Course Notes: A Crash Course on Causality – Week 3: Matching and Propensity Scores

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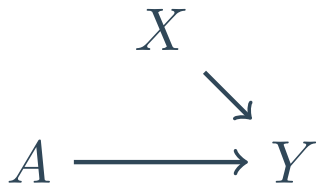
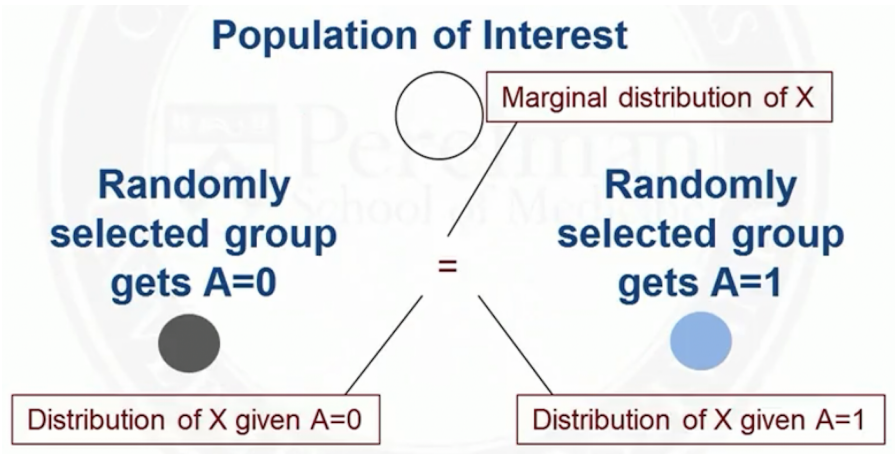
Randomized trials



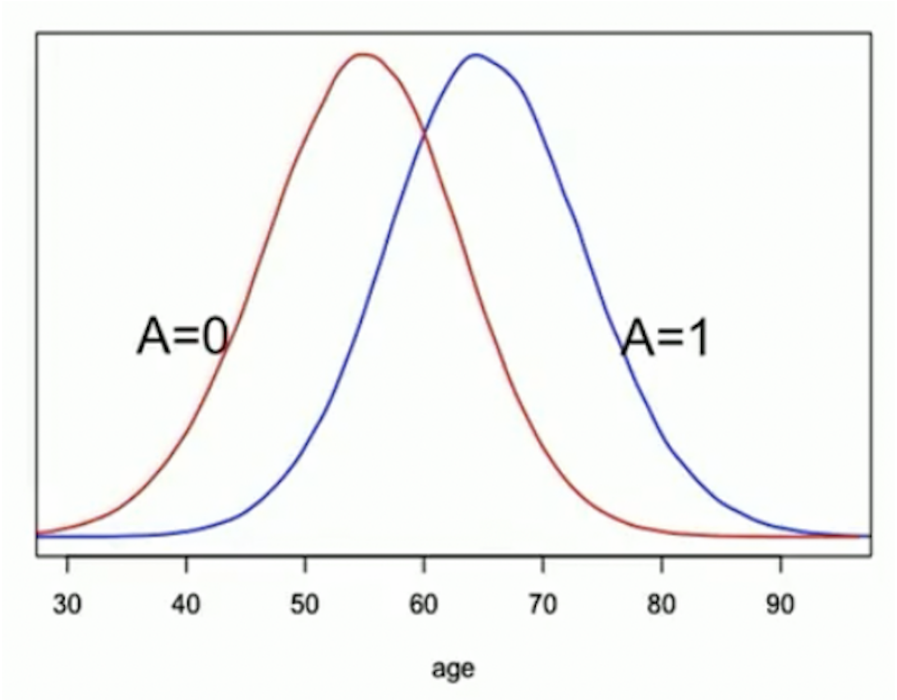
- In experiments, treatment A is determined by a coin toss; so there are no arrows from X to A, i.e., no backdoor paths
- Covariate balance: distribution of pre-treatment variables X are the same in both treatment groups



- Hence, if there is difference in the outcome, it is not because of X

Observational studies

- In observational studies, the distribution of X may differ between treatment groups
- For example, older people may be more likely to get treatment $A = 1$:



Matching

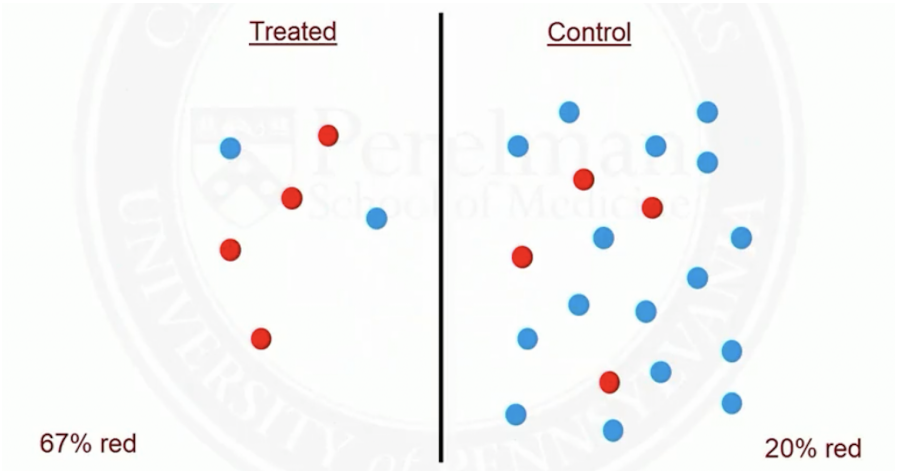
- Matching: a method that attempts to make an observational study more like a randomized trial
- **Main idea of matching**: match individuals in the treated group $(A = 1)$ to individuals in the control group $(A = 0)$ on the covariates X
  - Usually, the sample size of the treated group is smaller than the control group, so after matching, we will use all cases in the treated group, but only a fraction of the cases in the control group
- In the example where older people are more likely to get $A = 1$
  - At younger (older) ages, there are more people with $A = 0$ ($A = 1$)
  - In a randomized trial, for any particular age, there should be about the same number of treated and untreated people
  - This balance can be achieved by matching treated people to control people of the same age

Advantages of matching

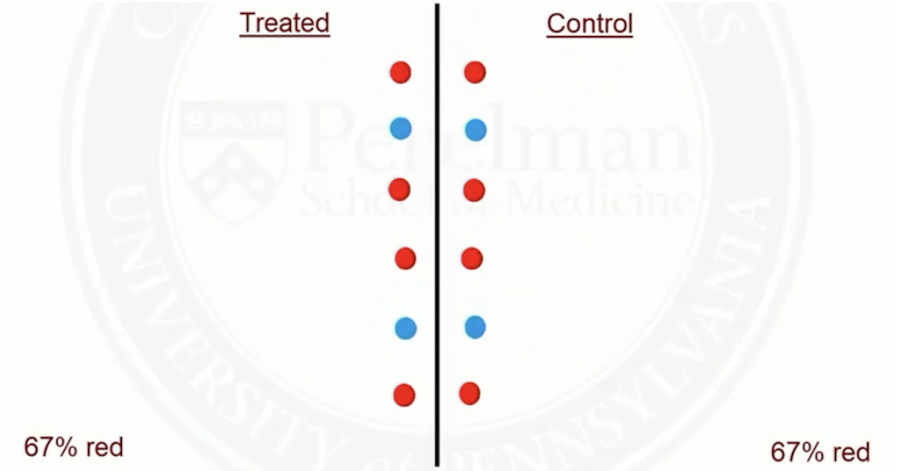
- Controlling for confounders is achieved at the design phase, i.e., without looking at the outcome
- Matching will reveal lack of overlap in covariate distribution
  - Positivity assumption will hold in the population that can be matched
- We can treated a matched dataset as if from a randomized trial
- Outcome analysis is simple

Match on a single covariate

- Suppose red patients are more likely to be treated than blue ones
- Before matching



- After matching

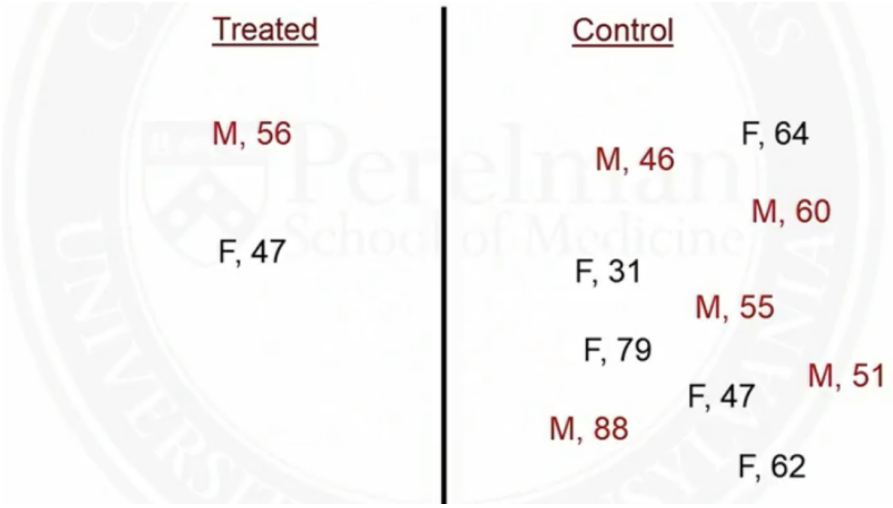


Match on many covariates

- We will not be able to exactly match on the full set of covariates
- In randomized trials, treated and control subjects are not perfect matches either; the distribution of covariates is balanced between groups (stochastic balance)
- Matching closely on covariates can achieve stochastic balance

Example of matching on two covariates: sex and age

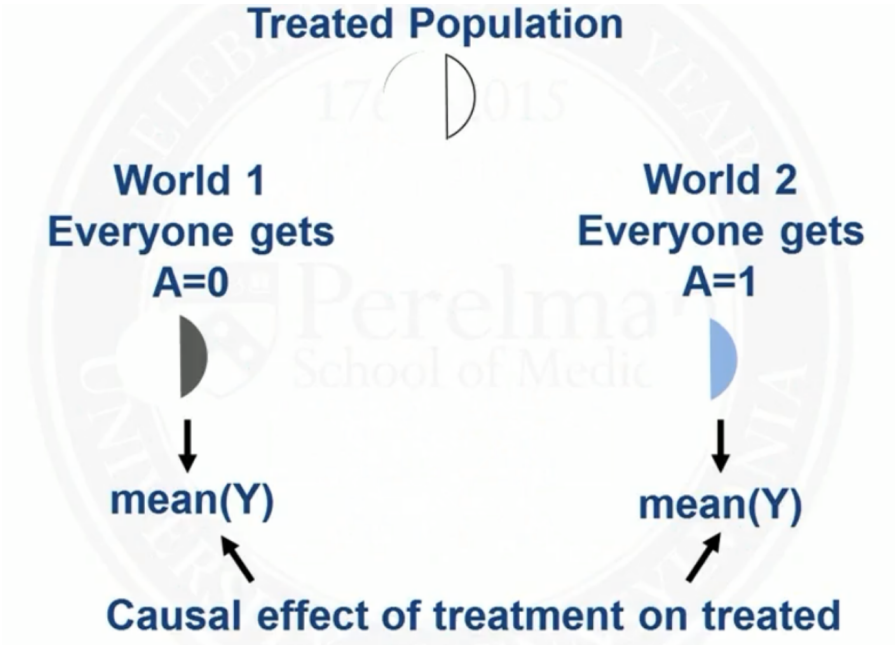
- Before matching



- After matching

Target population of matching: the treated

- By matching, we are making the distribution of covariates in the control population look like that in the treated population
- So we will analysis causal effect of treatment on the treated



- There are matching methods that can be used to target a different population (beyond scope of this course)

Fine balance

- Sometimes it is hard to find great matches, so we are willing to accept some non-ideal matches, **if treated and control groups have the same distribution of covariates (fine balance)**
- For the matches below, average age and percent female are the same in both groups, although neither match is great
  - Match 1: treated, male, age 40 and control, female, age 45
  - Match 2: treated, female, age 45 and control, male, age 40

Number of matches

- One to one (pair matching): match one control to every treated subject
- Many to one: match K (a fixed number) controls to every treated subject; e.g., 5 to 1 matching
- Variable: sometime match 1, sometimes more than 1 (if multiple good matches available), control to treated subjects

Metrics used in matching

- Mahalanobis distance between two vectors:

$$D(\mathbf{X}_i, \mathbf{X}_j) = \sqrt{(\mathbf{X}_i - \mathbf{X}_j)^T \mathbf{S}^{-1} (\mathbf{X}_i - \mathbf{X}_j)}, \quad \mathbf{S} = cov(\mathbf{X})$$

  - We use covariance to scale so that the M distance is invariant of unit change

Treated			Control			
Age	COPD	Female	Age	COPD	Female	**Distance**
78.17	0	1	70.25	1	0	4.23
			75.33	0	1	0.17
			86.08	1	1	3.72
			54.97	0	0	2.45
			43.63	0	0	2.89
			18.04	0	1	3.60

- Robust Mahalanobis distance: robust to outliers
  - Replace each covariate value with its rank
  - Constant diagonal on covariance matrix
  - Calculate the usual M distance on the ranks

Types of matching

- Greedy (nearest neighbor) matching
  - Not ideal, but computationally fast
- Optimal matching
  - Better, but computationally demanding

Setup

- We have selected a set of pre-treatment covariates X that satisfy the ignorability assumption
- We have calculated a distance $d_{i,j}$ between each treated subject i and each control subject j
- We have more control subjects than the treated subjects
- We will focus on pair matching (one-to-one)

Nearest neighbor matching (greedy)

1. Randomly order list of treated subjects and control subjects
2. Start with the first treated subject, match to the control with the smallest distance
3. Remove the matched control from the list of available matches
4. Move on to the next treated subject. Repeat until all treated subjects are matched

- Not invariant to order initial order of list
- Not optimal: always taking the smallest distance match does not minimize total distance
- R package: MatchIt, https://cran.r-project.org/web/packages/MatchIt/MatchIt.pdf

Many-to-one matching

- For K:1 matching: after everyone has 1 match, go through the list again and find 2nd matches. Repeat until K matches
- Pair matching (one-to-one) vs many-to-one matching: a bias-variance tradeoff
  - Pair matching: closer matches, faster computing time
  - Many-to-one matching: larger sample size

Caliper

- We may exclude a treated subject if there is no good matches for it
- Caliper: maximum acceptable distance
  - Only match a treated subject if the best match has distance less than the caliper
- If no matches within caliper, it is a sign of violation of the positivity assumption. So we should exclude these subjects
- Drawback: population harder to define

Optimal matching

- Optimal matching: minimized global distance measure, e.g., total distance
- Computational feasibility of optimal matching: depends on the size of the problem
  - Number of treatment-control pairing: product of number of treatment and number of control
  - 1 million treatment-control pairings is feasible on most computers (not quick, though)
  - 1 billion pairings is not feasible
- R packages: optmatch, rcbalance

Assessing matching balance

- Check covariate balance: compute standardized difference to see if each covariate has similar means between treatment and control

$$smd = \frac{\bar{X}_{\text{treatment}} - \bar{X}_{\text{control}}}{\sqrt{\frac{s^2_{\text{treatment}} + s^2_{\text{control}}}{2}}}$$

  - Does not depend on sample size
  - Often, absolute value of smd is reported
  - We calculate smd for each variable we match on
  - This analysis does not involve the outcome variable

- Rule of thumb:
  - $|smd| < 0.1$: adequate balance
  - $|smd| \in [0.1, 0.2]$: not too alarming
  - $|smd| > 0.2$: serious imbalance

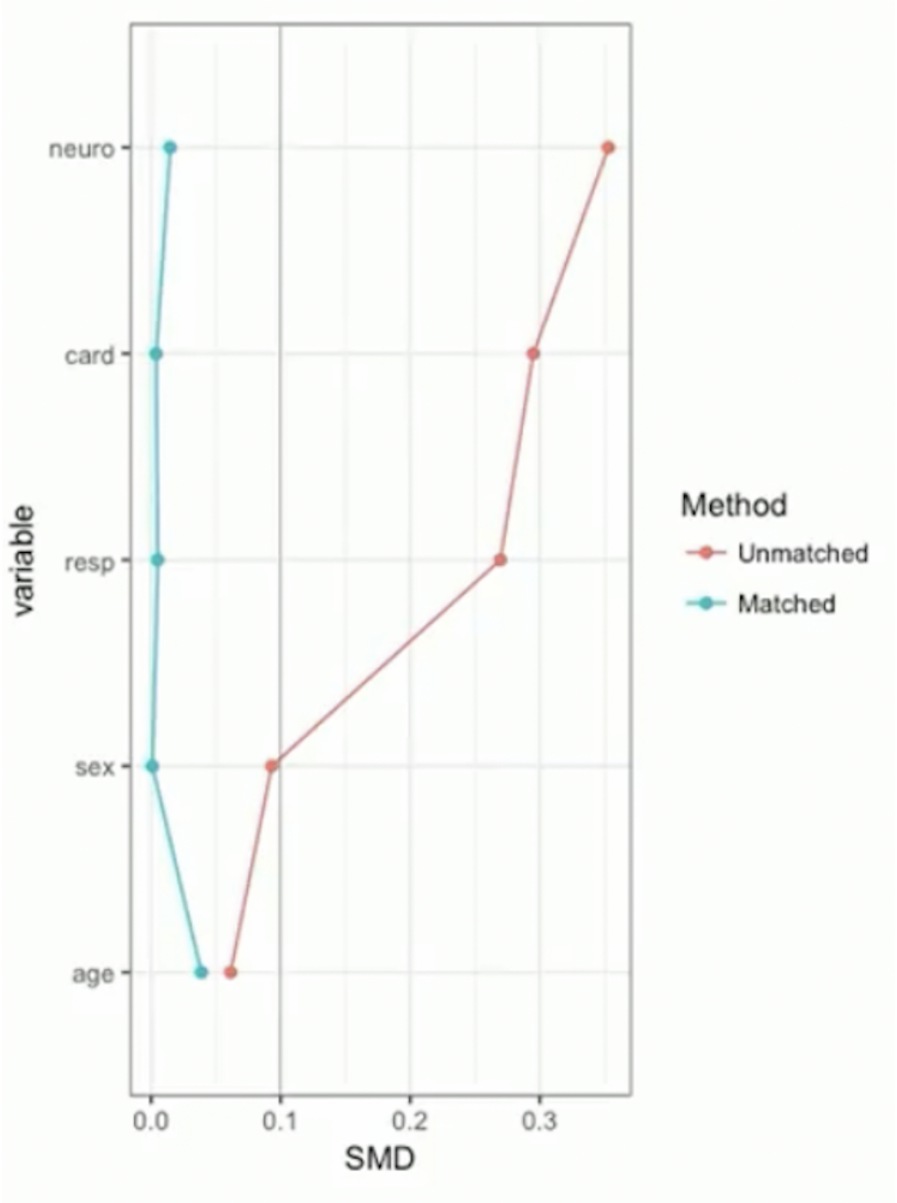
Example: right heat characterization (RHC) data

- Table 1: compares pre-matching and post-matching balance

	Unmatched			Matched		
	No RHC	**RHC**	**SMD**	**No RHC**	**RHC**	**SMD**
n	3551	2184		2082	2082	
age (mean (sd))	61.8 (17.3)	60.8 (15.6)	0.06	61.6 (16.7)	61.0 (15.8)	0.039
sex = Male (%)	53.9	58.5	0.09	56.9	56.9	0.001
resp = Yes (%)	41.7	28.9	0.27	30.6	30.4	0.005
card = Yes (%)	28.4	42.3	0.30	39.3	39.5	0.004
neuro = Yes (%)	16.2	5.4	0.35	5.3	5.7	0.015

Example continued: RHC data

- SMD plot: visualizes Table 1



After matching, proceed with outcome analysis

- Test for a treatment effect
- Estimate a treatment effect and confidence interval
- Methods should take matching into account

Randomization test

- Also known as permutation tests or exact tests
- Main ideas of randomization test
  - Compute test statistic from observed data, assuming null hypothesis of no treatment effect is true
  - Randomly **permute treatment assignment** within pairs and recompute test statistic
  - Repeat many times and see how unusual observed statistic is

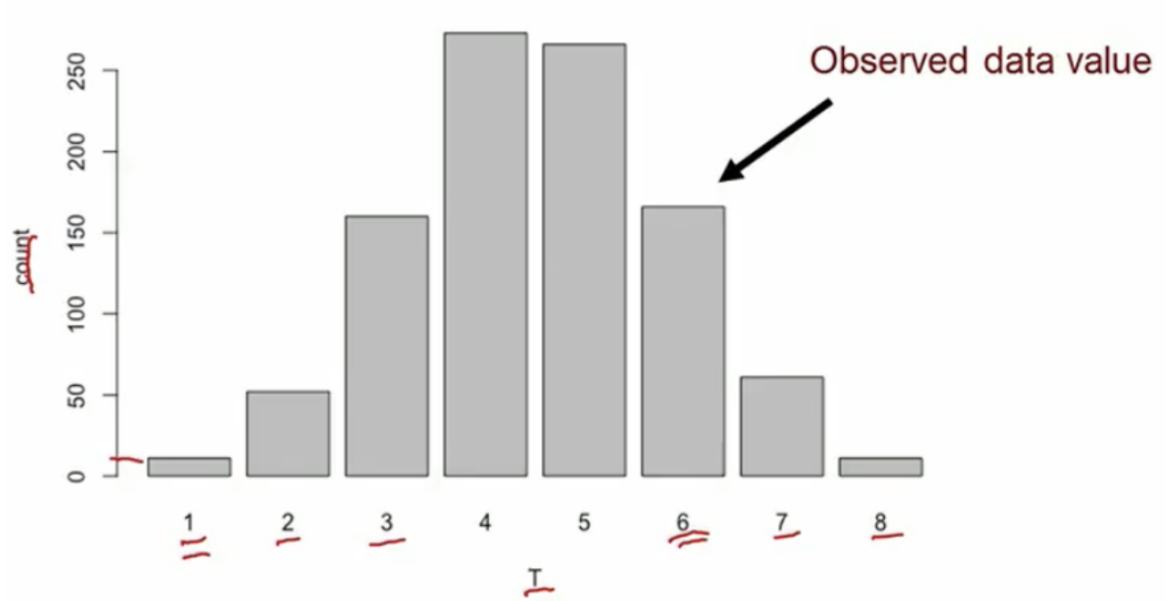
A binary outcome example

- Test statistic: the total number of events in the treated group
  - Test stat $T = 6$ in the observed data

Matched pair	Treated	Control
1	0	0
2	1	0
3	1	0
4	0	0
5	1	1
6	0	0
7	0	1
8	0	1
9	0	0
10	1	0
11	0	0
12	1	0
13	1	0

- In the observed data, discordant pairs (in red) are the only ones can change during treatment permutation

Permutation test for binary outcome: equivalent to a NcNemar test



		Control	
		Outcome	
	Outcome	1	0
Treatment	1	1	5
	0	2	5

```
> ex<-matrix(c(1,5,2,5),2,2)
> mcnemar.test(ex)

        McNemar's Chi-squared test with continuity correction

data:  ex
McNemar's chi-squared = 0.57143, df = 1, p-value = 0.4497
```

NcNemar test: whether row and column marginal frequencies are the same, for paired binary data

- Paired binary data, represented in a 2 by 2 contingency table

	Test 2 positive	Test 2 negative	Row total
Test 1 positive	a	b	$a+b$
Test 1 negative	c	d	$c+d$
Column total	$a+c$	$b+d$	N

- Hypotheses: whether $p_a + p_b = p_a + p_c$, or equivalently,

$$H_0 : p_b = p_c, \quad H_1 : p_b \neq p_c$$

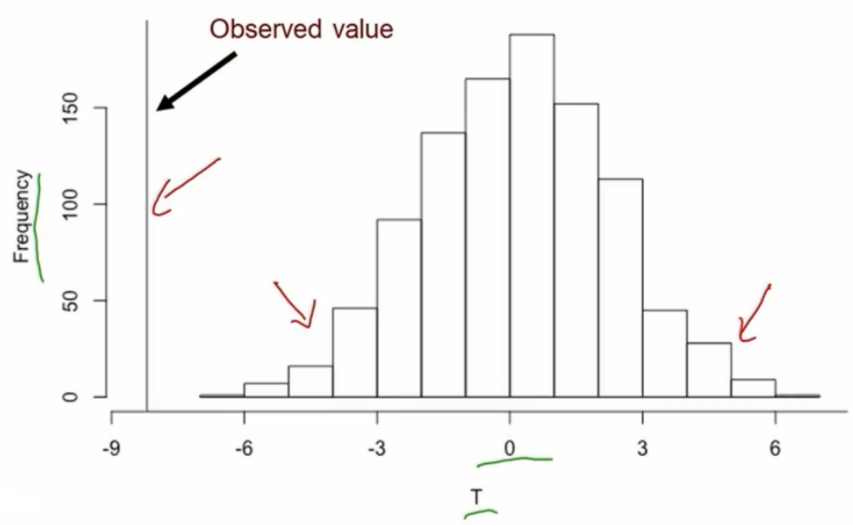
- Test statistic

$$\frac{(b-c)^2}{b+c} \underset{\sim}{\text{ under } H_0} \chi^2_{df=1}$$

- Source: https://en.wikipedia.org/wiki/McNemar%27s_test

Permutation test for continuous outcome: equivalent to a paired t-test

- Test statistic: difference in sample means




```
> t.test(txsbp,consbp,paired=TRUE)

        Paired t-test

data:  txsbp and consbp
t = -6.7416, df = 19, p-value = 1.928e-06
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -10.749497  -5.656137
sample estimates:
mean of the differences
              -8.202817
```

Other outcome models

- Conditional logistic regression
  - Matched binary outcome data
- Generalized estimating equations (GEE)
  - Match ID variable used to specify clusters
  - For binary outcomes, can estimate a causal risk difference, causal risk ratio, or causal odds ratio (depending on link function)

Propensity score

- Propensity score: probability of receiving treatment, given covariates X

$$\pi_i = P(A_i = 1 \mid X_i)$$

- Propensity score is a balancing score

$$P(X = x \mid \pi(X) = p, A = 1) = P(X = x \mid \pi(X) = p, A = 0)$$

  - Suppose two subjects have the same value of propensity score, but different covariate values X
  - This means that both subjects' X is just as likely to be found in the treatment group
  - So if we restrict to a subpopulation of subjects who have the same value of the propensity score, there should be balance in the treatment vs control groups

- We can match on propensity score to achieve balance

Logistic regression to estimate propensity score

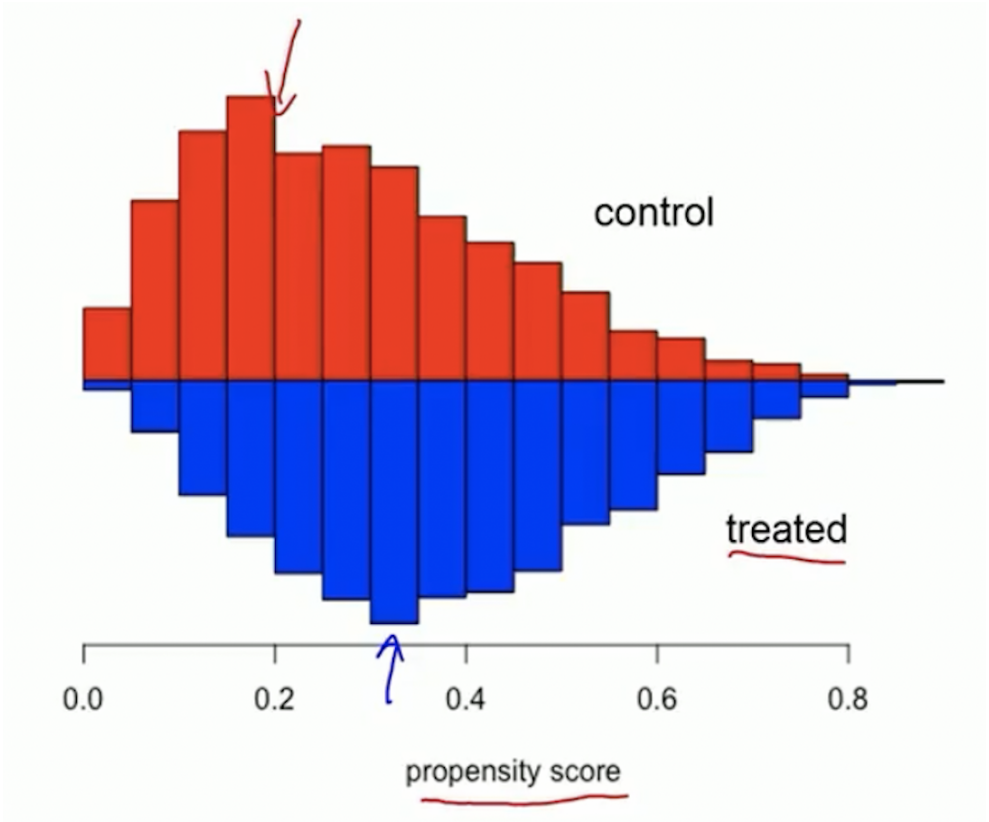
- In a randomized trial, the propensity score is known

$$P(A = 1 \mid X) = P(A = 0 \mid X) = 0.5$$

- In an observational study, we need to estimate the propensity score $P(A = 1 \mid X)$
  1. Fit a logistic regression: outcome A, covariates X
  2. Get the predicted probability (fitted value) for each subject as the estimated propensity score

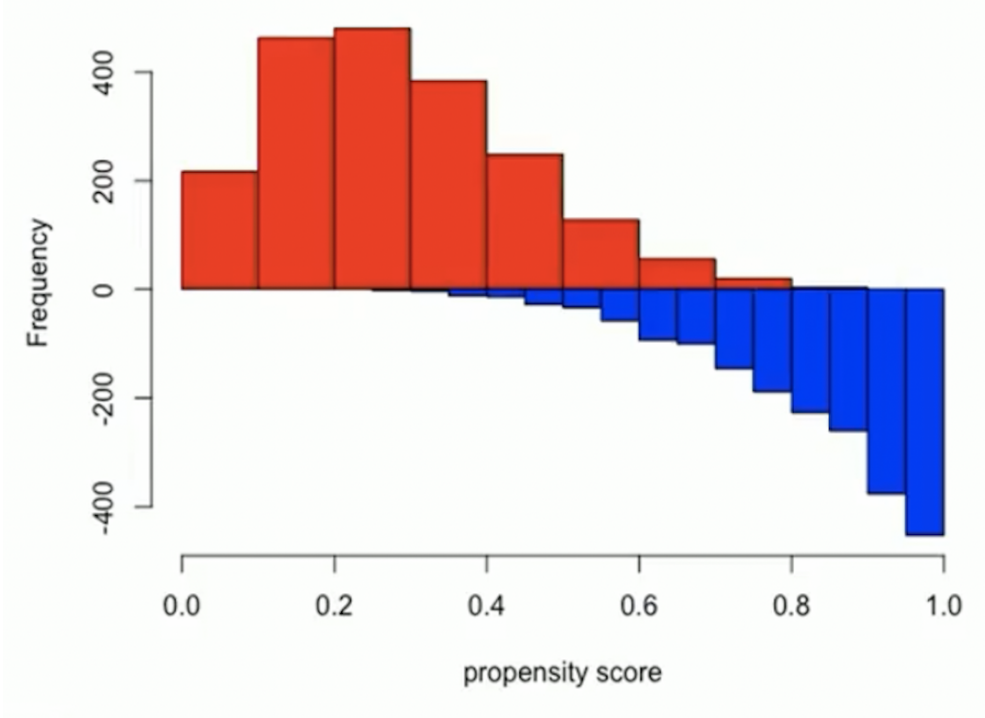
Before propensity score matching: check for overlap

- Propensity score matching is simple; it's matching on one variable
- After the propensity is estimated, but before matching, it is useful to look for overlap
  - This is to check positivity assumption
- Example of good overlap



Trim tails if there is a lack of overlap

- Example of bad overlap



- Trim tails: remove subjects who have extreme values of propensity score
  - Remove control subjects whose propensity score is less than the minimum in the treatment group
  - Remove treated subjects whose propensity score is greater than the maximum in the control group

Propensity score matching

- Compute a distrance between the propensity score for each treated subject with every control
- Use nearest neighbor or optimal matching
- In practice, logit of the propensity score is often used, rather than the propensity score itself
- A caliper can be used to avoid bad matches
- After matching: outcome analysis
  - Randomization tests
  - Conditional logistic regression, GEE, etc

References

- Coursera class: “A Crash Course on Causality: Inferring Causal Effects from Observational Data”, by Jason A. Roy (University of Pennsylvania)
  - https://www.coursera.org/learn/crash-course-in-causality