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Required Sample Size for Difference-in-Differences Analysis: Implications for Comparative Effectiveness Research

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Data collection for CER

- Comparative effectiveness research (CER) involves comparison of ≥ 2 treatments (or treatment vs. usual care)

- Approach lends itself to difference-in-differences (DD) analysis

Question for CER study design:

- What is the minimum required sample size to conduct a CER-DD study with a desired level of accuracy?

Outline

1. Review DD framework

2. Introduce Accuracy in Parameter Estimation (AIPE) framework

3. Describe approach for merging DD & AIPE frameworks

4. Illustrate calculations with an example

Statistical model for CER

- Difference-in-differences (DD) framework

	Period		
Group	**Pre**	**Post**	**Difference**
Treatment	A	B	B-A
Comparison	C	D	D-C
			DD estimate = (D-C) – (B-A)

- With observational data, multiple regression model needed to control for confounding factors

$$Y_{it} = \beta_0 + \beta_1 TREAT_i + \beta_2 POST_t + \beta_3 TREAT_i \cdot POST_t + \gamma W_{it} + \varepsilon_{it}$$

- DD estimate controlling for (observable) confounders is β_3

Accuracy in parameter estimation (AIPE)

- Key question: How large should the sample be to obtain an **accurate estimate** of β_3 ?
- **Accuracy** ==> confidence interval (CI) is "sufficiently small"
- Accuracy in parameter estimation (AIPE)
  - AIPE formulas well-established for "ordinary" regression models
  - Set desired accuracy = Half-width of CI
  - Input: Key model parameters (Prior/preliminary studies, guesses)
  - Output: Required sample size
- **Goal of the study**: Develop *adjustments* to AIPE formulas to account for the typical structure of DD models used for CER

Simple/heuristic adjustments to AIPE formulas

1. Structure of DD variable
   - Can be modeled in advance (proportion in each group & period)
   - Anticipate variance & collinearity between DD var and covariates
2. Binary outcomes (e.g., survival, readmission)
   - Linear probability model
   - Robust standard errors

   } Anticipate "worst case scenario" for variance of outcome variable
3. Group effects (e.g., patients within hospitals)
   - Group and time level fixed effects
   - Cluster adjustment for group-time interactions
   - Variance inflation factor (VIF): $N_c = [1 + (m-1)\rho]*N$
4. Autocorrelation
   - Issue for long time series (e.g., years of monthly data)
   - VIF for AR(1) process: $N_a = [(1+\theta)/(1-\theta)]*N$

Test data

- New Jersey Health Initiatives Expecting Success: Excellence in Cardiac Care (NJHI-ES) program

- Effort to reduce readmissions for heart failure patients
  - 10 intervention hospitals
  - 80 comparison hospitals

  } M=90 hospitals (N=503,231 total observations)

- Intervention timing
  - Intervention: July 2007 – December 2009
  - Baseline: January 2002 – June 2007

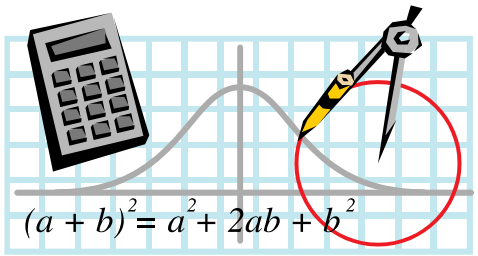
- Findings for likelihood of 90-day readmission

  Estimate for β_3 = -0.0585 with 95% CI: (-0.1124, -0.0047)

  Half-width = ± 0.0538

Calculations w/test data

- **Goal:** Use NJHI-ES data to determine required sample size for an evaluation of a similar future intervention
  - Impact of group effects/cluster adjustment
  - Impact of autocorrelation
- **Units of analysis:** Initial/index admission
  - Micro-units for required sample size (N)
- **Outcome variable:** 90-day readmission (yes/no)
- **Model:** Linear probability DD w/hospital-level group & monthly time effects



Required sample sizes to ensure that 95% CI for the DD parameter is within desired accuracy

Scenario 1: All observations are independent (i.e., no clustering & no autocorrelation)

Desired accuracy (Half-width for 95% CI)	Required total sample size (N)	N per hospital*
± 0.10	8,015	89
± 0.05	31,719	352
± 0.01	790,256	8,781

*Assuming M=90 hospitals available for the study.

Original NJHI-ES: Half-width = ± 0.05, N=503,231

Required sample sizes to ensure that 95% CI for the DD parameter is within desired accuracy

Scenario 2: Intraclass correlation coefficient ρ=0.01

Desired accuracy (Half-width for 95% CI)	Required total sample size (N) w/no cluster effect	Required total sample size (N) if M=90 hospitals	Required total sample size (N) if M=1,000 hospitals
± 0.10	8,015	72,501	8,626
± 0.05	31,719	∞	45,989
± 0.01	790,256	∞	∞

Required sample sizes to ensure that 95% CI for the DD parameter is within desired accuracy

Scenario 3: Autocorrelation for given AR(1) parameter θ

Desired accuracy (Half-width for 95% CI)	Required total sample size (N) w/no autocorr	Required total sample size (N) if θ=0.1	Required total sample size (N) if θ=0.5
± 0.10	8,015	9,796	24,045
± 0.05	31,719	38,768	95,157
± 0.01	790,256	965,868	2,370,768

Discussion

- Sample size formulas fairly straightforward
  - Input values: Study design, preliminary data, & scenarios
- Correlation of observations can have large effects on sample size requirements (clustering + autocorrelation together)
- Formulas based on several assumptions
  - Input parameters are known (not estimated)
  - "Intuitive" formulas (conservative assumptions)
  - Linear probability model
  - Treatment exogeneity (i.e., no unobserved selection bias)
- Our formulas may provide significant improvement over more simplified sample size formulas often used in study planning

QUESTIONS?

Questions later: ddelia@ifh.rutgers.edu