STANDARDIZATION TO ADJUST FOR CONFOUNDING

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LEARNING OBJECTIVES.

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

1. Describe standardization to estimate marginal effects.
2. Interpret standardized estimates
3. Use modeling to estimate standardized estimates with many covariates.
4. Describe bootstrapping to obtain 95% confidence intervals.

PLAN FOR TODAY: STANDARDIZATION.

1. Recap
2. Standardization without models
3. Standardization with models
4. Bootstrapping
5. Standardization example
6. Standardization versus IP weighting

RECALL: CAUSAL QUESTION OF INTEREST.

1. What is the effect of quitting smoking on weight gain?
2. What is the effect of quitting smoking on risk of death?

RECALL: MARGINAL CAUSAL EFFECTS.

Causal Question:
What is the effect of smoking cessation on weight gain?

We compare:

1. the average weight gain had everyone quit smoking

$$E[Y^{a=1}]$$

versus

2. the average weight gain had everyone *not* quit smoking

$$E[Y^{a=0}]$$

$E[Y^{a=1}] - E[Y^{a=0}]$ is a marginal causal effect

RECALL: CONDITIONAL CAUSAL EFFECTS.

Causal Question:
What is the effect of smoking cessation on weight gain?

We compare:

1. the average outcome had everyone in stratum $L = l$ quit smoking

$$\mathrm{E}[Y^{a=1}|L = l]$$

versus

2. the average outcome had everyone in stratum $L = l$ *not* quit smoking

$$\mathrm{E}[Y^{a=0}|L = l]$$

$\mathrm{E}[Y^{a=1}|L] - \mathrm{E}[Y^{a=0}|L = l]$ is a conditional causal effect

RECALL: IDENTIFIABILITY ASSUMPTIONS.

We need assumptions to estimate causal effects:

1. Conditional exchangeability: the mean outcome in the treated would have been the same as the mean outcome in the untreated, had they been treated, and vice versa, within levels of L

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

2. Positivity: the probability of being assigned to each treatment level is greater than 0 within levels of L

$$\Pr[A = a|L = l] > 0 \text{ for all } a, l \text{ if } \Pr[\mathrm{L} = \mathrm{l}] \neq 0$$

3. Consistency: an individual's counterfactual outcome under their observed treatment level is equal to their observed outcome

$$Y^a = Y \text{ when observed treatment } A \text{ is equal to } a$$

POLL QUESTION 1: IDENTIFIABILITY ASSUMPTIONS.

Consider the mean counterfactual outcome had everyone been treated among people with $L = l$:

$$\mathrm{E}[Y^{a=1} | L = l]$$

The following equality

$$\mathrm{E}[Y^{a=1} | L = l] = \mathrm{E}[Y^{a=1} | A = 1, L = l]$$

is true because of which assumption?

A. Conditional exchangeability
B. Consistency
C. Positivity
D. None of the above

RECALL: CONDITIONAL EXCHANGEABILITY.

$$\mathrm{E}[Y^{a=1}|L = l] = \mathrm{E}[Y^{a=1}|A = 1, L = l]$$

is true because of conditional exchangeability

- Within levels of L, the counterfactual outcome is independent of the observed treatment:

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

- Within levels of L, the mean counterfactual outcome should be the same regardless of whether we stratify on A or not (because Y^a and A are unrelated, conditional on L)

POLL QUESTION 2: IDENTIFIABILITY ASSUMPTIONS.

The following equality

$$\mathrm{E}[Y^{a=1}|A=1, L=l] = \mathrm{E}[Y|A=1, L=l]$$

is true because of which assumption?

A. Exchangeability
B. Consistency
C. Positivity
D. None of the above

RECALL: CONSISTENCY.

$$\mathrm{E}[Y^{a=1}|A=1, L=l] = \mathrm{E}[Y|A=1, L=l]$$

is true because of consistency

Among people with $A = 1$, their counterfactual outcome under treatment ($Y^{a=1}$) is equal to their observed outcome (Y).

RECALL: PUTTING THE ASSUMPTIONS TOGETHER.

$$\mathrm{E}[Y^a | L = l] = \mathrm{E}[Y^a | A = a, L = l] = \mathrm{E}[Y | A = a, L = l]$$

This equality is true because of conditional exchangeability.

This equality is true because of consistency.

We can estimate this quantity among people with $A = 1$ and among people with $A = 0$ in our observed data because of positivity.

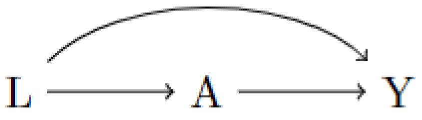
We can do this

- Non-parametrically: e.g., by calculating means in our data
- Parametrically: e.g., by fitting an outcome regression model

Using a parametric approach introduces additional assumptions.

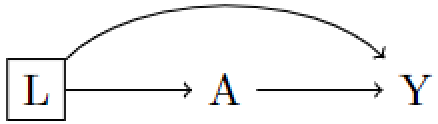
RECALL: METHODS TO ADDRESS CONFOUNDING.

Suppose we have confounders L for the effect of A to Y:

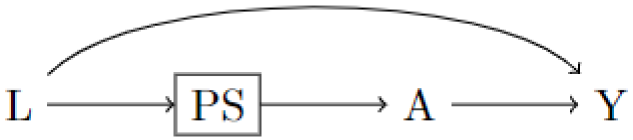


We can:

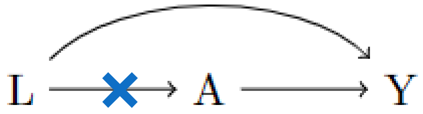
1. Stratify or condition on L to block the open backdoor path from A to Y (e.g., outcome regression)



2. Generate propensity scores and stratify, condition, or match on propensity scores



3. Use inverse probability of treatment weights (IPTW)



MARGINAL EFFECTS IN OBSERVATIONAL STUDIES.

We know how to obtain

- Conditional effects by using stratification/outcome regression
- Marginal effects by using inverse probability of treatment weighting

Standardization is another method to obtain marginal effects.

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STANDARDIZATION TO ESTIMATE MARGINAL CAUSAL EFFECTS.

To estimate marginal effects, we need to know

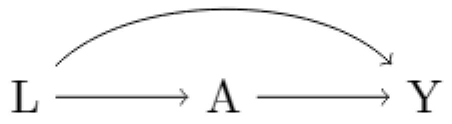
- The mean weight gain had everyone quit smoking

$$E[Y^{a=1}]$$

- The mean weight gain had everyone *not* quit smoking

$$E[Y^{a=0}]$$

However, in the presence of a confounder L:



- The mean outcome among the treated or untreated is not equal to the marginal counterfactual outcomes

$$E[Y|A=1] \neq E[Y^{a=1}]$$
$$E[Y|A=0] \neq E[Y^{a=0}]$$

- But we can estimate conditional counterfactual outcomes:

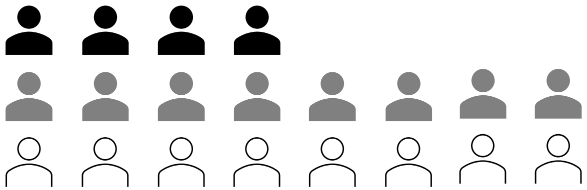
$$E[Y|A=1,L] = E[Y^{a=1}|L]$$
$$E[Y|A=0,L] = E[Y^{a=0}|L]$$

Using standardization, we can weight the conditional counterfactual outcomes to obtain marginal counterfactual outcomes.

ESTIMATING $\mathrm{E}[Y^{a=1}]$.

- Suppose exercise is our only confounder
- In our study population, we'd have a mix of people with:
  - $L = 0$: much exercise
  - $L = 1$: moderate exercise
  - $L = 2$: little or no exercise

- For example:

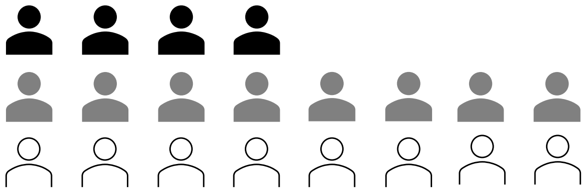


- What is the mean counterfactual outcome had everyone quit smoking?

- Hypothetically, to calculate $\mathrm{E}[Y^{a=1}]$, we could take the average of the counterfactual outcomes for:
  - the 4 people who do much exercise $(L = 0)$;
  - the 8 people who do moderate exercise $(L = 1)$; and
  - the 8 people who do little or no exercise $(L = 2)$

$\mathrm{E}[Y^{a=1}]$ AS A WEIGHTED AVERAGE.

The study population:



We can also think of $\mathrm{E}[Y^{a=1}]$ as a *weighted* average:

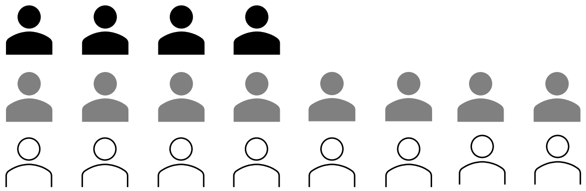
$$\mathrm{E}[Y^{a=1}] = \frac{(4 \times \text{black person}) + (8 \times \text{grey person}) + (8 \times \text{outlined person})}{20}$$

or

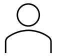
$$\mathrm{E}[Y^{a=1}] = \left(\frac{4}{20} \times \text{black person}\right) + \left(\frac{8}{20} \times \text{grey person}\right) + \left(\frac{8}{20} \times \text{outlined person}\right)$$

$E[Y^{a=1}]$ AS A WEIGHTED AVERAGE.

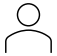
The study population:



We can also think of $E[Y^{a=1}]$ as a *weighted* average:

$E[Y^{a=1}] = \big[(4 \times$  $) + (8 \times$  $) + (8 \times$  $)\big] / 20$

or

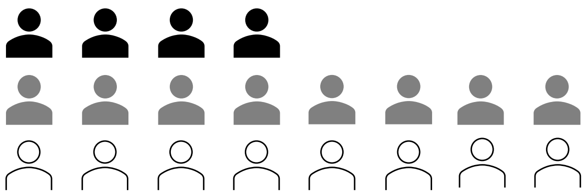
$E[Y^{a=1}] = \left(\frac{4}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right)$

These are the weights and correspond to the probability of observing an individual with a given exercise level:

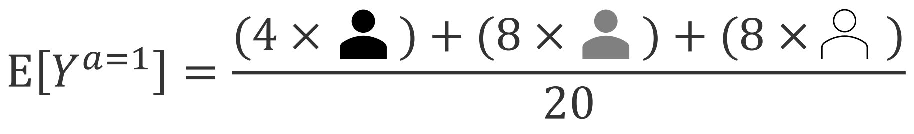
$$\Pr[L = l]$$

$\mathrm{E}[Y^{a=1}]$ AS A WEIGHTED AVERAGE.

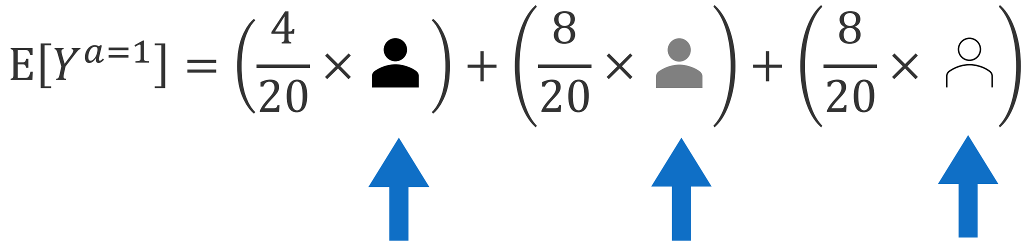
The study population:



We can also think of $\mathrm{E}[Y^{a=1}]$ as a *weighted* average:



or



These are the counterfactual means within levels of exercise:

$$\mathrm{E}[Y^{a=1} | L = l]$$

$\mathrm{E}[Y^{a=1}]$ AS A WEIGHTED AVERAGE: PUTTING IT ALL TOGETHER.

$\mathrm{E}[Y^{a=1}] = \left(\frac{4}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right)$

The counterfactual mean under treatment, $\mathrm{E}[Y^{a=1}]$, is a weighted average of the counterfactual means within each level of L, $\mathrm{E}[Y^{a=1}|L]$:

$$\begin{aligned}\mathrm{E}[Y^{a=1}] = \; & \Pr[L=0] \times \mathrm{E}[Y^{a=1}|L=0] + \\ & \Pr[L=1] \times \mathrm{E}[Y^{a=1}|L=1] + \\ & \Pr[L=2] \times \mathrm{E}[Y^{a=1}|L=2]\end{aligned}$$

$\mathrm{E}[Y^{a=1}]$ AS A WEIGHTED AVERAGE: PUTTING IT ALL TOGETHER.

$\mathrm{E}[Y^{a=1}] = \left(\frac{4}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right)$

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These probabilities can be calculated in our observed data.

These means are equal to $\mathrm{E}[Y|A=1, L=l]$ because the treated and untreated are exchangeable conditional on exercise

$\mathrm{E}[Y^{a=1}]$ AS A WEIGHTED AVERAGE: PUTTING IT ALL TOGETHER.

$\mathrm{E}[Y^{a=1}] = \left(\frac{4}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right) + \left(\frac{8}{20} \times\right.$  $\left.\right)$

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$$\begin{aligned}\mathrm{E}[Y^{a=1}] = \; & \Pr[L=0] \times \mathrm{E}[Y|A=1, L=0] + \\ & \Pr[L=1] \times \mathrm{E}[Y|A=1, L=1] + \\ & \Pr[L=2] \times \mathrm{E}[Y|A=1, L=2]\end{aligned}$$

You may see this written in a more compact notation: $\mathrm{E}[Y^{a=1}] = \sum_{l=0}^{L} \Pr[L=l] \times \mathrm{E}[Y|A=1, L=l]$

WE CAN CALCULATE $\mathrm{E}[Y^a]$ USING OUR OBSERVED DATA.

$$\mathrm{E}[Y^{a=1}] = \sum_{l=0}^{L} \Pr[L = l] \times \mathrm{E}\,[Y|A = 1, L = l]$$

- Under the assumptions of
  - Conditional exchangeability
  - Positivity
  - Consistency
- We can similarly estimate $\mathrm{E}[\mathrm{Y}^{\mathrm{a}=0}]$
- Once we have estimates for $\mathrm{E}[\mathrm{Y}^{\mathrm{a}=1}]$ and $\mathrm{E}[\mathrm{Y}^{\mathrm{a}=0}]$, we can identify the marginal causal effect:

$$\mathrm{E}[\mathrm{Y}^{\mathrm{a}=1}] - \mathrm{E}[\mathrm{Y}^{\mathrm{a}=0}]$$

INTERPRETATION OF STANDARDIZED ESTIMATES.

- Our causal estimate was $\mathrm{E}[Y^{a=1}] - \mathrm{E}[Y^{a=0}] = 2.56 \text{ kg.}$
- Interpretation: Had everyone quit smoking, the mean weight gain would have been 2.56 kg higher than had everyone not quit smoking.
- Notice:
  - The use of counterfactual language ("had everyone quit smoking" and "had everyone not quit smoking")
  - Marginal interpretation (i.e. we don't specify "conditional on exercise")

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STANDARDIZATION WITH MULTIPLE CONFOUNDERS.

- Our causal estimate of $\mathrm{E}[Y^{a=1}] - \mathrm{E}[Y^{a=0}] = 2.56\ \mathbf{kg}$ assumes exercise is our only confounder
- We estimated the causal effect by calculating probabilities and conditional means in our data
- In general, we'd expect to adjust for multiple confounders
- With multiple L's, we have to calculate the probabilities and means for all combination of L's

$$\mathrm{E}[Y^a] = \sum_{l=0}^{L} \Pr[L = l] \times \mathrm{E}\,[Y|A = a, L = l]$$

POLL QUESTION: STANDARDIZATION WITH MULTIPLE CONFOUNDERS

Suppose we have three dichotomous confounders. How many means would we have to calculate to estimate the counterfactual mean under treatment, $\mathrm{E}[Y^{a=1}]$?

$$\mathrm{E}[Y^{a=1}] = \sum_{l=0}^{L} \Pr[L = l] \times \mathrm{E}\left[Y|A = 1, L = l\right]$$

A. Three

B. Six

C. Eight

D. Twelve

STANDARDIZATION: THE CURSE OF DIMENSIONALITY.

- With three dichotomous confounders, we have to calculate:
  - Eight probabilities, $\Pr[L = l]$
  - Eight conditional means, $\mathrm{E}[Y|A = 1, L = l]$

  just to estimate $\mathrm{E}[Y^{a=1}]$
- Then we have to do it again to estimate $\mathrm{E}[Y^{a=0}]$
- The number of quantities that we have to calculate grows exponentially as we include more and more confounders
- To handle high-dimensionality, we need models

WHERE DO MODELS COME IN WITH STANDARDIZATION?

Recall our formula for standardization:

$$\mathrm{E}[Y^a] = \sum_{l=0}^{L} \Pr[L = l] \times \mathrm{E}\left[Y | A, L = l\right]$$

- We'll first consider how to use models to estimate the mean outcome, conditional on treatment and confounders
- With multiple and/or continuous Ls, we can use an outcome model:

$$\mathrm{E}[Y|A, L] = \beta_0 + \beta_1 A + \beta_2 L_1 + \beta_3 L_2 + \cdots \beta_{p+1} L_p$$

- This is the same model that we saw in outcome regression!

TRADE-OFFS WHEN USING MODELS.

Just like with outcome regression, there are trade-offs when using models for standardization.

BENEFITS OF USING MODELS:

- Estimates are more efficient (narrower confidence intervals)
- We have to because we have finite data

RISKS OF USING MODELS:

- These models impose *a priori* restrictions/assumptions, e.g.
  - No product terms between variables
  - The contribution of continuous variables to the outcome is linear
- If these assumptions are wrong, we get biased estimates

WHAT ABOUT $\Pr[L = l]$?

- Now that we have $\mathrm{E}[Y|A = a, L = l]$ from our model, we have to weight these conditional means according to $\Pr[L = l]$:

$$\mathrm{E}[Y^a] = \sum_{l=0}^{L} \Pr[L = l] \times \mathrm{E}\,[Y|A, L = l]$$

- There is a trick that we can use that allows us to avoid actually estimating $\Pr[L = l]$

There are four steps to the method:

1. Expansion of the dataset
2. Outcome modelling
3. Prediction
4. Standardization by averaging

STANDARDIZATION USING STATISTICAL SOFTWARE.

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1. Expansion of the dataset
2. Outcome modelling
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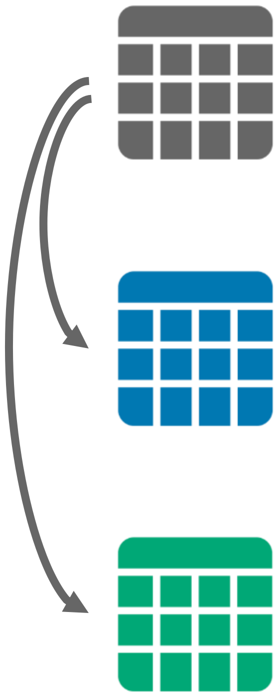

Create two copies of the original dataset.

In the first copy, we set $A = 1$ for everyone (i.e., dataset for the counterfactual world where everyone been treated).

In the second copy, we set $A = 0$ for everyone (i.e., dataset for the counterfactual world where everyone had been untreated).

STANDARDIZATION USING STATISTICAL SOFTWARE.

There are four steps to the method:

1. Expansion of the dataset
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$$\mathrm{E}[Y|A,L] = \beta_0 + \beta_1 A + \beta_2 L_1 + \beta_3 L_2 + \cdots \beta_{p+1} L_p$$

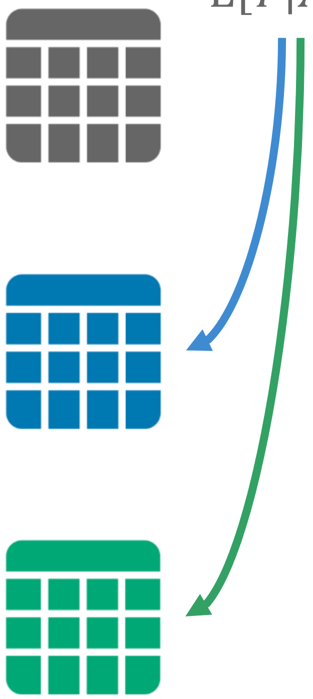
Fit our outcome regression model in the original dataset.

STANDARDIZATION USING STATISTICAL SOFTWARE.

There are four steps to the method:

1. Expansion of the dataset
2. Outcome modelling
3. Prediction
4. Standardization by averaging

$$\mathrm{E}[Y|A, L] = \beta_0 + \beta_1 A + \beta_2 L_1 + \beta_3 L_2 + \cdots \beta_{p+1} L_p$$



Using our fitted model, obtain the predicted conditional means, $\hat{\mathrm{E}}[Y|A, L]$, for our two copies of the dataset.

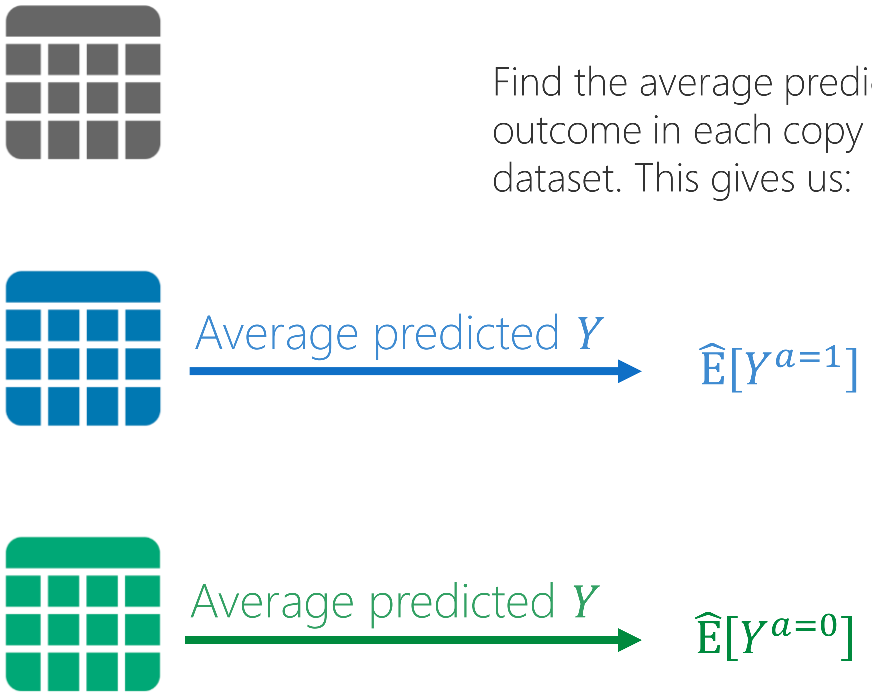
- Expected outcome for each individual had they been treated
- Expected outcome for each individual had they been untreated

STANDARDIZATION USING STATISTICAL SOFTWARE.

There are four steps to the method:

1. Expansion of the dataset
2. Outcome modelling
3. Prediction
4. Standardization by averaging

Find the average predicted outcome in each copy of the dataset. This gives us:



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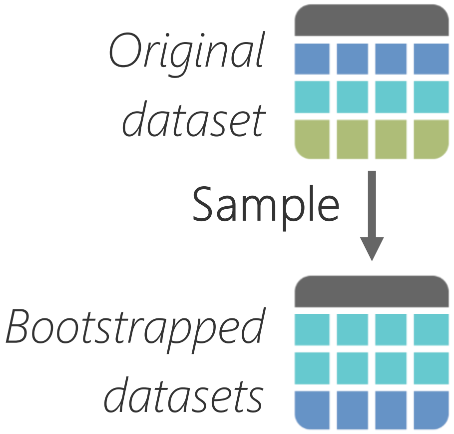
BOOTSTRAPPING TO OBTAIN 95% CONFIDENCE INTERVALS.

In order to calculate an approximate 95% confidence interval, we need to use a method called bootstrapping:

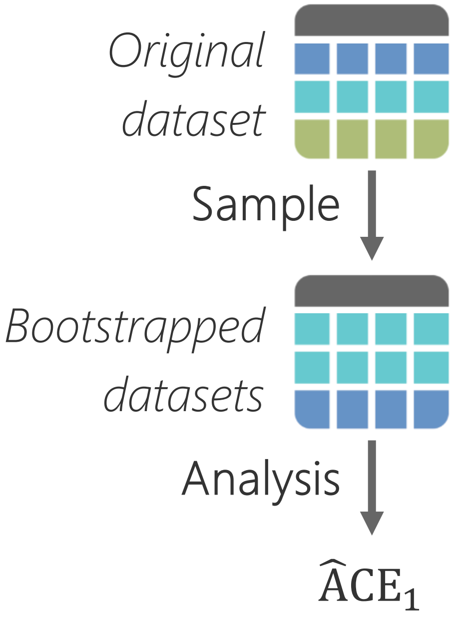
1. Sample with replacement from the original dataset.
    - Some individuals may get selected more than once; some not at all
    - Creates a new (bootstrapped) dataset that should have the same number of observations as the original dataset



BOOTSTRAPPING TO OBTAIN 95% CONFIDENCE INTERVALS.

In order to calculate an approximate 95% confidence interval, we need to use a method called bootstrapping:

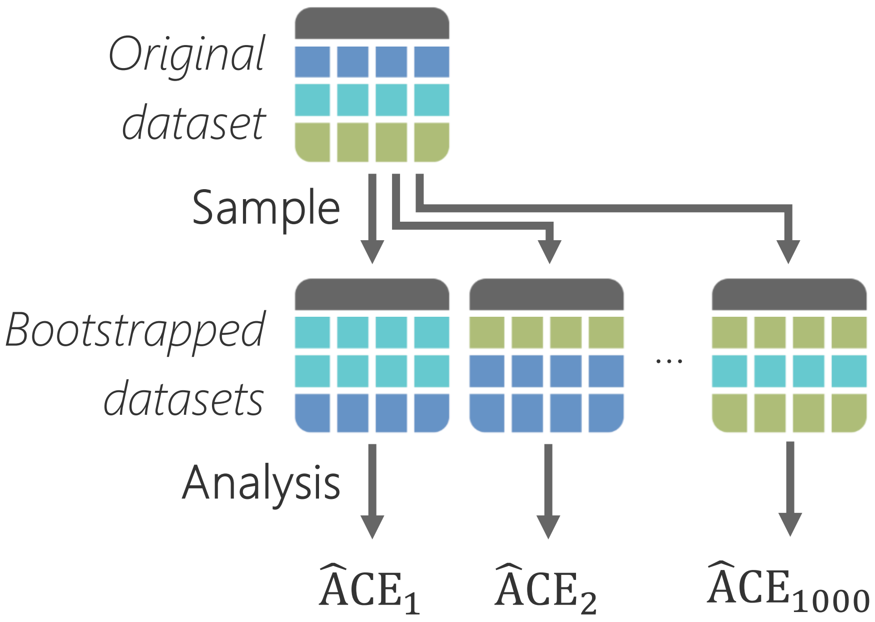
1. Sample with replacement from the original dataset.
2. Calculate the marginal average causal effect (ACE) using standardization in your bootstrapped dataset.
   - Expansion, outcome model, prediction, standardize by averaging



BOOTSTRAPPING TO OBTAIN 95% CONFIDENCE INTERVALS.

In order to calculate an approximate 95% confidence interval, we need to use a method called bootstrapping:

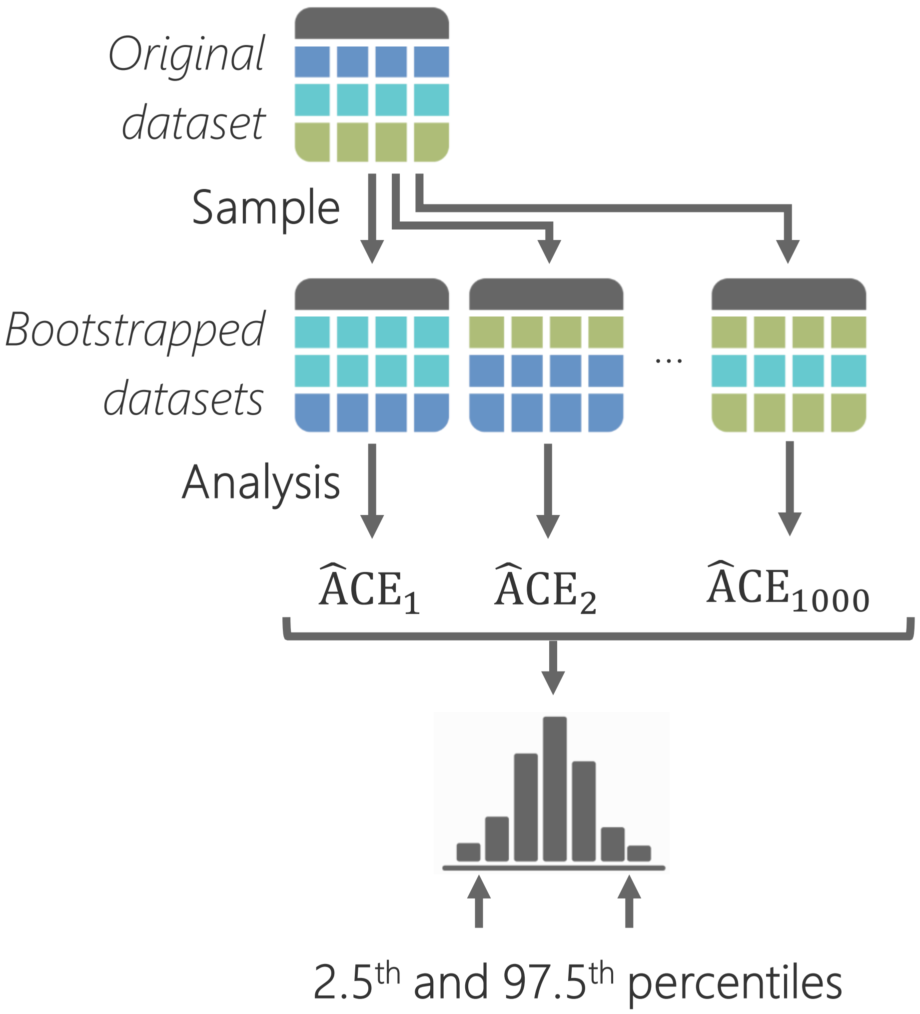
1. Sample with replacement from the original dataset.
2. Calculate the standardized estimate in your bootstrapped dataset.
3. Repeat steps 1-2 for 1,000 times.
   - End up with 1,000 bootstrapped estimates for the standardized effect



BOOTSTRAPPING TO OBTAIN 95% CONFIDENCE INTERVALS.

In order to calculate an approximate 95% confidence interval, we need to use a method called bootstrapping:

1. Sample with replacement from the original dataset.
2. Calculate the standardized estimate in your bootstrapped dataset.
3. Repeat steps 1-2 for 1,000 times.
4. Use the 2.5th and 97.5th percentiles of the 1,000 estimates as the 95% CI limits



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STANDARDIZATION EXAMPLE.

Estimating the Effects of Potential Public Health Interventions on Population Disease Burden: A Step-by-Step Illustration of Causal Inference Methods

Jennifer Ahern, Alan Hubbard, and Sandro Galea

STANDARDIZATION EXAMPLE: BACKGROUND.

- Data: New York Social Environment Study
- Exposure: neighborhood smoking norms (proportion of residents who believe it is unacceptable to smoke cigarettes)
- Outcome: individual smoking behavior
- What are some potential confounders of this relationship?

(Ahern et al., 2009)

STANDARDIZATION EXAMPLE: ANALYSIS.

The authors included the follow variables in their model:

- Smoking norms (exposure)
- Smoking history
- Age
- Race
- Sex
- Marital status
- Birthplace
- Survey language
- Years lived in neighborhood
- Income
- Education
- Unemployed
- Smoking history × smoking norms

Why do you think the authors wanted to use standardization?

(Ahern et al., 2009)

STANDARDIZATION EXAMPLE: ANALYSIS.

Recall the four steps of standardization:

1. Expansion of the dataset
2. Outcome modelling
3. Prediction
4. Standardization by averaging

(Ahern et al., 2009)

STANDARDIZATION EXAMPLE: OUTCOME MODELLING.

The table on the left presents some of results from the author's logistic outcome model*.

The authors present an odds ratio of 0.27 for neighborhood smoking norms. Is this a marginal or conditional effect?

*The authors actually use a generalized estimating equation logistic model to deal with clustering by neighborhood. For simplicity, we'll treat it as a regular logistic model.

	Odds Ratio
Intercept	
Neighborhood smoking norms	0.27
Smoking before moved to neighborhood	
Never smoked	1.00
Ever smoked/tried smoking	0.98
Weekly smoker	15.21
Daily smoker	17.49
Age, years	
18–24	3.58
25–34	2.25
35–44	1.40
45–54	1.00
55–64	0.57
≥65	0.18
Missing	2.14
Race	
White	1.00
African American	0.96
Asian	0.73
Hispanic	1.12
Other	1.69
Missing	1.45

Table continues

(Ahern et al., 2009)

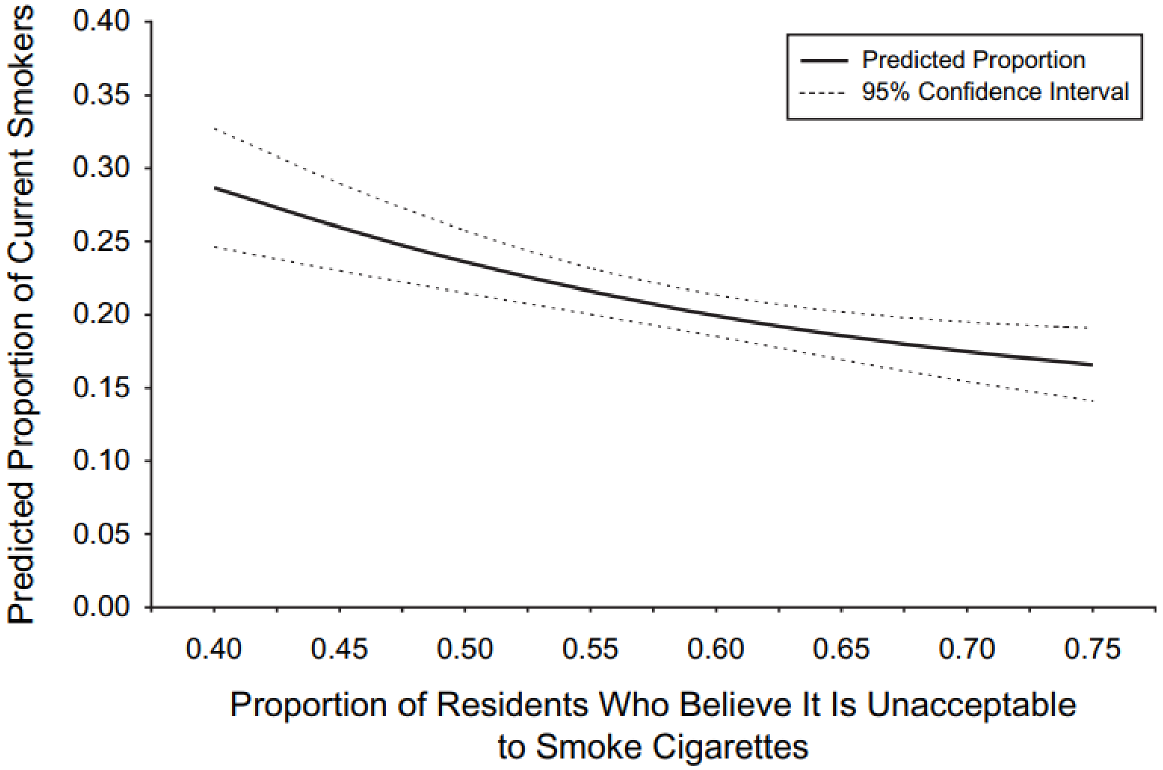
STANDARDIZATION EXAMPLE: STANDARDIZATION.

- Recall that we have a continuous exposure (proportion of residents who believe it is unacceptable to smoke cigarettes)
- Many possible counterfactual outcomes, e.g.
  - What is one's expected smoking behavior if 1% of the neighborhood residents believed it is unacceptable to smoke cigarettes ($Y^{a=0.01}$)
  - What is one's expected smoking behavior if 25% of the neighborhood residents believed it is unacceptable to smoke cigarettes ($Y^{a=0.25}$)

(Ahern et al., 2009)

STANDARDIZATION EXAMPLE 3: RESULTS.

(Y^a)



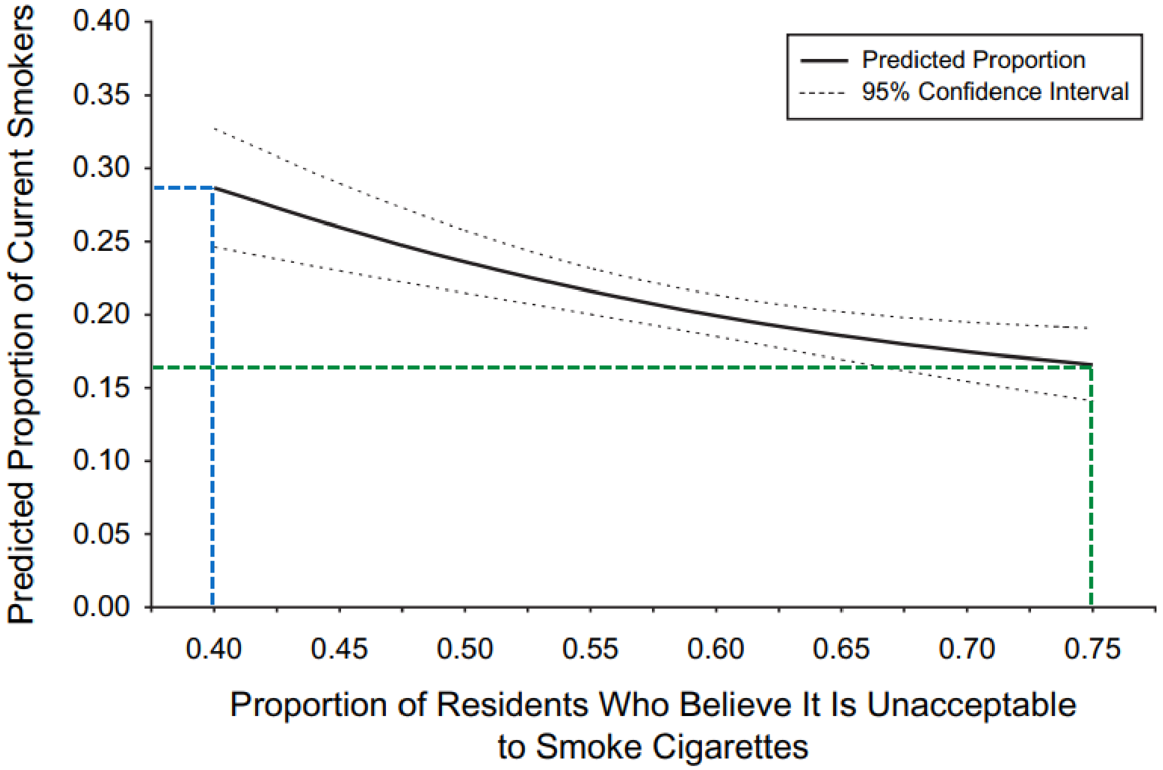
$(A = a)$

What is the estimate for $\mathrm{E}[Y^{a=0.75}] - \mathrm{E}[Y^{a=0.40}]$?

(Ahern et al., 2009)

STANDARDIZATION EXAMPLE 3: RESULTS.

(Y^a)



$(A = a)$

$$\mathrm{E}[Y^{a=0.75}] - \mathrm{E}[Y^{a=0.40}] \approx 0.12$$

However, there are an infinite number of causal contrasts that we could make with a continuous exposure.

(Ahern et al., 2009)

PLAN FOR TODAY: STANDARDIZATION.

1. Recap
2. Standardization without models
3. Standardization with models
4. Bootstrapping
5. Standardization example
6. Standardization versus IP weighting

IP WEIGHTING OR STANDARDIZATION?

- Both methods give us estimates for the marginal effect:
$$\mathrm{E}[Y^{a=1}] - \mathrm{E}[Y^{a=0}]$$
- Using non-parametric models for IPW and standardization will give us identical estimates from the two approaches
- Using parametric models for IPW and standardization may give us slightly different results:
  - Fitting different models
    - IPW: model for treatment A to calculate weights
    - Standardization: model for outcome Y
  - Different modelling assumptions
- Large differences between the IPW and standardized estimates alerts us to model misspecification in one or both models

STANDARDIZATION WITH TIME-VARYING TREATMENTS.

- The g-formula extends the standardization procedure that we've described to time-varying treatments and confounders
- Can be very computationally extensive
- See Chapter 21.2 of *Causal Inference: What If* for more information

LEARNING OBJECTIVES.

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

1. Describe standardization to estimate marginal effects.
2. Interpret standardized estimates
3. Use modeling to estimate standardized estimates with many covariates.
4. Describe bootstrapping to obtain 95% confidence intervals.