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Bias and Confounding

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Why is it important to know about Bias and Confounding?
Most epidemiological studies try to determine if an association exists between a risk factor and outcome. In appraising the observed relationship, it is important to keep in mind that the association may arise from either chance, bias or confounding or a combination of these. The role of 'chance' is dealt with through calculating probability values of study results being true or due to chance alone, i.e., through the use of 'p values' and 'confidence intervals'1. Bias and confounding also affect observations and lead to false conclusions regarding association between a risk factor and outcome, as discussed below.

What is Bias?
Bias is the distortion of results due to a systematic error introduced into a study during the design phase (sampling, subject recruitment), or the data collection phase (measuring exposure and outcome). There are many types of bias encountered in epidemiology. Four types of bias are briefly described below according to the study phases where they might occur:

A. Design Phase:
In this phase the bias that mainly results is due to (1) sampling and (2) selection of study subjects.
1. Sampling bias can occur if, for example, a household examination survey is conducted during morning hours to assess the prevalence of joint problems in the adult population. As healthy adults would be at work and those at home would most likely be older retired persons, this procedure would result in a biased higher prevalence of joint disorders.
2. Selection bias results if selection criteria differ for cases and controls, or exposed and unexposed subjects. For example, the odds ratio might be higher than expected in studying the relationship between smoking and lung cancer, if controls are chosen from amongst volunteers. This is possibly because individuals who volunteer to be studied, are also likely to be more health conscious and not indulge in risky behaviour like smoking.

B. Data Collection:
The following are some types of bias commonly encountered in this phase of the study.
1. Observation bias can result if an interviewer is aware of the study hypothesis and probes cases for history of exposure to a risk factor more than in controls (interviewer bias). On the other hand, persons have experienced an event are more likely to recall exposure to a factor compared to controls. For example, mothers with deformed children might be more likely to remember if they had or were exposed to rubella during that pregnancy (recall bias) compared to controls.
2. Misclassification bias results if there are problems with measurement, due to faulty equipment or bad technique on the part of the persons recording a measurement. For example, if the person weighing children does not standardize the scale prior to weighing the child, borderline children will be mistakenly classified either as being malnourished or well nourished depending on what that scale registers at rest.

What is the Effect of the Various Biases on the Measure of Association?
As the effect of biases is similar whether the measure of association is the odds ratio or the relative risk, the odds ratio is used in the table below to illustrate such effects.

What is Confounding?
This is the differential effect of unknown or uncontrolled factors on study groups, e.g., cases and controls. For example, in assessing the relationship between chewing betel nut and oral cancer, gender

of individuals is a potential confounder. If the proportion of females in the overall sample is small, the association between chewing \'paan\' and oral cancer is likely to be underestimated especially if females are likely to be paan chewers. Thus a third unknown or uncontrolled factor may be differentially present in the groups divided according to exposure to the suspected risk factor and also have an independent association with the outcome.

Example:

In step 1, calculation of the crude odds ratio (OR= 1) shows no difference between cases and controls regarding exposure to paan chewing, i.e., paan chewing is not associated with oral cancer.

Step 2 examines the risk of exposure to paan in cases and controls separately for males and females. Results for each of these strata show that cases are twice as likely as controls to have been paan chewers (OR= 2). The difference between the crude analysis (Step 1) aI3d stratified analysis (Step 2) is that in this example females were more likely to have oral cancer (n= 140) compared to males (n= 110) but were under-represented in the overall sample.

How do I minimize the effect of Bias and Confounding in the Study?

The effect of bias and confounding cannot be eliminated entirely, but can be minimized if the researcher is aware of the potential types of biases and confounders that might distort study results. Bias can be taken into account in the different phases as follows:

1. Design phase: This can be accomplished by avoiding situations for selective sampling or subject recruitment. The example of sampling bias described earlier can be overcome by conducting the examination survey during evening hours as well as on the weekend to ensure representation from adults that are away at work on weekdays. To overcome the selection bias caused by using volunteers as controls in studying the effect of smoking on lung cancer, it might be wise to select controls randomly from hospital records or from the community.

2. Data collection phase: 'Blinding' the interviewer or examiner to the study outcome will prevent selective probing for certain types of answers or measurements, thus reducing interviewer bias. Providing the same amount of information to study subjects without disclosing the research hypothesis and keeping them unaware auto study status, i.e., case or control, will reduce recall bias as in the case of mothers with and without deformed children. Use of objective, close ended questions and not leading questions will help to reduce bias. Training of interviewers, better supervision and quality checks will eliminate misclassification bias to a great extent. For example, training interviewers to standardize equipment before weighing would reduce the misclassification bias regarding the nutritional status of the children described above. Obtaining data from pre-existing records and cross-checking information from multiple sources will decrease the possibility of reporting bias.

Confounding can be dealt with in a similar manner.

1. Design phase: Cases and controls are matched to ensure similarity with regard to potential confounding variables, e.g., age and sex. Matched analysis is required to assess the odds ratio in this case, the method of which can be found in textbooks on epidemiology[2].

2. Data analysis phase: Forming strata on the basis of the confounding variable is one method of analysis. Analyzing the relationship between chewing paan and oral cancer separately in males and females, as discussed above, will provide information whether chewing paan is related to oral cancer, independent of the effect of gender. More sophisticated methods of analysis may be used to minimize confounding. Fikree3 describes an example of confounding and how direct adjustment can be used to remove such an effect on study results.

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