Study designs and statistical methods for current observational studies

7. Feb. 2024

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Health Transition

1900 1920 1940 1960 1980 2000 2020

Disease Structure

Acute Infection

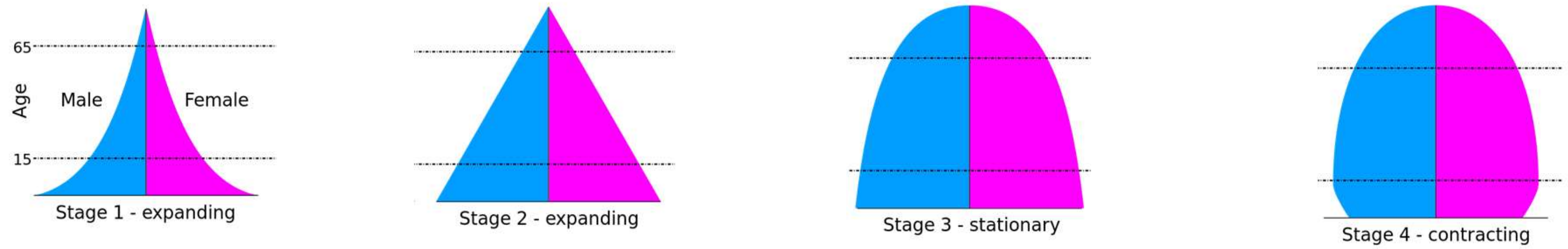
Chronic Infection

Cancer/Stroke/Cardiovascular

Social /Environment

Population Structure

High infant mortality → Increased workforce → Low birthrate and aging



Industrial Structure

Primary → Secondary → Tertiary → IoT/AI

Healthcare Structure

Quantitative expansion → Technological innovation → Quality and quantity optimization

Current features of observational research

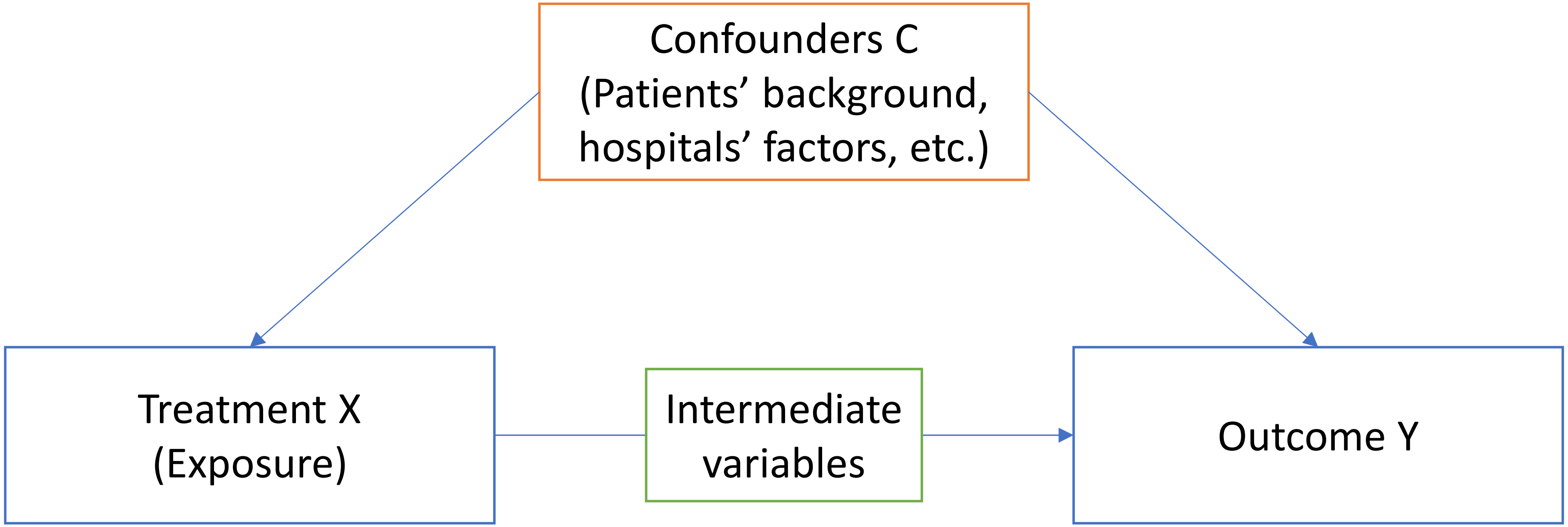
- Observational data

(i.e., administrative data, claims data, and GPS data)

- Improved PC computing power

- Development of research questions that we need to consider many confounders and unmeasured confounders

Confounding



- Confounders associate with the outcome and treatment. They are not intermediate variables between treatment and outcome.
- We often use the <u>adjustment, stratification, matching, and weighting</u> to deal with confounders.

Issues on the regression analysis

- If there are many confounders and unobserved confounders, the following issues would occur.

  - Misconfiguration of the model

  - If too many variables need to be included in a model relative to the number of events, the estimates from these models can be incorrect.

Am J Epidemiol 2003; 158. 280-7

Study designs and statistical analysis in current observational studies

1. Difference-in-Differences
2. Instrumental Variable Analysis
3. Regression Discontinuity

} Natural experimental methods (Quasi-experimental methods)

4. Panel Data Analysis / Interrupted Time-Series

5. Propensity Score Analysis (matching, weighting, stratification, and adjustment using propensity scores)
6. Adjustment(regression), weighting, stratification, and matching

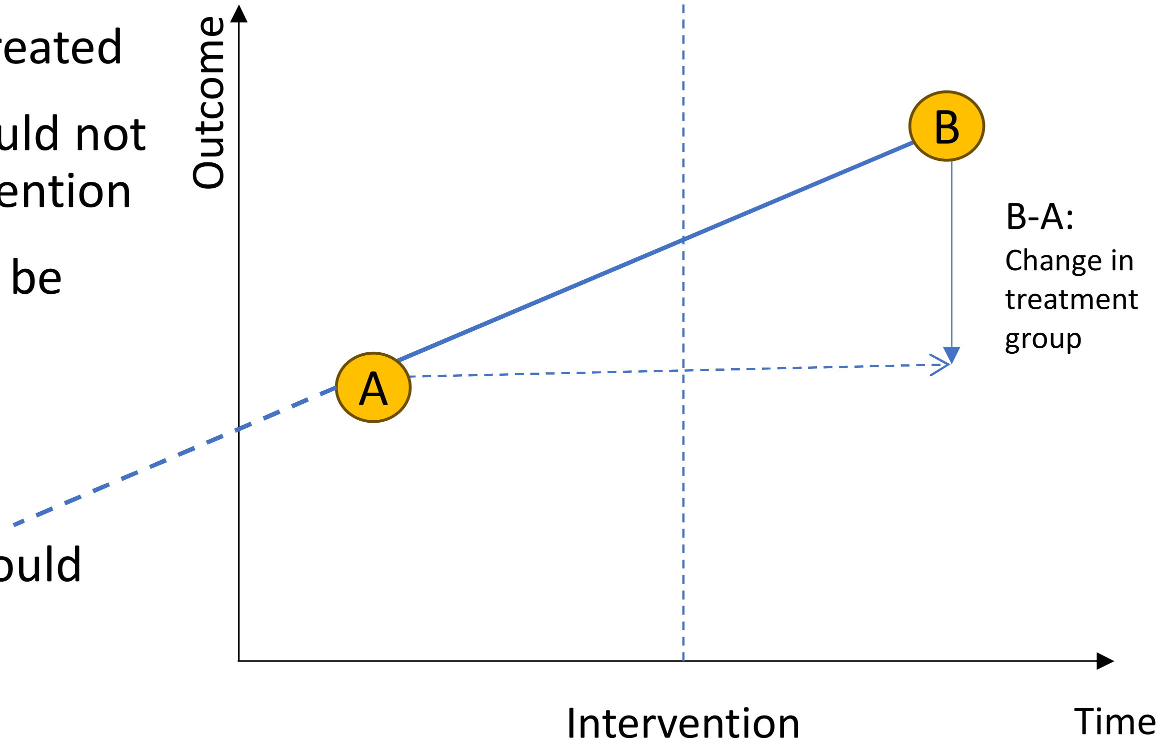
Difference-in-Differences Analysis

Reference:

Dimick, J. B. and A. M. Ryan (2014). Methods for evaluating changes in health care policy: the difference-in-differences approach. JAMA 312(22): 2401-2402.

Pre-post comparison

- Only one group: everyone gets treated
- Counterfactual: the outcome would not have changed without the intervention
- Assumption: the outcome would be constant before and after the intervention



- "Simple differences" over time could represent:
  - Actual interventional effect
  - Other factors that may have affected the group over time
  - Mix of both

➔Absolute changes are weak evidence for causal effects

	Treatment
Before	A
After	B
Change	B-A

Difference-in-Differences design

Key assumptions

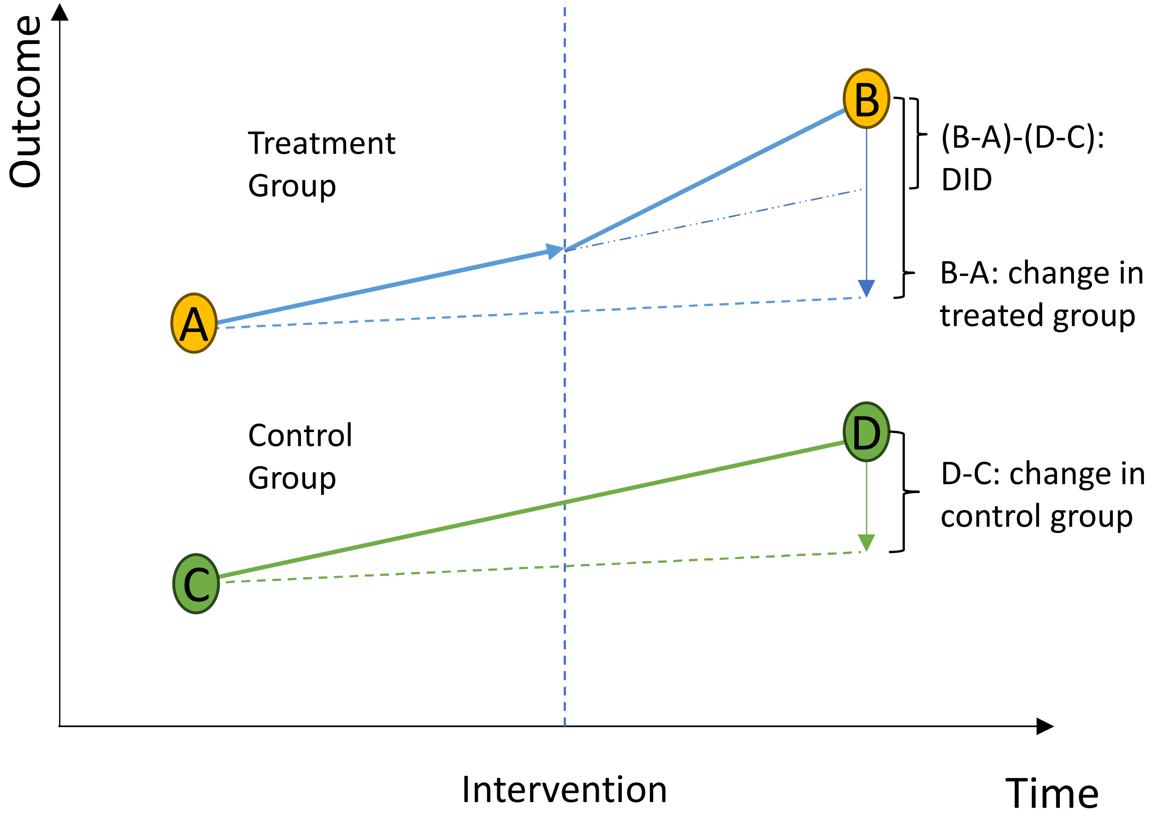
1. <u>Parallel trends assumption</u>

If there is no intervention, the outcomes of the treatment and control group would be a parallel trend.

Demonstrate that the outcomes of the treatment and control groups are parallel at several time points before the intervention.

2. <u>Common shocks assumption</u>

There are no other exogenous events occurring that affect pre- and post-intervention outcomes, or if they occur, they affect the two groups in the same way.



DID

= (change in treatment) – (change in control)

= ($\text{Treat}^{\text{After}}$ - $\text{Treat}^{\text{Before}}$) – ($\text{Control}^{\text{After}}$ - $\text{Control}^{\text{Before}}$)

	Treatment	**Control**
Before	A	C
After	B	D
Change	B-A	D-C
DID	(B-A) – (D-C)	

DID example

Did the first COVID-19 policy announced by the Japanese government affect asthma patients?

Intervention: COVID-19 policy (Week 9)

Treatment: 2020

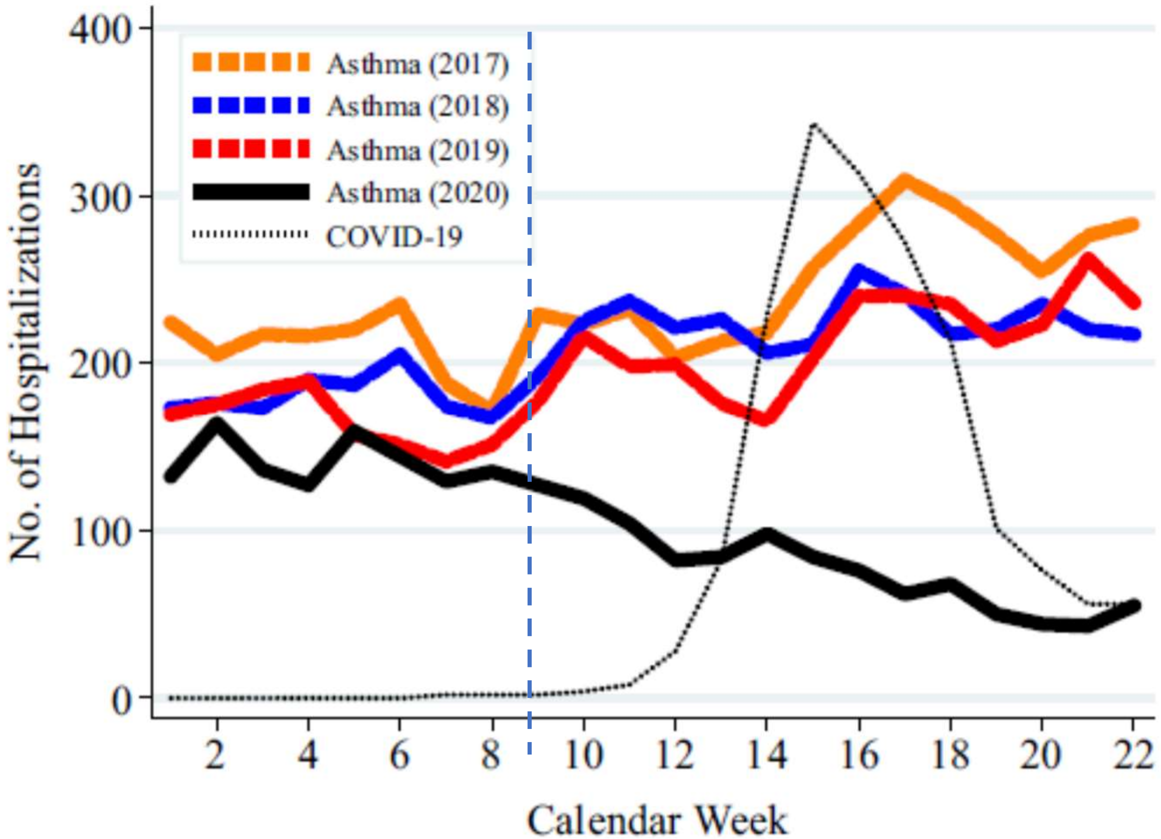
Control: 2017-2019

DID

=(78.3-140.8)-(229.9-184.9)

= -107.5 per week

FIGURE 1. Trends in hospitalizations for asthma and COVID-19 for Japanese acute-care hospitals, 2017 through 2020.



Average number of hospitalizations per week					
2017-2019			2020		
Weeks 1-8	Weeks 9-22	Ratio (difference)	Weeks 1-8	Weeks 9-22	Ratio (difference)
184.9	229.9	1.24 (45.0)	140.8	78.3	0.56 (−62.5)

Abe K, Miyawaki A, Nakamura M, Ninomiya H, Kobayahi Y. Trends in Hospitalizations for Asthma During the COVID-19 Outbreak in Japan. The Journal of Allergy and Clinical Immunology: In Practice. 2020;9(1):494-6.e1.

To be continued