**Sample size re-estimation incorporating prior information on a nuisance parameter**

Tobias Mütze, Novartis Pharma AG, Basel

Prior information is often incorporated informally when planning a clinical trial. Here, we present an approach on how to incorporate prior information, such as data from historical clinical trials, into the nuisance parameter–based sample size re-estimation in a design with an internal pilot study. We focus on trials with continuous endpoints in which the outcome variance is the nuisance parameter. For planning and analyzing the trial, frequentist methods are considered. Moreover, the external information on the variance is summarized by the Bayesian meta-analytic-predictive approach. To incorporate external information into the sample size re-estimation, we propose to update the meta-analytic-predictive prior based on the results of the internal pilot study and to re-estimate the sample size using an estimator from the posterior. By means of a simulation study, we compare the operating characteristics such as power and sample size distribution of the proposed procedure with the traditional sample size re-estimation approach that uses the pooled variance estimator. The simulation study shows that, if no prior-data conflict is present, incorporating external information into the sample size re-estimation improves the operating characteristics compared to the traditional approach. In the case of a prior-data conflict, that is, when the variance of the ongoing clinical trial is unequal to the prior location, the performance of the traditional sample size re-estimation procedure is in general superior, even when the prior information is robustified. When considering to include prior information in sample size re-estimation, the potential gains should be balanced against the risks.

Schmidli, H., Neuenschwander, B., & Friede, T. (2017). Meta-analytic-predictive use of historical variance data for the design and analysis of clinical trials. Computational Statistics & Data Analysis, 113, 100-110.

Mütze, T., Schmidli, H., & Friede, T. (2018). Sample size re-estimation incorporating prior information on a nuisance parameter. Pharmaceutical statistics, 17(2), 126-143.