Module 1: Introduction to systematic reviews

Learning objectives

- Be familiar with the rationale for systematic reviews
- Understand the concept of bias
- Be familiar with different types of questions that can be posed about the effects of health care interventions
- Consider study designs which are most likely to give a valid answer to these questions
- Be aware of practical problems in finding, appraising and synthesising non-RCT evidence

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

- Chapter 1: Introduction

Other relevant material

- *Rationale for systematic reviews* by Cynthia Mulrow (Mulrow CD. Rationale for systematic reviews. BMJ 1994; 309:597-9.)

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Too much information, too little time

This is the essence of an important problem facing people who make decisions about health care. There is simply too much information around for people to keep up to date. On top of this, high quality information is often not easy to find.

The rationale for systematic reviews is explained in the article by Cynthia Mulrow, which you should now read. If you don't have access to it, the main points are summarised below for you.

Read the article 'Rationale for systematic reviews' by Cynthia Mulrow

The full text of the article is available at:

http://www.bmj.com/cgi/content/full/309/6954/597

The rationale for systematic reviews can be summarised like this:

- People making decisions about treatment choices, or other health care interventions, need reliable information
- There is too much information around for decision makers to keep up to date
- Therefore, decision makers need reviews of existing information
- Reviews can be unscientific and biased in the way they collect, appraise and summarise information
- Systematic reviews attempt to minimise these biases to provide a reliable basis for making decisions

Are reviews science?

Systematic reviews aren't new, and have been used in the natural sciences, such as physics, for some time. The idea behind them is simple. Science is cumulative, with new ideas being based on previous knowledge and observation, and new advances in science should help us make sense of what we already know and have observed. But if we don't collect previous knowledge and observation in a systematic way, we are unlikely to make progress as quickly as we could. For example, if we are not aware of relevant research done by someone in another country, we cannot use that to help formulate our own research. We might even choose to do exactly the same research, without realising it has already been done. This is wasteful.

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You might imagine that researchers do this routinely, but a study of controlled trials in leading medical journals showed that these studies are often published without reference to what we know already, and without discussion of what the new study adds to our knowledge. The reader is expected to go and find out all that for herself. Try the activity on the left.

Activity: Find a recent report of a research study. Does it tell you what research has been done before? And does it tell you what the study added to our body of knowledge?

The need to be more scientific about how science progresses is increasingly being recognised in health care. For instance, the UK Medical Research Council now requires evidence that a systematic review has been prepared before it will commission a new trial. This ensures that the question has not already been answered, and that the results of previous research are used in designing the new trial.

What is bias?

You've probably already noticed that the word 'bias' has been used in this module. This word has a meaning here which is similar to its meaning in common usage. Bias means something that will cause a consistent deviation from the truth. This is different from the play of chance.

Bias means something that will cause a consistent deviation from the truth

For example, if we took a random sample of five people on a shopping street, four of them might be men. Would we then predict that four out of every five people are men? No, the play of chance meant that the sample we took was not representative of the whole population. The next sample of five people may well have had four, or even five, women.

If, however, we tried to estimate the proportion of men in the whole population by taking samples from a football crowd, we would probably find that, even if we took a very large sample, there would be more men than women. This is simply because we are taking a sample from a place which is not typical of the world at large – we have introduced a bias into our sampling which will cause us always to overestimate the proportion of men in the population.

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Minimising bias

This is an expression you will see a lot in relation to systematic reviews. Because the aim is to provide reliable information, we need to do as much as possible to minimise the effects of anything that will cause the results to deviate from the truth. In other words, we need to minimise bias.

There are many possible sources of bias, which we will look at in various modules. For now, they can be grouped into two areas: bias arising from the studies included in the review, and bias arising from the way the review is done.

We'll come back to bias in the studies collected for a review shortly. The 'systematic' part of systematic reviews is all about minimising bias in the way the review is carried out. People have tried to identify the major sources of bias and error in reviews, and to design a system that will minimise them. The process involved in a systematic review goes like this:

The steps of a systematic review

- Define the question
- Look for all studies reliably addressing the question
- Sift the studies to select relevant ones
- Assess the quality of the studies
- Calculate results for each study (and combine them if appropriate)
- Interpret results

This general approach is followed in all systematic reviews, although the latter steps depend on finding some suitable studies.

The component studies of a review

There is no point taking a very systematic approach to preparing a review if the individual studies within it are not capable of answering the question your review poses. Just as we want to minimise bias in the review process, so we want to choose component studies that are likely to give us an answer close to the truth. There will always be the effects of chance and we can only overcome this by collecting as much evidence as possible, and taking account of it in the way we analyse and interpret results. But our only means of minimising the effects of bias, is to include only studies that are less likely to be biased.

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Choosing studies likely to give a valid answer to the question

Cochrane reviews address question of the effectiveness of health care interventions

These modules are mainly concerned with systematic reviews of health care interventions – questions of the type 'Does intervention A have different effects to intervention B in this health problem?' The Cochrane Collaboration has also recently started to conduct reviews of diagnostic test accuracy however it does not currently address other types of health questions such as prevalence, prognosis or genetic predisposition.

Examples of questions about interventions, from published reviews, are:

- Does the application of compression bandages or stockings aid venous ulcer healing?
- What are the effects of topical treatments applied during pregnancy on the later development of stretch marks?

These questions are about comparing different interventions and measuring their effects. This means there should be comparison groups, where one group receives one intervention and the other group receives the alternative.

Comparison groups should be as similar as possible

An important issue in designing studies like this is the generation of the comparison groups. We want the two groups to be identical in every respect, except for the different interventions they get. If the groups are not identical, we are often not sure whether differences in the outcomes between the two groups are due to these differences in the groups, or due to the interventions we wanted to study.

For example, if we wanted to compare the effect of compression bandages for venous ulcers with doing nothing, we would want comparison groups which had similar ages of patients, similar proportions of people with diabetes, similar proportions of smokers, etc. In fact, we would want anything that might affect wound healing to be equal in the two groups, and the only difference to be that one group gets compression bandages and the other doesn't.

We could try to make sure of this by 'matching' patients – for every person in the group getting compression bandages, we could try to find another person with similar age, same sex, diabetes and smoking status, and put them in the group not getting compression bandages.

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Randomisation will ensure, in the long run, that comparison groups are similar

As well as taking a lot of effort, the problem is that there may be factors influencing wound healing that we haven't thought about, or don't know about. We can't match for these. This is where the power of randomisation lies. If each person coming into the study has an equal chance of going into either group, over the long run all factors, known and unknown, will be equally distributed.

So, randomisation should produce comparable groups, and the groups are more likely to be comparable the more people are randomised. This means we are more certain about concluding that differences in the outcome are due to the treatment. In short, the studies are less likely to be biased, and we are more likely to believe the results. Studies that randomise participants to groups are called randomised controlled trials (RCTs).

There are other practical reasons for focussing on randomised controlled trials. These reflect some of the methodological work done in this area, and some of the work done by the Cochrane Collaboration over the last few years:

- A considerable amount of work has gone into making randomised trials easier to find, so that we don't find a non-representative, or biased, group of studies
- We are beginning to understand how to tell an unbiased trial from a biased one

The same amount of background work has not been put into the location and utilisation of other study designs. For this reason, concerns about interpreting results will be greater if we choose study designs other than randomised controlled trials. Most Cochrane reviews therefore use the presence of randomisation as a minimum quality criterion when deciding which studies to include and, therefore, only include randomised trials.

What if there aren't any trials?

Randomised controlled trials are more common in some areas of health care than others, for example where the interventions are drugs. What do we do if we have an important question, but there are no randomised controlled trials addressing the question?

Well, there's absolutely nothing 'wrong' with a systematic review that has been done to a high standard, but finds no studies. In fact, these reviews are very useful because they highlight important gaps in our knowledge. Research funders are increasingly looking at the results of systematic reviews to help them decide what studies to commission. So a review that finds no studies can stimulate new research that will be able to answer the question.

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Activity: Find a recent systematic review and read it.

See what you think of a review

It's a good idea to have a look at a systematic review for yourself. Find a recently published systematic review, for example by looking at *The Cochrane Library*, or searching PubMed (http://www.ncbi.nlm.nih.gov/sites/entrez) using the term 'systematic review'. Read the review, and ask yourself how well you think it summarises the evidence.

There's no need to carry out a formal appraisal of it; just think about how relevant it is, and how accurate you think it is. Can you think of any ways in which it could have been done better? Make some notes and keep them somewhere, so that you can come back to them at the end of these modules and think again about the quality of this review, and how you could do it better.

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