Machine Learning for Healthcare
HST.956, 6.S897

Lecture 15: Causal Inference Part 2

David Sontag

Acknowledgement: adapted from slides by Uri Shalit (Technion)

Reminder: Potential Outcomes

- Each unit (individual) x_i has two potential outcomes:
  - $Y_0(x_i)$ is the potential outcome had the unit not been treated: "***control outcome***"
  - $Y_1(x_i)$ is the potential outcome had the unit been treated: "***treated outcome***"

- Conditional average treatment effect for unit i:
  $CATE(x_i) = \mathbb{E}_{Y_1 \sim p(Y_1|x_i)}[Y_1|x_i] - \mathbb{E}_{Y_0 \sim p(Y_0|x_i)}[Y_0|x_i]$
- Average Treatment Effect:
$$ATE = \mathbb{E}_{x \sim p(x)}[CATE(x)]$$

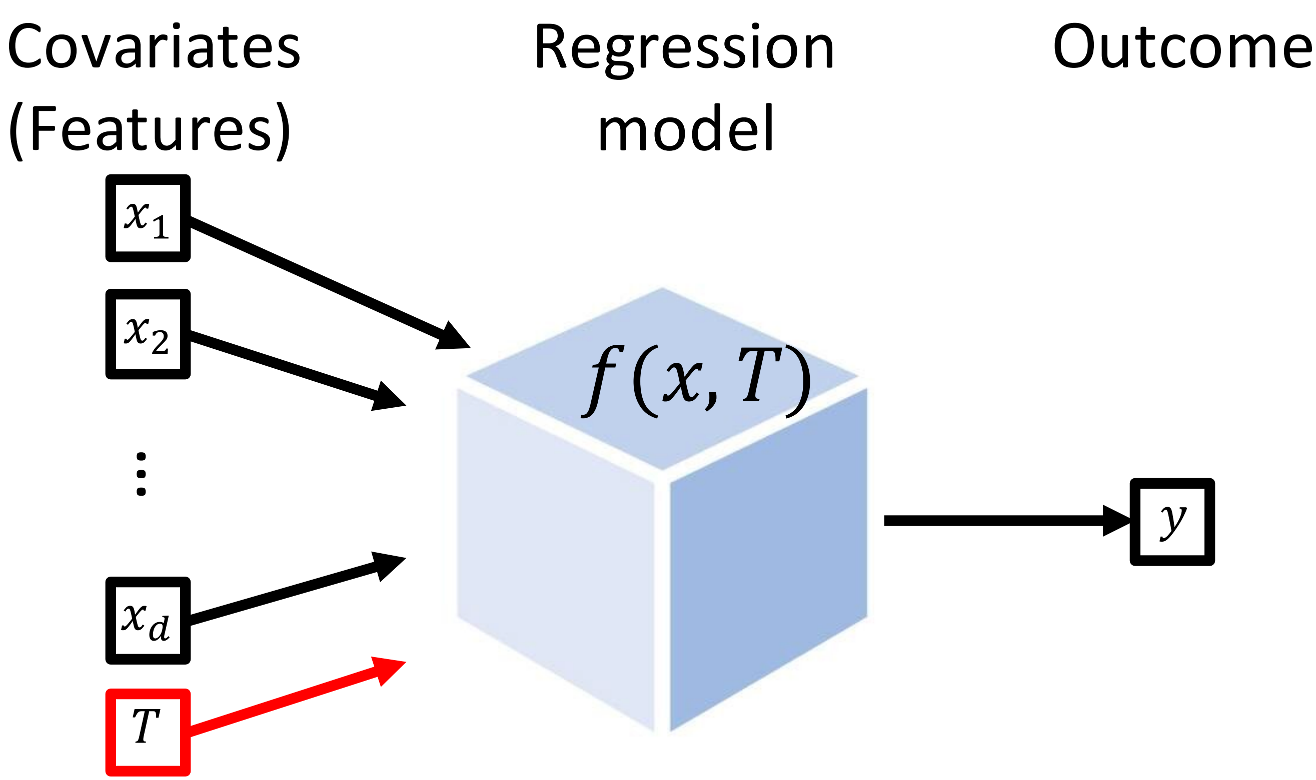
Two common approaches for counterfactual inference

Covariate adjustment

Propensity scores

Covariate adjustment (reminder)

Explicitly model the relationship between treatment, confounders, and outcome:



Covariate adjustment (reminder)

- Under ignorability,
  $CATE(x)$ =
  $\mathbb{E}_{x\sim p(x)}\Big[\,\mathbb{E}[Y_1|T=1,x]-\mathbb{E}[Y_0|T=0,x]\Big]$

- Fit a model $f(x,t)\approx\mathbb{E}[Y_t|T=t,x]$, then:
  $\widehat{CATE}(x_i)=f(x_i,1)-f(x_i,0)$.

Covariate adjustment with linear models

- Assume that:

Blood pressure **age** **medication**

$$Y_t(x) = \beta x + \gamma \cdot t + \epsilon_t$$
$$\mathbb{E}[\epsilon_t] = 0$$

- Then:

$$CATE(x) := \mathbb{E}[Y_1(x) - Y_0(x)] =$$

Covariate adjustment with linear models

- Assume that:

Blood pressure **age** **medication**

$$Y_t(x) = \beta x + \gamma \cdot t + \epsilon_t$$
$$\mathbb{E}[\epsilon_t] = 0$$

- Then:

$$CATE(x) := \mathbb{E}[Y_1(x) - Y_0(x)] =$$
$$\mathbb{E}[(\cancel{\beta x} + \gamma + \epsilon_1) - (\cancel{\beta x} + \epsilon_0)] = \gamma$$

$$\boxed{ATE := \mathbb{E}_{p(x)}[CATE(x)] = \gamma}$$

Covariate adjustment with linear models

- Assume that:

Blood pressure age medication

$$Y_t(x) = \beta x + \gamma \cdot t + \epsilon_t$$
$$\mathbb{E}[\epsilon_t] = 0$$

$$\boxed{ATE := \mathbb{E}_{p(x)}[CATE(x)] = \gamma}$$

- For causal inference, need to estimate γ well, not $Y_t(x)$ - **Identification, not prediction**
- *Major difference between ML and statistics*

What happens if true model is not linear?

- True data generating process, $x \in \mathbb{R}$:

$$Y_t(x) = \beta x + \gamma \cdot t + \delta \cdot x^2$$
$$ATE = \mathbb{E}[Y_1 - Y_0] = \gamma$$

- Hypothesized model:

$$\widehat{Y_t}(x) = \hat{\beta} x + \hat{\gamma} \cdot t$$

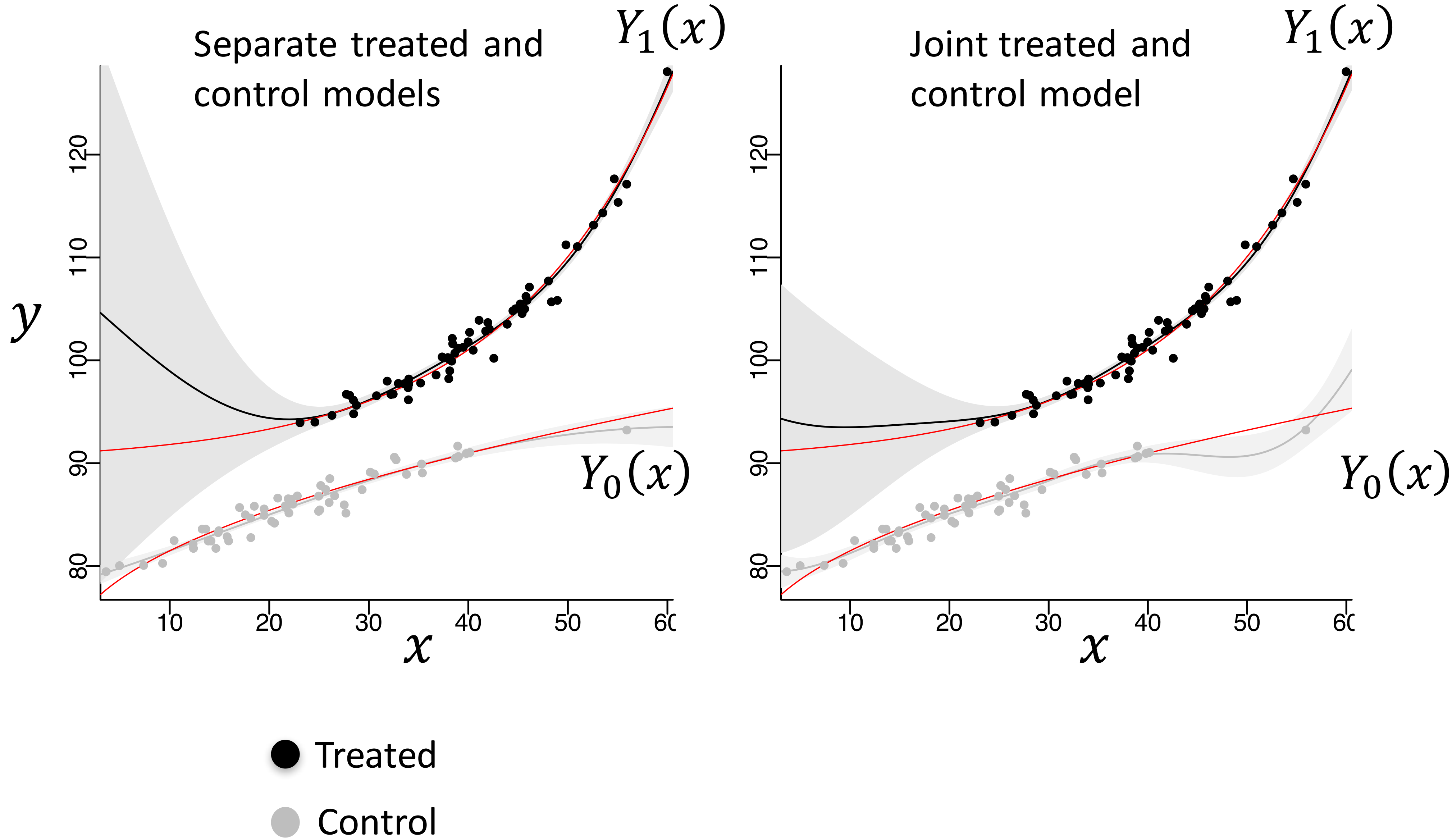
$$\hat{\gamma} = \gamma + \delta \frac{\mathbb{E}[xt]\mathbb{E}[x^2] - \mathbb{E}[t^2]\mathbb{E}[x^2 t]}{\mathbb{E}[xt]^2 - \mathbb{E}[x^2]\mathbb{E}[t^2]}$$

Depending on δ, can be made to be arbitrarily large or small!

Covariate adjustment with non-linear models

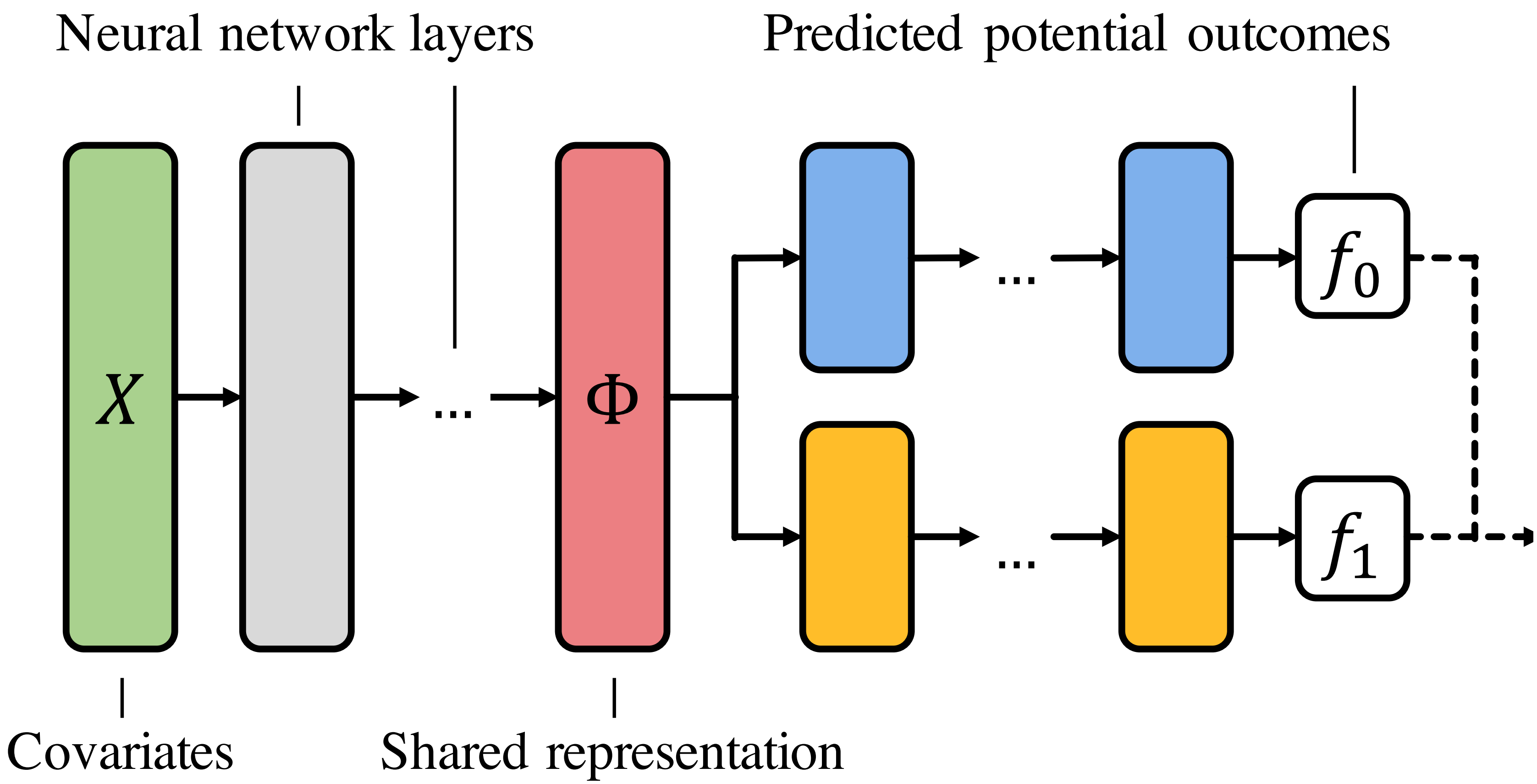
- Random forests and Bayesian trees
  Hill (2011), Athey & Imbens (2015), Wager & Athey (2015)
- Gaussian processes
  Hoyer et al. (2009), Zigler et al. (2012)
- Neural networks
  Beck et al. (2000), Johansson et al. (2016), Shalit et al. (2016), Lopez-Paz et al. (2016)

Example: Gaussian processes



Figures: Vincent Dorie & Jennifer Hill

Example: Neural networks



Shalit, Johansson, Sontag. *Estimating Individual Treatment Effect: Generalization Bounds and Algorithms*. ICML, 2017

Matching

- Find each unit’s long-lost counterfactual identical twin, check up on his outcome

Matching

- Find each unit's long-lost counterfactual identical twin, check up on his outcome

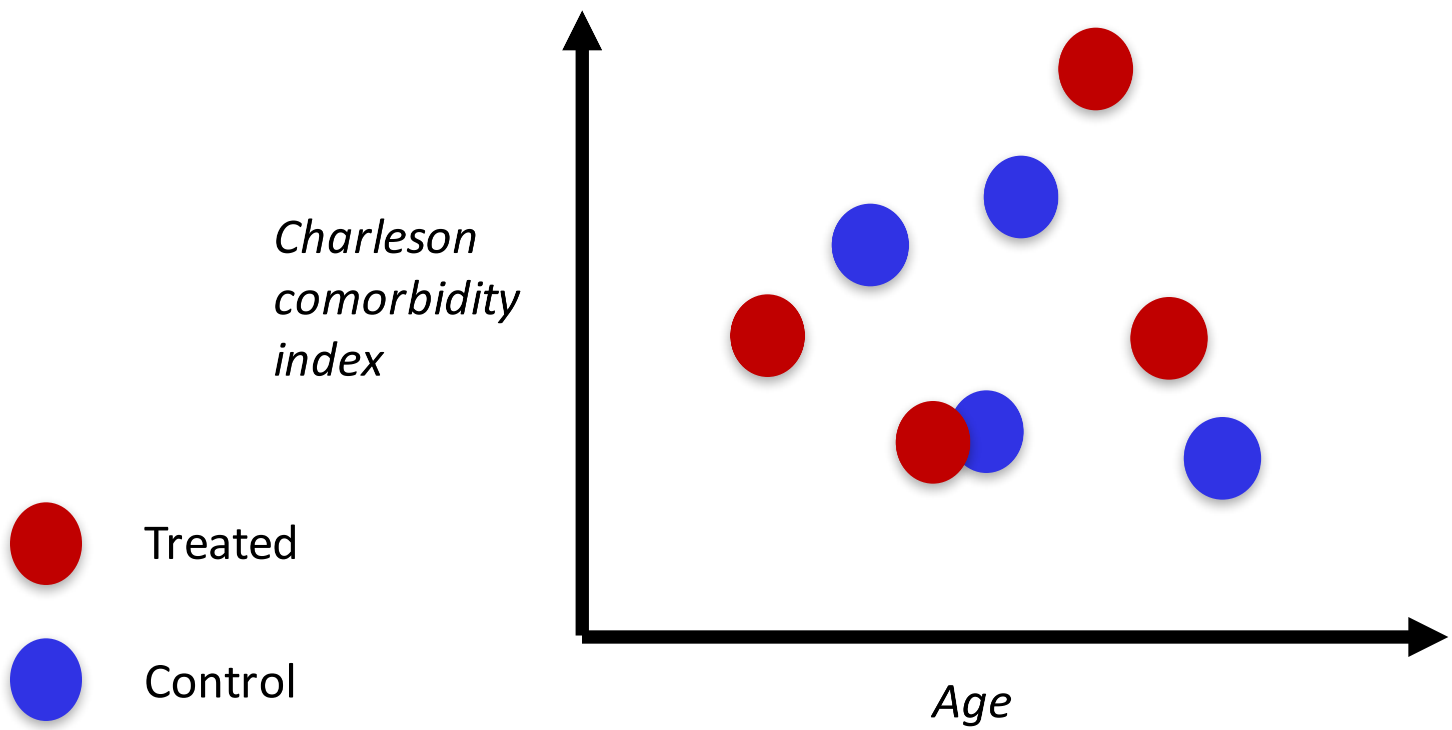
Obama, had he gone to law school

Obama, had he gone to business school

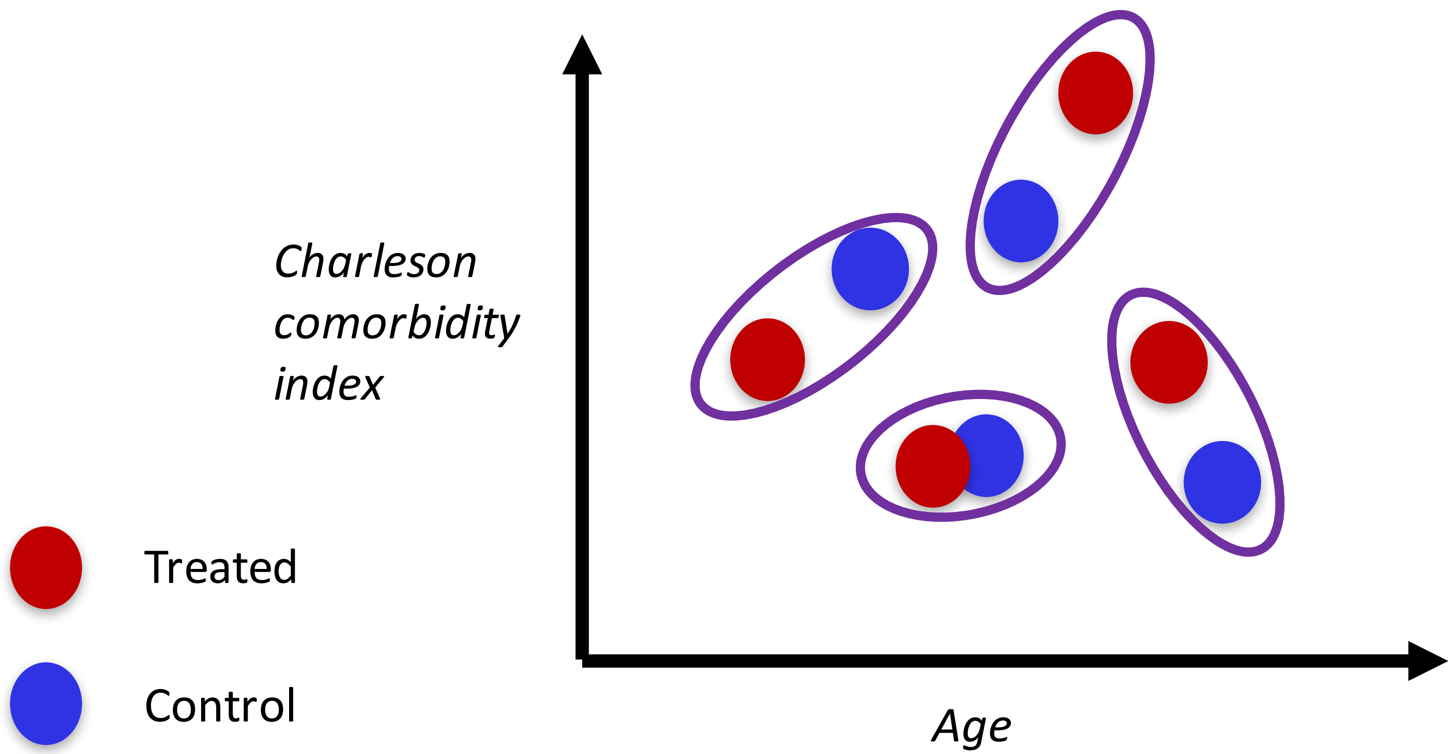
Matching

- Find each unit’s long-lost counterfactual identical twin, check up on his outcome
- Used for estimating both ATE and CATE

Match to nearest neighbor from opposite group



Match to nearest neighbor from opposite group



1-NN Matching

- Let $d(\cdot,\cdot)$ be a metric between x's
- For each i, define $j(i) = \underset{j \text{ s.t. } t_j \neq t_i}{\operatorname{argmin}} \; d(x_j, x_i)$

  $j(i)$ is the nearest counterfactual neighbor of i
- $t_i = 1$, unit i is treated:

$$\widehat{CATE}(x_i) = y_i - y_{j(i)}$$

- $t_i = 0$, unit i is control:

$$\widehat{CATE}(x_i) = y_{j(i)} - y_i$$

1-NN Matching

- Let $d(\cdot,\cdot)$ be a metric between x's
- For each i, define $j(i) = \underset{j \text{ } s.t. \text{ } t_j \neq t_i}{\operatorname{argmin}} \; d(x_j, x_i)$

  $j(i)$ is the nearest counterfactual neighbor of i

- $\widehat{CATE}(x_i) = (2t_i - 1)(y_i - y_{j(i)})$
- $\widehat{ATE} = \frac{1}{n}\sum_{i=1}^{n} \widehat{CATE}(x_i)$

Matching

- Interpretable, especially in small-sample regime
- Nonparametric
- Heavily reliant on the underlying metric
- Could be misled by features which don’t affect the outcome

Covariate adjustment and matching

- Matching is equivalent to covariate adjustment with two 1-nearest neighbor classifiers:
$\hat{Y}_1(x) = y_{NN_1(x)}$, $\hat{Y}_0(x) = y_{NN_0(x)}$
where $y_{NN_t(x)}$ is the nearest-neighbor of x among units with treatment assignment
$$t = 0,1$$

- 1-NN matching is in general inconsistent, though only with small bias (Imbens 2004)

Two common approaches for counterfactual inference

Covariate adjustment

Propensity scores

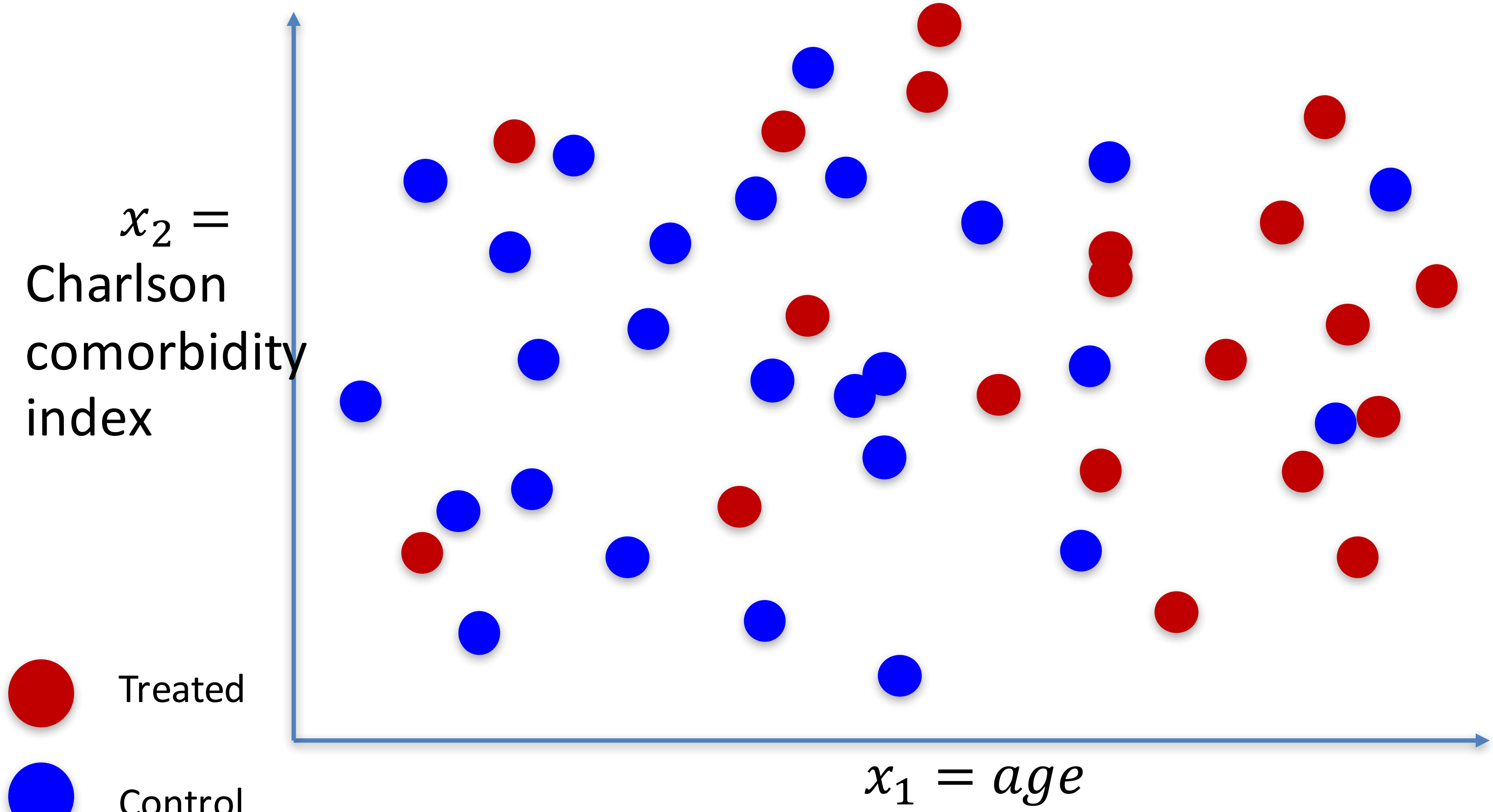
Propensity scores

- Tool for estimating ATE
- Basic idea: turn observational study into a pseudo-randomized trial by re-weighting samples, similar to importance sampling

Inverse propensity score re-weighting

$$p(x \mid t=0) \cdot w_0(x) \neq p(x \mid t=1) \cdot w_1(x)$$

reweighted control *reweighted treated*



Propensity score

- Propensity score: $p(T = 1|x)$, using machine learning tools
- Samples re-weighted by the inverse propensity score of the treatment they received

Propensity scores – algorithm

Inverse probability of treatment weighted estimator

How to calculate ATE with propensity score for sample $(x_1, t_1, y_1), \ldots, (x_n, t_n, y_n)$

1. Use any ML method to estimate $\hat{p}(T = t|x)$
2. $$A\hat{T}E = \frac{1}{n} \sum_{i \text{ s.t. } t_i=1} \frac{y_i}{\hat{p}(t_i = 1|x_i)} - \frac{1}{n} \sum_{i \text{ s.t. } t_i=0} \frac{y_i}{\hat{p}(t_i = 0|x_i)}$$

Propensity scores – algorithm

Inverse probability of treatment weighted estimator

How to calculate ATE with propensity score for sample $(x_1, t_1, y_1), \ldots, (x_n, t_n, y_n)$

1. Randomized trial $p(T = t|x) = 0.5$
2. $$\hat{ATE} = \frac{1}{n} \sum_{i \text{ s.t. } t_i=1} \frac{y_i}{\hat{p}(t_i = 1|x_i)} - \frac{1}{n} \sum_{i \text{ s.t. } t_i=0} \frac{y_i}{\hat{p}(t_i = 0|x_i)}$$

Propensity scores – algorithm

Inverse probability of treatment weighted estimator

How to calculate ATE with propensity score for sample $(x_1, t_1, y_1), \ldots, (x_n, t_n, y_n)$

1. Randomized trial $p(T = t|x) = 0.5$
2. $\hat{ATE} = \frac{1}{n} \sum_{i \text{ s.t. } t_i=1} \frac{y_i}{0.5} - \frac{1}{n} \sum_{i \text{ s.t. } t_i=0} \frac{y_i}{0.5} =$

Propensity scores – algorithm

Inverse probability of treatment weighted estimator

How to calculate ATE with propensity score for sample $(x_1, t_1, y_1), \dots, (x_n, t_n, y_n)$

1. Randomized trial $p = 0.5$

2. $$\hat{ATE} = \frac{1}{n} \sum_{i \text{ s.t. } t_i = 1} \frac{y_i}{0.5} - \frac{1}{n} \sum_{i \text{ s.t. } t_i = 0} \frac{y_i}{0.5} =$$
$$\frac{2}{n} \sum_{i \text{ s.t. } t_i = 1} y_i - \frac{2}{n} \sum_{i \text{ s.t. } t_i = 0} y_i$$

Propensity scores – algorithm

Inverse probability of treatment weighted estimator

How to calculate ATE with propensity score

for sample $(x_1, t_1, y_1), \ldots, (x_n, t_n, y_n)$

Sum over $\sim \frac{n}{2}$ terms

1. Randomized trial $p = 0.5$

2. $$\hat{ATE} = \frac{1}{n} \sum_{i \text{ s.t. } t_i=1} \frac{y_i}{0.5} - \frac{1}{n} \sum_{i \text{ s.t. } t_i=0} \frac{y_i}{0.5} =$$

$$\frac{2}{n} \sum_{i \text{ s.t. } t_i=1} y_i - \frac{2}{n} \sum_{i \text{ s.t. } t_i=0} y_i$$

Propensity scores - derivation

- Recall average treatment effect:

$$\mathbb{E}_{x\sim p(x)}\left[\ \mathbb{E}\left[Y_1|x,T=1\right]-\mathbb{E}\left[Y_0|x,T=0\right]\ \right]$$

- We only have samples for:

$$\mathbb{E}_{x\sim p(x|T=1)}\left[\ \mathbb{E}\left[Y_1|x,T=1\right]\right]$$

$$\mathbb{E}_{x\sim p(x|T=0)}\left[\ \mathbb{E}\left[Y_0|x,T=0\right]\right]$$

Propensity scores - derivation

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Propensity scores - derivation

- We only have samples for:

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- We need to turn $p(x|T=1)$ into $p(x)$:

$$p(x|T=1)\cdot \quad ? \quad = p(x)$$

Propensity scores - derivation

- We only have samples for:

$$\mathbb{E}_{x \sim p(x|T=1)}\left[\,\mathbb{E}\left[Y_1|x, T=1\right]\right]$$

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- We need to turn $p(x|T=1)$ into $p(x)$:

$$p(x|T=1) \cdot \frac{p(T=1)}{p(T=1|x)} = p(x)$$

Propensity score

Propensity scores - derivation

- We only have samples for:

$$\mathbb{E}_{x \sim p(x|T=1)}\left[\ \mathbb{E}\left[Y_1|x, T=1\right]\right]$$

$$\mathbb{E}_{x \sim p(x|T=0)}\left[\ \mathbb{E}\left[Y_0|x, T=0\right]\right]$$

- We need to turn $p(x|T=0)$ into $p(x)$:

$$p(x|T=0) \cdot \frac{p(T=0)}{p(T=0|x)} = p(x)$$

Propensity score

- We want: $\mathbb{E}_{x \sim p(x)}[Y_1(x)]$
- We know that:

$$p(x|T=1) \cdot \frac{p(T=1)}{p(T=1|x)} = p(x)$$

- Thus:

$$\mathbb{E}_{x \sim p(x|T=1)}\left[\frac{p(T=1)}{p(T=1 \mid x)} Y_1(x)\right] = \mathbb{E}_{x \sim p(x)}[Y_1(x)]$$

- We can approximate this empirically as:

$$\frac{1}{n_1} \sum_{i \text{ s.t. } t_i=1} \left[\frac{n_1/n}{\hat{p}(t_i = 1 \mid x_i)} y_i\right] = \frac{1}{n} \sum_{i \text{ s.t. } t_i=1} \frac{y_i}{\hat{p}(t_i = 1 \mid x_i)}$$

(similarly for $t_i=0$)

Problems with IPW

- Need to estimate propensity score (problem in all propensity score methods)
- If there's not much overlap, propensity scores become non-informative and easily mis-calibrated
- Weighting by inverse can create large variance and large errors for small propensity scores
  - Exacerbated when more than two treatments

Many more ideas and methods

- Natural experiments & regression discontinuity
- Instrumental variables

Many more ideas and methods – Natural experiments

- Does stress during pregnancy affect later child development?
- Confounding: genetic, mother personality, economic factors…
- Natural experiment: the Cuban missile crisis of October 1962. Many people were afraid a nuclear war is about to break out.
- Compare children who were in utero during the crisis with children from immediately before and after

Many more ideas and methods – Instrumental variables

- Informally: a variable which affects treatment assignment but not the outcome
- Example: are private schools better than public schools?
- Confounding: different student population, different teacher population
- Can’t force people which school to go to

Many more ideas and methods – Instrumental variables

- Informally: a variable which affects treatment assignment but not the outcome
- Example: are private schools better than public schools?
- Can’t force people which school to go to
- Can *randomly* give out vouchers to some children, giving them an opportunity to attend private schools
- The voucher assignment is the instrumental variable

Summary

- Two approaches to use machine learning for causal inference:
  1. Predict outcome given features and treatment, then use resulting model to impute counterfactuals (*covariate adjustment*)
  2. Predict treatment using features (*propensity score*), then use to reweight outcome or stratify the data
- Causal graphs important for thinking through whether problem is setup appropriately and whether assumptions hold