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ENDGAMES

STATISTICAL QUESTION

The purpose of control groups

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Researchers investigated the effectiveness of a monovalent rotavirus vaccine against severe rotavirus diarrhoea in children under 2 years. A matched case-control study design was used. Cases were 323 children under 2 years admitted to hospitals in El Salvador with laboratory confirmed rotavirus diarrhoea. Controls were 969 children matched to cases for age and neighbourhood in a ratio of 3:1.[1]

Details of vaccination with the monovalent rotavirus vaccine were confirmed retrospectively by inspection of vaccination cards held by parents. Details about further risk factors were collected from hospital records or in interviews with parents. The researchers concluded that monovalent rotavirus vaccine was highly effective against acquiring rotavirus diarrhoea severe enough to lead to hospital admission in children under 2 years.

Which of the following statements, if any, are true for the above case-control study?

a) When recruited all participants had severe rotavirus diarrhoea

b) The control group allowed the natural epidemiology of severe rotavirus diarrhoea to be studied

c) The control group comprised active controls

Answers

Statements *a*, *b*, and *c* are all false.

A control group is used in comparative studies. The aim of the above study was to investigate the effectiveness of a monovalent rotavirus vaccine against severe rotavirus diarrhoea in children under 2 years. A matched case-control study, observational in design, was used. Two groups of children were identified on the basis of their disease status—those that had been admitted to hospital with laboratory confirmed rotavirus diarrhoea (the cases), and children that were otherwise healthy (the controls) (*a* is false). The study was retrospective in design. Information about the risk factor of interest—the monovalent rotavirus vaccine—was collected from inspection of vaccination cards held by parents. Data on past exposure to other potential risk factors were collected from hospital records or in interviews with parents. If the cases and controls differed in vaccination rates, or other risk factors, it would indicate that exposure was associated with severe rotavirus diarrhoea.

The composition and purpose of a control group in a case-control study differ from those of a randomised controlled trial. A control group is essential in clinical trials (except for crossover trials where participants act as their own controls).[2] Trial participants are randomly allocated to an experimental treatment, such as a new drug, or to the control group. At baseline, participants in the control group will have a similar health status to that of those in the experimental treatment group. This is different from the above example, where the cases had laboratory confirmed rotavirus diarrhoea and the control group was made up of healthy children (*a* is false).

The control group in a trial receives no treatment, a placebo, or the standard treatment. All groups are then followed prospectively to observe the effects of treatment. The control group is described as concurrent or parallel. It is essential that controls are concurrent rather than historical. Historical controls are patients who have already been treated and assessed. It is possible that the causes and epidemiology of the disease or condition being studied change with time. If controls are concurrent, then the natural course of the disease or condition can be evaluated and compared with the experimental treatment group. This is unlike the control group in a case-control study. None of the controls in the example above had experienced severe rotavirus diarrhoea, so the control group did not allow the natural epidemiology of severe rotavirus diarrhoea to be studied (*b* is false).

An active control is a member of a control group in a trial who receives an existing treatment. In case-control trials, such as the one described here, controls receive no treatment (*c* is false). Active controls in a trial are sometimes described as positive controls, as compared with negative controls, who do not receive an active treatment—that is, they receive a placebo or no treatment. In the example above, the controls were matched controls. For each case, three controls of the same age (born within 30 days of the case) and living in the same neighbourhood were recruited.

The composition and purpose of a control group in a nested case-control study design are similar to those in a case-control

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study. Described in a previous question,[3] the nested case-control study is an observational design that incorporates a case-control study within a cohort study. Typically the cohort is prospective in design. Members of the cohort will be identified as a case if they experience the disease or condition of interest. For each case one or more controls will be identified from the same cohort—that is, cohort members who had not experienced the disease or condition. Cases and controls are usually matched. The cases and controls may then be followed prospectively. A nested case-control study is typically conducted instead of an analysis of the entire cohort for reasons of cost. In contrast to a case-control study, information in a nested case-control is collected prospectively and is therefore not prone to recall bias.

Competing interests: None declared.

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2 Sedgwick P. Crossover trials. *BMJ* 2012;344:e3710.
3 Sedgwick P. Observational study design. *BMJ* 2012;345:e5856.

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