


Methods which can accommodate observed confounders

Advanced Epidemiology

Dr Michael Green

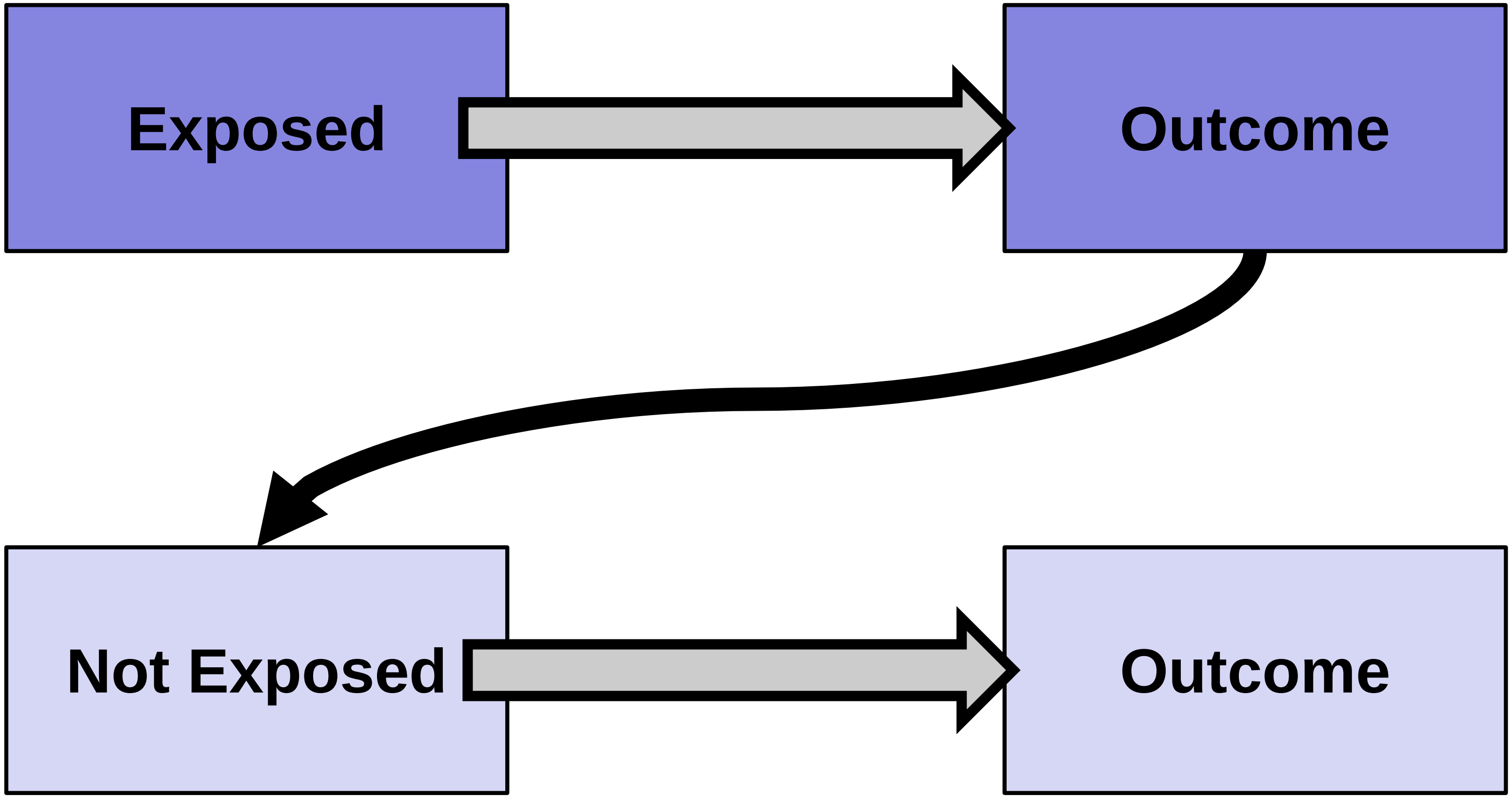
MRC/CSO Social and Public Health Sciences Unit, University of Glasgow

6th March 2018

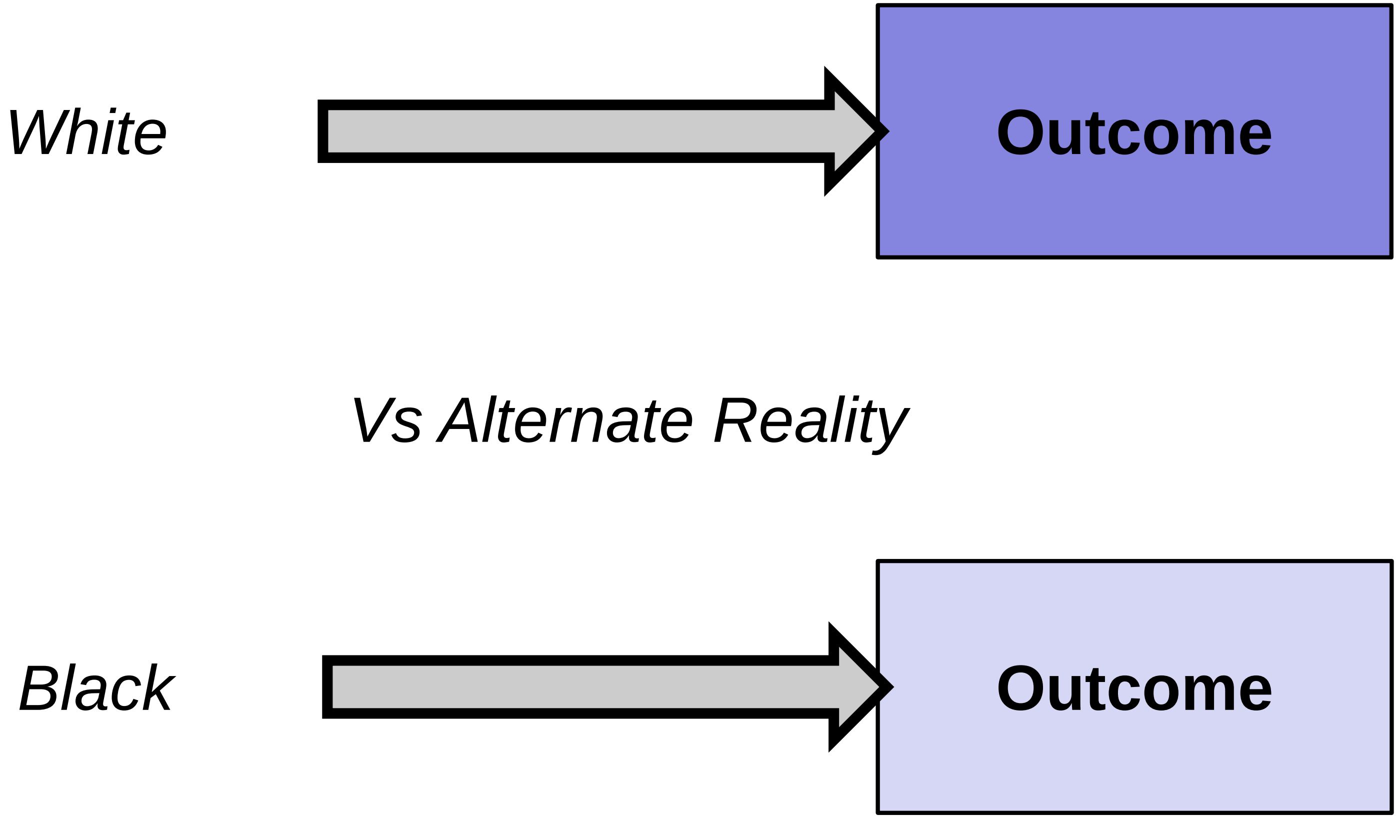
Lecture– Outline

- Causal Inference from Observational Research
- DAGS (recap) & mutually adjusted regression
- Collider bias and stratification/selection
- Propensity weighting (IPW)

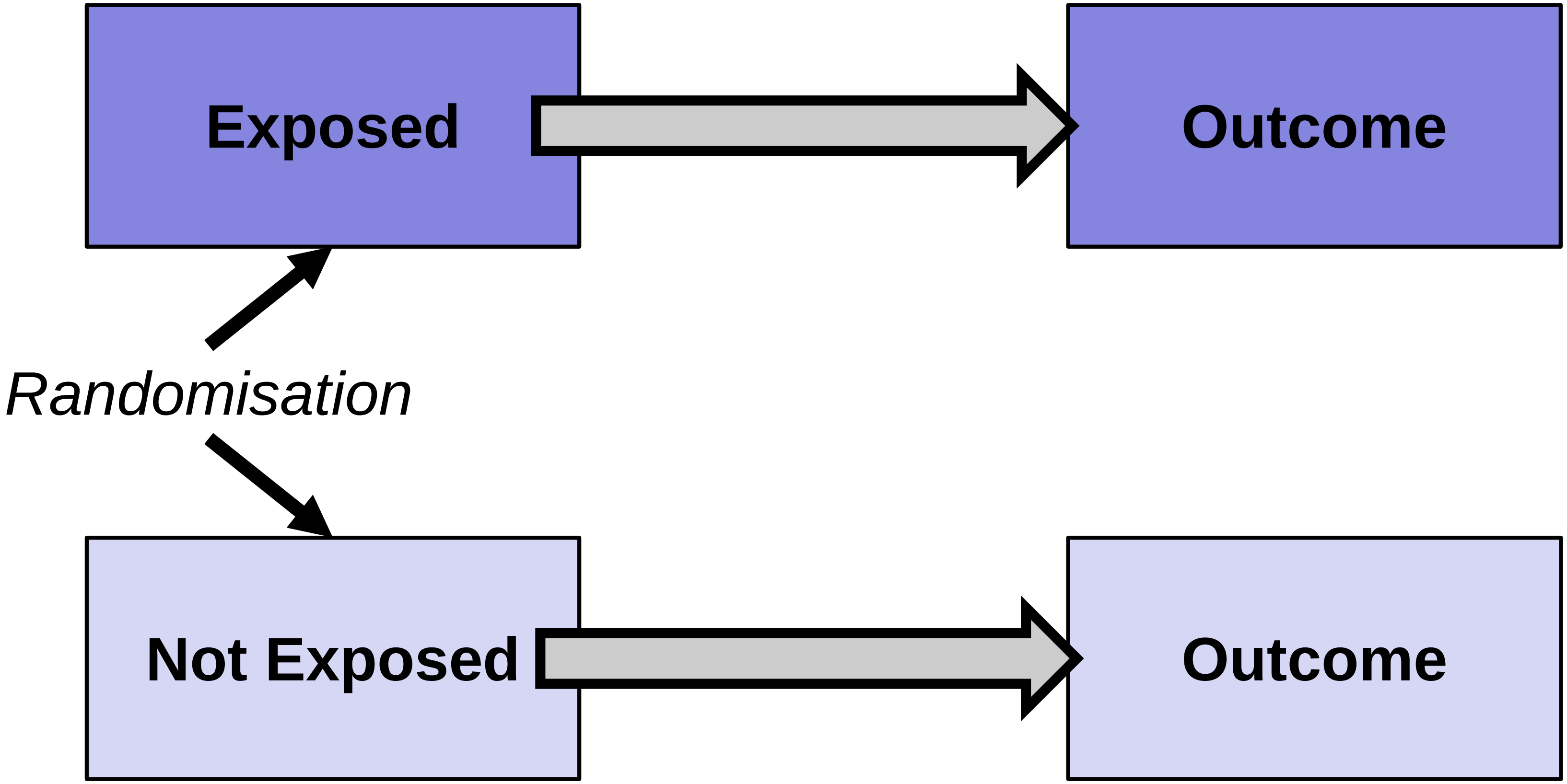
Fundamental Problem of Causal Inference



Fundamental Problem of Causal Inference

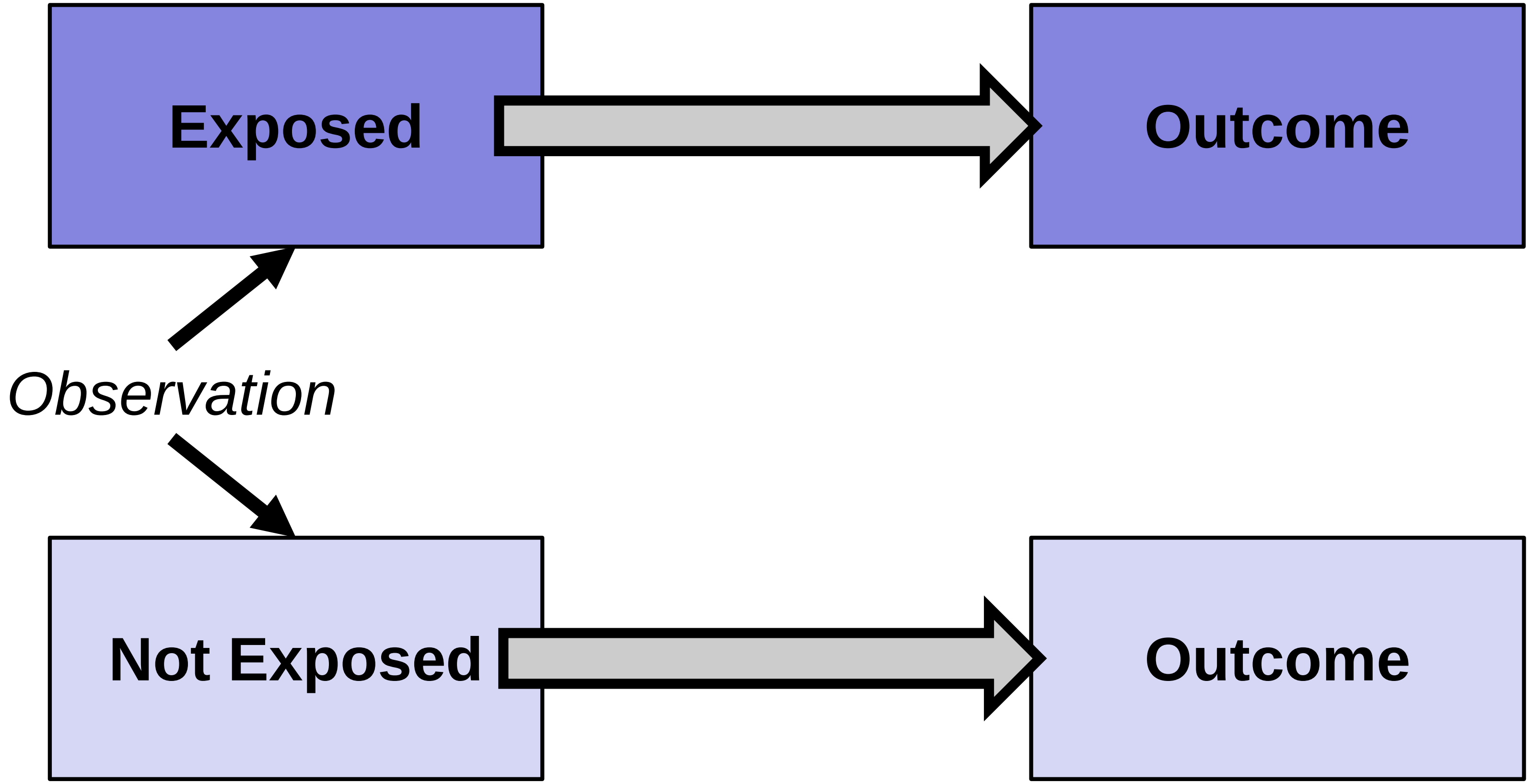


Fundamental Problem of Causal Inference



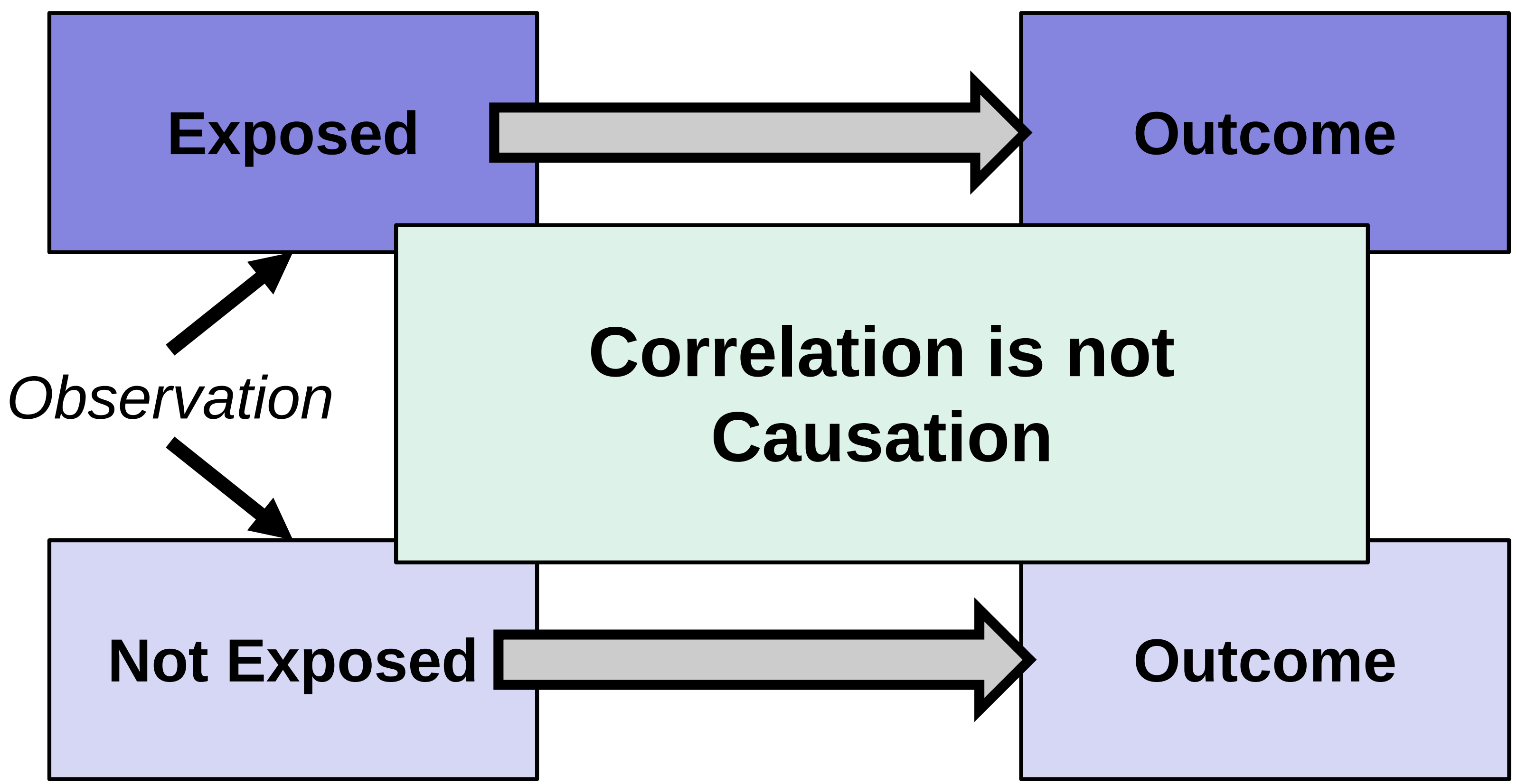
*Randomisation -> **Exchangeability***

Fundamental Problem of Causal Inference



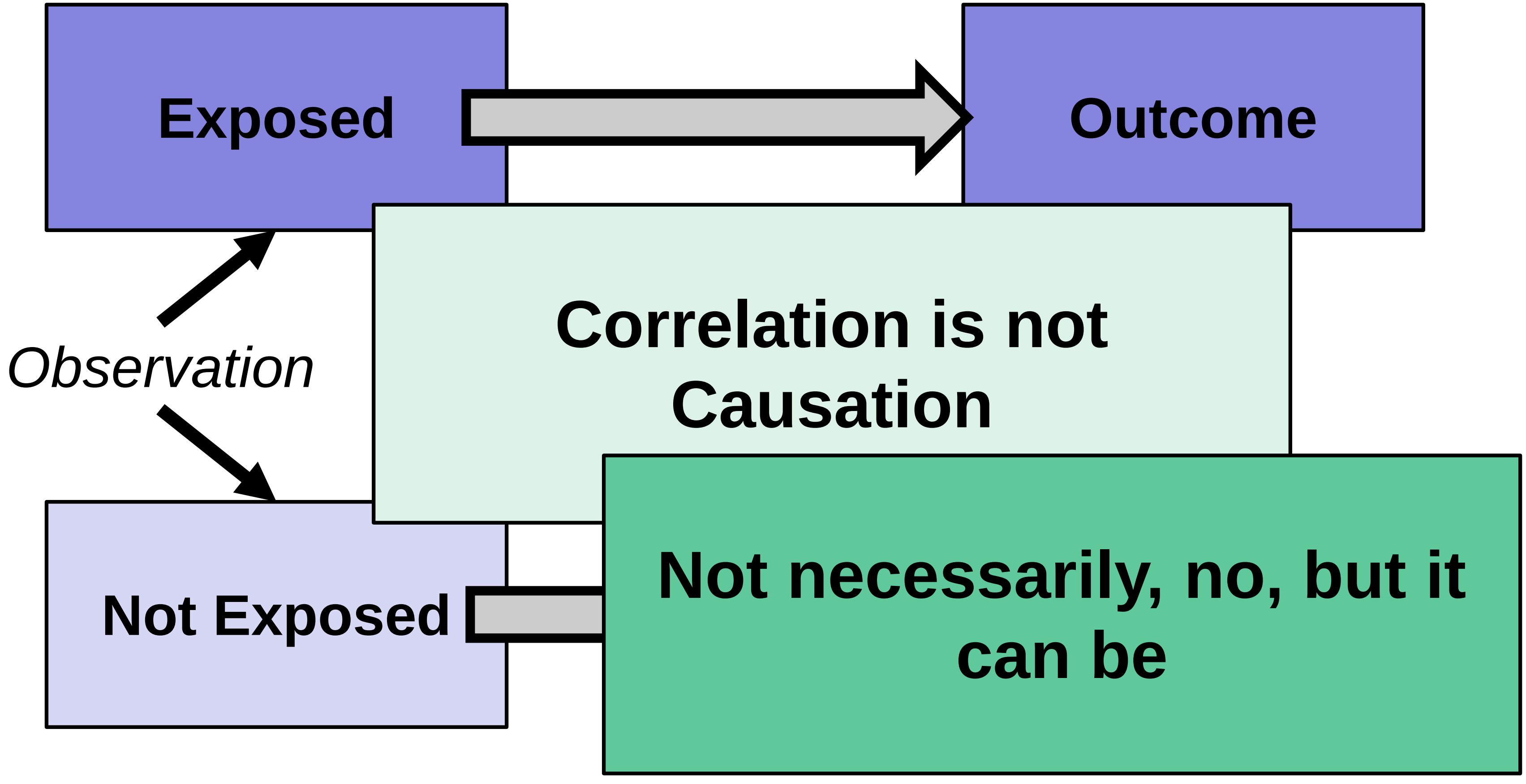
Observation ≠ ***Exchangeability***

Fundamental Problem of Causal Inference



Observation ≠ ***Exchangeability***

Fundamental Problem of Causal Inference



Observation $\neq$ ***Exchangeability***

Why do observational research?

Lots of problems aren’t well suited to randomised experiments:

- Consider ethics of randomly exposing people to a risk factor you think may be dangerous
- Randomised experiments are costly to run, so tend to focus more on short-term effects
- Internal vs External Validity
- Some variables aren’t randomisable, eg Gender, Race etc

Causal Language and Estimation

- **The C-Word**: many prefer to speak of associations rather than causal effects
- But, do we want to estimate an association or a causal effect?

Hernán MA. The C-Word: Scientific Euphemisms Do Not Improve Causal Inference From Observational Data. *American Journal of Public Health* 2018; 108: 616-9.

Contrast these definitions:

- **Calculate:** determine a value by mathematical means
- **Estimate:** provide an informed, approximate calculation, based on specific assumptions

Causal Language and Estimation

"A calculated association between two variables in a given population could be considered an "estimate" of the causal effect of one on the other, but even with very narrow confidence intervals it may not be our "best estimate." Confidence intervals are commonly used to express statistical uncertainty, but there may also be less easily quantifiable (and often implicit) logical uncertainties around a given estimate. Ideally, our "best estimate" would acknowledge and strive to eradicate potential sources of bias, be rooted in existing knowledge and theory, and rest on plausible assumptions. Causal thinking can be an important and useful tool to evaluate the quality of our estimates, make our assumptions explicit, and consider whether our estimates are as good as they could be."

Green MJ. Calculating Versus Estimating Causal Effects. *American Journal of Public Health* 2018; **108**: e4-e5.

Observational Studies

- Often use adjusted regression, eg:

Health = a + b*X1 + c*X2 + d*X3 + error

- Where X1,2,3 etc are different exposure measures
- Coefficients b,c,d etc interpreted as effects ‘independent’ of other factors in the model

However, care is needed when interpreting **mutually adjusted** coefficients such as these…

Observational Studies

- Often use adjusted regression, eg:

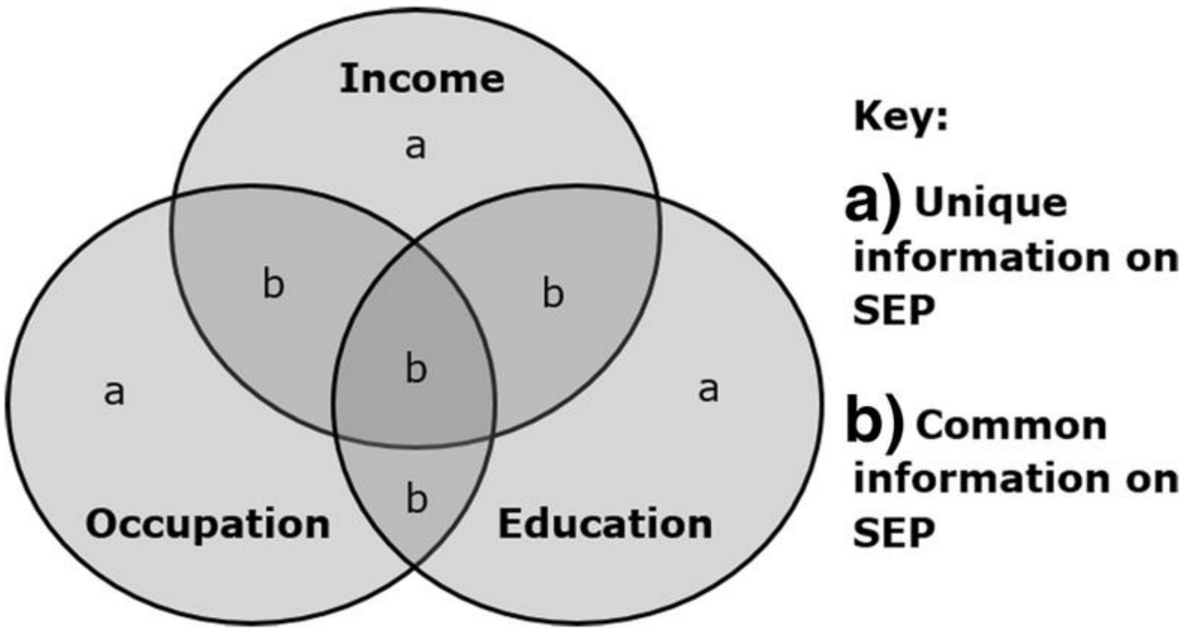
$$\textbf{Health} = a + b*\mathbf{X1} + c*\mathbf{X2} + d*\mathbf{X3} + \text{error}$$

- Where X1,2,3 etc are different exposure measures
- Coefficients b,c,d etc interpreted as effects ‘independent’ of other factors in the model

However, care is needed when interpreting **mutually adjusted** coefficients such as these…

Mutual Adjustment

Health = **education** + **occupation** + **income**



Green MJ, Popham F. Interpreting mutual adjustment for multiple indicators of socioeconomic position without committing mutual adjustment fallacies. *BMC Public Health 2019; 19: 10*

Which areas of the diagram do the coefficients for education, occupation & income represent?

Directed Acyclic Graphs (DAGs)

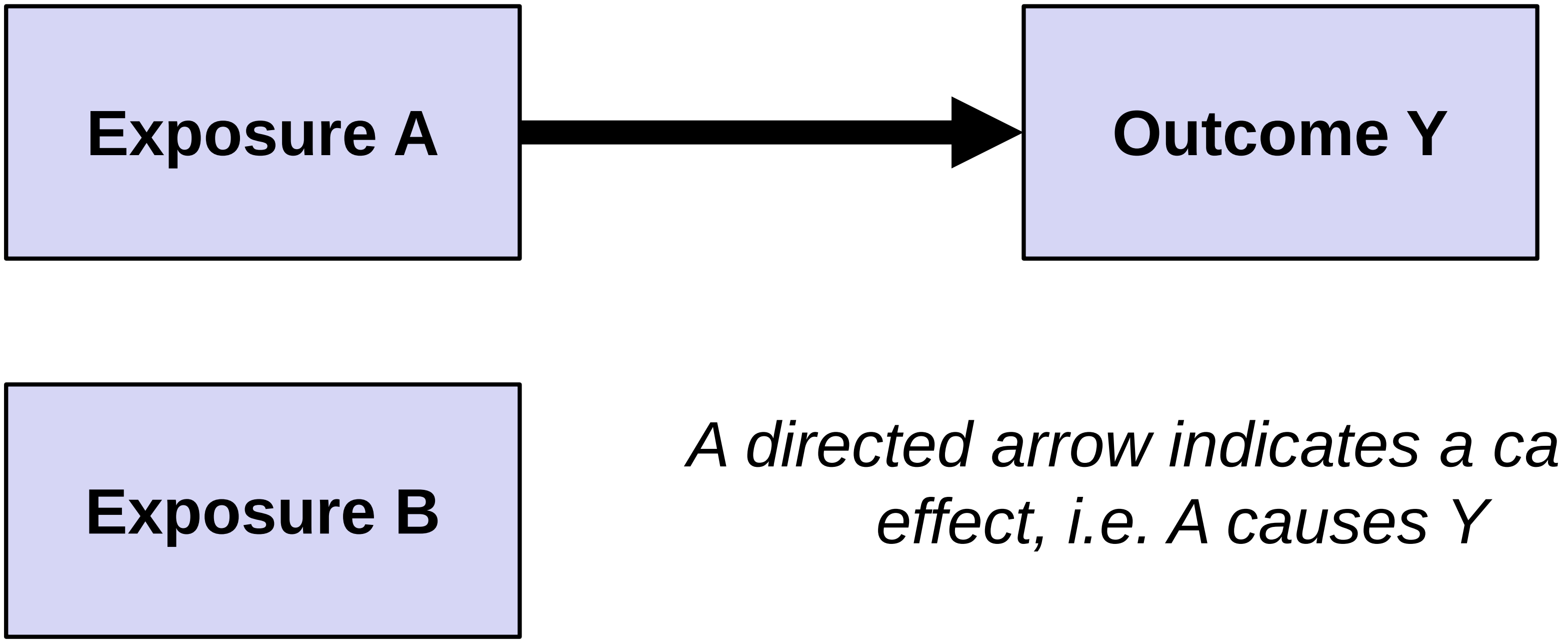
Diagrams intended to provide **clarity** about:

- the **assumptions** that statistical conclusions are based on
- how effects should be **interpreted** based on those assumptions

Great online software:

- http://www.dagitty.net/

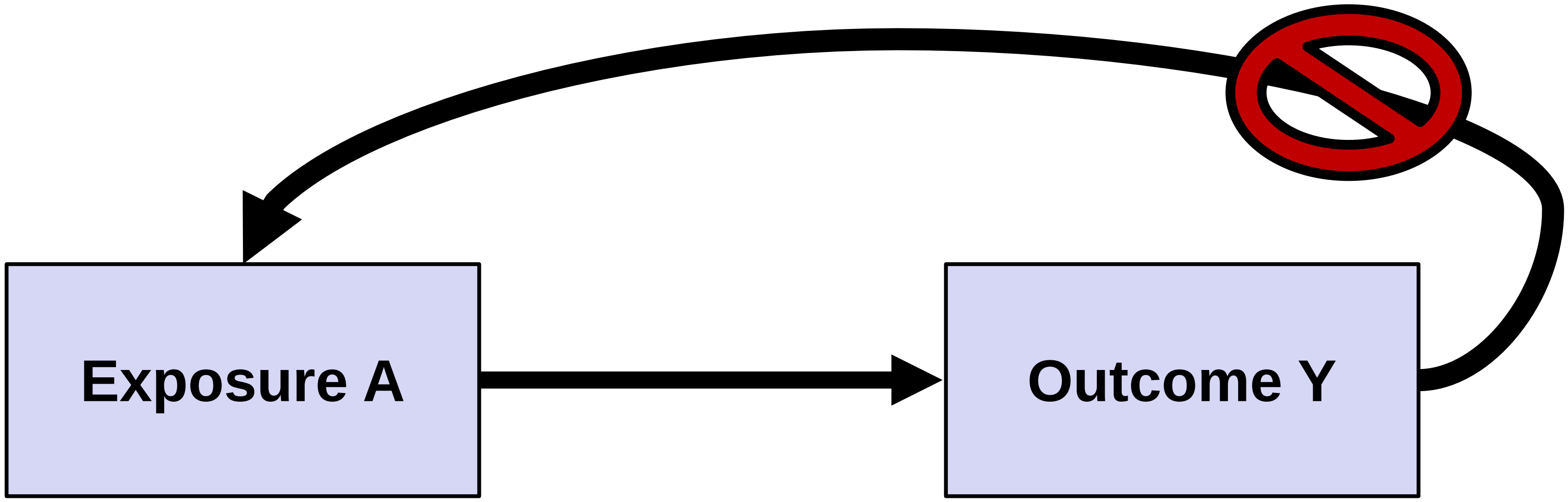
DAGS - Basics



A directed arrow indicates a causal effect, i.e. A causes Y

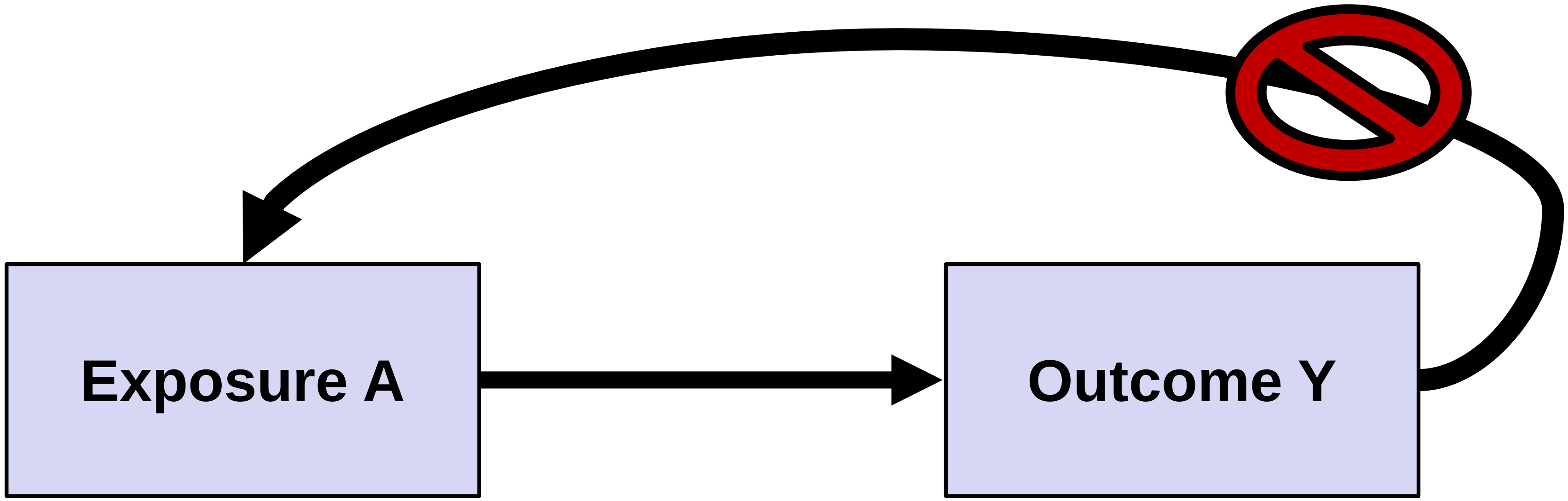
No directed arrow indicates no causal effect, i.e. B does not cause Y

DAGS - Basics



Reciprocal/Feedback loops are not allowed

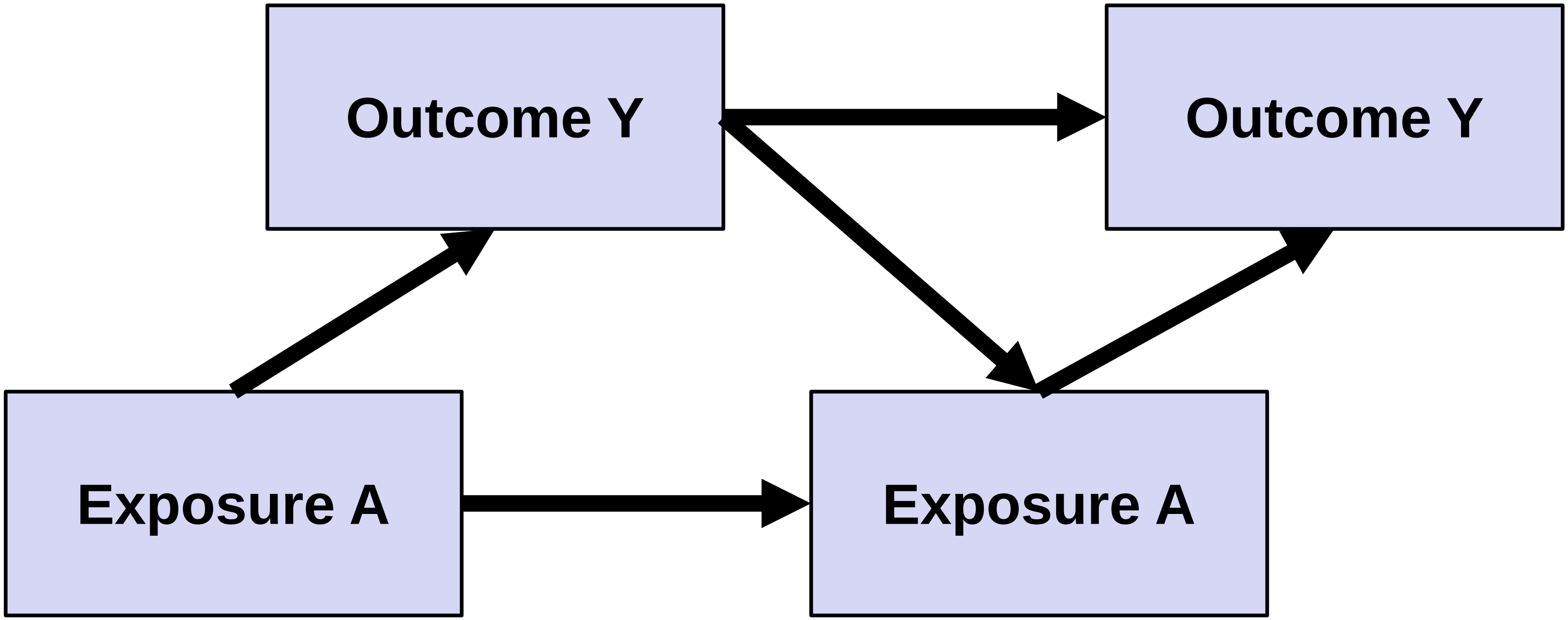
DAGS - Basics



Reciprocal/Feedback loops are not allowed

So how do we account for these?

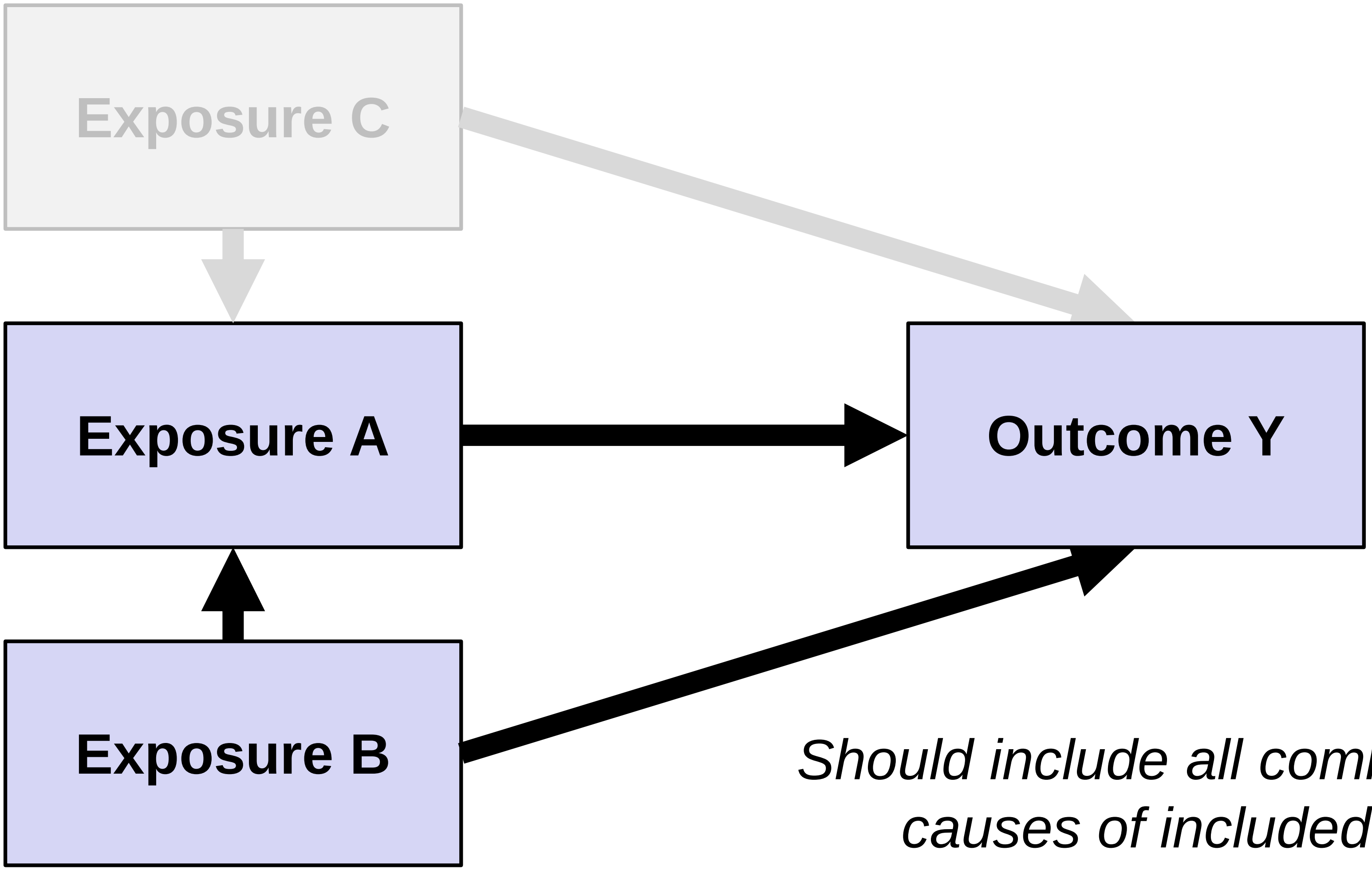
DAGS - Basics



Reciprocal/Feedback loops are not allowed

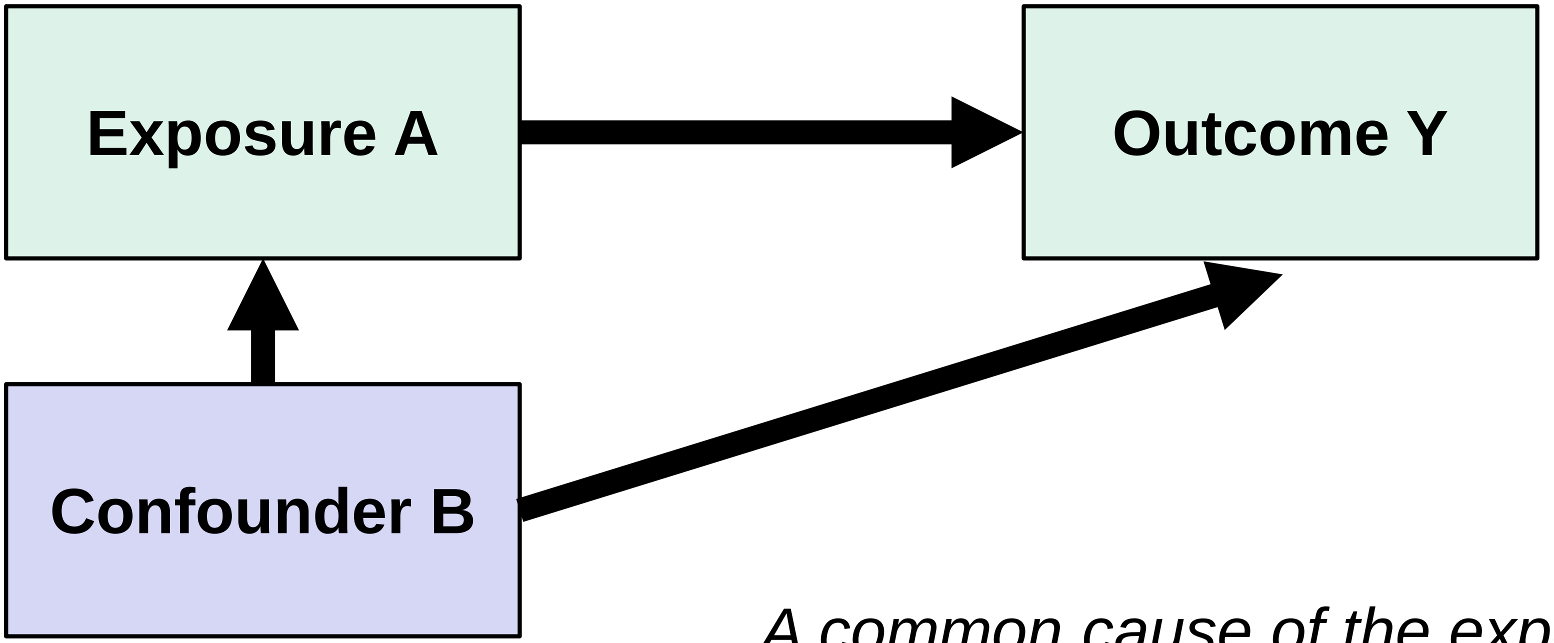
But can be incorporated with multiple measures over time

DAGS - Basics



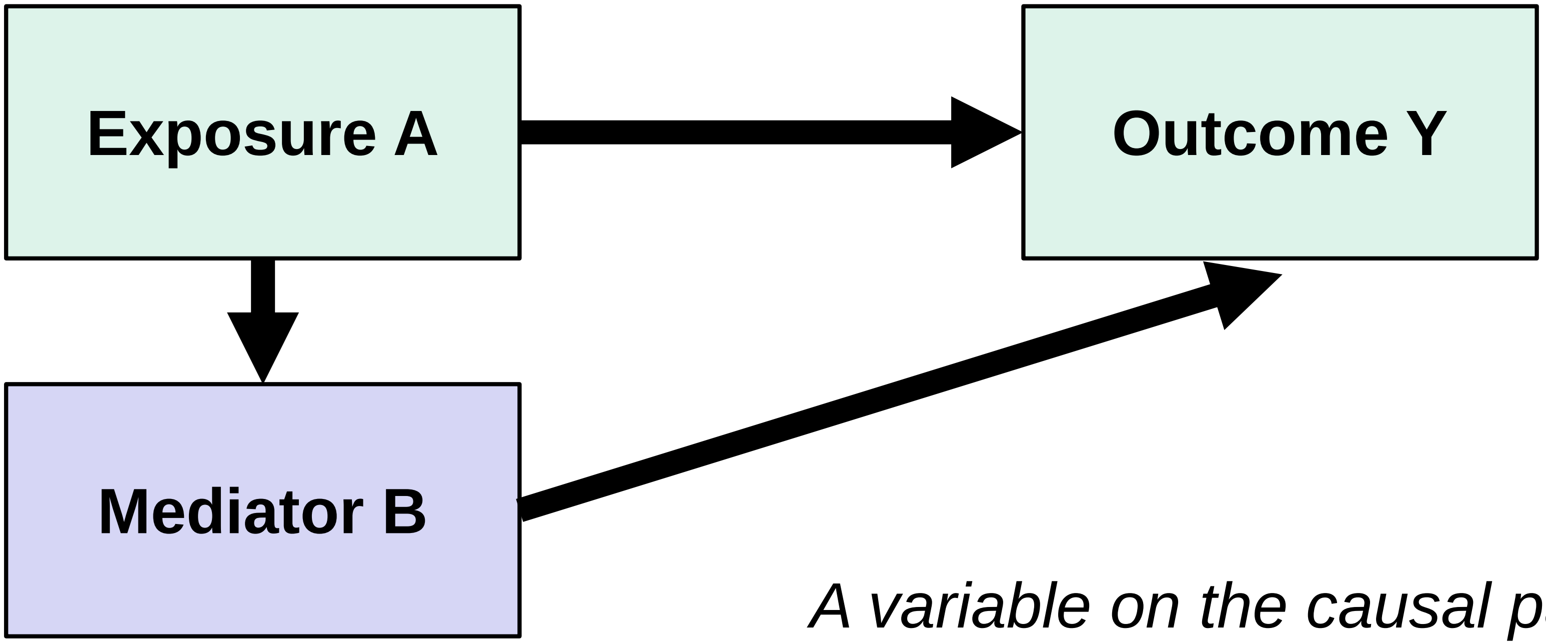
Should include all common causes of included variables

DAGS – Confounding vs Mediation



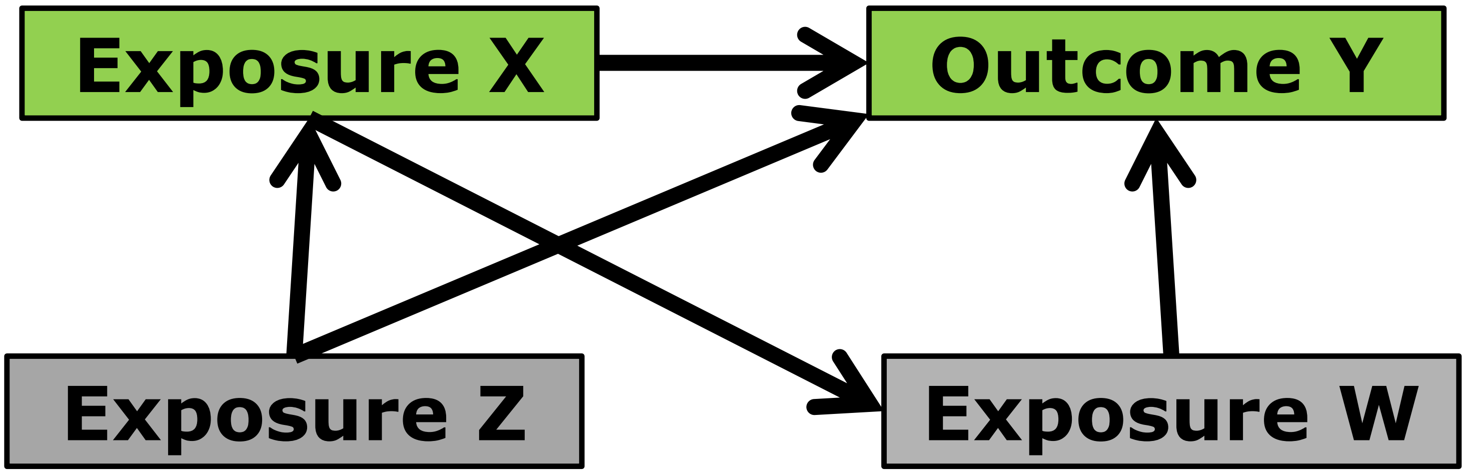
A common cause of the exposure and outcome of interest is a ***confounder***

DAGS – Confounding vs Mediation



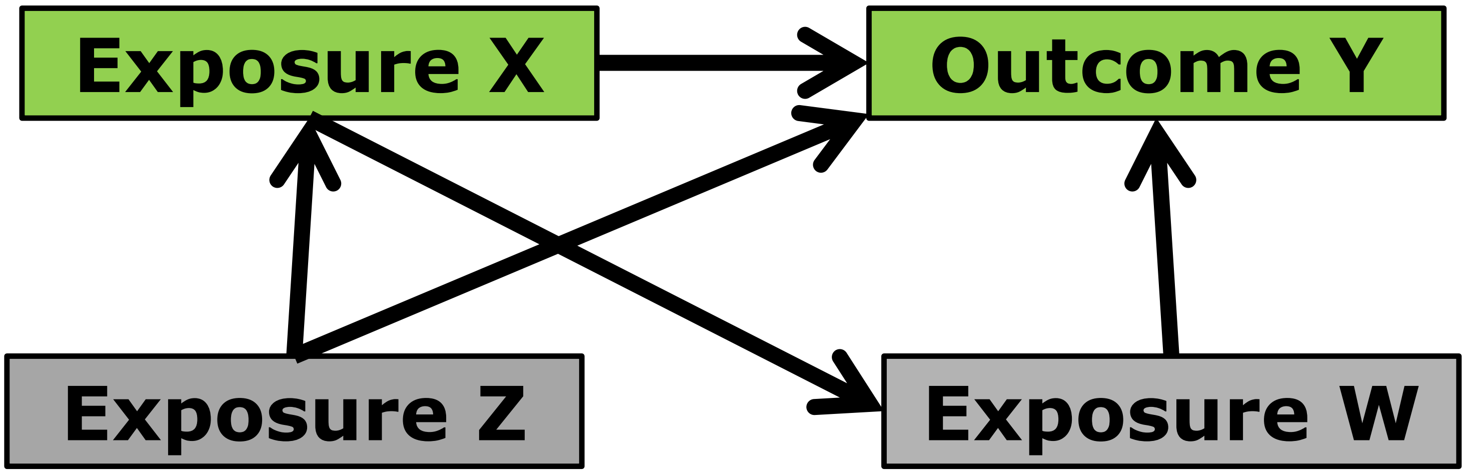
A variable on the causal path between the exposure and outcome of interest is a ***mediator***

DAGs and Regression



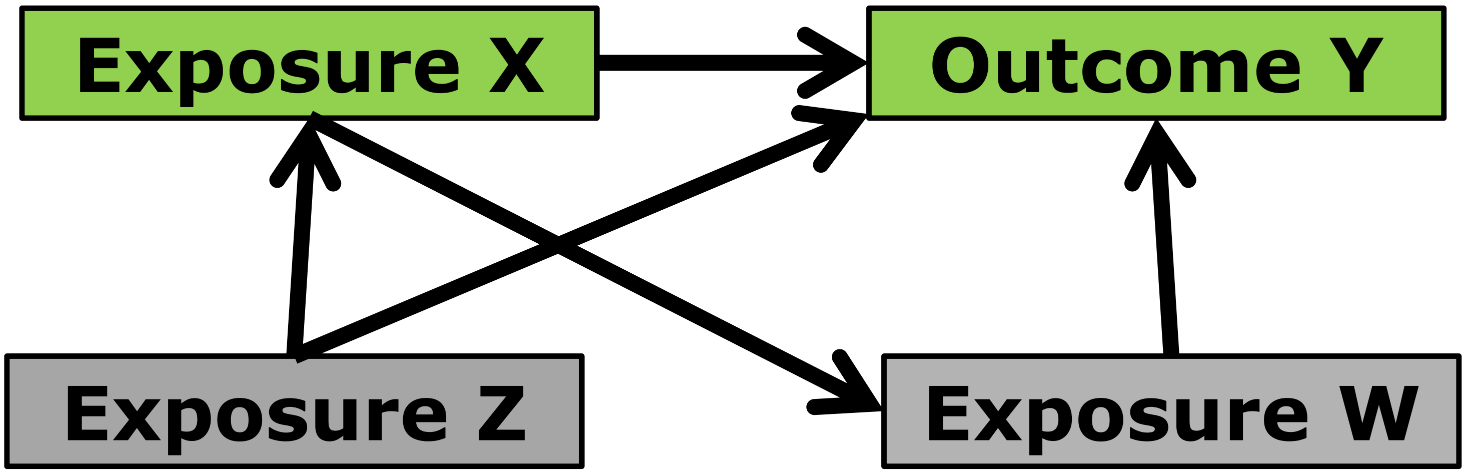
- Interest is in effect of X on Y
- Regression: Y = a + b*X + error
  - Coefficient for X is effect on Y

DAGs and Regression



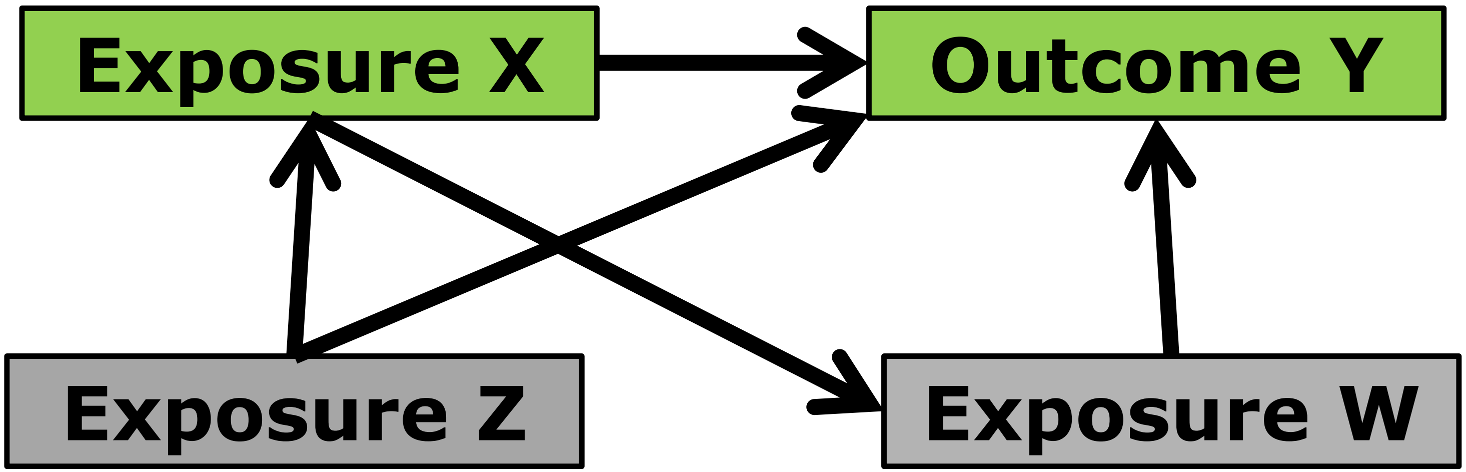
- Interest is in effect of X on Y
- Regression: Y = X
  - Why will this estimate be biased?

DAGs and Regression



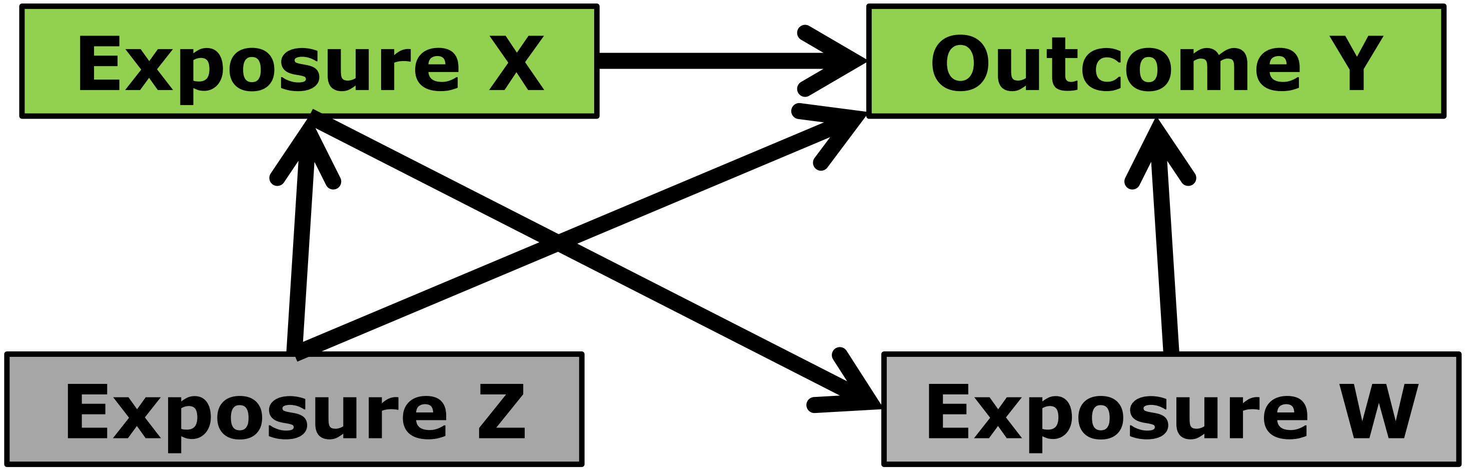
- Interest is in effect of X on Y
- Regression: Y = X + Z
  - The effect of X is **confounded by Z**, so Z needs to be adjusted out

DAGs and Regression



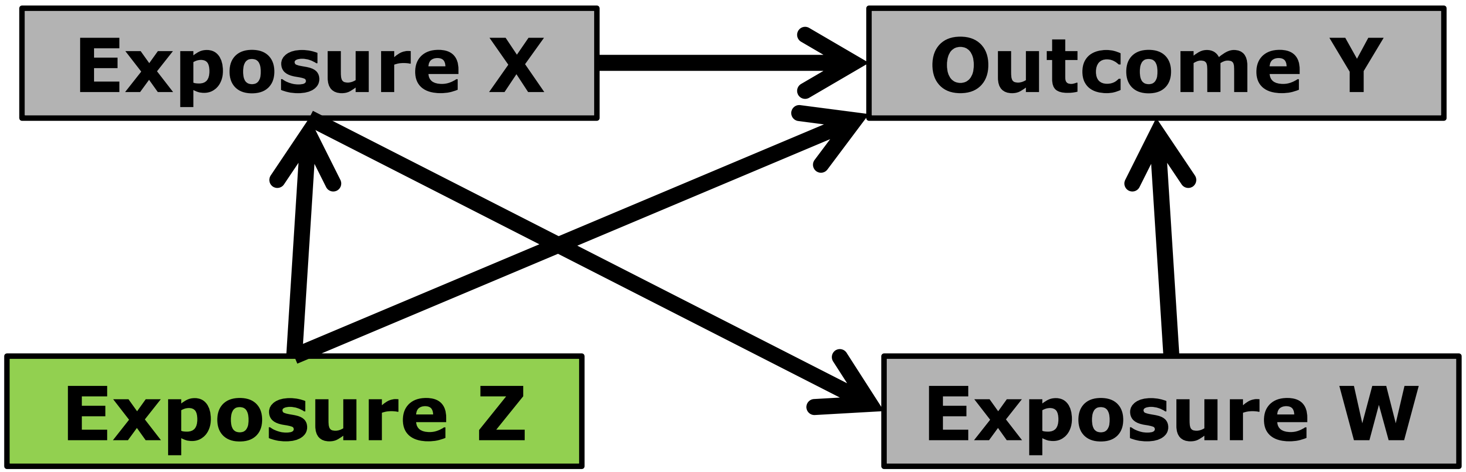
- Interest is in effect of X on Y
- Regression: Y = X + Z + W
  - Why would an estimate that also adjusts for W be biased?

DAGs and Regression



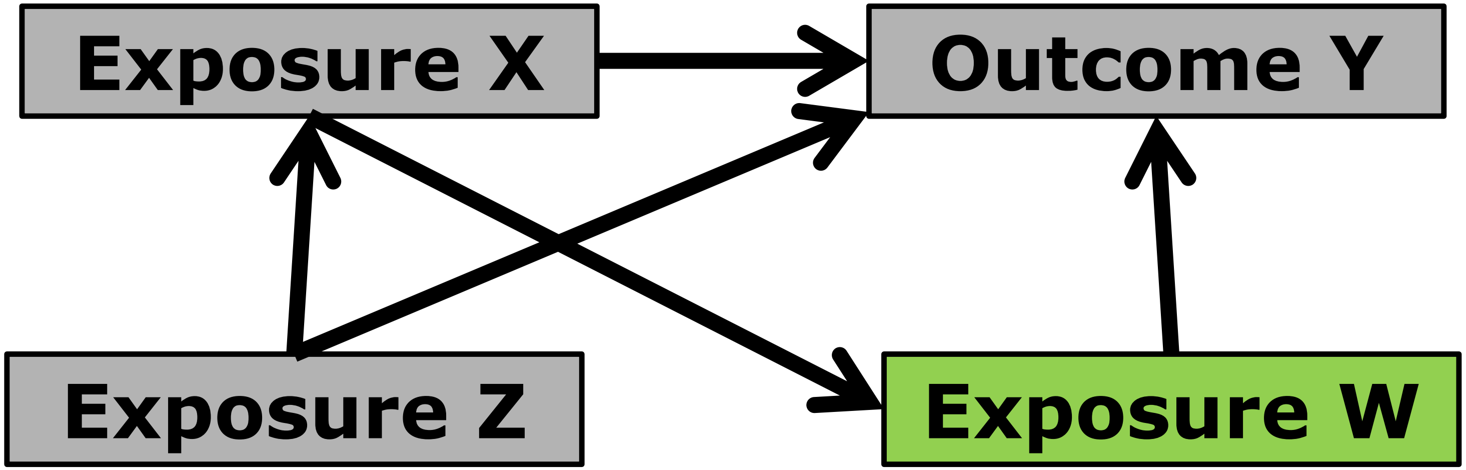
- Regression: Y = X + Z + W
  - W is a **mediator** of the effect of X on Y
  - Adjusting for W only leaves the **direct** effect of X on Y

DAGs and Regression



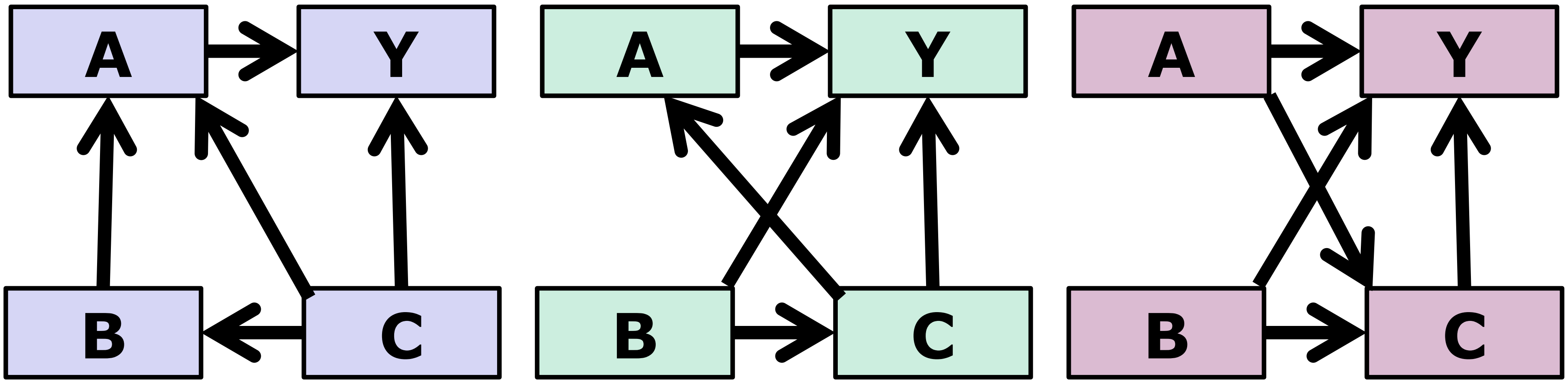
- **Adjust for confounders**
- Don’t adjust for mediators

DAGs and Regression



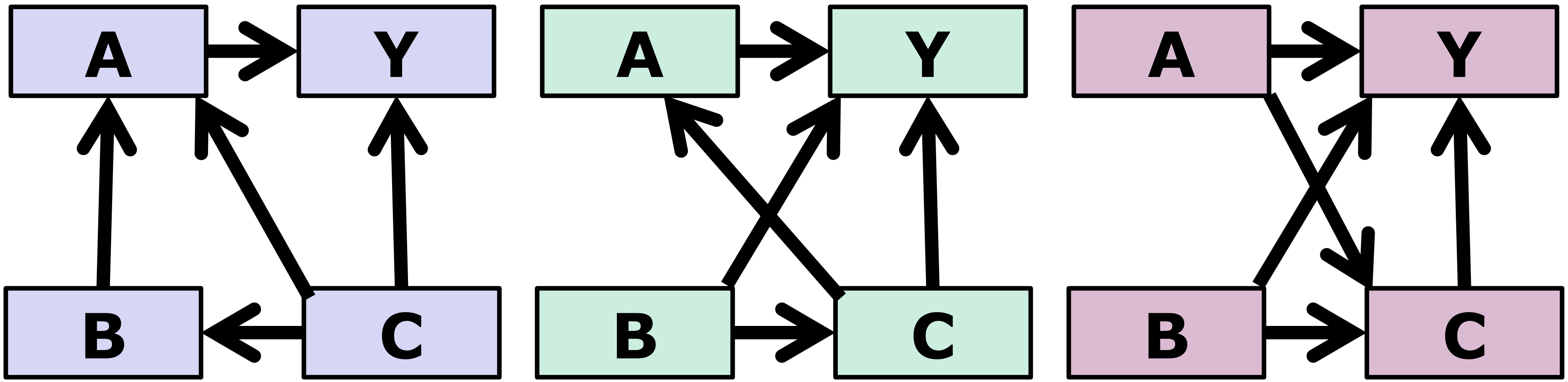
- Adjust for confounders
- **Don't adjust for mediators**

Directed Acyclic Graphs (DAGs)



- Might be multiple ways to draw diagram, representing different assumptions
- Different exposures/diagrams require different analyses

Directed Acyclic Graphs (DAGs)

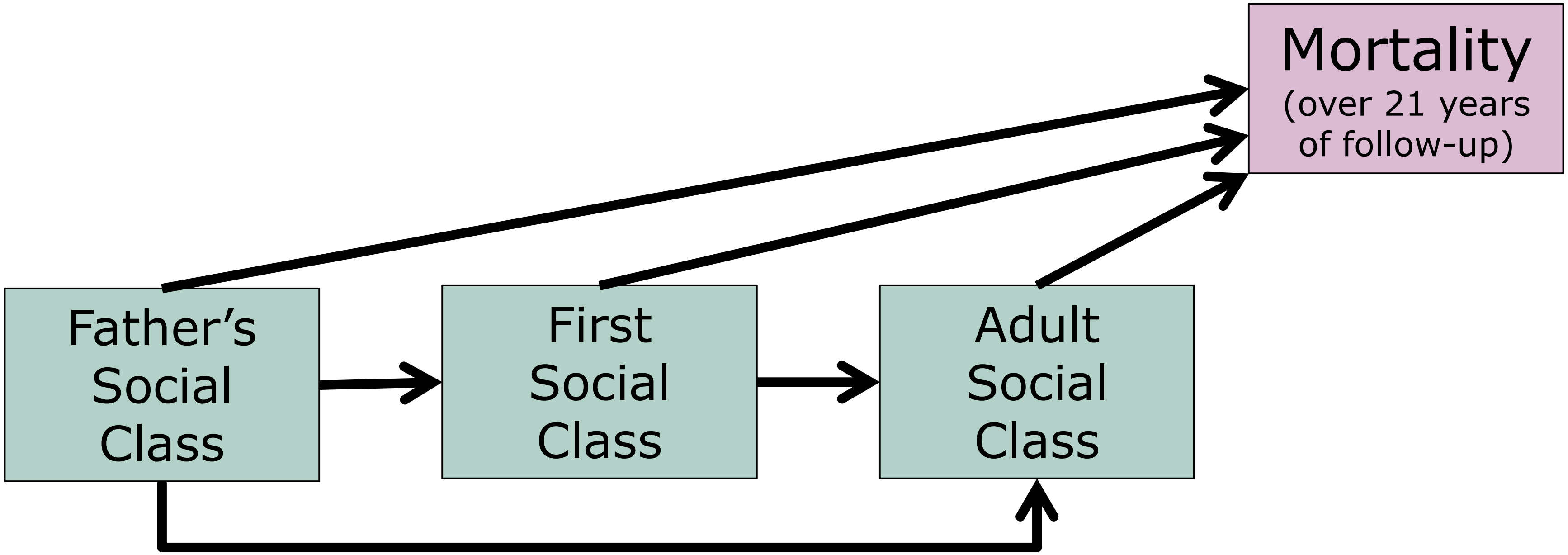


- In the three scenarioes shown here, if you want **effect of C on Y**
  - Should you adjust for A?
  - Should you adjust for B?

An example

- DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

- A study of mortality in relation to social class (manual vs. non-manual) at three stages of the lifecourse



DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

	Unadjusted Hazard Ratio (95% CI)	**Mutually Adjusted Hazard Ratio (95% CI)**
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 (1.16-1.43)	1.01 (0.89-1.16)
Adult Social Class	1.40 (1.27-1.55)	1.29 (1.14-1.47)

- Does Father's or Adult Social Class have the stronger effect on mortality?
- Which two cells should you compare?

DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

	Unadjusted Hazard Ratio (95% CI)	Mutually Adjusted Hazard Ratio (95% CI)
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 [illegible].43)	1.01 (0.89-1.16)
Adult Social Class	1.40 [illegible].55)	1.29 (1.14-1.47)

Total effect of
Father's Social Class

DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

	Unadjusted Hazard Ratio (95% CI)	Mutually Adjusted Hazard Ratio (95% CI)
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 (1.16-1.43)	1.01 [illegible].16)
Adult Social Class	1.40 (1.27-1.55)	1.29 [illegible].47)

Direct effect of Father's Social Class
not mediated by First or Adult Social Class

DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

	Unadjusted Hazard Ratio (95% CI)	Mutually Adjusted Hazard Ratio (95% CI)
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 (1.16-1.43)	1.01 (0.89-1.16)
Adult Social Class	1.40 (1.27-1.55)	1.29 (1.14-1.47)

Total effect of Adult Social Class confounded by First or Father's Social Class

DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

	Unadjusted Hazard Ratio (95% CI)	Mutually Adjusted Hazard Ratio (95% CI)
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 (1.16-1.43)	1.01 (0.89-1.16)
Adult Social Class	1.40 (1.27-1.55)	1.29 (1.14-1.47)

Total effect of Adult Social Class
not confounded by First or Father's Social Class

DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

	Unadjusted Hazard Ratio (95% CI)	Mutually Adjusted Hazard Ratio (95% CI)
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 (1.16-1.43)	1.01 (0.89-1.16)
Adult Social Class	1.40 (1.27-1.55)	1.29 (1.14-1.47)

- Comparing these 2 cells the total effect of Father's Social Class is greater than that of Adult Social Class

DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

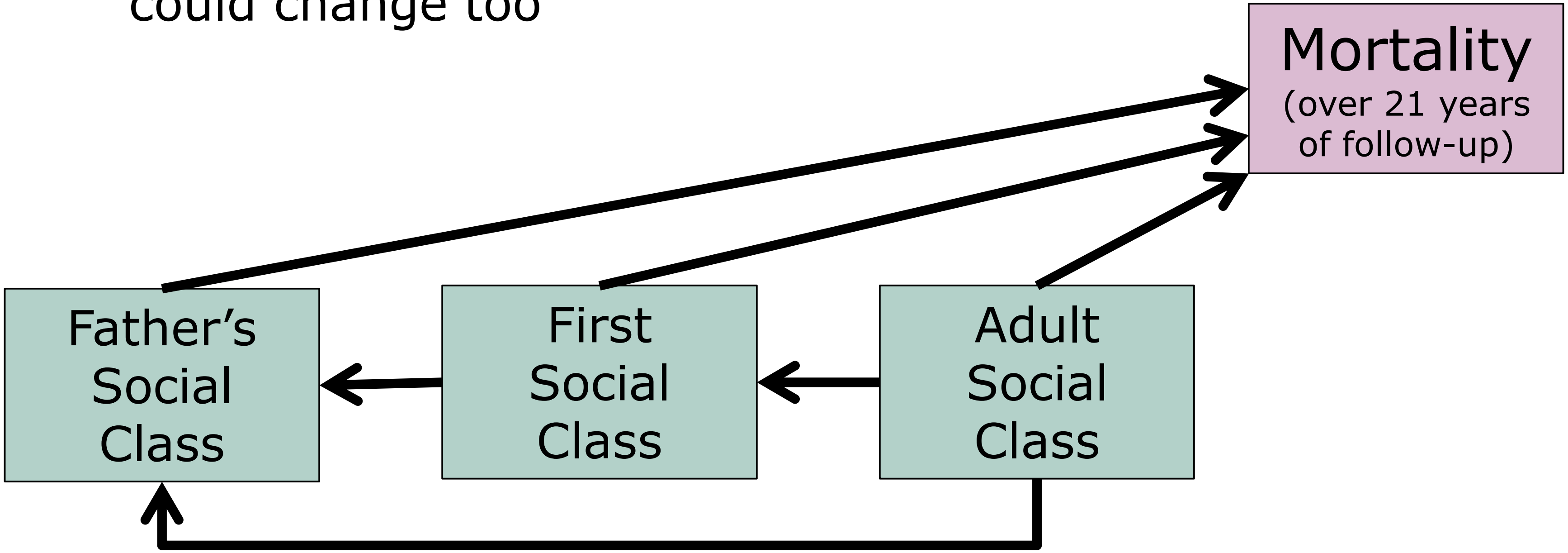
	Unadjusted Hazard Ratio (95% CI)	Mutually Adjusted Hazard Ratio (95% CI)
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 (1.16-1.43)	1.01 (0.89-1.16)
Adult Social Class	1.40 (1.27-1.55)	1.29 (1.14-1.47)

- The total effect of Adult Social Class is roughly equivalent to the direct effect of Father's Social Class
- ~1/2 the total effect of Father's Social Class is **mediated** by First and Adult Social Class

Alternative assumptions

- DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

- If we changed our assumptions regarding the causal direction between these variables, our interpretation could change too



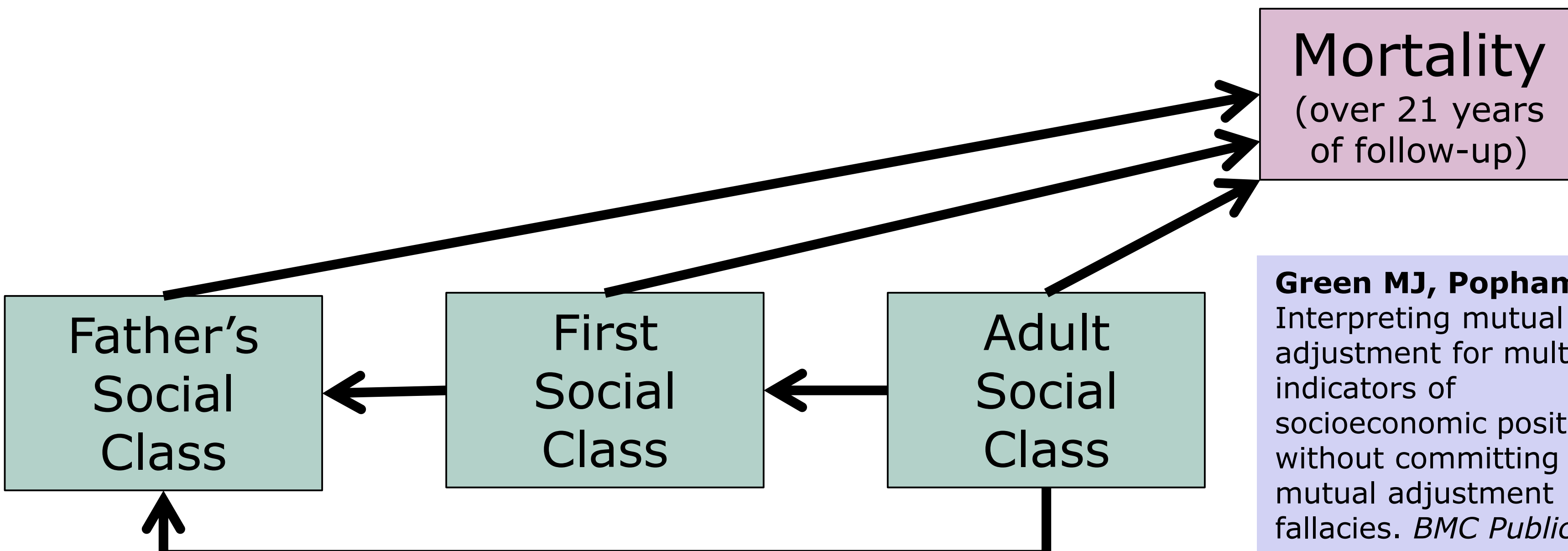
DAVEY SMITH G., HART C., BLANE D., GILLIS C., HAWTHORNE V. Lifetime socioeconomic position and mortality: prospective observational study, BMJ 1997: 314: 547.

	Unadjusted Hazard Ratio (95% CI)	**Mutually Adjusted Hazard Ratio (95% CI)**
Father's Social Class	1.44 (1.27-1.64)	1.28 (1.11-1.47)
First Social Class	1.29 (1.16-1.43)	1.01 (0.89-1.16)
Adult Social Class	1.40 (1.27-1.55)	1.29 (1.14-1.47)

- Under reversed causal diagram we would compare these two cells to get at whether father's or adult social class is more important (and get a different answer)

Alternative assumptions

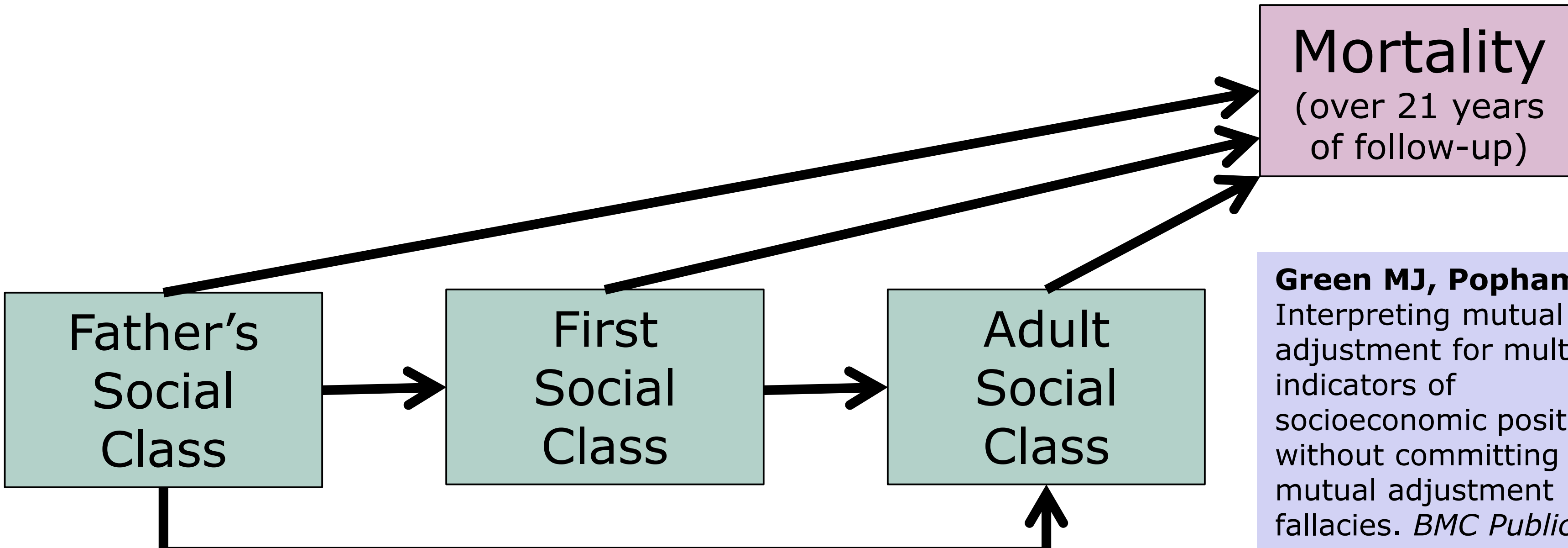
- Important to specify our assumptions, so that readers can understand how we're interpreting mutually adjusted coefficients
- Mutually adjusted coefficients could be compared if you wanted to compare causal estimates under different causal assumptions
- But 'mutual adjustment' is poor short-hand for this
- When we speak of effects being 'independent' it's important to specify whether we mean from confounders or mediators



Green MJ, Popham F. Interpreting mutual adjustment for multiple indicators of socioeconomic position without committing mutual adjustment fallacies. *BMC Public Health 2019; 19: 10*

Alternative assumptions

- Important to specify our assumptions, so that readers can understand how we're interpreting mutually adjusted coefficients
- Mutually adjusted coefficients could be compared if you wanted to compare causal estimates under different causal assumptions
- But 'mutual adjustment' is poor short-hand for this
- When we speak of effects being 'independent' it's important to specify whether we mean from confounders or mediators



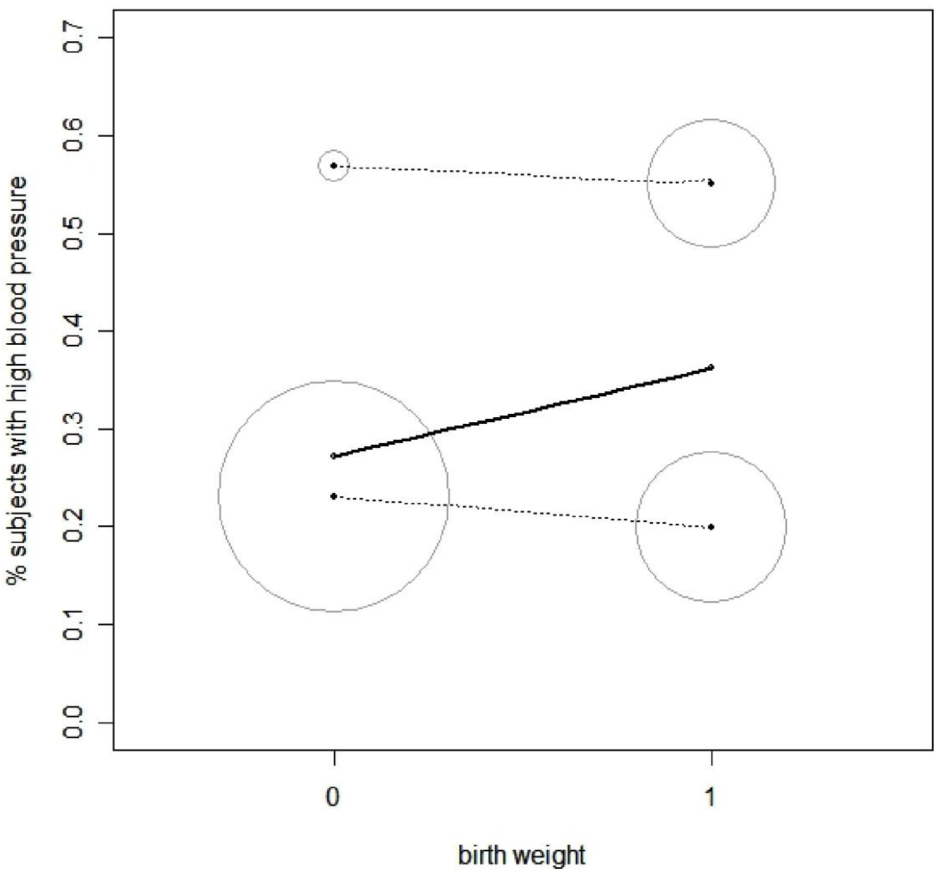
Green MJ, Popham F. Interpreting mutual adjustment for multiple indicators of socioeconomic position without committing mutual adjustment fallacies. *BMC Public Health 2019; 19: 10*

Another example: birthweight, current weight & blood pressure

	Normal BP	High BP	Total	Percentage of subjects with high BP
Overall:				
Low birth weight	354	132	486	27.2%
High birth weight	328	186	514	36.2%
Total	682	318	1,000	31.8%
Current weight < = 90 Kg				
Low birth weight	329	99	428	23.1%
High birth weight	221	55	276	19.9%
Total	550	154	704	21.9%
Current weight > 90 Kg				
Low birth weight	25	33	58	56.9%
High birth weight	107	131	238	55.0%
Total	132	164	296	55.4%

Source: Tu, Y.-K., Gunnell, D., & Gilthorpe, M.S. (2008). Simpson's Paradox, Lord's Paradox, and Suppression Effects are the same phenomenon - the reversal paradox. *Emerging Themes in Epidemiology, 5, 2.*

Why does this happen?



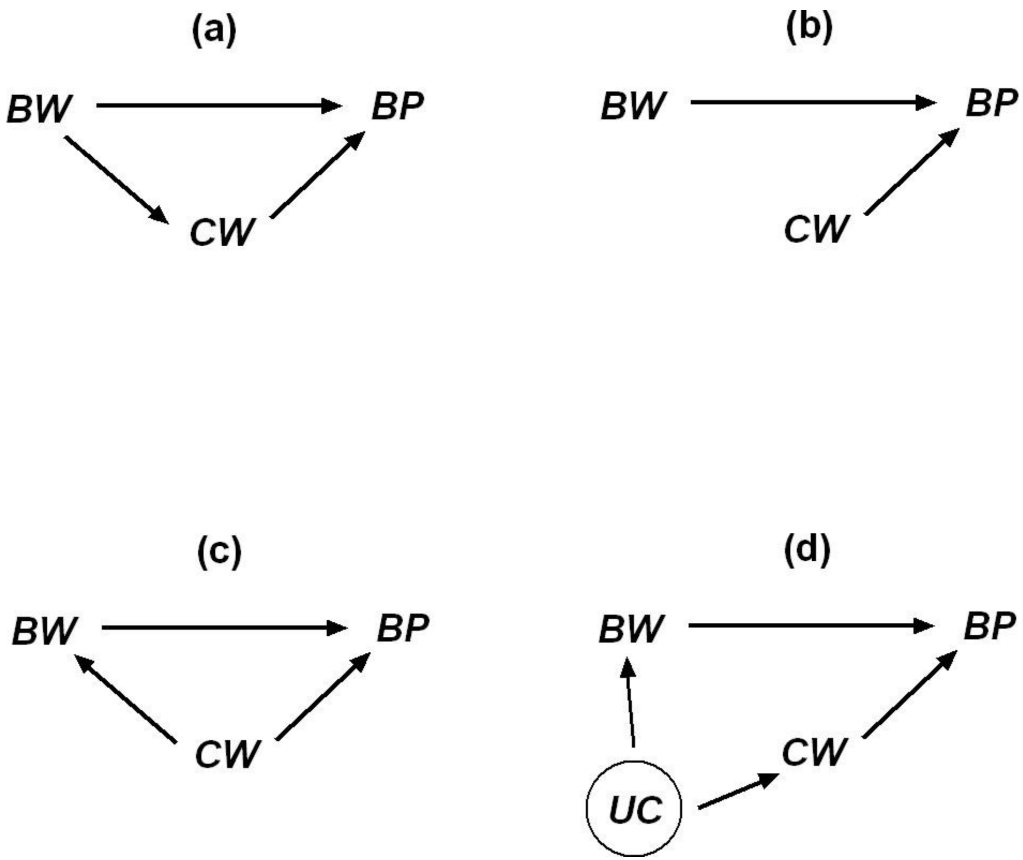
- Upper circles = high current weight
- Lower circles = low current weight
- Circle size = n

- Thick line = overall association between birth weight and BP

- Dotted lines = association between birth weight and BP, **conditional on current weight**

Source: Tu, Y.-K., Gunnell, D., & Gilthorpe, M.S. (2008). Simpson's Paradox, Lord's Paradox, and Suppression Effects are the same phenomenon - the reversal paradox. *Emerging Themes in Epidemiology, 5, 2.*

Importance of Theory



- Figures a, c & d can explain correlations between BW, CW & BP
- How we estimate true effect of BW on BP depends on which DAG is correct

BW=Birthweight
CW=Current Weight
BP=Blood Pressure

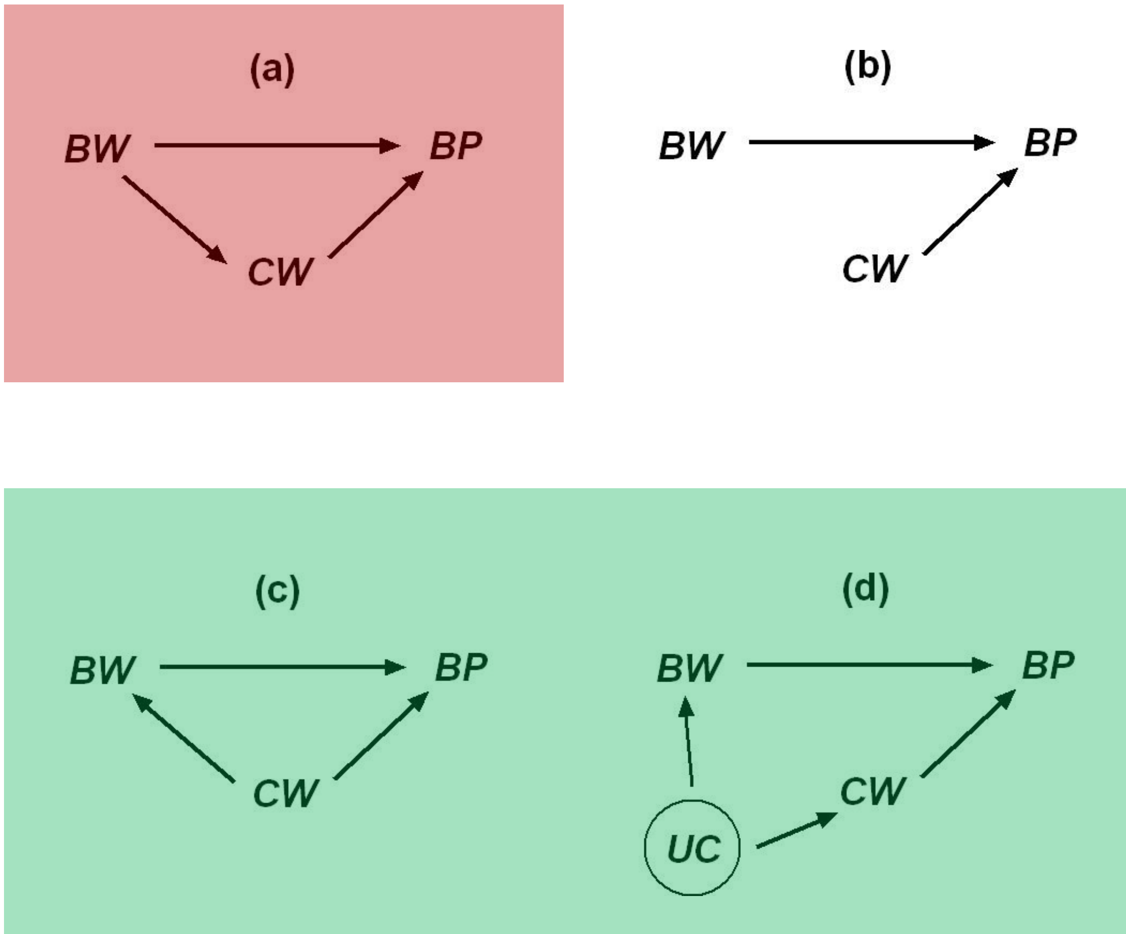
Source: Tu, Y.-K., Gunnell, D., & Gilthorpe, M.S. (2008). Simpson's Paradox, Lord's Paradox, and Suppression Effects are the same phenomenon - the reversal paradox. *Emerging Themes in Epidemiology, 5, 2.*

Birthweight & Blood Pressure

Huxley & Collins **(2002)** *Unravelling the fetal origins hypothesis: is there really an inverse association between birthweight and subsequent blood pressure?* Lancet, **360** (9334): 659-665

- Reviewed 55 studies showing associations between birthweight and blood pressure
- Most showed an inverse association (but with a trend towards smaller effects in larger studies)
- 49 of the 55 studies had adjusted for current weight

Importance of Theory



- Majority of the evidence base in that review is either:
  - Based on fig c or fig d

Or:

  - Wrong based on fig A

Brief Re-cap…

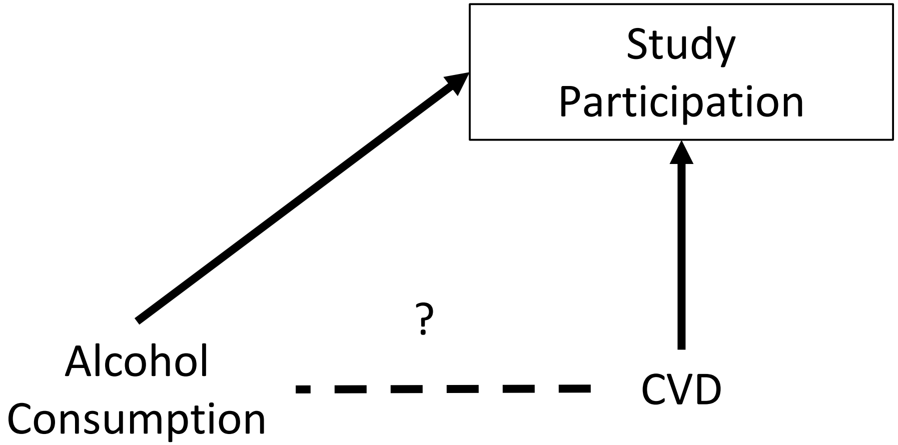
Health = Exp1 + Exp2 + Exp3

- Take care when interpreting **'mutually adjusted'** co-efficients such as these

- Interpretation are not equivalent and depend on assumptions about how exposures relate to one another

- Important distinction between **Total** and **Direct** effects

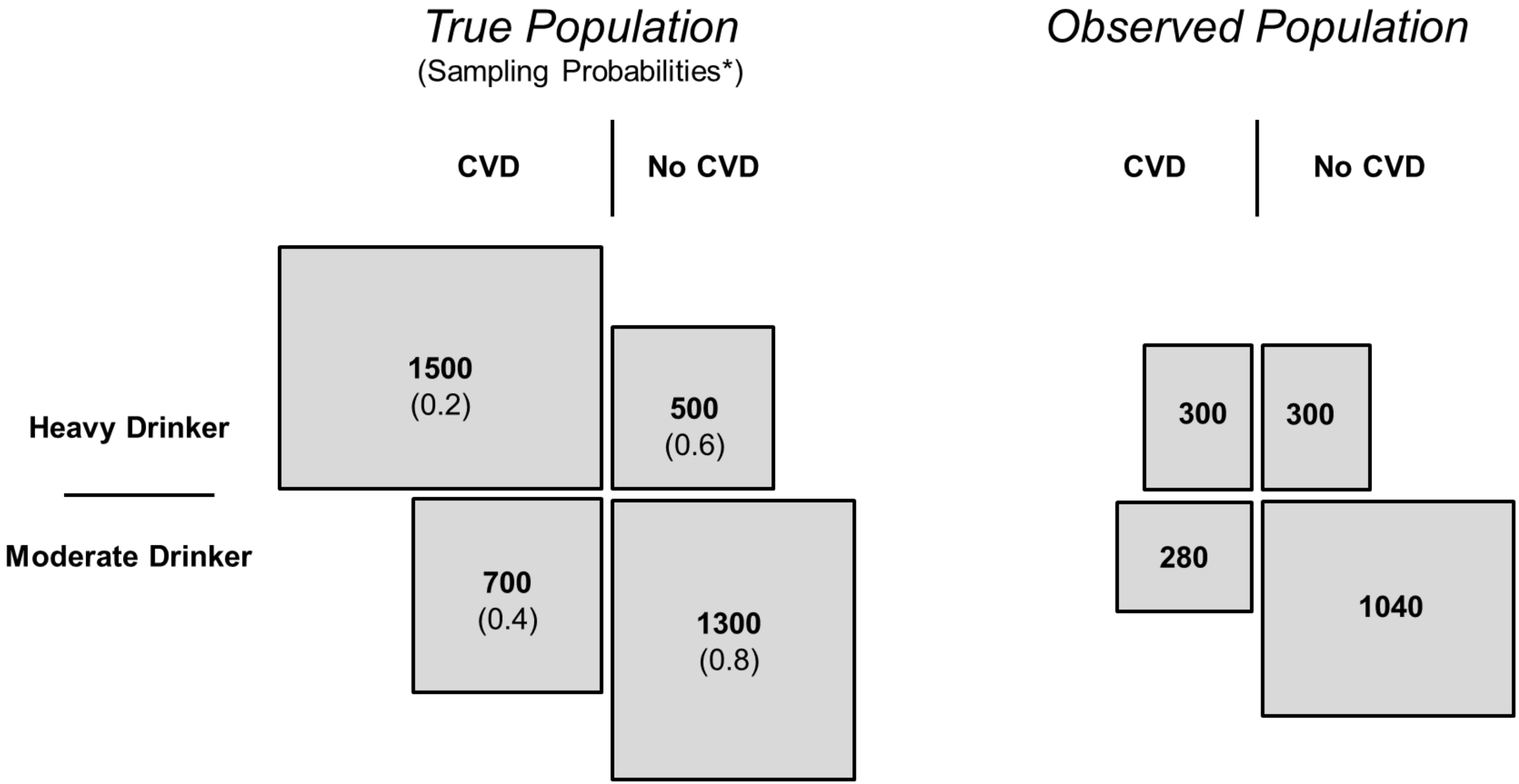
Selection Bias



If participation is caused by both the exposure of interest and the outcome, this can induce a spurious correlation between them

Katikireddi SV, Green MJ, Taylor AE, Davey Smith G, Munafò MR. Assessing causal relationships using genetic proxies for exposures: an introduction to Mendelian randomization. *Addiction* 2018; 113: 764-74

Selection Bias

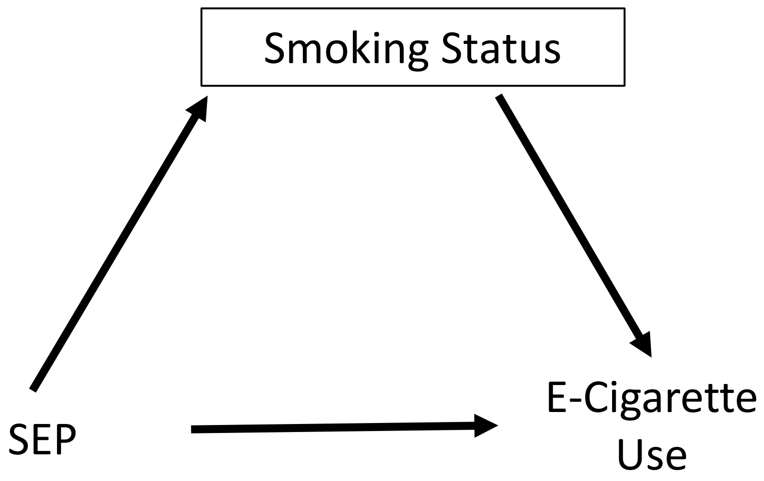


Relative Risk: 2.14
Odds Ratio: 5.57

Relative Risk: 2.36
Odds Ratio: 3.71

*Sampling probabilities were assigned as 0.8, with reductions of 0.4 for having CVD and 0.2 for being a heavy drinker.

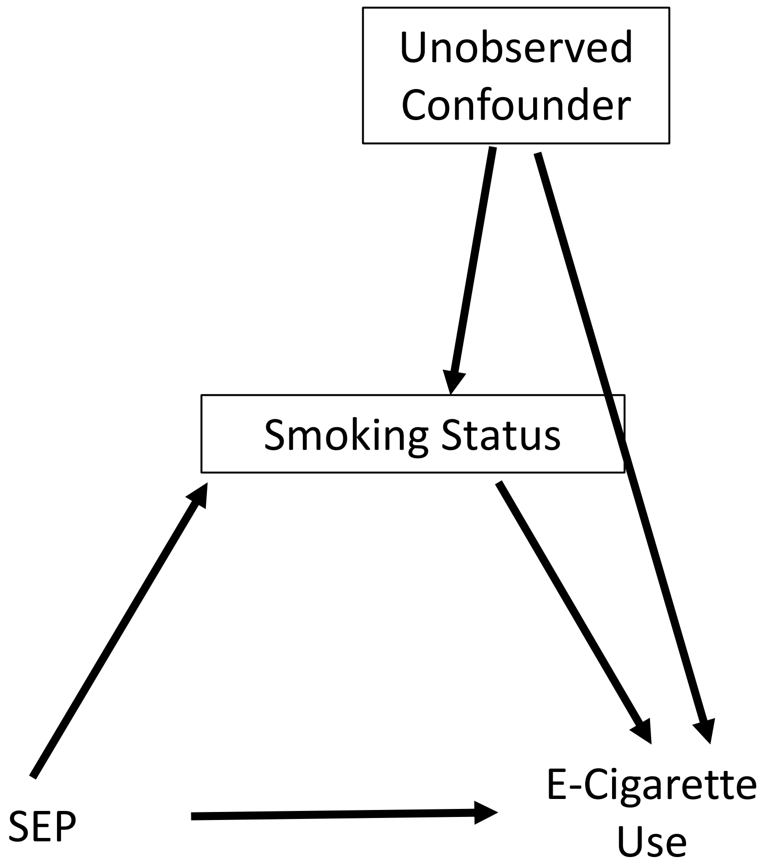
Collider Bias



Say we're interested in effects of SEP on E-Cigarette Use, but want to stratify by smoking status.

Why might the results be biased?

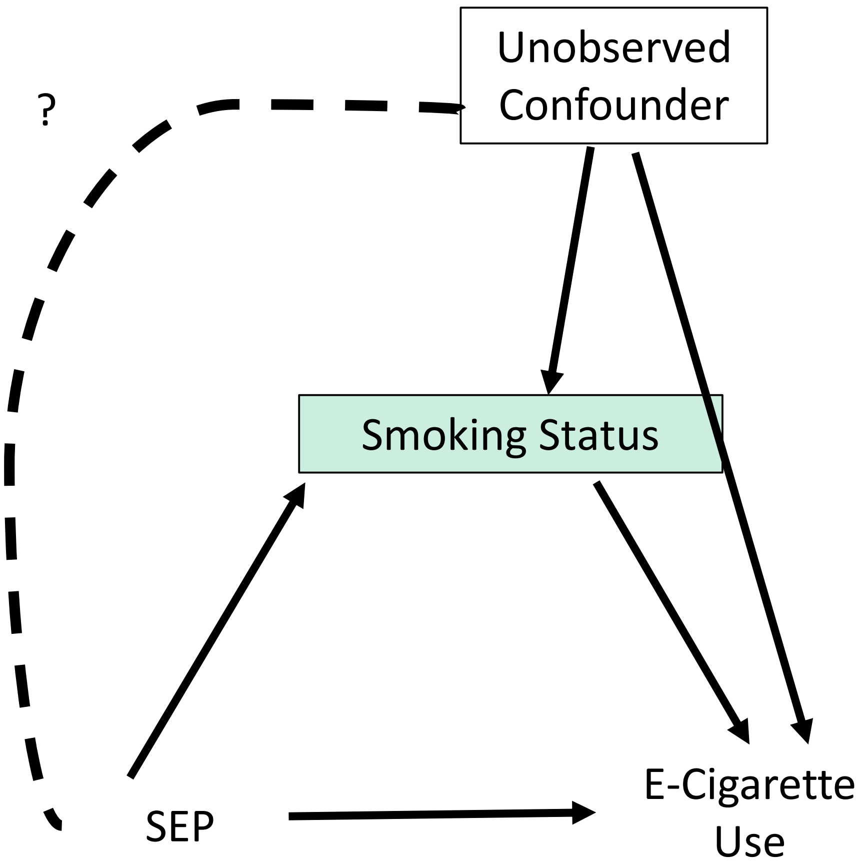
Collider Bias



Say we're interested in effects of SEP on E-Cigarette Use, but want to stratify by smoking status.

Why might the results be biased?

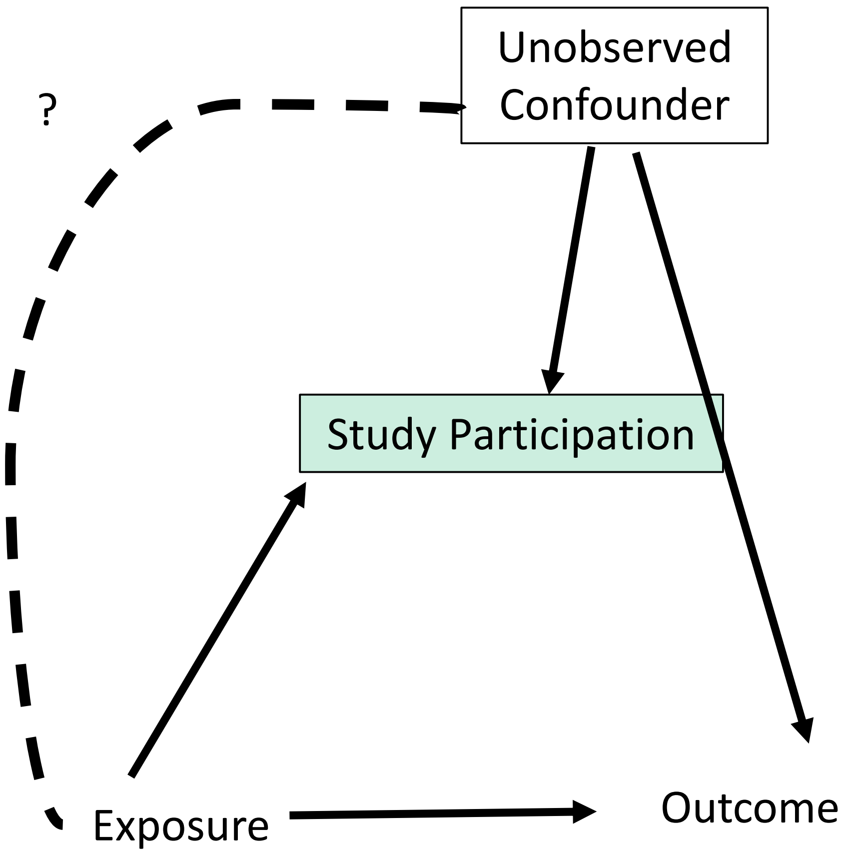
Collider Bias



Say we're interested in effects of SEP on E-Cigarette Use, but want to stratify by smoking status.

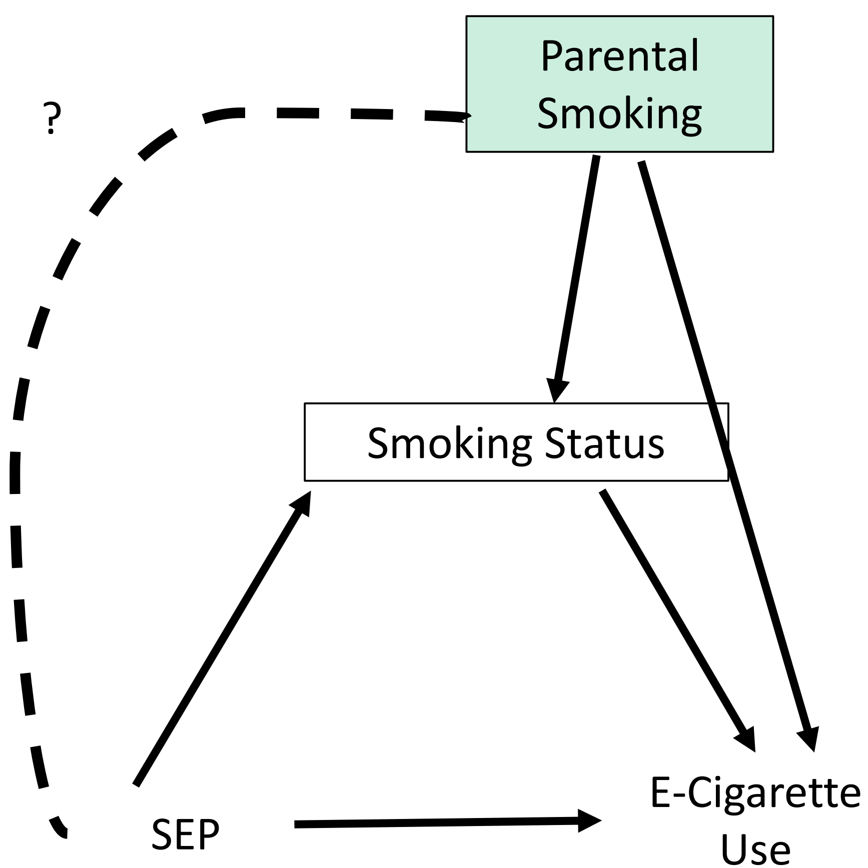
Why might the results be biased?

Selection & Collider Bias



*Study participation doesn't **have** to be determined by the outcome to be a problem*

Collider Bias

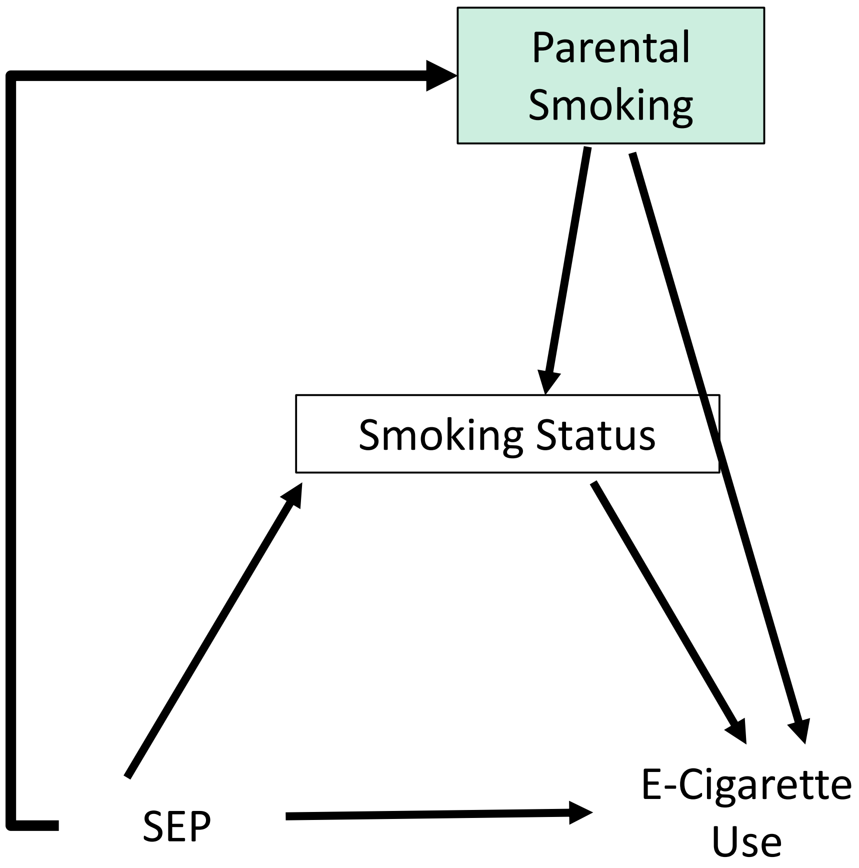


What if we measure and adjust for the unobserved confounder?

Blocks the 'back-door' path…

Unless…

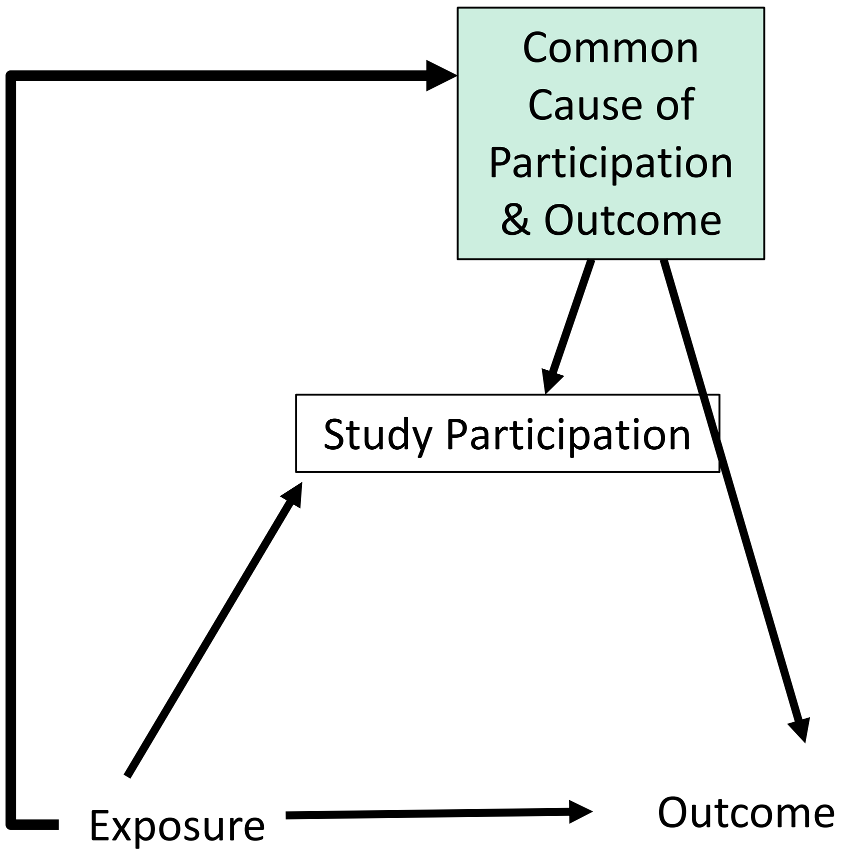
Collider Bias



If the mediator-outcome confounder is caused by the exposure of interest:

- Not adjusting for it induces collider bias
- Adjusting for it removes part of the effect of interest

Selection & Collider Bias



If the mediator-outcome confounder is caused by the exposure of interest:

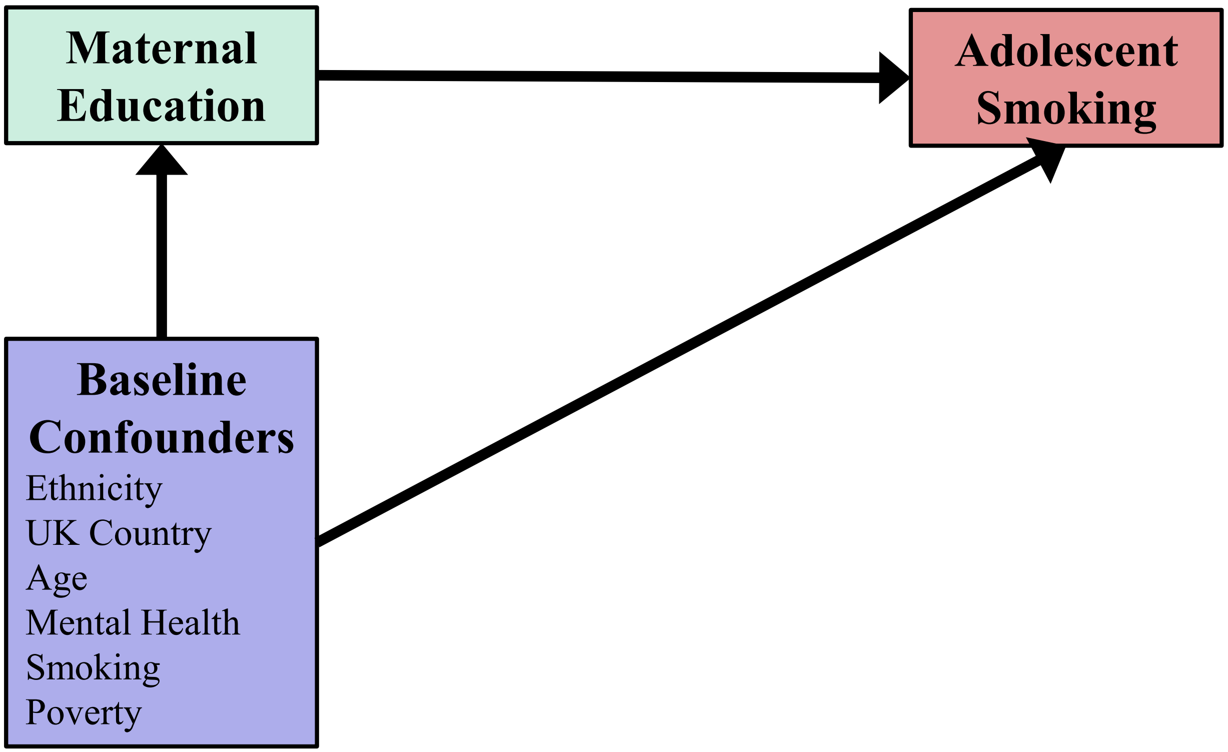
- Not adjusting for it induces collider bias
- Adjusting for it removes part of the effect of interest

Break

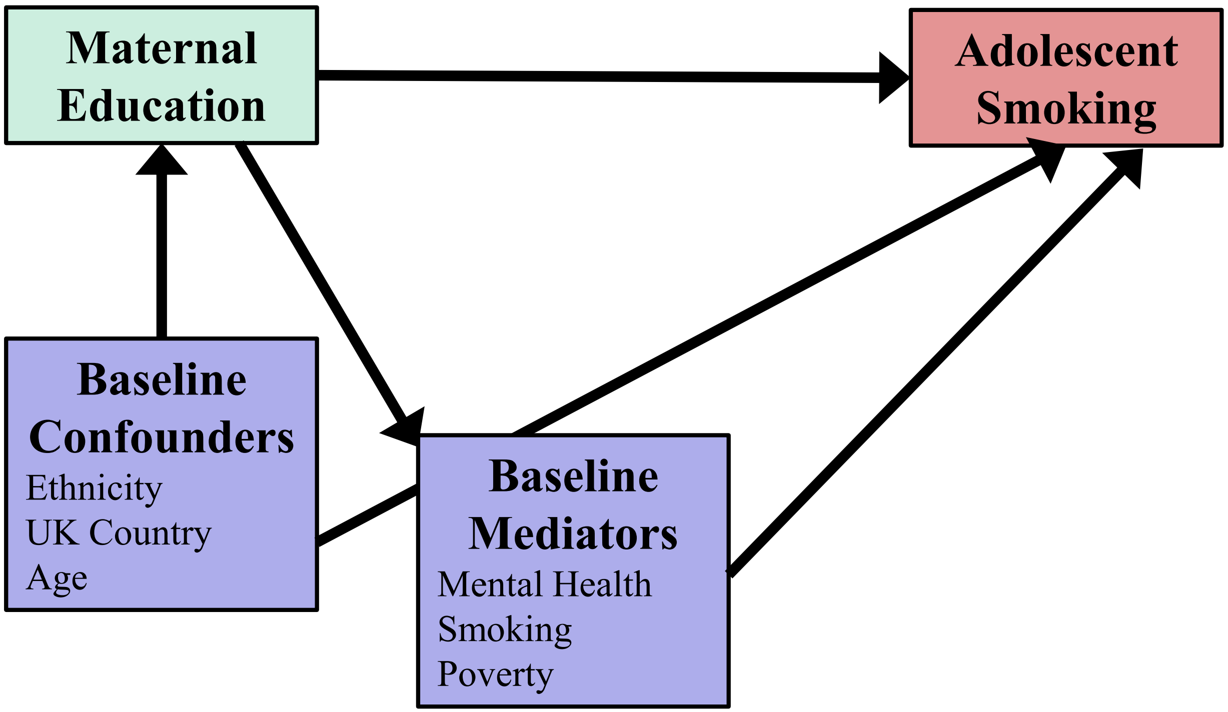
Exercise 1

Exercise 1

Exercise 1

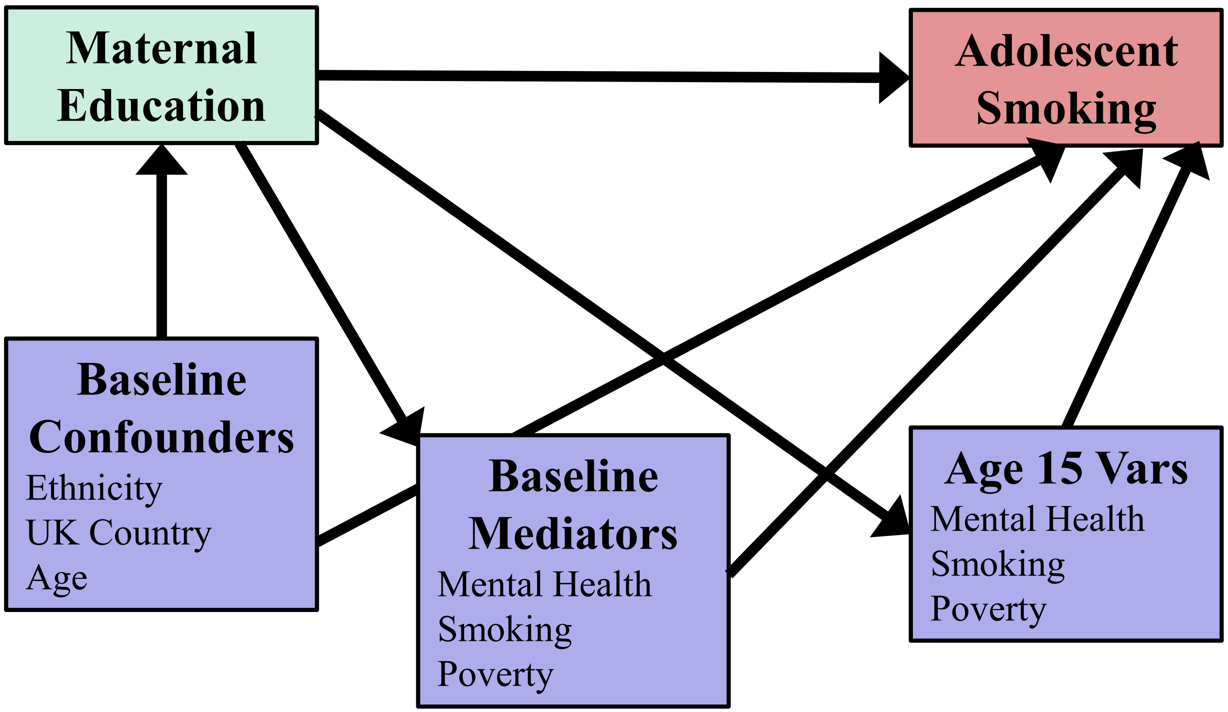

Maternal Education
Adolescent Smoking
Baseline Confounders
Ethnicity
UK Country
Age
Mental Health
Smoking
Poverty

Exercise 1



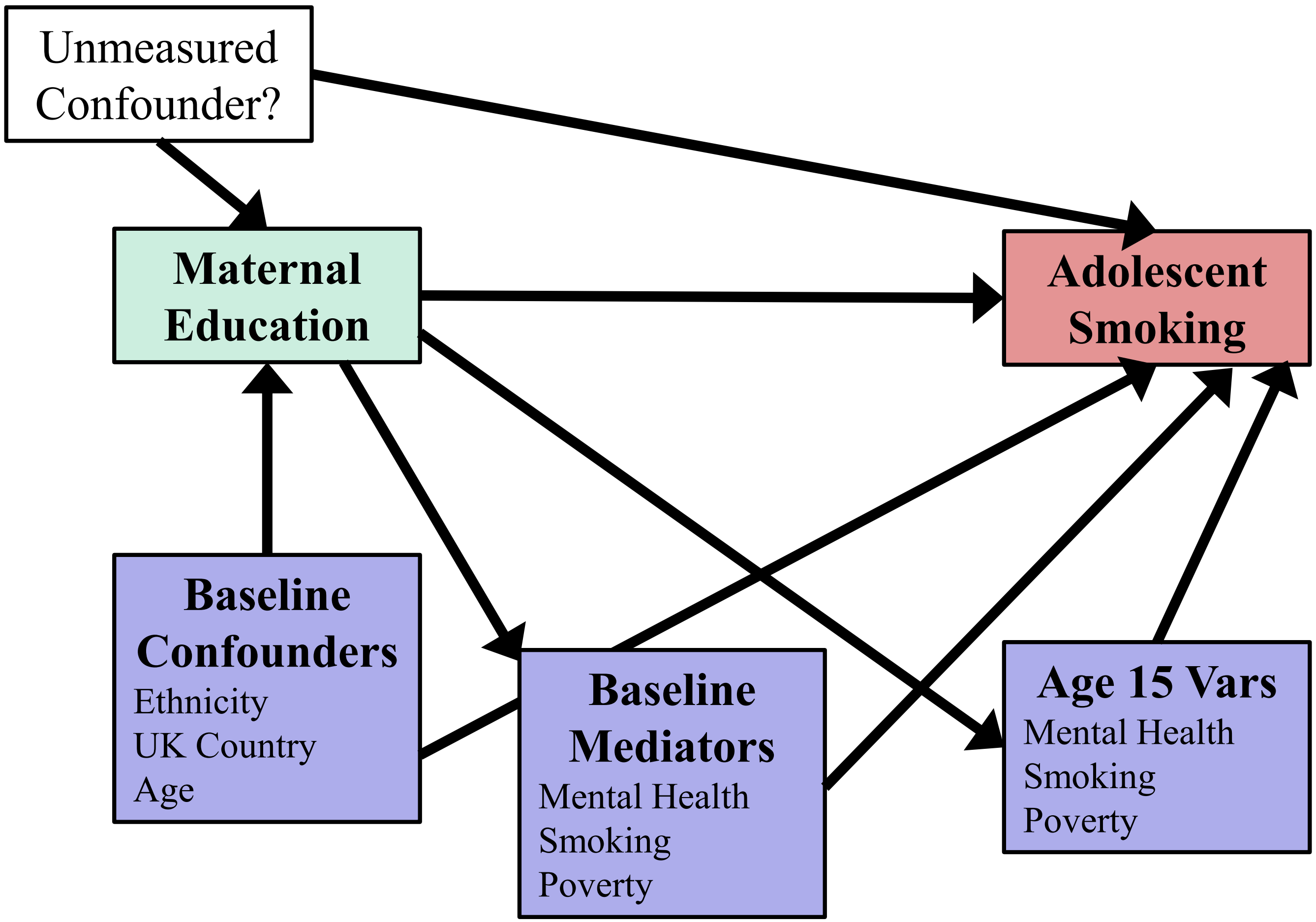
Maternal Education
Adolescent Smoking
Baseline Confounders
Ethnicity
UK Country
Age
Baseline Mediators
Mental Health
Smoking
Poverty

Exercise 1

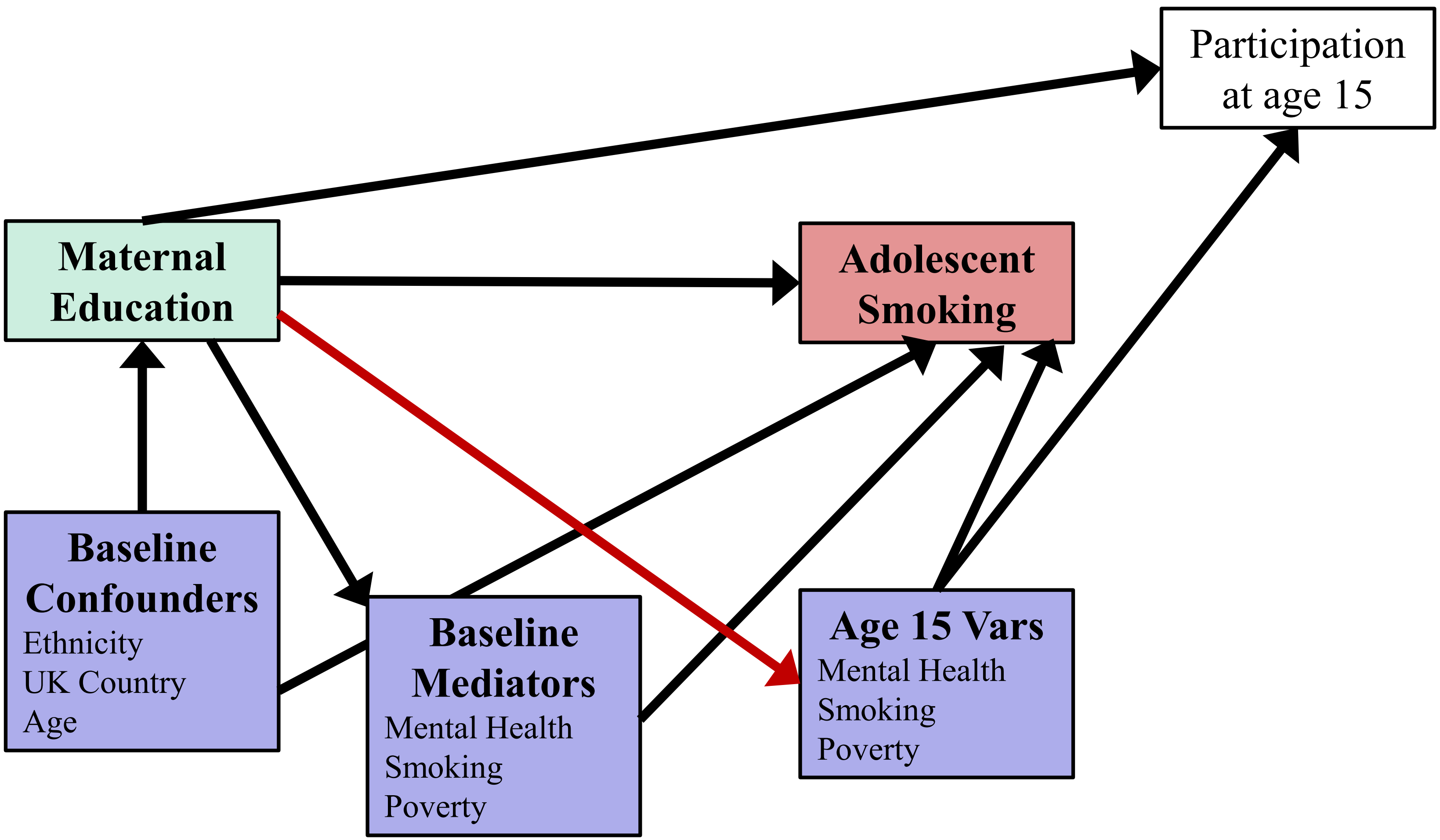


Maternal Education
Adolescent Smoking
Baseline Confounders
Ethnicity
UK Country
Age
Baseline Mediators
Mental Health
Smoking
Poverty
Age 15 Vars
Mental Health
Smoking
Poverty

Exercise 1

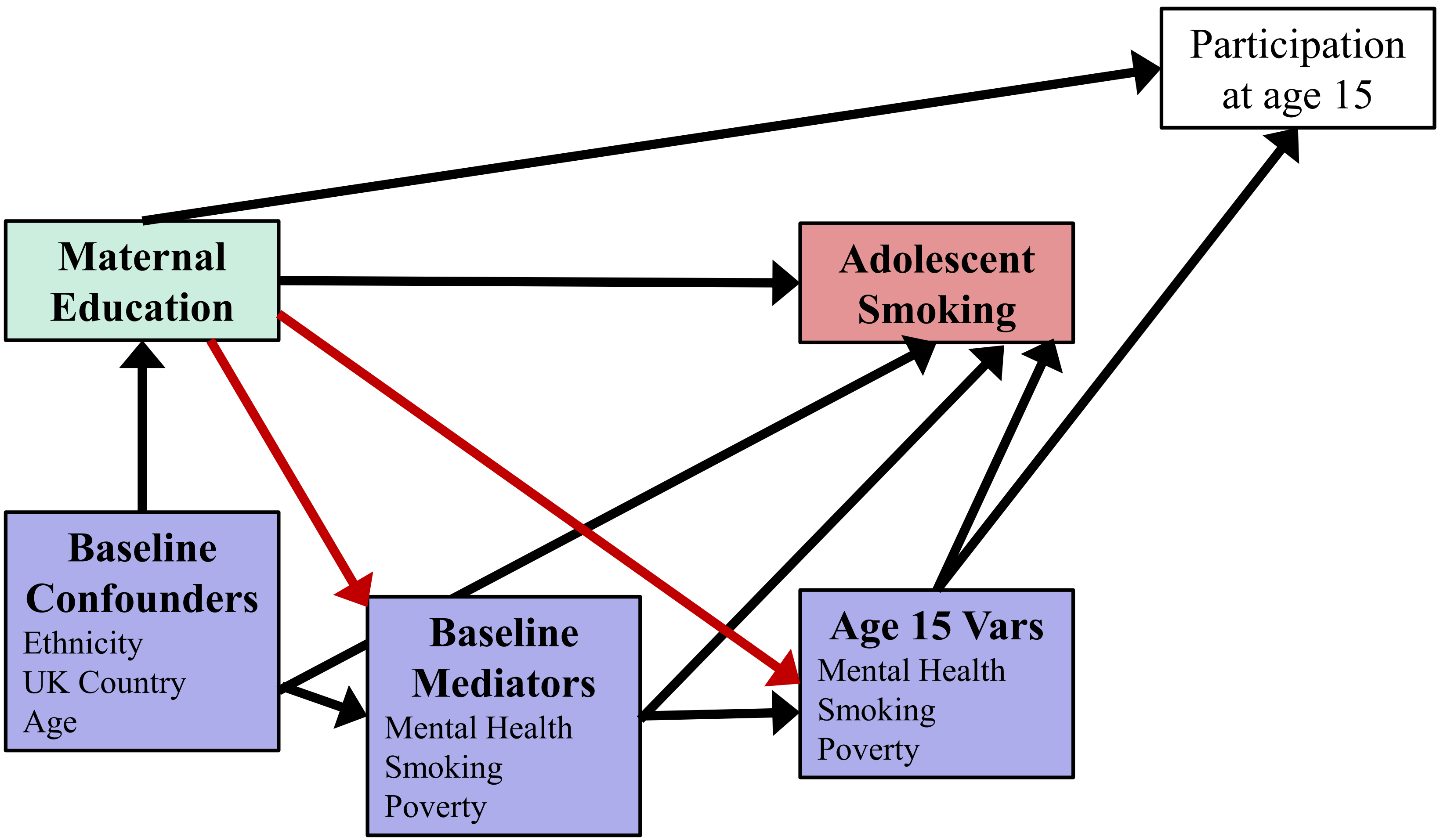

Unmeasured Confounder?
Maternal Education
Adolescent Smoking
Baseline Confounders
Ethnicity
UK Country
Age
Baseline Mediators
Mental Health
Smoking
Poverty
Age 15 Vars
Mental Health
Smoking
Poverty

Exercise 1



Participation at age 15
Maternal Education
Adolescent Smoking
Baseline Confounders
Ethnicity
UK Country
Age
Baseline Mediators
Mental Health
Smoking
Poverty
Age 15 Vars
Mental Health
Smoking
Poverty

Exercise 1

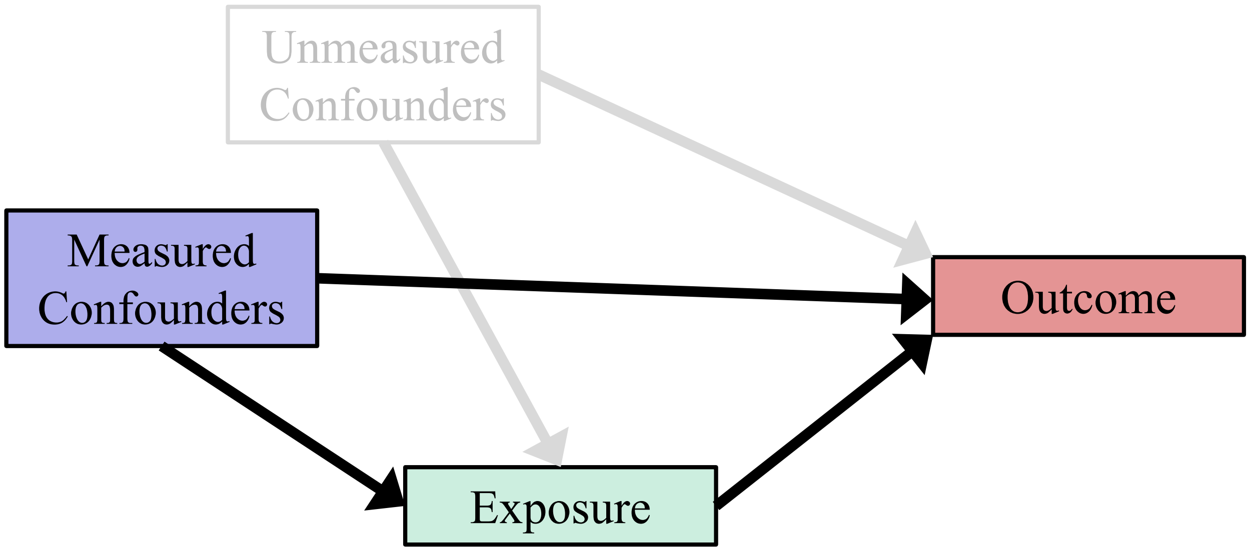


Participation at age 15
Maternal Education
Adolescent Smoking
Baseline Confounders
Ethnicity
UK Country
Age
Baseline Mediators
Mental Health
Smoking
Poverty
Age 15 Vars
Mental Health
Smoking
Poverty

Recap: What are we trying to do?

- Trying to mimic randomised experiment
- Control condition & treatment (or exposure) condition
- In an experiment randomisation aims to provide ‘balance’
- In observational studies exposures are not assigned randomly so conditions may be ‘unbalanced’

Confounder Adjusted Regression



So we can use regression to estimate causal effect of exposure on outcome, based on explicit assumptions

More assertive than saying exposure is associated with outcome but correlation ≠ causation

Causal Effect Definitions

What works, for whom, and in which circumstances?

- Acknowledges effect heterogeneity

We can distinguish (at least) two types of treatment effect:

- **Average Treatment Effect (ATE):** whole population is exposed vs no-one is exposed
- **Average Treatment Effect among the Treated (ATT):** effect of exposure for those who actually experienced it; observed level of exposure vs no-exposure
  - *Why might these estimates differ?*

Propensity Scores

- **Propensity score**= probability of treatment/exposure, given measured confounders
- Usually estimated in some kind of logistic regression model
- Variety of ways to use these to achieve (observed) confounder balance:
  - Propensity Matching
  - Propensity Stratification
  - Propensity Regression
  - **Propensity Weighting (aka Inverse-Probability Weighting: IPW)**

Propensity Matching

- Form pairs of subjects in exposed/unexposed groups with similar propensity scores
- Lots of different methods for matching
  - With/Without replacement
  - Greedy/optimal
  - With/Without caliper
  - Many-1/1-1
- If you match exposed participants to unexposed participants with similar propensity scores then this **estimates the ATT**

Propensity Stratification

- Rank subjects by their propensity score
- Stratify into groups (eg quintiles)
- Estimate difference between exposed/unexposed within each group
- Average results
  - ATE: straight average of group estimates
  - ATT: group estimates weighted by proportion of treated subjects in group

Propensity Regression

- Regression of exposure on outcome with adjustment for propensity score
- Can be used to estimate ATE or ATT, but doesn’t perform well in simulations

Propensity (or Inverse-Probability) Weighting (IPW)

	Unexposed re-weighted to resemble…	**Exposed** re-weighted to resemble…	**Interpretation of the comparison:**
Average Treatment Effect (ATE)	Whole population **W=P/P^**	Whole population **W=P/P^**	All exposed vs no exposure
Average Treatment Effect among the Treated (ATT)	Exposed **W=(1-P^)/P^**	Exposed **W=1**	Observed level of exposure vs no exposure

W=Weight
P=Overall probability of individual's observed exposure level
P^=Probability of individual's observed exposure level conditional on confounders

Comparison of propensity methods

- **Matching & weighting** perform better at removing bias than stratification and regression
- **Matching and weighting** equivalent in some settings; matching moderately better in others
- **Weighting easily gives ATE or ATT, while matching only gives ATT**
- Weighting uses all your data, matching discards some
- Matching is complicated (lots of decisions), while **weighting is relatively simple**

IPW Steps/stages

- Estimate a model predicting exposure based on observed confounders and use this to calculate weights
- Check overlap of propensity score distributions between exposed/unexposed
- Check confounder balance between exposed/unexposed

- (repeat these steps as necessary until balance is achieved)

- **Only then estimate treatment effect on outcome**
  - Important as separates analysis from results

IPW Steps/stages

- **Estimate a model predicting exposure based on observed confounders and use this to calculate weights**
- Check overlap of propensity score distributions between exposed/unexposed
- Check confounder balance between exposed/unexposed

- (repeat these steps as necessary until balance is achieved)

- Only then estimate treatment effect on outcome
  - Important as separates analysis from results

IPW Steps/stages: Modelling exposure

- Estimate a model for the exposure
  - e.g. logistic regression for binary exposure
  - Conditional on observed confounders
- Use this to estimate predicted probabilities for each individual's observed exposure value, e.g. if Px is predicted probability of exp=1 based on confounders, then:
  - If exp=1, P^=Px
  - If exp=0, P^=(1-Px)
- Calculate weights for ATE/ATT as indicated earlier

Propensity (or Inverse-Probability) Weighting (IPW)

	Unexposed re-weighted to resemble…	**Exposed** re-weighted to resemble…	**Interpretation of the comparison:**
Average Treatment Effect (ATE)	Whole population **W=P/P^**	Whole population **W=P/P^**	All exposed vs no exposure
Average Treatment Effect among the Treated (ATT)	Exposed **W=(1-P^)/P^**	Exposed **W=1**	Observed level of exposure vs no exposure

W=Weight
P=Overall probability of individual's observed exposure level
P^=Probability of individual's observed exposure level conditional on confounders

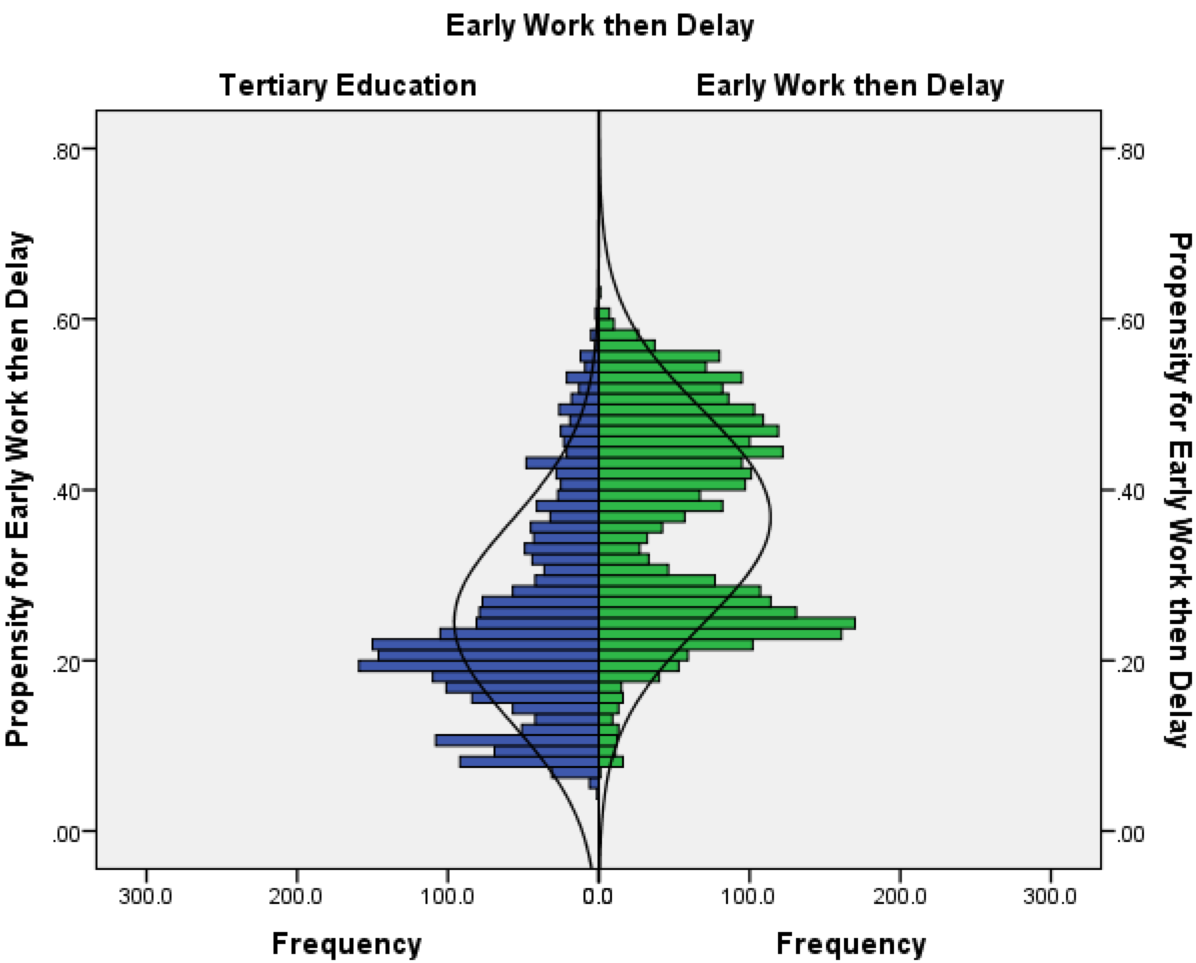
IPW Steps/stages

- Estimate a model predicting exposure based on observed confounders and use this to calculate weights
- **Check overlap of propensity score distributions between exposed/unexposed**
- Check confounder balance between exposed/unexposed

- (repeat these steps as necessary until balance is achieved)

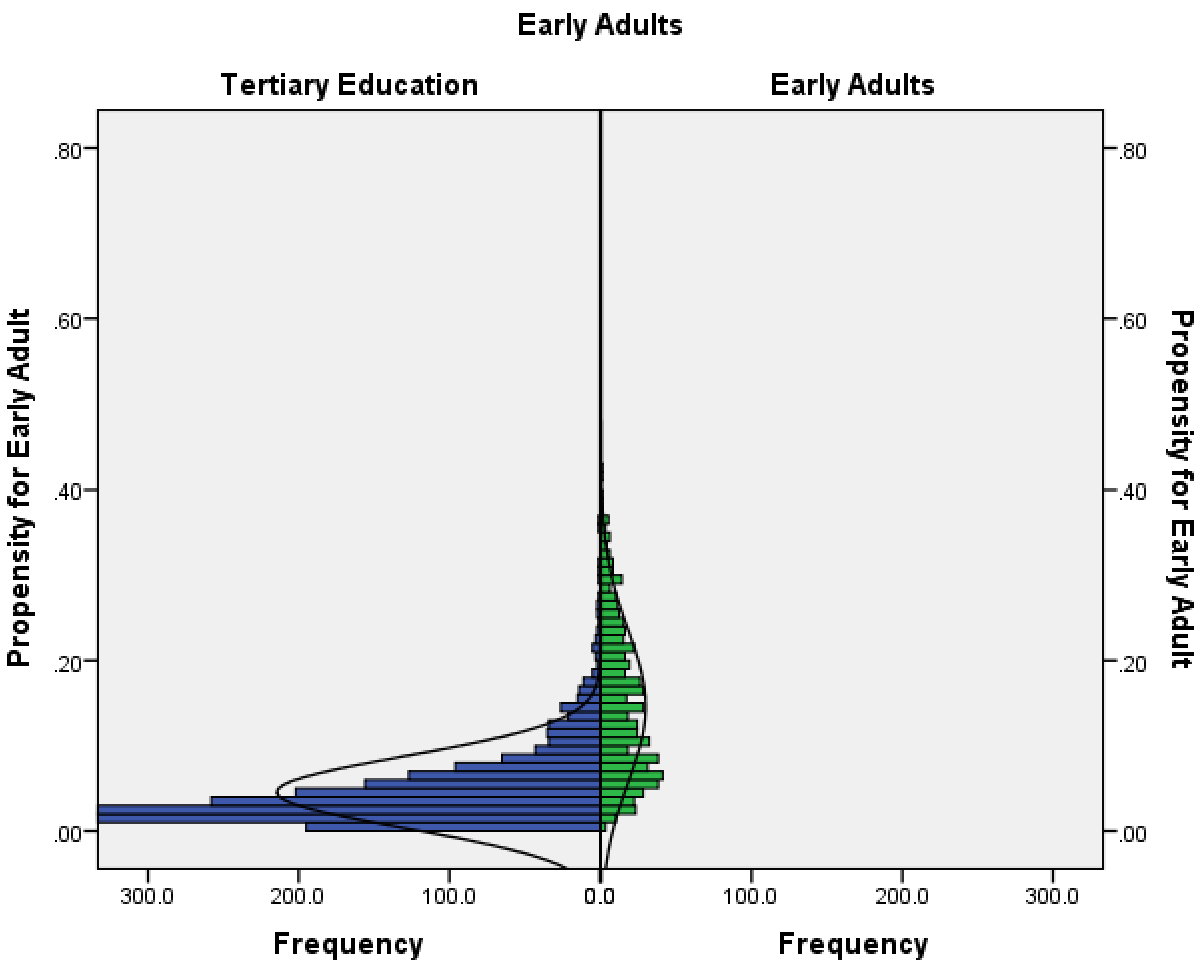
- Only then estimate treatment effect on outcome
  - Important as separates analysis from results

Propensity distributions comparisons



Green MJ, Leyland AH, Sweeting H, Benzeval M. Causal effects of transitions to adult roles on early adult smoking and drinking: Evidence from three cohorts. *Social Science and Medicine* 2017; 187: 193-202.

Propensity distributions comparisons



Green MJ, Leyland AH, Sweeting H, Benzeval M. Causal effects of transitions to adult roles on early adult smoking and drinking: Evidence from three cohorts. *Social Science and Medicine* 2017; 187: 193-202.

Propensity distributions comparisons

- If distributions are clearly separated, then there is a risk of **off-support inference**, i.e. exposure groups are so different from each other that you don’t have enough information for causal inference
  - **This risk will still be there if you use regression, but is less explicit/obvious**

- Comparing distributions can be informative BUT
- No clear threshold for what constitutes sufficient over-lap for causal inference

Other indicators of limited information:

- Mean ATE weights should be close to 1, if not suggests some subjects being assigned extreme weights
- Effect estimates/confounder balance are sensitive to truncation of weights (e.g. at 95% percentile)

IPW Steps/stages

- Estimate a model predicting exposure based on observed confounders and use this to calculate weights
- Check overlap of propensity score distributions between exposed/unexposed
- **Check confounder balance between exposed/unexposed**

- (repeat these steps as necessary until balance is achieved)

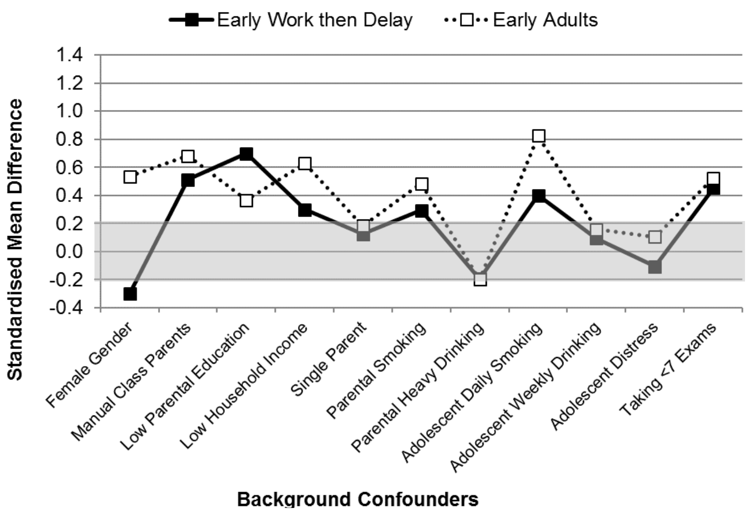
- Only then estimate treatment effect on outcome
  - Important as separates analysis from results

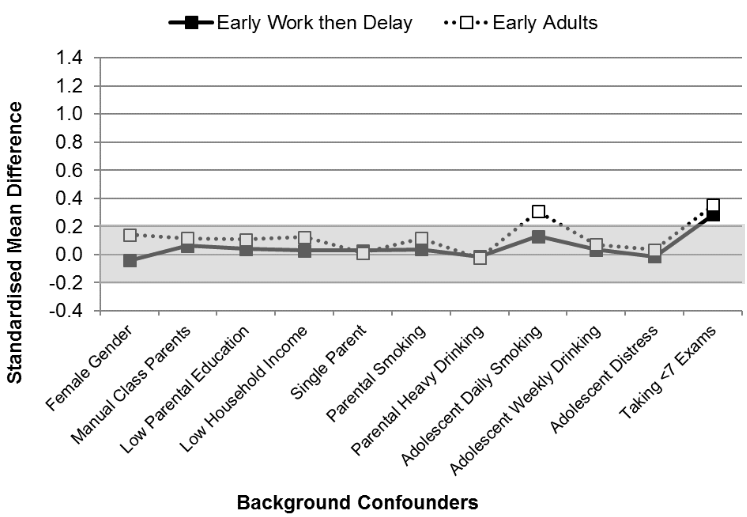
Checking Confounder Balance

Unpublished results deleted

Standardised Mean Differences in Confounders associated with Youth use of e-cigarettes

Checking Confounder Balance





- Regression and IPW both assume no **unmeasured** confounding
- BUT in both, you may not entirely remove **measured** confounding either

If balance not achieved:

- Revisit your exposure prediction model
- Otherwise, report and acknowledge potential bias

Green MJ, Leyland AH, Sweeting H, Benzeval M. Causal effects of transitions to adult roles on early adult smoking and drinking: Evidence from three cohorts. *Social Science and Medicine* 2017; 187: 193-202.

IPW Steps/stages

- Estimate a model predicting exposure based on observed confounders and use this to calculate weights
- Check overlap of propensity score distributions between exposed/unexposed
- Check confounder balance between exposed/unexposed
- (repeat these steps as necessary until balance is achieved)

- **Only then estimate treatment effect on outcome**
  - Important as separates analysis from results

Estimate Causal Effects

Unpublished results deleted

ORs associated with Youth use of e-cigarettes

Interpretation of effects

E-Cigarette example:

ATE: smoking rates would be higher if all youths used e-cigarettes, compared to no youth using them

ATT: smoking rates are higher because some youth currently use e-cigarettes and would reduce if we intervened to stop current usage

Estimates on previous slide showed less evidence for the ATT interpretation than the ATE, so:

- Effect of e-cigarette use varies depending on the background factors predicting usage

IPW vs Adjusted Regression

- Both assume no unmeasured confounding
- IPW approach has explicit checks for off-support inference and confounder balance
- Separation of design and analysis; less temptation to modify regression model until desired outcome is achieved
- Regression can be suspect to a catch-22 where a variable is both a confounder and a mediator
  - Extensions of IPW can get around this
- It is not clear what population regression effect estimates based on (i.e. ATE or ATT?)

What population are regression estimates based on?

	No Weight			IPW		Outcome Regression	
	Total	X = 0	X = 1	X = 0	X = 1	X = 0	X = 1
Z = 0	*49.1*	47.2	54.7	49.1	49.1	52.7	52.7
Z = 1	*50.9*	52.8	45.3	50.9	50.9	47.3	47.3
Q = 0	*86.7*	85.3	90.4	86.7	86.7	89.4	89.4
Q = 1	*13.3*	14.7	9.6	13.3	13.3	10.6	10.6
Z = 0, Q = 0	*43.2*	40.8	49.9	43.2	43.2	47.6	47.6
Z = 0, Q = 1	*6.0*	6.4	4.8	6.0	6.0	5.2	5.2
Z = 1, Q = 0	*43.5*	44.5	40.5	43.5	43.5	41.8	41.8
Z = 1, Q = 1	*7.4*	8.3	4.8	7.4	7.4	5.4	5.4

IPW indicates inverse probability weighting.

- Two confounders Z and Q and exposure of interest X

Popham F, Leyland AH. Assessing Confounder Balance in Outcome Regressions. *Epidemiology* 2018; **29**: e47-e8.

What population are regression estimates based on?

	No Weight			IPW		Outcome Regression	
	Total	X = 0	X = 1	X = 0	X = 1	X = 0	X = 1
Z = 0	*49.1*	47.2	54.7	49.1	49.1	52.7	52.7
Z = 1	*50.9*	52.8	45.3	50.9	50.9	47.3	47.3
Q = 0	*86.7*	85.3	90.4	86.7	86.7	89.4	89.4
Q = 1	*13.3*	14.7	9.6	13.3	13.3	10.6	10.6
Z = 0, Q = 0	*43.2*	40.8	49.9	43.2	43.2	47.6	47.6
Z = 0, Q = 1	*6.0*	6.4	4.8	6.0	6.0	5.2	5.2
Z = 1, Q = 0	*43.5*	44.5	40.5	43.5	43.5	41.8	41.8
Z = 1, Q = 1	*7.4*	8.3	4.8	7.4	7.4	5.4	5.4

IPW indicates inverse probability weighting.

- IPW ATE balances Z and Q at population average

Popham F, Leyland AH. Assessing Confounder Balance in Outcome Regressions. *Epidemiology* 2018; **29**: e47-e8.

What population are regression estimates based on?

	No Weight			IPW		Outcome Regression	
	Total	X = 0	X = 1	X = 0	X = 1	X = 0	X = 1
Z = 0	*49.1*	47.2	54.7	49.1	49.1	52.7	52.7
Z = 1	*50.9*	52.8	45.3	50.9	50.9	47.3	47.3
Q = 0	*86.7*	85.3	90.4	86.7	86.7	89.4	89.4
Q = 1	*13.3*	14.7	9.6	13.3	13.3	10.6	10.6
Z = 0, Q = 0	*43.2*	40.8	49.9	43.2	43.2	47.6	47.6
Z = 0, Q = 1	*6.0*	6.4	4.8	6.0	6.0	5.2	5.2
Z = 1, Q = 0	*43.5*	44.5	40.5	43.5	43.5	41.8	41.8
Z = 1, Q = 1	*7.4*	8.3	4.8	7.4	7.4	5.4	5.4

IPW indicates inverse probability weighting.

- Outcome regression balances Z and Q at levels different from the population average

Popham F, Leyland AH. Assessing Confounder Balance in Outcome Regressions. *Epidemiology* 2018; **29**: e47-e8.

Thanks

Exercise 2