

Design and Analysis of Stepped Wedge Cluster Randomized Trials

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Randomized Trial (RT)

- Randomize (independent) subjects to intervention arm
 - Q: Why bother?
- Criteria for assessing intervention
 - Safety
 - Efficacy
 - Effectiveness
- Q: What is a different type of RT?

Cluster Randomized Trial (CRT)

- Randomize (independent) clusters to intervention arm
 - Subjects within clusters are correlated
- Q: Why are CRTs useful?

Partner Notification

- Public health authorities contact sex partner
 - Of potential exposure to sexually transmitted infection (STI)
 - To seek treatment
 - Drawback: Implementation expensive
- Alternative: Patient Delivered Partner Therapy
 - Infected patient brings treatment to sex partner
 - Drugs or drug vouchers

Expedited Partner Therapy (EPT)

- Individually randomized trial [Golden et al., 2005]
 - 1998 to 2003 in King County, WA
 - Notification strategies (Intervention arms)
 - Patient delivered partner therapy, referred to as EPT
 - Standard partner notification (control)
 - **Goal:** To compare **effectiveness** of notification strategies for treating chlamydia and/or gonorrhea
 - **Primary outcome:** “presence of persistent or recurrent infection in the original index patient 3 – 19 weeks after treatment”
 - Study results
 - Significantly **increased proportion** of partners treated
 - **Decreased risk** of infection in patients
- **Q:** Successful trial, but are we done?

Limitation of EPT

- Q: What about all the other counties in WA state?
 - King county is **not representative** of every county in WA
- Goal for WA: To implement EPT in **every county**
 - Q: How?

Motivation for CRT

- Individually randomized trial completed
 - But only for **one** county (King)
- New trial
 - Counties represent **clusters**
 - **Q:** What kind of CRT should we use?

Possible CRT Designs

- Parallel
- Crossover
- Stepped wedge

<u>Parallel</u>		<u>Crossover</u>		<u>Stepped Wedge</u>					
Time		Time		Time					
	1		1 2		1	2	3	4	5
Cluster 1	1	Cluster 1	1 0	Cluster 1	0	1	1	1	1
Cluster 2	1	Cluster 2	1 0	Cluster 2	0	0	1	1	1
Cluster 3	0	Cluster 3	0 1	Cluster 3	0	0	0	1	1
Cluster 4	0	Cluster 4	0 1	Cluster 4	0	0	0	0	1

- Q: Which design is **best** from a **scientific** perspective?
- Q: Which design is **best** from a **statistical** perspective?

Comments on Designs

- Some argue that stepped wedge design is **only preferable to no randomized trial** [Kotz et al., 2012]
 - Takes longer
 - Stepped wedge **only** has higher power because more data than parallel
- Hussey and Hughes
 - Stepped wedge is **not** a design to **always** implement
 - But represents a **viable** option in **some** situations

Scientific Perspective

- Criteria for best design
 - Ethical
 - Logistical
 - Feasible

Statistical Perspective

- Criteria for **best** design
 - **Power**
 - Probability of rejecting null when alternative is true
 - **For stepped wedge**: Consider different effect sizes (i.e., number of clusters randomized at each time point)
 - **Coefficient of Variation (CV)**
 - **Ratio** of between-cluster standard deviation over mean prevalence
 - **Sample sizes within clusters**
 - Equal versus unequal

Analysis of CRT

- Population-level approach
 - Generalized Estimating Equations (GEE)
- Individual-level approaches
 - Linear Mixed Models (LMM)
 - Generalized Linear Mixed Models (GLMM)
- Some considerations
 - Known versus unknown variance components
 - Normal versus non-normal data

Summary

- Motivated CRTs
 - Expedited Partner Therapy individually randomized trial
 - Three designs: parallel, crossover, stepped wedge
 - After scientific consideration, we want to consider statistical aspects of the three designs
 - Power
 - CV (prevalence estimated from cross-sectional sampling)
- Next steps:
 - Work through the derivations/computation to assess CRTs
 - Focusing on Power calculations
 - Extension: Compare Power for parallel versus stepped wedge
 - More comparable sample sizes
 - Different time steps