Probability and hazard ratio for combined endpoints: extending CompARE.

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Randomized clinical trials are commonly designed to compare treatment effects. The choice of the primary endpoint at the design stage is of paramount importance. The decision is often based on whether a combination of several endpoints has to be included as part of the primary endpoint. A case study from the cardiovascular area is the LIFE trial, where the combined relevant endpoint consisting of the union of cardiac death and myocardial infarction, plus the additional endpoint stroke were used as the primary composite endpoint. Gómez and Lagakos develop a methodology to evaluate the relative efficiency (ARE) of a composite endpoint versus a relevant subset of its components. In order to calculate the ARE, the anticipated combined probabilities and hazard ratios are required. However, investigators might know the specific values of each component rather than their corresponding combined values. These combined parameter values will play and important role in the ARE computations and therefore in sample size calculations.

With the main aim of making the ARE method widely applicable to the scientific community, we built the web-based platform CompARE. It provides a tool to compute ARE values, returning results for different scenarios through plots and tables. Moderate correlation and exponential distributions for the marginal laws are considered by default. CompARE is extended to other distributions allowing as well the possibility of combinations of more than two events for the primary endpoint.

In this talk we present how to derive combined probabilities and hazard ratios appropriately from the marginal components. We have implemented several options in CompARE to assign probabilities and hazard ratios. These options are constrained to the interval of plausible values and might depend on the anticipated values of the correlation between components. We illustrate these findings by means of the LIFE study.

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