

# DESIGN EXTENSIONS OF EXPERIMENTS WITH NORMALLY DISTRIBUTED OUTCOME AND UNKNOWN VARIANCE

N. Timmesfeld, H. Schäfer, H.-H. Müller<sup>†</sup>

*Institute of Medical Biometry and Epidemiology, Philipps-University, Marburg, Germany*

<sup>†</sup> E-mail: *muellerh@med.uni-marburg.de*

In experiments with t-distributed test statistics the required sample size depends on the unknown variance. Using estimates of the nuisance parameter from previous studies for sample size calculation often leads to uncertainty regarding specification of the sample size. Even a small underestimation of the true variance may lead to a considerable loss of power. Re-estimation of the variance from the collected data and checking the sample size is attractive. Whenever insufficient power becomes apparent during the course of the experiment and a re-calculated sample size can practically be achieved, an immediate extension of the experiment is desired. However, one has to consider that preservation of the type I error level is an important issue, particularly in confirmatory clinical trials.

In all presented methods till now there is at least one of the following disadvantages: control of the type I error rate is not ensured, sample size modification is only possible at a preplanned interim analysis, sample size re-calculation depends on a pre-specified rule, the method uses approximation of distributions.

Refining the conditional rejection probability approach, we propose a method for design extensions having none of the listed disadvantages. Moreover, when no design changes are prompted, the efficient pre-specified design using a (group sequential) t-test will be retained until the end of the experiment.