Diabetes and pre-diabetes affect a substantial proportion of US adults. Stakeholders such as public health officials, governments, health systems, and health insurers often enact policies and interventions aimed at preventing or improving diabetes. In recent years, health care reform at the national and state levels has created changes affecting individuals with diabetes. These changes are often “natural experiments” that can provide valuable information about improving diabetes outcomes if studied rigorously. This talk will define natural experiments and quasi-experiments, discuss how to find natural experiments created by health reform, review challenges when studying large health system data, and suggest best practices for analyzing health reform natural experiments.
Analyzing Health Reform Natural Experiments that Affect People with Diabetes

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Outline

I. What are natural experiments and quasi-experiments?
II. Finding natural experiments that affect people with diabetes
III. Practical issues and challenges when using large health system data to study natural experiments
IV. Recommendations for analyzing health reform natural experiments
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Natural Experiments

• Definition:
  • Occur when individuals are exposed to experimental and control conditions by factors outside control of investigators, and typically without overt randomization
• Some also distinguish “quasi-experiments:”
  • Investigators have some control over assigning intervention group, but assignment is not randomized
Classifying Experimental Type

Degree of investigator control over "intervention" assignment

- Assigned by investigators
  - Intervention is randomized
    - Randomized controlled experiment
  - Intervention is exogenous
    - Strong quasi-experiment
- Occurred naturally or not influenced by investigators
  - Intervention is exogenous
    - Strong natural experiment
  - Intervention is endogenous (self-selected)
    - Weak observational study

Natural Experiment

Outcome Unit vs. Month:

-11 -8 -5 -2 1 4 7 10 13 16 19 22 25 28 31 34

Outcome Unit:

0 1 2 3 4
Natural Experiment

Before intervention

Intervention
Natural Experiment

Before intervention

干预前

干预组

Control Group

Control组

After intervention

干预后

Month

干预

Outcome Unit

Outcomes

干预的实施
Key Features of Natural Experiments

• Manner in which “intervention” carried out allows inference about whether intervention caused an outcome (i.e., “causal inference”)
• External validity (generalizability) typically better than RCTs, but internal validity typically worse
• Researchers can use a variety of study designs to study effects of intervention on outcome measures
  • Cross-sectional
  • Pre-post with comparison group
  • Interrupted time series with control series

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Finding Natural Experiments that Affect People with Diabetes

**Preliminary questions to ask:**
- What are the hypothesized intended and unintended effects of a population-level intervention?
- Do those effects change mediators of diabetes health outcomes?

![Example Conceptual Model](image)

- Medicaid Expansion
- Access to antiglycemic drugs
- Use of antiglycemic drugs
- Acute complications
Natural EXperiments for Translation in Diabetes (NEXT-D & NEXT-D2)


Example Health Reform Natural Experiments that Might Affect Diabetes

• Medicare Modernization Act of 2003:
  • Incentivized high-deductible plans among employers

• Affordable Care Act of 2010:
  • Some states expanded Medicaid eligibility
  • Allowed states to establish Medicaid Health Homes for chronically ill patients

• Centers for Medicare & Medicaid Services:
  • Offered $0 coverage for intensive behavioral therapy for obesity in 2012
  • Introduced billing code for non-face-to-face chronic care management services in 2015

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My Evolution in Using Large Health System Data

2004

My Evolution in Using Large Health System Data: Overview

2004  →  2018
Data storage and processing

Programming flow & coordination
Data storage and processing
Key Approaches to Taming Large Health System (Claims) Data

• Get your hands dirty in the data
• Create calendar trends of all numerator and denominator counts
• Use contemporaneous control groups
• Beware of co-interventions and selection
The Importance of Calendar Trends

\[\text{Mental Health Assessment Rates}\]

\[\text{Count of Specific Mental Health Codes}\]

Count

Calendar Month
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Broad Recommendations for Analyzing Health Care Reform

1. Consider conceptual model carefully
2. Maximize internal validity (causal inference)
3. Present results in an intuitive manner
4. Consider alternate approaches for rare / unstable measures
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Change of Approach after Considering Conceptual Model

Interrupted Time Series / Segmented Regression

Time-to-event / Cox Proportional Hazards Regression

Wharam et al. JAMA-IM. 2017. *p<0.05
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Recommendations for Optimizing and Testing Internal Validity

A. Study strong quasi-experiments or natural experiments
B. Aim high on the hierarchy of study design
C. Match to enhance comparability of the intervention and control groups
D. Develop supporting evidence
A. Study strong quasi-experiments or natural experiments

Degree of investigator control over "intervention" assignment

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B. Aim high on the hierarchy of design

Assuming exogenous intervention

- Cross-sectional designs
- Before-after without control group (pre-post)
- Before-after with control group
- Interrupted time series (ITS) without control group
- ITS with control group (+/- matched)
- Randomized controlled trials
- Multiple randomized controlled trials
Interrupted Time Series with Control Series Study Design

C. Match to enhance comparability of the intervention and control groups

• (Only applicable if subjects continuously in denominator during both baseline and follow-up)
• Use clinical/researcher intuition regarding matching variables
  • What variables would I include in a block randomized trial?
• Approach: we have transitioned to using coarsened exact matching
• Ideal if matching on baseline characteristics leads to similar pre-intervention trends in outcomes
  • If different or unclear, consider matching on baseline trend of the outcome measure
Within-study Comparison Design

![Diagram showing Comparison Design with POPULATION, Randomized Experiment, and Natural Experiment branches.]

Gold Standard Effect Estimate

Estimated Treatment Effect

Bias Reduction: Matching on Covariates +/- Baseline Outcomes

![Graph showing RCT result with different covariates levels: No covariates, All covariates minus pretest, One pretest covariate, Two or more pretest covariates, and All covariates.]

D. Develop supporting evidence

- Examine unaffected outcome measures or less affected subpopulations
- Falsification tests (e.g., move index date back 1 year)
- Other context-specific approaches, E-value, etc
Acute Diabetes Complication Visits to Emergency Department

Wharam et al. JAMA-IM. 2017. *p<0.05

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Interrupted Time Series with Control Series Study Design

Relative annual change in HDHP group: $-5.5\%^*$ $-7.1\%^*$

Wharam et al. JAMA-IM. 2017. *p<0.05

Strengthening Presentation Approaches


Interrupted-time-series plot
Broad Recommendations for Analyzing Health Care Reform

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Alternate Approaches for Rare / Unstable Measures

• If interrupted time series unstable, consider using cumulative interrupted time series display or time-to-event designs
• Match on baseline characteristics including baseline trend of the outcome measure
  • But careful not to create regression to the mean
• Use coarsened exact matching rather than propensity score matching
Delayed Major Macrovascular Disease Care in Diabetes

Follow-up delay

- Major Symptom or Sign: 1.5 months*
- Major Diagnostic Test: 1.9 months*
- Major Treatment: 3.1 months*

Wharam et al. In press. 2018. *p<0.05

Summary

- Health reform natural experiments: opportunity to rigorously assess effects of major policies on important diabetes outcomes
- Studying natural experiments with big data creates substantial, but surmountable, challenges
- Recommendations for studying natural experiments:
  - Study changes that are exogenous to diabetes patients
  - Consider coarsened exact match, including on baseline trend
  - Use interrupted time series design/display of data
  - Present intuitive plots and effect estimates
  - Consider alternate approaches for rare outcomes
Thank you!

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