More evidence needed

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

3.2e Consider the need for further fair comparisons.

Explanation

There is always some uncertainty about the effects of treatments. If that uncertainty affects decisions that are important to people, the uncertainty should be reduced by further fair comparisons whenever possible. Individuals should consider participating in those fair comparisons when they are uncertain about which alternative to choose because of uncertainty about the effects of the alternatives. Participating in a fair comparison is a good hedging strategy when there is important uncertainty about effects. Moreover, people in fair comparisons sometimes fare better than people outside of fair comparisons. In addition, the results of fair comparisons can help to generate reliable information on which to base future decisions.

Willingness to contribute to the collective good and to help others is commonly thought to be the key motivating factor for participation in randomized trials. However, although willingness to help others might incline people towards participation, participation may be conditional, to some extent, on expectations of personal benefit. For example, a study interviewed people about their motivation to participate in a trial of surgery compared to medical management of gastroesophageal reflux (heartburn and regurgitation caused by stomach contents regurgitating into the oesophagus (tube connecting the mouth and stomach) *[McCann 2010 (RS)]*. It found that people invited to participate viewed:

- recruitment appointments as an opportunity for learning and review,
- participation as potentially offering access or faster access to surgery, and
- participation as offering careful monitoring.

Participants reported that being inclined to help others predisposed them towards trial participation, but considerations of the implications of trial participation for them personally also influenced decisions about participation. For the people who agreed to be randomized, trial participation seemed to be a win-win situation – one in which they could both help others and benefit (or at least not be harmed) personally.

Basis for this concept

A systematic review of factors that affect decisions to participate in randomized trials found 29 studies of experiences of being invited to participate in a trial and of choosing whether to participate *[Houghton 2020 (SR)]*. People were less likely to participate if they were discouraged by other people, felt they had nothing to gain, perceived participation as burdensome, felt they had something to lose, or if there was ineffective trial communication. Conversely, they were more likely to participate if they were encouraged by other people, felt they had something to gain, felt they could help others, felt they had nothing to lose, and if there was effective trial communication. The possible benefits of taking part were key to the decision. Individuals were influenced by the chance of improvement to their health. In addition, many welcomed the opportunity to participate for altruistic reasons or to make a difference by contributing to science.

Some people consider trial participants to be “guinea pigs” *[Sackett 2005]*. Concerns that participants in trials are being “sacrificed” originated from, and are perpetuated by, the examination of single trials or very selective collections of them. Reports of abuse of trial participants are sufficiently publicised that they cause some to question whether randomized trials generally do more harm than good to their participants. However, individual cases and selective reviews are not the best ways to address questions about the benefits and harms of participating in randomized trials.

Several reviews have assessed whether it is beneficial or harmful to participate in randomized trials *[Braunholtz 2001 (SR), Fernandes 2014 (SR), Gross 2006 (SR), Nijjar 2017 (SR), Peppercorn 2004 (SR), Stiller 1994 (SR)]*. Some have compared patients who were treated within trials with those treated outside the trials, regardless of differences between the treatments or between the participants and non-participants. They suggest that participants in trials sometimes have better outcomes than patients outside of trials, and do not have worse outcomes. But it is uncertain whether the results reflect the effects of participating in a randomized trial (trial effects), differences in the treatments in and outside of the trials (treatment effects), or differences between participants and non-participants. A systematic review of studies that compared outcomes in participants who participated in randomized trials with comparable non-participants who received the same or similar treatment found that, on average, participants in randomized trials had similar outcomes to comparable patients who received the same or similar treatments outside the trials *[Vist 2008 (SR), Vist 2005]*. A systematic review of studies that compared patients treated by health professionals or institutions that take part in research found that there may be greater adherence to guidelines and more use of evidence by health professionals and institutions that take part in trials *[Clarke 2011 (SR)]*. However, the consequences for patient health were uncertain.

A common reason for not participating in randomized trials is a strong preference for (or against) one of the treatments being compared *[McCann 2010 (RS)]*. In addition to personal considerations about the pros and cons of participating in a randomized trial, people should only participate in trials if:

- the trial protocol has been registered and made publicly available (see Concept 2.2b),
- the protocol refers to a systematic review showing that the trial is justified (see Concept 2.2a), and
- you receive written assurance that the full study results will be published and sent to all participants who indicate that they wish to receive them (see Concept 2.2b).

In addition, to increase the value of research and reduce waste, new randomized trials should address the needs of users of research (patients, health professionals, and policymakers) and be informed by systematic reviews of existing research *[Chalmers 2014]*.

Implications

Consider advocating for and participating in fair comparisons of treatments when there are important uncertainties about the effects of the treatments.

References

Systematic reviews

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