

TITLE: Enhancing Pediatric Clinical Trials: A Shiny App for Bayesian Adaptive Semiparametric Design, Communication and Implementation

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ABSTRACT:

Effectively communicating the importance and the characteristics of advanced designs to non-statistical experts involved in the trial conduction presents a significant challenge. Effective communication ensures that clinicians can easily apply the complex Bayesian methodologies in their practice, bridging the gap between statistical innovation and clinical implementation. This research discusses the development and utilization of a Shiny application designed to support Bayesian adaptive semiparametric design implementation in pediatric randomized controlled trials (RCTs). The application aims to address challenges in pediatric clinical trials, such as efficiently handling primary and secondary endpoints, especially in the presence of sparse or conflicting prior data. The app incorporates Bayesian adaptive design principles enhanced with B-Spline semiparametric priors, allowing dynamic updating of priors with ongoing data, thus improving the accuracy and efficiency of treatment effect estimation.

The Shiny app provides an interactive and user-friendly interface for researchers to input trial parameters, perform simulations, and visualize results in real time. Key features include the ability to assess the design operative characteristics, conduct Monte Carlo simulations, evaluate stopping rules based on the Highest Posterior Density Interval (HDI) and assess the impact of various prior distributions on trial outcomes. The app is designed to be highly flexible, accommodating different trial designs and endpoints, and can integrate historical data or expert opinions seamlessly.

One of the significant advantages of the Shiny app is its capacity to automate complex statistical calculations, making advanced Bayesian methods accessible to researchers without extensive statistical expertise. By offering real-time data analysis and visualization, the app aids in making informed decisions during the trial, such as determining sample sizes, evaluating interim results, and deciding on early stopping for efficacy or futility.

The development of the Shiny app was motivated by real-world applications, specifically the REnal SCarring Urinary infEction Trial (RESCUE), a pediatric RCT that faced multiple challenges in trial conduction. Through simulation studies inspired by this trial, the app demonstrated its ability to correctly declare treatment effects and stop trials early for futility, thereby enhancing the overall efficiency and ethical conduct of pediatric trials. Simulation results indicated that the semiparametric design, supported by the Shiny app, required a smaller sample size to achieve the target power of 0.8 compared to traditional parametric methods when using informative priors.

The Shiny app offers an accessible platform for clinicians to understand and apply complex Bayesian methodologies in their trials. The app facilitates robust, ethical, and efficient trial outcomes by improving clinician engagement and understanding through accessible communication tools and real-time data analysis.