

2. The Target Trial

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Cornell Info 6751: Causal Inference in Observational Settings
Fall 2022

25 Aug 2022

Learning goals for today

At the end of class, you will be able to:

1. Define the target trial (hypothetical experiment) that a causal study seeks to emulate
2. Understand how the target trial clarifies causal questions

Logistics

- ▶ Problem Set 1 is due on Monday at 5pm on Canvas
- ▶ We are getting one or more TAs

Logistics

From Tuesday's reading

Randomized experiments: Two key benefits

- Exchangeability

- Precise questions

Group Exercises

General discussion

Logistics

From Tuesday's reading

Randomized experiments: Two key benefits

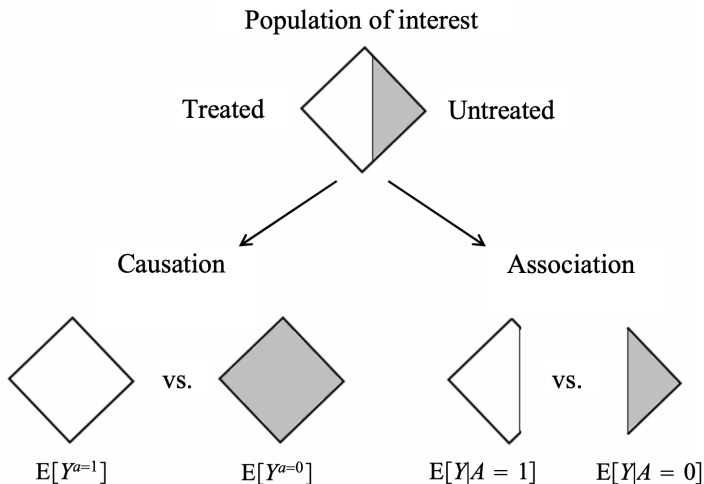
Exchangeability

Precise questions

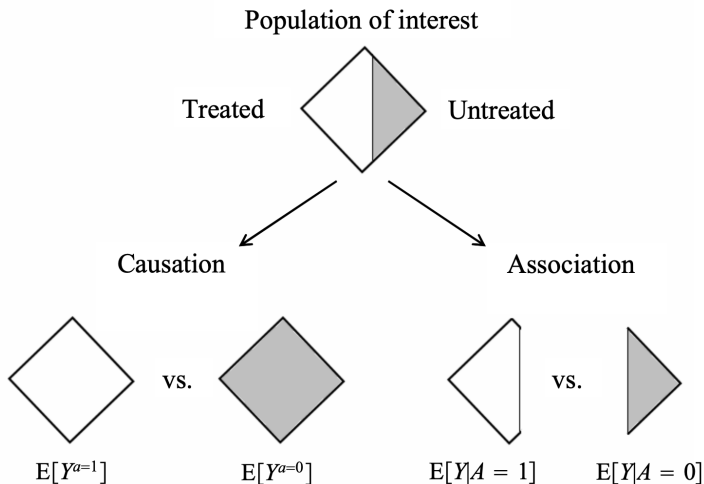
Group Exercises

General discussion

Revisit a figure from Tuesday's reading



Revisit a figure from Tuesday's reading



Question: What if a coin flip assigned units to the white or gray?

The white and gray are **exchangeable**

The white and gray are **exchangeable**

We will discuss this key idea in three ways:

- ▶ By an experimental procedure
- ▶ By a science table
- ▶ By a mathematical statement of independence

Exchangeability: By an experimental procedure

Exchangeability: By an experimental procedure

Flip a coin

Two groups of people: heads and tails

Exchangeability: By an experimental procedure

Flip a coin

Two groups of people: heads and tails

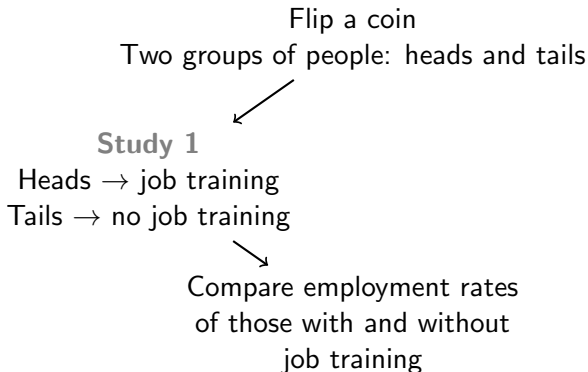


Study 1

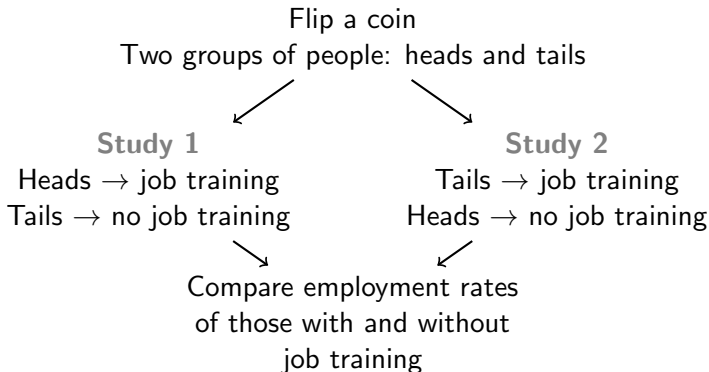
Heads → job training

Tails → no job training

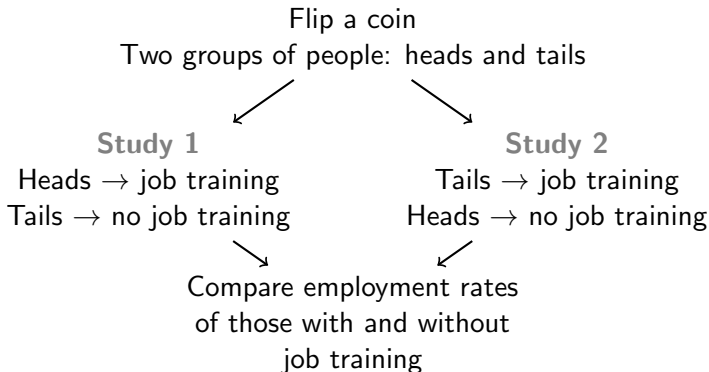
Exchangeability: By an experimental procedure



Exchangeability: By an experimental procedure

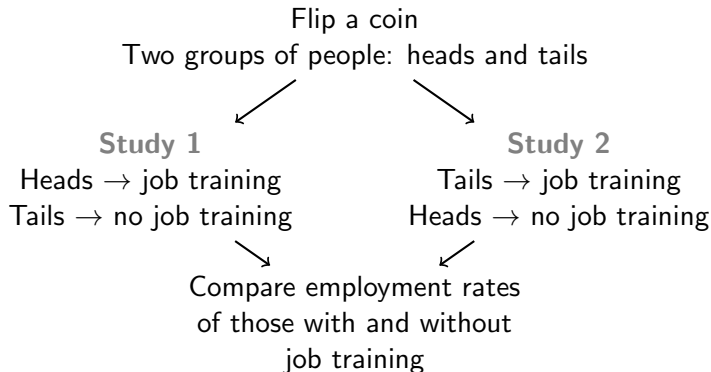


Exchangeability: By an experimental procedure



Question: Are both studies valid?

Exchangeability: By an experimental procedure



Question: Are both studies valid?

Yes. The (H/T) groups are **exchangeable**.

Any statistical pattern between (H/T) and employment can only arise from the causal effect of job training

Exchangeability¹: In a Table

- ▶ Treatment A : Job training or no job training
- ▶ Outcome Y : Employed or jobless

	<u>Outcome With Job Training</u>	<u>Outcome Without Job Training</u>
Person 1	Employed	Employed
Person 2	Employed	Employed
Person 3	Employed	Jobless
Person 4	Employed	Jobless

¹See Hernán and Robins 2.1

Exchangeability¹: In a Table

- ▶ Treatment A: Job training or no job training
- ▶ Outcome Y: Employed or jobless

	<u>Treatment</u>	<u>Outcome With Job Training</u>	<u>Outcome Without Job Training</u>
Person 1	Job Training	Employed	Employed
Person 2	None	Employed	Employed
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Person 4	Job Training	Employed	Jobless

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Exchangeability²: In Math

²See Hernán and Robins 2.1

Exchangeability²: In Math

- Job training A affects employment Y

²See Hernán and Robins 2.1

Exchangeability²: In Math

- ▶ Job training A affects employment Y
- ▶ Statistically, A tells us something about Y

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Exchangeability²: In Math

- ▶ Job training A affects employment Y
- ▶ Statistically, A tells us something about Y
 - ▶ Received job training \rightarrow more likely to be employed

²See Hernán and Robins 2.1

Exchangeability²: In Math

- ▶ Job training A affects employment Y
- ▶ Statistically, A tells us something about Y
 - ▶ Received job training \rightarrow more likely to be employed
- ▶ But A tells us nothing about $Y^{\text{Job training}}$

²See Hernán and Robins 2.1

Exchangeability²: In Math

- ▶ Job training A affects employment Y
- ▶ Statistically, A tells us something about Y
 - ▶ Received job training \rightarrow more likely to be employed
- ▶ But A tells us nothing about $Y^{\text{Job training}}$
 - ▶ Some people would be employed if they received job training

²See Hernán and Robins 2.1

Exchangeability²: In Math

- ▶ Job training A affects employment Y
- ▶ Statistically, A tells us something about Y
 - ▶ Received job training \rightarrow more likely to be employed
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 - ▶ Some people would be employed if they received job training
 - ▶ Some people would not

²See Hernán and Robins 2.1

Exchangeability²: In Math

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 - ▶ Some people would not
 - ▶ The coin flip A is unrelated to which kind of person one is

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Exchangeability²: In Math

- ▶ Job training A affects employment Y
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 - ▶ Some people would not
 - ▶ The coin flip A is unrelated to which kind of person one is

In math:

$$A \perp\!\!\!\perp Y^a \quad \text{for all } a$$

In words:

The treatment A is independent
of the potential outcomes Y^a
for all treatment values a

²See Hernán and Robins 2.1

Experiments are great because exchangeability holds by design.

Experiments are great because exchangeability holds by design.

But they are also great for other reasons.



Phase 3 Clinical Trial of Investigational Vaccine for COVID-19 Begins

Multi-Site Trial to Test Candidate Developed by Moderna and NIH

July 27, 2020

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³Published 27 July 2020. <https://www.niaid.nih.gov/news-events/phase-3-clinical-trial-investigational-vaccine-covid-19-begins>

The Moderna trial⁴: What do we like about this design?

⁴Published 27 July 2020. <https://www.niaid.nih.gov/news-events/phase-3-clinical-trial-investigational-vaccine-covid-19-begins>

The Moderna trial⁴: What do we like about this design?

- ▶ “Trial volunteers will receive two intramuscular injections approximately 28 days apart.”

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The Moderna trial⁴: What do we like about this design?

- ▶ “Trial volunteers will receive two intramuscular injections approximately 28 days apart.”
- ▶ “Participants will be randomly assigned 1:1 to receive either two 100 microgram (mcg) injections of mRNA-1273 or two shots of a saline placebo.”

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The Moderna trial⁴: What do we like about this design?

- ▶ “Trial volunteers will receive two intramuscular injections approximately 28 days apart.”
- ▶ “Participants will be randomly assigned 1:1 to receive either two 100 microgram (mcg) injections of mRNA-1273 or two shots of a saline placebo.”
- ▶ “The trial is blinded, so the investigators and the participants will not know who is assigned to which group.”

⁴Published 27 July 2020. <https://www.niaid.nih.gov/news-events/phase-3-clinical-trial-investigational-vaccine-covid-19-begins>

The Moderna trial⁵: What do we like about this design?

Person 1

Person 2

Person 3

Person 4

⁵Published 27 July 2020. <https://www.niaid.nih.gov/news-events/phase-3-clinical-trial-investigational-vaccine-covid-19-begins>

The Moderna trial⁵: What do we like about this design?

	<u>Treatment</u>
Person 1	mRNA-1273
Person 2	Saline
Person 3	Saline
Person 4	mRNA-1273

⁵Published 27 July 2020. <https://www.niaid.nih.gov/news-events/phase-3-clinical-trial-investigational-vaccine-covid-19-begins>

The Moderna trial⁵: What do we like about this design?

	<u>Treatment</u>	<u>Outcome Under mRNA-1273</u>	<u>Outcome Under Saline</u>
Person 1	mRNA-1273	Healthy	?
Person 2	Saline	?	Healthy
Person 3	Saline	?	Hospitalized
Person 4	mRNA-1273	Healthy	?

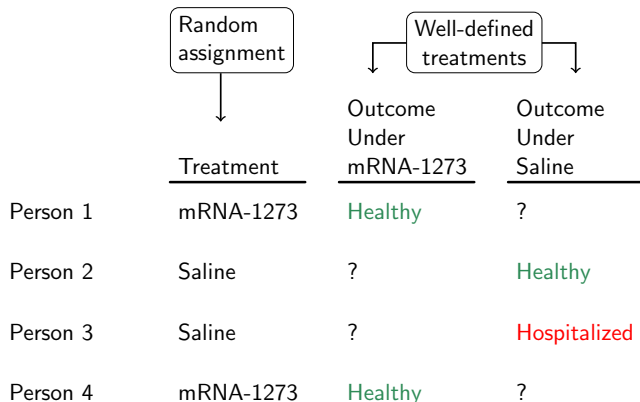
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The Moderna trial⁵: What do we like about this design?

<div>Well-defined treatments</div>			
	<u>Treatment</u>	<u>Outcome Under mRNA-1273</u>	<u>Outcome Under Saline</u>
Person 1	mRNA-1273	Healthy	?
Person 2	Saline	?	Healthy
Person 3	Saline	?	Hospitalized
Person 4	mRNA-1273	Healthy	?

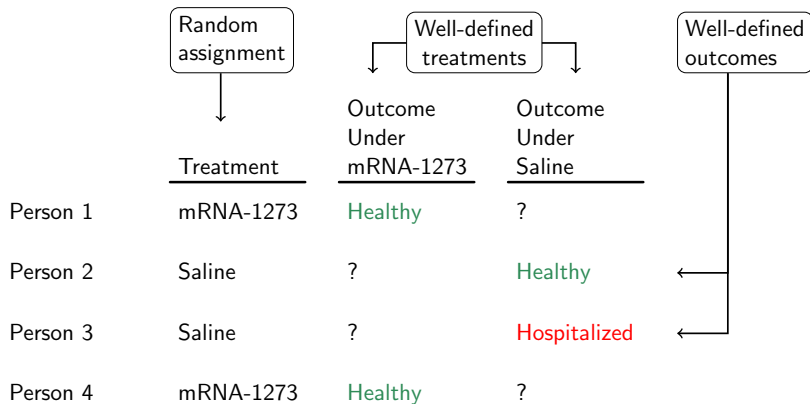
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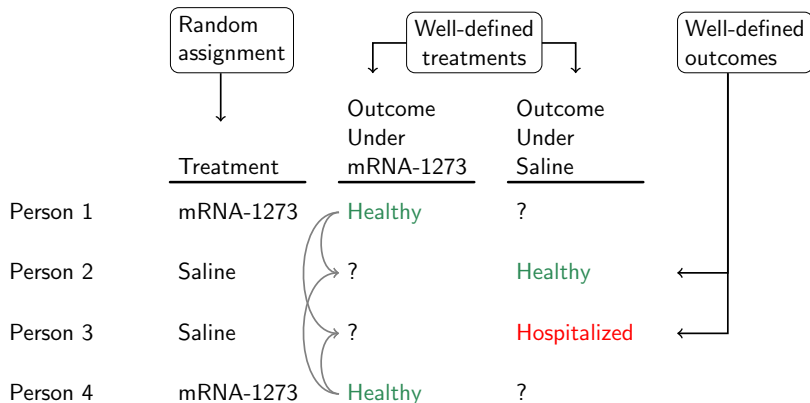
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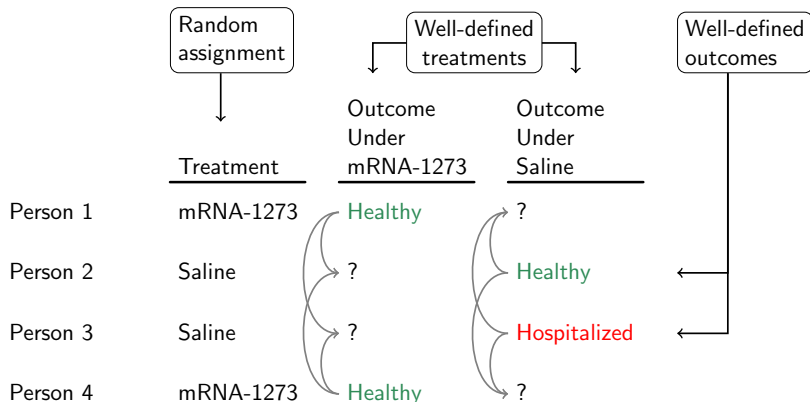
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The Moderna trial⁶: What do we like about this design?

- ▶ Eligibility criteria clear

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The Moderna trial⁶: What do we like about this design?

- ▶ Eligibility criteria clear
- ▶ Blinded

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The Moderna trial⁶: What do we like about this design?

- ▶ Eligibility criteria clear
- ▶ Blinded
- ▶ Defined follow-up period

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The Moderna trial⁶: What do we like about this design?

- ▶ Eligibility criteria clear
- ▶ Blinded
- ▶ Defined follow-up period
- ▶ Well-defined outcome

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The Moderna trial⁶: What do we like about this design?

- ▶ Eligibility criteria clear
- ▶ Blinded
- ▶ Defined follow-up period
- ▶ Well-defined outcome
- ▶ Randomized assignment

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The Moderna trial⁶: What do we like about this design?

- ▶ Eligibility criteria clear
- ▶ Blinded
- ▶ Defined follow-up period
- ▶ Well-defined outcome
- ▶ Randomized assignment
- ▶ Pre-registered hypotheses

⁶Published 27 July 2020. <https://www.niaid.nih.gov/news-events/phase-3-clinical-trial-investigational-vaccine-covid-19-begins>

Media Advisory

Wednesday, December 30, 2020

Peer-reviewed report on Moderna COVID-19 vaccine publishes

Data from Phase 3 clinical trial confirm vaccine is effective.

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⁷<https://www.nih.gov/news-events/news-releases/peer-reviewed-report-moderna-covid-19-vaccine-publishes>

Logistics

From Tuesday's reading

Randomized experiments: Two key benefits

- Exchangeability

- Precise questions

Group Exercises

General discussion

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Randomized experiments: Two key benefits

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Part 1) Design a randomized trial

This page had links to Google docs for 8 groups to work on the exercise (see exercise on next slides)

Odd numbered groups

You are a medical researcher focused on high blood pressure. Your research points toward a new drug—MiraclePill—which you believe will cause lower blood pressure in patients who are at risk (you are the expert, so you can define this). You aren't sure of the correct dosage: you think somewhere between 0 and 100 mg per week.

How would you design a randomized trial to assess MiraclePill?

1. What is the intervention?
2. What is the outcome?
3. What is the follow-up period between treatment and outcome?
4. Who is the target population?
5. How are unit-level quantities aggregated to a population-level summary?

Even numbered groups

You are a social scientist focused on the underrepresentation of women in computer science at the BA level. You develop a new mentorship program to connect entering first-year women computer science majors with recent women Cornell alumni from CS. The alumni agree to meet one-on-one with the first-year undergraduates a couple times a year. You want to randomize some element of this program in order to test its effectiveness.

How would you design a randomized trial to assess the mentorship program?

1. What is the intervention?
2. What is the outcome?
3. What is the follow-up period between treatment and outcome?
4. Who is the target population?
5. How are unit-level quantities aggregated to a population-level summary?

Observational evidence

Scroll down to Part 2

Odd numbered groups

Another medical researcher comes to you with observational evidence. “I had 100 people in my office today. 50 of them tell me they take MiraclePill 100mg once per week. The other 50 tell me they do not take MiraclePill. Average blood pressure was lower for those who take MiraclePill.”

What do you say to this researcher? How is their evidence different from your target trial?

Even numbered groups

Another social scientist comes to you with observational evidence. "Today I was at a gathering of women Cornell alumni from the CS and English departments. I went around and asked them if they ever engaged with CS alumni during college. 75% of the CS graduates said yes, but only 10% of the English graduates said yes. I think engaging with alumni is key to persistence in CS."

What do you say to this researcher? How is their evidence different from your target trial?

Hypothetical target trial

Scroll down to Part 3

Odd numbered groups

A researcher (with whom you may disagree) says to you: “Coming to office hours frequently causes student success in the classroom.”

Your task is to create the details that would make this observational claim specific. What is the target trial?

1. What is the hypothetical intervention?
2. What is the outcome?
3. What is the follow-up period between treatment and outcome?
4. Who is the target population?
5. How are unit-level quantities aggregated to a population-level summary?

Even numbered groups

A researcher (with whom you may disagree) says to you: “Single parenthood causes poverty. If poor women would marry, then they would no longer be poor.”

Your task is to create the details that would make this observational claim specific. What is the target trial?

1. What is the hypothetical intervention?
2. What is the outcome?
3. What is the follow-up period between treatment and outcome?
4. Who is the target population?
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General discussion

In an observational study, you cannot randomize.

⁸Hernán, M. A., & Robins, J. M. (2016). Using big data to emulate a target trial when a randomized trial is not available. *American Journal of Epidemiology*, 183(8), 758-764.

In an observational study, you cannot randomize.

But you can do all the other things⁸

⁸Hernán, M. A., & Robins, J. M. (2016). Using big data to emulate a target trial when a randomized trial is not available. *American Journal of Epidemiology*, 183(8), 758-764.

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- ▶ Eligibility criteria

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- ▶ Eligibility criteria
- ▶ Treatment strategies

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- ▶ Eligibility criteria
- ▶ Treatment strategies
- ▶ Assignment procedures (to discuss more Sep 6)

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- ▶ Eligibility criteria
- ▶ Treatment strategies
- ▶ Assignment procedures (to discuss more Sep 6)
- ▶ Follow-up period

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- ▶ Eligibility criteria
- ▶ Treatment strategies
- ▶ Assignment procedures (to discuss more Sep 6)
- ▶ Follow-up period
- ▶ Outcome
- ▶ Causal contrasts of interest

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- ▶ Eligibility criteria
- ▶ Treatment strategies
- ▶ Assignment procedures (to discuss more Sep 6)
- ▶ Follow-up period
- ▶ Outcome
- ▶ Causal contrasts of interest
- ▶ Analysis plan

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Learning goals for today

At the end of class, you will be able to:

1. Define the target trial (hypothetical experiment) that a causal study seeks to emulate
2. Understand how the target trial clarifies causal questions

Let me know what you are thinking

tinyurl.com/CausalQuestions

Office hours TTh 11am-12pm and at
calendly.com/ianlundberg/office-hours
Come say hi!