Mi-Ok Kim, PhD
Associate Professor
Biostatistics and Epidemiology
Department of Pediatrics
Cincinnati Children's Hospital Medical Center

Utility of Sequentially Monitored Response-Adaptive Designs for Multi-Center Clinical Trials

Clinical trials usually involve multiple competing objectives such as minimizing the sample size and protecting more people from possibly inferior treatments. Statistical techniques that have developed to balance competing objectives and attain efficiency include sequential monitoring and response-adaptive randomization. In this paper we examine the utility of sequentially monitored response adaptive randomization for confirmatory clinical trials. Many confirmatory clinical trials have delayed primary outcomes, include interim analysi(e)s to stop early for futility or efficacy, involve subgroups defined by stratification, and involve multi-center, across which attaining balance in randomization is often desirable. Delay in the primary outcome variable is challenging for sequential monitoring and response adaptive randomization, as it creates a lag between the number of subjects accrued and the information known at the time of the analysis. Earlier work has proposed imputation based doubly adaptive biased coin designs (DBCD) to address delayed outcomes (Kim et al, 2014). We adapt the imputation based DBCD to accommodate multiple interim analyses and attain balance in randomization across multiple centers.