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Collider Stratification Bias I: Principles and Structure

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Collider stratification bias is frequently discussed among epidemiologists as a threat to validity of study inferences. This is part 1 of a 2-part series, in which we address: 1) the structure of collider stratification bias and underlying theoretical framework, and 2) the magnitude of bias introduced by conditioning on a collider in common scenarios in epidemiologic research.

WHAT IS COLLIDER STRATIFICATION BIAS?

In directed acyclic graphs (DAGs), causal effects are represented by arrows pointing from one variable (node) to another. A common effect of exposure and outcome will have at least 2 arrows that "collide" at that variable, hence the term "collider." Conditioning on a common effect of 2 otherwise unrelated factors creates a statistical association between those factors in at least 1 stratum of the collider, or collider stratification bias (1). Collider stratification bias can arise due to restriction, as when the sample comprises a single stratum of a collider. Alternatively, collider stratification bias can occur when estimating stratum-specific effects within strata of a collider, or conditioning on a collider to estimate a weighted average effect across strata. The structural basis of this bias allows for illustration using DAGs. Figure 1A–B represents a scenario in which 2 variables, *A* and *B*, are causally independent (i.e., neither is a cause of the other) but are both causes of a third variable, *C* (Figure 1A). Stratification on *C* results in collider bias (indicated by the dotted line in Figure 1B).

Extending this simple scenario, consider Figure 1C, focusing on collider stratification due to restriction in a study of the relationship between 2 variables, height and running speed. For the sake of simplicity, suppose there is no causal relationship between height and speed in the general population, just as we previously assumed variables *A* and *B* were causally independent. This may not be entirely true (2), but we treat these as unrelated for pedagogical purposes. Now, if you were to restrict your study from the general population to professional basketball players, such as National Basketball Association (NBA) players, you might reach a different conclusion about an association between height and speed (Figure 1C). Most professional basketball players are very tall; tall players have a distinct advantage for rebounding, blocking shots, and jumping above defenders to score points. It is possible to make it to the NBA without being very tall, but shorter individuals who make it to the NBA are likely to have other special skills, and are thus more likely to be very fast. Some NBA players may be both tall and fast, but a professional basketball player who is short is likely very fast. In a sample of professional basketball players, height and speed are clearly related—knowing an NBA player is short tells you something about their running speed. In this example, we are "conditioning" on the collider (being in the NBA) by restricting the study population to NBA players. As a result, we have induced a noncausal association between height and speed that does not exist in the general population. The association between height and speed in NBA players is noncausal because there is no true causal relationship between height and speed (recall, as stated above, height and speed are independent). The association between height and speed is an artifact of conditioning on the collider, in this case due to restriction (i.e., to NBA players).

COLLIDER STRATIFICATION BIAS IN EPIDEMIOLOGIC RESEARCH

The simple scenario above demonstrates how conditioning on a collider can introduce a noncausal association between previously uncorrelated variables in a selected sample. But how does this extend to epidemiologic research aiming to estimate a causal relationship between an exposure and outcome? The same underlying principles apply. Collider stratification bias can introduce a spurious relationship or distort an existing relationship between two variables, one of which is usually the exposure of interest. The spurious or distorted correlation between these variables may then result

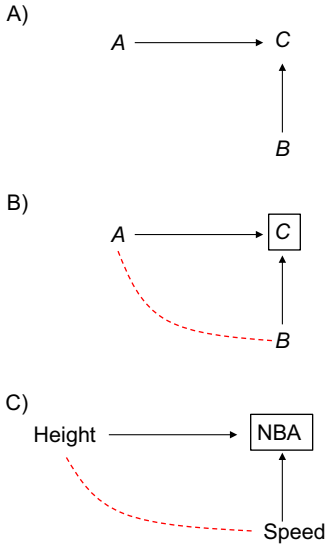

Figure 1. Directed acyclic graphs (DAGs) depicting 2 independent variables that are both causes of a third variable (a collider). A) *A* and *B* are causally independent, but both cause *C*, a collider. B) The square box around *C* indicates conditioning on the collider, *C*, introducing collider stratification bias and a noncausal association between variables *A* and *B*. C) The noncausal association induced between height and running speed when the study data are restricted to National Basketball Association players.

in biased estimates of the exposure-outcome relationship of interest.

Consider an extension to the NBA scenario above. Suppose a research team is interested in understanding the relationship between height and atrial fibrillation, a type of irregular heartbeat (arrythmia). Prior research has demonstrated being tall is a risk factor for atrial fibrillation (3). The researchers want to seek out a population with a high prevalence of exposure (i.e., a tall group of people) and decide to restrict their study population to a group of professional NBA players. They collect data on a comprehensive set of potential confounders of the exposure-outcome relationship, mainly related to genetics, family history, and personal medical history. One variable they did not collect data on is running speed, which is closely related to physical fitness level, another unmeasured variable. Unbeknownst to them, running speed (i.e., physical fitness level) is a strong predictor of becoming a professional basketball player, and level of physical fitness is also a predictor of atrial fibrillation (4). Results of multivariable analysis examining the relationship between height and arrythmia, confusingly, indicate a weak protective association between being tall and risk of atrial fibrillation. Basketball players who were taller were at a lower risk of atrial fibrillation than shorter players. Could collider stratification bias affect these results? Yes! Being a professional basketball player is a collider on the path between height and atrial fibrillation (Figure 2). It is a direct effect of exposure, as tall people are more likely to become professional basketball players, and there are uncontrolled common causes associated with being a

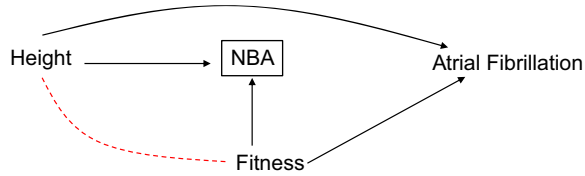

Figure 2. Directed acyclic graph illustrating the relationship between height and atrial fibrillation among National Basketball Association players.

professional basketball player and atrial fibrillation. Thus, conditioning on being a professional basketball player by restriction again introduces collider stratification bias, distorting the causal association between the exposure (height) and outcome (atrial fibrillation).

We refer readers to previously published articles for examples of DAGs representing different causal structures that produce collider stratification bias (e.g., Berkson's bias, bias due to informative censoring, healthy worker effect, M-bias) (5). M-bias is another extension of collider stratification bias in which the collider has no causal effect on either exposure or outcome but is associated with both exposure and outcome via shared common causes (Figure 3). Bias due to stratification on a collider—whether due to selection or adjustment—has been proposed to explain the birth weight paradox (where stratification is due to adjustment), the obesity paradox (where stratification is due to restriction), and as the structural basis for associations resulting from selective attrition (6–8).

COLLIDER STRATIFICATION AND SELECTION BIAS

The relationship of collider stratification bias with selection bias has been a source of confusion. Collider stratification bias is a type of selection bias, but it is also possible to have selection bias without a collider present. Selection bias broadly refers to systematic differences in the true quantity of interest in the target population (e.g., distribution of disease in a descriptive study or effect of interest when causal inference is the goal) versus in the sample arising from the processes by which individuals are selected from the target population into the analytical sample. Collider stratification bias arises from conditioning (via adjustment, restriction, or stratification) on a collider. Bias that occurs when available data are restricted to a single stratum of a collider (e.g., due to censoring if censored (yes/no) = no) is a type of selection bias and a special case of collider stratification bias ("collider restriction bias") (9). Note that

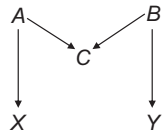

Figure 3. An example of M-bias, a type of collider stratification bias.

in such an instance, the effect estimates are not reflective of any causal relationship for any population. It is a sort of epidemiologic sleight of hand: Effect estimates from a sample comprised of only a single stratum of a collider are not valid causal effects even for the sample because of the induced correlation results from conditioning on a collider. To illustrate this concept, imagine conducting an observational study with the goal of estimating effects of cigarette smoking on lung cancer (even though this relationship is one of the most robust epidemiologic findings ever reported). It is well established that cigarette smoking decreases life expectancy. Now, imagine that you choose to recruit only individuals who are at least 100 years of age into your study, with the goal of estimating effects of cigarette smoking on lung cancer among centenarians. Restricting the study sample to only those who have survived to age 100 years would induce collider stratification bias if there are unmeasured or uncontrolled common causes of survival to age 100 and lung cancer (i.e., survival to age 100, and therefore selection into your study, is a collider). Let us say, further, that your analyses indicate a protective association between smoking and lung cancer in centenarians. Does this mean that smoking is not harmful among individuals over age 100? Absolutely not. Even though smoking is truly harmful in the population, regardless of age, a protective association could be observed in centenarians due to collider stratification bias alone. This apparently protective effect is entirely spurious even among centenarians; it would be incorrect to conclude that smoking is truly protective among centenarians.

CONCLUSION

The structural conditions that give rise to collider stratification bias are very common in epidemiologic research—whether in the design or analysis phase—as we have described here. Beyond questions about the presence or absence of bias, magnitude—the degree to which effect estimates deviate from the truth—is a critical consideration. We address magnitude of collider stratification in the next paper in this series.

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