Seminar

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Statistical Inference for Response-Adaptive Designs in Multi-Center Clinical Trials

Abstract:
We discuss methods for comparing two treatments A and B. We investigate the performance of response-adaptive (RA) and covariate-adjusted response-adaptive (CARA) designs in multi-center clinical trials. First, we discuss applying RA designs to maximize the well-being of participating patients in multi-center clinical trials. We assume that the centers are selected from a large population of centers and develop a generalized linear mixed model (GLMM) to examine the treatment effect. The asymptotic properties of the maximum likelihood (ML) estimators of model parameters are derived using the influence function method. We verified their theoretical properties through simulation studies. The techniques are then applied to a real data that were obtained from a multi-center clinical trial designed to compare two cream preparations (active drug/control) for treating an infection. Secondly, we investigate the efficiency of statistical inference and ethics for participating patients under RA, CARA, and completely randomized (CR) designs for a generalized linear model (GLM). We consider the logit model to measure efficiency and ethics. Furthermore, we showed that ML estimators of GLM parameters are consistent and asymptotically follow multivariate normal distribution for adaptive designs. A simulation study was conducted to verify these theoretical results. Finally, we provide a justification of why asymptotic results for Wald-type test for adaptive designs can be used. We proved that the choice of adaptive designs affects the statistical power of hypothesis testing via these quantities: the target allocation proportion, the bias of the randomization procedure from the target, and the variability induced by the randomization process. Moreover, we showed that the statistical power increases when the design variability decreases for a covariate in a logit model. Our theoretical findings are verified by simulation results.