Belief that research isn't relevant to real life

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

1.2e Do not assume that fair comparisons are not applicable in practice.

Explanation

Assumptions that fair comparisons of treatments in research are not applicable in practice can be misleading. People may claim that evidence from fair comparisons of treatments cannot be applied to everyday practice. This is likely to be true if there are important differences between the fair comparisons and everyday practice. The effects of treatments are unlikely to differ substantially unless there are compelling reasons why everyday practice is so different from the fair comparisons that the treatments are unlikely to work in the same way *[Dans 1998]*.

Deciding whether there are compelling reasons depends on evidence outside of fair comparisons of treatments (for example, basic science research that demonstrates how a treatment causes an outcome) and judgement. Reasons for uncertainty about the applicability of research only become compelling when there is compelling evidence or compelling logical reasons for expecting the effects of a treatment to be substantially different in practice.

For example, human biology tends to be more similar than different across people from different countries, races, and ethnicities. So, you would expect medicines to have similar effects most of the time. Thus, it is not necessary to conduct randomized trials of medicines in every country with large samples of people from every race and ethnicity. But there are sometimes important differences. For example, the benefits of lowering elevated blood pressure in reducing strokes and other cardiovascular morbidity and mortality are well established. However, several different types of medicine are used to lower blood pressure and there has been uncertainty about which of these should be used. There has also been uncertainty about whether these medicines worked the same in Black people and in non-Black people, particularly for angiotensin-converting enzyme (ACE) inhibitors. This is because ACE inhibitors were found to be less effective for lowering blood pressure in Black people than in non-Black people. For this reason, a randomized trial designed to compare different medicines for lowering blood pressure planned to do a subgroup analysis for Black participants in the trial, which included 33,357 participants (35% Black) in the U.S. and Canada *[Wright 2005 (RS)]*. The results of this study were largely similar for Blacks and non-Blacks, except for the effect of the ACE inhibitor on strokes. Black participants assigned to the ACE inhibitor were more likely to have a stroke than Black participants assigned to the thiazide diuretic, but not non-Black participants.

Various terms are used to describe the "applicability" of research, including transferability, generalisability, external validity, and relevance. Although these terms have been defined differently, checklists designed to assess these concepts include broadly similar criteria *[Munthe-Kaas 2019 (SR)]*. These include differences between fair comparisons and everyday practice in the characteristics of the people, characteristics of the treatments, and characteristics of the context. It is possible to generate long lists of things that could potentially be different. For example, differences in patient characteristics could include differences in age, sex, education, income, race, ethnicity, weight, comorbidity, genetic markers, astrological sign, baseline risk, etc. To avoid being misled by spurious assumptions about fair comparisons not being relevant, only those factors for

which there are compelling reasons why a treatment is unlikely to work the same way in practice as it did in fair comparisons should be considered when assessing the applicability of the results.

It should be noted that most often the relative effect will be similar for people with different baseline risks. Differences in baseline risk will, however, often lead to differences in the absolute effect.

Basis for this concept

There have been at least 136 comparisons of outcomes of patients who participated in randomized trials and outcomes of patients who were eligible for the trial and received a similar treatment but did not participate *[Vist 2008 (SR)]*. The comparisons include both comparisons of the 'experimental' or new treatment inside and outside of the trial, and 'control' treatment comparisons. On average, the outcomes of patients participating and not participating in trials were similar. Among the 136 comparisons, 21 comparisons found statistically significant differences in outcomes. Eleven of those reported better outcomes for patients within trials and ten reported worse outcomes for patients treated within trials. These results challenge the assertion that the results of randomized trials are not applicable in practice.

However, the results of some randomized trials may be less likely to be applicable than others. Some trials are largely explanatory. That is, they are designed to assess the effects of a treatment given in ideal circumstances *[Thorpe 2009]*. Those trials may be less likely to be applicable in practice than trials that are largely pragmatic, i.e., designed to assess the effects of a treatment given in the circumstances of everyday practice.

A systematic review that compared treatment effects on mortality from randomized trials conducted in more developed versus less developed countries found similar effects in 128 out of 139 cases (92%). A few cases (8%) showed, on average, more favourable treatment effects in less developed countries. The extent to which those discrepancies reflect biases in reporting or study design versus genuine differences in treatment effects (for example, due to differences in treatment implementation or baseline risk) is uncertain.

There are statistical and logical reasons for thinking that relative measures of effect are more likely to be consistent across different baseline risks. For example, a large risk difference, say 50%, is not possible in a group of people with a baseline risk that is less than 50%. There is also empirical evidence that relative measures of effect tend to be more consistent across people with different baseline risks than absolute risks *[Guyatt 2013a]*, although that evidence has been brought into question *[Poole 2015 (OR)]*. It cannot be assumed that relative risks are consistent and can be applied in practice to people with different baseline risks. However, most of the time it is more likely that relative effects are applicable in practice across groups with different baseline risks than it is that absolute risks are applicable. Moreover, this is only a concern when it is possible to identify groups of people with important differences in baseline risk.

Implications

Do not assume fair comparisons are not applicable because of differences between fair comparisons and everyday practice, unless there are compelling reasons why treatments would work differently.

References

Systematic reviews

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