful suggestions. Once your review group has approved your protocol, it is published in *The Cochrane Library*. As well as enabling people to send you comments, this is one way we can try to make sure different people don't start the same review without realising it, and so avoid duplication of effort.

Protocols help to make sure no-one else is doing the same work without realising it

Minimising bias

Writing down exactly what you plan to do, in advance, is one of the ways you can minimise bias. A systematic review is retrospective – you're looking back at a set of studies that have already been done. It's easy to imagine that if you are familiar with the results of these studies, it might change the way you define the question, set the selection criteria, decide which interventions to compare, and choose which outcomes to look for.

Protocols help to minimise bias

However, most people starting a review know at least some of the studies relevant to their question, simply because they are interested in the topic. So are we being unrealistic to think we can rid ourselves of our biases by writing a protocol? It's probably impossible to get rid of all bias, which is why we talk about minimising it. Writing a protocol is one way we should be able to reduce bias, even if we can't eliminate it, by being transparent about what we plan to do in advance.

Can I change my protocol?

It is unreasonable to expect that it will always be possible to prepare a protocol containing a plan for every situation that might arise in a systematic review. Your selection criteria might be worded in a way that just doesn't work when you try to use them on a set of studies, or the data you are able to collect might need analysing in a way you hadn't thought of. It's better to change the protocol than to finish up with a review that's not helpful for users.

The type of changes you should be particularly wary of are those that mean you will include or exclude different studies than you had originally intended. This is especially important if you know what effect your rule change will have on the results of the review.

If you have to change your protocol after it's published, you should report major changes and the effect they have had on the results

What you can, and should, always do is report in your review any changes you made along the way and what effect this had. If the results change, it's probably sensible to present all the analyses, with and without the changes, so that readers can make up their own minds which results they believe.

Writing your protocol

You will probably have several versions of the protocol as you agree on the content with your co-reviewers and review group. Many people prefer to do this in a word-processing package they know well, rather than put it straight into RevMan. If you plan to do this, it is easy to copy and paste text directly into RevMan after you have written it in another piece of software. However, fancy fonts, formatting, tables, etc don't paste across well, so keep the text simply formatted.

You should also remember that the target audience for your review is the same as for a general medical journal. So try to imagine the audience when you're writing, and write for them. If they cannot understand what you are proposing in your protocol, they might not be able to understand the results and conclusions of your review.

The Title

The title of your review is important. When someone using *The Cochrane Library* is browsing through a list of reviews, it is the first thing they will see. So the title has to provide enough information to help the reader decide if the review is relevant to them.

The reader will need some succinct information about the participants and interventions that are the focus of the review. They won't want to be distracted with unnecessary words. The Cochrane Collaboration has decided on a standard format for titles which helps to convey information as quickly as possible:

[Intervention] for [problem] in [category]

The last of these three parts is not always needed. Here are some examples:



Try to write out your title in this format

Acupuncture for chronic asthma
Antihistamines versus aspirin for itching in late pregnancy
Case management for people with severe mental disorders

Try writing out your title in this format. Try it out on some people and see if they understand what your review is about. You'll get further help from your review group in deciding on the title.

By the time readers finish your Background section they should be able to understand why you are asking the question

The Background section

In the Background section you need to explain to people reading your review why you are asking the review question. Don't forget to write this section in plain English. Here's a list of the sort of things you might like to cover:

- How important is the problem?
- Is there any uncertainty about how to deal with the problem?
- Why do people think this intervention might work?
- What is the intervention supposed to achieve?

The background should cover the size of the problem, uncertainty about dealing with it, why the intervention might work, and what it is supposed to achieve

When you discuss the importance of the health problem addressed by your review, you should cover how common the problem is and what effect it has on people or communities. For example, the common cold affects millions of people, has only minor effects on most people, but is responsible for a lot of time off work which costs the economy money. Multiple sclerosis is not very common, but affects some people very severely. You should try to attach some numbers to these types of statement (and reference them), and also consider how the situation might vary around the world.

Many people undertake reviews because they know there is uncertainty about how to deal with the health problem. If you know of evidence of uncertainty, put it here. For example, you might be aware of a survey showing that different doctors use different drugs in the same situation.



Read [section 4.5](#) of the *Cochrane Handbook for Systematic Reviews of Interventions*

It's not always obvious why people think an intervention might work, or why people tried it in the first place. So include some explanation of the reasoning behind the use of the intervention. For drugs, this might be some biological information about how the drug acts on a cell; for other interventions it might be psychological or sociological theory. However, don't get too technical! This section of a review should be understandable to a wide readership. If you think there needs to be some very detailed information for expert readers, you could put a section at the end of the Background with a subheading called 'technical information'.



Try to explain to someone who doesn't know much about the topic what your review is about. Give yourself a time limit of 5 minutes and try to get all the important points in.

Finally, you should explain what the intervention is supposed to achieve. Is it supposed to cure the problem, or help with a specific symptom?

At the end of this section, the reader should understand why you are asking the review question, and the next part of the review shouldn't come as a surprise. A good way to see if your background contains the right information is to use it to explain to someone what your review is about.

Objectives



Write out the main questions your review addresses in a few sentences

In this section you should write down the main questions to be addressed in your review. This should only take a sentence or two. Try it now.....

Defining the question

Getting the question right is the most important step in doing your review. As well as telling others what the review is about, it will guide how you collect studies, how you check whether studies are eligible and how you do the analysis. So take your time over it, discuss it with your co-reviewers and show it to others.

Chapter 5 of the *Cochrane Handbook for Systematic Reviews of Interventions* covers this in some detail, so this section just summarises what's in there and adds a few comments. Defining the question is also the focus of 'Developing a protocol for a review' workshops – these can be a good place to try your ideas out on other people and learn from the review questions being thought about by other people. For details of these, and other, workshops contact your review group or look at the dates of workshops on www.cochrane.org.



Read [Chapter 5](#) of the *Cochrane Handbook for Systematic Reviews of Interventions*

It's also worth having a look on *The Cochrane Library*, or checking with your review group, for reviews of similar topics to your's to see how others have defined their questions.

Types of participants

Define the health problem. Be careful about using definitions that depend on

- Time
- Place
- Technology

For example, diagnostic criteria that were first developed in the UK in 1994 couldn't have been used before then, and may not be used by people in other countries at all. Expensive or recent tests may not be available in many countries. So be careful. Don't risk setting conditions that will force you to exclude studies that would otherwise be relevant to your objective.

Define the population and setting. Think about

- Age
- Sex
- Race
- Other factors that may make some people respond very differently to the intervention
- Where the participants are (hospital, community, etc)

Again, take care with these, as you may find that setting rigid criteria means you have to throw studies out. It is often better to be over inclusive at this stage. If, for example, you restrict the age to people aged eighteen or older, what will you do with a study of hundreds of participants that has three sixteen-year-olds in it?

Types of interventions

Define the interventions. For drugs, think about

- Drug preparation
- Route of administration
- Dose
- Duration
- Frequency

Be careful not to limit the question too much. For example, think about when a drug regimen is so different that it would have a totally different effect, rather than just specifying the commonly used dose.

For non-drug interventions, defining the intervention can be a bit more difficult. You'll need to think about describing similar bits of interventions or concepts – exactly what was done, how often it was done, who did it, were they trained, etc. It can be particularly tricky where the intervention is complex, for example where a set of interventions is performed by one or more people. You may need to end up with a set of core parts to the intervention, and then some other non-core parts.

A review of assertive community treatment for people with severe mental disorders is a good example of a complex intervention clearly defined, and the reasons why it was defined in that way justified. (Marshall M, Lockwood A. [Assertive community treatment for people with severe mental disorders](#). *Cochrane Database of Systematic Reviews* 1998, Issue 2. Art. No.: CD001089. DOI: 10.1002/14651858.CD001089)

“For an intervention to be accepted as ACT it must have been described in the trial report as: Assertive Community Treatment, Assertive Case Management or PACT; or as being based on the Madison, Treatment in Community Living, Assertive Community Treatment or Stein and Test models. Trials of case management that did not meet the criteria for ACT are considered in (a separate review). The review did not consider the use of ACT as an alternative to acute hospital admission. The review also excluded studies of 'Home-Based Care' (which involves a multi-disciplinary team assessing and treating urgent psychiatric referrals at home).

Home-based care is a form of crisis intervention which deals with those who are usually acutely ill, and should not be classified with either ACT or case management as these are long-term interventions for severely and persistently ill people.”

Define the comparisons. Here, you need to decide whether the group you will be comparing the intervention group with have

- A placebo
- Nothing
- Some other treatment

To help you understand this it may be helpful to look at an example, a Cochrane Review of magnesium sulphate and other anticonvulsants for women with pre-eclampsia (Duley L, Gülmezoglu AM, Henderson-Smart DJ. [Magnesium sulphate and other anticonvulsants for women with pre-eclampsia](#). *Cochrane Database of Systematic Reviews* 2003, Issue 2. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025).

In this review the part of the question related to types of intervention and comparisons is defined as “comparisons of an anticonvulsant with placebo (or no anticonvulsant), and of one anticonvulsant with another”. From the analysis section of this review (below) you can see how the reviewers have organised some of their comparisons.

- 5 Magnesium sulphate versus none/placebo
 - 5.1 Maternal death
 - 5.2 Eclampsia
 - 5.3 Stillbirths and neonatal deaths
 - 5.4 Any reported side effects
- 6 Magnesium sulphate versus phenytoin
 - 6.1 Eclampsia
 - 6.2 Complications of labour
 - 6.3 Caesarean section
 - 6.4 Mortality for the fetus or infant
 - 6.5 Infant morbidity
- 7 Magnesium sulphate versus diazepam
 - 7.1 Eclampsia
 - 7.2 Caesarean section
 - 7.3 Stillbirths and neonatal deaths
- 8 Magnesium sulphate versus nimodipine
- 9 Magnesium salts versus methyl dopa
 - 9.1 Other antihypertensive therapy
 - 9.2 Admission to special care baby unit

Types of outcomes

List all important outcomes as inclusion criteria in your review

The general rules are to list the outcomes of interest to decision-makers, particularly those who have the health problem of interest. Think about

- How the outcomes might be measured
- When the outcomes should be measured
- Which are the most important outcomes
- Bad outcomes as well as good outcomes

As with defining the participants, be careful about choosing outcomes where the definition changes over time and place.

Even if you believe certain outcomes are unlikely to be reported, you should list them if they are important. Then when you are writing up the review, you can comment that you looked for information on those outcomes but the studies didn't report it. This will define a gap in the research and hopefully encourage researchers to include that outcome in future trials.

There is more in later modules about the types of data you may encounter, and how you might handle them.

Types of studies

Most Cochrane reviews focus on randomised controlled trials both because of concerns about bias in other types of study design, and bias in retrieving other study types, as explained in module 1.

There are occasions when randomised controlled trials are unlikely ever to be done. For example, if an intervention saves people with a condition where previously everyone died, it would not be appropriate to do a randomised trial in which some of the participants did not get treated. Other examples would be where the intervention is applied at a level that makes randomisation impractical, such as tobacco taxes at a national level. If you think your topic fits into categories like these, you'll need to discuss it with your review group.

You should not choose to look for other study types, where randomised controlled trials are feasible, simply because you don't believe trials have been done. There are reviews with no trials – if the question is important enough for a review, then the lack of trials is an important finding.



*Activity:
Work through
the table to
help you
clarify your
review
question and
criteria*

Building up your table of comparisons

The table below is designed to help you construct your review question and subsequently set your inclusion and exclusion criteria. Using what you have learned and thought about in the above section, complete this table and finalise your question.

| | |
|---------------|--|
| Participants | <p>How is the disease/condition defined? What are the most important characteristics that describe the participants relevant to your review? Are there any relevant demographic factors? (ie age, sex, ethnicity) What is the setting? (eg hospital, community etc) Who should make the diagnosis? Are there any co-morbidities to be excluded? Are there any other types of people who should be excluded from your review (because they are likely to react to the intervention in a different way)? How will studies involving only a subset of relevant participants be handled?</p> <p>In one sentence describe your population, for example "All adults with tennis elbow (pain on lateral aspect of the elbow aggravated by use of the wrist or hand), diagnosed by a health care worker."</p> |
| Interventions | <p>What are the experimental and control (comparator) interventions of interest? Does the intervention have variations (eg dosage, mode of delivery, personnel who deliver it, frequency of delivery, duration of delivery, timing of delivery)? Are all variations to be included (for example is there a critical dose below which the intervention may not be clinically appropriate)? How will trials including only part of the intervention be handled? How will trials including the intervention of interest combined with another intervention (co-intervention) be handled?</p> <p>In one sentence describe your intervention.</p> |
| Comparisons | <p>What are you interested in comparing the intervention to? This depends on the primary question of the review. Are you only interested in whether the intervention offers benefit over the natural course of the disorder (ie a comparison to placebo or no treatment), or are you interested in whether the intervention offers benefit over other interventions.</p> <p>List your possible comparisons:</p> |

| | |
|----------------|--|
| Outcomes | <p>How do you think it is important to measure change with respect to this intervention in this population?</p> <p>List all the outcomes you are including in your review. Consider outcomes relevant to all potential decision-makers, including economic data.</p> <p>Divide your outcomes into primary (essential) outcomes and secondary. The main conclusions of your review will be based on the primary outcomes (usually three or fewer) so give this considerable thought. Primary outcomes are the two or three outcomes from among the main outcomes that the review would be likely to be able to address if sufficient studies are identified, in order to reach a conclusion about the effects (beneficial and adverse) of the intervention(s). Secondary outcomes include the remaining main outcomes (other than primary outcomes) plus additional outcomes useful for explaining effects.</p> <p>Ensure the outcomes cover potential as well as actual adverse effects.</p> <p>Consider the type and timing of outcome measurements. Are there any methods of measurement or times to exclude (eg timing of outcomes that are clinically inappropriate or measurement tools that are not valid)</p> |
| Types of study | <p>There may be some study methodology aspects that, if present, you feel renders that study so invalid to your review that it should be excluded. Some more common ones are lack of randomisation, failure to conceal allocation or, in reviews where the outcomes are very subjective (eg global assessment of improvement or levels of depression), blinding of the outcome assessor.</p> <p>Are there any exclusions related to trial methodology in your review?</p> |
| Review title | <p>As we have discussed already, the title of a Cochrane review usually follows the format:</p> <p><i>Intervention for Problem in Category</i></p> |



Getting it into RevMan

This is covered in the first part of the RevMan Tutorial, which you should now do, if you haven't done it already

*Try part one of
the RevMan
Tutorial, if you
haven't
already done
so*