Bayesian Robustness
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ROBUST BAYESIAN DESIGN AND ANALYSIS OF CLINICAL TRIALS VIA PRIOR PARTITIONING[1]

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Unlike traditional approaches, Bayesian methods enable formal combination of expert opinion and objective information into interim and final analyses of clinical trials data. However, in cases where a broad group must be convinced by the results, a practical approach for studying and communicating the robustness of conclusions to prior specification is required. Rather than adopt the traditional method of modifying a single, initial prior and repeating the posterior calculation, in this paper we give a partial characterization of the class of priors leading to a given decision (such as stopping the trial and rejecting the null hypothesis) conditional on the observed data. We employ an interval null hypothesis based on the indifference zone approach of Freedman and Spiegelhalter, and restrict attention to priors having certain prespecified quantiles. We illustrate the application of our approach to interim monitoring using data from a recent AIDS clinical trial. We also indicate the method's usefulness in the design of future trials, creating simulation-based Bayesian analogues of the classical sample size table.

1. Introduction. Recently, Bayesian methods have seen increasing usage in the design, interim monitoring, and final analysis of clinical trials data. They allow for greatly simplified designs, due to the independence of the inference from the stopping rule, as well as more realistic sample size determination based on the full range of the experimenter's prior beliefs. Advanced Monte Carlo integration algorithms such as the Gibbs sampler enable fast and accurate computation of relevant posterior distributions, providing a more informative estimate of the treatment effect and the associated uncertainty. Moreover, Bayesian methods free the user from prespecifying the number of looks at the data or the form of an "α-spending function" (see e.g. Carlin et al., 1993). Finally, the Bayesian methodology is easily blended with formal decision-theoretic tools in settings where policymakers must do more than simply summarize a trial's results (e.g., in determining whether it is ethical to run a given trial in the first place). Thorough reviews of the use of Bayesian methodology in clinical trials are provided by Berry (1993) and Spiegelhalter, Freedman and Parmar (1994).

Despite these potential advantages, many practitioners are either skeptical of Bayesian methods or reluctant to use them. This apprehension is often

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