

A Theory For Testing Hypotheses Under Covariate-Adaptive Randomization

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Abstract

The covariate-adaptive randomization method was proposed for clinical trials a long time ago but very little theoretical work has been done for statistical inference associated with it. Practical users often apply test procedures available for simple randomization, which is controversial since procedures valid under simple randomization may not be valid under other randomization. We provide some theoretical results for testing hypotheses after covariate-adaptive randomization. We show that one way to obtain a valid test procedure is to use a correct model between outcomes and covariates, including those used in randomization. We also show that the simple two sample t-test, without using any covariate, is conservative under covariate-adaptive biased coin randomization in terms of its type I error, and that a valid bootstrap t-test can be constructed. The power of several tests are examined theoretically as well as empirically. Our study provides a guidance for applications and sheds light on further research in this area.