Stepped Wedge Cluster Randomized Trials

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Outline

- Introduction
- Analysis of stepped wedge cluster randomized trials
- 3 Investigation of simulation study
- Extensions to basic model
- 6 Conclusion

Introduction

Background

Paper by Hussey and Hughes [1] can be viewed as entry point to stepped wedge cluster randomized trials (SW-CRT)

- Provides an overview of motivation, design and analysis of SW-CRTs
- Focuses on technical aspects of practical interest such as power and estimators
- Presents ideas in an accessible and succinct format

Main limitations and weaknesses from our perspective:

- Limited breadth: discussion is restricted to primarily one SW-CRT setting
- Minimal depth: technical details are only briefly explained or omitted entirely
- **3** Writing: unclear which aspects are novel; some typos and/or errors

Objective

Our main goal is to address the limitations of Hussey and Hughes [1]:

- 1 Address missed technical details, explanations and derivations
- 2 Clarify their simulation procedure and attempt to replicate their simulation results
- 3 Discuss extensions to their basic model for different SW-CRT settings



Assumed SW-CRT setting

Washington State Community Expedited Partner Treatment (EPT) Trial:

- Hypothesis: EPT public health programs decrease prevalence of chlamydia and incidence of gonorrhea in young women
- Method: Program implemented in 23 local health jurisdictions (LHJ) in 4 waves; primary outcomes were prevalence (incidence) of chlamydia (gonorrhea) in tested women

Primary SW-CRT setting based on EPT trial that Hussey and Hughes [1] work under:

- ullet SW-CRT with I=24 clusters and T=5 measured time points
- \bullet Cross-sectional design with N=100 units at each cluster-time

Statistical model

Individual-level model under assumed SW-CRT setting:

$$Y_{ijk} = \mu + \alpha_i + \beta_j + X_{ij}\theta + e_{ijk}$$
$$= \mu_{ij} + e_{ijk}$$

- ullet μ is the mean across clusters and time
- $\alpha_i \sim N(0, \tau^2)$ is a random effect for cluster $i \in \{1, \dots, I\}$
- β_j is a fixed effect for time point $j \in \{1, \dots, T-1\}$ ($\beta_T = 0$ for identifiability)
- X_{ij} is a treatment indicator for cluster i at time j (1 denotes intervention)
- ullet θ is the treatment effect of interest
- $e_{ijk} \sim N(0, \sigma^2)$ are i.i.d. noise

Methods for estimating treatment effect θ [1]

- Within-cluster estimator
 - Consistent if no time effects ($\beta_j = 0$ for all j); biased otherwise [A1]
- 2 Linear mixed effects model (LMM) via weighted least squares (WLS)
 - Useful if τ^2 and σ^2 known or clusters roughly equal sized; loss of power otherwise due to misspecified weights
 - More efficient than within-cluster estimator if no time effects; note Liao et al. [2] found an error in Hussey and Hughes' relative efficiency [A2]
- 3 Generalized linear mixed effects model (GLMM)
 - Weights are appropriately weighted even if variance components unknown
 - Link function allows choice of how expected response is modeled
- 4 Generalized estimating equations (GEE)
 - Consistent even if correlation structure misspecified as long as mean is correctly specified

Power calculation

Hussey and Hughes [1] prescribe using a Wald test to test $H_0: \theta = 0$

• Power for a test of size α is approximately

$$\Phi\left(\frac{\theta_a}{\sqrt{\operatorname{Var}(\hat{\theta})}} - Z_{1-\frac{\alpha}{2}}\right)$$

where Φ is the cumulative distribution function of a standard normal [A3]

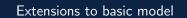
Hussey and Hughes [1] also show that

- power is maximized when each cluster crosses over at its own time point [A4]
- delays in treatment effect decreases power [A5]



Procedure

Results



Conclusion

Multiple factor analysis

- Factor analysis: estimate latent factors underlying observed data
- Principal Component Analysis: given data matrix $A \in \mathbb{R}^{n \times d}$, returns scaled loadings $V \in \mathbb{R}^{d \times d}$ and principal components (PCs) $S \in \mathbb{R}^{n \times d}$ s.t.

$$S = AV$$

- \Rightarrow Represent and estimate factors by the leading $k \leq d$ PCs
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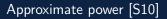
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- \bullet ?]: rotate PCs to make coefficients as sparse as possible (i.e., $\approx 0)$

References I

- [1] Hussey, M. A. and Hughes, J. P. (2007). Design and analysis of stepped wedge cluster randomized trials. *Contemporary Clinical Trials*, 28(2):182–191.
- [2] Liao, X., Zhou, X., and Spiegelman, D. (2015). A note on "Design and analysis of stepped wedge cluster randomized trials". *Contemporary Clinical Trials*, 45(Pt B):338.









Delay in treatment effect [S10]