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ENDGAMES

STATISTICAL QUESTION

What is intention to treat analysis?

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Researchers investigated the effectiveness of a home based early intervention on children's body mass index at age 2 years. A randomised controlled trial was used. The intervention consisted of eight home visits from specially trained community nurses in the first 24 months after birth. This intervention was in addition to the usual childhood nursing services from community health service nurses. The control group received the usual childhood nursing services alone. Participants were first time mothers and their infants.[1]

The primary outcome was the child's body mass index at age 2. In total, 667 first time mothers and their infants were recruited to the trial; 337 were allocated to intervention and 330 to control. An intention to treat analysis showed that mean body mass index was significantly lower in the intervention group (16.53) than in the control group (16.82) (mean difference −0.29, 95% confidence interval −0.55 to −0.02; P=0.04).

Which of the following statements, if any, describe intention to treat analysis?

a) Maintains original group composition achieved after randomisation

b) Minimises confounding between treatment groups

c) Provides a pragmatic estimate of the benefit of the intervention

d) Typically provides a smaller estimate of the true effect of the intervention

Answers

Statements *a*, *b*, *c*, and *d* all describe intention to treat analysis.

The effectiveness of the home based early intervention on children's body mass index at age 2 years was investigated using a randomised controlled trial. The trial was analysed using the principle of intention to treat. This meant that all participants recruited to the trial were analysed and participants were compared in their outcome measurements on the basis of the treatment group to which they were originally randomly allocated. This was regardless of whether participants started the treatment allocated, subsequently withdrew from treatment, deviated from the treatment protocol, or received a different treatment.

Intention to treat analysis has two main purposes. Firstly, it maintains the original comparability of treatment groups achieved after randomisation (*a* is true). Providing the sample is large enough, the treatment groups will be similar in their baseline characteristics. Therefore, potential confounding between treatment groups will be minimised (*b* is true). Confounding factors are those that may influence treatment and outcome measures, such as demographics, prognostic factors, and other characteristics that might influence someone to participate in or withdraw from a trial. Any differences between treatment groups at the end of the study will therefore be the result of differences in treatment received and not potential confounding between treatment groups.

The second purpose of intention to treat analysis is a pragmatic one—it reflects what would happen in clinical practice (*c* is true). Treatments and interventions are not always acceptable or well tolerated. Patients often do not start, complete, or continue with their prescribed treatment. Therefore, intention to treat analysis provides an assessment of the practical effects and benefits of treatment in clinical practice.

Intention to treat analysis is usually thought to provide a smaller estimate of the true effect of an intervention compared with control treatment (*d* is true). This is because the estimated effect of the intervention would be expected to be reduced by the inclusion of participants that were non-adherent to or deviated from the protocol.

An intention to treat analysis depends on all trial participants providing a measurement of the outcome variables. However, in the trial above the researchers reported that 170 (25.5%) of the trial participants were lost to follow-up and did not provide a measurement of the child's body mass index at age 2. Because the primary outcome was collected two years after randomisation, it was inevitable that a large proportion of participants would be lost to follow-up. Reasons for loss to follow-up included loss of contact with participants, in addition to participants having moved away, no longer being interested, being too busy, being ill, or having died.

To perform an intention to treat analysis, the only alternative to omitting participants was for the researchers to estimate the missing data using complex methodology. Missing data were

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estimated using the approach of multiple imputation by chained equations. This involved predicting the missing values of body mass index at age 2 on the basis of all observed values of body mass index, demographics, and prognostic factors recorded during follow-up for all trial participants. Missing data and other methods of imputation will be discussed in future endgames.

The CONSORT guidelines encompass various initiatives and were developed to alleviate problems arising from inadequate reporting of randomised controlled trials. The guidelines recommend using intention to treat analysis as standard practice. Typically, a per protocol analysis will also be performed alongside an intention to treat approach. The per protocol approach will be described in a future endgame.

Competing interests: None declared.

1 Wen LM, Baur LA, Simpson JM, Rissel C, Wardle K, Flood VM. Effectiveness of home based early intervention on children's BMI at age 2: randomised controlled trial. *BMJ* 2012;344:e3732.

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