

ENDGAMES

STATISTICAL QUESTION

Open clinical trials

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Researchers assessed the effectiveness of adenotonsillectomy in children with mild symptoms of throat infections or adenotonsillar hypertrophy. An open randomised controlled trial was performed. Control treatment consisted of watchful waiting. In total, 300 children aged 2-8 years were recruited and randomised to adenotonsillectomy (n=151) or control (n=149).¹

The main outcome measures included episodes of fever, throat infections, upper respiratory tract infections, and health related quality of life. The researchers reported that adenotonsillectomy had no major clinical benefits over watchful waiting in children with mild symptoms of throat infections or adenotonsillar hypertrophy.

Which of the following types of bias, if any, might this open clinical trial be liable to?

- a) Allocation bias
- b) Ascertainment bias
- c) Assessor bias
- d) Detection bias
- e) Response bias

Answers

Options *b*, *c*, *d*, and *e* are all true, whereas *a* is false.

Clinical trials are referred to as “open” or simply “unblinded” if the participants, investigators, and all peripheral staff are aware which treatment the participants are allocated. If an open trial involves the investigation of a drug then it is typically referred to as “open label.” Open trials do not have to involve randomisation or include a control treatment. Phase I and phase II trials, described in a previous question,² are often open.

In the example above, the participants would have undergone informed consent before recruitment and would therefore know which treatments they could receive—adenotonsillectomy or watchful waiting. After randomisation the participants and investigators would obviously have been aware of the treatment allocation.

Ascertainment bias is the systematic distortion of the assessment of outcome measures by the investigators or trial participants because they were aware of treatment allocation. Ascertainment bias is sometimes referred to as detection bias. Because the trial was open, ascertainment or detection bias may have occurred (*b* and *d* are true). Ascertainment bias would have occurred, for example, if the researchers favoured adenotonsillectomy and wished to show it was more effective than watchful waiting. The investigators were aware of treatment allocation, and therefore could have been biased in their assessment—subconsciously or otherwise—towards adenotonsillectomy. Ascertainment bias could also have occurred, for example, if participants knew their treatment allocation; they might have been disappointed if allocated the control treatment and reported worse scores than they experienced, particularly for outcomes measured subjectively, resulting in an exaggerated difference between the treatments in outcome. When ascertainment bias occurs on behalf of the investigators it is called assessor bias, and when it occurs on behalf of the participants it is known as response bias. Therefore, because the trial was open it was liable to assessor and response bias (*c* and *e* are true).

Allocation bias is the systematic difference between participants in how they are allocated to treatment. Allocation bias did not occur because participants were randomised to treatment (answer *a* is false). Each participant, therefore, had an equal probability of being allocated to adenotonsillectomy or control.

Competing interests: None declared.

- 1 Van Staaij BK, van den Akker EH, Rovers MM, Hordijk GJ, Hoes AW, Schilder AGM. Effectiveness of adenotonsillectomy in children with mild symptoms of throat infections or adenotonsillar hypertrophy: open, randomised controlled trial. *BMJ* 2004;329:651.
- 2 Sedgwick P. Phases of clinical trials. *BMJ* 2011;343:d6068.

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