Adjustment Criteria for Generalizing Experimental Findings

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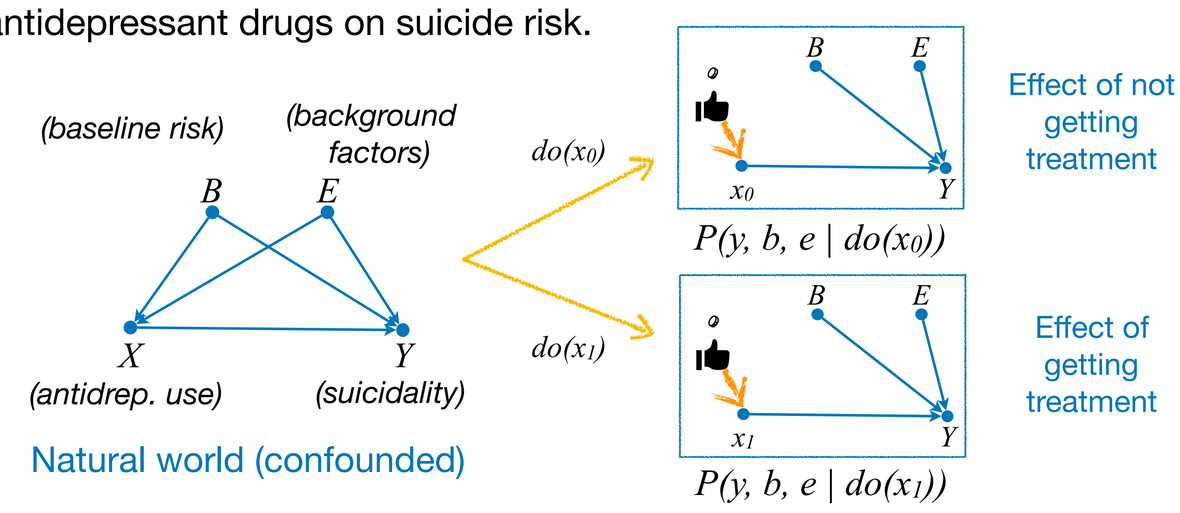
1 Introduction

Proper experimentation guarantees internal validity, that is, causal conclusions obtained from it hold true for the domain from where the sample was drawn.

However, most experimental findings are intended to be generalized to a broader, or even different, target domain (in other words, population, setting, or environment).

2 Motivating Example [Greenhouse et al. 2008]

- The FDA performed randomized controlled trials to assess the effect of antidepressant drugs on suicide risk.



Natural world (confounded)

- RCTs suggested that youths receiving antidepressants had approximately twice the amount of suicidal thoughts and behaviors compared to the control groups.

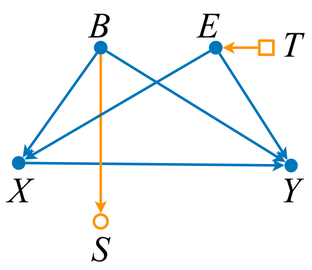
$$P(Y=1\,|\,do(x_1)) > P(Y=1\,|\,do(x_0))$$

- Results led to the addition of a strict warning to the drug's label.
- Surprisingly, following the warning, a decrease in prescriptions was reported together with an increase of suicidal events in the corresponding age group.

$$P^*(Y=1\,|\,do(x_1)) < P^*(Y=1\,|\,do(x_0))$$

- Several observational studies reported positive results for patients using the same antidepressants, even after accounting for access to mental health-care and other confounding factors.

$$\tilde{P}^*(Y=1\,|\,do(x_1)) < \tilde{P}^*(Y=1\,|\,do(x_0))$$



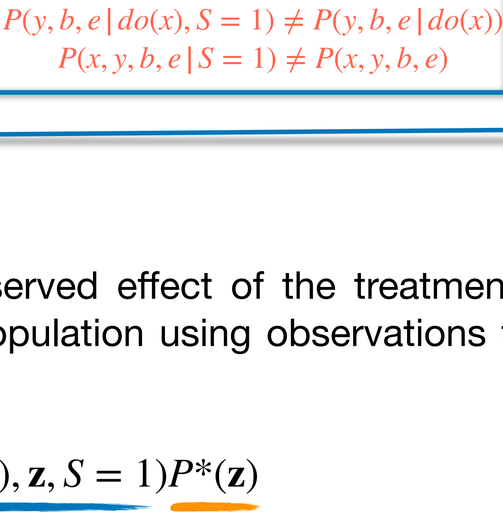
(Selection Diagram D)

$$\underbrace{P^*(y\,|\,do(x))}_{\text{causal effect in target domain}} = \sum_{b,e} \underbrace{P(y\,|\,do(x),b,e,S=1)}_{\text{experimental data from the source under selection bias}} \underbrace{P^*(b,e)}_{\text{measurements from the target domain}}$$

3 Challenges

1. Transportability

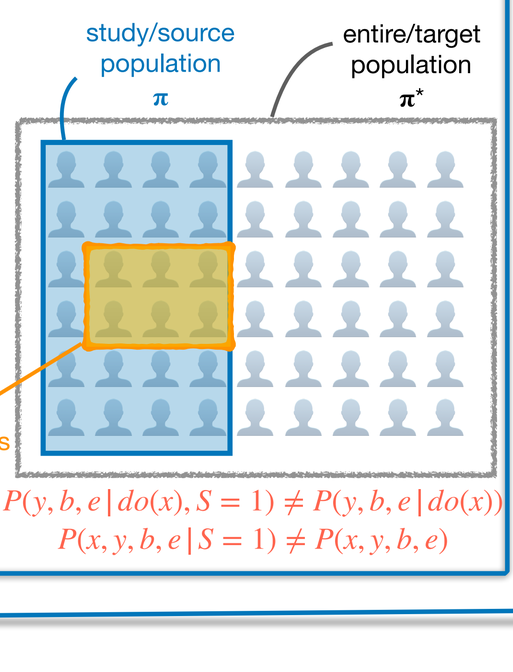
There is a mismatch between the study population $\boldsymbol{\pi}$ and the general clinical population $\boldsymbol{\pi}^*$ regarding ethnicity, race, and income (covariates named *E*).



$$P^*(e) \neq P(e)$$

2. Selection Bias

FDA's studies sampled from a distinct population by excluding youths with elevated baseline risk for suicide (B) from their cohorts.



$$P(y,b,e\,|\,do(x),S=1) \neq P(y,b,e\,|\,do(x))$$
$$P(x,y,b,e\,|\,S=1) \neq P(x,y,b,e)$$

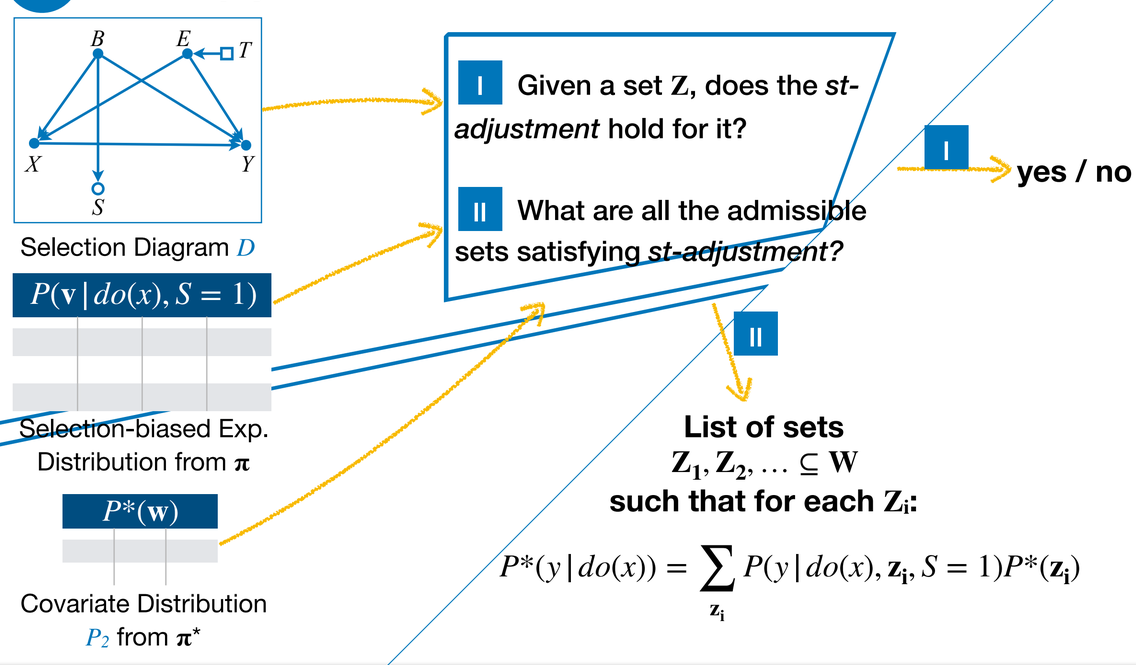
4 st-Adjustment

Strategy. Recalibrate the observed effect of the treatment on the outcome in the studied population using observations from the target population.

$$\underbrace{P^*(y\,|\,do(x))}_{\text{unbiased target effect in } \boldsymbol{\pi}^*} = \sum_{\mathbf{z}} \underbrace{P(y\,|\,do(x),\mathbf{z},S=1)}_{\text{experiment results in source domain } \boldsymbol{\pi}} \underbrace{P^*(\mathbf{z})}_{\text{observations from the target domain } \boldsymbol{\pi}^*}$$

Given a candidate set $\mathbf{Z}$, special attention needs to be paid to those *affected by the treatment* that are *correlated with the outcome* given pre-treatment covariates. Call them $\mathbf{Z_p}$.

5 Task(s) Overview



6 Result I: Graphical Criterion

A set of covariates $\mathbf{Z}$ is admissible for *st-adjustment* in D relative to treatment $\mathbf{X}$ and outcome $\mathbf{Y}$ if:

(i) Variables in $\mathbf{Z_p}$ are independent of the treatment given all other covariates, and

(ii) The outcome $\mathbf{Y}$ is independent of all the transportability (T) and selection bias nodes (S) given the covariates $\mathbf{Z}$ and the treatment $\mathbf{X}$.

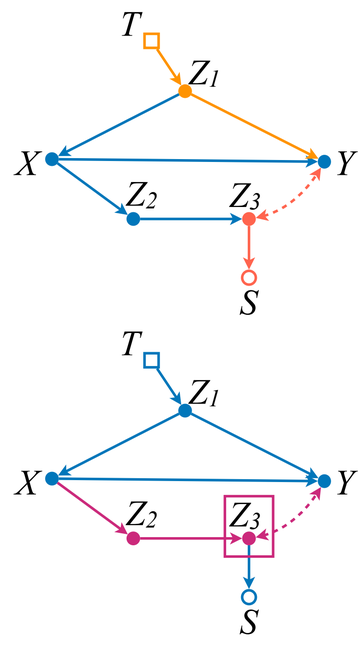
Thm. The causal effect $P^*(y \mid do(x))$ is identifiable by *st-adjustment* on a set $\mathbf{Z}$ with D if and only if the conditions above hold for $\mathbf{Z}$ relative to $\mathbf{X}$ and $\mathbf{Y}$.

7 Result II: Search Algorithm

The paper gives a procedure to list valid adjustment sets given what variables can be measured.

Task: Compute $P^*(y \mid do(x))$

- Consider the set $\mathbf{Z}=\{Z_1, Z_2, Z_3\}$, where $\mathbf{Z_p}=\{Z_3\}$.
- The outcome Y is affected by differences in the distribution of Z_1 between the source and target domains.
- The variable Z_3 affects the likelihood of units being sampled.
- If we adjust for Z_3 to control for selection bias, we introduce spurious correlation. Hence, we should also control for Z_2.



$$P^*(y\,|\,do(x)) = \sum_{z_1,z_2,z_3} P(y\,|\,do(x),z_1,z_2,z_3,S=1)P^*(z_1,z_2,z_3)$$