

ENDGAMES

STATISTICAL QUESTION

Randomised controlled trials with full factorial designsPhilip Sedgwick *reader in medical statistics and medical education*

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Researchers explored the effectiveness of three interventions in preventing falls among older people. The three interventions were group based exercise, home hazard management, and vision improvement. A randomised controlled trial with a full factorial design was used. The control treatment was no intervention. The study design allowed the effectiveness of each intervention to be evaluated plus exploration of their effects when combined. The researchers recruited 442 participants aged 70 years and over living at home in an urban community in Melbourne, Australia. The main outcome measure was self reported time to first fall after randomisation.¹

The researchers reported that group based exercise was the most effective single intervention in reducing the number of falls. Falls were further reduced by the addition of home hazard management or vision management, or both.

How many treatment groups were there in the above randomised controlled trial that incorporated a full factorial design?

- a) Four
- b) Six
- c) Seven
- d) Eight

Answer

There were eight (answer *d*) treatment groups in the randomised controlled trial.

The standard clinical trial typically investigates the effects of a single intervention compared with control. The interventions of group based exercise, home hazard management, and vision improvement could have been compared against control in three separate trials. However, this would have been statistically inefficient, much time and effort would have been spent in recruiting participants, and it would have been expensive. A four arm parallel trial could have been carried out, comparing group based exercise versus home hazard management versus vision improvement home versus control. Such a trial would have needed a larger sample size than any of the individual trials, although it would not have been as large as the combined sample size for three separate trials.

A full factorial design was used in the randomised controlled trial. This design allowed the effects of each intervention—group based exercise, home hazard management, and vision improvement—to be separately compared with the control. It also allowed interventions to be combined and their effects to be evaluated when compared with the control. The full factorial design was more efficient than a four arm parallel trial.

The above trial is referred to as a 2^3 full factorial design because it involved three interventions. There would have been two possible exposures for each intervention, including the control arm. Because the three interventions were compared against control in a factorial trial, the number of possible treatment groups a patient could have been allocated was 2^3 ; that is, $2 \times 2 \times 2 = 8$ treatment groups in total (answer *d*). To be allocated to one of eight groups, participants in effect underwent three separate randomisations. Let group based exercise be denoted by A, home hazard management by B, vision improvement by C, and control by D. In the first randomisation, participants were allocated to group A or D. In the second one each participant already allocated to A or D was allocated to B or D, resulting in treatment groups AB, AD, DB, and DD. In the third allocation, each participant in these four groups was subsequently allocated to C or D, resulting in the groups ABC, ABD, ADC, ADD, DBC, DBD, DDC, and DDD. The letters indicate which combination of treatments participants received. For example, participants allocated to the group ABC received all three interventions. Intervention D is control treatment which consists of no treatment. Therefore, the eight group combinations become A, B, C, AB, AC, BC, ABC, and D.

In practice the eight treatment groups were identified in advance so the participants did not have to undergo three separate random allocations. The researchers reported that 442 participants were recruited to the trial. These participants could have been randomly allocated to a treatment group. However, simple random allocation does not guarantee equal numbers of participants in each group. Therefore, to ensure balance of group numbers the researchers used an “adaptive biased coin” technique. This will be described in a future question.

The factorial design is viewed as a versatile experimental design because it allows researchers to investigate whether combining

interventions increases their effectiveness. It is the only design that enables this information to be obtained. The above trial was a full factorial trial because all possible treatment combinations were investigated. Factorial trials require particular considerations, especially at the design and analysis stages. The simplest factorial trial is a 2×2 design—one that involves two interventions each compared against a control treatment. Described in a previous question,² the 2×2 design incorporates four treatment groups and enables researchers to investigate the

effects of each intervention alone and both interventions combined against the control.

Competing interests: None declared.

- 1 Day L, Fildes B, Gordon I, Fitzharris M, Flamer H, Lord S. Randomised factorial trial of falls prevention among older people living in their own homes. *BMJ* 2002;325:128.
- 2 Sedgwick P. Factorial trials. *BMJ* 2010;340:c3401.

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