Statistical issues in trial designs with composite binary endpoints

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Abstract. Composite endpoints, defined as the union of two binary endpoints, are widely chosen as primary endpoint in clinical trials. However, its use entails difficulties in designing the study as well as in interpreting the results.

This talk has a two-folded aim. First, we present a methodology to quantify the gain in efficiency of using a composite binary endpoint instead of its most relevant component as primary endpoint to lead the trial[1]. The methodology, based on the Asymptotic Relative Efficiency (ARE), is given by the correlation between the components of the composite endpoint, the event proportion, and the effect of therapy on each component.

Second, we propose a procedure for sizing trials with composite binary endpoints, doing so on the basis of anticipated values on the components parameters even if the correlation between them is unknown. Our proposal calculates the minimum sample size that guarantees the pre-specified power while accounting for the uncertainty of the correlation value and plausible deviations in the components parameter values[2].

We have implemented the ARE methodology and the sample size procedure in a web-platform called CompARE[3]. We illustrate both proposals with a cardiovascular trial using the platform CompARE. We conclude with an outlook for the ongoing research on the relationship between the ARE and the reciprocal ratio of the sample sizes.

Keywords

Asymptotic Relative Efficiency; Clinical Trial; Composite Endpoint.

References

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