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# An extension to generalized pairwise comparisons for prioritized outcomes with censoring

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## Résumé

Generalized pairwise comparisons have been proposed to permit a comprehensive assessment of several prioritized outcomes between two groups of observations [1]. We propose an extension of generalized pairwise comparisons for time-to-event outcomes that takes into account the time to censored observations. We show how pairwise scores can be calculated from the Kaplan-Meier estimates of the survival function in the presence of right-censored data. These scores are used to estimate the chance of a better outcome with treatment than with control, which is defined as where the outcome is captured by the variable in the treatment group and by the variable in the control group. A randomization test can be used to test the null hypothesis, and to calculate a confidence interval for . The extended procedure for generalized pairwise comparisons is more efficient than the standard procedure. When several outcomes are prioritized in a single assessment of the overall treatment effect (i.e. benefit-risk assessment), the estimation of the chance of a better outcome varies only slightly with the censoring pattern. Since the way the censoring occurs is independent of the parameters of interest (benefits and risks of an investigational treatment), the censoring rate on the survival outcome should not have a large impact on the estimation of the chance of a better outcome.

To facilitate the use of generalized pairwise comparisons we have developed an R package `BuyseTest`, which we will present. The package includes the standard procedure of generalized pairwise comparisons, and two extensions for time-to-event outcome analyses. The standard procedure of pairwise scoring for time-to-event variable is to classify as ‘uninformative’ all the pairs not known to be favorable or unfavorable because of censoring. When only one time-to-event outcome is considered, this approach is equivalent to Gehan’s extension of the Wilcoxon test for censored data [2]. The first extension estimates using the Kaplan-Meier estimate of the survival function based on all observations, following Latta’s modification of Efron’s test and Peto and Peto’s test [3]. The second extension estimates using the Kaplan and Meier estimates of the survival function of the two groups of patients, following the Efron’s generalization of the Wilcoxon test [4]. The R package `BuyseTest` also includes a function to compute sample size while designing randomized trials.

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