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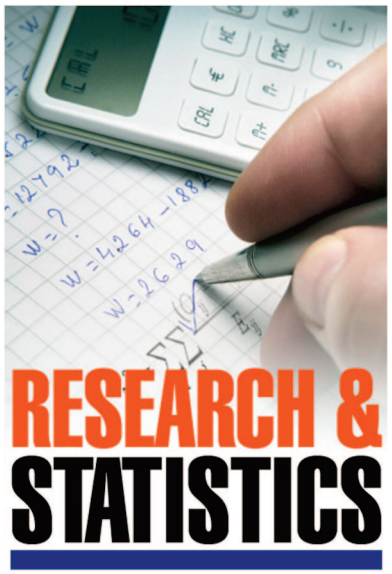

Understanding and Identifying Bias in Research Studies

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Case Study

You are seeing a healthy 18-year-old patient who is interested in contraception and, specifically, the "Depo shot" or medroxyprogesterone. The information you have gathered from her during your visit and her medical history suggest that she is a good candidate. You take a few minutes out of the visit to review the literature for issues of safety. Most of the articles and reviews suggest that medroxyprogesterone is a good choice for healthy young women, but a recent study shows an association between medroxyprogesterone and the development of hypertension. You look more closely at the study and discover that the young women taking medroxyprogesterone had their vital signs (including blood pressure) checked every 3 months when they came in for the medroxyprogesterone injection. The other women included in the study for comparison only had their vital signs checked every year at annual health supervision visits. You are unclear about whether the study design might have introduced bias and how the bias might affect your reading of the study results.

Bias Defined

Bias is a major issue in epidemiologic research studies and can lead to inferences that systematically deviate from truth. Bias has been defined as "any systematic error in the design, conduct or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of disease." (1) Bias has been written about extensively. In this article, we review a few of the most common types of bias encountered in epidemiologic studies, discuss common reasons for the biases, and provide a guide for identifying bias when reviewing or reading research studies.

Common Types of Bias

Surveillance bias may result from one population being monitored more closely or more frequently than the general population. In the study described, in which an association was found between medroxyprogesterone and hypertension, the young women taking medroxyprogesterone were monitored at a greater frequency, every 3 months, than were the young women who were not taking medroxyprogesterone, who were monitored annually. The difference in the rate of monitoring may have introduced a surveillance bias. Because hypertension typically is diagnosed only after at least three blood pressure readings have been elevated above a certain level, the young women who were monitored more frequently had more of an opportunity to have hypertension diagnosed. The young women who were monitored less frequently (annual visits only) may have had the same prevalence of hypertension, but they may have had less of an opportunity to have hypertension diagnosed because of the lower frequency of visits. The systematic difference in the monitoring of the young women taking medroxyprogesterone compared with the young women not taking medroxyprogesterone may have resulted in a spurious association.

Selection bias has two primary varieties. One arises from systematic differences in the characteristics between individuals selected for a study compared with those not selected for the study.

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(2) In the study described, for example, the study sample population consisted entirely of individuals attending the clinic, who may differ from the general population. Therefore, associations found are not necessarily generalizable to the larger population.

The second variety of selection bias arises from systematic differences in the selection of cases and controls or exposed and unexposed individuals. Such systematic differences can lead to fallacious associations that really do not exist but, rather, are a result of the selection bias. The medroxyprogesterone study described serves as an example of this type of selection bias.

Despite the flaws in the described study, a follow-up study was designed. That study prospectively follows individuals taking medroxyprogesterone (exposed) and those not taking medroxyprogesterone (unexposed) to determine the incidence of hypertension in each group and to test for differences between the two groups. The eligibility criteria for the two groups include all females between the ages of 12 and 18 years attending a teen health clinic. Additional eligibility criteria for the exposed group require that all females currently are taking medroxyprogesterone. Do you have any concerns about the selection criteria?

One of our concerns is that in the prospective study, individuals selected for the study in the two groups may differ systematically from one another. For example, the young women taking medroxyprogesterone presumably are sexually active, are aware of medroxyprogesterone as a contraceptive option, and may be more likely to attend their clinic visits regularly. The young women in the nonmedroxyprogesterone group, on the other hand, may not be sexually active and may differ in other measurable and unmeasurable factors (eg, health insurance status, reliable transportation to and from clinic). If the differences related to the selection of the two groups also are related to the likelihood of hypertension, the study may show findings that are fallacious.

Misclassification bias results from misclassifying individuals into diseased or nondiseased groups or into exposed and unexposed groups. Individuals in the medroxyprogesterone study, who were followed less frequently (only for annual visits), may have had less opportunity to have hypertension diagnosed. This circumstance may have resulted in their misclassification into the nonhypertensive (nondiseased) group. This type of misclassification bias is termed differential misclassification because the rate of misclassification differs in the comparison study groups. (3) Differential misclassification can lead to identifying an association where one does not exist or a lack of an association where one does, indeed, exist.

Misclassification bias also can occur as a result of nondifferential misclassification. (3) This error occurs when cases and controls (exposed and unexposed individuals) are misclassified at similar rates and the misclassification is not related to case-control or exposure status. Nondifferential misclassification usually results in an attenuation of a relative risk or odds ratio, resulting in less likelihood of an association appearing, although it may exist.

How to Identify Bias

Knowing the more common types of bias in epidemiologic research studies may not be enough to identify bias in research studies. Following are some basic tips on how to assess a research study for bias.

The most likely areas to contain biases are in the study design and methods of the study, so the reader should look closely at the description of these procedures. Has the study design been identified clearly, including the general approach (descriptive or hypothesis testing), the level of measurement (individual or ecologic), and the specific design (cohort, retrospective cohort, cross-sectional, case-control, experimental, quasi-experimental)?

The next step is to examine how the study sample was selected. Have the authors clearly stated where and from what population the study sample was selected? What were the eligibility and ineligibility criteria for study selection? How may the study sample selection criteria have created a study population that is representative of the population sampled? If the study population selection criteria suggest that the study population is no longer representative of the larger population, it is likely that some biases have been introduced and that the study will have limited generalizability.

The strategies of sampling for controls or other comparison group is important. Were there any systematic differences in their selection? Try to assess whether the controls were selected similarly to the cases, such as similar eligibility and ineligibility criteria, and whether the controls are comparable to the cases. The comparison groups should be similar in all characteristics except for one: the disease or exposure under study. Finally, in considering the results, try to determine whether the results and any associations found have sufficient supporting evidence to suggest plausibility and, if available, whether the results are consistent with those of other studies.

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