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Maintaining the validity of inference in stepped-wedge cluster randomized trials under random effects misspecification

Mixed-effect regression is commonly used in stepped-wedge cluster randomized trials (SW-CRTs). A key requirement is to account for the complex correlation structures. Common structures are exchangeable (random intercept), nested exchangeable (random cluster-by-period), and exponential decay (discrete-time decay). In recent years, more complex models (e.g., random intervention models) have been proposed. In practice, it is challenging to specify appropriate random effects and obtain valid statistical inferences. Robust variance estimators (RVE) that have been widely discussed under the generalized estimating equations framework may also be applied in mixed-effect regression to deal with random-effect misspecifications. However, relevant discussion in SW-CRT has been limited. In this study, we first review five RVEs that are available for linear mixed models via R. Then, we describe the results of a simulation study to investigate the performance of RVE under mixed-effect regression. We focused on SW-CRTs with continuous outcomes assuming the data were generated from models with 1) exponential decay and random intervention effects, or 2) random cluster-by-period and random intervention effects. For each data generator, we found that the use of RVE with either the random intercept or the random cluster-by-period model was sufficient to provide valid statistical inference. With the Satterthwaite degrees of freedom approximation, among the five RVEs we investigated, CR3 (a small-sample corrected RVE that approximates the leave-one-cluster-out jackknife variance estimator) consistently gave the best coverage results, even though it might be slightly anti-conservative when the number of clusters was below sixteen.