LETTER TO THE EDITOR

Many continuous variables such as the duration of the common cold should be analyzed using the relative scale

Alba et al. [1] compared the heterogeneity of meta-analyses on the basis of the type of outcome, and concluded that meta-analyses that evaluate continuous outcomes showed substantially higher I^2 values than meta-analyses of binary outcomes. However, in a proper comparison, like should be compared with like.

First, their measure of effect on binary outcomes was a relative effect (risk ratio, odds ratio), whereas their measure of effect on the continuous outcomes was an absolute effect or effect in standard deviation units (standardized mean difference). Second, there is great variability in the kind of phenomena that are measured by continuous outcomes. For example, quite diverse scales are used in psychiatry, and they are analyzed as continuous variables, yet those outcomes are quite different from, say, the occurrence of lung cancer (binary) or the duration of the common cold (continuous). The latter two directly measure biological phenomena and they might substantially differ from arbitrary scales. These two issues were not considered by Alba et al. [1].

Effects in binary outcomes are usually better captured by the relative scale than by an absolute scale, for example, the 10-fold increase in lung cancer risk by smoking. Similarly, the relative effect can better capture the differences between the compared groups in many biological phenomena that are measured as continuous outcomes.

Our Cochrane review on vitamin C and the common cold showed the shortest average duration of colds in a placebo group of children to be 2.6 days, whereas the longest was 14 days (Analysis 2.1.2 in [2]). Such a great variation in cold duration in the placebo groups is explained by variations in viruses and in operational outcome definitions between different trials, and so forth. An ideal treatment might shorten the long colds by 10 days, whereas such an effect on short colds is impossible. Thus, the absolute effect scale is not feasible for analyzing effects on the duration of colds. Therefore, we used the relative scale in our analysis. We calculated that the heterogeneity in the effect of vitamin C on cold duration over 14 trials on children was $I^2 = 27\%$ ($P = 0.17$; Analysis 2.1.2 in [2]). The same set of studies gives $I^2 = 46\%$ ($P = 0.03$) when the analysis is done on the absolute scale. The latter I^2 is 19 percentage points more (1.7-fold) than the I^2 of the relative scale (See Appendix). Thus, meta-analyses on different scales can lead to divergent I^2 values. Different metrics may have biased the comparison of meta-analyses on binary and continuous outcomes [1].

Alba et al. cited a meta-analysis on zinc and the common cold [3] as a specific example of great heterogeneity in meta-analyses on continuous outcomes. However, much of the heterogeneity in that particular meta-analysis was explained by the apples and oranges problem [4]. Heterogeneity over 13 trials on zinc lozenges and the common cold ($I^2 = 89\%$) was largely explained by the dose of zinc and the type of zinc salt used in the lozenges [5]. Thus, separating apples from the oranges can explain a substantial part of heterogeneity in some meta-analyses. For the previously mentioned reasons, the conclusions of Alba et al. [1] do not seem justified.

Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.jclinepi.2016.03.020.

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