Belief in big data

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

1.2c Do not assume that more data is better data.

Explanation

Claims that are based on "big data" (data from large databases) or "real world data" (routinely collected data) can be misleading. More data simply gives a more statistically precise estimate of whatever biases there might be in a treatment comparison that uses routinely collected data. When using routinely collected data, it is only possible to control for confounders that are already known and have been measured. Unfortunately, routinely collected data often do not include sufficient detail to confidently conclude that any association found between a treatment and an outcome means that the treatment caused the outcome.

For example, routinely collected (real world) data have been used in non-randomized comparisons of different types of coronary artery bypass surgery. Twelve studies including 34,019 patients used a non-randomized study design that is believed to reduce the risk of bias due to confounders (propensity-score matching) *[Gaudino 2018 (SR)]*. They found that using two internal thoracic arteries compared to using one artery was associated with a lower risk of dying within one year. A more likely explanation is that the association was because of confounders that had not been measured. Using two arteries instead of one increases the complexity and invasiveness of the surgery. It is likely that surgeons tend to reserve this type of surgery for patients perceived as healthier and expected to live longer. This type of bias in allocating patients to different treatments (e.g., based on the individual surgeon's judgement) is very difficult to quantify. The statistics can only be adjusted for the measured confounders *[Agoritsas 2017]*. As a further illustration of this problem, a large randomized trial found little or no difference in survival after 10 years. This contrasts with 14 non-randomized studies using propensity-score matching with 24,123 patients, which found that using two arteries improved survival compared to one artery *[Gaudino 2019 (SR)]*. This was due to both lower survival in patients in randomized trials, who were allocated to the two-artery group, and higher survival in the group allocated to the one-artery group compared to the studies using "real world data".

Describing routinely collected data as "real world data" implies that data collected in carefully designed fair comparisons of treatments do not come from the real world. Databases of routinely collected data may indeed include a broader spectrum of people than data collected in fair comparisons of treatments that have narrow eligibility criteria. However, routine collection of data is rarely planned to include the information that is needed to ensure fair comparisons, and randomized trials can be designed to have wide eligibility criteria.

Basis for this concept

A systematic review of studies that evaluated the effectiveness of treatments on mortality using propensity scores found that most of the studies explored effects of treatments that had already been compared in randomized trials *[Hemkens 2016b (SR)]*. The so-called "real world" studies seemed to have little impact.

Another systematic review compared treatment effects found in non-randomized studies using routinely collected ("real world") data and propensity-score matching with those found in

randomized trials *[Hemkens 2016a (SR), Sterne 2018]*. The review found that the non-randomized studies using routinely collected data systematically and substantially overestimated mortality benefits of treatments compared with subsequent trials investigating the same question. This is consistent with the findings of another systematic review comparing studies using propensity score methods with randomized trials *[Dahabreh 2012 (SR)]*. A third systematic review compared treatment effects found in non-randomized studies using "real world data" with those found in randomized trials for mortality and other outcomes *[Ewald 2020 (SR)]*. That review did not find a systematic difference in treatment effects, but it found important differences, including effects going in the opposite direction for eight of the 19 included comparisons. A fourth systematic review of comparisons between non-randomized studies using real world data and randomized trials found only two substantial differences in treatment effects out of 15 comparisons *[Mathes 2021 (SR)]*.

As with comparisons of other types of non-randomized studies with randomized trials, there are many reasons why both randomized trials and non-randomized studies can either overestimate or underestimate the effects of treatments *[Anglemyer 2014 (SR), Goodman 2017 , Kleijnen 1997 , Mathes 2021 (SR), Sterne 2016]*. So, it is difficult to draw firm conclusions about how often the results of non-randomized studies using real world data will differ substantially from the results of randomized trials. However, evaluations of treatment effects using "real world data" are unlikely to be reliable if there are not high-quality data *[Bian 2020 (SR)]*, and important confounders have not been measured *[Franklin 2019]*.

The main argument for studies using "real world data" is that the findings of randomized trials are not applicable to the real world. However, the fourth systematic review of comparisons between non-randomized studies using real world data and randomized trials found little impact of factors related to the applicability of the findings on the estimated treatment effects *[Mathes 2021 (SR)]*. Limited applicability of the randomized trials was mostly due to the trials being designed to assess the effects of treatments under ideal circumstances ("explanatory studies") (e.g., having narrow eligibility criteria) rather than under normal, everyday circumstances ("pragmatic studies") *[Thorpe 2009]*.

The finding that the results of the randomized trials appeared to be largely applicable to the "real world" is consistent with the findings of a systematic review of studies comparing outcomes in patients receiving a treatment in a randomized trial to similar patients receiving the same treatment outside of a randomized trial *[Vist 2008 (SR)]*. On average, participants in randomized trials were found to have similar outcomes compared to similar people who received a similar treatment outside of a randomized trial.

Implications

Do not assume that an association between a treatment and an outcome found using "big data" or "real world data" means that the treatment caused the outcome unless other possible reasons for the association have been ruled out.

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Systematic reviews

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