



THE UNIVERSITY  
*of* EDINBURGH

# Methods for Causal Inference

## Lecture 6: Instrumental variable method

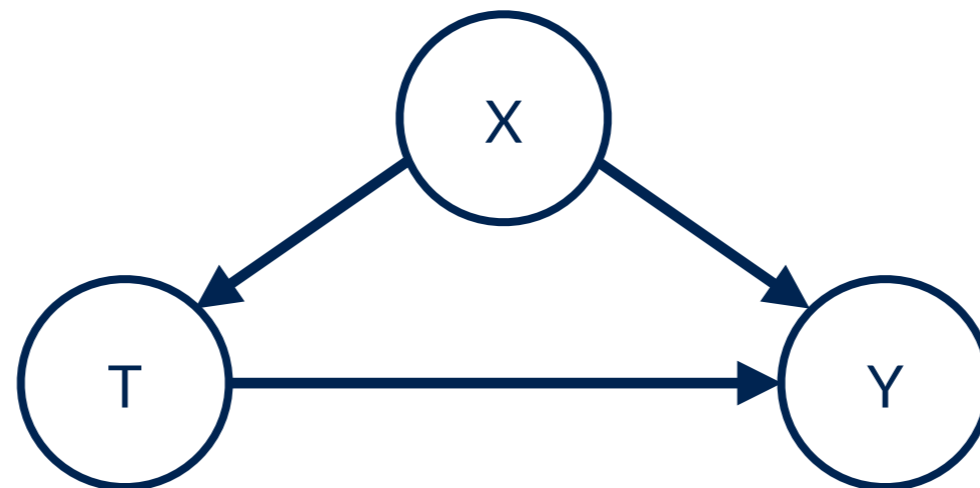
---

Ava Khamseh

School of Informatics  
2023-2024

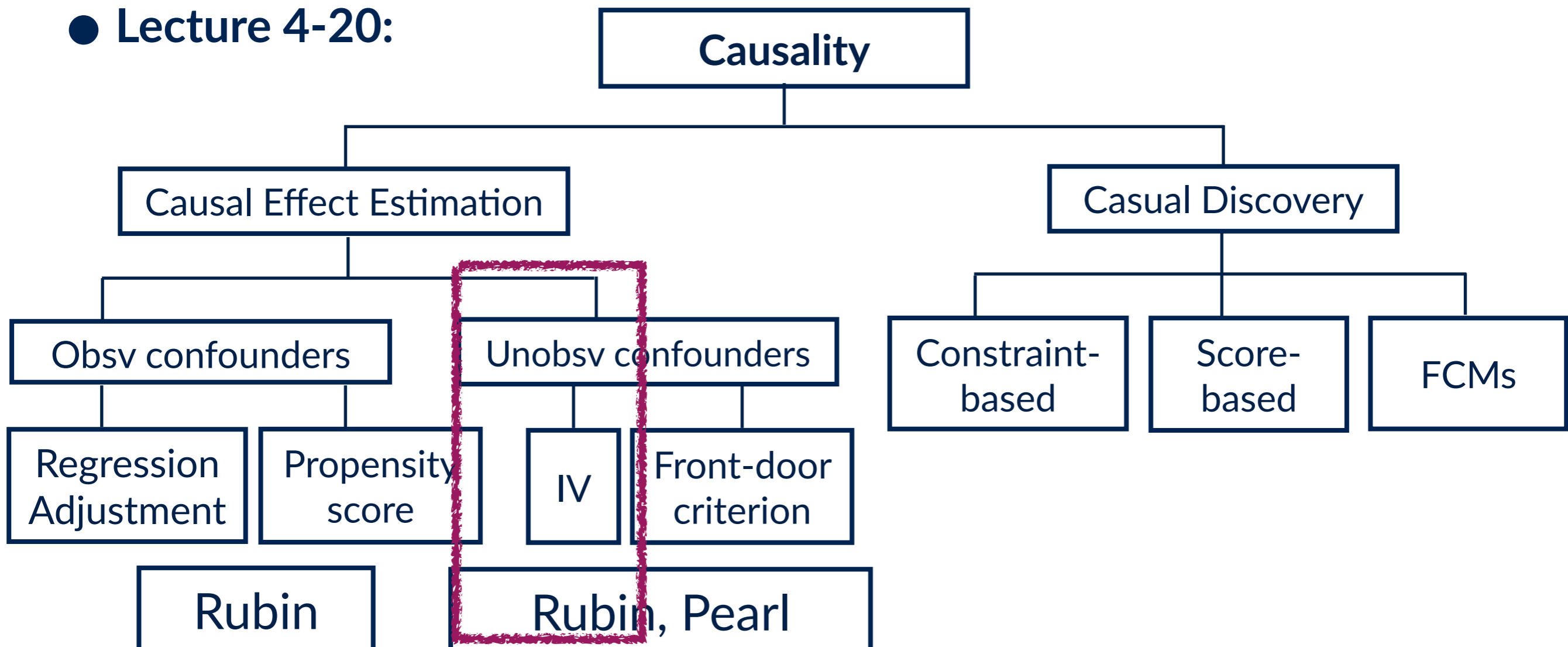
So far ...

## Causal inference with observed confounders



# Overview of the course

- **Lecture 1:** Introduction & Motivation, why do we care about causality? Why deriving causality from observational data is non-trivial.
- **Lecture 2:** Recap of probability theory, variables, events, conditional probabilities, independence, law of total probability, Bayes' rule
- **Lecture 3:** Recap of regression, multiple regression, graphs, SCM
- **Lecture 4-20:**



# Randomised Controlled Trials (RCTs)

Randomised Control Trials (RCT): Subjects are assigned at random to various groups (treatment or control)

RCTs are sometimes referred to 'gold standard' of scientific research, used in biological, medical and behavioural sciences

# Randomised Controlled Trials (RCTs)

Randomised Control Trials (RCT): Subjects are assigned at random to various groups (treatment or control)

RCTs are sometimes referred to 'gold standard' of scientific research, used in biological, medical and behavioural sciences

But RCT's can be impossible, imperfect or unethical:

- Can be very costly and difficult to organise (demanding resources)

# Randomised Controlled Trials (RCTs)

Randomised Control Trials (RCT): Subjects are assigned at random to various groups (treatment or control)

RCTs are sometimes referred to 'gold standard' of scientific research, used in biological, medical and behavioural sciences

But RCT's can be impossible, imperfect or unethical:

- Can be very costly and difficult to organise (demanding resources)
- Perfect control is hard to achieve (imperfect compliance): Adverse reaction to an experimental drug means dose has to be reduce no avoid harm

# Randomised Controlled Trials (RCTs)

Randomised Control Trials (RCT): Subjects are assigned at random to various groups (treatment or control)

RCTs are sometimes referred to 'gold standard' of scientific research, used in biological, medical and behavioural sciences

But RCT's can be impossible, imperfect or unethical:

- Can be very costly and difficult to organise (demanding resources)
- Perfect control is hard to achieve (imperfect compliance): Adverse reaction to an experimental drug means dose has to be reduce no avoid harm
- Unethical: Asking pregnant women to smoke to observe child birth weight  
Denying the control subjects a drug, e.g. treatment could have been potentially life saving for cancer patients

# Randomised Controlled Trials (RCTs)

Randomised Control Trials (RCT): Subjects are assigned at random to various groups (treatment or control)

RCTs are sometimes referred to 'gold standard' of scientific research, used in biological, medical and behavioural sciences

But RCT's can be impossible, imperfect or unethical:

- Can be very costly and difficult to organise (demanding resources)
- Perfect control is hard to achieve (imperfect compliance): Adverse reaction to an experimental drug means dose has to be reduce no avoid harm
- Unethical: Asking pregnant women to smoke to observe child birth weight  
Denying the control subjects a drug, e.g. treatment could have been potentially life saving for cancer patients
- Randomisation may influence participation and behaviour



# Randomising an instrument

Causal inference from studies in which subjects have a final choice

Randomisation is confined to an indirect **instrument** that encourages or discourages participation in treatment or control programmes.

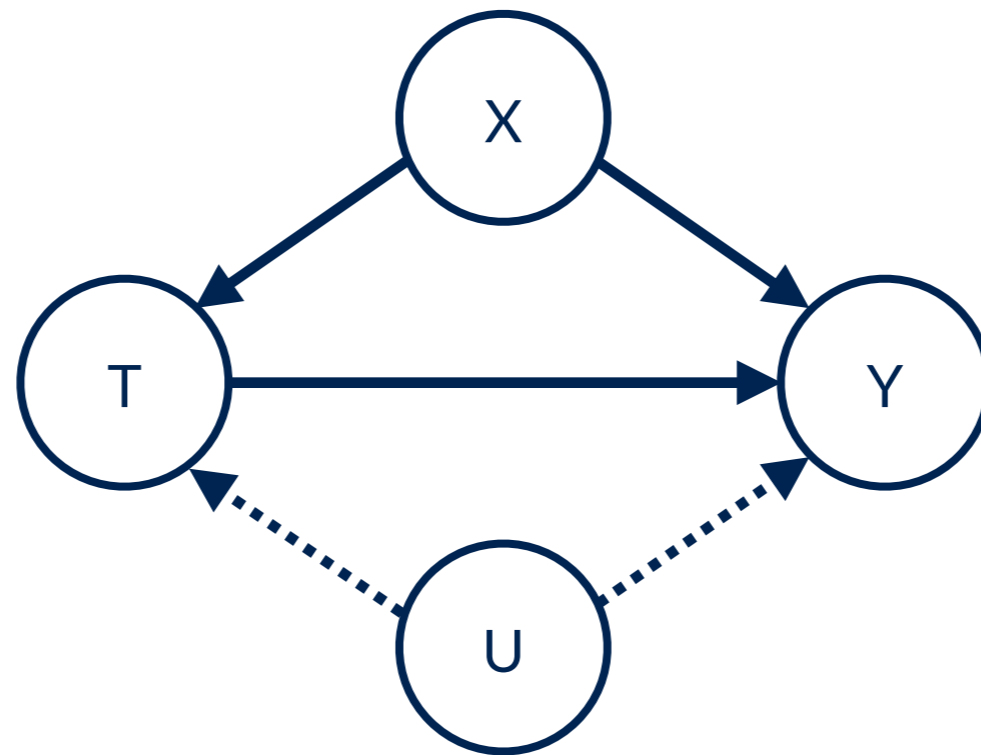
(However, imperfect compliance poses a problem, e.g., subjects that declined taking the drug are precisely those who would have responded adversely. So an experiment might conclude the drug is more effective than it actually is.

-> more complex methods, e.g. bounds)

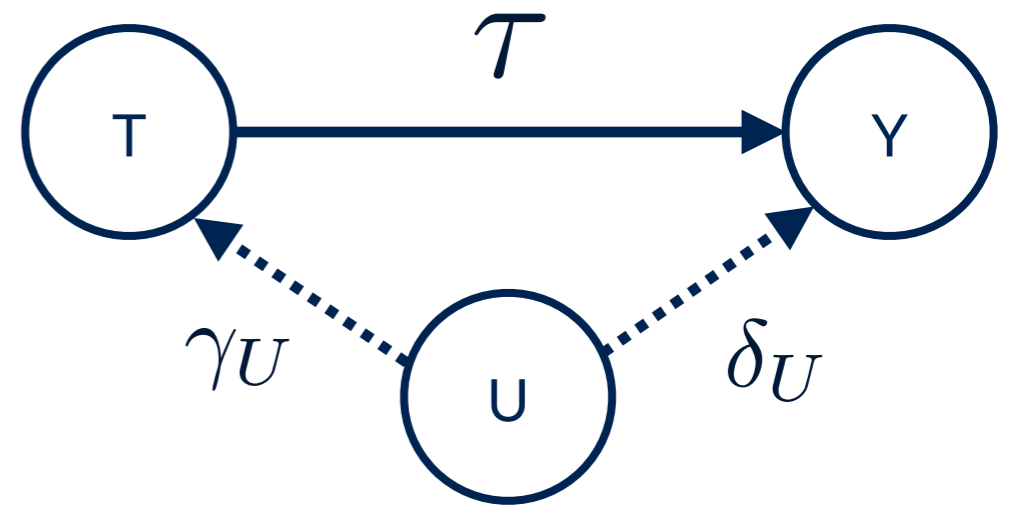
# Instrumental Variable

Unobserved confounders (U), **violates unconfoundedness**, i.e. conditioning on X alone, would not results in a randomised treatment assignment

Unconfoundedness is fundamentally unverifiable

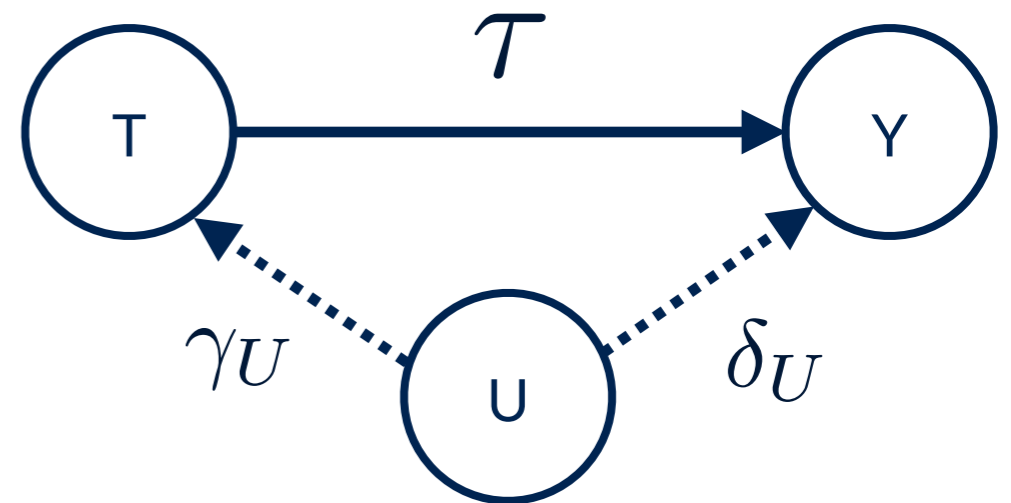


# Naive regression leads to bias



$$Y = \tau T + \delta_U U$$
$$T = \gamma_U U$$

# Naive regression leads to bias



What happens if we naively perform a linear regression of Y on T:

$$Y = \tau T + \delta_U U$$
$$T = \gamma_U U$$

$$\frac{\text{Cov}[T, Y]}{\text{Var}[T]} = \frac{\tau \text{Var}[T] + \gamma_U \delta_U \text{Var}[U]}{\text{Var}[T]} = \tau + \frac{\gamma_U \delta_U \text{Var}[U]}{\text{Var}[T]} = \tau + \frac{\delta_U}{\gamma_U}$$

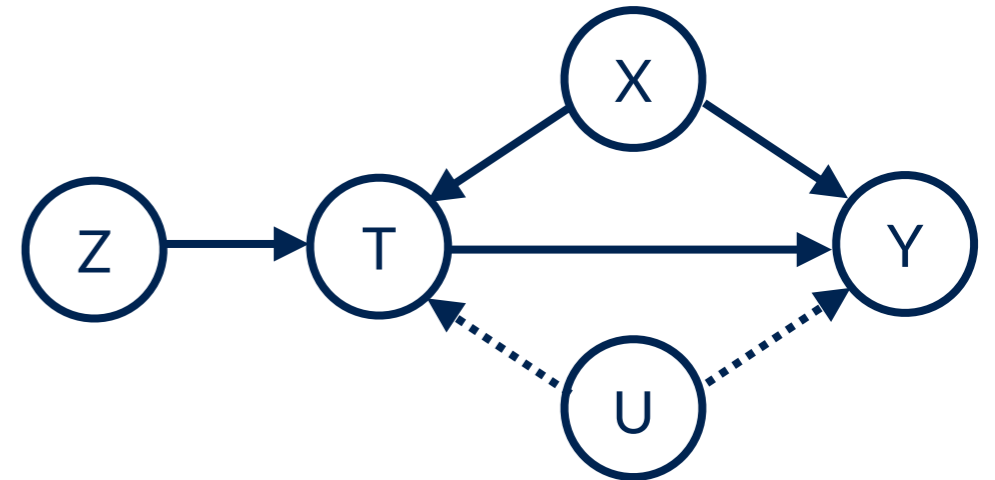
causal term

Bias term

# Instrumental Variable example

- **Example 1:**

- T: smoking during pregnancy
- Y: birthweight
- X: parity, mother's age, weight, ...
- U: Other unmeasured confounders



- Randomise Z (intention-to-treat): either receive encouragement to stop smoking ( $Z=1$ ), or receive usual care ( $Z=0$ )
- Intention-to-treat analysis gives causal effect estimator of encouragement  $z$  on outcome  $y$ :

$$\mathbb{E}(y|z = 1) - \mathbb{E}(y|z = 0)$$

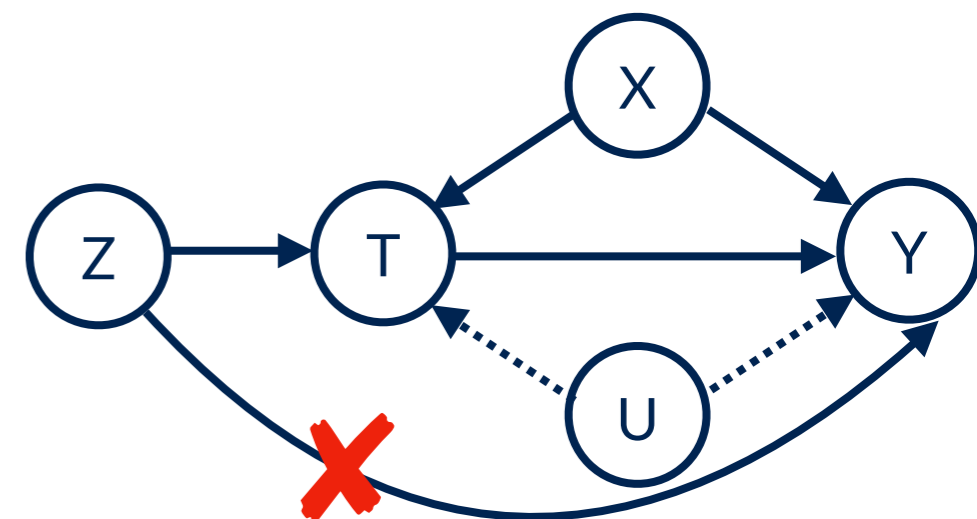
- What can we say about the causal effect of smoking itself?

# Instrumental Variable assumptions

- **SUTVA:** Potential outcomes for each individual  $i$  are unrelated to the treatment status of other individuals:

$$Y^{(i)}(\mathbf{Z}, \mathbf{T}) = Y^{(i)}(Z^{(i)}, T^{(i)}) , \quad |\mathbf{Z}| = |\mathbf{T}| = N \text{ individuals}$$

- **Non-zero average/relevant:** Treatment assignment  $Z$  associated with the treatment  $\mathbb{E} \left[ \left( T^{(i)} | z = 1 \right) - \left( T^{(i)} | z = 0 \right) \right]$
- Treatment assignment  $Z$  is random ( $Z$  and  $Y$  do not share a cause).



# Instrumental Variable assumptions

- **SUTVA:** Potential outcomes for each individual  $i$  are unrelated to the treatment status of other individuals:

$$Y^{(i)}(\mathbf{Z}, \mathbf{T}) = Y^{(i)}(Z^{(i)}, T^{(i)}) , \quad |\mathbf{Z}| = |\mathbf{T}| = N \text{ individuals}$$

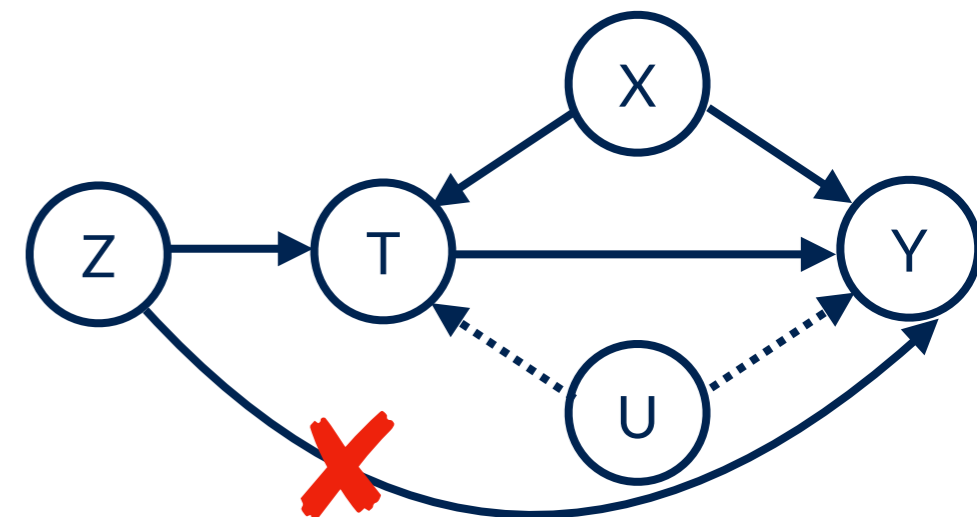
- **Non-zero average/relevant:** Treatment assignment  $Z$  associated with the treatment  $\mathbb{E} \left[ \left( T^{(i)} | z = 1 \right) - \left( T^{(i)} | z = 0 \right) \right]$
- Treatment assignment  $Z$  is random ( $Z$  and  $Y$  do not share a cause).

$$\left( Y^{(i)} | z = 1, t \right) = \left( Y^{(i)} | z = 0, t \right)$$

- **Exclusion Restriction:** Any effect of  $Z$  on  $Y$  is via an effect of  $Z$  on  $T$ , i.e.,  $Z$  should not affect  $Y$  when  $T$  is held constant

- **Monotonicity** (increasing encouragement “dose” increases probability of treatment, no defiers):

$$\left( T^{(i)} | z = 1 \right) \geq \left( T^{(i)} | z = 0 \right)$$



# Instrumental Variable: Potential values of T

Population	T z=0	T z=1	Description
Never-takers	0	0	Causal effect of Z on T is zero, since $\left(T^{(i)} z=1\right) - \left(T^{(i)} z=0\right) = 0$
Compliers	0	1	<u>causal effect inference:</u> $\left(T^{(i)} z=1\right) - \left(T^{(i)} z=0\right) = 1$ $\left(Y^{(i)} T^{(i)}=1\right) - \left(Y^{(i)} T^{(i)}=0\right)$
Defiers	1	0	Rule out by <b>monotonicity</b> , since $\left(T^{(i)} z=1\right) - \left(T^{(i)} z=0\right) = -1$
Always-takers	1	1	Causal effect of Z on Y is zero, since $\left(T^{(i)} z=1\right) - \left(T^{(i)} z=0\right) = 0$

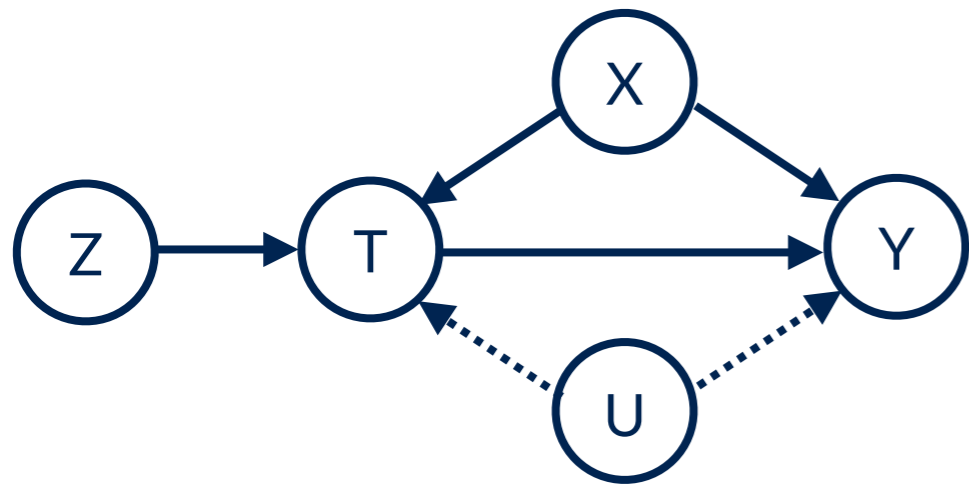
Notation: T=1 is **not** smoking



# Instrumental Variable: The estimand

Want ATE:

$$\mathbb{E} [Y_{T=1} - Y_{T=0}]$$



“Almost”

Will estimate:

$$\tau = \frac{\mathbb{E} [(Y|z = 1) - (Y|z = 0)]}{\mathbb{E} [(T|z = 1) - (T|z = 0)]}$$

# Instrumental Variable: The estimand

**Want ATE:**  $\mathbb{E} \left[ \left( Y^{(i)} | t^{(i)} = 1 \right) - \left( Y^{(i)} | t^{(i)} = 0 \right) \right]$

**Derivation:**

$$\tau = \frac{\mathbb{E} [(Y|z = 1) - (Y|z = 0)]}{\mathbb{E} [(T|z = 1) - (T|z = 0)]}$$

$$\begin{aligned} & \left( Y^{(i)} | T^{(i)}(z = 1) \right) - \left( Y^{(i)} | T^{(i)}(z = 0) \right) \quad \text{t is either t=0 or t=1, and exclusion restriction} \\ = & \left[ Y^{(i)} \left( t^{(i)} = 1 \right) \cdot \left( t^{(i)} | z = 1 \right) + Y^{(i)} \left( t^{(i)} = 0 \right) \cdot \left( 1 - \left( t^{(i)} | z = 1 \right) \right) \right] \\ - & \left[ Y^{(i)} \left( t^{(i)} = 1 \right) \cdot \left( t^{(i)} | z = 0 \right) + Y^{(i)} \left( t^{(i)} = 0 \right) \cdot \left( 1 - \left( t^{(i)} | z = 0 \right) \right) \right] \\ = & \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \cdot \left( \left( t^{(i)} | z = 1 \right) - \left( t^{(i)} | z = 0 \right) \right) \end{aligned}$$

Hence, the causal effect of Z on Y for individual i, is the product of the causal effect of Z on T, and, the casual effect of T on Y.

# Instrumental Variable: The estimand

**Want ATE:**  $\mathbb{E} \left[ \left( Y^{(i)} | t^{(i)} = 1 \right) - \left( Y^{(i)} | t^{(i)} = 0 \right) \right]$

**Derivation:**

$$\tau = \frac{\mathbb{E} [(Y|z = 1) - (Y|z = 0)]}{\mathbb{E} [(T|z = 1) - (T|z = 0)]}$$

$$\begin{aligned} & \left( Y^{(i)} | T^{(i)}(z = 1) \right) - \left( Y^{(i)} | T^{(i)}(z = 0) \right) \quad t \text{ is either } t=0 \text{ or } t=1, \text{ and exclusion restriction} \\ = & \left[ Y^{(i)} \left( t^{(i)} = 1 \right) \cdot \left( t^{(i)} | z = 1 \right) + Y^{(i)} \left( t^{(i)} = 0 \right) \cdot \left( 1 - \left( t^{(i)} | z = 1 \right) \right) \right] \\ & - \left[ Y^{(i)} \left( t^{(i)} = 1 \right) \cdot \left( t^{(i)} | z = 0 \right) + Y^{(i)} \left( t^{(i)} = 0 \right) \cdot \left( 1 - \left( t^{(i)} | z = 0 \right) \right) \right] \\ = & \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \cdot \left( \left( t^{(i)} | z = 1 \right) - \left( t^{(i)} | z = 0 \right) \right) \end{aligned}$$

Hence, the causal effect of Z on Y for individual i, is the product of the causal effect of Z on T, and, the causal effect of T on Y.

# Instrumental Variable: The estimand

**Want ATE:**  $\mathbb{E} \left[ \left( Y^{(i)} | t^{(i)} = 1 \right) - \left( Y^{(i)} | t^{(i)} = 0 \right) \right]$

**Derivation:**

$$\tau = \frac{\mathbb{E} [(Y|z = 1) - (Y|z = 0)]}{\mathbb{E} [(T|z = 1) - (T|z = 0)]}$$

$$\begin{aligned} & \left( Y^{(i)} | T^{(i)}(z = 1) \right) - \left( Y^{(i)} | T^{(i)}(z = 0) \right) \quad \text{t is either t=0 or t=1, and exclusion restriction} \\ = & \left[ Y^{(i)} \left( t^{(i)} = 1 \right) \cdot \left( t^{(i)} | z = 1 \right) + Y^{(i)} \left( t^{(i)} = 0 \right) \cdot \left( 1 - \left( t^{(i)} | z = 1 \right) \right) \right] \\ - & \left[ Y^{(i)} \left( t^{(i)} = 1 \right) \cdot \left( t^{(i)} | z = 0 \right) + Y^{(i)} \left( t^{(i)} = 0 \right) \cdot \left( 1 - \left( t^{(i)} | z = 0 \right) \right) \right] \\ = & \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \cdot \left( \left( t^{(i)} | z = 1 \right) - \left( t^{(i)} | z = 0 \right) \right) \end{aligned}$$

Hence, the causal effect of Z on Y for individual i, is the product of the causal effect of Z on T, and, the casual effect of T on Y.

# Instrumental Variable: The estimand

To continue the derivation, we use the fact that:

$$\mathbb{E}[XY] = \int \int xy p(x, y) dx dy = \int dy y p(y) \int dx x p(x|y) = \int dy y p(y) \mathbb{E}[x|y]$$

and write,

$$\begin{aligned} & \mathbb{E} \left[ \left( Y^{(i)} | T^{(i)}(z=1) \right) - \left( Y^{(i)} | T^{(i)}(z=0) \right) \right] \\ &= \mathbb{E} \left[ \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \cdot \left( \left( t^{(i)} | z = 1 \right) - \left( t^{(i)} | z = 0 \right) \right) \right] \end{aligned} \quad \begin{array}{l} \nearrow \\ \mathbf{0, 1, -1} \end{array}$$

# Instrumental Variable: The estimand

To continue the derivation, we use the fact that:

$$\mathbb{E}[XY] = \int \int xy p(x, y) dx dy = \int dy y p(y) \int dx x p(x|y) = \int dy y p(y) \mathbb{E}[x|y]$$

and write,

$$\begin{aligned} & \mathbb{E} \left[ \left( Y^{(i)} | T^{(i)}(z=1) \right) - \left( Y^{(i)} | T^{(i)}(z=0) \right) \right] \quad \xrightarrow{\quad} \mathbf{0, 1, -1} \\ &= \mathbb{E} \left[ \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \cdot \left( \left( t^{(i)} | z=1 \right) - \left( t^{(i)} | z=0 \right) \right) \right] \\ &= \mathbb{E} \left[ \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \mid \left( \left( t^{(i)} | z=1 \right) - \left( t^{(i)} | z=0 \right) \right) = 1 \right] \cdot \\ & \quad P \left( \left( t^{(i)} | z=1 \right) - \left( t^{(i)} | z=0 \right) = 1 \right) \\ & - \mathbb{E} \left[ \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \mid \left( \left( t^{(i)} | z=1 \right) - \left( t^{(i)} | z=0 \right) \right) = -1 \right] \cdot \\ & \quad P \left( \left( t^{(i)} | z=1 \right) - \left( t^{(i)} | z=0 \right) = -1 \right) \\ & \quad \xleftarrow{\quad} \mathbf{0, \text{by monotonicity}} \end{aligned}$$

# Instrumental Variable: The estimand

$$\frac{\mathbb{E} [(Y^{(i)} | T^{(i)}(z = 1)) - (Y^{(i)} | T^{(i)}(z = 0))]}{\mathbb{E} [(t^{(i)} | z = 1) - (t^{(i)} | z = 0)]}$$
$$= \mathbb{E} \left[ \left( Y^{(i)} \left( t^{(i)} = 1 \right) - Y^{(i)} \left( t^{(i)} = 0 \right) \right) \mid \left( \left( t^{(i)} | z = 1 \right) - \left( t^{(i)} | z = 0 \right) \right) = 1 \right]$$

i.e. restricting to **compliers**, the average causal effect of Z on Y is proportional to the average causal effect of T on Y.

$$\tau = \frac{\mathbb{E} [(Y | z = 1) - (Y | z = 0)]}{\mathbb{E} [(T | z = 1) - (T | z = 0)]}$$

- In this example, Z was randomly assigned as part of the study
- IV can also be randomised in nature (nature randomiser):
  - Mendelian randomisation

# Instrumental Variable: Mendelian Randomisation

Population genetics:

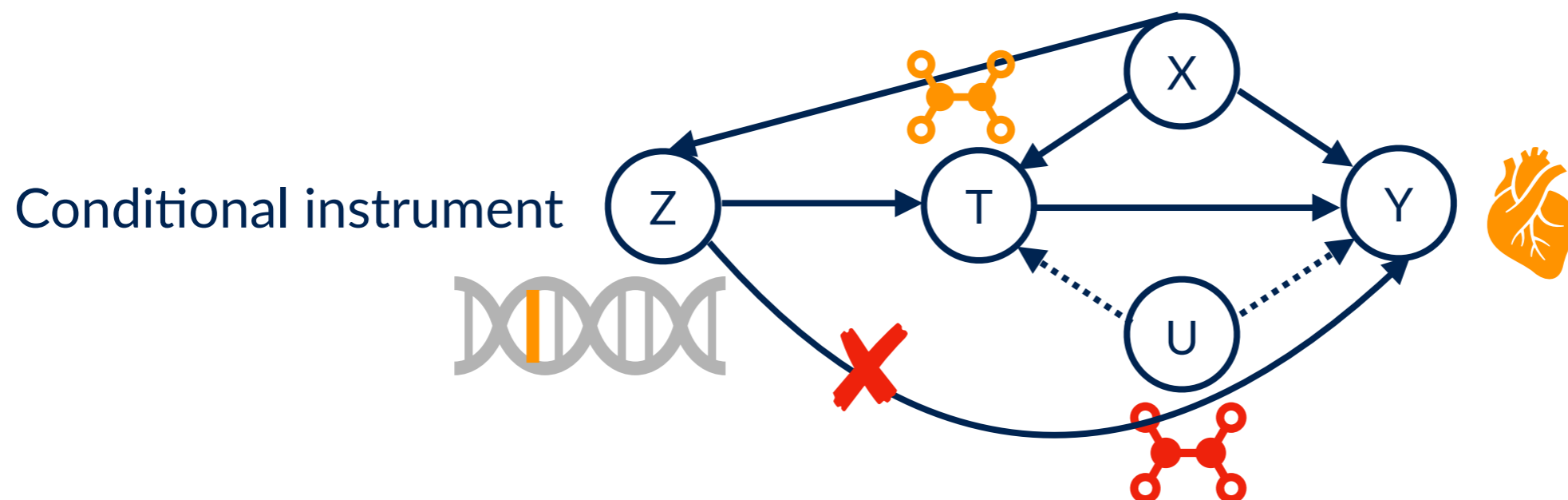
Z = a DNA variant associated with a particular exposure T

T = exposure, e.g. lipid levels in the blood

Y = heart disease

X = population stratification (might affect Z, need to adjust)

U = unobserved variables affecting both lipid levels and disease





# Instrumental Variable: Economics

How does price of a product casually affect demand?

Z = Market supply

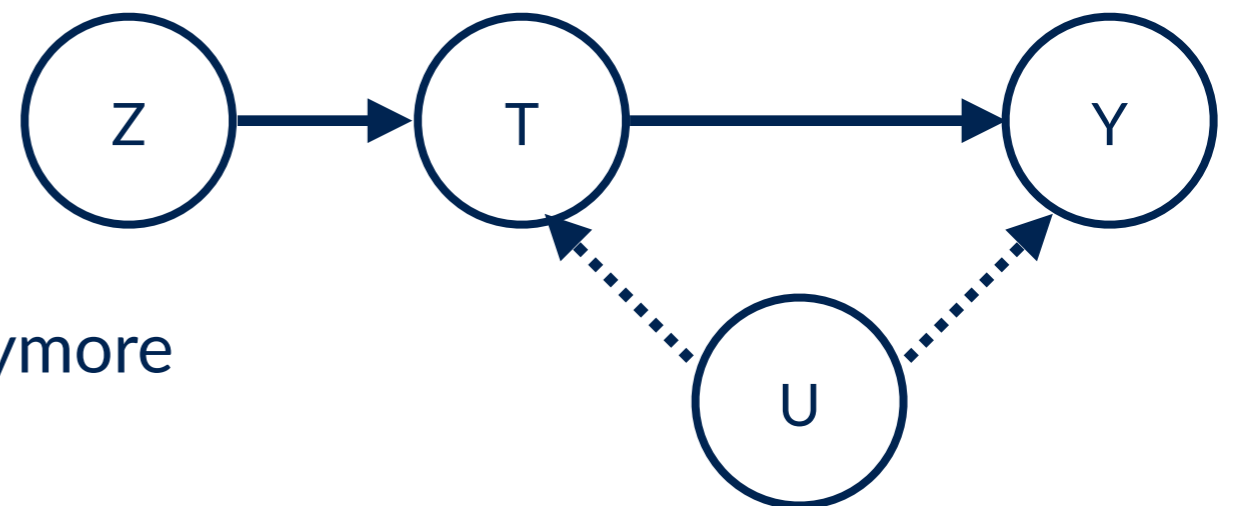
T = Price

Y = Demand

U = Factors confounding influencing price and demand  
(e.g. tax imposed)

Exclusion restriction requires that market supply  
does not affect demand  
(e.g. COVID-19 toilet paper fiasco! )  
(e.g. Pokemon cards)

Also, individuals may not be independent anymore



# The Wald Estimator (for binary variables)

$$\tau = \frac{\mathbb{E}[(Y|z=1) - (Y|z=0)]}{\mathbb{E}[(T|z=1) - (T|z=0)]}$$



$$\hat{\tau} = \frac{\frac{1}{n_{z=1}} \sum_{i \in z=1} Y^{(i)} - \frac{1}{n_{z=0}} \sum_{i \in z=0} Y^{(i)}}{\frac{1}{n_{z=1}} \sum_{i \in z=1} T^{(i)} - \frac{1}{n_{z=0}} \sum_{i \in z=0} T^{(i)}}$$

# IV Estimator: continuous variables case

Linear case:

$$\tau = \frac{\text{Cov}(Y, Z)}{\text{Cov}(T, Z)}$$



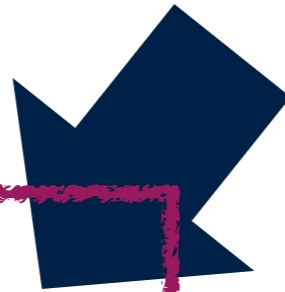
$$\hat{\tau} = \frac{\hat{\text{Cov}}(Y, Z)}{\hat{\text{Cov}}(T, Z)}$$

Two-Stage Least-squares  
Estimator

# IV Estimator: continuous variables case

Linear case:

$$\tau = \frac{\text{Cov}(Y, Z)}{\text{Cov}(T, Z)}$$

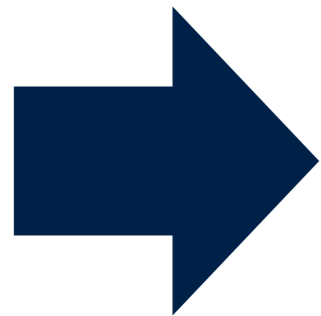


$$\hat{\tau} = \frac{\hat{\text{Cov}}(Y, Z)}{\hat{\text{Cov}}(T, Z)}$$

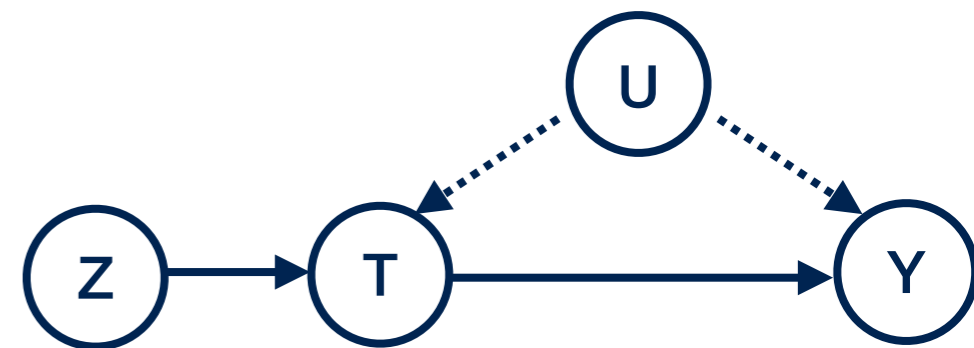
Two-Stage Least-squares  
Estimator

# IV Estimator: continuous variables case

$$\text{Cov}(Y, Z) = \mathbb{E}[YZ] - \mathbb{E}[Y]\mathbb{E}[Z]$$



$$\hat{\tau} = \frac{\hat{\text{Cov}}(Y, Z)}{\hat{\text{Cov}}(T, Z)}$$

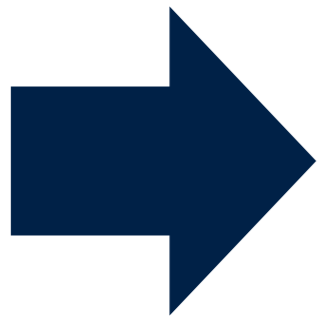


$$Y = \tau T + \delta_U U$$

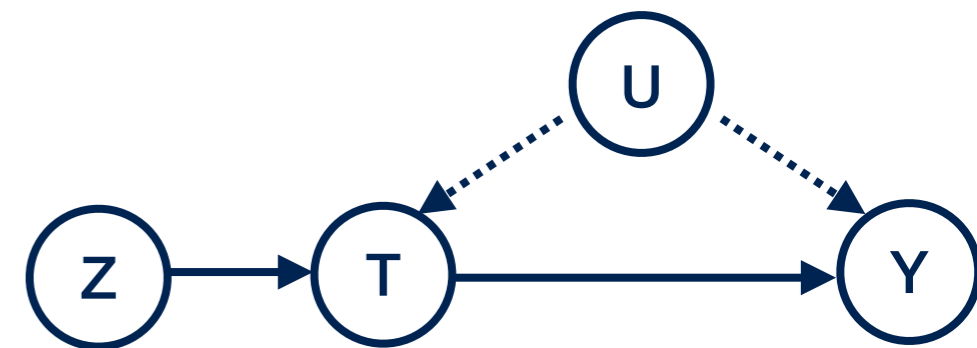
# IV Estimator: continuous variables case

$$\begin{aligned}\text{Cov}(Y, Z) &= \mathbb{E}[YZ] - \mathbb{E}[Y]\mathbb{E}[Z] \\ &= \mathbb{E}(\tau T + \delta_u U)Z] - \mathbb{E}[\tau T + \delta_u U]\mathbb{E}[Z]\end{aligned}$$

By linearity and  
exclusion restriction



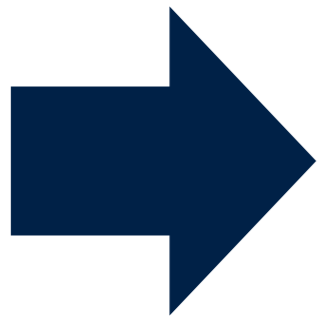
$$\hat{\tau} = \frac{\hat{\text{Cov}}(Y, Z)}{\hat{\text{Cov}}(T, Z)}$$



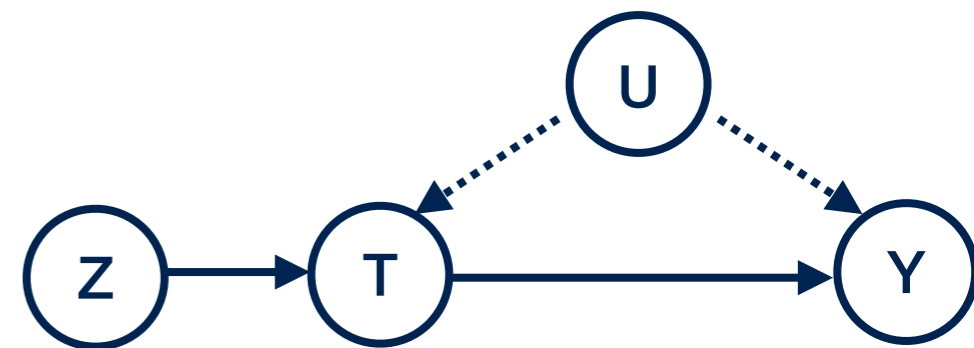
$$Y = \tau T + \delta_U U$$

## IV Estimator: continuous variables case

$$\begin{aligned}\text{Cov}(Y, Z) &= \mathbb{E}[YZ] - \mathbb{E}[Y]\mathbb{E}[Z] \\ &= \mathbb{E}(\tau T + \delta_u U)Z] - \mathbb{E}[\tau T + \delta_u U]\mathbb{E}[Z] \\ &= \tau\mathbb{E}[TZ] + \delta_u\mathbb{E}[UZ] - \tau\mathbb{E}[T]\mathbb{E}[Z] - \delta_u\mathbb{E}[U]\mathbb{E}[Z]\end{aligned}$$



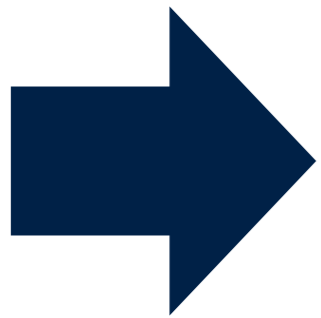
$$\hat{\tau} = \frac{\hat{\text{Cov}}(Y, Z)}{\hat{\text{Cov}}(T, Z)}$$



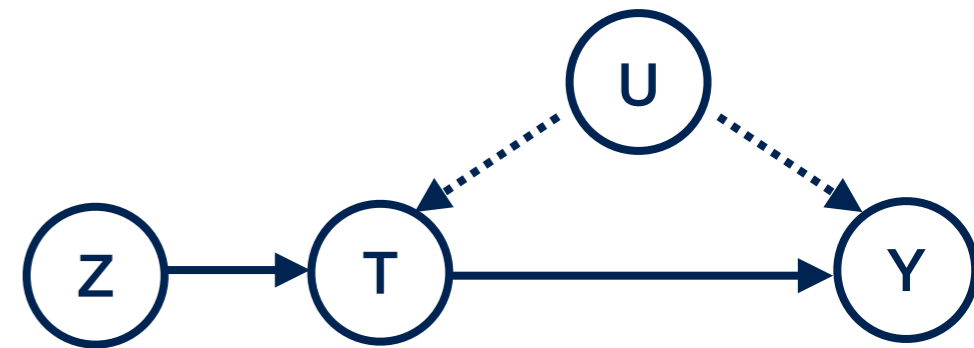
$$Y = \tau T + \delta_U U$$

# IV Estimator: continuous variables case

$$\begin{aligned}\text{Cov}(Y, Z) &= \mathbb{E}[YZ] - \mathbb{E}[Y]\mathbb{E}[Z] \\ &= \mathbb{E}(\tau T + \delta_u U)Z] - \mathbb{E}[\tau T + \delta_u U]\mathbb{E}[Z] \\ &= \tau \mathbb{E}[TZ] + \delta_u \mathbb{E}[UZ] - \tau \mathbb{E}[T]\mathbb{E}[Z] - \delta_u \mathbb{E}[U]\mathbb{E}[Z] \\ &= \tau \text{Cov}(T, Z) + \delta_U \text{Cov}(U, Z)\end{aligned}$$



$$\hat{\tau} = \frac{\hat{\text{Cov}}(Y, Z)}{\hat{\text{Cov}}(T, Z)}$$



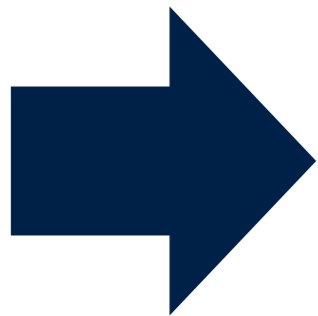
$$Y = \tau T + \delta_U U$$



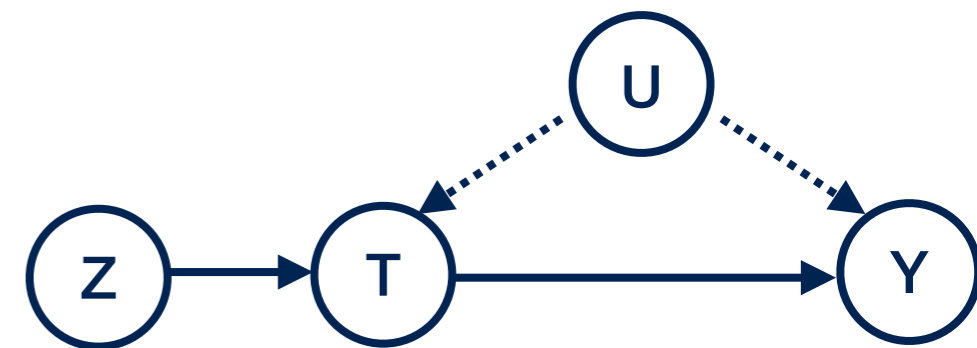
# IV Estimator: continuous variables case

$$\begin{aligned}\text{Cov}(Y, Z) &= \mathbb{E}[YZ] - \mathbb{E}[Y]\mathbb{E}[Z] \\ &= \mathbb{E}(\tau T + \delta_u U)Z] - \mathbb{E}[\tau T + \delta_u U]\mathbb{E}[Z] \\ &= \tau\mathbb{E}[TZ] + \delta_u\mathbb{E}[UZ] - \tau\mathbb{E}[T]\mathbb{E}[Z] - \delta_u\mathbb{E}[U]\mathbb{E}[Z] \\ &= \tau\text{Cov}(T, Z) + \delta_U\text{Cov}(U, Z) \\ &= \tau\text{Cov}(T, Z)\end{aligned}$$

Instrument is not  
confounded by U



$$\hat{\tau} = \frac{\hat{\text{Cov}}(Y, Z)}{\hat{\text{Cov}}(T, Z)}$$

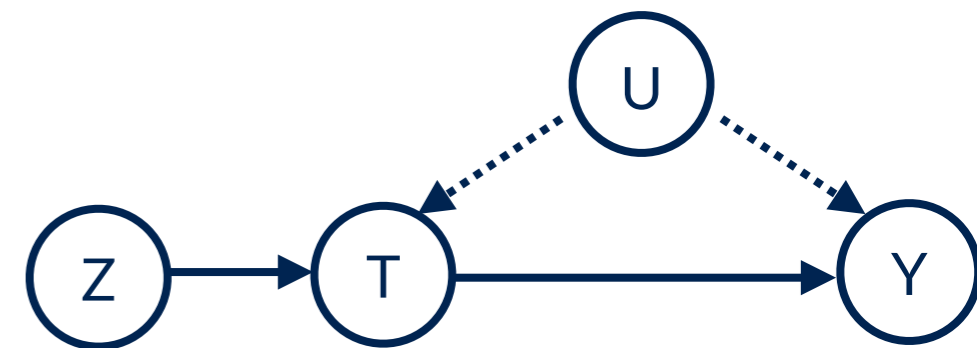


$$Y = \tau T + \delta_U U$$

# IV Estimator: continuous variables case

Two-Stage Least Squares Estimator (linear regression):

1. Estimate  $\mathbb{E}[T|Z]$ , to obtain  $\hat{T}$  in subspace
2. Estimate  $\mathbb{E}[Y|\hat{T}]$ , to obtain  $\hat{\tau}$ , which is the fitted coefficient in front of  $\hat{T}$  in this regression.

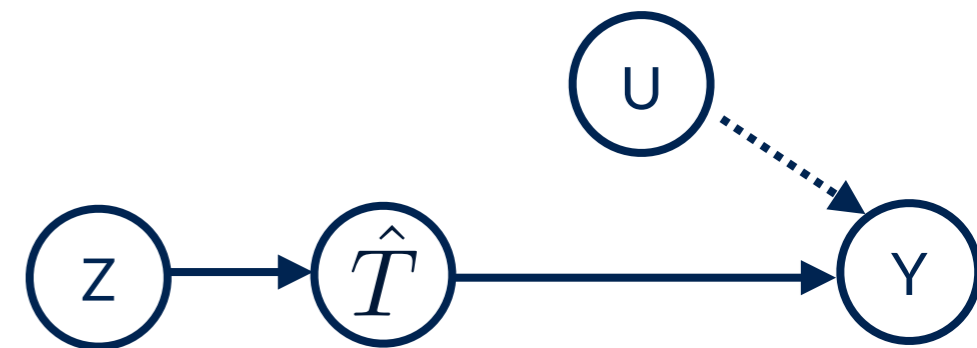


$$Y = \tau T + \delta_U U$$

# IV Estimator: continuous variables case

Two-Stage Least Squares Estimator (linear regression):

1. Estimate  $\mathbb{E}[T|Z]$ , to obtain  $\hat{T}$  in subspace
2. Estimate  $\mathbb{E}[Y|\hat{T}]$ , to obtain  $\hat{\tau}$ , which is the fitted coefficient in front of  $\hat{T}$  in this regression.



$$Y = \tau T + \delta_U U$$

# Other remarks

## Double-blind studies:

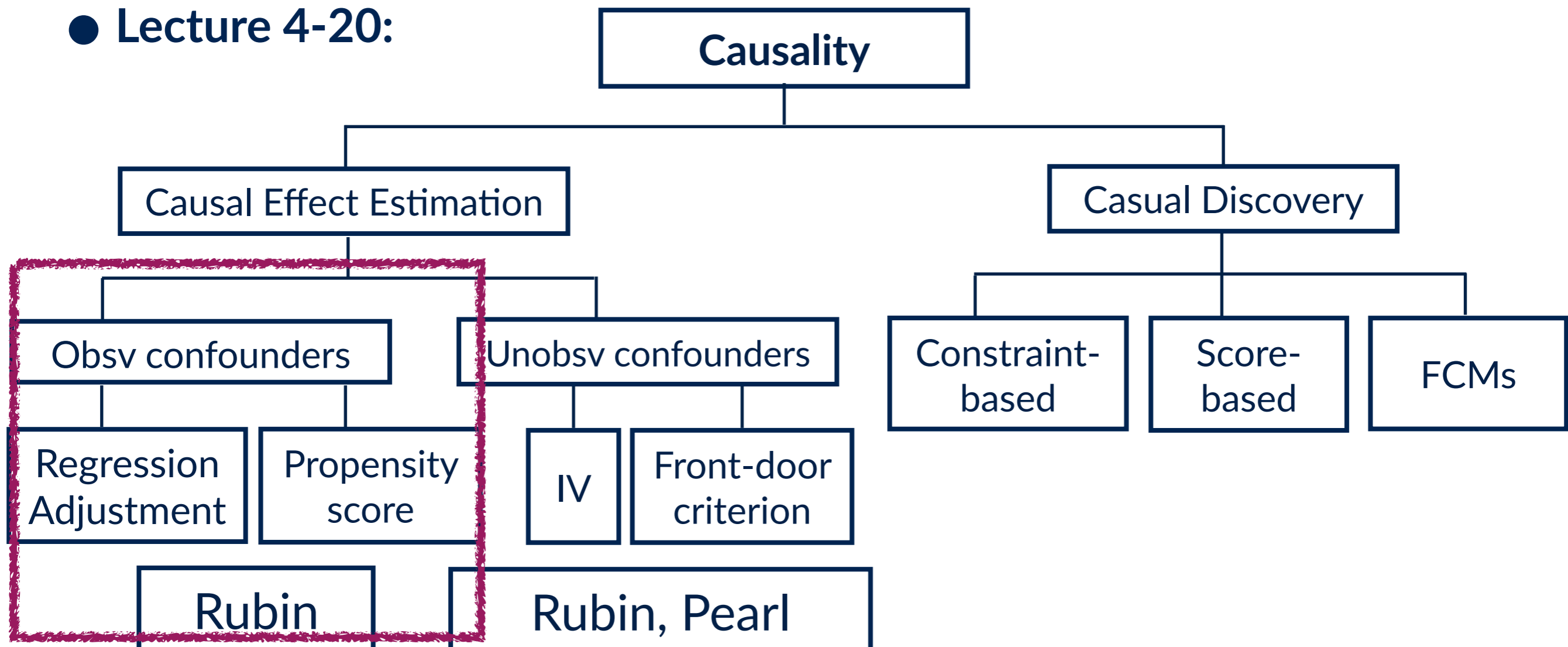
To ensure exclusion restriction, investigators withhold knowledge of the assigned treatment  $Z$  from participants and doctors

Example: Those randomly assigned  $z=1$ , receive aspirin, but those assigned  $z=0$  receive placebo, do not. The pills look identical. Neither doctor nor patient knows which is which, “double-blind placebo-controlled” randomised experiment.

Often not feasible, e.g. heart surgery, has no convincing placebo!

# Overview of the course

- **Lecture 1:** Introduction & Motivation, why do we care about causality? Why deriving causality from observational data is non-trivial.
- **Lecture 2:** Recap of probability theory, variables, events, conditional probabilities, independence, law of total probability, Bayes' rule
- **Lecture 3:** Recap of regression, multiple regression, graphs, SCM
- **Lecture 4-20:**





THE UNIVERSITY  
*of* EDINBURGH

# Methods for Causal Inference

## Lecture 6: Instrumental variable method

---

Ava Khamseh

School of Informatics  
2023-2024