Improving efficiency of inferences in randomized clinical trials using auxiliary covariates

Anastasios A. Tsiatis *
North Carolina State University

The primary goal of a randomized clinical trial is to make comparisons among two or more treatments. For example, in a two-arm trial with continuous response, the focus may be on the difference in treatment means; with more than two treatments, the comparison may be based on pairwise differences. With binary outcome, pairwise odds-ratios or log-odds ratios may be used. In general, comparisons may be based on meaningful parameters in a relevant statistical model. Standard analyses for estimation and testing in this context typically are based on the data collected on response and treatment assignment only. In many trials, auxiliary baseline covariate information may also be available, and there has been considerable debate regarding whether and how these data should be used to improve the efficiency of inferences. Taking a semiparametric theory perspective, we propose a broadly-applicable approach to achieving more efficient estimators and tests in the analysis of randomized clinical trials, where "adjustment" for auxiliary covariates is carried out in such a way that concerns over the potential for bias and subjectivity often raised for other covariate adjustment methods may be obviated. Simulations and applications demonstrate the performance of the methods.

*This is joint work with Marie Davidian, Min Zhang, and Xiaomin Lu.