Belief that association means causation

From: Key Concepts for assessing claims about treatment effects and making well-informed treatment choices (Version 2022)

1.2b Do not assume that association is the same as causation.

Explanation

The fact that a possible treatment outcome (i.e. a potential benefit or harm) is associated with a treatment does not mean that the treatment caused the outcome. The association or correlation could instead be due to chance or some other underlying factor. For example, people who seek and receive a treatment may be healthier and have better living conditions than those who do not seek and receive the treatment. Therefore, people receiving the treatment might appear to benefit from the treatment, but the difference in outcomes could be because they are healthier and have better living conditions, rather than because of the treatment.

An obvious example of confusing an association with causation would be to assume that going to the doctor causes people to be sick because going to the doctor is associated with being sick. It is more likely that people went to the doctor because they were sick than that going to the doctor caused them to be sick. Another obvious example would be to assume that eating ice cream causes people to drown because ice cream sales are associated with drowning. A more likely explanation for that association is that when it is hot people eat more ice cream and they also swim more. In this example, hot weather is a confounder – it is associated with the “treatment” (eating ice cream) and it affects the “outcome” (the number of people who drown).

A less obvious example of confusing an association with causation was the assumption that hormone replacement therapy (HRT) prevented cardiovascular disease (CVD). For many years, experts and doctors believed that HRT reduced the risk of CVD, based on an association found in studies that compared women who chose to take HRT and women who did not. However, large, randomized trials showed no benefit or an increased risk of CVD in women assigned to HRT. An explanation for this is that socio-economic status was a confounder in the non-randomized studies. Women with lower socio-economic status are more likely to have CVD and they are less likely to take HRT. So, a reason for the association found in the non-randomized studies was the difference in socio-economic status between the comparison groups, not the difference in whether they took HRT or not *[Humphrey 2002 (SR)]*.

Basis for this concept

Researchers, press releases from universities and journal publishers, and news reports frequently use causal language when reporting associations found in non-randomized studies of treatments *[Lazarus 2015 (RS), Oxman 2022 (SR), Yu 2020 (RS)]*. This is likely to be misleading.

As illustrated by the examples above, there is a compelling logical basis for not assuming that an association between a treatment and an outcome means that the treatment caused the outcome. However, it is less clear how often assumptions about causation based on an association are wrong or when it is correct to assume that an association ***does*** mean that a treatment caused an outcome.

When there are very strong associations, it is very unlikely that they result from confounding *[Glasziou 2007]*. However, very strong associations are uncommon *[Nagendran 2016 (SR), Oxman 2012a , Pereira 2012 (SR)]*.

When there are not very strong associations, one way of assessing the likelihood of being misled by assumptions about causation based on an association is to compare associations found in non-randomized studies to the findings of randomized trials. Non-randomized studies can only adjust for potential confounders if these are known and have been measured. On the other hand, randomly assigning people to comparison groups in large, randomized trials tends to balance the distribution of both measured and unmeasured risk factors (potential confounders) across treatment comparison groups. How much is known about potential confounders and to what extent they have been measured varies. Often, what is known and measured is limited. For example, a systematic review of non-randomized studies published in major psychiatry journals found that confounding was widely ignored in interpreting the results *[Munkholm 2020 (SR)]*.

Some reviews of comparisons between the results of non-randomized studies and randomized trials have found important differences in results, while others have found little or no difference *[Anglemyer 2014 (SR), Rush 2018 (SR)]*. There are several possible reasons for these variable findings and why both randomized trials and non-randomized studies can either overestimate or underestimate the effects of treatments *[Kleijnen 1997 , Sterne 2016]*. This includes confounding that can occur after randomisation, particularly in trials that measure long-term effects of treatments *[Hernán 2013 , Manson 2016]*. So, it is difficult to draw firm conclusions about how often assumptions about causation based on an association observed outside the context of randomized trials are misleading.

Before assuming that an outcome associated with a treatment has been caused by the treatment, other reasons for an association should be considered in a systematic review of fair comparisons as the basis for judging the extent to which other reasons for an association have been ruled out *[Sterne 2016]*.

Implications

Do not assume that an outcome associated with a treatment was caused by the treatment unless other reasons for the association have been ruled out in a systematic review of fair comparisons.

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