Online Supplement for "Review of Recent Methodological Developments in Group-Randomized Trials: Part 2 – Analysis"

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GLOSSARY

This online supplement contains a glossary of terms arranged according to the sections of the manuscript.

ANALYSIS OF PARALLEL GROUP-RANDOMIZED TRIALS

Equivalence: Assessing whether the new intervention is equivalent to the comparison intervention.

Non-inferiority: When a trial is designed to show that the new intervention is not worse than the comparison intervention.

Superiority: When a trial is designed to establish whether a new intervention is superior to the comparison intervention (e.g., another drug, a placebo, enhanced usual care). However, the statistical test is still two-sided, allowing for the possibility that the new intervention is actually worse than the comparison.

Methods for the Intervention Effect

On treatment analyses: When groups are analyzed "according to the intervention they actually received."[1]

Per protocol analyses: When groups "not receiving the correct intervention are excluded."[1]

Methods Based on Randomization Scheme

Constrained randomization: Refers "to those designs that go beyond the basic design constraints to specify classes of randomization outcomes that satisfy certain balancing criteria, while retaining validity of the design."[2]

Model-Based Methods

Augmented GEE: "Augmenting the standard GEE with a function of baseline covariates."[3] These methods adapt semiparametric theory developed by Robins[4] and Robins, Rotnitzky, and Zhao[5] for observational studies with time-varying exposures and missing data problems, respectively. They consist of leveraging the estimating equation by a predictor function for counterfactual outcomes under the intervention not received by the group/cluster considered missing.[3]

Baseline covariate balance: The group-level and individual-level covariate distributions are similar in all study arms.[6]

Choice of balancing criterion: Li et al. describe several balancing criteria to assess how well a GRT is balanced across covariates. These include the "best balance" (BB) metric of de Hoop et al.,[7] the balance criterion (B) of Raab and Butcher,[11] and the total balance score introduced by Li et al.[8]

Cohort GRT design: A cohort of individuals is enrolled at baseline and those same individuals are followed up over time.

Cross-sectional GRT design: A different set of individuals is obtained at each time point.

Design balance at the group level: When there are equal numbers of groups randomized to each study arm.

G-computation estimator: A computational method to estimate causal effect in structural nested models. These models are designed to deal with confounding by variables affected by intervention.[9]

Informative cluster size: When the outcome measured is related to the size of the cluster.[10]

Within-cluster resampling: Randomly sample one observation from each cluster, with replacement. Then analyze this resampled dataset. Repeat this process a large number of times. "The within-cluster resampling estimator is constructed as the average" of all of the resample-based estimates (see Hoffman et al.[11] pp. 1122-3).

DEVELOPMENTS IN THE ANALYSIS OF ALTERNATIVES

Stepped-Wedge GRTs

Stepped Wedge GRT: "A one-directional crossover GRT in which time is divided into intervals and in which all groups eventually receive the intervention."[12,13]

Network-Randomized GRTs

Network-Randomized GRT: "The network-randomized GRT is a novel design that uses network information to address the challenge of potential contamination in GRTs of infectious diseases."[12,14,15,16]

Pseudocluster Randomized Trials

Pseudocluster randomized trial: Intervention is allocated to individuals in a two-stage process. "In the first stage, providers are randomized to a patient allocation-mix…. In the second stage, patients recruited to the PCRT are individually randomized to intervention or control according to the allocation probability of their provider."[12]

Individually Randomized Group-Treatment Trials

Individually Randomized Group-Treatment Trials: "Studies that randomize individuals to study arms but deliver treatments in small groups or through a common change agent."[12,17]

DEVELOPMENTS IN ADRESSING DATA CHALLENGES

Missing Outcome Data

Covariate-dependent missingness (CDM) assumption: The assumption that "missingness in outcomes depends on covariates measured at baseline, but not on the outcome itself."[18]

Doubly-robust augmented GEE approach: Combining augmented GEE and IPW, a doubly-robust estimator is obtained, which provides an unbiased estimate if either the marginal mean model or the missing data model is correctly specified.[19,20]

Missing at Random (MAR) assumption: Rubin's (1976) definition is that "data are missing at random if for each possible value of the parameter φ [the parameter of the conditional distribution of the missing data indicator given the data], the conditional probability of the observed pattern of missing data, given the missing data and the value of the observed data, is the same for all possible values of the missing data."[21]

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