Quasi-experimental designs with application to small populations

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Acknowledgements/Disclosure

The LASSY study “Longitudinal Assessment of SSRI Warnings and Suicidality Among Youth”

- Investigators of 11 sites of the Mental Health Research Network, Health Care Systems Research Network
- DPM study team: Chris Lu, Steve Soumerai (study PI), Jeanne Madden, Martin Kuldorff, Darren Toh, Matt Lakoma
- Funding: NIMH

Other funding: NHGRI, NIDDK, NCI, PCORI, CDC, FDA, Harvard Pilgrim Health Care Institute
Overview of presentation

- Quasi-experimental designs
  - Overview
  - Example 1, Effects of FDA regulatory actions
  - Example 2, Effects of prior authorization
- Strengths and challenges of using quasi-experimental designs to examine effects of policies/interventions
Impacts of health policies, programs, interventions

- Health policies: eg FDA drug warnings, cost-containment policies
- May have intended and unintended consequences
  - Desirable or undesirable
  - Anticipated or unanticipated
  - Direct or indirect
  - Obvious or latent
Interrupted Time Series

$X =$ Intervention (e.g., a policy) \hspace{1cm} O_t =$ Measurement at time $t$
Pre-post with Comparison Group

Intervention Group

Comparison Group

\[ X = \text{Intervention (e.g., a policy)} \quad O_t = \text{Measurement at time } t \]
Other designs

- Pre-post only
  - Intervention Group
  - Time: \( O_1 \times O_2 \)

- Post-only
  - Intervention Group
  - Time: \( X \times O_1 \)

- Post-only with comparison group
  - Intervention Group
  - Comparison Group
  - Time: \( X \times O_1 \)
## Hierarchy of study designs

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Interrupted Time Series

□ When to use ITS
  ▪ Sharply-defined intervention date
  ▪ Outcomes available over time

□ Basic Design
  ▪ Compare longitudinal trends before & after the intervention

□ Major assumption
  ▪ Baseline trend reflects what would have happened without intervention
ITS Logic and Parameters Estimated by Segmented Linear Regression

Assumption: Baseline trend correctly reflects what would have happened without intervention

Adapted from Schneeweiss et al, Health Policy 2001
Pre-post with comparison group

- **Region 1 (Intervention group)**
- **Region 2 (Comparison group)**

The graph shows a comparison between Region 1 (Intervention group) and Region 2 (Comparison group) over the years 2010 and 2011. The y-axis represents the percentage of members, ranging from 0% to 100%. The intervention is indicated by the vertical dashed line.
Pre-post with comparison group
Example: FDA antidepressant warnings

- Aim: To evaluate impact of FDA’s safety warnings* & media attention on rates of
  - Antidepressant dispensings
  - Suicide attempts
  - Completed suicides

- A longitudinal, multi-site study (2000 to 2010)
- Data source: Health administrative & claims data

*The FDA released several public health advisories before the BBW in October 2004

Data Networks

Avoid limitations of multi-site research

- Pulling together data elements needed from each site on a project by project basis is time-consuming & expensive
- Each system has its own data specs
- Data sharing might be a concern

Data networks (& analytical toolbox) exist

- Data networks take time & money to develop
- HCSRN VDW: ~15 million individuals
- Sentinel: ~223 million individuals
- PCORnet: ~10 million individuals
Harmonized multiple databases

Time & money to develop

Adapted from: http://www.hcsrn.org/asset/b9efb268-eb86-400e-8c74-2d42ac57fa4F/VDW.Infographic031511.jpg
Children / Adolescents

Relative change:
-31% (-33, -29)

FDA's warnings & media coverage

22% (5, 38)

Antidepressant dispensings

Suicide attempts by poisoning

Example: Prior Authorization Policies

- A natural experiment: MaineCare
  - July 2003: PA for non-preferred second generation antipsychotics & anticonvulsants
  - New Hampshire: comparison group
- Bipolar disorder: disabling & costly illness
- Medications are effective for managing bipolar
- Variations in response to drug treatment
- Rx discontinuation & health status could affect health services use

Lu et al. Med Care 2010; 48(1):4-9
Lu et al. Psych Serv 2011; 62(2):186-193
Impact on Drug Initiation

FIGURE 1. Proportion of patients initiating on bipolar medications (including antipsychotics, anticonvulsants and lithium) in the prepolicy (July 2002 to April 2003) and policy (August 2003 to February 2004) periods. Note: Interrupted time series models did not include points in the phase-in period (May 2003 to July 2003).

Lu et al. Med Care 2010; 48(1):4-9
Impact on Drug Discontinuation

aHR=2.28 (1.15-4.52), controlling for the relative hazard ratios between pre-policy & policy cohorts in the comparison state.

Zhang et al. Psych Serv 2009
Sicker and less sick patients

Sicker patients:
\[ \text{aHR} = 1.73 \ (1.04-2.88) \]

Less sick patients:
\[ \text{aHR} = 1.30 \ (1.05-1.61) \]

Lu et al. Psych Serv 2011; 62(2):186-193
ITS: Strengths

- Sharply-defined intervention
- Controls common threats to internal validity
- Direct estimate of effects
- Intuitive visual display
- Easy to communicate results than other methods e.g., propensity score matching, instrumental variables
ITS: Challenges

- Requires reasonably stable data
- Linear trend might not be realistic
- Stronger if 8+ points per segment
- Sensitive to points near end of segment
- May not work well with rare outcomes (e.g., death)

- Co-interventions
  - Widespread media coverage
  - Impact of media coverage cannot be separated

- Changes in instrumentation
Take-home Messages

- Evaluating impacts of policies or intervention is important
  - Choose data sources
  - Use strong study designs
  - Measure intended vs. unintended consequences
  - Measure short-term vs. long-term outcomes

- Leverage existing data networks if possible
  - Self-reported race/ethnicity
  - Zip code to define rurality
  - Other demographic or clinical information available
Thank you!

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Threats to Internal Validity

- **Selection:** Pre-intervention differences between study and control groups
- **History:** An event occurring between pre- and post-intervention when the event is not the intervention of interest
- **Maturation:** Subjects growing older, healthier, sicker etc. between pre and post-intervention
- **Instrumentation:** A change in the measuring instrument