#### Instrumental Variables

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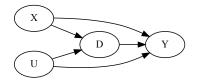
#### Contents

- Instrumental Variables
- 2 Randomized Trials with Non-compliance
- IVs in Observational Studies
- 4 Two Stage Least Squares
- References
- 6 Appendix

Instrumental Variables



## If we can't satisfy the backdoor path criterion

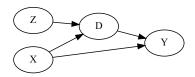


- This happens if there are unmeasured variables that make is impossible to block the backdoor path.
- These are also known as unmeasured confounders.
- If such variables exist, then we *cannot* use Matching, Regression, and Reweighing.



# Instrumental Variables (IV) can save us!

- IVs do not rely on the ignorability assumption.
- An IV is a variable that affects the treatment but not the outcome (directly)



- In this example, Z is the IV.
- The IV should be a randomized process that only affects the treatment.

## Sample Use Case for IVs: Randomized Encouragement

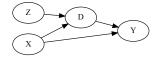
Sexton and Hebel 1984. "A clinical trial of change in maternal smoking and its effect of birth weight."

- Variables:
  - D: Smoking During Pregnancy
  - Y: Birthweight
  - X: Mother's age, order of birth, weight, etc.
  - Z: Randomize to either receive **encouragement** to stop smoking (Z=1) or receive usual care (Z=0).
- While it is unethical to randomly tell mothers to smoke, it is okay to randomly discourage smoking.

Randomized Trials with Non-compliance

#### IVs to adjust for non-compliance in randomized trials

 Non-compliance – not everyone assigned to a treatment will take the treatment.



- Variables:
  - Z: treatment assignment
  - D: treatment received
  - Y: outcome
  - X: confounders there could be variables that affect both D and Y. e.g. less healthy people might be less likely to take the prescribed treatment.
- Example: Sending out an email to customers vs. customers actually opening the emails.

## Compliance Classes

• There are 4 classes based on *potential treatment*:

Label	$D^{Z=0}$	$D^{Z=1}$
Never-takers	0	0
Compliers	0	1
Defiers	1	0
Always-takers	1	1

 Local Average Treatment Effect (LATE). To distinguish this from ATE, since we can only measuring the treatment effect of the *Compliers* instead of the entire population.

$$\begin{split} \mathsf{LATE} &= E[Y^{Z=1} - Y^{Z=0} | D^0 = 0, D^1 = 1] \\ &= E[Y^{D=1} - Y^{D=0} | \mathsf{Compliers}] \end{split}$$

LATE is also known as CATE (Complier Average Treatment Effect).

#### How do we get the Potential Treatment?

- Problem: in the actual data, we don't get to see  $D^{Z=z}$ .
- We can narrow it down to 2 classes:

Z	D	$D^0$	$D^1$	Class
0	0	0	?	Never-takers or compliers
0	1	1	?	Always-takers or defiers
1	0	?	0	Never-takers or defiers
1	1	?	1	Always-takers or <b>compliers</b>

# Monotonicity Assumption narrows down the Potential Classes

#### **Monotonicity Assumption**

- There are no defiers.
- Encouragement should not decrease the probability of treatment.

Z	D	$D^0$	$D^1$	Class
0	0	0	?	Never-takers or compliers
0	1	1	?	Always-takers or <del>defiers</del>
1	0	?	0	Never-takers or <del>defiers</del>
1	1	?	1	Always-takers or compliers

The goal is to estimate LATE

$$\mathsf{LATE} = E[Y^{D=1} - Y^{D=0} | \mathsf{compliers}]$$

But what we can directly measure is the Intention to Treat Effect (ITT), so we can start there.

$$\mathsf{ITT} = E[Y^{Z=1} - Y^{Z=0}] = E[Y|Z=1] - E[Y|Z=0]$$

This equality hold since Z is randomly assigned (Ignorability Assumption).

$$\begin{split} E[Y|Z=1] &= E[Y|Z=1, \text{always takers}] P(\text{always takers}) \\ &+ E[Y|Z=1, \text{never takers}] P(\text{never takers}) \\ &+ E[Y|Z=1, \text{compliers}] P(\text{compliers}) \end{split}$$

Note that  $Z \perp\!\!\!\perp (D^0, D^1)$  for always-takers and never-takers, so we can simplify the expression above.

$$\begin{split} E[Y|Z=1] &= E[Y|Z=1, \text{always takers}] P(\text{always takers}) \\ &+ E[Y|Z=1, \text{never takers}] P(\text{never takers}) \\ &+ E[Y|Z=1, \text{compliers}] P(\text{compliers}) \end{split}$$

$$\begin{split} E[Y|Z=1] &= E[Y|\text{always takers}]P(\text{always takers}) \\ &+ E[Y|\text{never takers}]P(\text{never takers}) \\ &+ E[Y|Z=1,\text{compliers}]P(\text{compliers}) \end{split}$$
 
$$E[Y|Z=0] &= E[Y|\text{always takers}]P(\text{always takers}) \\ &+ E[Y|\text{never takers}]P(\text{never takers}) \\ &+ E[Y|Z=0,\text{compliers}]P(\text{compliers}) \end{split}$$
 
$$E[Y|Z=1] - E[Y|Z=0] = E[Y|Z=1,\text{compliers}]P(\text{compliers}) \\ &- [Y|Z=0,\text{compliers}]P(\text{compliers}) \\ &\frac{E[Y|Z=1] - E[Y|Z=0]}{P(\text{compliers})} = E[Y^{D=1} - Y^{D=0}|\text{compliers}] = \text{LATE} \end{split}$$

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$$\mathsf{LATE} = \frac{E[Y|Z=1] - E[Y|Z=0]}{P(\mathsf{compliers})}$$

From the table above, we get an expression for P(compliers):

$$\begin{split} E[D|Z=1] &= P(\mathsf{compliers}) + P(\mathsf{always\text{-}takers}) \\ E[D|Z=0] &= P(\mathsf{always\text{-}takers}) \\ \therefore P(\mathsf{compliers}) &= E[D|Z=1] - E[D|Z=0] \end{split}$$

Therefore we can estimate LATE using

LATE = 
$$\frac{E[Y|Z=1] - E[Y|Z=0]}{E[D|Z=1] - E[D|Z=0]}$$

This expression is also known as the **Wald Estimator**.



#### Estimating LATE: Summary

We can estimate LATE using the Wald Estimator.

$$\mathsf{LATE} = \frac{E[Y|Z=1] - E[Y|Z=0]}{E[D|Z=1] - E[D|Z=0]}$$

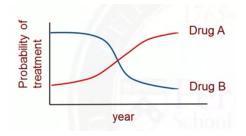
- From the Wald estimator, we see that the ITT underestimates the LATE.
- Remember that this estimator will only work under 2 assumptions:
  - Exclusion Restriction The IV should not be associated with the outcome except through the treatment.
  - Monotonicity Assumption Encouragement (the IV) should not decrease the likelihood of treatment, i.e. there are no defiers.

IVs in Observational Studies

#### IVs as "Natural Experiments"

- We can use certain randomized natural processes as IVs. Some examples are:
  - Mendelian randomization
  - Quarter of Birth (see example)
  - Geographic distance to specialty care provider
- The key is to find variables that satisfy the *exclusion restriction* this heavily relies on subject matter knowledge.

#### Example 1: Calendar Time as IV



#### For example:

- Treatment: Sulfonylureas vs. Metformin
- IV: Time (e.g. in the past sulfonylureas were more "encouraged")
- Outcome: BMI

Source: Ertefaie et al. (2017) "A tutorial on the use of instrumental variables in pharmacoepidemiology"

#### Example 2: distance as IV

Distance to a clinic or specialty care center is commonly used as an IV for healthcare outcomes.

- Shorter distance → stronger encouragement.
- We have to argue/defend (using domain expertise) if distance is a valid IV.
   e.g. It could be that income affects both distance to clinic and health outcomes.

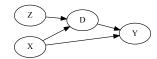
For example – investigating the difference in delivery outcomes for NICU and regular hospitals:

- Treatment: Delivery at NICU vs. Regular Hospital
- IV: Travel time from nearest hospital vs nearest NICU
- Outcome: Mortality

Source: Baiocchi et al. (2010). "Building a Stronger Instrument in an Observational Study of Perinatal Care for Premature Infants"

Two Stage Least Squares

#### Two Stage Least Squares



This method also relies on the IV assumptions.

• Stage 1: Regress Treatment on the IV

$$D_i = \alpha_0 + \alpha_1 Z_i + \epsilon_i$$

• Stage 2: Regress the Outcome with the predicted value of the treatment

$$Y_i = \beta_0 + \beta_1 \hat{D}_i + \epsilon_i$$

 $\beta_1$  from Stage 2 is the Causal Effect Estimate.

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22 / 27

References



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Appendix



# Why does IV even work?

ullet Ideally, if X where measured we can just run a regression of the form

$$Y_i = \beta_0 + \kappa_i + \beta_1 X_i + u_i$$

ullet since we don't have data on X, all we can do is

$$Y_i = \beta_0 + \kappa D_i + v_i$$

where  $v_i = \beta_1 X_i + u_i$ 



## Why does IV even work?

$$Y_i = \beta_0 + \kappa D_i + v_i$$
$$v_i = \beta_1 X_i + u_i$$

• Now, let's try to recover the treatment effect  $\kappa$ . Given an IV Z,

$$Cov(Z,Y) = Cov(Z,\beta_0 + \kappa D_i + v_i)$$

$$= \kappa Cov(Z,D) + Cov(Z,v)$$

$$\therefore \kappa = \frac{Cov(Z,Y)}{Cov(Z,D)} = \frac{Cov(Z,Y)/Var(Z)}{Cov(Z,D)/Var(Z)}$$

- Cov(Z, v) = 0 since  $Z \perp \!\!\! \perp X$
- ullet For binary Y and D, kappa is equivalent to the LATE Wald Estimator.

$$\kappa = \frac{Cov(Z,Y)/Var(Z)}{Cov(Z,D)/Var(Z)} = \frac{E[Y|Z=1] - E[Y|Z=0]}{E[D|Z=1] - E[D|Z=0]}$$

