Module 15: Publication Bias

Learning objectives

- Understand what publication bias is and describe how it could arise
- Be familiar with the design and interpretation of funnel plots
- Be aware of other relationships which can cause funnel plot asymmetry
- Be aware of other forms of bias in the reporting of studies, especially duplicate publication, selective reporting of outcomes and subscales, and subgroups of data.
- Consider methods of reducing the potential impact of publication bias on the results of a systematic review
- Be aware of ongoing research in this field

Other relevant material

- Presentation on reading a funnel plot

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

- Chapter 10: Addressing reporting biases

Where does this go in a Cochrane review?

- Ensure your search strategy is as sensitive as it can be to reduce the chances of missing negative studies, possibly attempt to measure publication bias as part of the analysis of your review in RevMan and consider the likelihood of publication bias in your review's Discussion.

What is publication bias?

Publication bias results in it being easier to find studies with a 'positive' result

Systematic reviews aim to find and assess for inclusion *all* high quality studies addressing the question of the review. But finding all studies is not always possible and we have no way of knowing what we have missed. Does it matter if we miss some of the studies? It will certainly matter if the studies we have failed to find differ systematically from the ones we have found. Not only will we have less information available than if we had all the studies, but we might come up with the wrong answer if the studies we have are unrepresentative of all those that have been done.

We have good reason to be concerned about this, as many researchers have shown that those studies with significant, positive, results are easier to find than those with non-significant or 'negative' results. The subsequent over-representation of positive studies in systematic reviews may mean that our reviews are biased toward a positive result.

Reporting bias is a group of related biases potentially leading to over-representation of significant or positive studies in systematic reviews

Publication bias is just one type of a group of biases termed reporting bias. We have quite a lot of evidence that these biases exist, so it is fair to assume that most systematic reviews will be subject to reporting bias to some extent.

Publication bias and other related biases can be summarised as statistically significant, 'positive' results being:

- More likely to be published (publication bias)
- More likely to be published rapidly (time lag bias)
- More likely to be published in English (language bias)
- More likely to be published more than once (multiple publication bias)
- More likely to be cited by others (citation bias)

All of these reporting biases make positive studies easier to find than those with non-significant results, something that we can try to minimise by extensive searching.

Managing publication bias

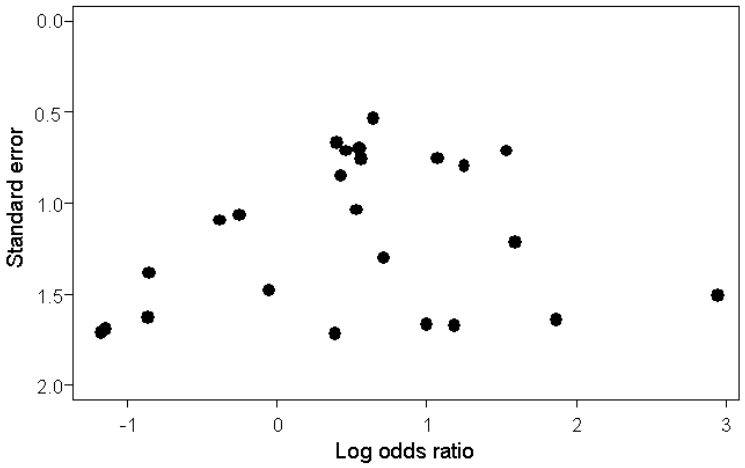
If we accept that your review will almost certainly be subject to publication bias to some extent, we are left with the problem of estimating how big a problem it is in your review, and what to do about it. There are several methods for getting an idea about how much of a problem this may be, and the method available in RevMan is the funnel plot. This means you should use the funnel plot option to investigate the presence of publication bias in your review and then discuss this in the Discussion section of the text of your review. If you suspect there may be a problem in your review, you need to bear this in mind when making your conclusions and recommendations. The likeliest scenario is that the results of your review are biased to the positive.

The slides at the end of this module explain the parts of a funnel plot and you should familiarise yourself with it before progressing any further.

In the absence of publication bias we might expect a symmetrical funnel plot.

Interpreting funnel plots

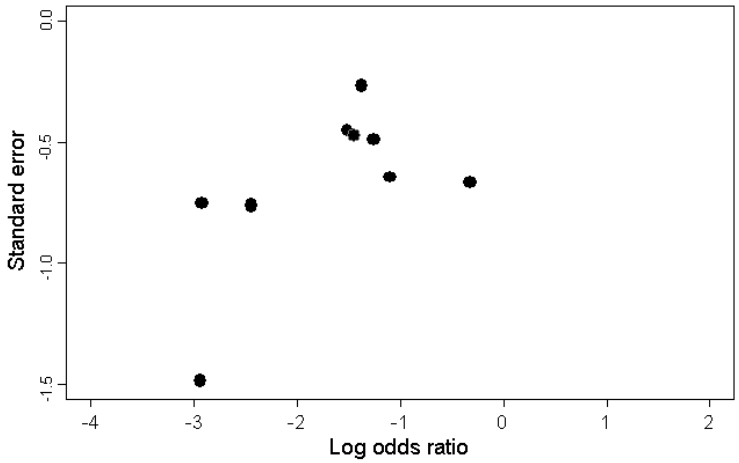
If publication bias is not present, you would expect your funnel plot to be roughly symmetrical, as in the example below:



As the studies become less precise (i.e. higher standard error), you would expect the results (given here as a log odds ratio) of the studies to be more variable, scattered to both sides of the more precise larger studies.

When you plot your studies onto a funnel plot, you may find it is not symmetrical and does not resemble an inverted funnel. This may be due to publication bias, however there are other factors leading to an asymmetrical plot.

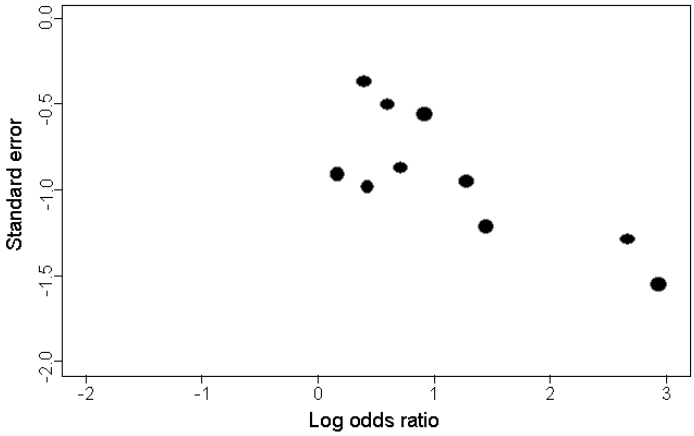
The next funnel plot is from a review of prevention for chronic non-steroidal anti-inflammatory medication induced gastro-intestinal toxicity.



An asymmetrical funnel plot may be due to study factors other than publication bias

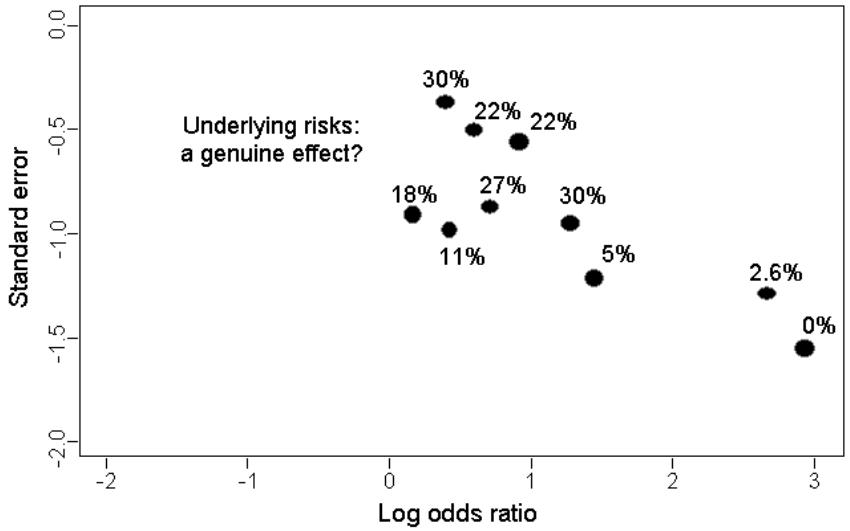
As you can see it is not symmetrical, although this impression is mainly caused by one small study to the left of the most common effect. This may indicate publication bias, but there are other possible explanations. The small study may be of lesser quality, and poor quality studies, especially those failing to conceal allocation, often result in exaggerated treatment effect sizes. Or this small study may have been performed in a particularly high risk population where the effect is large. In looking at this plot, we can only report that there may be publication bias.

Look at the plot below from a review of Aversive Smoking for smoking cessation. The outcome is risk of quitting, so the larger the OR the better aversive smoking works.



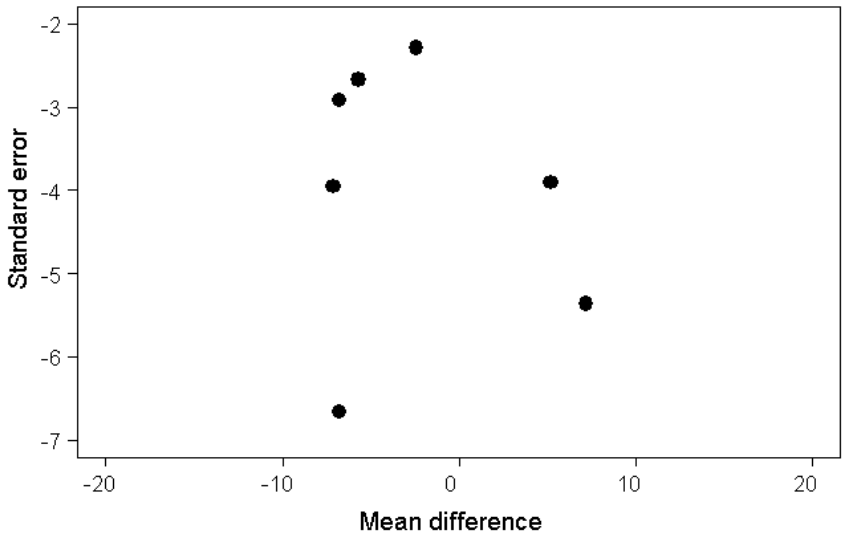
Does this look symmetrical? At first look it appears that the smaller, less precise studies are all much more positive than the larger, more precise studies, and there are no smaller studies to the left (negative) side of the graph. This appears to be a good example of publication bias.

If however, we add the control event rates (quit rate in the control group) to the plot, the interpretation may be different.



The trials with the lowest control event rates demonstrate the most positive results. We could convince ourselves when looking at this that the pattern of greater effect with lower control event rates represented a true relationship, adverse smoking works better in those more addicted people less likely to give up anyway (i.e. without the experimental intervention). Or it could be publication bias. There are lots of possible explanations for this pattern. The point is that from the funnel plot it is impossible to know.

Another possible type of funnel plot is a hollow plot, like this one from a review of dieting to reduce body weight for controlling hypertension in adults.



Here there are some trials to the right of the point of no effect, indicating that dieting increases blood pressure (measured as the mean difference on a continuous scale) and some to the left, indicating that dieting reduces blood pressure. There are no trials around no difference. This is possibly publication bias of the type where significant studies (i.e. those showing the intervention is significantly beneficial and those showing the intervention is significantly harmful) are published or found systematically more than those showing no difference.

From these examples, we can see that a funnel plot is not a very reliable method of investigating publication bias, although it does give us some idea of whether our study results are scattered symmetrically around a central, more precise effect. Funnel plot asymmetry may be due to publication bias, but it may also result from clinical heterogeneity between studies (for example different control event rates) or methodological heterogeneity between studies (for example failure to conceal allocation).

Even if there is publication bias in a review, it may not result in an asymmetrical funnel plot, for example when the plot is hollow.

There are some statistical tests for detecting funnel plot asymmetry (e.g. Egger's linear regression test and Begg's rank correlation test) but these have low power and are rarely used in Cochrane reviews. If you would like to use them, you should discuss this with a statistician.

Correcting for publication bias.
From what we have seen in this module so far, we know that the methods we have for detecting the possibility of publication bias in systematic reviews are not very good. Any methods for attempting to correct for this perceived bias are therefore also not ideal, but the following methods have been suggested. These are rarely used in Cochrane reviews but are included here for completeness.

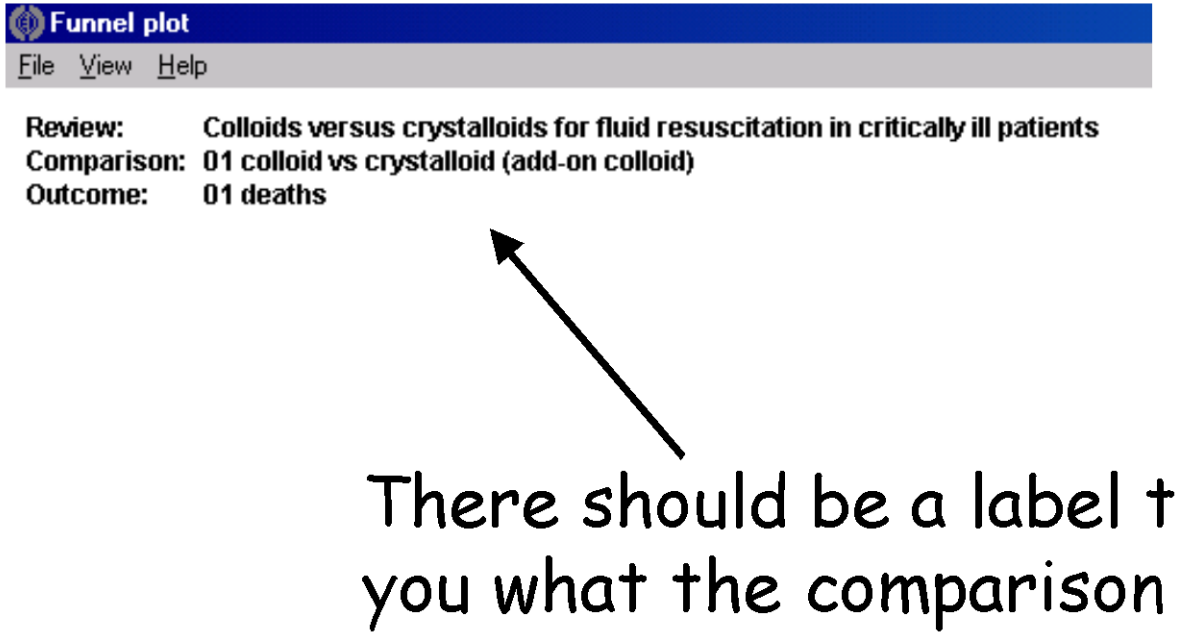
"Trim and fill method"
In this method the tail of the side of the funnel plot with the smaller studies is chopped off to make the funnel plot symmetrical, and it is then replicated and added back to both sides so the plot becomes symmetrical. The centre and variability of the filled funnel plot are then estimated (there are complicated statistical methods to do this formally).

Fail safe N
Here, the number of null studies (of similar size) which would be required to remove an observed significant effect is estimated. This method may give you an idea of the likely importance of any publication bias present. For example, if it tells you that several large negative trials would need to exist to overturn your positive result, you may decide it is quite unlikely that these were missed. This remains, however, a judgement.

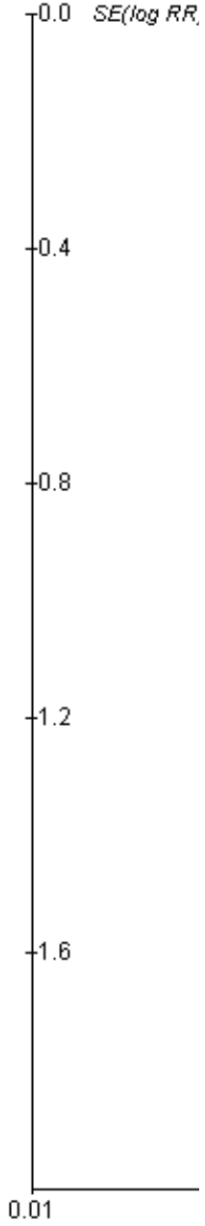
Modelling
Models for the probability that studies with particular results do or do not get published can be designed and used to investigate possible publication bias.

Summary
There is quite a lot of work being undertaken, both in the form of trials registers and more intensive searching to try to help reviewers identify all trials, and methodological research to advance the ways we measure and account for publication bias in systematic reviews. Currently however, the only thing we know for certain about publication bias is that it exists. Our methods for assessing its presence can only provide suggestions, not definite answers.

The main purpose of including issues to do with publication bias in your review is to ensure that you, and readers of your review, are aware of the fact that publication bias is possible, and to attempt, at least in part, to estimate how big an impact it might have on the results of your review.



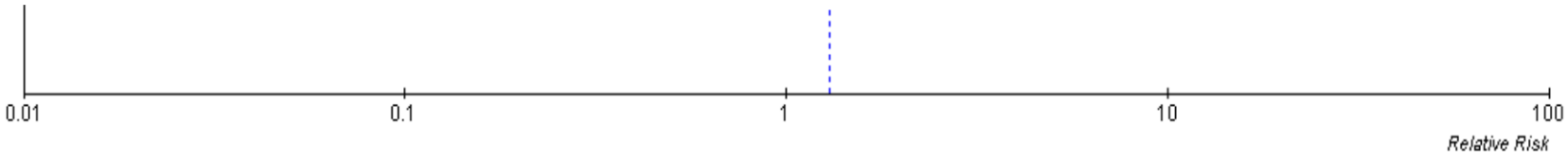
There should be a label telling you what the comparison is



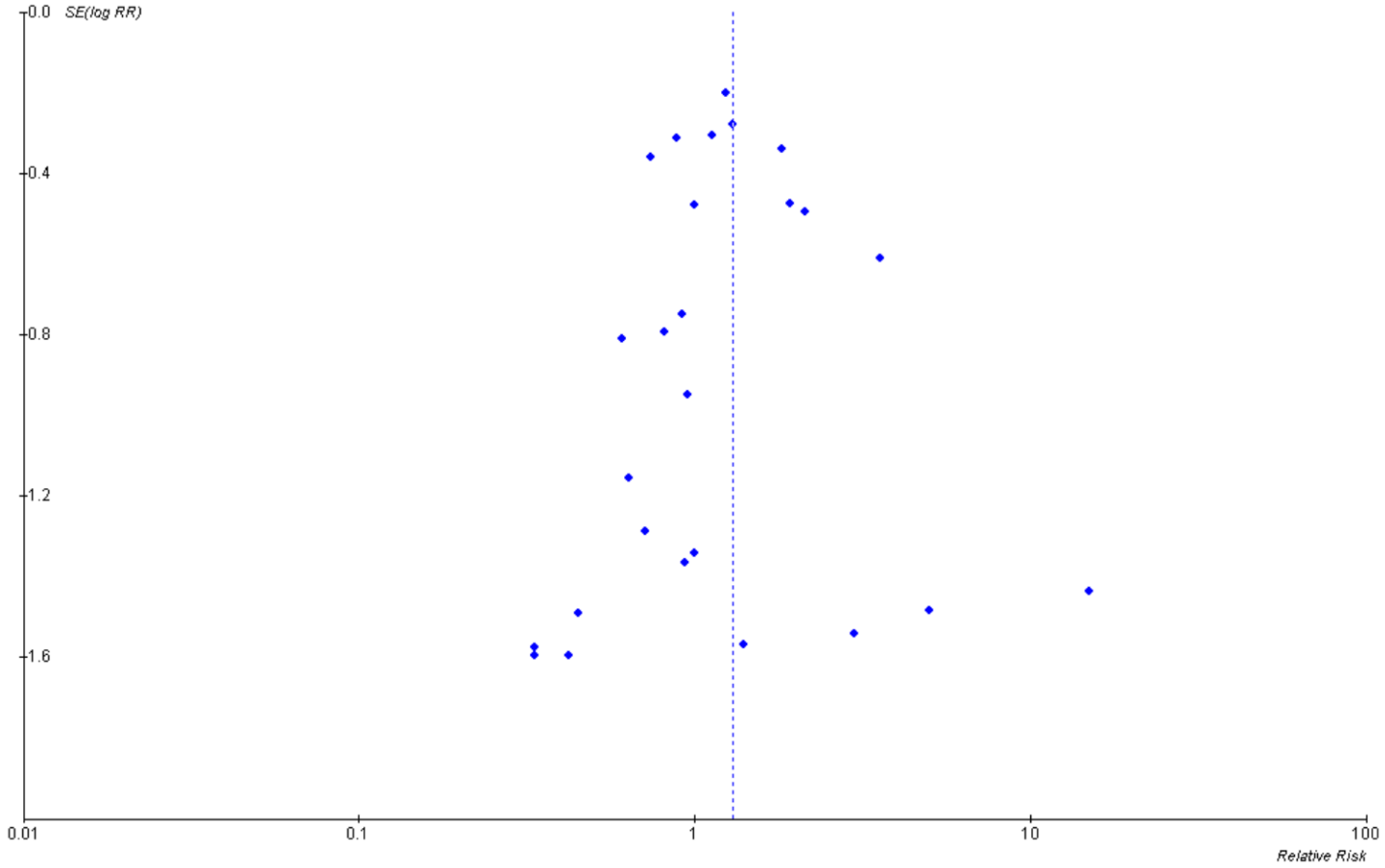
The vertical axis is some measure of the precision of the estimate of the treatment effect. So the smaller the confidence interval, the more precise the study, and the further up the study is placed.

Here, the measure of precision is the standard error of the log RR. Elsewhere, you may see sample size or weight used.

The horizontal axis measures the treatment effect – here it is the relative risk, on a log scale so that the distance from 0.1 to 1 is the same as from 1 to 10



The point estimate from each study is then plotted, and a vertical line added (this line isn't added in all packages) where the pooled estimate from the meta-analysis lies



We would expect less precise studies (with fewer participants and events) to be more affected by the play of chance, and so more widely scattered about the pooled estimate.

As studies get bigger with more events, we expect them to be closer to the pooled estimate. Overall, this should produce a triangular shape, or inverted funnel (depending on how the axes are plotted)