

論文要旨

Dynamic borrowing with a bias tolerance cap in augmented randomized controlled trials

(バイアスの許容上限を与えた外部対照の動的利用法に関する研究)

生物統計情報学コース

49-236604

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Randomized controlled trials (RCTs) have long been considered the gold standard for evaluating treatment efficacy and safety. However, RCTs often face challenges such as high costs, extended trial durations, patient recruitment difficulties, and ethical constraints. To address these feasibility issues, incorporating external control data as a hybrid control group (augmented RCTs) has emerged as a promising solution. Although various statistical methods have been developed for this purpose, few account for the impact of confounding caused by imbalances in unknown or unmeasured covariates between the external control and the control group of the current RCT. In this study, we introduce a novel approach to account for the effects of unmeasured covariates using parametric standardization, inverse probability weighting (IPW), and augmented IPW (AIPW) for continuous and binary outcomes. To facilitate dynamic borrowing of external data, we propose a weighted mean estimator, where the weights flexibly adjust based on the estimated effects of unmeasured covariates. Our framework also allows for intuitive consideration of the bias-variance trade-off by specifying a bias tolerance cap. Simulation studies demonstrate that the proposed method keeps bias within a pre-specified tolerance cap, regardless of the extent of confounding by unmeasured covariates. Furthermore, our approach shows notable improvements in statistical power and efficiency compared to existing methods that only address measured confounders. To illustrate the practical utility, we apply our proposed methodology to Japanese RCTs and electronic health record data for patients with unresectable pancreatic cancer.