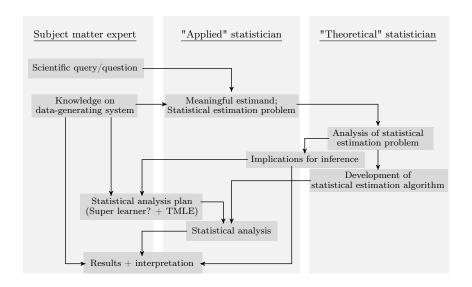
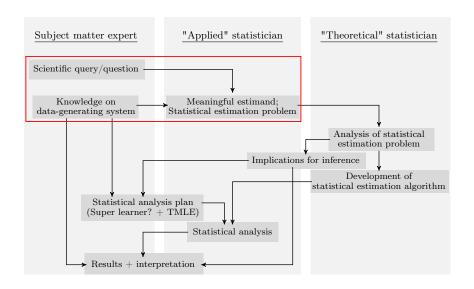
# Day 1, Lecture 2

#### In this lecture, our goal is to:

- Develop an understanding of the utilization of causal inference tools to define nonparametric targets of estimation, highlighting the role of counterfactual reasoning and hypothetical interventions.
- 2. Differentiate between causal and statistical parameters, and list the assumptions necessary for the translation between them.





- ▶ A clearly defined goal as a starting-point for any analysis
  - necessary to talk about estimator performance
  - semiparametric/nonparametric efficiency theory (and TMLE) requires a clearly defined goal
- Brief introduction to the setting of a typical causal inference problem
  - example: average treatment effect
  - model-free and estimator-free definition of parameters

# Moving targets with different logistic regression models

- $X \sim \text{Unif}(-2,2)$
- ► *A* ~ Bernouilli(0.5) (no confounding)
- ▶  $Y \in \{0, 1\}$

Say that the distribution of Y given X and A follows the parametric model:

$$\operatorname{logit} \mathbb{E}[Y \mid A, X] = \beta_0 + \beta_A A + \beta_X^{\mathsf{T}} X^2$$

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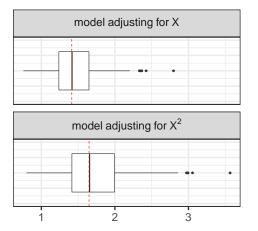
$$\operatorname{logit} \mathbb{E}[Y \mid A, X] = \beta_0 + \beta_A A + \beta_X^{\mathsf{T}} X^2$$

The odds ratio  $\exp(\beta_A)$  is a different parameter than  $\exp(\alpha_A)$  in a different model:

$$\operatorname{logit} \mathbb{E}[Y \mid A, X] = \alpha_0 + \alpha_A A + \alpha_X^{\mathsf{T}} X$$

# Moving targets with different logistic regression models

- ▶ The variables X we include in the model to assess the effect of A on Y changes the parameter (conditional OR).
- Only one of the models can be true at a time.



The upper panel does not show a biased estimator, just an estimator targeting a different parameter (dashed red line).

#### Causal inference

What we obtain moving on to a causal inference setting: 1) An interpretable and relevant target of estimation, and 2) a model-free definition of a target parameter.

<sup>&</sup>lt;sup>1</sup>And, if you are already familiar, consider this a small repetition and introduction to the notation.

#### Causal inference

What we obtain moving on to a causal inference setting: 1) An interpretable and relevant target of estimation, and 2) a model-free definition of a target parameter.

- We are only going to go briefly over the "causal inference concepts",<sup>1</sup> but we need this part to very clear about with it is we are estimating.
  - For today and tomorrow we consider just the simple example where the target of estimation is the average treatment effect (ATE).
- For the causal inference notation, we follow the book by Hernán and Robins (which, if you are interested, you can find here: https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1268/2021/03/ciwhatif\_hernanrobins\_30mar21.pdf).
  - ► I will leave out DAGs/SCMs.

<sup>&</sup>lt;sup>1</sup>And, if you are already familiar, consider this a small repetition and introduction to the notation.

### Steps of the roadmap

- Step 1 Go from scientific question to target causal estimand (stated in the language of counterfactuals)
- Step 2 Assess whether we can go from target causal estimand to target statistical estimand = assess "identifiability"

In a given data situation, we want to explicitly clarify:

- Observed data
- 2. Causal model
- 3. Causal question and target causal estimand
- 4. Identifiability

### An example we can have in the back of our minds

#### Scientific question:

Does having a planned cesarian section (intended cesarian section) among women who gave birth twice change the risk of postpartum haemorrhage (PPH) during the second delivery?



Goal: Translate this is into a precise formulation of a statistical estimation problem.

Observed data 
$$O = (X, A, Y) \in \mathbb{R}^d \times \{0, 1\} \times \{0, 1\} = \mathcal{O}$$

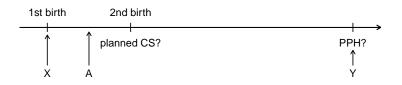
- \*  $X \in \mathbb{R}^d$  are covariates ex: age at 2nd delivery, information of PPH at first delivery, ...
- \*  $A \in \{0,1\}$  is a binary exposure variable (treatment decision) ex: decision to have a planned cesarian section.
- \*  $Y \in \{0,1\}$  is a binary outcome variable ex: PPH (postpartum haemorrhage).

We observe a sample  $O_1, \ldots, O_n \stackrel{iid}{\sim} P_0 \in \mathcal{M}, n \in \mathbb{N}$ .

 ${\cal M}$  is the set of all possible probability distributions for our data.

Implicit assumptions for the data structure:<sup>2</sup>

- ▶ X are covariates known before the treatment decision A was made
- Outcome Y is observed after treatment decision was made



<sup>&</sup>lt;sup>2</sup>This ordering could also be encoded in a structural causal model.

Our statistical model  $\mathcal{M}$  for  $P_0$  contains possible distributions P for the observed data O.

The density p of  $P \in \mathcal{M}$  can be factorized into:

$$p(o) = \mu_Y(y \mid a, x)\pi(a \mid x)\mu_X(x),$$

- $\mu_{Y}(y \mid A, X) = P(Y = y \mid A, X)$
- $\pi(a | X) = P(A = a | X)$
- $\mu_X$  is the marginal density of X (with respect to an appropriate dominating measure)

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We assume that  ${\mathcal M}$  is a nonparametric model.

- \* Throughout, we make no parametric restrictions on  $\mu_Y$ ,  $\mu_X$ .
- \* We could impose some parametric structure on  $\pi$ , but let us assume that we do not.

# Operators on functions of the observed data<sup>3</sup>

For a function  $h: \mathcal{O} \to \mathbb{R}$  and distribution P

$$Ph = \mathbb{E}_P[h(O)] = \int hdP = \int_{\mathcal{O}} h(o)dP(o)$$

where  $\mathcal{O} = \mathbb{R}^d \times \{0,1\} \times \{0,1\}$  is the sample space of O = (X,A,Y).

<sup>&</sup>lt;sup>3</sup>van der Vaart, A. W. (2000). Asymptotic statistics (Vol. 3). Cambridge university press.

# Confounding

How can we define a causal effect?

The contrast  $\mathbb{E}_P[Y \mid A=1] - \mathbb{E}_P[Y \mid A=0]$  tells us about the risk difference in the two exposure groups.

Any such difference is likely due to other factors than the decision to initiate treatment or not

\* the exposure decision is confounded.

#### Counterfactuals

To answer a causal question, we ideally want to know

- Scenario 1 What happened to a subject had they been exposed?
- Scenario 2 What would have happened to the same subject had they not been exposed?

We imagine a model with two outcomes for each subject:

- $\triangleright$  a variable  $Y^1$  corresponding to scenario 1, and
- $\triangleright$  a variable  $Y^0$  corresponding to scenario 2
- = the "counterfactuals" (aka potential outcomes).

#### Counterfactuals

- \*  $Y^1$  = outcome if exposed
- \*  $Y^0$  = outcome if not exposed

We use the counterfactual outcomes to define precisely what a causal effect is:

- $\rightarrow$  on the individual level,  $Y^1 = 1$  and  $Y^0 = 0$  for a particular subject would tell us that this subject would experience outcome under exposure and not otherwise
- $\rightarrow$  on the population level,  $\mathbb{E}_P[Y^1] \neq \mathbb{E}_P[Y^0]$  tells us that the risk changes depending on whether exposed or not

# Target causal estimand: Average causal effect (ATE)

The average causal effect<sup>4</sup> (ATE/ACE) measures the average effect in the population

$$ATE = \mathbb{E}_{P}[Y^{1}] - \mathbb{E}_{P}[Y^{0}]$$

→ It is interpreted as the difference in risk had everyone in the population been exposed and had everyone in the population been unexposed.

<sup>&</sup>lt;sup>4</sup>or average treatment effect.

Can we estimate the causal effect from the observed data?

 $\triangleright$  only  $Y^1$  or  $Y^0$  is observed for each individual.

Identifying  $\mathbb{E}_P[Y^1] - \mathbb{E}_P[Y^0]$ 

= write  $\mathbb{E}_P[Y^1] - \mathbb{E}_P[Y^0]$  as a parameter of the observed data distribution.

requires three overall assumptions (identifiability assumptions).

- 1. Consistency:  $Y^a = Y$  if A = a, a = 0, 1
  - Requires that the "treatment intervention" is well-defined and no interference between subjects.
  - Example of a violation: effect of vaccines (one subject's effect of a vaccine depends on whether other subjects are vaccinated or not).

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- 2. Exchangeability:  $Y^a \perp A \mid X$ , for a = 0, 1
  - Conditional on covariates, the exposed group tells us what would happen to the unexposed if they had been exposed and vice versa.
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  - Conditional on covariates, the exposed group tells us what would happen to the unexposed if they had been exposed and vice versa.
  - ▶ Requires that there is no unmeasured confounding.
- 3. Positivity:  $P(A = a \mid X) > 0$  for a = 0, 1 and almost surely all X
  - We cannot investigate the effect of an intervention that was never "tested" in the observed data (conditional on covariates X).

Under these assumptions:

$$\mathbb{E}_{P}[Y^{1}] - \mathbb{E}_{P}[Y^{0}]$$

$$= \mathbb{E}_{P}[\mathbb{E}_{P}[Y^{1} \mid X] - \mathbb{E}_{P}[Y^{0} \mid X]]$$

$$\stackrel{?}{=} \mathbb{E}_{P}[\mathbb{E}_{P}[Y^{1} \mid A = 1, X] - \mathbb{E}_{P}[Y^{0} \mid A = 0, X]]$$

$$\stackrel{1}{=} \mathbb{E}_{P}[\mathbb{E}_{P}[Y \mid A = 1, X] - \mathbb{E}_{P}[Y \mid A = 0, X]]$$

$$= \Psi(P)$$

(3. (positivity) ensures that the conditional expectations are well-defined).

Goal achieved: Right hand side is expressed only in terms of observable quantities.

Under the assumptions:

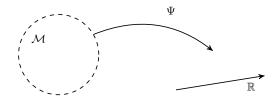
$$\mathbb{E}_{P}[Y^{1}] - \mathbb{E}_{P}[Y^{0}] = \underbrace{\mathbb{E}_{P}[\mathbb{E}_{P}[Y \mid A=1,X] - \mathbb{E}_{P}[Y \mid A=0,X]]}_{(*)} = \Psi(P),$$

for any  $P \in \mathcal{M}$ .

In our statistical analysis, we proceed with (\*).

"Causal inference part" is over.

Now we are exactly in the situation we wanted:



#### Average treatment effect (ATE)

- $O = (X, A, Y) \in \mathbb{R}^d \times \{0, 1\} \times \{0, 1\}$
- ▶ The ATE is defined for  $P \in \mathcal{M}$  as

$$\Psi(P) = \mathbb{E}_P[\mathbb{E}_P[Y \mid A=1,X] - \mathbb{E}_P[Y \mid A=0,X]]$$

### Target statistical estimand: g-formula

We can write the target parameter as:

$$\begin{split} \Psi(P) &= \mathbb{E}_{P} \big[ \mathbb{E}_{P} \big[ Y \mid A = 1, X \big] - \mathbb{E}_{P} \big[ Y \mid A = 0, X \big] \big] \\ &= \mathbb{E}_{P} \big[ f(1, X) - f(0, X) \big] \\ &= \int_{\mathbb{R}^{d}} \big( f(1, X) - f(0, X) \big) d\mu_{X}(X) = \tilde{\Psi}(f, \mu_{X}) \end{split} \tag{*}$$

where

$$f(a,x) = \mathbb{E}[Y \mid A = a, X = x]$$

and  $\mu_X$  is the marginal distribution of X.

We refer to this as the g-formula.

# Target statistical estimand: IP-weighting

We can also rewrite the target parameter as:

$$\Psi(P) = \int_{\mathbb{R}^{d}} (f(1,x) - f(0,x)) d\mu_{X}(x) \qquad (*)$$

$$= \int_{\mathbb{R}^{d}} \sum_{y=0,1} y (\mu_{Y}(y \mid 1,x) - \mu_{Y}(y \mid 0,x)) d\mu_{X}(x)$$

$$= \int_{\mathbb{R}^{d}} \sum_{y=0,1} \sum_{a=0,1} y (a\mu_{Y}(y \mid a,x) - (1-a)\mu_{Y}(y \mid a,x)) d\mu_{X}(x)$$

$$= \int_{\mathbb{R}^{d}} \sum_{y=0,1} \sum_{a=0,1} \left( \frac{ay}{\pi(a \mid x)} - \frac{(1-a)y}{\pi(a \mid x)} \right) \mu_{Y}(y \mid a,x) \pi(a \mid x) d\mu_{X}(x)$$

$$= \tilde{\Psi}_{ipw}(\pi,p) \quad (**)$$

where  $\pi(a | x) = P(A = 1 | X = x)$ .

The g-formula:

$$\widetilde{\Psi}(f, \mu_X) = \int_{\mathbb{R}^d} (f(1, x) - f(0, x)) d\mu_X(x) 
= \mathbb{E}_P[f(1, X) - f(0, X)].$$
(\*)

The IP-weighted formula:

$$\widetilde{\Psi}_{ipw}(\pi, p) = \int_{\mathbb{R}^d} \sum_{a=0,1} \sum_{y=0,1} \left( \frac{ay}{\pi(a \mid x)} - \frac{(1-a)y}{\pi(a \mid x)} \right) dP(o) 
= \mathbb{E}_P \left[ \frac{AY}{\pi(1 \mid X)} - \frac{(1-A)Y}{\pi(0 \mid X)} \right]$$
(\*\*)

- f and (the average over)  $\mu_X$  are nuisance parameters for the g-formula.
- $\blacktriangleright$   $\pi$  and (the average over) p are nuisance parameters for the IP-weighted formula.

Yet another representation of the target parameter is

$$\widetilde{\Psi}_{ee}(f, \pi, p) = \int_{\mathbb{R}^{d}} \sum_{a=0,1} \sum_{y=0,1} \left\{ \left( \frac{a}{\pi(a \mid x)} - \frac{1-a}{\pi(a \mid x)} \right) (y - f(a, x)) + f(1, x) - f(0, x) \right\} p_{Y}(y \mid a, x) \pi(a \mid x) d\mu_{X}(x)$$

$$= \mathbb{E}_{P} \left[ \left( \frac{A}{\pi(A \mid X)} - \frac{1-A}{\pi(A \mid X)} \right) (Y - f(A, X)) + f(1, X) - f(0, X) \right]$$

• f,  $\pi$  and (the average over) p are nuisance parameters for this parametrization.

Yet another representation of the target parameter is

$$\widetilde{\Psi}_{ee}(f, \pi, \rho) = \int_{\mathbb{R}^{d}} \sum_{a=0,1} \sum_{y=0,1} \left\{ \left( \frac{a}{\pi(a \mid x)} - \frac{1-a}{\pi(a \mid x)} \right) (y - f(a, x)) + f(1, x) - f(0, x) \right\} \rho_{Y}(y \mid a, x) \pi(a \mid x) d\mu_{X}(x)$$

$$= \mathbb{E}_{P} \left[ \left( \frac{A}{\pi(A \mid X)} - \frac{1-A}{\pi(A \mid X)} \right) (Y - f(A, X)) + f(1, X) - f(0, X) \right]$$

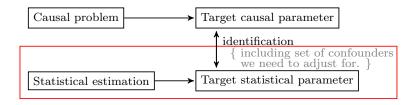
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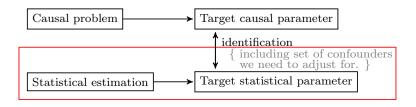
#### SMALL EXERCISE:

- 1. Note that  $\tilde{\Psi}_{\rm ee}(f,\pi,p) = \tilde{\Psi}(f,\mu_X) + [\text{an extra term}]_1$ . Show that it can also be written as  $\Psi_{\rm ee}(f,\pi,p) = \tilde{\Psi}_{\rm ipw}(\pi,p) + [\text{an extra term}]_2$ .
- 2. Show that  $\tilde{\Psi}_{ee}(f, \pi, p) = \mathbb{E}_P[Y^1] \mathbb{E}_P[Y^0]$  under the identifiability assumptions (consistency, exchangeability and positivity).

- Causal parameter (now fixed).
- Causal model: How do the observed variables affect one another?
  - are the covariates we observe sufficient to remove confounding? which variables do we need to adjust for to make treatment groups comparable?
- Identifiability
  - identifiability assumptions allow us to write causal parameter as statistical parameter.
  - the assumptions may not hold, but we can state and discuss them.
- Statistical parameter
  - Statistical interpretation: The average effect in the population, standardized to the distribution of covariates.







- one estimator is not more causal than another.
- different estimators are based on different nuisance parameters and have different statistical properties (bias/variance).

### On a sidenote: Other simple causal parameters

We focus on the ATE as an example of a causal parameter.

But note that other simple causal parameters can be constructed from  $\mathbb{E}[Y^1]$  and  $\mathbb{E}[Y^0]$ .

Like:

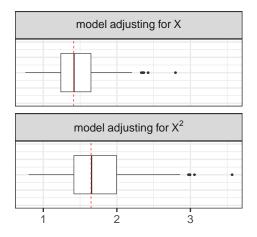
$$\Psi^{\mathsf{RR}}(P) = \frac{\mathbb{E}[Y^1]}{\mathbb{E}[Y^0]},$$

or,

$$\Psi^{\mathsf{OR}}(P) = \frac{\mathbb{E}[Y^1]/(1 - \mathbb{E}[Y^1])}{\mathbb{E}[Y^0]/(1 - \mathbb{E}[Y^0])}.$$

### On a sidenote: Other simple causal parameters

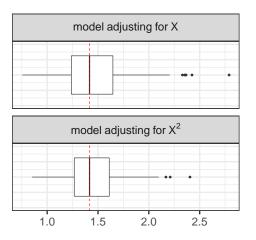
log(OR) as a regression coefficient is a moving target in different logistic regression models:



The upper panel does not show a biased estimator, just an estimator targeting a different parameter (dashed red line).

### On a sidenote: Other simple causal parameters

The corresponding causal odds ratio is a fixed target — and the target does not change depending on adjustment for X or  $X^2$ :



... but these are different statistical estimators, and they have different statistical properties.

#### Last slide of this lecture

#### Summarizing this lecture:

- b take 5 minutes to write down 3−10 keywords/concepts/formulas from this lecture;
- b discuss the keywords with the person sitting next to you, and explain their significance in the overall targeted learning framework (5 min).