Introduction to Causal Inference

Yan Li

SURV/SURVMETH 740

Yli6@umd.edu

OUTLINE

Introduction to Causal Inference

- Correlations vs. Causation
- Individual causal effects
- Average causal effects (ACE)
- Measures of causal effects
- Measures of Association
- Causal Assumptions to Make Connections

Directed Acyclic Graphs (DAGs)

- Marginal independence
- Conditional independence
- Rules for d-separation (d: dependence)

Introduction to Causal Inference

Simple cause and effect:

One action directly causes one immediate result

E.g. Alarm → wake up on time; pour milk → milk comes out

More complex causality:

Multiple cases over time with delayed and unclear effect

E.g. eat healthy + exercises + genes… → longevity

Causal questions (What If questions):

- If a firm wants to raise price of produces, what *would* have happened?
- If the congress passes a law, what *would* have happened?
- What would have been the election outcome if the candidate had not been an incumbent?
- Would the two countries have fought each other if they had been both autocratic?
- How many more disadvantaged youths would get employed under the new job-training program?

Therefore,

Causal inference is about the inference of counterfactuals: “If I intervene or change something, some specific outcome will happen?”

Correlations vs. Causation

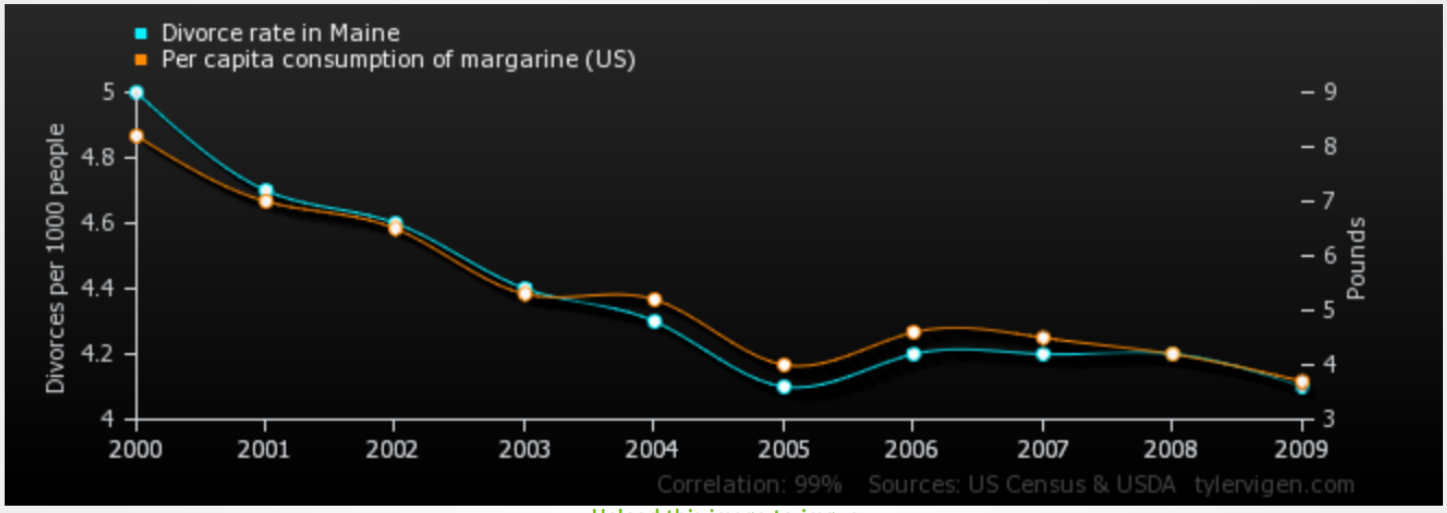
- A **correlation** is a relationship that you observe between two variables that appear to be related.
- If you see a correlation between two variables in the data that does not mean there is a *casual* relationship!
- Causally unrelated variables might happen to be highly correlated with each other over some period of time.

E.g. divorce rate in Maine correlated per capita consumption of margarine (https://www.bbc.com/news/magazine-27537142)

Divorce rate in Maine

correlates with

Per capita consumption of margarine (US)



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	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Divorce rate in Maine *Divorces per 1000 people (US Census)*	5	4.7	4.6	4.4	4.3	4.1	4.2	4.2	4.2	4.1
Per capita consumption of margarine (US) *Pounds (USDA)*	8.2	7	6.5	5.3	5.2	4	4.6	4.5	4.2	3.7

Correlation: 0.992558

Examples of Correlations:

1. Subway $ vs. Pizza $ (Inflation)

Correlation: the price of a ride on the subway tends to fall and rise with the price of a slice of pizza

The prices that pizza vendors choose to set for their pizza do not actually influence the pricing that the MTA sets for the subway

2. Bad Smells vs. Disease (Germs)

Correlation: The sick tended to smell unpleasant, appear together, so the two phenomena were correlated

Both were caused by a third variable Germs

The **difference** between correlation and causation

“Correlation helps you predict the future, because it gives you an indication of what’s going to happen. Causality lets you change the future!”

How to estimate the causal effect quantitatively?

Individual causal effects

Rubin causal model:

$$A \rightarrow Y$$

A: Intervention, exposure or treatment

Y: Outcome variable

- Indicator of treatment for unit i, where $i = 1, \ldots, N$

  $A_i = \begin{cases} 1 \text{ if unit } i \text{ received the treatment or under treatment} \\ 0 \text{ if unit } i \text{ did not reveive the treatment or under control} \end{cases}$

- Potential or Counterfactual outcome: Outcome that *would* have been realized if unit i received the treatment a (=0 or 1), denoted by $Y_i^a = \begin{cases} Y_i^0 \text{ Potential outcome for unit } i \text{ if untreated} \\ Y_i^1 \text{ Potential outcome for unit } i \text{ if treated} \end{cases}$

- Actual outcome: outcome actually observed based on the assigned treatment, denoted by Y_i.

Example:

$$A \rightarrow Y$$

A = no heart transplant or heart transplant (0/1);

Y = alive or death (0/1)

Data: Zeus: heart transplant → death

- Actual outcome for Zeus is Y_i=death
- Potential outcome for Zeus is ${Y_i}^{a=0}$ and ${Y_i}^{a=1}$
- **Individual Causal Effect** (ICE): causal effect of the treatment on the outcome for unit i is the difference between its two potential outcomes for individual i:

$$\tau_i = {Y_i}^1 - {Y_i}^0$$

- How potential outcomes (Y_i^0 and Y_i^1) relate to observed outcome Y_i?

  Assumption of **Consistency** (EPI), also called stable unit treatment value assumption (**SUTVA)** (ECON), implies no interference b/t units, one version of each treatment level:

  A subject i with observed treatment level $A_i = a$ has observed outcome Y_i and $Y_i = Y_i^a$. That is, observed outcome is the potential outcome of the observed treatment a.

  e.g. For Zeus: $Y_i^1 = 1$ is equal to his observed outcome Y=1.

  Zeus and Alice NOT influence each other and receive same version of medicine.

Fundamental problem of causal inference: we only can observe one potential outcome for each person (No Y_i^0 from Zeus)

Average causal effects (ACE)

Individual causal effects are fundamentally impossible

We instead focus on averages.

Assume we observe all units in the population of size *N*.

Definition: An average causal effect of treatment A on outcome Y is present if $E[Y^{a=1}] \neq E[Y^{a=0}]$ in the population of interest, that is "average outcome if all population units take the treatment (a=1) ≠ average outcome if all population units take no treatment (a=0)," can be measured by

$$\tau = E(Y^1 - Y^0) = \frac{1}{N}\sum_{i=1}^{N}[\,Y_i^1 - Y_i^0]$$

- Average of individual causal effect over the entire population

For example:

$$\tau = \frac{1}{N}\sum_{i=1}^{N}[Y_i^1 - Y_i^0]$$

Y: systolic blood pressure (BP)

A: Medicaid or no Medicaid

Interpretation of τ = -20mm Hg

In the population of hypertensive patients, if all had Medicaid, their average systolic blood pressure would be 20 mmHg lower than if they all had no Medicaid.

The fundamental problem of causal inference still there!

How to identify ACE τ?

Example: Zeus extended family (hypothetically)

Table 1.1

	$Y^{a=0}$	$Y^{a=1}$
Rheia	0	1
Kronos	1	0
Demeter	0	0
Hades	0	0
Hestia	0	0
Poseidon	1	0
Hera	0	0
Zeus	0	1
Artemis	1	1
Apollo	1	0
Leto	0	1
Ares	1	1
Athena	1	1
Hephaestus	0	1
Aphrodite	0	1
Cyclope	0	1
Persephone	1	1
Hermes	1	0
Hebe	1	0
Dionysus	1	0

Q: What is Average Causal Effect?

1) The proportion of individuals that would have developed the outcome had all population subjects received treatment $a = 1$ is $E(Y^1) = Pr[Y^{a=1} = 1] = \frac{10}{20} = 0.5$;

2) The proportion of individuals to develop outcome had all population subjects did not receive treatment $a = 0$ is

$E(Y^0) = Pr[Y^{a=0} = 1] = \frac{10}{20} = 0.5.$

Therefore, it does not matter whether all or none of the individuals receive a heart transplant: half of them would die in either case.

Measures of causal effects

Effect measures:

- Causal risk difference (RD, additive scale): compute the absolute number of cases of a disease attributable to the treatment

$$E(Y^1 - Y^0) = \Pr[Y^{a=1} = 1] - \Pr[Y^{a=0} = 1]$$

- Causal relative risk (RR, multiplicative scale): compute how many times the risk of disease increases with treatment, compared to no treatment $\frac{E(Y^1)}{E(Y^0)} = \frac{\Pr[Y^{a=1}=1]}{\Pr[Y^{a=0}=1]}$

- Causal Odds ratio (OR): compute how many…odds of disease…..

$$\frac{\mathrm{E}[Y^1]}{1-\mathrm{E}[Y^1]} \Big/ \frac{\mathrm{E}[Y^0]}{1-\mathrm{E}[Y^0]} \text{ or } \frac{\Pr[Y^{a=1}=1]}{\Pr[Y^{a=1}=0]} \Big/ \frac{\Pr[Y^{a=0}=1]}{\Pr[Y^{a=0}=0]}$$

For example: Imagine a large population in which 3 in a million individuals would develop the outcome if treated, and 1 in a million individuals would develop the outcome if untreated.

Compute the causal RD, RR

The causal risk ratio is 3 (*Having the treatment, relative to no treatment, increase disease risk by 3 times*), and the causal risk difference is 0.000002 (*2 in a million cases of the disease attributable to the treatment*)

The causal **RR** highlights how much more likely the outcome is in the treatment group, while the causal **RD** emphasizes the real-world implications of the treatment in terms of additional cases. The choice between them depends on the context and the audience for which you are presenting the findings.

Measures of Association

In the real world, we only get to observe one of potential outcomes

Table 1.2

	A	Y
Rheia	0	0
Kronos	0	1
Demeter	0	0
Hades	0	0
Hestia	1	0
Poseidon	1	0
Hera	1	0
Zeus	1	1
Artemis	0	1
Apollo	0	1
Leto	0	0
Ares	1	1
Athena	1	1
Hephaestus	1	1
Aphrodite	1	1
Cyclope	1	1
Persephone	1	1
Hermes	1	0
Hebe	1	0
Dionysus	1	0

Y: observed outcome

Using data in Table 1.2,

→ Proportion of subjects that developed the outcome Y=1 among those subjects who happened to receive treatment value a in the population

$Pr[\mathrm{Y} = 1|A = 1] = \frac{7}{13}$; $Pr[\mathrm{Y} = 1|A = 0] = \frac{3}{7}$

Associational risk difference, risk ratio, and odds ratio are:

1) $Pr[\mathrm{Y}=1|A=1]-Pr[\mathrm{Y}=1|A=0]$

2) $\frac{Pr[\mathrm{Y}=1|A=1]}{Pr[\mathrm{Y}=1|A=0]}$

3) $\frac{Pr[\mathrm{Y}=1|A=1]/\Pr[\mathrm{Y}=0|\mathrm{A}=1]}{Pr[\mathrm{Y}=1|A=0]/\Pr[Y=0|A=0]}$

- By definition: Independent $\mathrm{Y} \perp A$ if

$$Pr[\mathrm{Y}=1|A=1]=Pr[\mathrm{Y}=1|A=0];$$

Otherwise, Y and A are associated

- Associational RD, RR and OR (association measure) quantify the strength of the association
- In our example, tables 1.1 and 1.2 show NO causal effect from A→Y, but there IS an association between A and Y

In general, $ACE = E(Y^1 - Y^0) \neq E(Y|A = 1) - E(Y|A = 0)$

Right side: for example,

$E(Y|A = 1)$: Expected value of Y given A=1

- This is restricting to the subpopulation of people of actually had A=1. They might differ from the whole population in important ways.

  For example, people at higher risk for flu (Y=1) might be more likely to get a flu shot (A=1), average difference in Y between the treatment group and the control group would have **selection bias** to estimate the ACE

Left side:

- $E(Y^1)$: mean of Y if the whole population was treated
- $E(Y^0)$: mean of Y if NO one in the whole population was treated

Assumptions to Make Connections between associational and causal effect

In order to identify Average Causal Effect:

- Recall: Stable-unit-treatment-value-assumption (**SUTVA**), also called **Consistency** (in Epidemiology):

$$E(Y^a|A = a) = E(Y|A = a)$$

- **Ignorability or Unconfoundedness or Exchangeability**

$$E(Y^a|A = a) = E(Y^a|A \neq a) = E(Y^a)$$

  - If a=0, $E(Y^0|A = 0) = E(Y^0|A = 1) = E(Y^0)$: The mean potential outcome under control, Y^0, for those in the *control* group (A=0) is same as those in the treatment group (A=1).

- If a=1, $E(Y^1|A = 1) = E(Y^1|A = 0) = E(Y^1)$: The mean potential outcome under treatment, Y^1, for those in the *treatment* group (A=1) is same as those in the *control* group (A=0).

In summary, treated and the untreated would have experienced the same risk of outcome if they had received the same treatment level (either A = 0 or A = 1). This means that the individuals in the treatment and control groups are ***exchangeable***. We have:

$$ACE = E(Y^1) - E(Y^0) = E(Y^1|A = 1) - E(Y^0|A = 0)$$

This assumption can be achieved by **random assignment** of individuals to treated and untreated group (in a randomized experiment).

- **Positivity**

  There is a probability greater than zero–a **positive** probability–of being assigned to each of the treatment levels.

$$1 > \Pr(A = a) > 0 \text{ for all } a$$

  There are no certain individuals (groups) are always treated or never treated.

Example:

a) Assuming positivity assumption hold, use the hypothetical data provided (next slide) to assess the two assumptions: Consistency, Exchangeability.

b) If all three assumptions (Consistency, Exchangeability, and Positivity) hold, can the causal risk difference (RD) be estimated using the associational RD?

id	**A**	Y^1	Y^0	**Y**
1	**1**	10	3	**10**
2	**1**	16	5	**16**
3	**1**	14	7	**14**
4	**1**	12	10	**12**
5	**1**	16	9	**16**
6	**1**	10	11	**10**
7	**1**	8	13	**8**
8	**1**	9	5	**9**
9	**1**	13	7	**13**
10	**1**	13	10	**13**
11	**1**	19	9	**19**
12	**1**	17	11	**17**
13	**1**	12	4	**12**
14	**0**	10	6	**6**
15	**0**	8	8	**8**
16	**0**	13	10	**10**
17	**0**	16	5	**5**
18	**0**	9	6	**6**
19	**0**	15	13	**13**
20	**0**	20	8	**8**

Consistency: observed outcome under the actual treatment a subject received Y|A=a is equal to the potential outcome under that treatment Y^a. In other words, for a subject who received treatment (A = 1), their observed outcome (Y) should equal their potential outcome Y^1 (outcome if treated). Similarly, for a subject who did not receive treatment (A = 0), their observed outcome should equal Y^0 (outcome if untreated): Check if the observed outcome Y matches the corresponding potential outcome (Y^1 for treated, Y^0 for untreated) for each individual.

To assess **Exchangeability** using the provided data, we need to check whether the potential outcome distributions are comparable between the treated (A=1) and untreated (A=0) groups: you would typically visualize the distributions of Y^1 and Y^0 in each group using histograms or summary statistics or some statistical testing.

Directed Acyclic Graphs (DAGs)

Directed Acyclic Graphs (DAGs)

We can describe the assumed causal relationships by DAGs.

"**Directed**" because each arrow implies a direction: because the arrow from A to B is into B, A may cause B, but not the other way around.

"**Acyclic**" because there are no cycles: a variable cannot cause itself, either directly or through another variables.

DAG composed of:

- Nodes: representing variables in the causal model
- Directed edges or arrows: representing possible causal effect

- A→ Y

  This is a directed graph with two nodes A and Y and 1 edge from A to Y (A→Y)

- A – Y

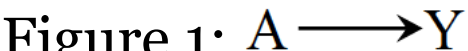
  This is an undirected graph

In summary:

Directed acyclic graphs (DAGs)

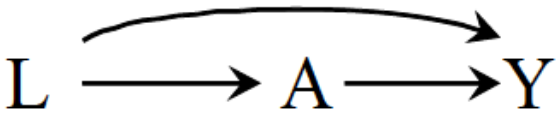
1. No undirected paths
2. No cycles

Causal diagrams and marginal independence

Figure 1: 

- Causal effect from A to Y.
- $\Pr[Y^{a=1} = 1] - \Pr[Y^{a=0} = 1] = E(Y^1 - Y^0) \neq 0$
- Individuals are randomly assigned to heart transplant (A) with the same probability to study causal effect from A to Y (death)

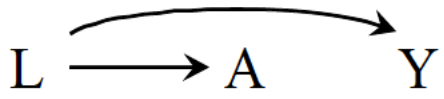
- Suppose individuals are randomly assigned to heart transplant (A) with a probability that depends on their *disease severity* (L).

Figure 2: 

- Information from L flows to both A and Y (Fork)
- E.g., *L* (disease severity) is a common cause of A (Heart Transplant) and Y (Death), *L* is called confounder.

- Information also flows from L→A→Y (Chain).
- Effect of L on Y is not direct but occurs through A, and A is a mediator between L and Y

Figure 3

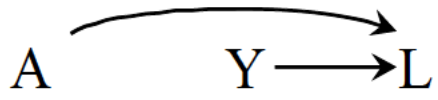


- Information flow from L to A and from L to Y, but there is no information flow from A to Y
- E.g. Cigarette smoking (L) has a causal effect on both

  carrying a lighter (A) and lung cancer (Y). However, carrying a lighter has NO causal effect on anyone's risk of lung cancer, i.e., $\Pr[Y^{a=1} = 1] = \Pr[Y^{a=0} = 1]$

Question: Are A and Y marginally independent (no statistical association), i.e., $\Pr[Y = 1|A = 1] = \Pr[Y = 1|A = 0]$ in Figures 1 - 3?

Figure 4



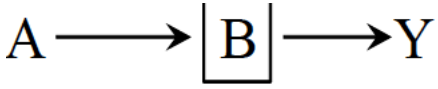
- Both A and Y affects L (collider), no information flow from L to either A or Y (Inverted forks). No information can be reached from A to Y or Y to A (collision).
- E.g. A is "getting the flu" and Y is "getting hit by a bus," with L "being in the hospital." Getting the flu doesn't cause someone to get hit by a bus, so no causal effect of A on Y.
- E.g. Haplotype A does not have a causal effect on air pollution (Y); however, both haplotype A and air pollution (Y) do have causal effects on lung cancer (L).

Q: A and Y are marginally independent in Figure 4?

In Summary from Figures 1-4

Two variables are (marginally) associated/correlated if one causes the other, or if they share common causes. Otherwise, they will be (marginally) independent (e.g. if they have common effect).

Causal diagrams and conditional independence

Figure 5: 

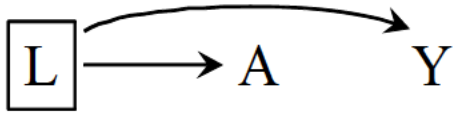
- The box placed around the node B: Restrict the analysis to the subset of individuals with specified level of B
- In the subset of individuals, say B = 0, treatment A and outcome Y are independent: $\Pr[Y = 1|A = 1, B = 0] = \Pr[Y = 1|A = 0, B = 0]$

Question: is there an A-Y association within levels of B (conditional independent)?

E.g., parental involvement → study time → academic performance

Graphically, a box placed around variable B blocks the flow of information through the chain path A → B → Y.

Figure 6

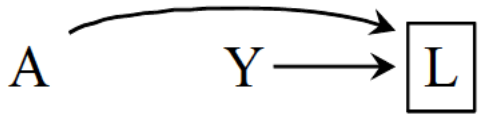


<u>Question</u>: is there A - Y association conditional on L?

- Even though A and Y are marginally associated, A and Y are conditionally independent given L
- E.g. Given a specified smoking level (L), the risk of lung cancer (Y) is the same for people with and without lighters (A): $P[cancer = 1|ligher = 1, smk = l] = P[cancer = 1|lighter = 0, smk = l]$ for all l

Graphically, the flow of information between A and Y is interrupted because the fork path is A ← L → Y is blocked by the box round L.

Figure 7

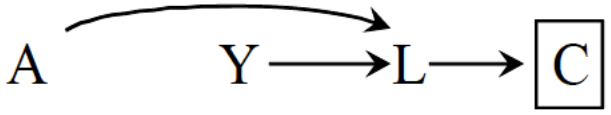


<u>Question</u>: is there an A - Y association conditional on L?

- Back to haplotype/air pollution example: <u>Given a subject with lung cancer (L),</u> the absence of haplotype A provides insight into her air quality. Without haplotype A, it is more likely that another cause of lung cancer, air pollution, is contributing to the outcome
- Back to flu/bus example: conditional on <u>being in the hospital (L)</u>, there is negative relationship between the flu and getting hit by bus (A and Y).

Graphically, A and Y are conditionally and inversely associated within levels of their common effect L.

Figure 8



- A and Y are conditionally and inversely associated within levels of C because C is a common effect of A and Y.
- E.g. back to haplotype/air pollution example

  C: Steroids medication, whose use is a consequence of a diagnosis of lung cancer.

In summary

Three structural reasons why two variables may be *associated* (information flow from one to the other variable):

- One causes the other (chains)
- They share common causes (fork)s, or
- They share a common effect but the analysis is restricted to certain level of that common effect (conditional on colliders or their descendants).

Blocking information to achieve independence

- A→G→B: Condition on G in Chains, we block the path A to B, For example: Outside temp. → Whether or not sidewalks are icy → whether or not someone falls.

- Conditional on the confounders in Forks
- Unconditional on Colliders or their descendants
    1. A is the state of an on/off switch
    2. B is the state of a different on/off switch
    3. G is whether the lightbulb is lit up

  A and B are *independent*: If I tell you that B is on, it tells you nothing about A; A and B are *dependent*: Given G, if I tell you that the light is off (G), then A must be off if B is on, and vice versa. You open a path by blocking G.

Rules for d-separation of a path

- Control for a set of notes (C) that separate two variables on given paths to achieve independence between variables:

- Contains a chain and the middle part of the chain is in C
- Contains a fork and the middle part of the fork (i.e. the confounder) is in C
- Contains an inverted fork and the middle part of the fork (i.e. the collider or any descendants of it) is **not** in C

Two nodes, A and B, are d-separated by a set of nodes C if C blocks every path from A to B, denoted by $A \perp B|C$.

Example:

Identify all nodes: X, Y, Z_1, Z_2, Z_3

Identify all paths from X to Y:

$X \leftarrow Z_3 \rightarrow Y$

$X \leftarrow Z_1 \rightarrow Z_3 \rightarrow Y$

$X \leftarrow Z_3 \leftarrow Z_2 \rightarrow Y$

$X \leftarrow Z_1 \rightarrow Z_3 \leftarrow Z_2 \rightarrow Y$

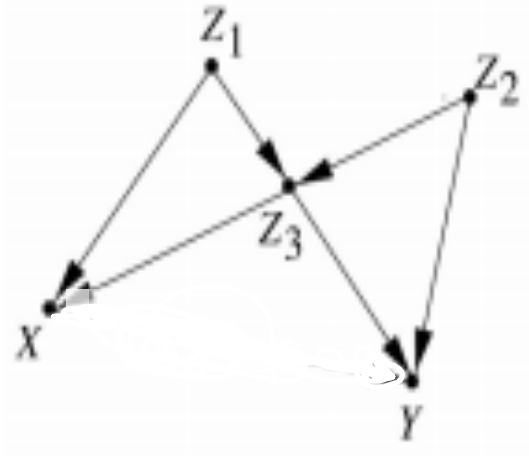


Figure 9

Z_1 is parent of X and Z_3; X and Z_3 are children of Z_1

Z_1 is ancestor of Y. Y is a descendant of Z_1

- X and Y are d-separated by set C=$\{Z_1, Z_2, Z_3\}$. How about $\{Z_3\}$ or (Z_2, Z_3) or (Z_1, Z_3) or (Z_1, Z_2)?
- List C variables to d-separate Z_1 and Z_2?

Pearl's back-door criterion is a way to rule out confounding via conditioning, thus identifying the causal effect of one variable on another. For identifying the causal effect of X on Y, the backdoor criterion has two parts:

First, the conditioning set C may not include any descendent of X. That means, anything that X affects cannot be conditioned on (c.f. post-treatment bias).

Second, the conditioning set C must block all back-door paths from X to Y. That is, by conditioning on our set C, we should break any back-door paths that may simultaneously generate confounded covariance in X and Y.

- Which of the following are NOT back door paths from X to Y?

1. $X \leftarrow Z_3 \rightarrow Y$
2. $X \rightarrow W_3 \rightarrow Y$
3. $X \leftarrow W_1 \leftarrow Z_1 \rightarrow Z_3 \rightarrow Y$
4. $X \leftarrow Z_3 \leftarrow Z_2 \rightarrow W_2 \rightarrow Y$
5. $X \leftarrow W_1 \leftarrow Z_1 \rightarrow Z_3 \leftarrow Z_2 \rightarrow W_2 \rightarrow Y$

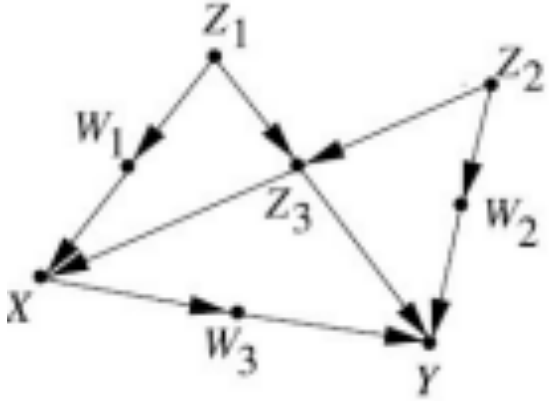


Figure 10

- <u>Which set of variables</u> should be controlled for in order to identify the causal effect from X to Y?

  a) $\{W_1, W_2\}$; b) $\{Z_1, Z_2\}$; c) $\{Z_1, Z_3\}$; d) $\{Z_3, W_3\}$; e) $\{Z_3\}$

In-class practices:

1. Researchers are studying the relationship between **physical activity** and **heart disease**. They believe the following factors are relevant:

   - **Age** (Older people tend to exercise less and are more prone to heart disease.)
   - **Smoking** (Smoking is associated with lower levels of physical activity and increased risk of heart disease.)
   - **Genetic Predisposition** (Some individuals are genetically predisposed to heart disease, regardless of their physical activity level.)

1)Draw a DAG that represents the relationships above.

2)What are the potential confounders? Should you adjust for them?

2. In a study on the effects of **diet** on **diabetes**, researchers collect data from individuals attending a specialized clinic. They believe the following relationships exist:

   - **Exercise** reduces the risk of diabetes.
   - **Diet** and **Exercise** are related (people who exercise are more likely to maintain a healthy diet).
   - **Clinic Attendance** is influenced by both **Exercise** and **Diabetes** (people who exercise less and have diabetes are more likely to attend the clinic).

1) Draw a DAG for this scenario, including the above variables.
2) What is the variable **Clinic Attendance** called in DAG?
3) What impact would adjusting for **Clinic Attendance** have on the analysis of the relationship between **Diet** and **Diabetes**?

3. Researchers are studying the effect of **education level** on **income**. They believe that **job type** is a mediator (i.e., higher education leads to better job opportunities, which in turn increases income). Additionally, they suspect that **family background** influences both **education** and **income**.

Questions:

1) Draw a DAG that includes the above variables.

2) Is **Job Type** a mediator or confounder in this DAG?

3) To measure direct causal effect from education on income, what are the variables you need to control?

4. You are tasked with investigating the relationship between **air pollution** and **asthma** in children. Consider the following:

   - **Parental Smoking** increases the likelihood of both **air pollution exposure** and **asthma** in children.
   - **Living in an urban area** increases exposure to **air pollution** but is not directly related to **asthma**.

Questions:

1) Draw a DAG including the above variables.
2) What are the confounders you should adjust for?
3) Should you adjust for **Urban Living**? Explain why or why not based on your DAG.

R package to draw DAG

```
# Install the packages if not already installed
install.packages("ggdag")
install.packages("dagitty")
install.packages("ggplot2")

library(ggdag)
library(dagitty)
library(ggplot2)

####-----Example
dag = dagify(y.HrtDis ~ x.Phy.Act + Age + Smoking + Gene,
             x.Phy.Act ~ Age + Smoking,
             exposure = "x.Phy.Act",
             outcome = "y.HrtDis")

ggdag(dag, node_size=20, text_size=3.5, edge_type="link",label_size = 4)
  + theme_dag_blank()
```