Topics in Causal Inference

STAT41530

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Lecture 2

Topic: Potential outcome framework

- Observational Study
  - Observational studies conceptualized as conditional randomized experiments
  - Stratification
  - Matching
  - Sensitivity analysis (very basic ideas)

Some slides are borrowed from slides of Prof. Fan Li at Duke Uni.

Identify causal effects from observational data

- Association ≠ causation

$$\mathbb{E}\left[Y(a)\right] \neq \mathbb{E}\left[Y \mid A = a\right]$$

- Analyze observational data as if treatment has been randomly assigned conditional on measured covariates L: $Y(a) \perp A|\, L$ for all a (also called unconfoundedness)

Key point: conceptualize observational studies as conditional randomized experiments

Therefore "what randomized experiment are you trying to emulate?" is a key question for causal inference from observational data. For each causal effect that we wish to estimate using observational data, we can describe (i) the target trial that we would like to, but cannot, conduct, and (ii) how the observational data can be used to emulate that target trial.

Observational study V.S. conditional randomized experiments

1. Conditional randomized experiment: $Y(a) \perp A|\, L$ is a fact as we control treatment assignment mechanism

   Observational study: $Y(a) \perp A|\, L$ is an assumption. It is always possible that this assumption is violated.

2. Conditional randomized experiment: $P(A = a \mid L)$ is known

   Observational study: $P(A = a \mid L)$ needs to be estimated. Can introduce bias and suffer from estimation uncertainty

Evaluate identifiability assumptions carefully

- Consistency (read book Chapters 3.4 and 3.5)
  - Can any variable have a causal effect? Are there multiple versions of assignment?

    We need “sufficiently well-defined interventions”

    Example: effect of sex, heart transplant by different techniques
  - $Y(A) = Y$?
- Positivity (overlap)

  $P[A = a \mid L] > 0$ for all l where $P[L = l] > 0$ in the target population.
  - Guaranteed by the nature of experiments
  - Not guaranteed in observational studies
- L only contains pre-treatment covariates

Stratification

Under the Assumption $Y(a) \perp A | L$

- If L has K levels, divide the data into K strata based on L
  - Treat data within each strata as a completely randomized experiment
  - Estimating average treatment effect: $\hat{\tau} = \sum_k (\bar{Y}_{k,1} - \bar{Y}_{k,0}) \frac{n_k}{n}$
- If L is continuous, split L into K classes/blocks
- Select $K \geq 5$ to remove bias for continuous L (Cochran 1968)

Stratification based on L works well only when the dimension of L is small

Stratification v.s. Standardization

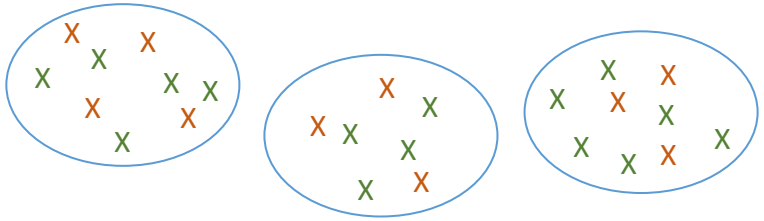
Standardization:

$$\mathbb{E}\left[Y(a)\right] = \mathbb{E}\left[\mathbb{E}\left[Y \mid L, A = a\right]\right]$$

- Estimate $\mathbb{E}\left[Y \mid L, A = a\right] = f_a(L)$
- Estimate $E[Y(a)]$ by $\frac{1}{n}\sum_i \hat{f}_a(L_i)$
- Standardization is also called the outcome regression approach

Stratification:

- Divide individuals into K blocks based on L
- Within each block, treat data as from a completely randomized experiment



Propensity score $e(L) = \mathbb{P}[A = 1 \mid L]$

positivity: $0 < e(L) < 1$

Property of propensity score
(Rosenbaum and Rubin, 1983)

$A \perp Y(a) \mid e(L)$ for all a

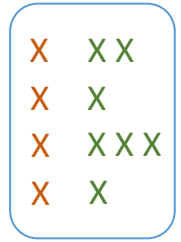
$$
\begin{aligned}
&\mathbb{P}[A = 1 \mid Y(a), e(L)] \\
=&\mathbb{E}[A \mid Y(a), e(L)] \\
=&\mathbb{E}[\mathbb{E}[A \mid Y(a), e(L), L] \mid Y(a), e(L)] \\
=&\mathbb{E}[\mathbb{E}[A \mid Y(a), L] \mid Y(a), e(L)] \\
=&\mathbb{E}[\mathbb{E}[A \mid L] \mid Y(a), e(L)] \quad \text{(conditional exchangeability)} \\
=&\mathbb{E}[e(L) \mid Y(a), e(L)] = e(L) = \mathbb{P}[A = 1 \mid e(L)]
\end{aligned}
$$

Stratification using propensity score

- Make use of the conditional exchangeability $Y(a) \perp A | e(L)$
- Adjusting for differences in $e(L)$ removes all biases associated with differences in L
- $e(L)$ reviewed as summary score of the confounder effects

- Divided individuals into K blocks by the corresponding quantiles of the estimated propensity scores

Matching



- For each treated unit, find the closest control unit(s) where the distance can be based on $\hat{e}(L)$ or L
- Can also do this for each controlled unit, typically # of control > # of treated
- Within each matched pair, treat assignment of the units as from a completely randomized experiment
- As we have a matched pair for each treated unit, we are estimated average causa effect on treated

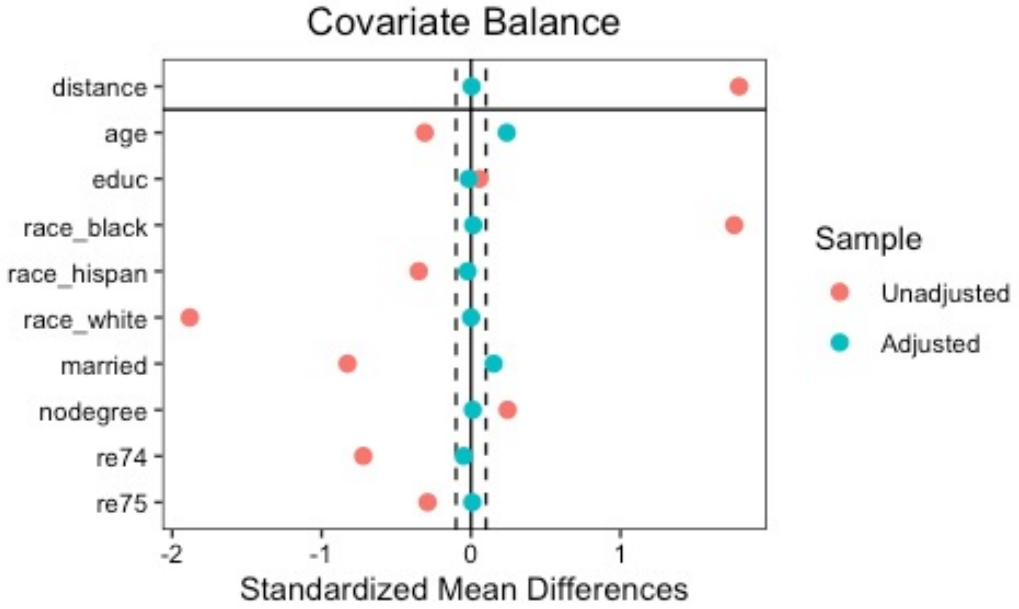
$$E[Y(a) \mid A = 1]$$

Covariate balancing

Covariate balance
$A \perp L \mid e(L)$

$$
\begin{aligned}
&\mathbb{P}\left[A = 1 \mid e(L)\right] \\
=&\mathbb{E}\left[\mathbb{E}\left[A \mid e(L), L\right] \mid e(L)\right] \\
=&\mathbb{E}\left[\mathbb{E}\left[A \mid L\right] \mid e(L)\right] = e(L) = \mathbb{P}\left[A = 1 \mid e(L), L\right]
\end{aligned}
$$

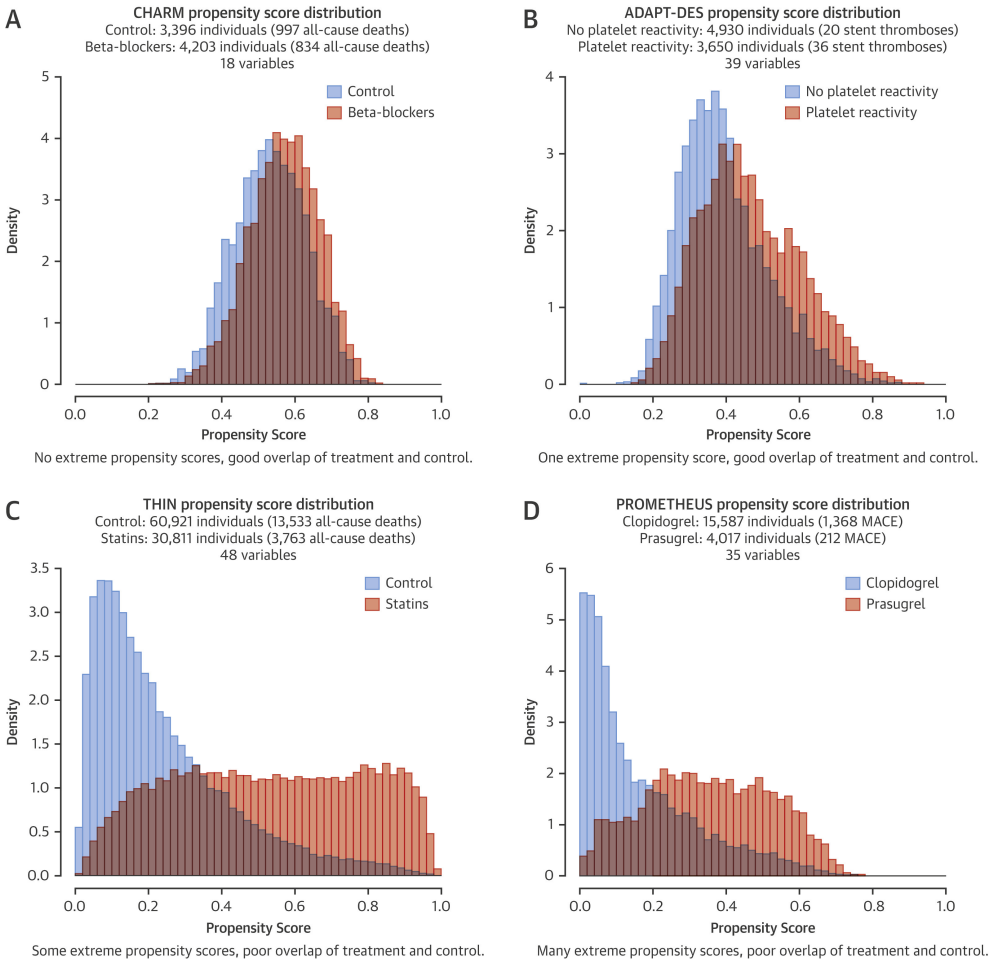
- After matching, the distribution of L is the same (balanced) for A = 0 and A = 1
- We can check covariates balancing to see if $e(L)$ is properly estimated



An illustration
https://cran.r-project.org/web/packages/cobalt/vignettes/cobalt.html

Check for positivity / overlap

- $0 < P[A = 1 \mid L] = e(L) < 1$ is a checkable assumption



Elze, Markus C., et al. "Comparison of propensity score methods and covariate adjustment: evaluation in 4 cardiovascular studies." *Journal of the American College of Cardiology* 69.3 (2017): 345-357.

Evaluate the conditional exchangeability assumption

Are there any unmeasured confounding?

Negative control treatments

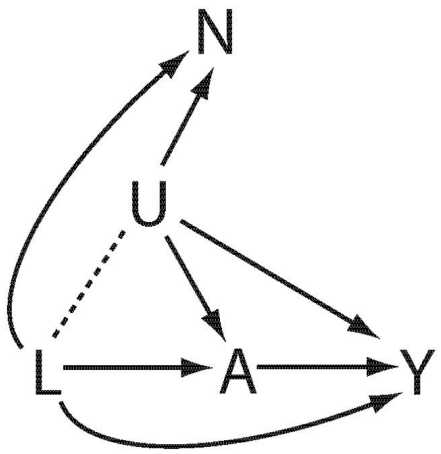
- Suppose we have three treatment levels: $a = -1, 0, 1$ (ineligibles, eligible nonparticipants, participants).
- Negative control treatment: know a priori: $Y_i(-1) = Y_i(0)$
- A testable hypothesis: $Y_i(0) \perp 1_{A_i=0} \mid L_i, A_i \in \{-1, 0\}$
- Whether this test has much bearing on the conditional exchangeability assumption depends on whether the extension of the assumption is plausible

Evaluate the conditional exchangeability assumption

Are there any unmeasured confounding?

Negative control outcome

- The idea: the negative control outcome is also affected by the same set of confounding, but given it is observed before the treatment, it is unaffected by the treatment

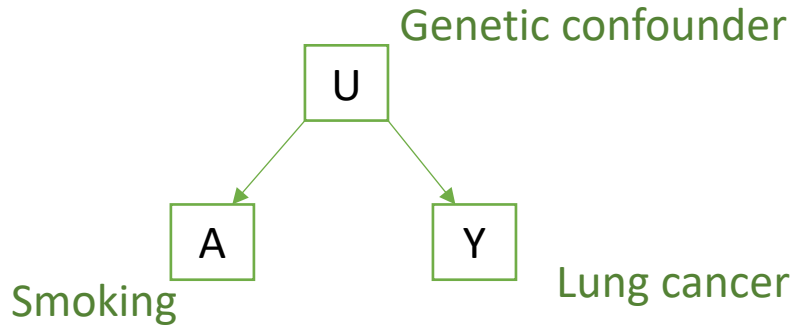


Lipsitch, M., Tchetgen, E. T., & Cohen, T. (2010). Negative controls: a tool for detecting confounding and bias in observational studies. *Epidemiology (Cambridge, Mass.)*, *21*(3), 383.

When conditional exchangeability may not hold

- Use other approaches
  - Instrumental variables (IV)
  - Front door criterion
  - Adjust by negative controls
- Sensitivity analysis

Sensitivity Analysis



A motivating example (Cornfield et al. 1959 JNCI)

- Fisher argued the association between smoking and lung cancer may be due to a common gene that causes both
- Cornfield showed that if Fisher is right, we have $RR_{AU} \geq RR_{AY} \approx 9$
- Such a genetic confounder is too strong to be realistic
- Thus, smoking should have a causal effect on lung cancer

$$p_1 = \mathbb{P}[U = 1 \mid A = 1], \quad p_2 = \mathbb{P}[U = 1 \mid A = 0]$$

$$\mathbb{P}[Y = 1 \mid A = 1, U = 1] = \mathbb{P}[Y = 1 \mid A = 0, U = 1] = r_1$$

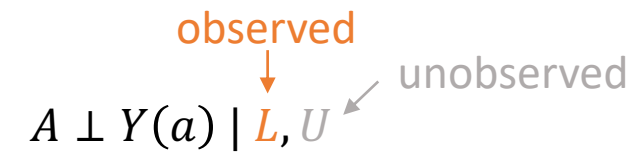
$$\mathbb{P}[Y = 1 \mid A = 1, U = 0] = \mathbb{P}[Y = 1 \mid A = 0, U = 0] = r_2$$

$$\text{We assume } p_1 \geq p_2, r_1 \geq r_2$$

$$\text{Then } RR_{AY} = \frac{\mathbb{P}[Y = 1 \mid A = 1]}{\mathbb{P}[Y = 1 \mid A = 0]} = \frac{p_1 r_1 + (1 - p_1) r_2}{p_2 r_1 + (1 - p_2) r_2} \leq \frac{p_1}{p_2} = RR_{AU}$$

Sensitivity Analysis

Idea:



- How sensitive is our estimate of causal effect to the presence of U ?

A model-based approach (Rosenbaum and Rubin, 1983 JRSS-B)

Assume that

$$U \sim \text{Bernoulli}(\pi)$$

$$\text{logit}\mathbb{P}\left[A = 1 \mid U, L\right] = r + \kappa L + \alpha U$$

$$\text{logit}\mathbb{P}\left[Y(a) = 1 \mid U, L\right] = \beta_a + \delta_a L + b_a U$$

Sensitivity parameters: $(\pi, \alpha, \delta_0, \delta_1)$

Set the sensitivity parameters to different values and see how estimates of causal effects change

Sensitivity Analysis

A more general approach (Rosenbaum book 2002)

Define $\pi_j = e(L_j, U_j)$. For a given Γ, assume

$$\frac{1}{\Gamma} \leq \frac{\pi_j(1-\pi_k)}{\pi_k(1-\pi_j)} \leq \Gamma \text{ for all } j,k \text{ with } L_j = L_k$$

Then we assess how the inference on causal effect change within the set for different Γ