



# What is Collider Bias and Why Should We Care?

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## Perspectives

Bias can threaten any study's internal validity compromising the findings. Bias is a nonrandom error that may affect the relationship between an exposure, risk factor, or treatment and the outcome. Bias can arise at any point in the research process, be it in the early stages of sample selection or the final stages of result rationalization and publication. There are 3 main types of bias: selection bias, information bias, and confounding bias.<sup>1</sup>

Selection bias is introduced when the target sample does not represent the study population. Examples include survivor treatment and health care access selection bias. Survivor treatment selection bias can arise in observational studies where patients who live longer are more likely to be administered a particular treatment. As such, investigators can falsely conclude that the treatment prolongs survival. Health care access bias occurs when studies on patients admitted to a health care institution do not represent the wider community. Health care access bias can stem from many reasons, such as the gravitation of patients with specific disorders toward clinicians or institutions of notable prestige, that is, centripetal bias, or the inclination of certain patients due to certain reasons, be it cultural or economic, toward diagnostic tests, that is, diagnostic access bias.<sup>1</sup> For instance, if an oral-maxillofacial surgeon only accepted private insurances, then the sample of patients based on the practice may not be a

representative of the population. As such, one would need to account for selection bias when conducting a clinical study on patients in the practice.

Information bias may be due to misclassification bias, ecological fallacy, and regression to the mean. Misclassification bias results from imperfections in measurements of the exposure/predictor variable. For example, observer/interviewer bias occurs when knowledge of the treatment arm or exposure status of the participant influences data collection. Ecological fallacy occurs when group analyses are used to make inferences at the level of the individual. For instance, one cannot conclude that fat intake is a risk factor for head and neck cancer on the grounds of head and neck cancer rates being higher in countries where fat comprises a larger share of the diet. Regression to the mean is a phenomenon where a variable that yields an extreme value in the first measurement yields a value closer to the mean in subsequent measurements. Investigators may attribute an outcome to an intervention when regression to the mean occurs. For example, a decrease in an individual's blood pressure after administering an antihypertensive can simply be a less-extreme consecutive measurement due to natural variation rather than the empirical effects of the antihypertensive.<sup>1</sup>

Confounding bias occurs by failing to identify and control for variables that are associated with both the exposure and the outcome. For instance, jaw size (confounder) is associated with both impacted teeth

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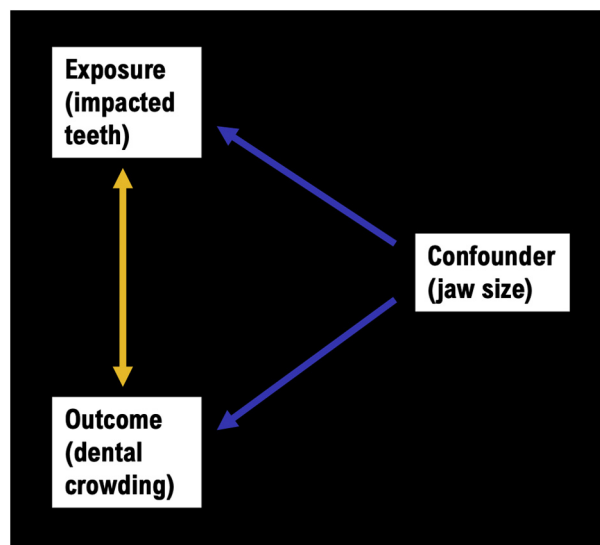
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(exposure) and dental crowding (outcome) (Fig 1). Failing to control for jaw size as a confounder could lead one to infer an association between impacted teeth and dental crowding. Nevertheless, controlling for a variable that can be independently caused by either the exposure or the outcome will, quite the opposite, introduce yet another bias—the collider bias.<sup>2</sup>

Collider bias is a form of selection bias that arises when the investigator controls for a variable (the collider) that occurs after the exposure and outcome. The exposure and outcome can both independently create a collider variable.<sup>2</sup> In contrast to the case of confounding, where the confounder is associated with both the exposure and outcome, the collider is created by both the exposure and outcome. For example, a spurious association may be made between jaw size (retrognathia), the exposure, and adenotonsillar hypertrophy, the outcome, when selecting for a sample of patients with obstructive sleep apnea, the collider (Fig 2).

One of the earliest clinical examples of the collider bias was provided by Sackett.<sup>3</sup> The authors detected an apparent association between locomotor and respiratory diseases. The caveat was that the study sample consisted solely of hospitalized patients. When the analysis was repeated with the general population, which included both hospitalized and nonhospitalized patients, the observed association vanished. Locomotor disease and respiratory diseases were both independently associated with hospitalization, which followed both variables in time. By controlling for the collider (hospitalization), Sackett<sup>3</sup> minimized the collider bias.

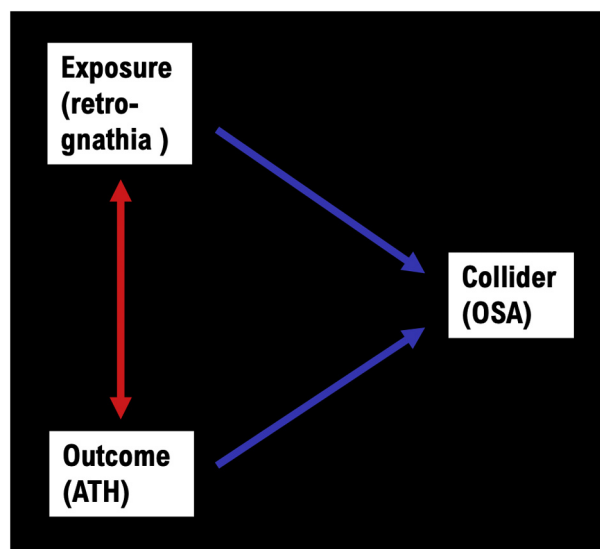
Within the domain of oral health, the possibility of collider bias has recently been identified in the reported association between periodontitis and carotid intima-media thickness (cIMT), a proxy variable for cardiovascular disease. Through conventional logistic regression, Leite et al located a positive association between periodontitis at the age of 24 years and cIMT at the age of 30 years.<sup>4</sup> Thereafter, the authors repeated the logistic regression for 2 different levels ( $\geq 3$  mg/L vs  $< 3$  mg/L) of high-sensitivity C-reactive protein (hsCRP). While the authors reported a significant association when hsCRP levels were  $\geq 3$  mg/L, no such association was seen for when hsCRP levels were  $< 3$  mg/L. Further, sensitivity analysis revealed that  $\geq 3$  mg/L hsCRP carried a 36% bias probability. When the authors assessed hsCRP as the collider, there was no association between periodontitis and cIMT. The authors suggest that the burden of periodontitis may require a period greater than what was investigated in the study (6 years) to exceed the threshold of systemic inflammation necessary for atherosclerosis. Periodontitis can independently lead to increased hsCRP levels. Concomitantly, high hsCRP levels is a predictor of both atherosclerosis and cIMT. While hsCRP was not a confirmed collider, the possibility remains.<sup>4</sup>



**FIGURE 1.** An illustration of confounding. The orange arrow represents a distorted association when failing to control for the confounder (jaw size) in the association between the exposure (impacted teeth) and the outcome (dental crowding). Abbreviations: ATH, adenotonsillar hypertrophy; OSA, obstructive sleep apnea.

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Impatient for solutions to our patients' health problems, surgeons may narrowly focus on the treatment, the outcome, and associations between the 2 variables. Nonetheless, it is vital not to rush the analyses; consider the myriad of biases apart from confounding bias, such as the collider bias. Indeed, the picture may not always be as clear as we think. Critically evaluating the research process is an iterative, albeit tedious, exercise but it may yield results that reflect the highest



**FIGURE 2.** An illustration of collider bias. The red arrow represents a distorted association when inappropriately controlling for the collider (OSA) in the association between the exposure (jaw size – retrognathia) and the outcome (adenotonsillar hypertrophy). Abbreviation: OSA, obstructive sleep apnea.

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levels of scientific truth, enable evidence-based clinical decision-making, and translate into effective care for our patients.

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