Module 18: Applying the results - inferences and uncertainty

This module will discuss the stage in a review when, having analysed and discussed the findings, we try to draw some conclusions.

Learning objectives

- Recognise inferences which may be misleading
- Be able to draw appropriate conclusions in the absence of evidence
- Be aware of uncertainty in clinical practice and health policy decision-making

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

- Section 12.7: Drawing conclusions

Where does this go in a Cochrane review?

- In the Discussion section of the review you will usually try to make some inferences from the findings
- The Authors' Conclusions section should succinctly summarise these inferences and any implications from the review for future practice
- The Authors' Conclusions section should also identify any implications from the review for future research

Starting at the end ….

We know that many people who read a review begin at the end, by looking at the conclusions and, often, the brief conclusions in the abstract. It is probably human nature as much as anything else to want a 'bottom line' from a research study or a review. Unfortunately, it is often very difficult or indeed impossible to provide this bottom line.

Whose conclusions?

Different users will draw different conclusions from the same review

As we have already seen in previous modules, users in different settings will often interpret the same evidence from the same review quite differently.

Within a review, any conclusions drawn are only those of the authors. For this reason Cochrane reviews specifically refer to *Authors' Conclusions* in order to highlight where these conclusions come from.

Usually there are three aspects to drawing conclusions:

- Does the intervention work at all? (as covered in module 16)
- What have we learned from this review that can be applied to clinical practice?
- What have we learned from this review about the need for further evaluation and research?

What are the implications for clinical practice

Weighing up the evidence – how do the scales balance out?

The first component of a conclusion is a bit like putting all the evidence you have obtained from the review on a balance scale and trying to see which way it tips and how confident you are about this interpretation. In essence, you need to decide, after taking all the possible outcomes into account, which of the alternatives (on balance) is likely to do more good than harm (and should be applied in practice) or more harm than good (in which case it should be abandoned from practice). However, more often than not your conclusion will probably be somewhere in between these two scenarios. It may be that there are important trade-offs between different outcomes (such as in the example of treating sore throats with antibiotics that we used in Module 17) and your conclusion needs to reflect this.

Uncertainty reigns

Sometimes there is insufficient evidence to draw a conclusion

Alternatively, you may find that there is insufficient evidence to arrive at a firm conclusion of any kind. In situations where there is still uncertainty (for example not enough or no trials, trials of poor quality or contradictory evidence from a group of trials), you may be wise to conclude that there is a need for further research in order to gain sufficient evidence to assess the effects of an intervention.

What are the implications for further research

Further research needs to be targeted wherever possible

While there may sometimes be a need for more research in order to gather sufficient evidence to address the original objectives of the review, it is often the case that the further research needs to be targeted to specific issues that have arisen out of the review. For example, in a review of nicotine replacement that has been maintained regularly since 1994, it was established that different nicotine replacement delivery systems (such as nicotine gum, patch, and inhaler) were more effective than placebo. However, further primary research was required to establish the effectiveness of a combination of different delivery formats. This was subsequently done and has now been included in updates of the review.

Each time a review is updated some questions that previously required further research might have been answered, and new questions may arise. This is why updating reviews regularly is so important.

Traps for the unwary

There are several common mistakes frequently made by reviewers:

Distinguish between 'no evidence of effect' and 'evidence of no effect'

i. Evidence of no effect versus no evidence of effect

Often, when there is inconclusive evidence we confuse '*no evidence* of effect' with 'evidence of *no effect'*. These two statements are not the same thing.

Often when there is insufficient evidence, a summary estimate will have wide confidence intervals that will include both the null and the possibility of quite big effects (either helpful or harmful). As an example, let's consider a summary relative risk of 1.02 with 95% confidence intervals that extend from 0.74 to 1.40. In this situation, there is no (or insufficient) evidence of effect, We can't say with any confidence that there is no effect, and it could be in either direction.

What we need is more evidence to increase our capability (or power) of detecting an important effect. If we wrongly concluded from the available evidence that the intervention had no effect when it really does, this would be referred to as Type II error (i.e. false negative, or missing an effect that is actually there). For this example it may be better to conclude along the lines of "the results of this review are consistent with the intervention being effective or not effective and further research is needed".

As a second example take the identical relative risk, but with much more precise 95% confidence intervals from 0.98 to 1.06. This time we can say there is evidence that, if there is an effect, it is small and might be too small to be important to users of health care. Statements like this will depend on what size of effect is clinically important. A 2% change in risk might be clinically important in some situations, but not others.

Irrespective of where the boundaries of the 95% confidence interval lie, we need to remember there is a 5% possibility that the true summary effect lies outside of these boundaries, and our result may be incorrect. If we wanted to be more certain, we could calculate the 99% confidence intervals around the summary estimate.

ii. *Evidence-conclusion mismatches*

Another error is a tendency to try and draw conclusions beyond the available evidence. It is very important that every statement you make in your review conclusions is backed up by your results, and all important results are dealt with in your conclusions. A trend towards an effect cannot be interpreted as a positive effect. It is important that you don't become guilty of reporting bias by only including the outcomes of review for which there was a significant effect in the conclusion and abstract of your review. As a minimum, results for the important outcomes should be reported in the conclusions and abstract.

iii. *"Further research is needed"*

A third common mistake is to be non-specific about the need for further research. A statement like "further research is needed" is not particularly helpful. The research that is needed should be described.

While it is hard to be prescriptive about how to draw inferences and conclusions from a review, try and practice by using these common mistakes as a form of check-list against which to try and improve conclusions from your own review. In doing a review you also need to remind yourself that no matter how well it is done, the review itself cannot make a health care decision, it can only assist in the process. Furthermore, once someone has used a review to make a decision there is no guarantee that they will derive the predicted benefits or avoid the potential harms. There never can be certainty in how individuals or groups of individuals will respond to an intervention. All we can hope to do is provide them with an objective summary of the best available evidence to inform their own treatment choices.

Try it for yourself

Activity: Look at the results of a review, and try writing your own conclusions

If you have access to *The Cochrane Library*, choose a review, read the results, without looking at the conclusions, and then try to write some conclusions. Then compare your conclusions with those of the authors. Are they the same? If not, why do you think they differ?