Key concepts for informed health choices. 2.3: descriptions of effects should clearly reflect the size of the effects

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This is the third of four essays in this series explaining key concepts about the trustworthiness of evidence from treatment comparisons. In this essay, we explain four considerations about how treatment effects are described. Be cautious of:

- verbal descriptions alone of the size of effects,
- relative effects of treatments alone,
- average differences between treatments and
- lack of evidence being interpreted as evidence of 'no difference'.

The basis for these concepts is described elsewhere.[1]

Be cautious of verbal descriptions alone of the size of effects

A treatment effect (a difference in outcomes in a comparison) is a numerical concept, but it may be difficult to understand quantitative information about the effects of treatments. Qualitative (descriptive) labels may be easier to understand and can be helpful. However, qualitative descriptions of effects may mean different things to different people, for example, saying that a treatment will 'slightly reduce', 'reduce' or 'greatly reduce' the likelihood of an undesirable outcome; or that a side effect is 'frequent' or 'rare'. In addition, verbal descriptions of treatments can be manipulative, for example, promising 'amazing results' or describing treatments as 'natural', implying that they are safe because of that.

Patients' perceptions of verbal descriptions of effects can affect their decisions. For example, a randomised comparison of verbal descriptors suggested by the European Union, such as 'common'

and 'rare' compared to numerical descriptions found, that those verbal descriptions were associated with overestimation of the likelihood of side effects.[2] Patients shown verbal descriptions had more negative perceptions of the medicine than those shown numerical descriptions, and they were more likely to say that the information would affect their decision to take the medicine.

Be cautious of relative effects of treatments alone

Relative effects are ratios, for example, the ratio of the probability of an outcome in one treatment group compared with that in a comparison group. They are insufficient for judging the importance of the difference (between the frequencies of the outcome). A relative effect may give the impression that a difference is more important than it actually is when the likelihood of the outcome is small to begin with. For example, if a treatment reduces the probability of getting an illness by 50% but also has harms, and the risk of getting the illness is 2 in 100, receiving the treatment may be worthwhile. If, however, the risk of getting the illness is 2 in 10,000, then receiving the treatment may not be worthwhile even though the *relative* effect is the same.

Absolute effects are differences, for example, the difference between the probability of an outcome in one treatment group compared with that in a comparison group. The absolute effect of a treatment is likely to vary for people with different baseline risks. Facemasks, for example, may have dramatically different effects depending on the baseline risk of infection.[3] Facemasks reduce transmission of viruses, including coronavirus, but it is uncertain how effective they are for preventing COVID-19 infections.[4–7]

If we assume a 40% relative reduction in the number of new COVID-19 infections, it is possible to estimate the absolute effect for different baseline risks (Table 1). If the baseline risk is zero, it does not make a difference whether facemasks are used. The number of new infections is zero either way. If there is a low baseline risk, for example, in the community when the incidence of COVID-19 is low (and not increasing), the difference is small (about eight fewer new infections if 10,000 people used facemasks for about two months). On the other hand, if the baseline risk is high, say for healthcare workers exposed to patients with COVID-19, the difference is much larger (about 700 fewer new infections per 10,000 people). In fact, the relative effect may also be larger for healthcare workers, if they use medical facemasks (rather than cloth masks), have training and more often use facemasks correctly compared to people in the community. The absolute effect would also then be larger.

Be cautious of average differences between treatments

Average effects do not apply to everyone. For outcomes that are assessed using scales (for example, to measure weight or pain) the difference between the average among people in one treatment group and the average among those in a comparison group may not make it clear how many people experienced a big enough change (for example, in weight or pain) for them to notice it, or that they would regard as important. In addition, many scales are difficult to interpret and are reported in ways that make them meaningless. This includes not reporting the lower and upper 'anchor', for example, whether a scale goes from 1 to 10 or 1 to 100; whether higher numbers are good or bad and whether someone experiencing

an improvement of, say, 5 on the scale would barely notice the difference, would consider it a meaningful improvement or would consider it a large improvement.

For example, the average difference in pain relief is not only hard to interpret, but misleading. When asked what they would consider treatment success, patients with chronic pain specify a large reduction in pain intensity, by 50% or more.[8] Most people tend to respond to painkillers (or a placebo) in two ways. Some people experience very effective pain relief (50% or more), whereas others experience very little (less than 15%). So, the average pain relief does not reflect what most people experienced in randomised trials of painkillers (analgesics) compared to placebos.[8] In Figure 1, the average difference in pain relief is about 28%. A less misleading and easier to

Figure 1. Proportions of patients with different degrees of pain relief.[8] *From Cochrane Pain, Palliative and Supportive Care. Acute postoperative pain: resources. Looking at outcomes, Slideset 3.
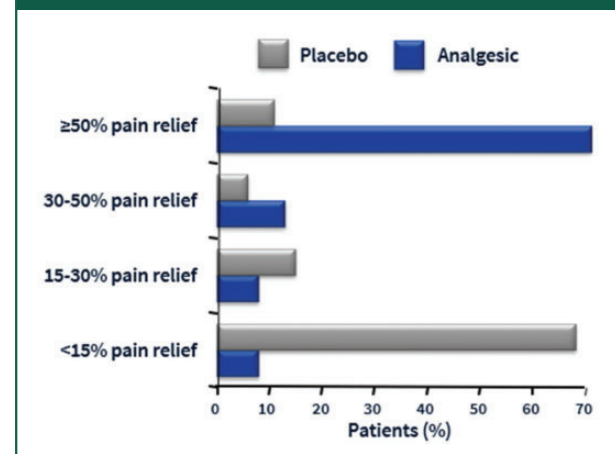
Table 1. Estimates of absolute effects (differences) for different baseline risks of COVID-19 assuming a 40% relative risk reduction.

	Baseline risk[a]	Risk with facemasks[b]	Difference[c]
No new infections	0	0	0
Low risk	0.2%	0.12%	0.08% (8 fewer per 10,000)
High risk	17.4%	10%	7% (700 fewer per 10,000)

[a]The low baseline risk corresponds to the number of new infections in eight weeks without facemasks if the two-week incidence is 50 per 100,000. The high risk is the assumed baseline risk from a systematic review.[4]
[b]The risk with facemasks is based on reducing the baseline risk by 40% (the assumed relative risk reduction).
[c]The difference between the baseline risk (without facemasks) and the risk with facemasks, showing how many fewer new infections there would be with using facemasks compared to not using facemasks.

understand way of reporting those results would be the difference between the proportion of participants in the analgesic group and the placebo group who were treated successfully (with ≥50% pain relief). In Figure 1, about 60% more participants were treated successfully with the analgesic compared to placebo.

Be cautious of lack of evidence being interpreted as evidence of `no difference'

Systematic reviews sometimes conclude that there is 'no difference' between the treatments compared. However, studies can never show that there is 'no difference' ('no effect'). They can only rule out, with specific degrees of confidence, differences of a specific size.

Misinterpreting 'statistically non-significant' results and failing to recognise uncertainty in estimates of effect can sometimes impede further research to reduce the uncertainty and result in delays in the uptake of effective treatments. For example, a systematic review of randomised trials of thrombolytic therapy (medicine that prevents blood clots from growing) given to patients after an acute heart attack found a 22% relative reduction in mortality that was highly unlikely to have occurred by chance alone.[9] But only 5 of the 24 trials had shown a 'statistically significant' effect ($P < 0.05$). The lack of 'statistical significance' of most of the individual trials and misinterpretation of those results led to a long delay before the value of thrombolytic therapy was appreciated.

Implications

- A verbal description of a treatment effect can be helpful, but it should be considered together with quantitative information about the size of the effect. Be wary of manipulative use of language in descriptions of treatment effects.
- Always consider the absolute effects of treatments – that is, the difference in outcomes between the treatment groups being compared. Do not make a treatment decision based on relative effects alone.
- When outcomes are assessed using scales, it cannot be assumed that every individual in the treatment comparison groups experienced the average effect. Be wary of differences on scales that are not explained or easily understood.
- Don't be misled by statements of 'no difference' between treatments ('no effect'). Consider instead the degree to which it is possible to confidently rule out a difference of a specified size.

Declarations
Competing Interests: None declared.

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