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ENDGAMES

STATISTICAL QUESTION

Prospective cohort studies: advantages and disadvantages

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Researchers investigated the association between opium use and subsequent risk of death. A prospective cohort study design was used. Participants were 50 045 people in north-eastern Iran aged 40-75 years at baseline. Recruitment took place between January 2004 and June 2008, and participants were followed until May 2011. The median length of follow-up was 4.7 years per participant. The main outcomes were death from all causes, plus all major subcategories.[1]

Information about opium use was collected at baseline. Participants were asked their age when they started using opium and subsequent length of use, typical amount used, frequency of use, and routes of administration. Information about exposure to a wide variety of other risk factors, including tobacco smoking and alcohol consumption, was also collected at baseline. During follow-up, participants were contacted annually by telephone with detailed questions about their health status and any hospital admissions or outpatient procedures. Opium use and exposure to other risk factors were not systematically updated.

The study concluded that opium users have an increased risk of death from multiple causes compared with non-users. Increased risks were also seen in people who had used low amounts of opium for a long period, plus those who had no major illness before use.

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

a) Recall bias was minimised

b) It was possible to estimate the population at risk

c) It can be inferred that opium use causes an increased risk of death

d) The results may be biased if a substantial number of cohort members were lost to follow-up

Answers

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

The purpose of the study was to investigate the association between opium use and subsequent risk of death from all causes, plus all major subcategories. A prospective cohort study design was used. Participants were 50 045 people in north-eastern Iran aged 40-75 years at baseline.

The cohort study was observational in design. Unlike a clinical trial, there was no intervention. The study recorded cohort members' use of opium at baseline and followed them until death or the end of the study, whichever came first. The median length of follow-up was 4.7 years per participant. To ascertain whether opium use was associated with an increased risk of death, mortality in cohort members who reported opium use was compared with mortality in those who did not use opium.

The study was prospective in design, with opium use recorded before participants were followed up. Therefore, recall bias would have been minimised (*a* is true). Recall bias, described in a previous question,[2] is typically associated with retrospective designs, such as case-control studies. It is the systematic difference in the accuracy of reported information about past exposure to risk factors between those diagnosed with a disease or condition (cases) and otherwise healthy people (controls). Recall bias will be present if participants have selective preconceptions about the association between the disease or condition and past exposure to the risk factor(s). Because information collected at baseline about opium use was about past behaviour, it is possible that the data were inaccurate. However, there was no reason to suspect there was a systematic difference between groups of study participants in the accuracy of reported information about opium use. The prospective nature of the study meant it was also possible to estimate the time course of events—that is, how length and frequency of opium use before recruitment affected subsequent length of life.

The prospective nature of the study meant that it was possible to estimate the population at risk (*b* is true). Estimating the population at risk has been described in a previous question.[3] The death rates in the cohort as a whole, and for participants who used opium and those who did not, estimated the death rates in the population. It is not possible to estimate the population at risk from observational studies that are retrospective in design.

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In the above study, in addition to the risk factor of opium use, exposure to a wide variety of other risk factors was also recorded at baseline. This is typical for a cohort study. However, it was not possible to measure and then control for, through statistical analysis, all factors that may have affected the outcome of death. It is therefore not possible to infer causation from the observed association between opium use and death because this association may have been due to confounding (*c* is false). Only association, and not causation, can be inferred from the results of an observational study. This is in contrast to an experimental study, such as a clinical trial, that uses random allocation to control for confounding at baseline. However, the statistician Austin Bradford-Hill proposed a set of criteria, which if fulfilled, may allow causation to be inferred from an association between a risk factor and outcome when widely and consistently seen in observational studies.[4] Further discussion of the criteria are beyond the scope of this article.

As is typical of most cohort studies, a large number of participants were recruited to and followed for a substantial period of time. The median length of follow-up was 4.7 years. This was to ensure that a sufficient number of cohort members experienced the outcome of death. More generally, a large number of cohort members will need to be recruited and followed for a long time period if the outcome is rare. It is often difficult to maintain contact with all cohort members, particularly if the cohort is large and the length of follow-up is extensive. Loss of contact with a large number of patients can lead to biased results (*d* is true), especially if the reason for loss to follow-up is related to the risk factor or outcome. The authors of the above trial reported that at the end of the study (May 2011) only 0.6% (n=293) of the study participants had been lost to follow-up. This was a relatively low proportion of the cohort, and extensive resources were needed to achieve this.

A consequence of a long follow-up period in a prospective cohort study is that it is sometimes difficult to ensure that risk factors and outcomes are measured consistently. In the above study, the diagnosis of death from some causes may have changed with time. The aetiology of some causes of death may also have changed with time. The risk factors were recorded only at baseline, as is typical in cohort studies. Opium use of cohort members probably changed during follow-up, and this would affect the validity of the reported association with mortality.

It has been suggested that by definition cohort studies are prospective in design. However, cohort studies may also be retrospective in design. Therefore, it is important that cohort studies are identified as prospective or retrospective. Retrospective cohorts are sometimes referred to as historical cohorts. In a retrospective cohort study, for example, health records for a group of patients would have already been collected and stored in a database. The study would involve looking back at events that have already taken place. In effect, it would be possible to identify a group of patients—the cohort—and reconstruct their experience as if they had been followed prospectively. Although the patient information would probably have been collected prospectively, the cohort would not have been initially identified with the aim of following the members prospectively and investigating the association between a risk factor and an outcome. In a retrospective design it is likely that not all pertinent risk factors would have been recorded. This may affect the validity of a reported association between a risk factor and outcome when adjusted for confounding. Furthermore, it is possible that the measurement of risk factors and outcome(s) would not have been as accurate and consistent as in a prospective cohort study. Retrospective cohort studies have distinct advantages and disadvantages compared with prospective cohort studies. Retrospective cohort studies will be discussed in further detail in a later question.

Competing interests: None declared.

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