Publication bias – teaching materials

- The attached slides can be used to teach people about publication bias

- There are notes beneath the slides with suggestions of how they might be used

- Prepared by Professor Amanda Burls and available from http://openaccess.city.ac.uk/13488/

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- *Publication bias* by Dr Amanda Burls is licensed under a Creative Commons Attribution 4.0 International License.

Who's heard of friendly bacteria?

You are seeing a patient and she asks...

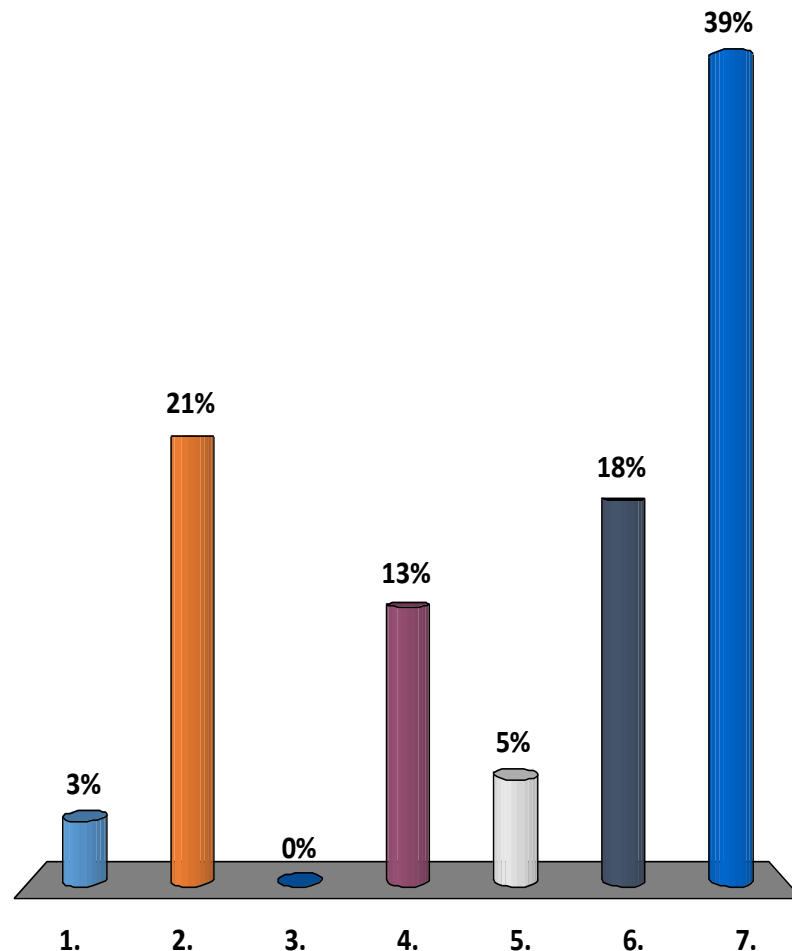*"Should I buy Activia™ to help with my tummy pain and improve my constipation?"*

You have 1 minute to discuss with your neighbour what you would tell her?

End

Which of the following is closest to your answer?

1. Try it - it can help some people

2. You need to ask a doctor a question like that

3. Yes, but any live yoghurt will do

4. No, there's no evidence it helps

5. I don't know

6. I don't know, but it can't do any harm

7. I don't know, but I'll look up the evidence and tell you next week

What is the evidence?

- What sort of study design would be best for answering this question?

Randomised Control Trial (RCT) of live yoghurt for Inflammatory Bowel Syndrome (IBS)

- P: Adults with IBS

- I: Activia (2 pots per day)

- C: Identical yoghurt with no live bacteria (2 pots per day)

- O: Adequate symptom relief

- T: 12 weeks

- Funded by Danone

- Undertaken by independent researchers at the University of Birmingham

RCT comparing live yoghurt with ordinary yoghurt IBS

- The trial ended in 2005
- What do you think the results showed?

Results for primary outcome

Table 3 Comparison of the proportions reporting adequate symptom relief in intention to treat analyses

Subjective global assessment (SGA)	Active product % (n)	Control product % (n)	Difference between the groups	p value active vs control
Week 4	56.7 (60)	53.1 (49)	3.61	0.707
Week 8	46.2 (52)	68.3 (41)	−22.1	0.027
Week 12	45.8 (48)	75.8 (33)	−29.9	0.004

End

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One participant in trial finally wrote to the investigator when these results had not been published five years later.

This was the reply…

Sent: 19 January 2010 15:45
To: Dr Amanda Burls
Subject: RE: Yoghurt trial

Dear Amanda,

The trial is not yet in press - this is in part due to the much longer than anticipated further analysis of the data at the funders request. In summary this was a negative trial - although both groups demonstrated benefit, those in the active product group did not show greater benefit and at times the difference actually favoured the control product….

Publication bias – the tendency not to publish negative findings

The trial was finally published eight years later (after pressure to do so)…

Roberts et al. BMC Gastroenterology 2013, 13:45
http://www.biomedcentral.com/1471-230X/13/45

RESEARCH ARTICLE

BMC Gastroenterology

Open Access

A randomised controlled trial of a probiotic 'functional food' in the management of irritable bowel syndrome

Lesley M Roberts[1], Deborah McCahon[1], Roger Holder[1], Sue Wilson[1] and FD Richard Hobbs[2*]

However, publication bias is

- Not only about not publishing
- Can also be about reporting outcomes that were positive but not mentioning those that were not (even when they were the primary outcome)
- Putting more positive results in the Abstract of the paper
- Distorting the Conclusions

Let's compare your conclusions to those in the paper

Conclusions: Significant improvements were reported for most outcomes in all trial participants but improvement did not differ by group. This trial does not provide evidence for effectiveness of a probiotic in IBS, in variance with a body of published literature and review conclusions. Differential drop out may however cloud interpretation of data.

Let's compare our implications for practice with those of the authors

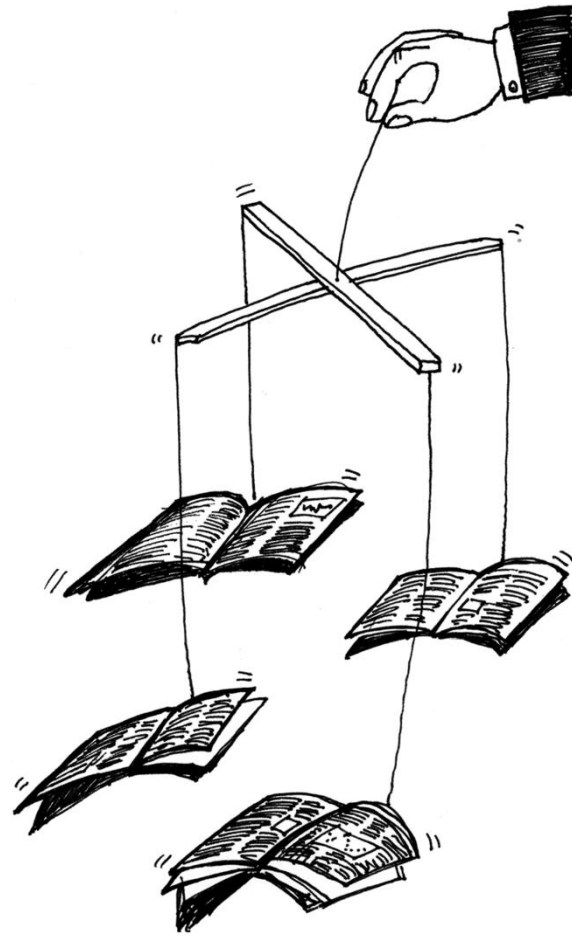**Implication for future research or clinical practice**
Clinicians advising patients with IBS managed in the community featuring a constipation element may wish to suggest the inclusion of a fermented dairy product, given that significant improvements were reported for most outcomes in all trial participants. The requirement of such products to contain a probiotic is not supported by this study.
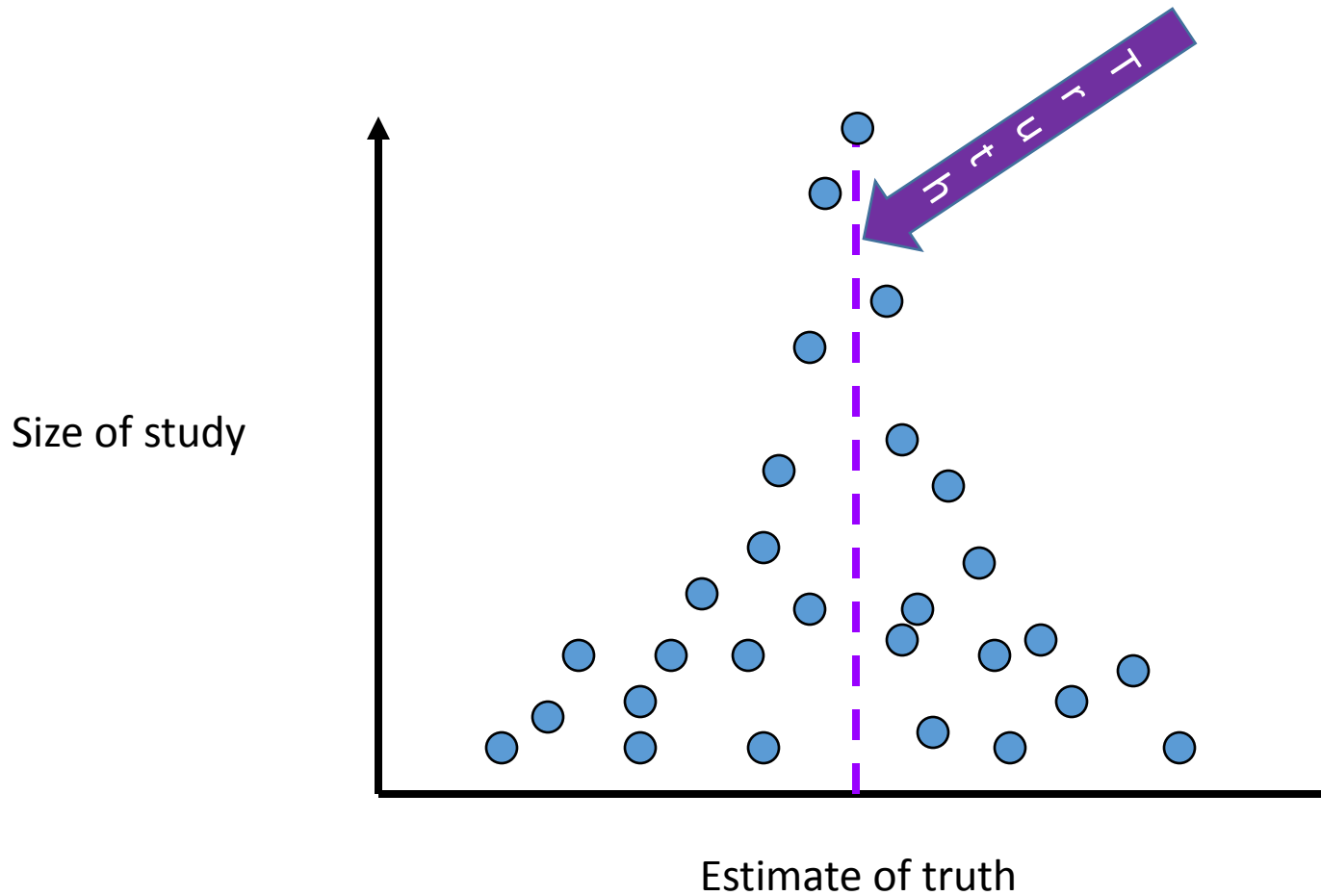
A biased conclusion - great for Danone!

- Activia was worse than the control yoghurt
- But, <mark>let's recommend fermented dairy products</mark> anyway!
- To back up such a recommendation randomized control trials are needed showing that fermented dairy products help patients with IBS compared to not having them.
- Otherwise we can't exclude bias or regression to the mean (that people get better anyway, without treatment!)

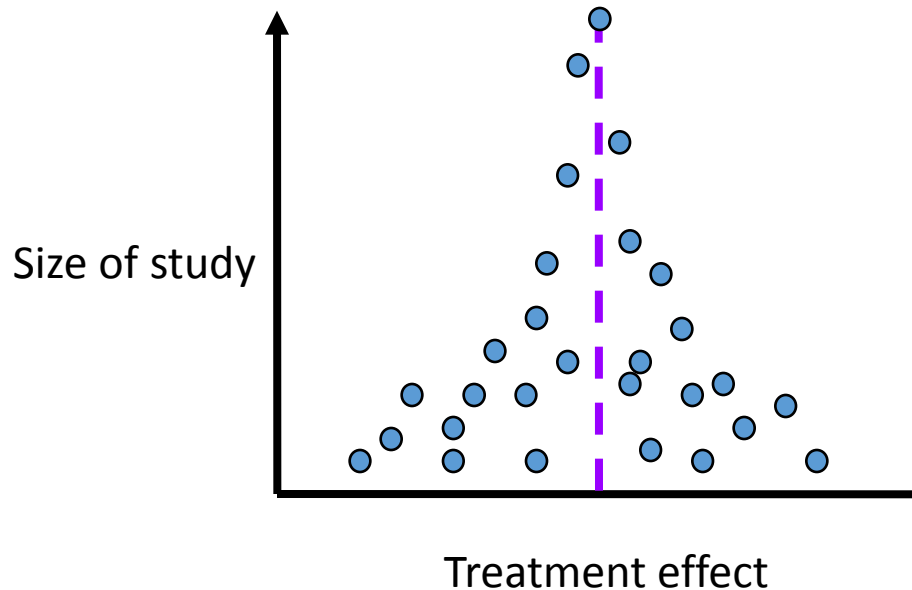# Further slides for later classes on publication bias

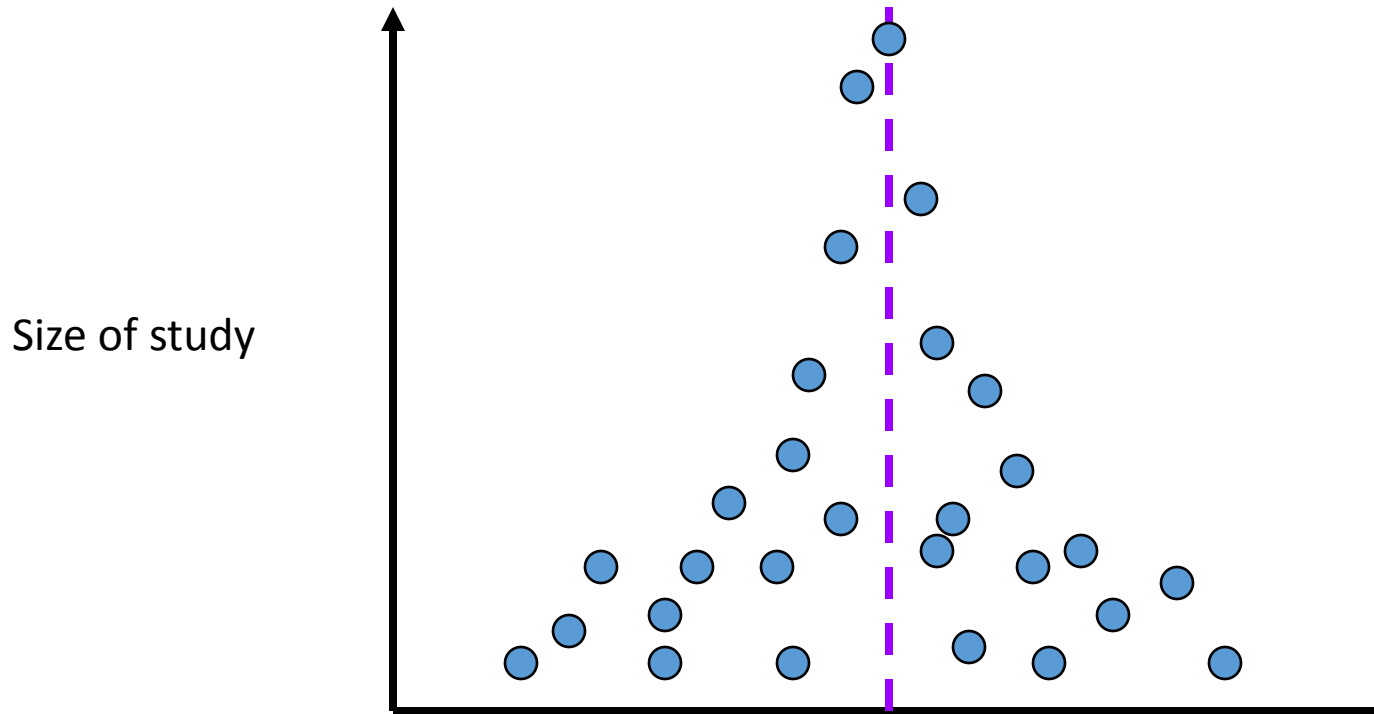# Looking for bias in systematic reviews

A funnel plot

Size of study

Estimate of truth

Funnel plots...

Size of study

Treatment effect
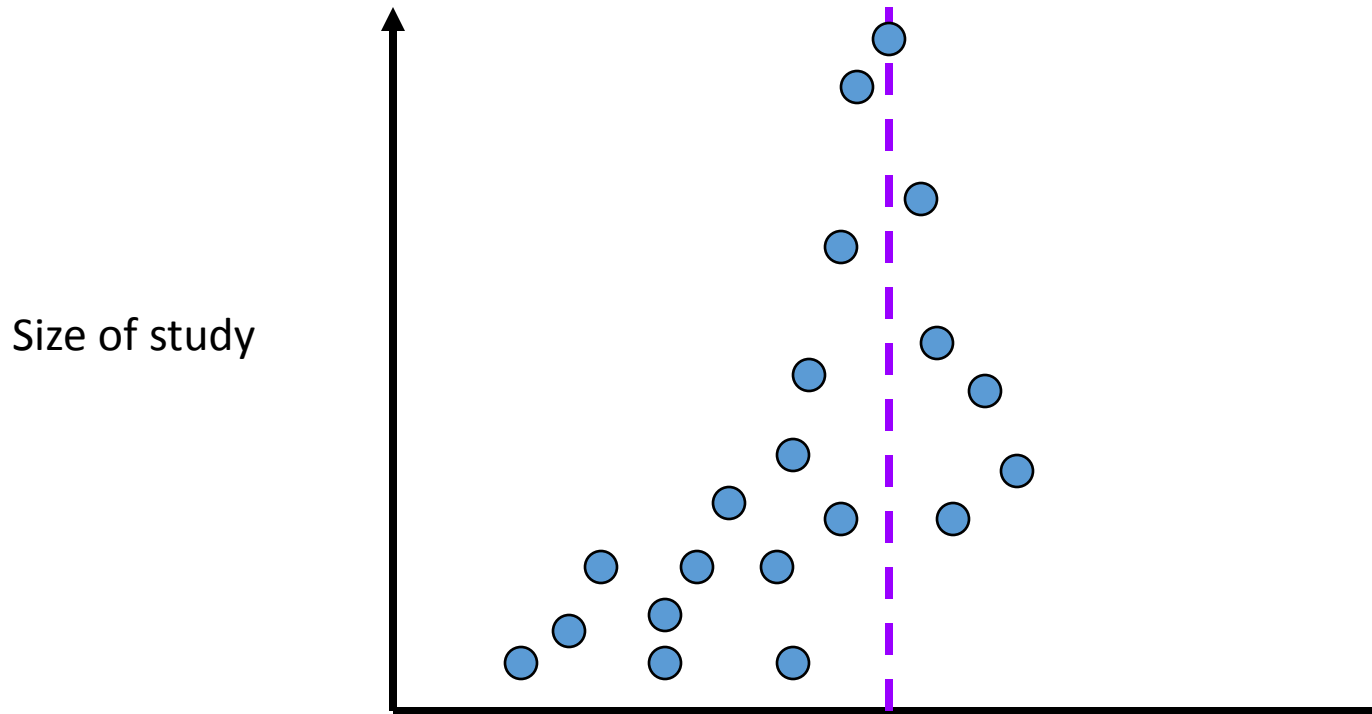
- …are scatter plots of treatment effect estimated from individual studies (x axis) against a measure of each study's sample size (y axis).

- The precision of the estimates of the treatment effect increases as sample size increases.

- Effect estimates from small studies scatter more widely at the bottom of the graph, with the spread narrowing among larger studies.

- In the absence of bias the plot should resemble a symmetrical inverted funnel.
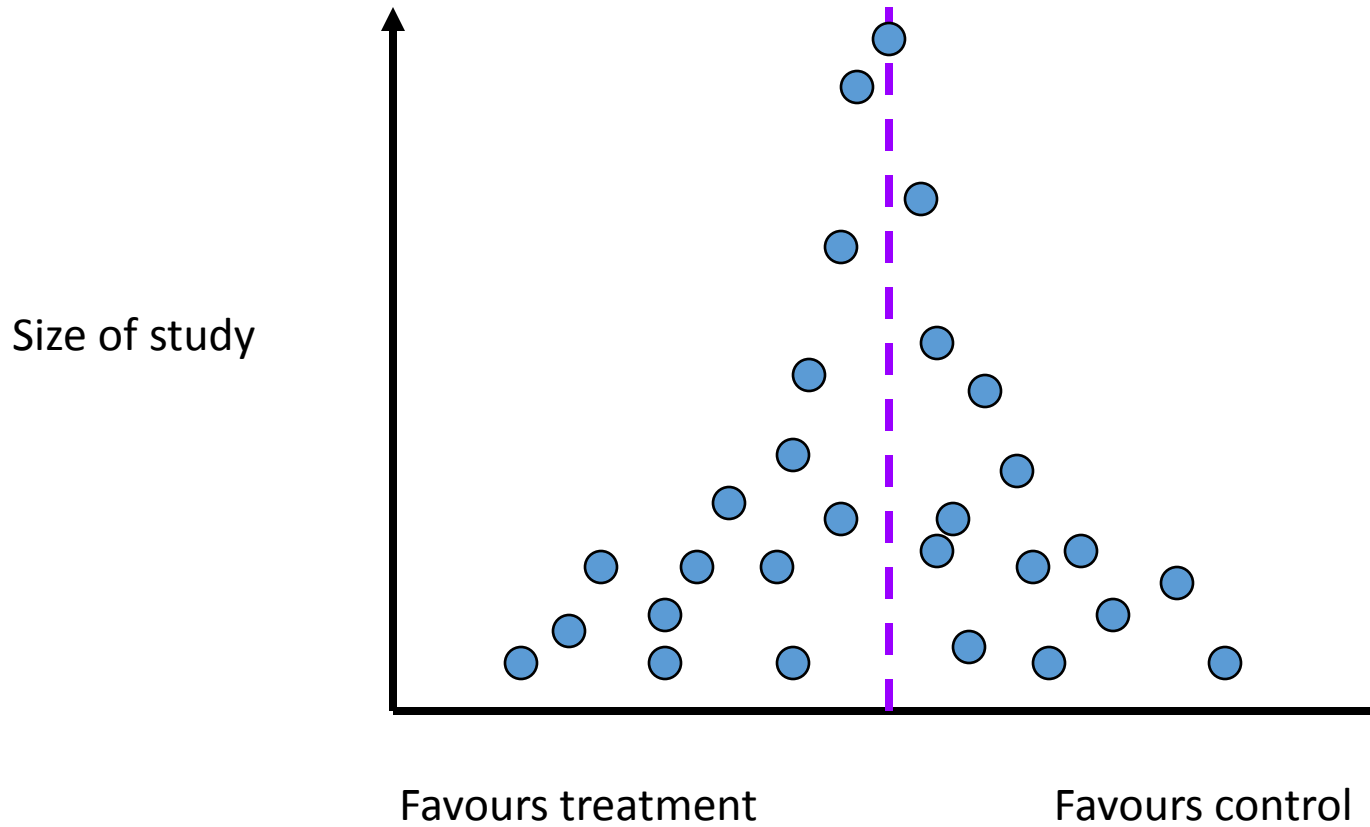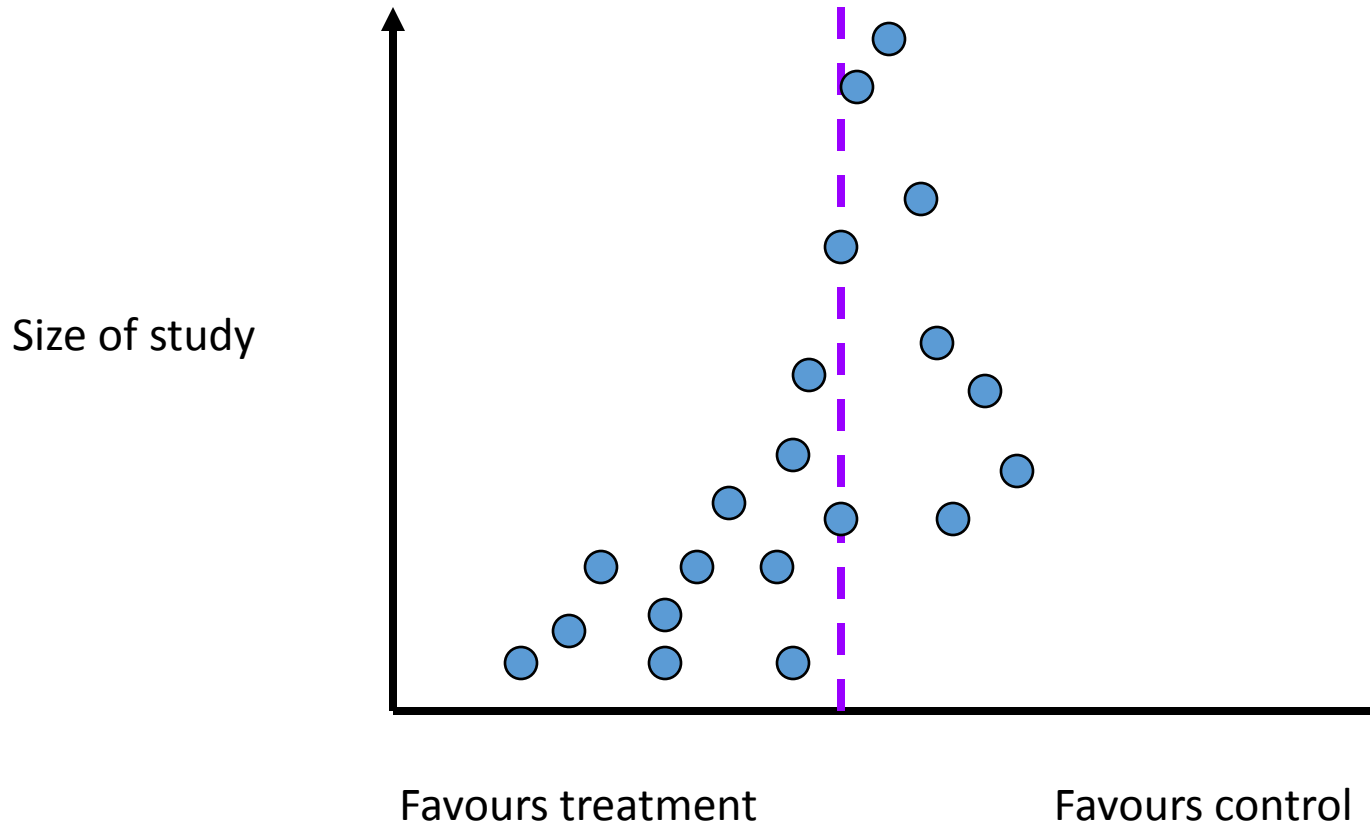
A funnel plot

Size of study

A funnel plot

Size of study

A funnel plot

Size of study

Publication bias distorts results

A funnel plot

Size of study

Favours treatment   Favours control

A funnel plot

Size of study

Favours treatment   Favours control

Sources of asymmetry

- Publication bias

- Poor methodological quality of smaller studies

- True heterogeneity i.e. size of effect differs according to study size

  - for example, due to differences in the intensity of interventions or differences in underlying risk between studies of different sizes

- Chance