

Response Adaptive Optimal Design in Clinical Trials - A Simulation Study Motivated by a Real Data Example

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Abstract

In this paper we summarize the theory of clinical trials, in particular their design, optimal design and adaptive design. We emphasize the two-stage optimal response-adaptive design and implement the theory of optimization on the nonlinear, multiparameter *E_{max}*-sigmoid model using two different optimization criteria, two optimization methods, three different parameter vectors and three different sample sizes. The aim of the paper is to study the distributional properties of an optimal design through simulations. We also propose an optimization method for computing the optimal design. The results reveal that a large variation in parameter estimates of the dose-response curve yields a large variation of the estimated optimal design. To explore this further we consider four different dose-response curve models. One of these models proves to give a reduction in variation and hence a reliable optimal design. However, our conclusion is that this model might not be realistic and that further investigation of the asymptotics of the estimated parameters should be carried out.

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