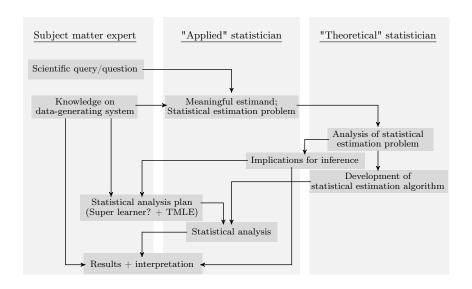
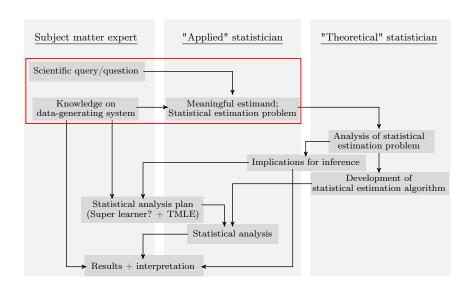
Day 1, Lecture 2

In this lecture, our goal is to:

- 1. Explain the utilization of causal inference tools to define nonparametric targets of estimation, highlighting the role of counterfactual reasoning and hypothetical interventions.
- 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 (ATE)
 - model-free and estimator-free definition of parameters

Moving targets with different logistic regression models

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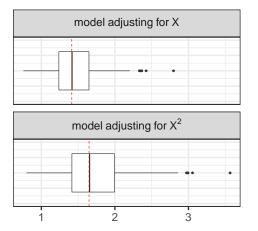
$$\operatorname{logit} \mathbb{E}[Y \mid A, X] = \beta_0 + \beta_A A + \beta_X^{\mathsf{T}} X^2$$

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.

¹And, 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",¹ but we need this part to very clear about with it is we are estimating.
 - ► To start with, 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.

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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:

- 1. 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:²

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



²This 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:

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

- $\mu_{Y}(y \mid A, X) = P(Y = y \mid A, X)$
- $\pi(a \mid X) = P(A = a \mid X)$
- μ_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 μ_Y , μ_X .
- * We could impose some parametric structure on π , but let us assume that we do not.

Operators on functions of the observed data³

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).

³van 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 between 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 effect⁴ (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.

⁴or 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
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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:

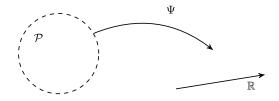
$$\mathbb{E}_{P}[Y^{1}] - \mathbb{E}_{P}[Y^{0}] = \underbrace{\mathbb{E}_{P}[\mathbb{E}_{P}[Y \mid A=1,X] - \mathbb{E}_{P}[Y \mid A=0,X]]}_{(*)} = \Psi(P),$$

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 μ_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:

$$\begin{split} \Psi(P) &= \int_{\mathbb{R}^d} \left(f(1,x) - f(0,x) \right) d\mu_X(x) \\ &= \int_{\mathbb{R}^d} \sum_{y=0,1} y \left(\mu_Y(y \mid 1,x) - \mu_Y(y \mid 0,x) \right) d\mu_X(x) \\ &= \int_{\mathbb{R}^d} \sum_{y=0,1} \sum_{a=0,1} y \left(a\mu_Y(y \mid a,x) - (1-a)\mu_Y(y \mid a,x) \right) d\mu_X(x) \\ &= \int_{\mathbb{R}^d} \sum_{y=0,1} \sum_{a=0,1} \left(\frac{ay}{\pi(a \mid x)} - \frac{(1-a)y}{\pi(a \mid x)} \right) \mu_Y(y \mid a,x) \pi(a \mid x) d\mu_X(x) \\ &= \tilde{\Psi}_{\mathrm{ipw}}(\pi,p) \quad (**) \end{split}$$

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) μ_X are nuisance parameters for the g-formula.
- \blacktriangleright π 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, π and (the average over) p are nuisance parameters for this parametrization.

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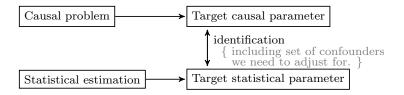
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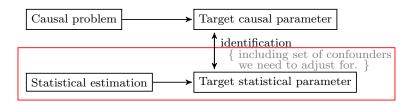
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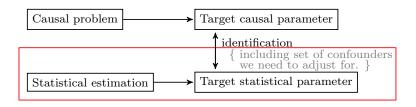
SMALL EXERCISE:

- 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 $\tilde{\Psi}_{\rm ee}(f,\pi,p) = \tilde{\Psi}_{\rm ipw}(\pi,p) + [\text{an extra term}]_2$.
- 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.







- Estimands (target parameters) defined as statistical functionals
 Ψ : M → Ψ(M) are independent of the specific estimation method used.
- One estimator is not more causal than another.
- Different estimators are based on different nuisance parameters and have different statistical properties (bias/variance).
- Whether one type of estimator or algorithm best fit the data does not affect the estimand, only estimation performance.

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:

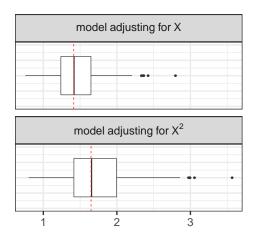
$$\Psi^{\mathsf{RR}}(P) = \frac{\mathbb{E}[Y^1]}{\mathbb{E}[Y^0]},$$

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

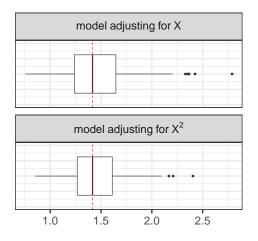
log(OR) as a regression coefficient is a moving target in different logistic regression models:



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.