ABSTRACT

Bayesian clinical trial designs offer the possibility of a substantially reduced sample size, increased statistical power, and reductions in cost and ethical hazard. However, when prior and current information conflict, Bayesian methods can lead to higher than expected Type I error, as well as the possibility of a costlier and lengthier trial. This motivates an investigation of the feasibility of hierarchical Bayesian methods for incorporating historical data that are adaptively robust to prior information that reveals it to be inconsistent with the accumulating experimental data. In this paper, we present novel modifications to the traditional hierarchical modeling approach that allows the commensurability of the information in the historical and current data to determine how much historical information is used. Here our primary focus is on the case of Gaussian linear models, and our primary tool is an extension of so-called modified power priors (Ibrahim and Chen, 2000). We compare the frequentist performance of our methods as well as existing, more traditional alternatives using simulation, calibrating our methods so they could be feasibly employed in FDA-regulated trials. We also give an example in a colon cancer trial setting where our proposed design produces more precise estimates of the model parameters, in particular conferring statistical significance to the observed reduction in tumor size for the experimental regimen as compared to the control regimen. Finally, summarize our findings, and indicate progress to date in extending our commensurability approach to the cases of binary and time-to-event data.

This work is joint with Mr. Brian Hobbs, PhD candidate, University of Minnesota.