

## Relevant outcomes

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

---

### 3.1b Consider the relevance of the outcomes measured in the research.

---

#### Explanation

A [fair comparison](#) may not include all [outcomes](#) – short- and long-term – that are important. Patients, professionals, and researchers may have different views about which outcomes are important. For example, studies often measure outcomes, such as heart rhythm irregularities, as [surrogates](#) for important outcomes, like death after heart attack. The effects of treatments on surrogate outcomes often do not provide a reliable indication of the effects on outcomes that are important. Similarly, short-term effects may not reflect long-term effects.

Despite dozens of [randomized trials](#) since the introduction of the first oral agent for treating type 2 diabetes, it has remained uncertain if any of those medicines favourably affects outcomes that are important to people, including morbidity, mortality, and quality of life [[Montori 2007](#)]. A key reason for this is that the trials have focused on glucose control measured with laboratory tests rather than on outcomes that are important to people with diabetes. Unfortunately, those laboratory tests (HbA) are not a reliable indicator of outcomes that are important to people with type 2 diabetes.

It is sometimes important to consider outcomes that are important to other people besides the person being treated. For example, the use of antibiotics may increase antibiotic resistance, and not being vaccinated for Covid-19 or not avoiding contact with other people may increase the risk of infection for others. Similarly, when decisions are made for a group of people rather than for individuals, the outcomes that are important to anyone who is affected should be considered.

#### Basis for this concept

A [systematic review](#) found 436 registered randomized trials that enrolled patients with diabetes [[Gandhi 2008 \(SR\)](#)]. Primary outcomes were patient-important outcomes in only 78 (18%) of the trials. One reason for trials measuring surrogate outcomes rather than patient-important outcomes is the preference of researchers and funding agencies to obtain results faster, with fewer patients and at lower costs. A major downside of this is that the results do not provide information about benefits that patients would consider important, given the paucity of validation of surrogate outcomes in diabetes and other conditions [[Bucher 1999](#)].

A systematic review of trials using surrogate outcomes compared to trials using patient relevant outcomes found that surrogate outcomes reported larger treatment effects than trials reporting patient relevant outcomes [[Ciani 2013 \(SR\)](#)]. This finding was not explained by differences in the risk of bias or characteristics of the two groups of trials. In the absence of patient relevant outcomes, it is important to consider whether surrogate outcomes have been validated and uncertainty about whether surrogate outcomes predict important benefits and harms.

#### Implications

Always consider the possibility that important outcomes may not have been addressed in fair comparisons. Avoid being misled by surrogate outcomes.

## References

### Systematic reviews

Ciani O, Buyse M, Garside R, Pavey T, Stein K, Sterne JA, et al. Comparison of treatment effect sizes associated with surrogate and final patient relevant outcomes in randomised controlled trials: meta-epidemiological study. *BMJ*. 2013;346:f457. <https://doi.org/10.1136/bmj.f457>

Gandhi GY, Murad MH, Fujiyoshi A, Mullan RJ, Flynn DN, Elamin MB, et al. Patient-important outcomes in registered diabetes trials. *JAMA*. 2008;299(21):2543-9. <https://doi.org/10.1001/jama.299.21.2543>

### Other references

Bucher HC, Guyatt GH, Cook DJ, Holbrook A, McAlister FA. Users' guides to the medical literature: XIX. Applying clinical trial results. A. How to use an article measuring the effect of an intervention on surrogate end points. Evidence-Based Medicine Working Group. *JAMA*. 1999;282(8):771-8.

<https://doi.org/10.1001/jama.282.8.771>

Montori VM, Gandhi GY, Guyatt GH. Patient-important outcomes in diabetes--time for consensus. *Lancet*. 2007;370(9593):1104-6. [https://doi.org/10.1016/s0140-6736\(07\)61489-5](https://doi.org/10.1016/s0140-6736(07)61489-5)