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

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Academy Health Annual Research Meeting
Orlando, FL
Monday June 25, 2012
Acknowledgement

This research was supported by the Agency for Health Care Research & Quality (Grant no. R24-HS019678)
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

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre</th>
<th>Post</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>A</td>
<td>B</td>
<td>B-A</td>
</tr>
<tr>
<td>Comparison</td>
<td>C</td>
<td>D</td>
<td>D-C</td>
</tr>
</tbody>
</table>

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 $\beta_3$
Accuracy in parameter estimation (AIPE)

- **Key question**: How large should the sample be to obtain an **accurate estimate** of $\beta_3$?

- **Accuracy** $\implies$ 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): $N_c = [1 + (m-1)p]N$

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

• Intervention timing
  – **Intervention**: July 2007 – December 2009

• Findings for likelihood of 90-day readmission
  Estimate for $\beta_3 = -0.0585$ 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)

<table>
<thead>
<tr>
<th>Desired accuracy (Half-width for 95% CI)</th>
<th>Required total sample size (N)</th>
<th>N per hospital*</th>
</tr>
</thead>
<tbody>
<tr>
<td>± 0.10</td>
<td>8,015</td>
<td>89</td>
</tr>
<tr>
<td>± 0.05</td>
<td>31,719</td>
<td>352</td>
</tr>
<tr>
<td>± 0.01</td>
<td>790,256</td>
<td>8,781</td>
</tr>
</tbody>
</table>

*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 $\rho=0.01$

<table>
<thead>
<tr>
<th>Desired accuracy (Half-width for 95% CI)</th>
<th>Required total sample size (N) w/no cluster effect</th>
<th>Required total sample size (N) if M=90 hospitals</th>
<th>Required total sample size (N) if M=1,000 hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>± 0.10</td>
<td>8,015</td>
<td>72,501</td>
<td>8,626</td>
</tr>
<tr>
<td>± 0.05</td>
<td>31,719</td>
<td>$\infty$</td>
<td>45,989</td>
</tr>
<tr>
<td>± 0.01</td>
<td>790,256</td>
<td>$\infty$</td>
<td>$\infty$</td>
</tr>
</tbody>
</table>
Required sample sizes to ensure that 95% CI for the DD parameter is within desired accuracy

Scenario 3: Autocorrelation for given AR(1) parameter $\theta$

<table>
<thead>
<tr>
<th>Desired accuracy (Half-width for 95% CI)</th>
<th>Required total sample size (N) w/no autocorr</th>
<th>Required total sample size (N) if $\theta=0.1$</th>
<th>Required total sample size (N) if $\theta=0.5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>± 0.10</td>
<td>8,015</td>
<td>9,796</td>
<td>24,045</td>
</tr>
<tr>
<td>± 0.05</td>
<td>31,719</td>
<td>38,768</td>
<td>95,157</td>
</tr>
<tr>
<td>± 0.01</td>
<td>790,256</td>
<td>965,868</td>
<td>2,370,768</td>
</tr>
</tbody>
</table>
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