Test and confidence intervals for secondary parameters in sequential clinical trials

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Abstract

For clinical trials carried out using a sequential design, analyses that neglect the monitoring aspect of the trial are potentially biased, and this holds for secondary parameters not directly used to determine whether the study should be stopped. Here we propose a hybrid resampling method to test secondary hypotheses and construct confidence intervals for secondary parameters in sequential clinical trials. This method does not require the asymptotic bivariate normal distribution assumption for the test statistics of the primary and secondary parameters. We examine the proposed method in detail in two commonly encountered scenarios: (1) the primary and secondary outcomes follow a joint bivariate normal distribution, the means of which are the parameters of interest; (2) the primary parameter is the treatment effect of overall survival, while the secondary parameter is the median survival in subjects with certain covariates.

This is a joint work with TL Lai (Stanford University) and Zheng Su (Stony Brook University).