Relevant health actions

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

3.1d Consider the relevance of the treatments that were compared.

Explanation

A fair comparison of the effects of a surgical procedure done in a specialised hospital or delivered by an experienced surgeon may not provide a reliable estimate of its effects and safety in other settings, or in the hands of less experienced surgeons.

For example, results from a large randomized trial showed that endarterectomy (surgical removal of part of the inner lining of an artery) for asymptomatic carotid stenosis (narrowing of the large arteries on each side of the neck) reduced the five-year absolute risk of stroke by about 5% *[Rothwell 2005]*. However, the trial only accepted surgeons with a good safety record, rejecting 40% of applicants and subsequently barring those who had adverse operative outcomes in the trial from further participation. The benefit from surgery was largely attributable to the low operative risk. Operative mortality was eight-fold higher outside of the trial and the risk of stroke and death was about three-fold higher.

Similarly, comparing a new drug to a drug or dose that is not commonly used (and which may be less effective or safe than those in common use) would not provide a relevant estimate of how the new drug compares to what is commonly done.

For example, in randomized trials of atypical antipsychotics for schizophrenia, haloperidol (one of the most frequently prescribed "typical" antipsychotics worldwide) was used as the comparison treatment *[Hugenholtz 2006 (SR)]*. However, the trials used haloperidol in doses that were higher than that recommended. In a meta-analysis of 52 randomized trials that controlled for the higher-than-recommended dose of comparator drugs, differences in effectiveness and overall tolerability between typical and atypical antipsychotics disappeared, suggesting that the perceived benefits of atypical antipsychotics were due to excessive doses of the comparison treatments, such as haloperidol *[Geddes 2000 (SR)]*.

Basis for this concept

Characteristics of treatments, including the duration, dose or intensity, mode of delivery, and skill of the person delivering the treatment can influence the effectiveness of a treatment. Unfortunately, characteristics such as these are poorly described. This can make it difficult to judge the relevance of treatments compared in studies to other contexts. For example, a review of randomized trials in oncology found that only 11% of 262 trials of cancer chemotherapy provided complete details of the trial treatments *[Duff 2010 (SR)]*. The completeness of treatment descriptions is often worse for non-pharmacological treatments. A review of 80 randomized trials and reviews found that 67% of descriptions of drug treatments were adequate compared with only 29% of non-pharmacological treatments *[Glasziou 2008 (SR)]*. Another review of 137 randomized trials of non-pharmacological treatments found that only 39% of treatments were adequately described *[Hoffmann 2013 (SR)]*.

Inadequate descriptions of treatments led to the development of the Template for Intervention Description and Replication (TIDieR) checklist *[Hoffmann 2014 , Hoffmann 2017]*. TIDieR has helped to improve descriptions of treatments, but further improvements are needed. An overview of 56

reviews that used the TIDieR checklist to evaluate the adequacy of treatment descriptions found that the names of treatments and reasons for using them were generally reported adequately *[Dijkers 2021 (SR)]*. However, only between 25% and 75% adequately reported other characteristics of treatments and as few as 10% of studies adequately reported modifications of treatments. Comparison treatments were reported less well than the treatment that was the focus of the comparison.

Another challenge with making judgements about the relevance of treatments is the choice of the comparison treatment, as illustrated by the example of treatments for schizophrenia presented above. This is often a problem for pharmacological treatments. Many drug trials are funded by industry and pharmaceutical companies typically choose to compare their drugs to a placebo rather than to another drug *[Dunn 2013 (SR), Lathyris 2010 (SR)]*. When there is more than one effective treatment available, people often need to decide which treatment to use, not whether to use a particular treatment or a placebo. Consequently, when direct comparisons of treatments are not available, as is often the case, indirect comparisons (across studies) must be used (see Concept 2.2c).

A related challenge for judgements about the relevance of pharmacological treatments is the assumption that drugs within a class are interchangeable *[Furberg 1999 , Furberg 2003 , McAlister 1999 , Mills 2014]*. Pharmaceuticals are categorised as members of existing "drug classes". The U.S. Food and Drug Administration (FDA) uses class labelling when "all products within a class are assumed to be closely related in chemical structure, pharmacology, therapeutic activity, and adverse reactions". However, this assumption can be dangerous. In addition to drugs within a class not being directly compared, new drugs are often approved based on randomized trials that measure surrogate outcomes rather than outcomes that are important to people (see Concept 3.1b). But there can be important differences in both beneficial and harmful effects of drugs within the same class. It should not be assumed that drugs within a class are interchangeable in the absence of reliable evidence of comparable benefits and long-term safety.

Implications

Be aware that treatments available to you may be sufficiently different from those in the research studies that the results may not apply to you.

References

Systematic reviews

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