Introduction to Causal Inference and Causal Data Science

Day 1: Causal Inference and Potential Outcomes

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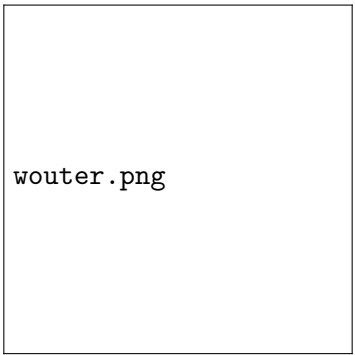
Slide on participants; backgrounds / logo's from different universities / disciplines

Your teachers

Oisín Ryan



Wouter van Amsterdam

Bas Penning de Vries

Why Causal Modeling?

Causal questions dominate scientific research

- Does smoking cause cancer?
- Does the expression of gene X produce phenotype Y?
- What is the effect of social media use on adolescent well-being?
- What effect could we expect a sugar tax to have on rates of adult-onset diabetes in the general population?
- Which treatment type will be most effective in reducing symptoms for this type of individual?

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Causal Modeling: When can we answer causal questions using *data*? And how should we go about doing this?

Why Causal Modeling?

Statistical modeling and **data science** give us a rich language to describe uncertainty in the world we see around us

- The language of *co-occurences*, *expected values*, *(joint, marginal and conditional) probabilities* and *statistical dependencies*.
- It helps us *describe* patterns and make (certain types of) *predictions*.

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But *by themselves*, statistical models have very little to say about causal relations!

Causal Modeling involves using concepts and techniques from statistical modeling and data science

- But causal models and causal information exist on a level **above** statistical information

Example

Imagine we are a team of health scientists.

We take a blood sample from a random sample of the population and record:

- The level of expression of a particular gene X
- The level of expression of a phenotype Y (e.g. blood insulin levels).

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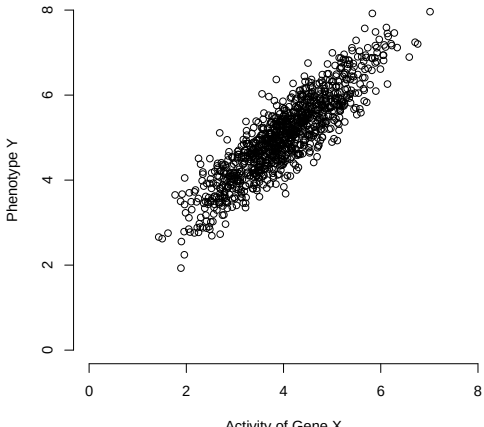

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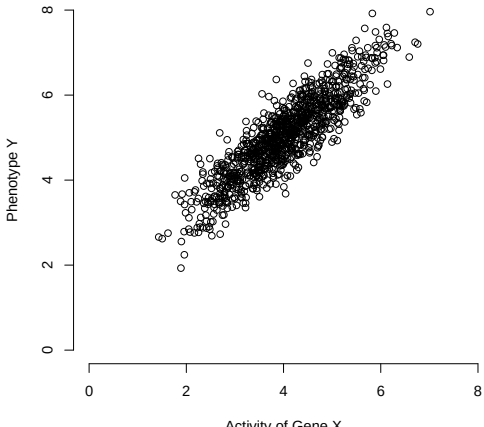
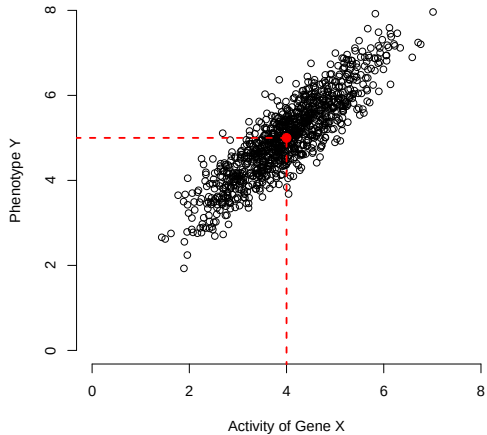


What kind of information can we extract from this data? What tasks can we perform, and what research questions can we answer using statistical techniques?

Example

Description:

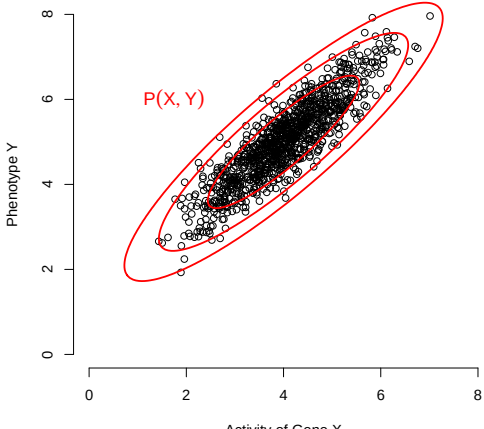
- What is the average level of gene expression in the sample ($\bar{X}$)?
- What does that tell us about the average level in our population ($E[X]$)?
- How *certain* are we about our *estimate* of the population mean?



Example

Models for (co-)occurence

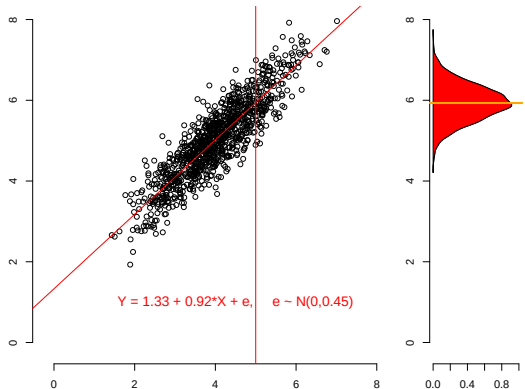
- What is the likelihood of observing a low level of gene expression (*Marginal Distribution* $P(X = x)$)?
- What is the probability that someone in the population has both a high insulin level and a high gene expression (*Joint distribution* $P(X, Y)$)?
- We can fit models, such as the normal distribution $P(X, Y) \sim N(\boldsymbol{\mu}, \boldsymbol{\Sigma})$ and ask how well this model fits the data



Example

Prediction:

- If I collect one more data point in *identical* circumstances and I observe a gene expression score of 5, what is my best guess of what phenotype level that person has?
- Answered by estimating / fitting models for the *conditional distribution* $P(Y|X)$
- Best guess is the *conditional expectation* $E[Y|X = 5]$, which we have to *estimate* somehow



Example

What kinds of questions can we **not answer**?

Example

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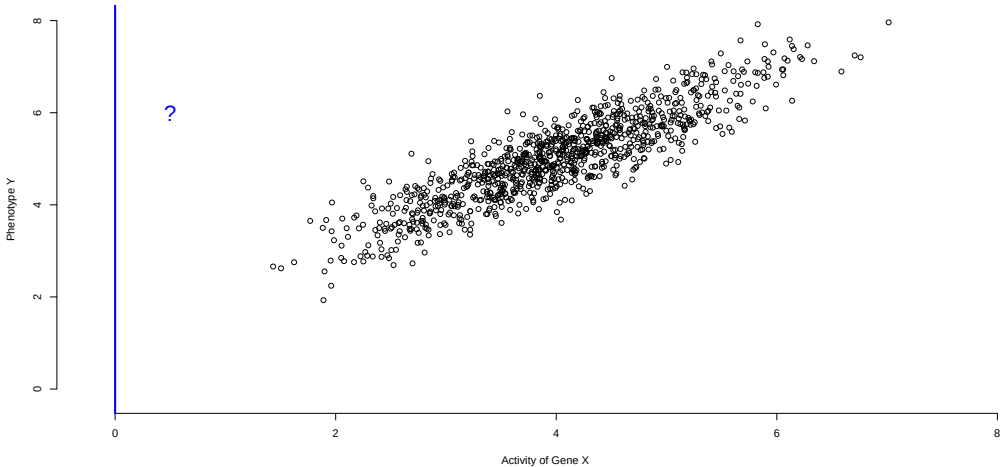
What if instead of just observing genes and phenotypes, I was to *manipulate*/ intervene on / *change* the expression of that gene.

- E.g., deactivating or suppressing gene expression entirely.

What level of phenotype expression would I expect to see if I did that?

- Predicting phenotype from gene expression in a different setting: The intervention setting instead of the observation setting

Example: Causal Reasoning



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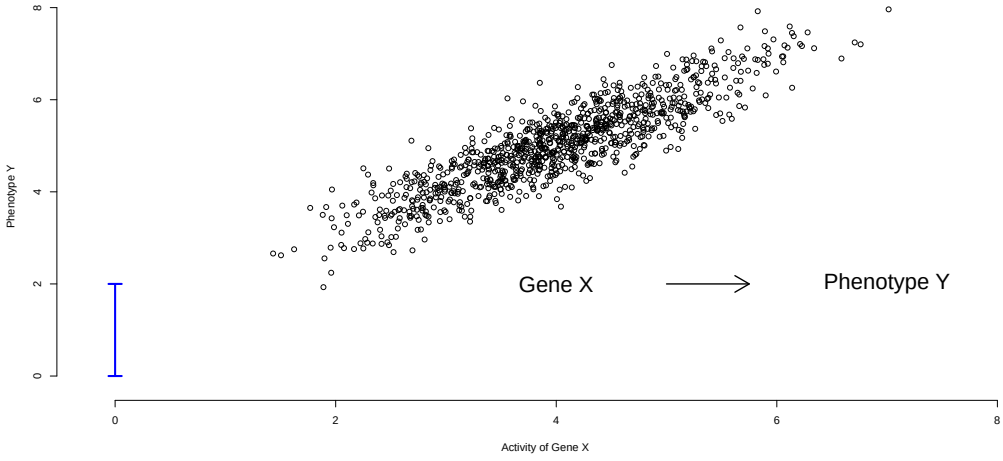
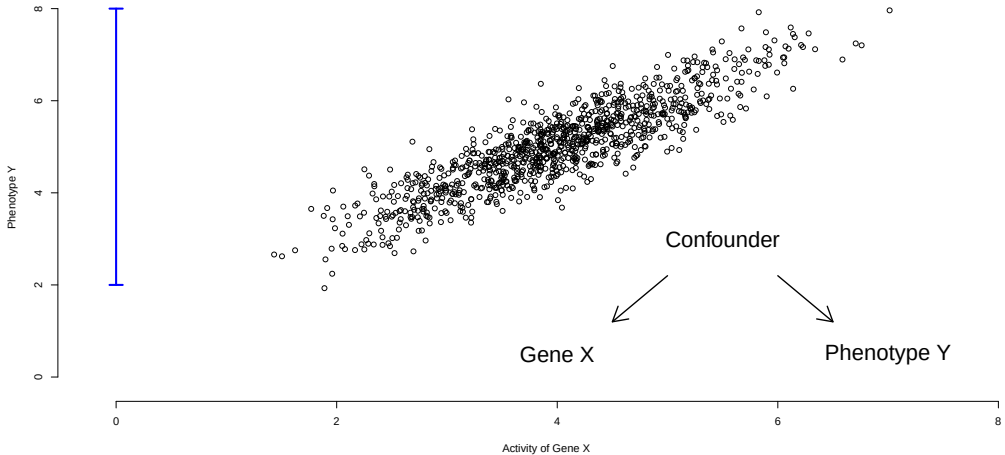
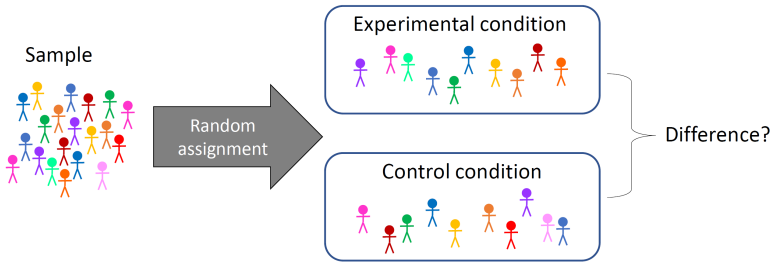


Example: Causal Reasoning



Randomized Control Trials

Randomized Control Trials (RCTs) are the gold standard for estimating causal effects.



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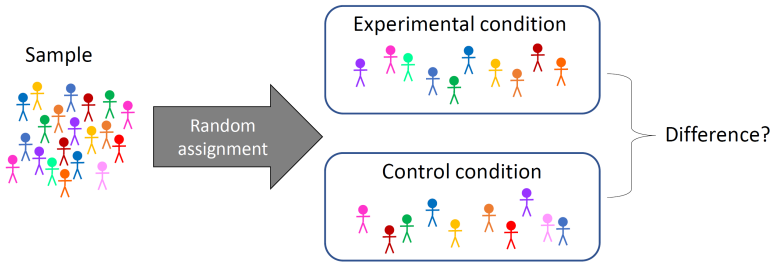


Great! But:

- What if the RCT doesn't work perfectly? What if I have non-compliance?
- What if I can't perform an RCT due to ethical or practical constraints? Observational / non-experimental data?

How can we perform causal modeling in practice? (rough)

Temptation to split the world up into two dimensions:

- Randomized Experiments : We can estimate and talk about causal effects
- Non-randomized experiments, observational data : Not a randomized experiment, so don't even discuss causal relations

This conflates the *means* with the *ends* (Hernan citation)
Leads to confusion; in reality, many causal reserach questions cannot or cannot efficiently/effectively/practicaly be answered using randomized experiments. - euphemisms, confusion

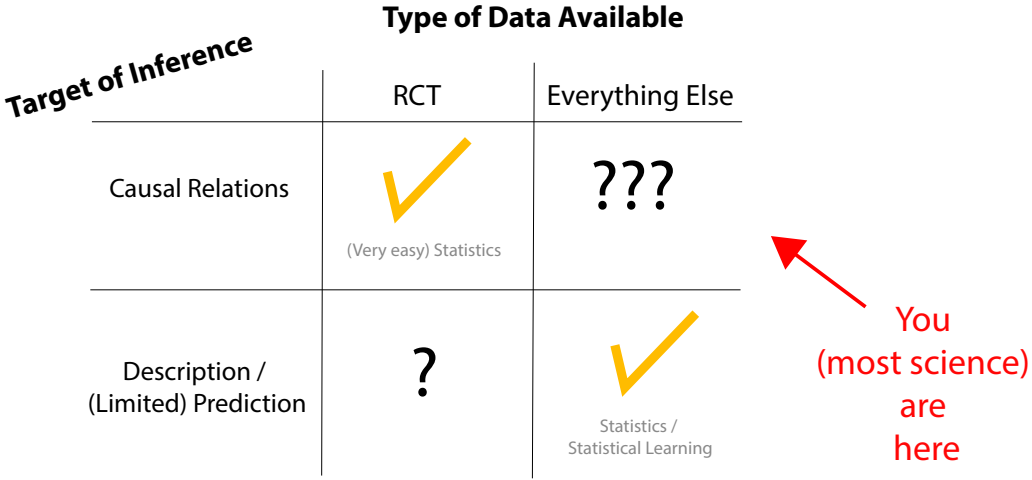
Science: A 2x2 table

Target of Inference	Type of Data Available: RCT	Type of Data Available: Everything Else
Causal Relations		
Description / (Limited) Prediction		

Science: A 2x2 table

Target of Inference	Type of Data Available: RCT	Type of Data Available: Everything Else
Causal Relations	✓ (Very easy) Statistics	???
Description / (Limited) Prediction	?	✓ Statistics / Statistical Learning

Science: A 2x2 table



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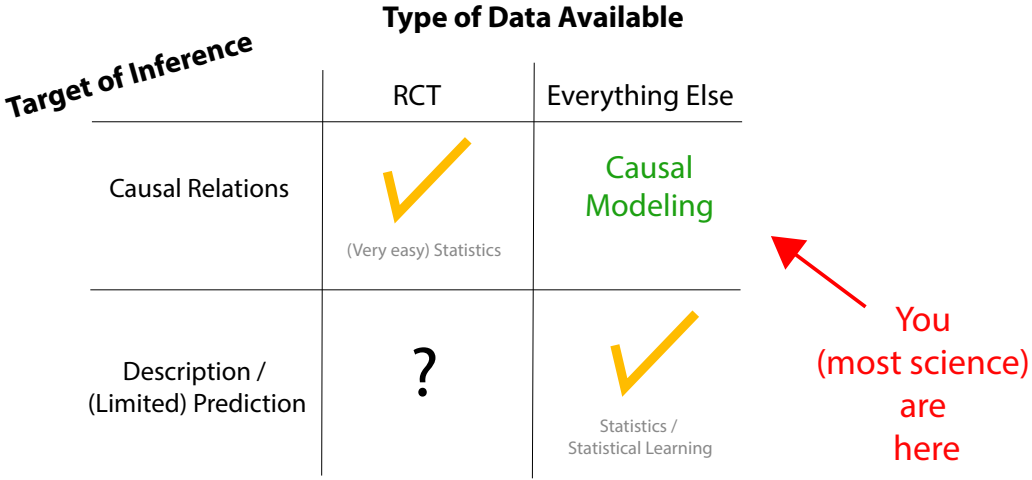

How can we perform causal modeling in practice? (rough)

Randomized experiments **are** special, but **why** are they special?
- what are the features / mechanisms / principles by which this study design allows for causal inference?
- by understanding these, can we understand if other designs might allow us to make the same types of inferences, e.g., by mimicing / accounting for those mechanisms etc.
We need a language to describe and understand causal inference

Two Frameworks / Languages for Causal Inference

Potential Outcomes (Part 1).

- Developed by statistician Don Rubin (m)
- Imbens (l) & Angrist (r): Nobel Prize for Economics 2021

Structural Causal Models (Part 2).

- Developed by Judea Pearl, a computer scientist
- "Bayesian Networks"

Outline

Outline

Structure of the course etc

Lecture, then lab
Lunch
(schedule for today)

Potential Outcomes I

Potential Outcomes

Headaches and Aspirin

- action: Aspirin ($X = 1$) or No Aspirin ($X = 0$)
- outcome: Headache gone ($Y = 1$) or Headache remains ($Y = 0$)

We want to know: Should I take an aspirin?

- I want to take aspirin if my headache level after taking aspirin is different than my headache levels if I don't take aspirin
- Two **potential versions of the outcome** for every person. Outcome if treated ($Y^{X=1}$) and outcome if not treated ($Y^{X=0}$)

A causal effect is defined as a **difference in potential outcomes**

Causal Effects

Individual causal effect:

$$ICE_i = Y_i^{X_i=1} - Y_i^{X_i=0}$$

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The fundamental problem of causal inference (Holland, 1986): We can only observe one potential outcome per unit

If you decide to take the aspirin ($x = 1$), in this situation I will observe your headache outcome under aspirin-taking: $Y_i^{X_i=1}$

- This is sometimes referred to as the **factual** outcome

But that means I cannot observe your headache outcome under aspirin-avoidance: $Y_i^{X_i=0}$

- This is then referred to as your **counterfactual** outcome

Causal Effects and Missing Data

- Highlights the basic structure of the causal inference problem from this perspective
- We have a missing data problem
- How can we approach this?
- Two "knobs" you can turn; 1) change the question you're asking, and 2) use information you do have to make guesses about the information you don't have
- In (2) the most crucial step is to understand in what situations we can use **information we do have** to make correct/useful/helpful guesses - These descriptions of "situations" are known as **assumptions**

Which causal effect?

Let's turn both knobs here; turns out ICE estimation is quite tricky in most situations - Instead it is often more feasible (and often of primary interest anyway) to estimate Average causal effects

Instead we typically focus on trying to infer the **average causal effect**

Average causal effect:

$$ACE = E[Y_i^{X=1} - Y_i^{X=0}] = E[Y^1] - E[Y^0]$$

Example: Aspirin and Headaches

	Potential outcomes		ICE
	Y_i^1	Y_i^0	$Y_i^1 - Y_i^0$
Charles	1	1	0
George	0	0	0
Susan	1	0	1
Tracy	1	1	0
Ken	0	1	-1
Pete	1	0	1
Helen	1	0	1
Kate	0	0	0

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Kate	0	0	0

$$ACE = E[Y^1] - E[Y^0]$$
$$ACE = 5/8 - 3/8 = 0.25$$

But we only observe one outcome per person

	Unobserved			Observed	
	Y_i^1	Y_i^0	$Y_i^1 - Y_i^0$	X_i	Y_i
Charles	1	1	0	0	1
George	0	0	0	1	0
Susan	1	0	1	1	1
Tracy	1	1	0	0	1
Ken	0	1	-1	0	1
Pete	1	0	1	1	1
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Pete	1	0	1	1	1
Helen	1	0	1	0	0
Kate	0	0	0	1	0

Expected value of recovery **aspirin takers** $(X = 1)$: (0+1+1+0)/4 = 0.5
Expected value of recovery **aspirin avoiders** $(X = 0)$: (1+1+1+0)/4 = 0.75

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$$E(Y|X = 1) - E(Y|X = 0) = -0.25$$

Naive conclusion: Aspirin decreases chances of headache relief.

What is the problem with observing?

Observing $\neq$ intervening

$E(Y|X = 1) - E(Y|X = 0)$ is **not the same** as $E(Y^1) - E(Y^0)$

Observing that $E(Y|X = 1) \neq E(Y|X = 0)$ (in words: the average value of headache levels for those who did and did not take aspirin are unequal), does not, in general, **imply a causal effect** of X on Y.

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In RCTs, we often use $E(Y|X=1) - E(Y|X=0)$ as an **estimate** of the *ACE*. But why? What makes an RCT so special?

NOTES

Rearrange below to make exchangeability first,
Split up SUTVA into no interference and consistency

Assumption 1: SUTVA

Stable unit treatment value assumption (SUTVA):

The potential outcomes for any unit do not vary with the treatments assigned to other units (i.e., **no interference**), and,
for each unit, there are **not different versions of each treatment level** that lead to different potential outcomes.

SUTVA is important when moving from a single unit (with an ICE), to multiple units (when we consider the ACE).

Different treatments

If there are multiple ways to raise X from 0 to 1, this means:

- there are **multiple treatments**
- these may have **different effects**
- and hence the causal question is **ill-defined**

Examples:

- What is the effect of obesity on health?
- Does physical punishment compromise children's well-being?
- Does alcohol undermine cognitive performance in young adolescents?

To formulate better questions, we should define the **target trial**: The randomized controlled trial we would have done, if it had been possible.

Assumption 2: Exchangeability

At best, **half** of the potential outcomes are **observed**; hence, causal inference is at its core a **missing data problem**.

The critical question is: What is the **missing data mechanism**?
Or: What is the **assignment mechanism**?

If there is a relation between the **assignment mechanism** and the **potential outcomes**, this may bias the estimation of the causal effect.

Exchangeability:

The actual treatment received (X) and the potential outcome given treatment Y^X are independent: $Y^x \perp\!\!\!\perp X$ for all x

This is also known as **unconfoundedness**: The missing potential outcome is missing **completely at random**. Individuals across treatment groups are **exchangeable**

Treatment NOT independent of potential outcomes

In a **non-randomized study**, treatment may depend on person features that also relate to the potential outcomes.

	Unobserved			Observed		Confounder
	Y_i^1	Y_i^0	$Y_i^1 - Y_i^0$	X_i	Y_i	Z_i
Charles	1	1	0	0	1	3
George	0	0	0	1	0	9
Susan	1	0	1	1	1	8
Tracy	1	1	0	0	1	5
Ken	0	1	-1	0	1	4
Pete	1	0	1	1	1	2
Helen	1	0	1	0	0	5
Kate	0	0	0	1	0	4

Average headache levels are higher among those who took the aspirin. But, people who took aspirin also scored higher on the covariate **dehydration levels** Z_i.

Conditional Exchangeability

Luckily, we don't need full exchangeability for causal inference. We only need **conditional exchangeability**; conditional on a set of observed covariates, the potential outcomes are independent of treatment assignment.

Conditional exchangeability:

The actual treatment received (X) and the potential outcome given treatment Y^X are independent within certain levels of Z: $Y^x \perp\!\!\!\perp X|Z$

This implies that data are *missing at random* (rather than *missing completely at random*).

Estimation of the ACE can proceed **as long as we can properly account for (i.e. condition on) the confounder** Z. But to be able to do this, we need...

Assumption 3: Positivity

There must be **exposed and unexposed participants** at every combination of values of Z in the population under study.

In an **RCT**, positivity is **present by design**.

In a **non-experimental study**, **violations** can be **detected** by:

- making tables of each categorical covariate and treatment (should be no empty cells)
- categorize a continuous covariate and make table (but this depends on number and width of categories)
- considering all combinations of covariates (becomes impossible)

Putting it Together

Three Conditions/Assumptions necessary for causal **identification**:

1. SUTVA
2. (Conditional) Exchangeability
3. Positivity

Causal Estimation:
Given our data and causal identification assumptions, how should we estimate the causal effect

Estimation

The Two "Tasks" of Causal Inference

Identification

Assuming I have **population-level statistical information** (given these variables but with an infinite sample size), can I infer the causal effect of interest?

What causal assumptions/conditions need to be met?

Estimation

Given that my causal effect is identified, how should I go about estimating this effect from sample data?

Statistical assumptions - functional form, distributions, etc.

Philosophy on causal inference and estimation:
- Make as few additional assumptions as possible - Mimic "randomization" using statistical tools; towards "non-parametric" **adjustment** approaches
Recall: we want to "adjust" for variables that determine which treatment your receive and which value of the outcome you are likely to have

Statistics in a nutshell

Statistical Estimand

Estimator

1. **Prepare Chocolate Cake Batter**
   Preheat oven to 350 degrees, and prepare Yo's Ultimate Chocolate Cake batter. Prepare your pans with parchment. Pour 2 ½ lbs into each 7" round pan, 1 ½ lbs into your 6" round pan, and divide the remaining batter evenly between your 5" round pans.

2. **Bake Cakes**
   Bake your 7" round cakes for 50 minutes, your 6" round cake for 40 minutes, and your 5" round cakes for 30 minutes, or until a toothpick comes out clean. Set aside to cool completely in their pans on a wire rack.

3. **Prepare Fillings & Simple Syrup**
   Prepare your dark chocolate ganache, Italian meringue buttercream, and simple syrup. Set aside until you're ready to decorate.

4. **Level Cakes**
   Remove your cooled cakes from their pans and level them with a ruler and serrated knife.

Estimate

Causal Inference in a nutshell

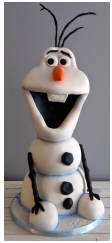
Causal Estimand	Causal Model	Statistical Estimand	Estimator	Estimate

Causal Inference in a nutshell

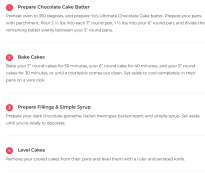
Causal Estimand

Causal Model

Statistical Estimand



Estimator



Estimate

Conditional Exchangeability by Conditioning

Recall: Conditional exchangeability
Within levels of the confounder, groups are comparable
Conditionally randomized trial

Adjustment by Stratification

- define strata ($Z = 0$, $Z = 1$)
- Estimate average effect within those strata
- ACE = weighted sum of these (more dehydrated than not, etc.)

Adjustment by matching

- like stratification taken to an extreme
- for every person in your dataset, find someone with the same set of covariate values
- take the difference in outcome in each matched pair
- the average of these = ACE

Propensity Scores

Propensity Scores are a tool used in the PO framework for causal estimation

Propensity scores (assuming no unobserved confounding):

The probability of exposure/treatment given confounders Z

$$\pi_i = P[X_i = 1|Z_i] = \frac{exp(Z_i'\phi)}{1+exp(Z_i'\phi)}$$

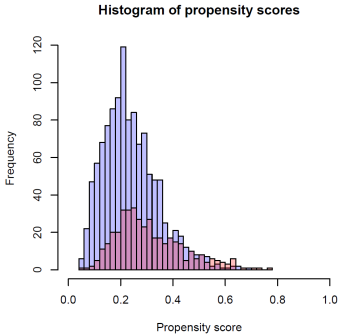
We estimate π_i using **logistic regression**

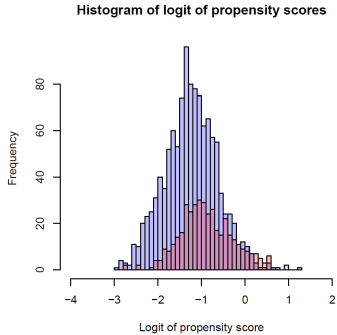
Propensity scores:

- Summarize information about the relationship between **pre-treatment** confounders (Z) and treatment (X)
- Are used to ensure *conditional exchangeability*

Get $Y^X \perp\!\!\!\perp X|\pi$ to replace $Y^X \perp\!\!\!\perp X|Z$

Overlap of propensity scores





The **distributions of logit**(π_i) for the treated and the untreated are typically different, but should fully (and properly) **overlap**:

- non-overlapping areas imply **violation of positivity assumption**
- non-overlapping areas **require extrapolation**
- areas with very few people in one groups imply there are **few matches**

Propensity Scores for Matching

Matching implies you **create pairs** that consist of a treated and a non-treated person, who have **identical propensity scores**.

Background: In an **RCT** we have: $P\big(Z|X=1\big) = P\big(Z|X=0\big)$

Balancing property:

$$P\big(Z|\pi=c, X=1\big) = P\big(Z|\pi=c, X=0\big)$$

If the propensity model is **correct**, then comparing treated and untreated **individuals with the same** π is a way of **mimicking an RCT**.

Propensity Scores for Weighting

Check if this will be covered in Day 3 (probably will be) The **probability of received treatment** is:

- π_i for those who were **treated** $(X_i = 1)$
- $1 - \pi_i$ for those who were **NOT treated** $(X_i = 0)$

Among **treated individuals**, those with large π_i are **overrepresented** in comparison to those with small π_i.

Among **untreated individuals**, those with large $1 - \pi_i$ are **overrepreseneted** in comparison to those with small $1 - \pi_i$.

To account for this inbalance, we **create a pseudo-population** where each case is **weighted** by the **inverse probability of received treatment**:

- $\frac{1}{\hat{\pi}_i}$ for $X_i = 1$
- $\frac{1}{1-\hat{\pi}_i}$ for $X_i = 0$

Causal Estimands

ATE and ATT
Matching/Weighting and ATE/ATT

Potential Outcomes: An Overview

Causal Inference is a missing data problem

- When can I infer $E[Y^1] - E[Y^0]$ if i don't fully observe either?

Steps (broadly):

- Assess SUTVA, Exchangeability and Positivity
- If you can meet those conditions, use covariate-based techniques like propensity scores to create balanced groups of treated and not treated, mimicing an RCT
- Estimate ACE by adjusting for group differences on confounders (e.g., weighting, matching)

Recommended Reading

Hernán, M. A. (2018). The C-word: scientific euphemisms do not improve causal inference from observational data. *American journal of public health*, 108(5), 616-619.
Rohrer, J. M. (2018). Thinking clearly about correlations and causation: Graphical causal models for observational data. *Advances in Methods and Practices in Psychological Science*, 1(1), 27-42.
Schafer, J. L., Kang, J. (2008). Average causal effects from nonrandomized studies: a practical guide and simulated example. *Psychological methods*, 13(4), 279.

Hernán MA, Robins JM (2020). Causal Inference: What If. Boca Raton: Chapman Hall/CRC.
Free copy: `https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1268/2021/03/ciwhatif_hernanrobins_30mar21.pdf`
Pearl, J., Glymour, M. & Jewell, N.P. (2016) Causal Inference in Statistics: A Primer