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

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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.
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

<table>
<thead>
<tr>
<th>Subjective global assessment (SGA)</th>
<th>Active product % (n)</th>
<th>Control product % (n)</th>
<th>Difference between the groups</th>
<th>p value active vs control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>56.7 (60)</td>
<td>53.1 (49)</td>
<td>3.61</td>
<td>0.707</td>
</tr>
<tr>
<td>Week 8</td>
<td>46.2 (52)</td>
<td>68.3 (41)</td>
<td>-22.1</td>
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<tr>
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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...
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)...
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, let’s recommend fermented dairy products 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...

- 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
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