Letter to the editor

Using risk difference as opposed to odds-ratio in meta-analysis

Andrea Messori *, Dario Maratea, Valeria Fadda, Sabrina Trippoli

HTA Unit, ESTAV Toscana Centro, Regional Health Service, 50100 Firenze, Italy

In comparing cardiovascular death between patients receiving intensified antiplatelet therapy after percutaneous coronary intervention and controls given standard-dose clopidogrel, the meta-analysis by Aradi et al. [1] handled a very critical data set because only 10 randomised studies were available and more than half of the event frequencies were zero (13 out of 20).

Besides this large number of zero frequencies, another weakness of this study is the choice of the odds-ratio (OR) as effect measure. More than 10 years ago, Walter [2] stressed that the OR tends to “exaggerate the effect of treatment” as a direct consequence of its mathematical definition. Another drawback pointed out by Walter [2] is that “the OR is undeniably the most difficult measure to intuit, so it is likely to be less useful that risk difference or relative risk for communicating risk”.

We reanalysed the data set of Aradi et al. [1] on cardiovascular mortality (Figure 2 of their article) by choosing the risk difference rather than the OR. All calculations (random-effect model) were carried out using the OMA software that automatically implements a correction for the presence of zero values as event frequencies [3].

The results of our analysis (Fig. 1) do not entirely confirm the findings of Aradi et al. [1]. In fact, while the p-value of Aradi et al. was 0.008 [1], our analysis found a p-value of 0.0515. More importantly, the benefit estimated by our analysis was a risk reduction of 0.47% (95% confidence interval: from a reduction of 0.89% to an increase of 0.003%).

It is interesting to see that a statistical level initially far from the conventional threshold of p=0.05 has been converted into a non-significant value by using a more conservative (and more appropriate) statistical analysis. Does this have any implication in interpreting Aradi’s findings?

References

Fig. 1. Comparison of cardiovascular mortality between patients receiving intensified antiplatelet therapy and controls given standard-dose clopidogrel. This meta-analysis was based on risk differences and random-effect model as implemented in the OMA software [3]. Black squares denote study-specific risk differences (with 95% confidence interval) while diamonds indicate pooled risk difference (with 95% confidence interval); I^2 is a measure of heterogeneity (accompanied by its level of statistical significance); the dotted vertical line highlights the meta-analytical value of risk difference. Abbreviations: Ev = number of events; Trt = number of treated patients. The complete references of the original studies have been reported by Aradi et al. [1].