ENDGAMES

STATISTICAL QUESTION

Allocation concealment versus blinding in randomised controlled trials

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Researchers investigated the effectiveness of the provision of whole food to enhance the completion of treatment for tuberculosis. A parallel group randomised controlled trial study design was used. The intervention was a nutritious culturally appropriate daily meal (weeks 1-8) and food package (weeks 9-32). Control treatment was nutritional advice alone at enrolment. Both intervention and control groups received standard care throughout the study period. The primary outcome was completion of treatment (clearance of acid fast bacilli from the sputum after treatment or the completion of eight months of treatment, or both).[1]

Participants were 270 adults (aged over 18 years) with previously untreated and newly diagnosed pulmonary tuberculosis, recruited from primary care clinics in Dili, Timor-Leste. Participants were randomised to treatment group after they had started standard tuberculosis treatment. The randomisation sequence was computer generated. Allocation concealment was ensured by the use of sequentially numbered, opaque, sealed envelopes. An independent observer, blinded to the allocated treatment, assessed the primary outcome.

There was no significant difference between treatment groups in the proportion of participants who achieved the primary outcome (intervention 76% *v* control 78%, P=0.7). It was concluded that provision of food did not improve outcomes in patients undergoing tuberculosis treatment in Timor-Leste.

Which of the following statements, if any, are true?

a) Allocation concealment ensured that the sequence in which patients would be allocated to treatment was not disclosed before random allocation

b) Allocation concealment minimised allocation bias

c) Allocation concealment meant that patients were blind to which treatment they had been allocated after random allocation

d) Allocation concealment ensured that the trial was double blind

Answers

Statements *a* and *b* are true, whereas *c* and *d* are false.

Allocation concealment and blinding in clinical trials are often confused. Allocation concealment involves not disclosing to patients and those involved in recruiting trial participants the allocation sequence before random allocation occurs (*a* is true). The allocation sequence is the order in which participants are to be allocated to treatment. Blinding involves not disclosing to patients and outcome assessors the treatment allocations after random allocation.

The purpose of the trial was to investigate the effectiveness of the provision of whole food to enhance the completion of treatment for tuberculosis. The control treatment was nutritional advice alone. Participants were randomised to treatment groups once they had started standard tuberculosis treatment. Random allocation was necessary so that the treatment groups had comparable baseline characteristics. Any differences in baseline characteristics between groups would have resulted in confounding. If this had been the case, any differences between treatment groups in the outcomes might not have been the result of differences in treatment received but the result of differences in baseline characteristics. Random allocation of participants was therefore crucial to be able to infer causation between treatment and outcomes. However, the success of random allocation was dependent on consecutively recruited patients being allocated to treatment groups according to the allocation sequence that was randomly generated by computer.

Allocation concealment involved not disclosing the allocation sequence to patients and those personnel involved in recruitment before the trial participants were recruited (*a* is true). It was important that this sequence was concealed because otherwise it might have been possible to subvert the recruitment and treatment allocation of participants. In particular, allocation concealment meant that it was not possible to influence which patient received the next treatment in the sequence.

If the researchers and personnel involved in recruiting patients knew the allocation sequence they may have selected,

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unconsciously or otherwise, which patients were recruited or the order in which this was done. They may have believed that some patients would not have accepted, or been unsuitable for, the next treatment in the sequence. Patients were also unaware of the allocation sequence. This ensured that they could not dictate their participation or "self selection" on the basis of knowledge of the subsequent treatment in the sequence.

Allocation concealment in the above trial minimised selection bias. Selection bias is the systematic difference between those patients who are recruited for a trial and those who are not. Selection bias results in a sample that is not representative of the patient population. Allocation concealment also minimised allocation bias (*b* is true)—that is, a systematic difference between participants in how they are allocated to treatment groups. Selection bias and allocation bias have been discussed in more detail in a previous question.[2]

Allocation concealment is always possible in trials and it is essential if blinding is to be achieved. However, blinding cannot always be achieved in trials. Despite allocation concealment, because of the nature of the intervention and control in the above trial, it was not possible to blind participants to their allocated treatment after they had been randomly allocated (*c* is false). Because trial participants were not blind to their treatment allocation, the trial was not double blind (*d* is false). Although the primary outcome was objectively measured, it was still possible for participants to show a response bias because of the lack of blinding. For example, because participants knew their treatment allocation, they might have been disappointed if allocated to the control group and felt less cared for, with the result that they were less likely to complete treatment or recover. The trial was "assessor blind" because an independent observer blinded to the allocated intervention assessed the primary outcome. Hence assessor bias was minimised.

Competing interests: None declared.

1   Martins N, Morris P, Kelly PM. Food incentives to improve completion of tuberculosis treatment: randomised controlled trial in Dili, Timor-Leste. *BMJ* 2009;339:b4248.
2   Sedgwick P. Selection bias versus allocation bias. *BMJ* 2013;346:f3345.

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