Quasi-experimental designs with application to small populations

Christine Lu, MSc, PhD

Department of Population Medicine

Harvard Pilgrim Health Care Institute

Harvard Medical School

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

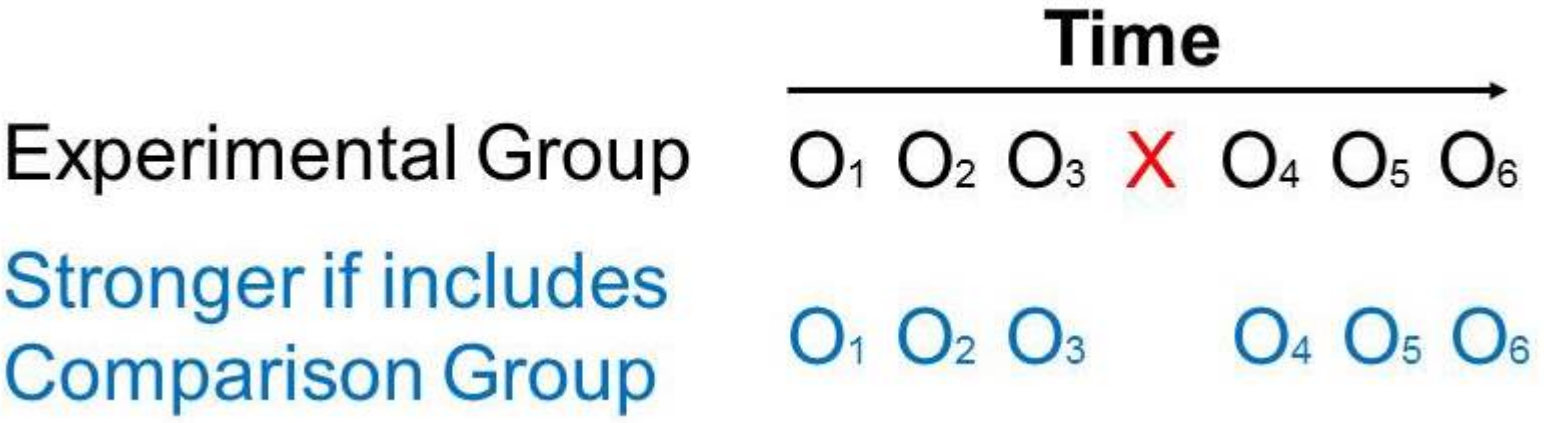
Overview of presentation

- 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) O_t=Measurement at time t

Pre-post with Comparison Group

X=Intervention (e.g., a policy) O_t=Measurement at time t

Other designs

Pre-post only

Intervention Group

Time →

O_1 X O_2

Post-only

Intervention Group

Time →

X O_1

Post-only with comparison group

Time →

Intervention Group X O_1

Comparison Group O_1

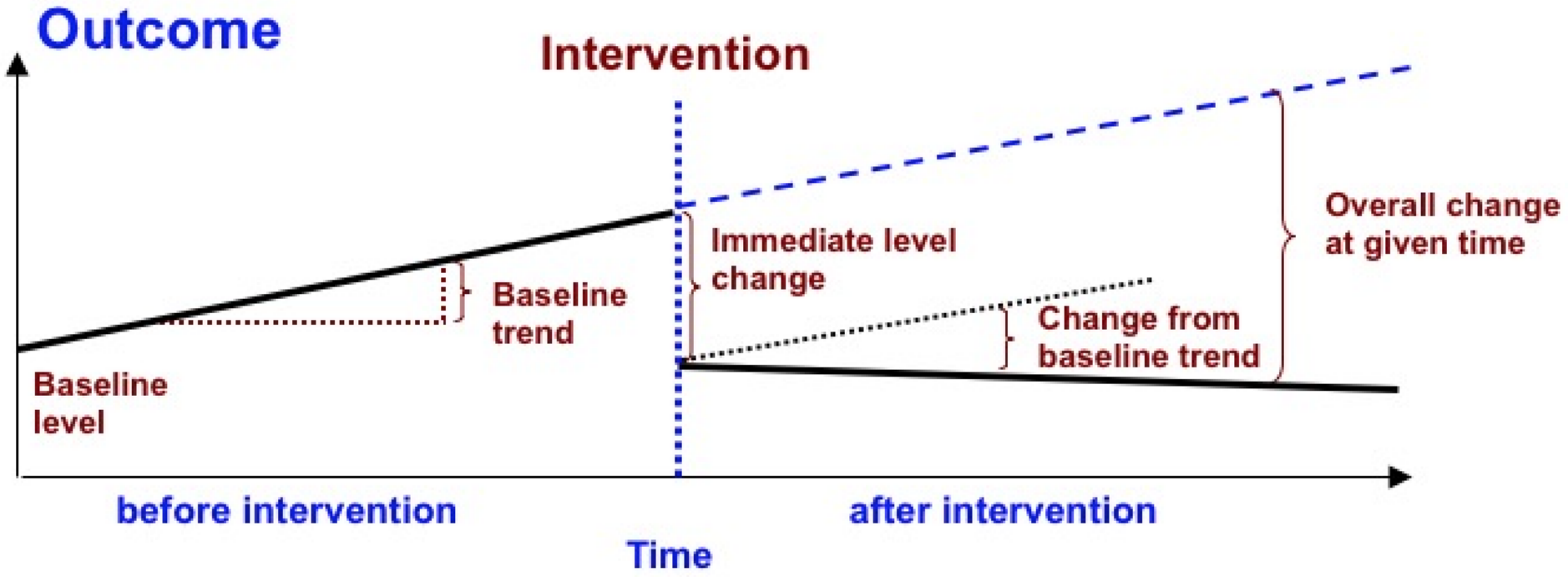
Hierarchy of study designs

Strong designs
Randomized Controlled Trials
Interrupted time series with comparison series
Intermediate designs
Single interrupted time series
Pre-post with comparison group
Weak designs
Pre-post only
Post-only
Post-only with comparison group

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

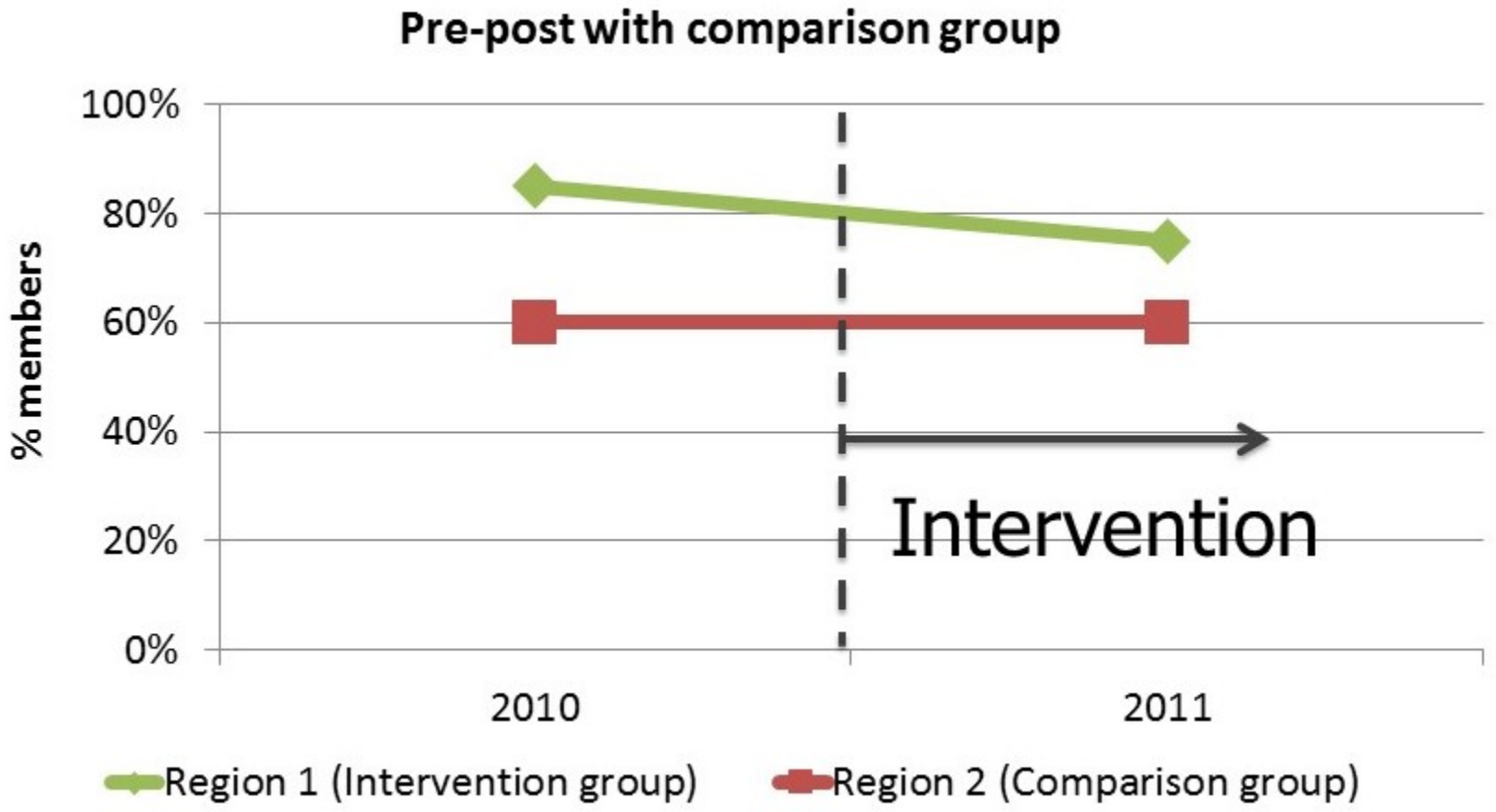
ITS Logic and Parameters Estimated by Segmented Linear Regression



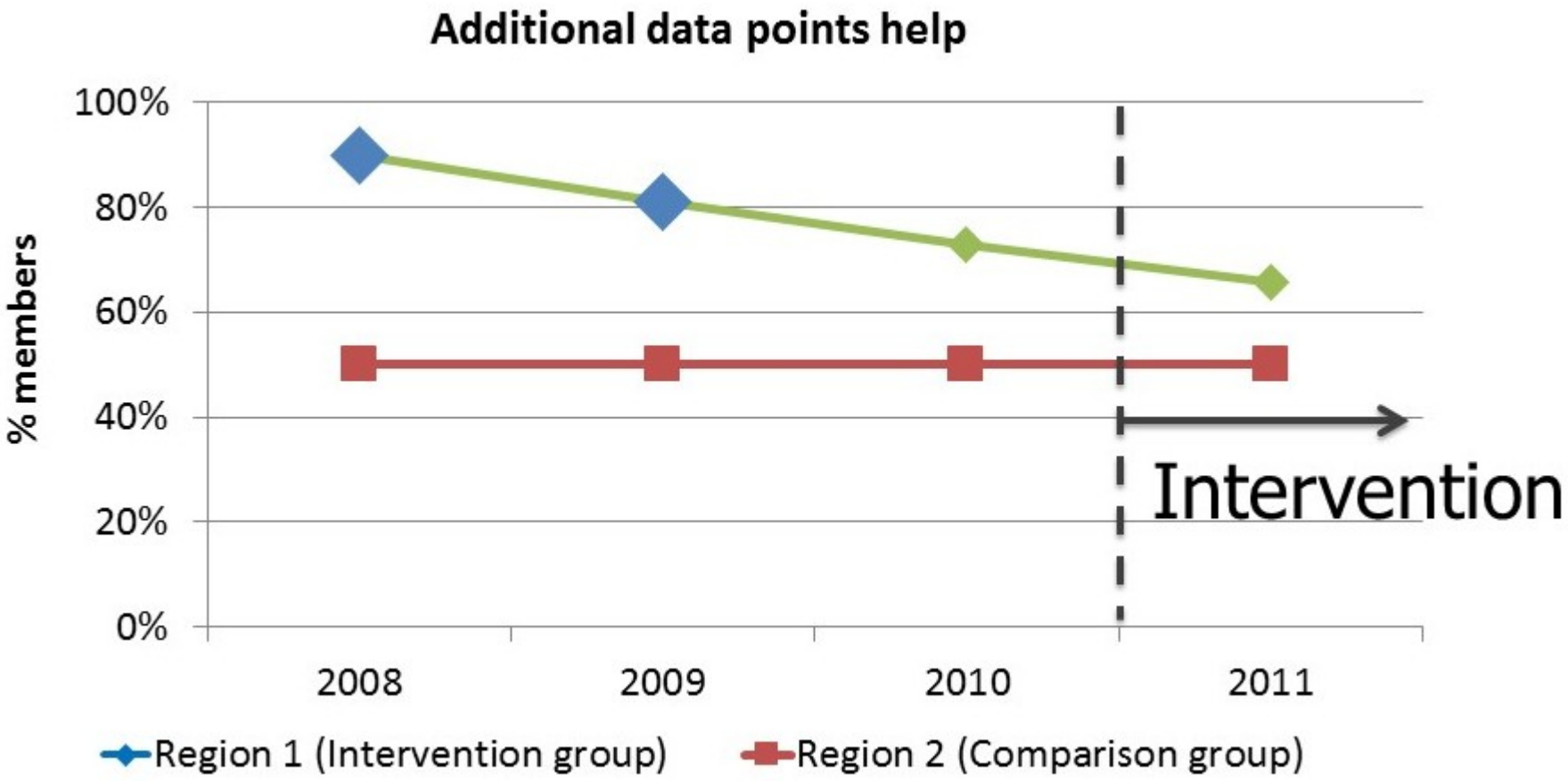
Assumption: Baseline trend correctly reflects what would have happened without intervention

Adapted from Schneeweiss et al, Health Policy 2001

Pre-post with comparison group



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

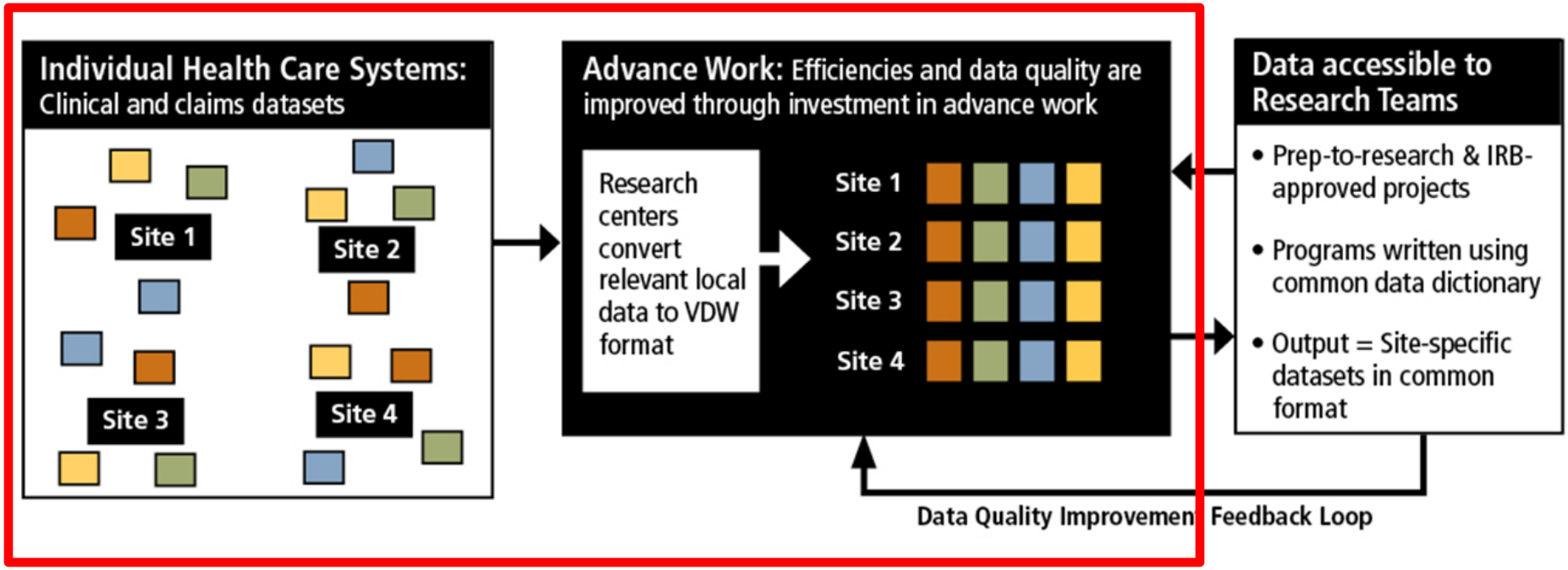
*The FDA released several public health advisories before the BBW in October 2004

Lu CY, et al. BMJ 2014

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

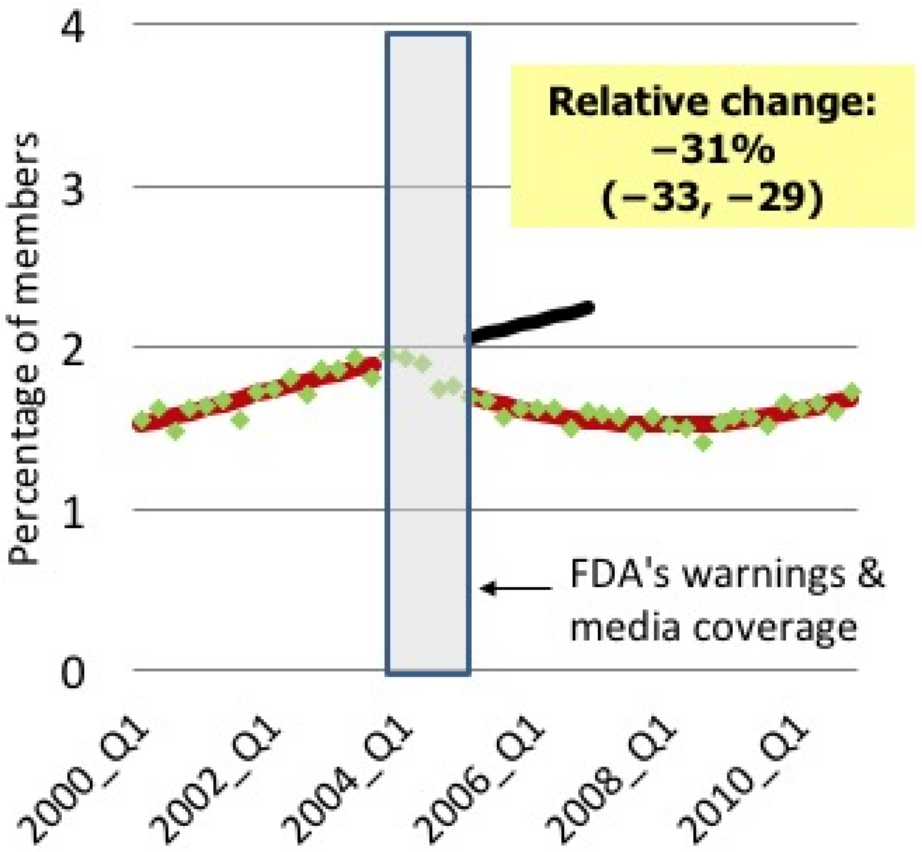
Harmonized multiple databases

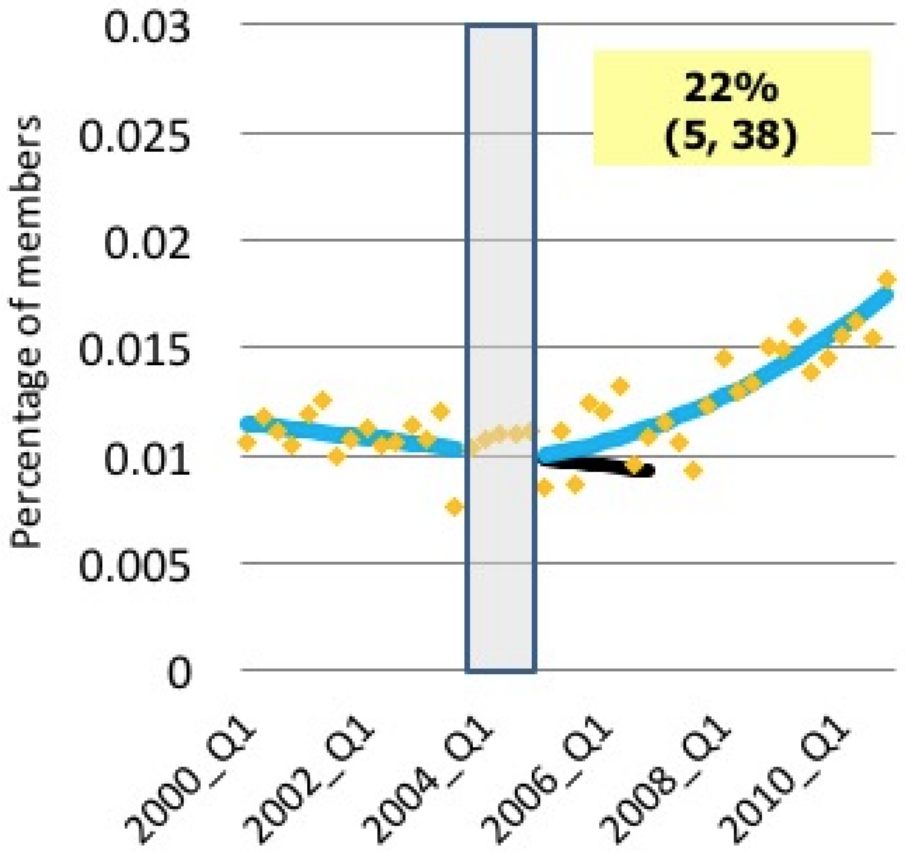


Time & money to develop

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

Children / Adolescents





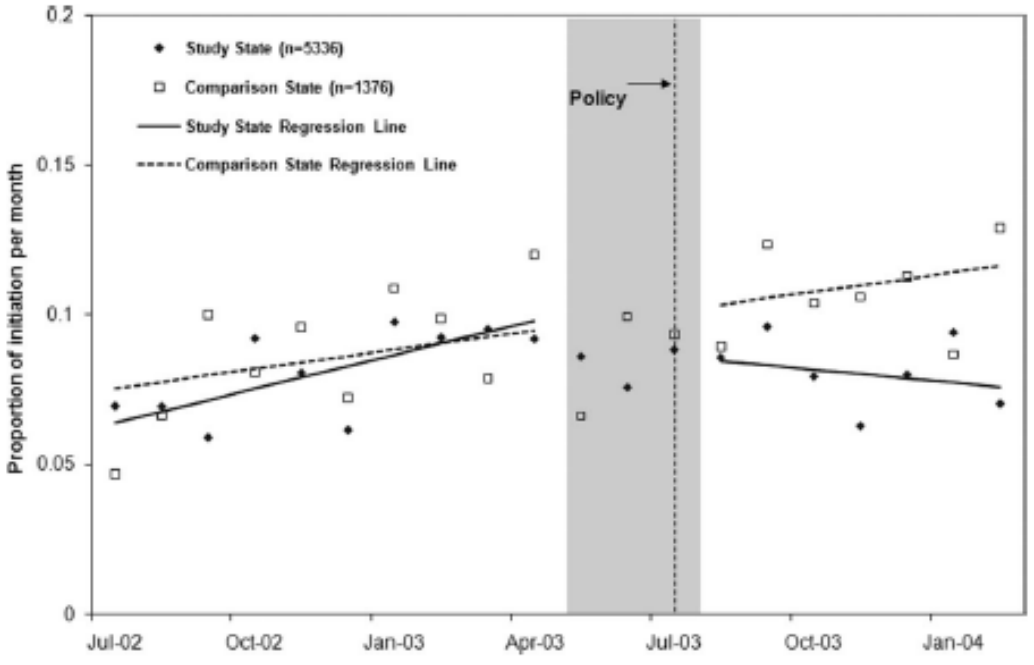
Lu CY, et al. BMJ 2014

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

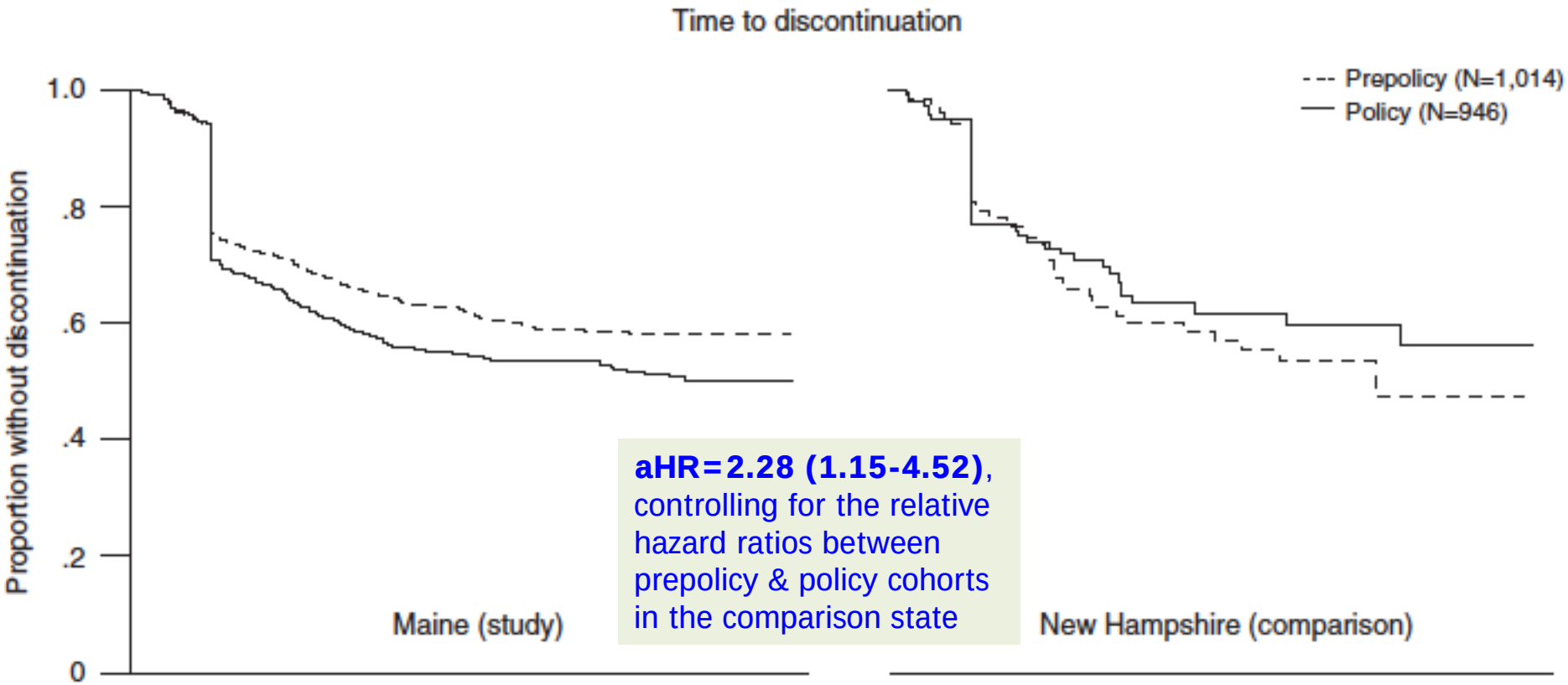


ITS with comparison series

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).

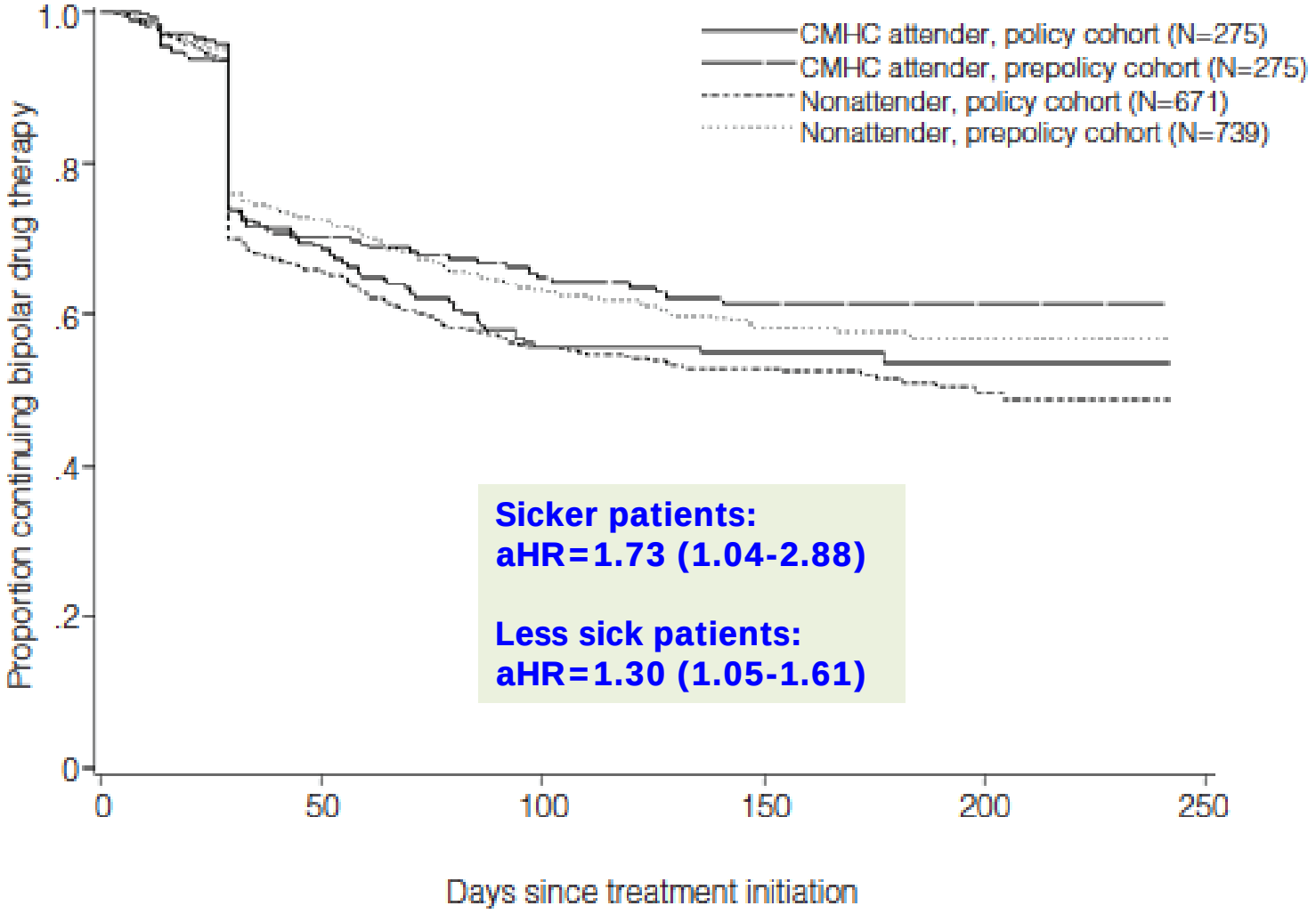
Lu et al. Med Care 2010; 48(1):4-9

Impact on Drug Discontinuation



Zhang et al. Psych Serv 2009

Sicker and less sick patients



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 (eg 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!

Chris Lu

Christine_lu@harvardpilgrim.org

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