MEASUREMENT BIAS

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LEARNING OBJECTIVES.

By the end of the session, you will be able to:

1. Define measurement error
2. Graphically represent independent/dependent errors and differential/non-differential errors

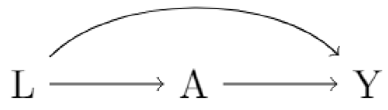
PLAN FOR TODAY: MEASUREMENT BIAS.

1. Recap
2. Measurement bias
3. Measurement error in the exposure or in the outcome
   a) Independent versus dependent measurement error
   b) Non-differential versus differential measurement error
4. Measurement error in the covariates
5. Approaches to measurement error
6. Measurement error example
7. Summary

RECALL: CONFOUNDING AND SELECTION BIAS.

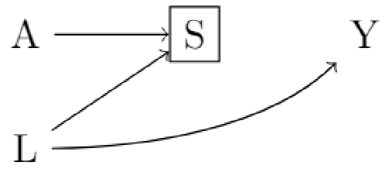
So far, we've focused on methods to address two main structural sources of bias: confounding and selection bias.

Confounding



- Common cause of exposure (A) and outcome (Y)
- Methods to address confounding include stratification, regression, standardization, propensity scores, IPTW

Selection bias



- Selection (S) of participants into a study and/or analysis
- Conditioning on a collider
- Methods to address selection bias include stratification, IPCW

AN ADDITIONAL SOURCE OF BIAS: MEASUREMENT BIAS.

- All our previous analyses assumed that all variables were perfectly measured
- Fairly unrealistic assumption – errors in measurement are often unavoidable
- Measurement bias can affect both randomized trials and observational studies

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MEASUREMENT BIAS.

- Arises from imperfect definition of study variables or flawed data collection procedures
- Also referred to as information bias, misclassification bias, recall bias, recall error
- Can result in:
  - Biased estimates
  - Incorrect confidence intervals
  - Spurious detection of effect modification

- Notation:
  - X: true value of variable X
  - X^*: measured value of variable X

- If $X \neq X^*$, then we have measurement bias
- E.g., in our randomized trial and observational study, we have data on A^* and Y^* but we're actually interested in A and Y
- Direction of the bias will depend on the structure of the measurement error

MEASUREMENT BIAS IN A DAG.

In a DAG, we may depict measurement error as follows:

$$\begin{array}{c} U_A \\ \downarrow \\ A^* \\ \uparrow \\ A \end{array}$$

- A is the true exposure
- A^* is the measured exposure
- U_A is the error in measuring the exposure (i.e. factors other than A that determine the value of A^*)

We can have something similar for the outcome as well:

$$\begin{array}{c} U_Y \\ \downarrow \\ Y^* \\ \uparrow \\ Y \end{array}$$

- Y is the true exposure
- Y^* is the measured exposure
- U_Y is the error in measuring the exposure (i.e. factors other than Y that determine the value of Y^*)

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INDEPENDENCE AND NON-DIFFERENTIALITY OF MEASUREMENT ERRORS.

When considering measurement error in the exposure and/or outcome, we look at the structure of these errors relative to each other and to the true value of the exposure or outcome.

Independent errors

- Error for the exposure (U_A)and error for the outcome (U_Y) are independent

$$f(U_Y, U_A) = f(U_Y)f(U_A)$$

Non-differential errors

- Error for the exposure is independent of the true value of the outcome

$$f(U_A|Y) = f(U_A)$$

- Error for the outcome is independent of the true value of the exposure

$$f(U_Y|A) = f(U_Y)$$

FOUR TYPES OF STRUCTURES FOR INFORMATION BIAS.

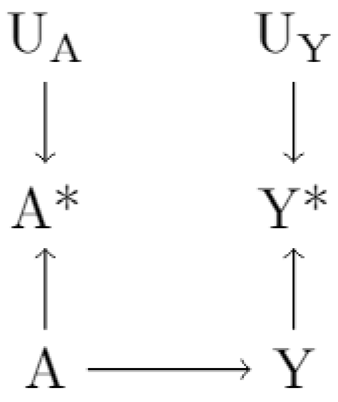
Can classify measurement error in the treatment and outcome as being

- Independent vs. dependent
- Nondifferential vs. differential

This gives us four types of measurement error:

1. Independent nondifferential
2. Dependent nondifferential
3. Independent differential
4. Dependent differential

(1) INDEPENDENT NONDIFFERENTIAL ERRORS.



Measurement errors U_A and U_Y are:

- Independent: the path from U_A to U_Y is blocked by colliders (A^* and Y^*)
- Non-differential: error for the exposure, U_A, is independent of the true outcome, Y (and similarly, U_Y is independent of A)

Example:

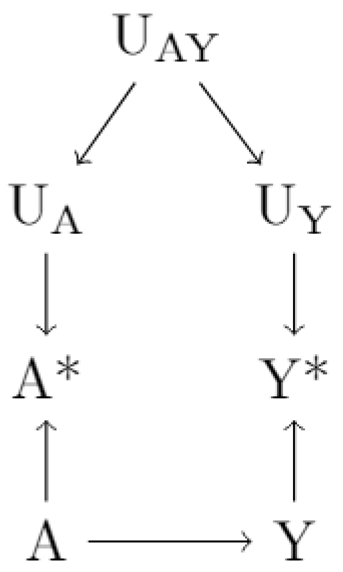
A: Vitamin D status

A^*: Self reported vitamin D intake using a food frequency questionnaire

Y: Mortality

Y^*: National Death Index

(2) DEPENDENT NONDIFFERENTIAL ERRORS.



Measurement errors U_A and U_Y are:

- Dependent: U_A to U_Y are associated through a common cause, U_{AY}
- Non-differential: error for the exposure, U_A, is independent of the true outcome, Y (and similarly, U_Y is independent of A)

Example:

A: Childhood chemical hair product use

A^*: Retrospectively self reported via questionnaire

Y: Age at menarche

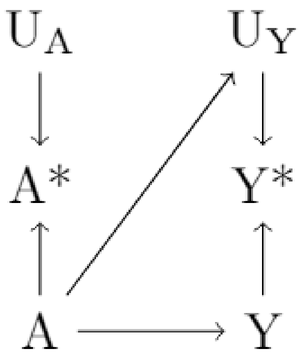
Y^*: Retrospectively self-reported via questionnaire

U_{AY}: Memory

(3) INDEPENDENT DIFFERENTIAL ERRORS.

Measurement errors U_A and U_Y are:

- Independent: the paths from U_A to U_Y is blocked by colliders (A^* or Y^*)
- Differential: U_A is associated with Y, or U_Y is associated with A

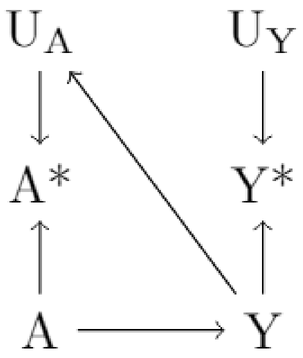


Example 1: error for the outcome is differential with respect to the exposure (i.e. U_Y is associated with A)

A: Elective surgery

Y: Quality of life

Y^*: Self-reported via questionnaire



Example 2: error for the exposure is differential with respect to the outcome (i.e. U_A is associated with Y)

A: Oral contraceptive use

A^*: Self-reported after knowing outcome status (e.g. case-control study)

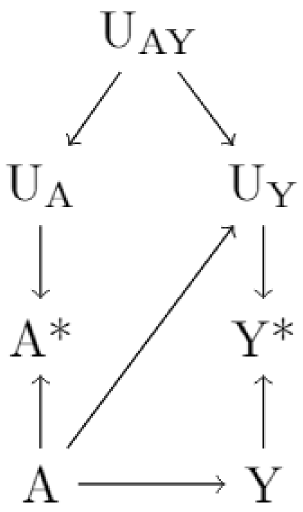
Y: Breast cancer

Note: often referred to as recall bias

(4) DEPENDENT DIFFERENTIAL ERRORS.

Measurement errors U_A and U_Y are:

- Dependent: U_A to U_Y are associated through a common cause, U_{AY}
- Differential: U_A is associated with Y, or U_Y is associated with A

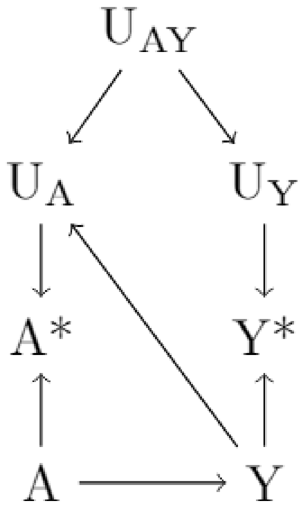


Example 1: error for the outcome is differential with respect to the exposure (i.e. U_Y is associated with A) and dependent errors

A: Chemotherapy

Y: Cancer progression

A^* and Y^*: Retrospectively collected using medical records



Example 2: error for the exposure is differential with respect to the outcome (i.e. U_A is associated with Y) and dependent errors

A: Cholesterol intake

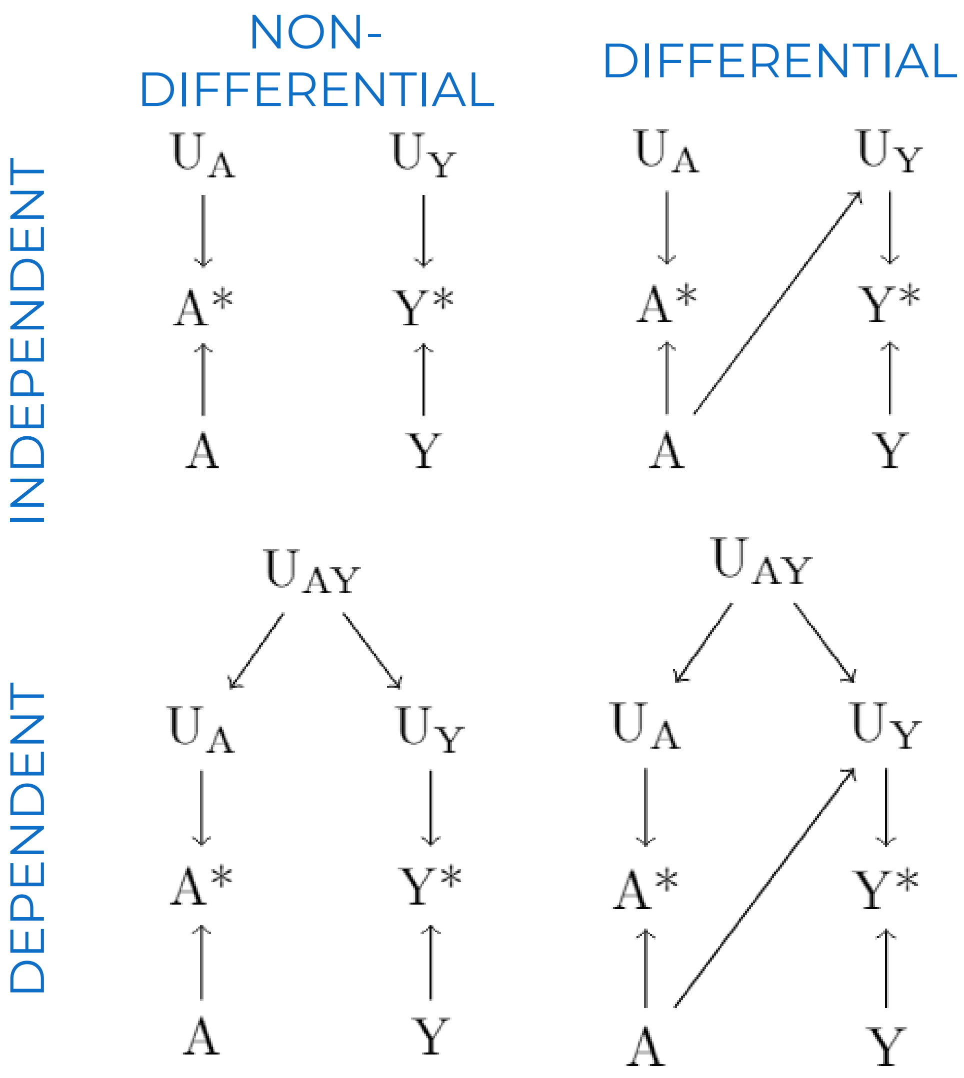
A^*: Retrospectively assessed via FFQ

Y: Dementia

Y^*: Self-reported dementia

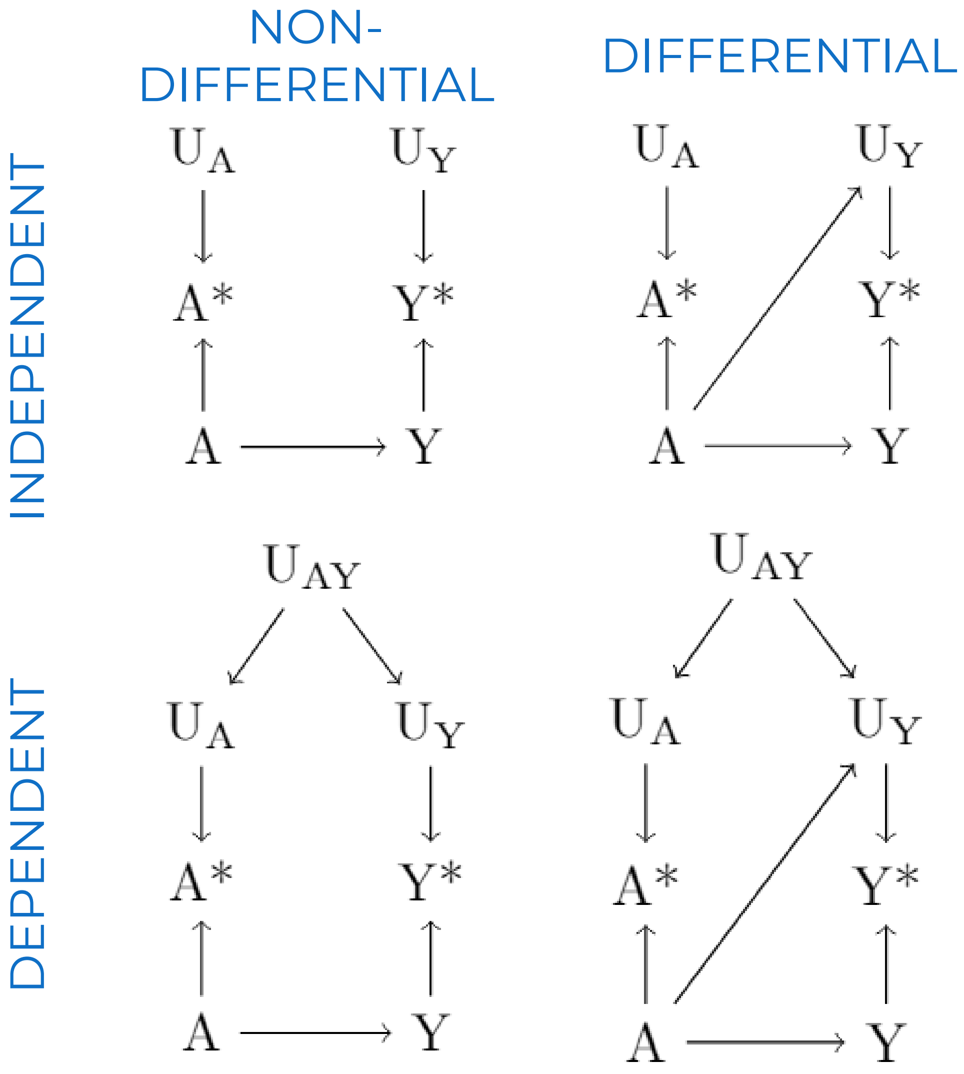
WHEN DOES MEASUREMENT ERROR CREATE BIAS?

- Bias arises from using A^* and Y^* to estimate the association between A and Y
- If we are under the null:
  - No bias if errors are independent and non-differential
  - Biased under all other scenarios (in any direction)



WHEN DOES MEASUREMENT ERROR CREATE BIAS?

- Bias arises from using A^* and Y^* to estimate the association between A and Y
- If we are not under the null:
  - Biased in all scenarios
  - Under certain (but not all) scenarios, expect independent nondifferential errors to bias towards null
  - Bias can be in any direction for others



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MEASUREMENT ERROR IN THE COVARIATES.

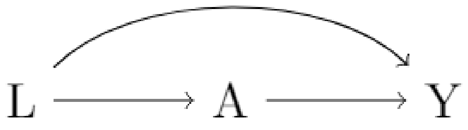
Similar to the notation that we used for measurement error in the exposure and outcome, we denote:

- L is the true value
- L^* is the measured value of the covariate L

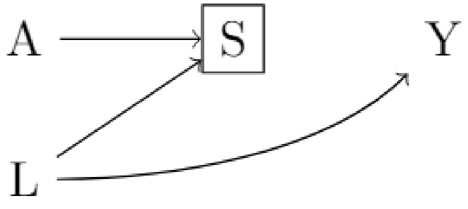
RESIDUAL BIAS DUE TO MEASUREMENT ERROR.

We may need to adjust for covariates L in order to address confounding or selection bias:

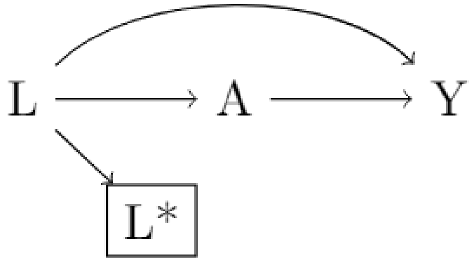
Confounding



Selection bias



If there is measurement error in L, then we are adjusting for L^*, not L:



- L^* acts as a surrogate confounder
- Partially blocks backdoor path but there is still residual confounding
- Could create more bias if the mismeasurement is in different directions relative to the exposure

EFFECT HETEROGENEITY DUE TO MEASUREMENT ERROR.

Measurement error in L can also make it look like an effect modifier. For example, suppose we have measured L^*:

- Among people with $L^* = 1$: everyone has $L = 1$ (i.e., those individuals were measured perfectly)
- Among people with $L^* = 0$: half of them have $L = 1$ and half of them have $L = 0$ (i.e., we have measurement error for *half* of the people with $L^* = 0$)

If A has no effect on Y, and we stratify on L^*:

- In the $L^* = 1$ strata: we'll find no association between A and Y because those people all have $L = 1$ (we've properly adjusted for confounding)
- In the $L^* = 0$ strata: we'll find an association between A and Y because we still have confounding (some people have $L = 0$ and some people have $L = 1$)

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APPROACHES TO MEASUREMENT ERROR.

Measurement error is difficult to address, because we don't have the true values of our mismeasured variables.

"No measurement error" is an untestable assumption.

Two general approaches to measurement error:

1. Conservative inference

- If errors are independent and non-differential, will sometimes bias towards null
- Researchers will
  - Make the argument that the measurement error in their study creates bias towards the null
  - Any association observed is a conservative estimate of the true causal effect

APPROACHES TO MEASUREMENT ERROR.

Measurement error is difficult to address, because we don’t have the true values of our mismeasured variables.

“No measurement error” is an untestable assumption.

Two general approaches to measurement error:

1. Conservative inference
2. Correction methods

Need an internal or external validation study to assess the extent of measurement error

- E.g., measure L^* and L in a smaller subset of a larger cohort
- Methods include regression calibration, multiple imputation

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EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

Let's suppose we design a randomized trial of to assess the effect of sleep medications on sleep deprivation.

Let's build a DAG to see how measurement bias could affect this study:

A: sleep medication

Y: sleep deprivation

$$A \longrightarrow Y$$

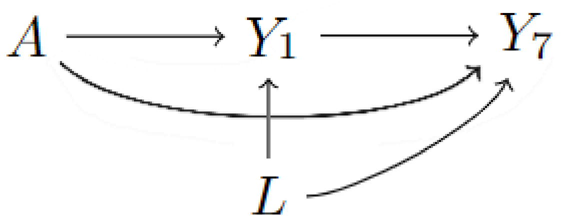
EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

Sleep deprivation is measured at day 1 and day 7 of follow-up

- Turn the node for Y into two nodes that represent the outcome measured at each of those time points:

$$Y_1 \text{ and } Y_7$$

- There may be common causes of sleep deprivation at the two time points: L



A: sleep medication use

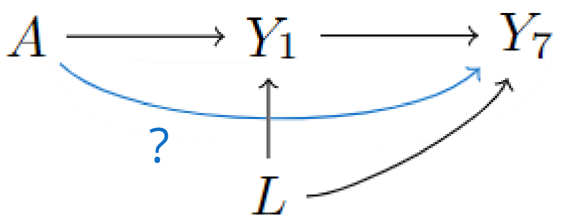
Y_1: sleep deprivation on day 1
Y_7: sleep deprivation on day 7

L: common causes of sleep deprivation measures

EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

Suppose we are interested in the direct effect of A on Y_7:

- Only interested in the direct path from A to Y_7
- Long term effect of sleep medications on sleep deprivation *not* mediated by its immediate effects on sleep deprivation



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EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

Suppose we are interested in the direct effect of A on Y_7:

- Only interested in the direct path from A to Y_7
- Long term effect of sleep medications on sleep deprivation *not* mediated by its immediate effects on sleep deprivation
- For simplicity, let's draw this DAG under the null (no direct effect of A on Y_7)

A: sleep medication use

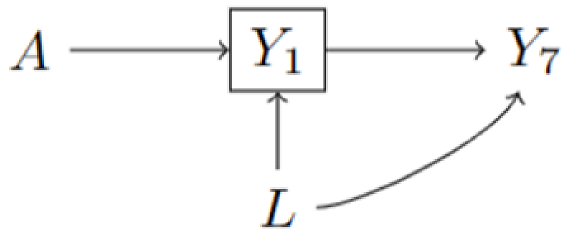
Y_1: sleep deprivation on day 1

Y_7: sleep deprivation on day 7

L: common causes of sleep deprivation measures

$$
\begin{tikzcd}
A \arrow[r] & Y_1 \arrow[r] & Y_7 \\
 & L \arrow[u] \arrow[ur, bend right] &
\end{tikzcd}
$$

MEASUREMENT ERROR: POLL QUESTION 1.



A: sleep medication use
Y_1: sleep deprivation on day 1
Y_7: sleep deprivation on day 7
L: common causes of sleep deprivation measures

What happens if we condition on Y_1?

A. We block the path: $A \rightarrow Y_1 \rightarrow Y_7$
B. We open the path: $A \rightarrow Y_1 \leftarrow L \rightarrow Y_7$
C. We block the path: $A \rightarrow Y_7$
D. A and B
E. A and C
F. B and C
G. A, B and C

EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

Conditioning on Y_1:

- Blocks the $A \rightarrow Y_1 \rightarrow Y_7$ path
- Opens the $A \rightarrow Y_1 \leftarrow L \rightarrow Y_7$ path

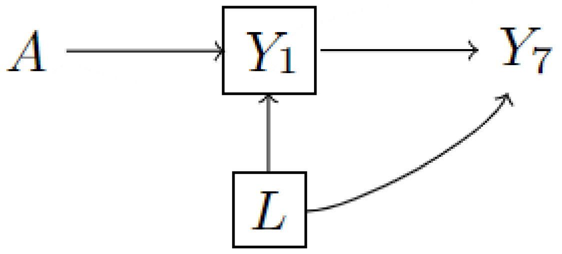
A: sleep medication use

Y_1: sleep deprivation on day 1
Y_7: sleep deprivation on day 7

L: common causes of sleep deprivation measures

The $A \rightarrow Y_1 \leftarrow L \rightarrow Y_7$ path is a form of selection bias

- Need to also adjust for L



EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

We measure sleep deprivation using a reaction test:

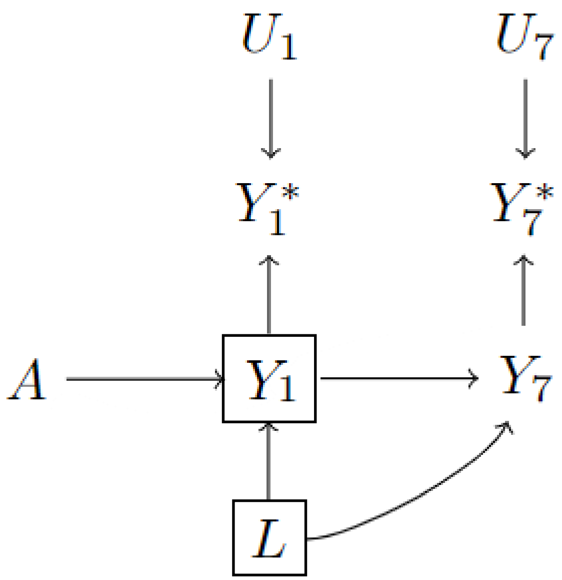
Y_1^*: results from the reaction test on day 1

Y_7^*: results from the reaction test on day 7

There are other factors that affect one's performance on the reaction test:

U_1: measurement error on day 1

U_7: measurement error on day 7



A: sleep medication use

Y_1: sleep deprivation on day 1
Y_7: sleep deprivation on day 7

L: common causes of sleep deprivation measures

Y_1^*: reaction test results on day 1
Y_7^*: reaction test results on day 7

U_1: measurement error on day 1
U_7: measurement error on day 7

MEASUREMENT ERROR: POLL QUESTION 2.

$$\begin{tikzcd} & U_1 \arrow[d] & U_7 \arrow[d] \\ & Y_1^* & Y_7^* \\ A \arrow[r] & Y_1 \arrow[u] \arrow[r] & Y_7 \arrow[u] \\ & L \arrow[u] \arrow[ur, bend right] & \end{tikzcd}$$

A: sleep medication use

Y_1: sleep deprivation on day 1
Y_7: sleep deprivation on day 7

L: common causes of sleep deprivation measures

Y_1^*: reaction test results on day 1
Y_7^*: reaction test results on day 7

U_1: measurement error on day 1
U_7: measurement error on day 7

What type of measurement error do we have for the outcome on day 1 and the outcome at day 7?

A. Independent nondifferential
B. Dependent nondifferential
C. Independent differential
D. Dependent differential

EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

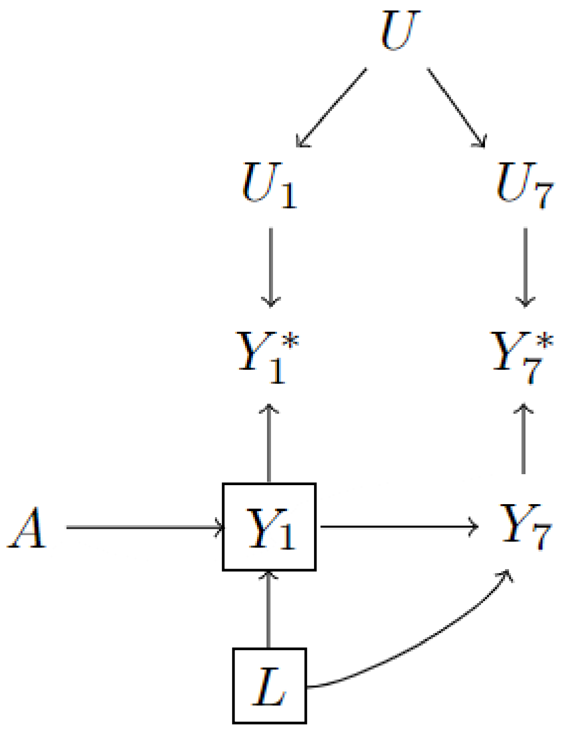
Even with this measurement error, there's no bias under the null.

- No biasing paths from A to Y_7^*

What if we add in factors that affect both the measurement error for the outcome at day 1 and at day 7?

- E.g., age, gender, physical fitness

Need to add a common cause of U_1 and U_7 to our DAG



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L: common causes of sleep deprivation measures

Y_1^*: reaction test results on day 1
Y_7^*: reaction test results on day 7

U_1: measurement error on day 1
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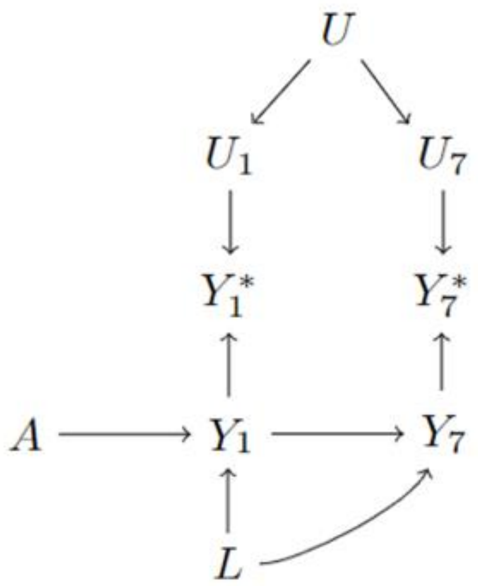
U: common causes of measurement errors

MEASUREMENT ERROR: POLL QUESTION 3.



A: sleep medication use

Y_1: sleep deprivation on day 1
Y_7: sleep deprivation on day 7

L: common causes of sleep deprivation measures

Y_1^*: reaction test results on day 1
Y_7^*: reaction test results on day 7

U_1: measurement error on day 1
U_7: measurement error on day 7

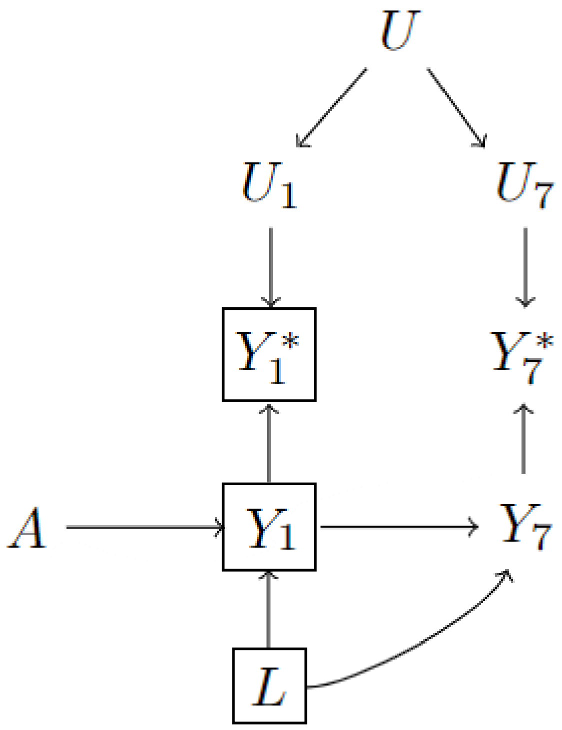
U: common causes of measurement errors

In the updated DAG, what type of measurement error do we have for the outcome on day 1 and the outcome at day 7?

A. Independent nondifferential
B. Dependent nondifferential
C. Independent differential
D. Dependent differential

EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

- Even with dependent nondifferential errors, we don't have bias under the null here
  - No biasing paths from A to Y_7^*
- However, in our analysis, we're not actually conditioning on sleep deprivation at day 1 (Y_1)
  - Unmeasured
- Conditioning on results of the reaction test on day 1 (Y_1^*)



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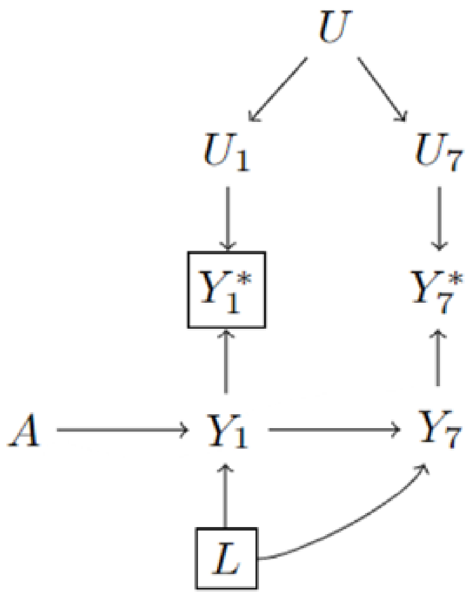
MEASUREMENT ERROR: POLL QUESTION 4.



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Y_1^*: reaction test results on day 1
Y_7^*: reaction test results on day 7

U_1: measurement error on day 1
U_7: measurement error on day 7

U: common causes of measurement errors

What happens when we condition on Y_1^* instead of Y_1?

A. Nothing, there are no biasing paths between A and Y_7^*.

B. We are no longer blocking the path mediated by Y_1.

C. We have introduced selection bias for the effect of A on Y_7^*.

D. A and B

E. A and C

F. B and C

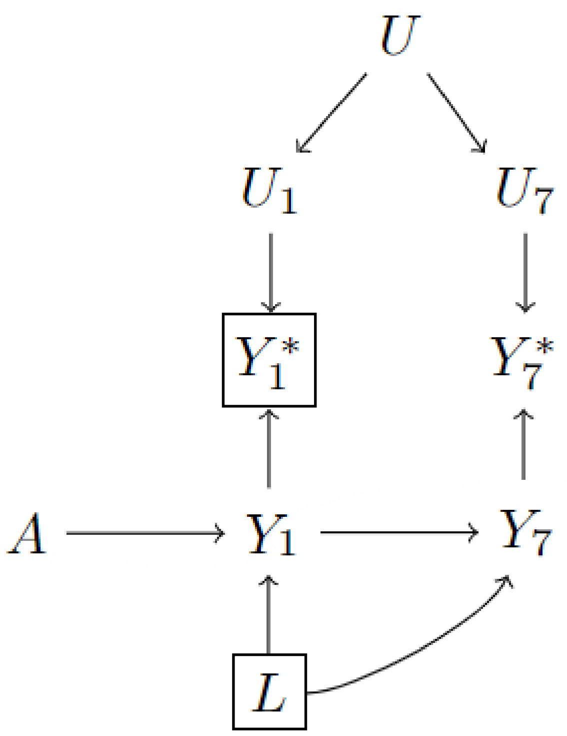
G. A, B and C

EXAMPLE: SLEEP MEDICATIONS AND SLEEP DEPRIVATION.

- We are no longer fully blocking the path from A to Y_7^*
- We are introducing selection bias through the path:

  $$A \to Y_1 \to Y_1^* \leftarrow U_1 \leftarrow U \to U_7 \to Y_7^*$$

- When we have a longitudinal outcome measured with error, need to be careful about conditioning on baseline or intermediate measures of the outcome



A: sleep medication use

Y_1: sleep deprivation on day 1
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Y_1^*: reaction test results on day 1
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U_1: measurement error on day 1
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By the end of the session, you will be able to:

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CAUSAL INFERENCE IS HARD!

We need to be aware of the assumptions that we're making:

- Conditional exchangeability
- Positivity
- Consistency

As well as potential threats to validity:

- Confounding
- Selection bias
- Measurement bias

With finite data, we also need to think about:

- Our modelling assumptions
- The role of chance

Strategies for better and more transparent research:

- Have a clear and well-defined research question
- Make your assumptions explicit (e.g. DAGs)
- Consider the target trial that you are trying to emulate

CAUSAL INFERENCE IS HARD!

In this course, we've primarily focused on:

- Time-fixed treatments
- Dichotomous treatments

However, most treatments of interest are time-varying, e.g.

- Medication use over time
- Diet
- Air pollution exposure

With time-varying treatments, the analyses become much more complex:

- Need to handle repeated measurements of the exposure and confounders
- Possible treatment-confounder feedback
- Need to use appropriate methods to address this (i.e., IPW and g-formula)

More on this in CI732!