Introduction to Causal Inference: Propensity Score

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- Historically, applied researchers have relied on the use of regression adjustment to account for differences in measured baseline characteristics between treated and untreated subjects.
- Recently, there has been increasing interest in methods based on the propensity score to reduce or eliminate the effects of confounding when using observational data.
- The Nobel Prize in Economics 2021 is awarded with one half to Card, and the other half jointly to Angrist and Imbens "for their methodological contributions to the analysis of causal relationships"

Confounding

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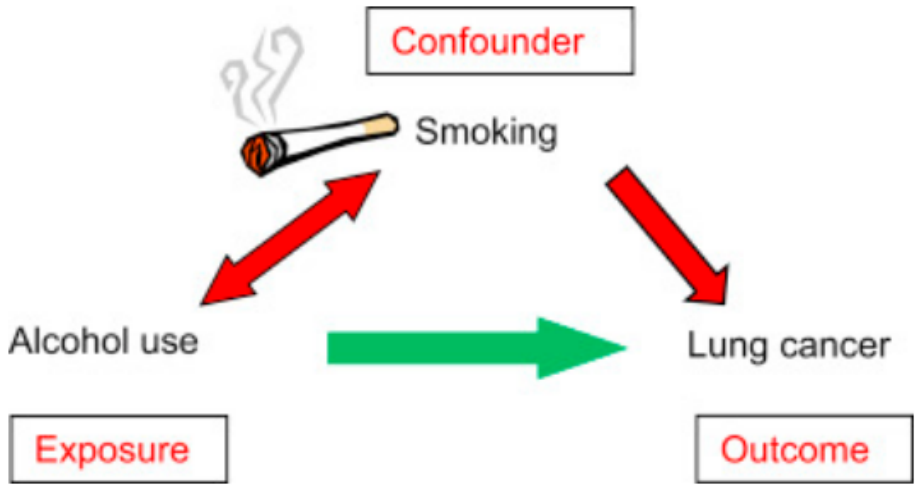


Confounding

- A confounder
  - is a risk factor for the outcome
  - is associated with the exposure
  - is not in the causal pathway between the exposure and the outcome

Example

Dental health and Heart disease

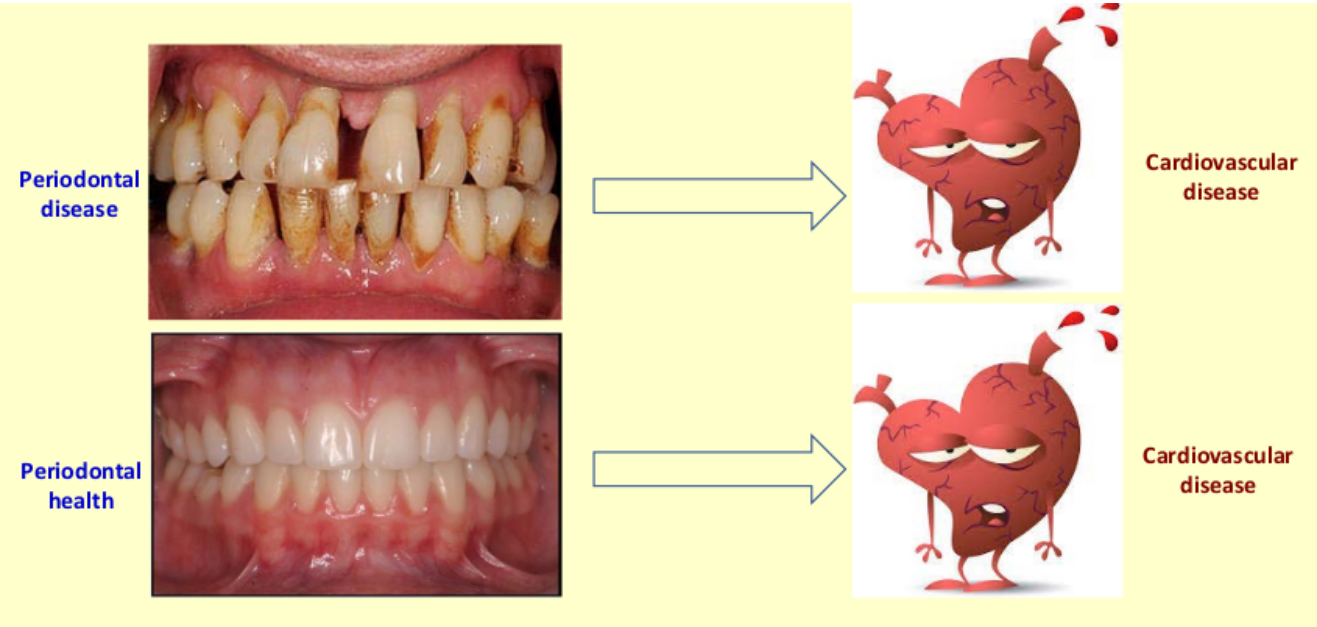
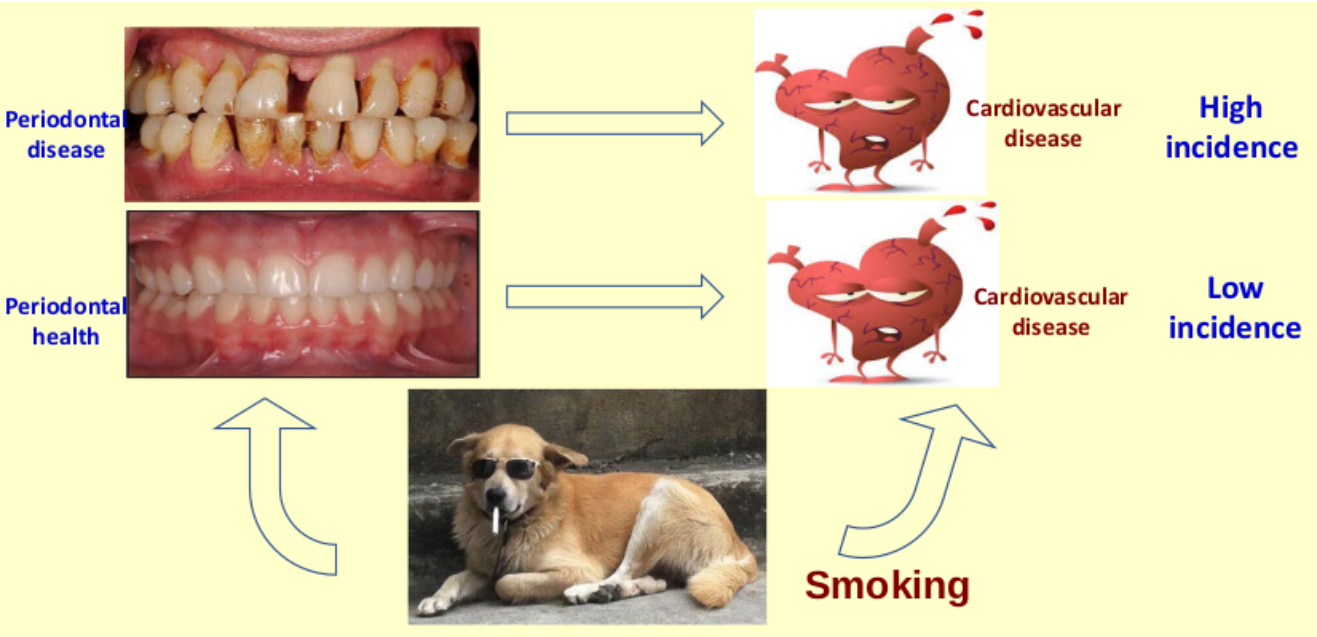


Figure: Example of confounding

Example

Dental health and Heart disease: We don't know whether the increase in the incidence is due to periodontal disease or smoking



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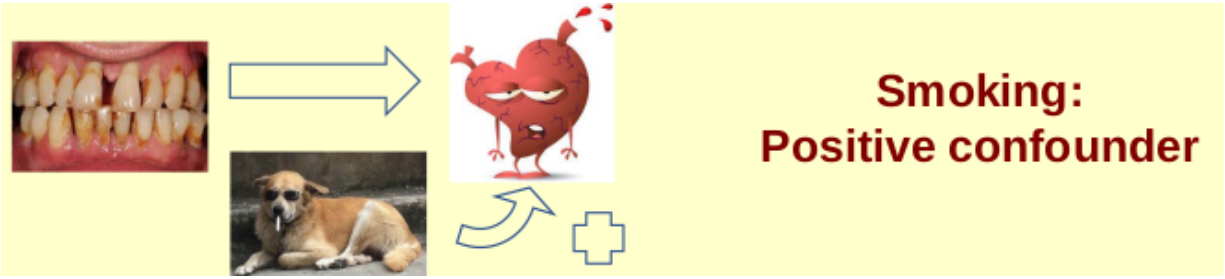

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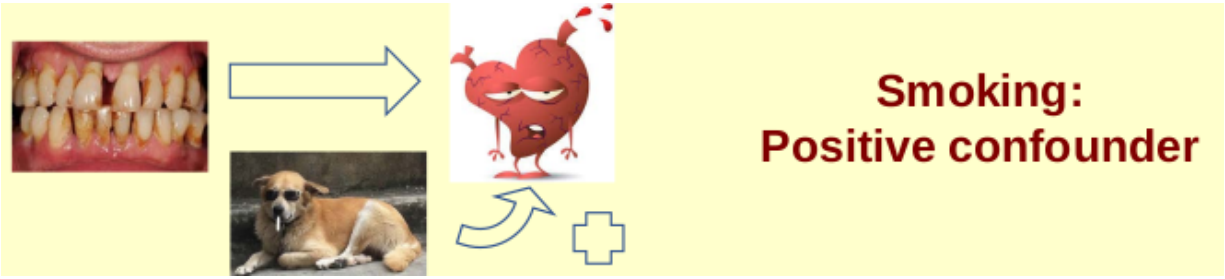

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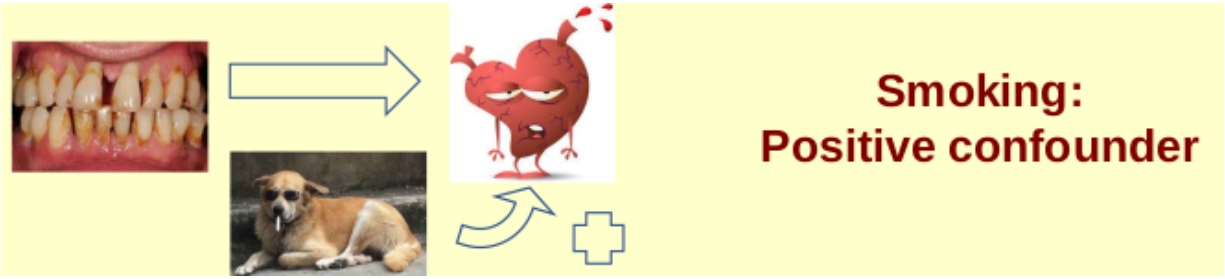

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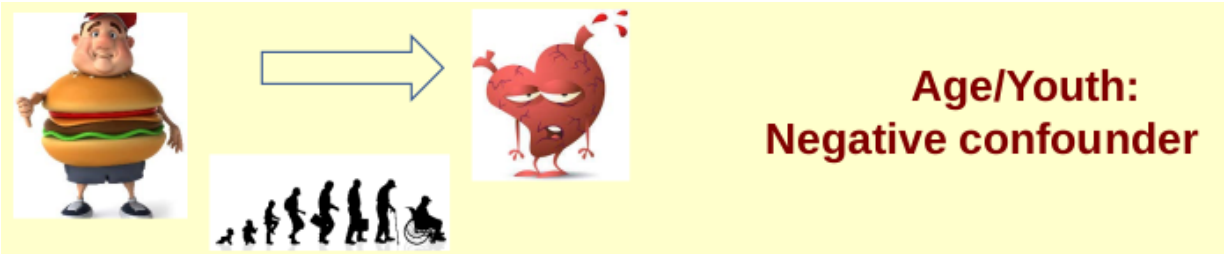

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Methods to address confounding

- Controlled in the design phase $\rightarrow$ experiment designs
  - Randomization
  - Restriction
  - Matching
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- Controlled in the design phase $\rightarrow$ experiment designs
  - Randomization
  - Restriction
  - Matching
  - Stratification
- Controlled in the analysis phase
  - Stratified analysis
  - Propensity scores

It is more desirable to handle it in the Design Phase; but some ideal methods might not be possible.

Design: randomization

Imagine an AB test

- Randomly assign subjects to the treatment or control group
- It removes bias in the treatment assignment
- It controls both known and unknown confounders
- It guarantees that statistical tests will have valid significance levels
- In short, it is the Gold Standard for experiment designs (in biomedical and social research)

Design: restriction

- Exclusion of individuals with confounding factors or restriction to specific groups.
  - Example 1: Exclusion of smokers from a heart disease study
  - Example 2: Inclusion only males between 40-45 years in a study of relationship between heart disease and overweight

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- Limitations
  - Reduces the number of eligible individuals
  - Restriction limits generalizability
  - Unable to evaluate the effects of factors that are restricted for

Design: matching

- Each pair of persons enrolled in a study are similar for one or more characteristics
  - Example: When study the causal relationship between periodontal disease and heart disease, if a 60 year-old Caucasian smoker with periodontal disease is entered then a 60 year old Caucasian smoker without periodontal disease will also be included

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- Limitations
  - Time-consuming and expensive
  - Limits sample size
  - Only for a small number of confounding factors
  - Unable to evaluate the effect of the factors that have been matched

It is very hard, even not possible, to match when there are many confounders or potential confounders; substantially reduced sample size.

Design/Analysis: stratification

- Control for confounding by creating two or more categories or subgroups (strata) in which the confounding variable does not vary.
  - Example 1: Divide subjects with and without periodontal disease into groups based on smoking status: smokers and non-smokers.
  - Example 2: Divide subjects into different age groups, such as ¡30, 30-35, 36-40, ...

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  - Unable to control simultaneously for multiple confounding variables
  - Limits sample size
  - Time consuming

Why not always randomized controlled experiments

In practice, though Randomized controlled experiments/trials is the best choice, sometimes it is hard to carry out.

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- Unethical: often in biomeical studies and clinical trials
- Infeasible
- Not scientifically or financially justified

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- Treatment selection is influenced by subject characteristics, which is a nonrandomized and uncontrolled process
- How to account for this systematic difference?

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- Propensity score is the probability of a subject being assigned to the treatment group conditional on observed baseline covariates (Rosebaum and Rubin, 1983)
- It uses logistic regression or other binary classification approaches

Propensity score: implementation

- Logistic regression (or other binary classification models capable of predictive probability)
  - Response variable: $z = 1$ for Treatment and 0 for Control
  - Covariates: all features $\boldsymbol{x}$, including all possible confounders

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  - Response variable: $z = 1$ for Treatment and 0 for Control
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- For each subject i with $\boldsymbol{x}_i$, the propensity score is $\hat{p}(z_i = 1 \mid \boldsymbol{x}_i)$

Propensity score: rationale

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- In particular, the propensity score is a balancing score: conditional on the propensity score, the distribution of observed baseline covariates will be similar between treated and untreated subjects.
- The propensity score as a scalar represents an overall status of high-dimensional covariates

Propensity score

- Three simple methods using propensity score
  - Matching on the propensity score
  - Stratification on the propensity score
  - Covariate adjustment using the propensity score

Propensity score matching

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  - If the outcome is continuous (e.g., a depression scale), the effect of treatment can be estimated as the difference between the mean outcome for treated subjects and the mean outcome for untreated subjects
  - If the outcome is binary (e.g., heart disease or not), the effect of treatment can be estimated as the difference between the proportion of subjects experiencing the event in each of the two groups (treated vs. untreated)

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- In **greedy matching**, a treated subject is first selected at random. The untreated subject whose propensity score is closest to that of this randomly selected treated subject is chosen for matching to this treated subject. This process is then repeated until one has exhausted the list of treated subjects.
- This process is called greedy because at each step in the process, the nearest untreated subject is selected for matching to the given treated subject, even if that untreated subject would better serve as a match for a subsequent treated subject.

Propensity score matching

- In **optimal matching**, matches are formed to minimize the total within-pair difference of the propensity score.
- Gu and Rosenbaum, 1993 (Comparison of multivariate matching methods: Structures, distances, and algorithms. Journal of Computational and Graphical Statistics 2, 405–420) compared greedy and optimal matching and found that optimal matching did no better than greedy matching in producing balanced matched samples.

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The processes of greedy and optimal matchings are different but the performance and results are similar

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- Subjects are ranked according to their estimated propensity scores, and then stratified into subsets based on predefined thresholds of the estimated propensity score
- A common approach is to divide subjects into five roughly equal sized groups using the quintiles (i.e., 20%, 40%, 60%, and 80% quantiles) of the estimated propensity score.

Stratification on the propensity score

- Cochran, 1968 (The effectiveness of adjustment by sub- classification in removing bias in observational studies; Biometrics 24, 295–313) demonstrated that stratifying on the quintiles of **a continuous confounding variable** eliminated approximately 90% of the bias due to that variable

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- Rosenbaum and Rubin, 1984 (Reducing bias in observational studies using sub-classification on the propensity score; Journal of the American Statistical Association 79, 516–524) extended this result to **stratification on the propensity score**, stating that stratifying on the quintiles of the propensity score eliminates approximately 90% of the bias due to measured **confounders** when estimating a linear treatment effect

Stratification on the propensity score

- Stratification on the propensity can be conceptualized as an analysis of a set of (five) randomized controlled trials. Within each stratum, the effect of treatment on outcomes can be estimated by comparing outcomes directly between treated and untreated subjects. The stratum-specific estimates of treatment effect can then be pooled across strata to estimate an overall treatment effect (e.g. using weighted average)

Covariate adjustment using the propensity score

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  - For a logistic model the treatment effect is interpreted as an adjusted odds ratio

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- Propensity score matching and stratification are model-free
- Covariate adjustment using the propensity score requires a linear or logistic regression; this method assumes that the relationship between the propensity score and the outcome has been correctly modeled
- Instead of using multiple predictors in a regression, all baseline characteristics are combined (through propensity score) into one "1index" (the propensity score). This makes it simpler to check for model assumptions

Comparison of the three propensity score methods

- Propensity score matching eliminates a **bigger** proportion of the systematic differences in baseline characteristics between treated and untreated subjects than stratification on the propensity score or covariate adjustment using the propensity score (Austin, P. C. Type I error rates, coverage of confidence intervals, and variance estimation in propensity-score matched analyses. The International Journal of Biostatistics, 5, Article 13; 2009)

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- However, propensity score matching is more time-consuming and potentially limits the sample size since some subjects may not able to match

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- In an observational study the true propensity score is not known. It must be estimated using the data
- An important component of any propensity score analysis is to examine whether the propensity score model has been adequately specified

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  - All measured baseline covariates
  - All baseline covariates that are associated with treatment assignment
  - All potential and true confounders
- In practice, it may be difficult to determine true confounders among baseline variables
- In many settings, most subject-level baseline covariates likely affect both treatment assignment and the outcome. Therefore, it is likely that one can safely include all measured baseline characteristics in the propensity score model.

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- `R` package: `MatchIt`

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- A short answer is NO
- A key assumption for propensity score methods to be valid is *unconfoundedness*; it is violated if there exist unobserved confounders
- Using propensity score methods, one assumes all confounders are observed as covariates in the data.
- In comparison, randomization controls both known and unknown confounders

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After Propensity Scores are generated, it is possible to estimate the treatment effect

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- If Matching is used, one can estimate within each pair, the average them out
- If Stratification is used, one can similarly estimate within each stratum, then weighted average them out
- If Covariate Adjustment is used, the effect of treatment is determined using the estimated regression coefficient from the fitted regression model

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Correlation between covariates and error terms is also known as *endogeneity*. In this situation, ordinary least squares produces biased and inconsistent estimates

Instrumental variable (IV)

An IV

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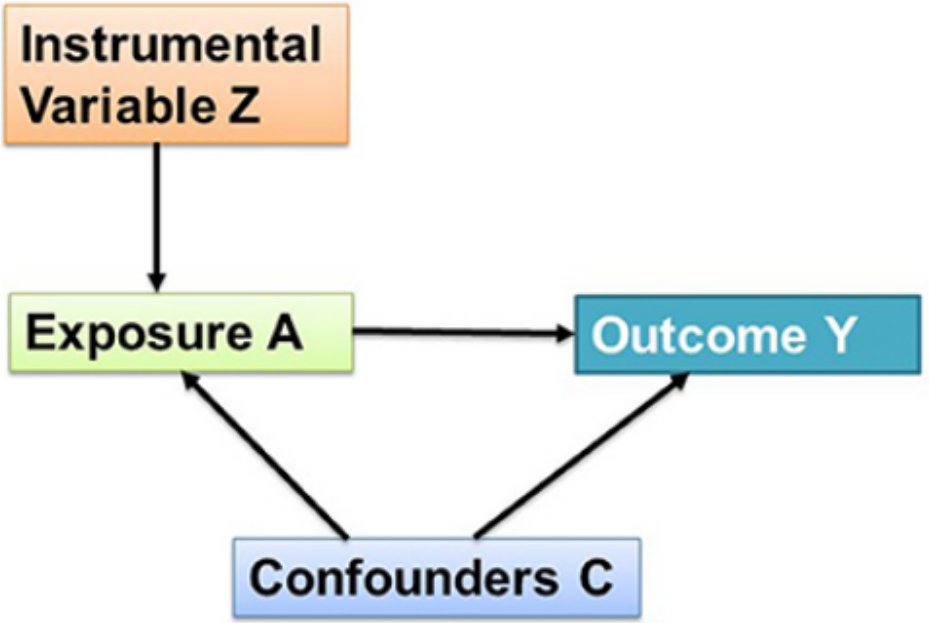

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- Try to find an IV whose effect on health is mediated through smoking $\rightarrow$ the tax rate for tobacco

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  lack of job $\rightarrow$ depression $\stackrel{?}{\rightarrow}$ smoking

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- Years of education $\stackrel{?}{\rightarrow}$ income

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  IV?
  Distance from home to a college/university $\rightarrow$ Years of education $\stackrel{?}{\rightarrow}$ income
  Any problem with the IV?

Instrumental variable: treatment effect estimates

Given IVs $\boldsymbol{Z}$,

- Stage 1: Regress each column of $\boldsymbol{X}$ on $\boldsymbol{Z}$; predict $\boldsymbol{X}$ by $\hat{\boldsymbol{X}}$ given $\boldsymbol{Z}$
- Stage 2: Regress $\boldsymbol{Y}$ on $\hat{\boldsymbol{X}}$
- The regression coefficients from stage 2 are the estimated effects

This method is only valid in linear models