INVERSE PROBABILITY WEIGHTING
Selection Bias

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Learning objectives
At the end of this lecture you will be able to

- Review the conditions for selection bias under the null
- Use IP weighting to adjust for selection bias when estimating causal effects

- Key concepts
  - Selection bias under the null
  - IP weights for selection
  - Differential loss to follow-up
  - Competing risks

Plan for today

A. Review of selection bias

B. IP weighting to adjust for selection bias

- Due to loss to follow-up/missing data

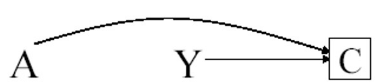
Selection bias

- Ubiquitous concept
- Bias that arises when the parameter of interest in a population differs from the parameter in the subset of individuals from the population that are available for analysis
  - Selection bias for descriptive measures (e.g., prevalence) because of non-random sampling
  - Selection bias for effect measures (e.g., causal risk ratio) because of differential loss to follow-up

Selection bias for effect measures

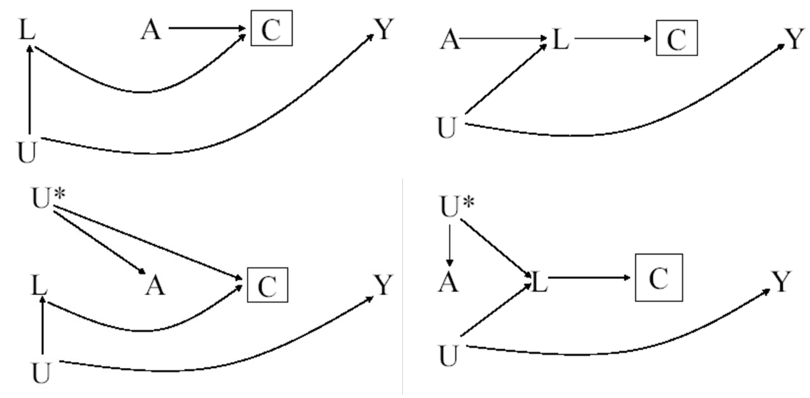
- Many different names
  - Inappropriate selection of controls, Berkson's bias, incidence-prevalence bias, loss to follow-up, nonresponse bias, missing data bias, volunteer bias, self selection, healthy worker effect…
- Here we focus on selection bias that arises even in the absence of a causal effect of treatment on the outcome
  - Selection bias under the null

The structure of selection bias under the null



- The bias arises as the consequence of conditioning on a common effect of treatment and outcome
  - or on a common effect of a cause of the treatment and a cause of the outcome
- That is, the design or the analysis is conditioned on "being selected for analysis" C=0

Missing data / Nonresponse
Censoring / Loss to follow-up



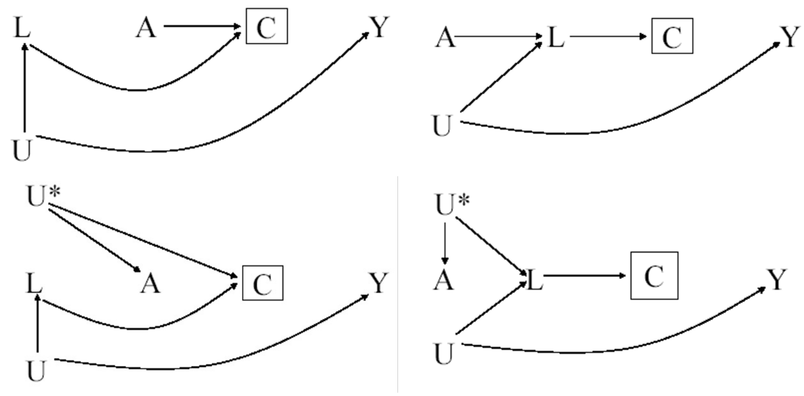
C: Missing data (1: yes, 0: no)

Bias due to differential loss to follow-up is possible in randomized experiments

True 0%

False 0%

Volunteer bias / Self-selection bias



Bias due to self-selection of participants at baseline is possible in randomized experiments

0

True

0%

False

0%

Aside: Internal vs. external validity in randomized experiments

- Internal validity
  - the estimated association has a causal interpretation in the studied population
  - i.e., no selection bias, no confounding
- External validity
  - the estimated association has a causal interpretation in another population
  - i.e., generalizability or transportability

- In randomized experiments
  - There is internal validity
  - Perhaps not external validity

A note on terminology

- The usage of the terms ‘confounding’ and ‘selection bias’ is not standardized

- Epidemiologists use ‘confounding’ and statisticians/econometricians ‘selection bias’ when referring to the same bias
- Others use ‘selection bias’ when ‘confounders’ are unmeasured
- Some use the term ‘selection-confounding’

A note on terminology

- We refer to the presence of common causes as confounding, and to conditioning on common effects as selection bias
  - This classification may not coincide perfectly with the traditional, often discipline-specific, terminologies
- Our goal is not to be normative about terminology
  - but rather to emphasize that there exist two distinct causal structures that lead to bias
  - regardless of the terms chosen to refer to them

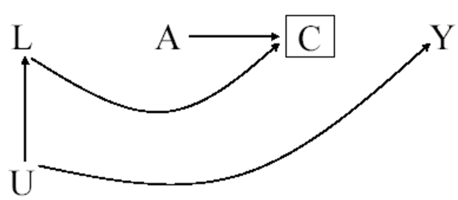
Selection bias in our study population?

- 1629 cigarette smokers
- Aged 25-74 years when interviewed in 1971-75 (baseline)
- Interviewed again in 1982
- Known sex, age, race, weight, height, education, alcohol use, and smoking intensity at both baseline and follow-up visits, and who answered the general medical history questionnaire at baseline

Key variables

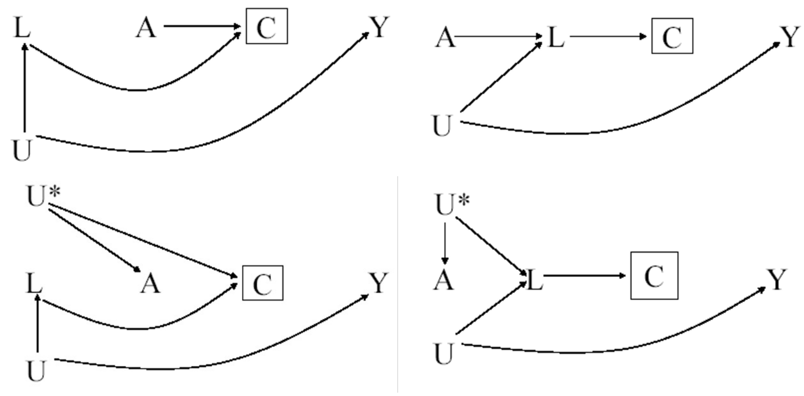
Treatment A	Quit smoking between baseline and 1982 1: yes, 0: no
Continuous outcome Y	Weight gain, kg Weight in 1982 minus baseline weight Available for 1566 individuals
Dichotomous outcome D	Death by 1992 1: yes, 0: no
Baseline (pre-treatment) covariates	Age, sex, race, alcohol use, intensity of smoking, weight…
Censoring C	Missing weight in 1982 1: yes, 0: no

Differential loss to follow-up / nonresponse or missing data



A: Smoking cessation, Y: weight gain,
C: Censoring (1: yes, 0: no),
L: Smoking intensity in 1971-75,
U: Lifetime history of smoking

Differential loss to follow-up



C: Missing data (1: yes, 0: no)

Plan for today

A. Review of selection bias

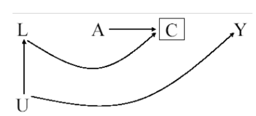
B. IP weighting to adjust for selection bias

- Due to loss to follow-up/missing data

Adjustment for selection bias

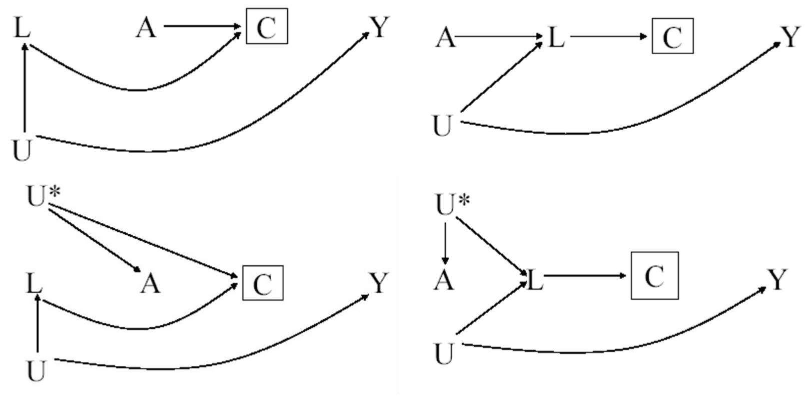
- Sometimes selection bias can be prevented by study design
  - e.g., sampling controls in a manner to ensure that they will represent the treatment distribution in the population
- Most often selection bias needs to be adjusted for via
  - Stratification
  - IP weighting

Stratification to adjust for selection bias



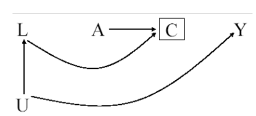
- The idea is blocking the path that was unblocked because of conditioning on the collider C
  - Can block it if L (or U) is measured
- The path is blocked by estimating the A-Y association in the selected within levels of L
  - That is, adding a box around L
- The conditional association measure is the causal effect within levels of L and C=0
  - a bit weird but unbiased under the null

Stratification to adjust for selection bias?



Conditional association measure not always causal!

IP weighting to adjust for selection bias

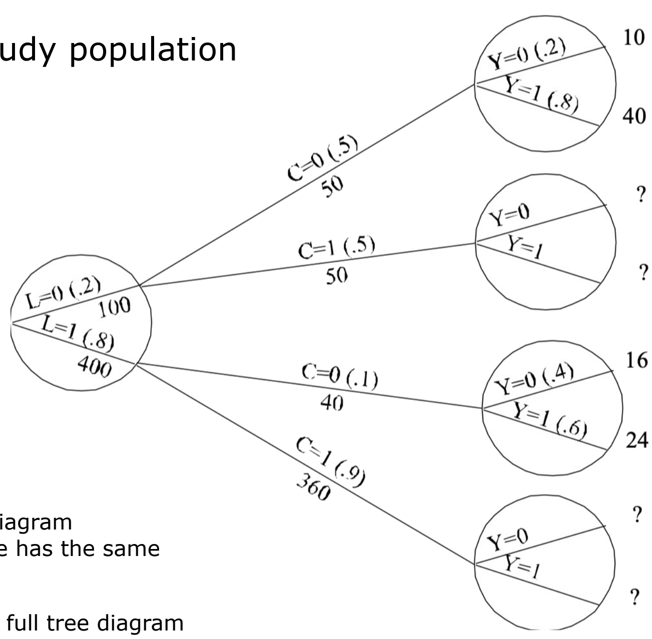


- ☐ The idea is eliminating the path that was unblocked because of conditioning on the collider C
  - ■ Can eliminate it if L (or U) is measured
- ☐ The path is eliminated by creating a pseudo-population in which everybody is selected (e.g., uncensored)
  - ■ Because then there are no arrows into C
- ☐ The association measure in the pseudo-population is the effect measure in the study population
  - ■ Unconditionally

Example

- 100 participants with same treatment and covariate history
  - untreated, men, aged 40-45, CD4 count >500
- 50 are lost to follow-up and do not contribute to the analysis (zero weight)
- The remaining 50 receive a weight=2
  - Probability of remaining uncensored is 0.5, weight for uncensored individuals is 1/0.5=2
  - IP weighting creates a pseudo-population in which the 100 participants are replaced by 2 copies of the 50 uncensored individuals

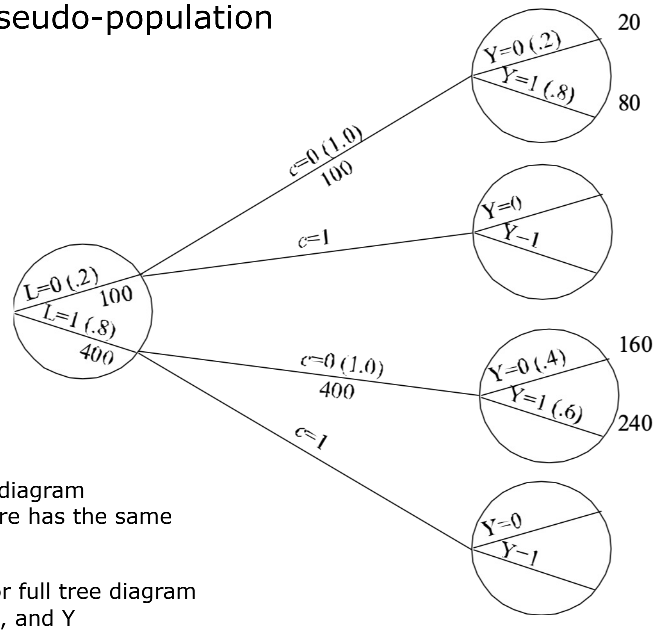
Study population



Note: Simplified tree diagram (assume everyone here has the same treatment A)

See course website for full tree diagram with nodes for L, A, C, and Y

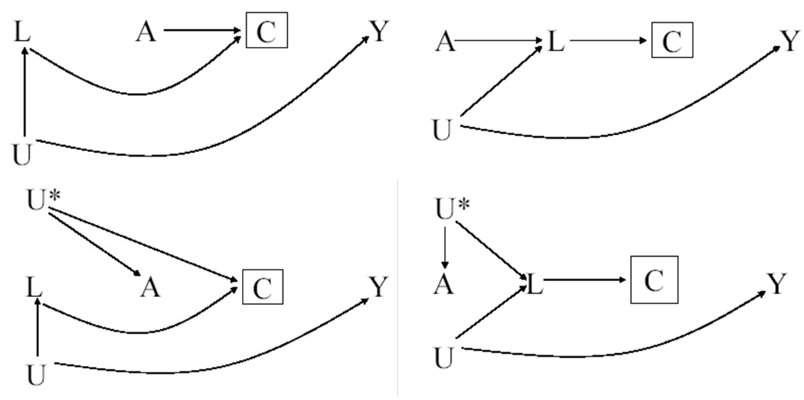
Pseudo-population



Note: Simplified tree diagram
(assume everyone here has the same treatment A)

See course website for full tree diagram with nodes for L, A, C, and Y

IP weighting to adjust for selection bias



Works in all four cases by removing arrows into *C*

Which assumption are we making?

$Y^{a,c=0} \amalg C|A,L$ for $c=0$

- Conditional exchangeability
  - within levels of A,L the risk in the unselected if selected is the same as the risk in the selected
  - or selection is randomized within levels of A,L
  - or no unmeasured confounding for selection C within levels of the measured variables A,L
- Also required:
  - Positivity: not all censored for some A,L levels
  - Consistency, including a well-defined intervention to eliminate censoring
    - problems with competing risks (see later)

IP weights for selection bias

$$W^C = \frac{1}{\Pr[C = 0|A, L]}$$

- Each selected individual in the population is weighted to create W^C individuals in the pseudo-population
  - Unselected individuals have weight zero
- The denominator of your weight is (informally) the probability of having been selected given your A,L values
  - Equal for all $C=0$ individuals with same A,L values

IP weights

- To adjust for confounding
  - Use IP weights W^A
  - A is the treatment variable
- To adjust for selection bias
  - Use IP weights W^C
  - C is the selection variable
- To adjust for both biases
  - Multiply $W^A \times W^C$

Stabilized IP weights for selection bias

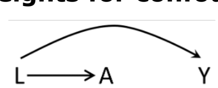
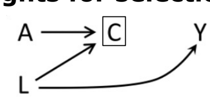
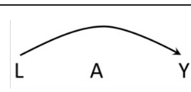
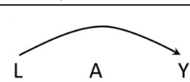
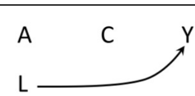
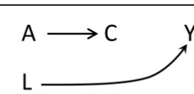
$$SW^C = \frac{\Pr[C = 0|A]}{\Pr[C = 0|A, L]}$$

- Same denominator as nonstabilized IP weights multiplied by an individual's probability of having been selected given their *A* values
- Each selected individual *i* in the population is weighted to create SW_i^C individuals in the pseudo-population

Stabilized IP weights

- To adjust for confounding
  - Use IP weights SW^A
  - A is the treatment variable
- To adjust for selection bias
  - Use IP weights SW^C
  - C is the selection variable
- To adjust for both biases
  - Multiply $SW^A \times SW^C$

Summary of IP weights for confounding and selection bias

	IP weights for confounding 		IP weights for selection bias 	
	Nonstabilized	**Stabilized**	**Nonstabilized**	**Stabilized**
Formula	$\frac{1}{f(A\|L)}$	$\frac{f(A)}{f(A\|L)}$	$\frac{1}{\Pr[C=0\|A,L]}$	$\frac{\Pr[C=0\|A]}{\Pr[C=0\|A,L]}$
DAG for pseudopopulation				
Size of pseudopopulation	Original N * number of levels of A	Original N	Original N before censoring	Original N after censoring

Nonstabilized weights eliminate censoring

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True

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False

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Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

Stabilized weights eliminate censoring

True

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False

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Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

Back to our data
Causal question 1

- Estimate the mean weight gain if everybody had quit smoking
  - $E[Y^{a=1}]$
- Estimate the mean weight gain if nobody had quit smoking
  - $E[Y^{a=0}]$
- Estimate the average causal effect on the additive scale
  - $E[Y^{a=1}] - E[Y^{a=0}]$

We have ignored censoring all this time!

- We restricted the analysis to the 1566 participants with non missing outcome
  - i.e., we did not use data from the 63 participants with missing outcome
- Effectively we assumed that the 1566 uncensored and the 63 censored participants were exchangeable
  - We assumed no selection bias due to censoring C

See ipw_selection.R, lines 6-9

Causal question 1 (what we really meant)

- Estimate the mean weight gain if everybody had quit smoking **and nobody had been censored**
  - $E[Y^{a=1,c=0}]$
- Estimate the mean weight gain if nobody had quit smoking **and nobody had been censored**
  - $E[Y^{a=0,c=0}]$
- Estimate the average causal effect
  - $E[Y^{a=1,c=0}] - E[Y^{a=0,c=0}]$

What model were we really fitting?

- We fit the weighted regression model

  $E[Y|A]= \theta_0 + \theta_1 A$
  - but restricted to individuals with nonmissing weight gain, i.e., conditional on C=0
- That is, we were really fitting the weighted regression model

  $E[Y|A,C=0]= \theta_0 + \theta_1 A$

What if this were a randomized experiment…

- … in which individuals had been randomly assigned to "quit smoking" or "remain as smokers"?
- Is the difference $\mathrm{E}[Y^{a=1,c=0}] - \mathrm{E}[Y^{a=0,c=0}]$ consistently estimated by $\hat{\theta}_1$ from the unweighted regression model?

  $\mathrm{E}[Y|A,C=0]= \theta_0 + \theta_1 A$
- Not in general
  - Post-randomization loss to follow-up/missing data may destroy the baseline exchangeability achieved by randomization

What if this were an observational study…

- … in which the treated and the untreated are exchangeable **at baseline**, conditional on measured confounders?
  - e.g., age, sex, race, alcohol, etc.
- IP weighting creates a pseudo-population with unconditional exchangeability **at baseline**
- In general, $\mathrm{E}[Y^{a=1,c=0}] - \mathrm{E}[Y^{a=0,c=0}]$ is not consistently estimated by $\hat{\theta}_1$ from the weighted regression model

  $\mathrm{E}[Y|A,C=0]= \theta_0 + \theta_1 A$

Which assumption were we making?

- Exchangeability
  - unconditional with respect to covariates L
  - selection is randomized within levels of A only
- This assumption is stronger than the assumption of conditional exchangeability
  - selection is randomized within levels of A,L
- Let's then conduct the analysis under the weaker assumption by using IP weighting

Doubly-weighted regression model

$E[Y|A,C=0]= \theta_0 + \theta_1 A$

- Adjusting for the following variables
  - Sex, age, race, hbp, education, active, smokeyrs, smokeintensity, exercise
    - squared terms for continuous variables
  - For both SW^A and SW^C
- Parameter estimates
  - $\hat{\theta}_0$ = 1.8
  - $\hat{\theta}_1$ = 3.3 (conservative 95% CI: 2.3, 4.3)
- Saturated model
  - 2 parameters, 2 quantities

See ipw_selection.R, lines 11-64

Censoring and the g-formula

- Did we adjust for censoring when using standardization?
- See homework

Summary: IP weighting adjusts for selection bias

- By creating a pseudo-population in which
  1. selection (e.g., censoring, missing data) is eliminated or randomly allocated
  2. the effect of the treatment is the same as in the original population
- The pseudo-population effect measure is equal to the effect measure had everybody been selected in the original population

Interpretation for different types of selection

- Censoring due to loss to follow-up
  - Effect had nobody, or only a random sample, been lost to follow-up
  - Appropriate
- Missing data, nonresponse
  - Effect had nobody, or only a random sample, had missing data
  - Appropriate
- Censoring due to competing risks
  - Effect had nobody, or only a random sample, been censored due to competing risks
  - Probably not interesting

Example of competing risks

- A study to estimate the effect of cigarette smoking on the risk of Alzheimer's disease

- Do we want effect estimates from a pseudo-population in which all other causes of death (cancer, heart disease, stroke, etc.) have been removed?
  - Pseudo-population does not correspond to any known human population
  - Plus, no well-defined intervention could possibly remove just one cause of death without affecting the others as well

Readings

- *Causal Inference, What If*. Chapter 8

- Greenland S. Quantifying biases in causal models: classical confounding versus collider-stratification bias. *Epidemiology* 2003; 14:300-306
- Hernán MA, Hernández-Díaz S, Robins JM. A structural approach to selection bias. *Epidemiology* 2004; 15:615–625

Progress report

1. Introduction to modeling
2. Stratified analysis:
   - outcome regression
   - propensity scores
3. Standardization
4. Inverse probability weighting
   - Marginal structural models
5. Instrumental variable estimation