Confounding

- Confounding $X$ (or common cause; see DAG) is the main complication/hurdle between association and causation

![Diagram](https://via.placeholder.com/150)

- Propensity score methods: need a model for $Z \sim X$
  - Stratification
  - Matching
  - Regression (need additional model for $Y \sim e(X)$)
  - Weighting (this lecture)
Inverse Probability Weighting (IPW)

- Inverse probability weighting (IPW), also known as inverse probability of treatment weighting (IPTW)
- Easy to show

\[
\mathbb{E} \left[ \frac{ZY}{e(X)} - \frac{(1 - Z)Y}{1 - e(X)} \right] = \tau_{ATE}.
\]

Observe

\[
\mathbb{E} \left[ \frac{ZY}{e(X)} \right] = \mathbb{E} \left\{ \frac{1}{e(X)} \mathbb{E} [ZY(1) \mid X] \right\} = \mathbb{E} \left\{ \frac{\mathbb{E}(Z \mid X)}{e(X)} \mathbb{E}[Y(1) \mid X] \right\}
\]

\[
= \mathbb{E} \{ \mathbb{E}[Y(1) \mid X] \} = \mathbb{E}[Y(1)]
\]

- Horvitz-Thompson (HT) estimator in survey sampling literature
Inverse Probability Weighting (IPW)

- Recall
  \[ \mathbb{E} \left[ \frac{ZY}{e(X)} - \frac{(1 - Z)Y}{1 - e(X)} \right] = \tau_{ATE}. \]

- Define the inverse probability weights (IPW):
  \[
  \begin{align*}
  w_1(X_i) &= \frac{1}{e(X_i)}, \quad \text{for } Z_i = 1 \\
  w_0(X_i) &= \frac{1}{1 - e(X_i)}, \quad \text{for } Z_i = 0.
  \end{align*}
  \]

- An unbiased nonparametric (moment-based) estimator of ATE:
  difference in the mean of the weighted outcomes between groups
  \[
  \hat{\tau}_{ipw,1} = \frac{1}{N} \left\{ \sum_{i=1}^{N} \frac{Y_i Z_i}{e(X_i)} - \sum_{i=1}^{N} \frac{Y_i (1 - Z_i)}{1 - e(X_i)} \right\} = \frac{1}{N} \sum_{i=1}^{N} \{ Y_i Z_i w_1(X_i) - Y_i (1 - Z_i) w_0(X_i) \}.\]
Normalize the weights

- When use any weighting method (e.g. IPW), good practice is to normalize weights – sum of the total of weights within one group should be 1

- Divide each unit’s weight by the sum of all weights in that group $w_i / \sum_{i:Z=z} w_i$ for $z = 0, 1$, i.e. the Hajek estimator:

$$
\hat{\tau}_{ipw,2} = \frac{\sum_{i=1}^{n} Y_i Z_i w_1(X_i)}{\sum_{i=1}^{n} Z_i w_1(X_i)} - \frac{\sum_{i=1}^{n} Y_i (1 - Z_i) w_0(X_i)}{\sum_{i=1}^{n} (1 - Z_i) w_0(X_i)}.
$$

- Reduce variance, $\mathbb{V}(\hat{\tau}_{ipw,2}) \leq \mathbb{V}(\hat{\tau}_{ipw,1})$, and lead to more stable estimate (Hirano, Imbens, Ridder, 2003)

- Normalized weights are also called “stabilized weights" (Hernan, Robins, Brumback, 2000)
Inverse Probability Weighting (IPW)

- IPW creates a weighted population (i.e. target population) – a population that the study sample is representative of

- In this weighted population, the covariates distributions between two groups are balanced: can show

\[
\mathbb{E}[XZ/e(X)] = \mathbb{E}[X(1 - Z)/(1 - e(X))].
\]

- The intuition behind: the less likely a subject is sampled, then the larger population it should represent

- Up-weigh “weirdos”: units whose treatment assignment is opposite to what the propensity score predicts
Inverse Probability Weighting (IPW): Variance

▶ What if the true PS $e(X)$ is known?

▶ Hirano, Imbens, Ridder (2003) shows that using the estimated PS instead of the true PS asymptotically gives more efficient estimate of treatment effect (projection)

▶ Closed-form sandwich estimator (M-estimator) of variance that takes into account of the uncertainty in estimating the propensity score (Lunceford and Davidian, 2004)

▶ Bootstrap: Resample units and refit PS and estimate the causal effects every time – computationally intensive for large sample
Inverse Probability Weighting (IPW)

**Advantages (general to weighting)**

- Simple, with theoretical foundation
- Smooth - explicit target population
- Global balance
- Extends to more complex settings

**Disadvantages (specific to IPW)**

- More sensitive to misspecification of propensity scores
- Propensity scores near 0 or 1 yield extreme weights
- Many ad hoc decisions to deal with this
- ATE might not always be the sensible estimand
Example: Framingham Heart Study re-visited

- **Goal:** evaluate the effect of statins on health outcomes

- **Patients:** cross-sectional population from the offspring cohort with a visit 6 (1995-1998)

- **Treatment:** statin use at visit 6 vs. no statin use

- **Outcomes:** CV death, myocardial infarction (MI), stroke

- **Confounders:** sex, age, body mass index, diabetes, history of MI, history of PAD, history of stroke...

- Significant imbalance between treatment and control groups in covariates motivates IPW (or some form of propensity score adjustment)
Balance in Framingham Study (Statins vs. Control)
Challenge to IPW: Poor overlap

![Graph showing propensity scores for untreated and on statins patients.]
Example: Poor Overlap (Brennen et al. 2016)
IPW Operational Challenges

- Propensity values near 0 and 1 yield extreme weights (after taking the inverse)

- Adverse finite-sample consequences – Basu’s elephant: severe bias and variance

- Normalization of weights helps, but not a lot

- Core problem: lack of overlap in the tail of the propensity distribution – causal comparisons of these units are highly uncertain
Other adjustment methods

How do poor overlap and extreme propensity scores impact other adjustment methods?

- Regression adjustment: Increases model sensitivity
- Matching: Many patients get excluded because they don’t have a match
- Stratification: Adds bias due to residual imbalance within strata

Better to fix IPW than to abandon weighting altogether.
Propensity Score Trimming and Truncation

- Symmetric trimming (*Crump et al.*, 2009)
  - exclude patients whose estimated PS is outside \([\alpha, 1 - \alpha]\)
  - rule of thumb \(\alpha = 0.1\)

- Asymmetric trimming (*Sturmer et al.*, 2010)
  - exclude patients with PS outside of the common PS range formed by the treated and control patients
  - among all units, further exclude those whose PS is below the \(q\) quantile of the treated units
  - among all units, exclude those whose PS is above the \((1 - q)\) quantile of the control units

- Propensity score truncation
  - Set the patients whose estimated PS is below \(\alpha\) to \(\alpha\), and whose estimated PS is above \(1 - \alpha\) to \(1 - \alpha\)
  - You can’t be more ad hoc than this!
## Trimming thresholds applied to Framingham

<table>
<thead>
<tr>
<th>Method</th>
<th>Left Excluded</th>
<th>Right Excluded</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetric $\alpha = 0.025$</td>
<td>1047</td>
<td>1</td>
<td>1048 (31%)</td>
</tr>
<tr>
<td>Symmetric $\alpha = 0.05$</td>
<td>1634</td>
<td>1</td>
<td>1635 (48%)</td>
</tr>
<tr>
<td>Symmetric $\alpha = 0.10$</td>
<td>2269</td>
<td>1</td>
<td>2270 (68%)</td>
</tr>
<tr>
<td>Asymmetric $q = 0.025$</td>
<td>1179</td>
<td>134</td>
<td>1313 (39%)</td>
</tr>
<tr>
<td>Asymmetric $q = 0.05$</td>
<td>1554</td>
<td>257</td>
<td>1811 (54%)</td>
</tr>
<tr>
<td>Asymmetric $q = 0.10$</td>
<td>1811</td>
<td>468</td>
<td>2279 (68%)</td>
</tr>
</tbody>
</table>
Symmetric Trimming $\alpha = 0.10$
Propensity Score Trimming - Cont’d

Reduce the impact of extreme PS and improve finite-sample property of IPW

Choice of threshold \( \alpha, q \) may be arbitrary

- conceptual challenge: ambiguous target population/interpretation
- operational challenge: causal estimates sensitive to trimming threshold
- operational challenge: bias-variance tradeoff
- operational challenge: refitting PS after trimming (a hidden message)
Extension Beyond IPW: Move the Goalpost

- A different approach: move the goalpost away from ATE (IPW). Other, user-specified target populations.

- Key question: ATE over what target population? (Thomas et al. 2020a)

- Often units who are “one the fence" (in the middle of PS distribution) are of interest. Examples:

  1. TAVR/SAVR
  2. Under clinical equipoise, the target population are units with the most “overlap” observed characteristics.
Extension Beyond IPW: Move the Goalpost

Motivating questions:

1. Is there a unified framework for weighting for different target populations?

2. Is there an intrinsic approach to define such “marginal population” while avoiding the pitfall of IPW?
IPW is a special case of a general class of balancing weights

Recall the conditional average treatment effect CATE is defined as

$$\tau(x) \equiv \mathbb{E}(Y(1)|X = x) - \mathbb{E}(Y(0)|X = x).$$

Assume density of the observed covariates, $f(x)$, exists wrt a measure $\mu$

Consider a target population, denoted by a density $g(x)$, possibly different from $f(x)$

The ratio $h(x) = g(x) / f(x)$ is called a tilting function, which re-weights the observed sample to represent the target population
A new class of estimands: the ATE over the target population $g$

$$
\tau_h \equiv \mathbb{E}_g [Y_i(1) - Y_i(0)] = \frac{\int \tau(x)f(x)h(x)\mu(dx)}{\int f(x)h(x)\mu(dx)} = \frac{\mathbb{E}\{h(x)\tau(x)\}}{\mathbb{E}\{h(x)\}}. \quad (1)
$$

$\tau_h$ is a general class of weighted ATE (WATE) estimands (Hirano et al., 2003)

When $h(x) = 1$, $f(x) = g(x)$, the target population is the observed population

Varying $h(x)$ defines varying target population. In practice, we pre-specify the tilting function $h(x)$
Let $f_z(x) = \Pr(X = x | Z = z)$ (covariate distribution within each group $z$), easy to show

$$f_1(x) \propto f(x)e(x), \quad f_0(x) \propto f(x)(1 - e(x))$$

For a given $h(x)$, to estimate $\tau_h$, we can weight $f_z(x)$ to the target population $g(x) = f(x)h(x)$ using analytic weights

$$
\begin{cases}
    w_1(x) \propto \frac{f(x)h(x)}{f_1(x)} = \frac{f(x)h(x)}{f(x)e(x)} = \frac{h(x)}{e(x)}, \\
    w_0(x) \propto \frac{f(x)h(x)}{f_0(x)} = \frac{f(x)h(x)}{f(x)(1-e(x))} = \frac{h(x)}{1-e(x)}.
\end{cases}
$$

The class of weights $(w_0, w_1)$ is called balancing weights: balance the distributions of the weighted covariates between comparison groups

$$f_1(x)w_1(x) = f_0(x)w_0(x) = f(x)h(x)$$
Examples: target population \((h)\) and balancing weights

- Choice of \(h(x)\) determines the target population, estimand, weights
- Statistical, scientific and policy considerations all come into play in selecting \(h(x)\)

<table>
<thead>
<tr>
<th>target population</th>
<th>(h(x))</th>
<th>estimand</th>
<th>weight ((w_1, w_0))</th>
</tr>
</thead>
<tbody>
<tr>
<td>combined</td>
<td>1</td>
<td>ATE</td>
<td>(\left(\frac{1}{e(x)}, \frac{1}{1-e(x)}\right)) [HT]</td>
</tr>
<tr>
<td>treated</td>
<td>(e(x))</td>
<td>ATT</td>
<td>(\left(1, \frac{e(x)}{1-e(x)}\right))</td>
</tr>
<tr>
<td>control</td>
<td>(1-e(x))</td>
<td>ATC</td>
<td>(\left(\frac{1-e(x)}{e(x)}, 1\right))</td>
</tr>
<tr>
<td>overlap</td>
<td>(e(x)(1-e(x)))</td>
<td>ATO</td>
<td>((1-e(x), e(x)))</td>
</tr>
<tr>
<td>trimming</td>
<td>(1(\alpha \leq e(x) \leq 1-\alpha))</td>
<td></td>
<td>(\left(\frac{1(\alpha \leq e(x) \leq 1-\alpha)}{e(x)}, \frac{1(\alpha \leq e(x) \leq 1-\alpha)}{1-e(x)}\right))</td>
</tr>
<tr>
<td>matching</td>
<td>(\min{e(x), 1-e(x)})</td>
<td></td>
<td>(\left(\frac{\min{e(x), 1-e(x)}}{e(x)}, \frac{\min{e(x), 1-e(x)}}{1-e(x)}\right))</td>
</tr>
</tbody>
</table>
Large-sample properties

Sample estimator of WATE

\[
\hat{\tau}_h = \frac{\sum_i w_1(x_i)Z_iY_i}{\sum_i w_1(x_i)Z_i} - \frac{\sum_i w_0(x_i)(1 - Z_i)Y_i}{\sum_i w_0(x_i)(1 - Z_i)}
\]  

(3)

Theorem 1. \(\hat{\tau}_h\) is a consistent estimator of \(\tau_h\).
Large-sample properties

**Theorem 2.** As $N \to \infty$, the expectation (over possible samples of covariate values) of the conditional variance of the estimator $\hat{\tau}_h$ given the sample $X = \{x_1, \ldots, x_N\}$ converges:

$$N \cdot E_x \mathbb{V}[\hat{\tau}_h \mid X] \to \int f(x)h(x)^2 \left[ \frac{v_1(x)}{e(x)} + \frac{v_0(x)}{1 - e(x)} \right] \mu(dx) / C_h^2,$$

where $v_z(x) = \mathbb{V}[Y(z) \mid X]$ and $C_h = \int h(x)f(x)d\mu(x)$ is a normalizing constant.

**Corollary 1.** The function $h(x) \propto e(x)(1 - e(x))$ gives the smallest asymptotic variance for the weighted estimator $\hat{\tau}_h$ among all $h$’s under homoscedasticity, and as $N \to \infty$,

$$N \cdot \min_h \{\mathbb{V}[\hat{\tau}_h]\} \to v / \int f(x)e(x)(1 - e(x)) \mu(dx).$$
Overlap Weights

Based on Corollary 1, LMZ propose a new type of weights, the overlap weights, by letting \( h(x) = e(x)(1 - e(x)) \):

\[
\begin{align*}
    w_1(x) &\propto 1 - e(x), & \text{for } Z = 1, \\
    w_0(x) &\propto e(x), & \text{for } Z = 0.
\end{align*}
\]

Each unit is weighted by its probability of being assigned to the opposite group.

As IPW, in practice one should always first normalize weights.
Overlap Weights

- Review: \( h(x) = e(x)(1 - e(x)) \),

\[
\begin{align*}
    w_1(x) &\propto 1 - e(x), \quad \text{for } Z = 1, \\
    w_0(x) &\propto e(x), \quad \text{for } Z = 0.
\end{align*}
\]

- **QUESTION**: what value of the propensity score \( e(x) \) gives highest \( h(x) \)?

- **ANSWER**: \( e(x) = 0.5 \) yields \( h(x) = 0.25 \)

- The relative weighting of \( f(x) \) by \( h(x) \) is greatest at 0.5

- **Target population**: the units whose characteristics could appear with substantial probability in either treatment group (most overlap)

- \( e(x)(1 - e(x)) \): harmonic mean, also Gini index in classification tree literature
Densities for two groups and overlap population

\[ f(x)h(x) \]

\[ f_0(x) \quad f_1(x) \]

Propensity score overlap weights and \( h(x) = e(x)(1-e(x)) \)

\[ w_1(x) = e(x) \quad w_0(x) = 1 - e(x) \]
Theorem 3. When the propensity scores are estimated by maximum likelihood under a logistic regression model,

\[
\text{logit}\{e(x_i)\} = \beta_0 + x_i'\beta,
\]

the overlap weights lead to exact balance in the means of any included covariate between treatment and control groups:

\[
\frac{\sum_{i=1}^{n} x_{ij}Z_i(1 - \hat{e}_i)}{\sum_{i=1}^{n} Z_i(1 - \hat{e}_i)} = \frac{\sum_{i=1}^{n} x_{ij}(1 - Z_i)\hat{e}_i}{\sum_{i=1}^{n} (1 - Z_i)\hat{e}_i}, \quad \text{for } j = 1, \ldots, p, \quad (4)
\]

where \( \hat{e}_i = \{1 + \exp[-(\hat{\beta}_0 + x_i'\hat{\beta})]\}^{-1} \) and \( \hat{\beta} = (\hat{\beta}_1, \ldots, \hat{\beta}_j) \) is the MLE for the regression coefficients.

- Remark: the exact balance property applies to any included covariate and derived covariate, including high order terms and interaction terms of the covariates.
Exact Balance: Outline of Proof

- The log likelihood function of the logistic PS model
  \[
  \text{logit}\{e(X_i)\} = \beta_0 + X_i'\beta
  \]
  is:
  \[
  L = \sum_{i=1}^{n} Z_i \log\{\hat{e}(x)\} + (1 - Z_i) \log\{1 - \hat{e}(x)\},
  \]
  where \(\hat{e} = \left\{1 + \exp(-x_i'\beta)\right\}^{-1} \).

- To obtain the MLE of \(\beta\)'s, one needs to solve for the score functions equating 0, which for each covariate \(k\) is:
  \[
  S_k = \frac{\partial \log L}{\partial \beta_k} = \sum_{i=1}^{n} x_{ik}(Z_i - \hat{e}), \quad \text{for } k = 0, 1, \ldots, p,
  \tag{5}
  \]
  where \(x_{0k} \equiv 1\).

- Equating to 0 and solving, the MLE \(\hat{\beta}\) satisfies (exercise)
  \[
  \sum_{i=1}^{n} Z_i = \sum_{i=1}^{n} \hat{e}_i, \quad \text{and} \quad \sum_{i=1}^{n} x_{ik}Z_i = \sum_{i=1}^{n} x_{ik}\hat{e}_i.
  \]
Corollary 2. If the postulated propensity score model includes any interaction term of a binary covariate, then the overlap weights lead to exact balance in the means in the subgroups defined by that binary covariate.

Remarks:

- If the true PS model has interaction terms, then overlap weights using PS estimated from any model that nests the true model gives exact balance in the subgroups defined by the interaction terms.
Exact Balance of Overlap Weights: More Remarks

- For binary treatment, the exact balance property only hold for the logistic link (the canonical link).

- Also holds if use a linear regression of $Z$ on $X$ to estimate $e(x)$: identity link is the canonical link.

- Double-edge sword: The exact balance property holds regardless of the validity of the PS model – a peculiar math artifact of the canonical link of GLM.

- Exact (mean) balance is a nice by-product of but not the main motivation behind overlap weights (minimize variance).

- In practice, one should always try to fit a good PS model even if this may break the exact balance.
Overlap Weights: Statistical Advantages

- **Minimum variance** of the nonparametric estimator among all balancing weights (the homoscedasticity assumption is not crucial in practice)

- **Exact balance** for means of included covariates in logistic propensity score model

- Weights are **bounded** (unlike IPW)

- Avoids *ad hoc* truncating weights or eliminating cases: a continuous version of trimming
Overlap Weights: Adaptive

- Overlap weights are adaptive, ATO approximate
  - ATE: if treatment and control groups are nearly balanced in size and
distribution (for \( e(x) \approx 1/2 \), \((1 - e(x), e(x)) \approx \left( \frac{0.25}{e(x)}, \frac{0.25}{1 - e(x)} \right) \))
  - ATT: if propensity to treatment is always small (for \( e(x) \approx 0 \),
\((1 - e(x), e(x)) \approx \left(1, \frac{e(x)}{1 - e(x)} \right) \))
  - ATC: if propensity to control is small
Overlap Weights: Scientific Relevance

► Overlap weights focus on the (sub)population closest to the population in RCT

► Overlap weights put emphasis on internal validity

► The overlap population is of intrinsic substantive interest, for example

  ▶ In medicine, patients in clinical equipoise

  ▶ In policy, units whose treatment assignment would be most responsive to a policy shift as new information is obtained

► Overlap weighting mimics attributes of a randomized clinical trial. Useful in situations where large RCT is not immediately available, e.g. COVID-19 studies (Thomas et al. 2020b)

► Overlap weighting was first proposed by A Zaslavsky and applied in medical journals since 2001 (Schneider et al. 2001)
Characterize the Target Population

- An easy way to characterize and compare different target populations is to present a table of covariate means, both unadjusted and weighted (commonly known as Table 1 in medical papers)

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Statin users N=348</td>
<td>No statins N=3008</td>
</tr>
<tr>
<td>Age – yr*</td>
<td>64 (57, 70)</td>
<td>57 (50, 65)</td>
</tr>
<tr>
<td>Female sex</td>
<td>44.3</td>
<td>54.3</td>
</tr>
<tr>
<td>Systolic Blood Pressure – mmHg</td>
<td>131 (119, 144)</td>
<td>125 (114, 138)</td>
</tr>
<tr>
<td>Diastolic Blood Pressure – mmHg</td>
<td>76 (69, 82)</td>
<td>75 (68, 81)</td>
</tr>
<tr>
<td>BMI – kg/m²</td>
<td>29 (26, 32)</td>
<td>27 (25, 31)</td>
</tr>
<tr>
<td>History of CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>16.4</td>
<td>3.0</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Peripheral Artery Dis.</td>
<td>7.5</td>
<td>2.2</td>
</tr>
<tr>
<td>Any ASCVD</td>
<td>35.3</td>
<td>8.9</td>
</tr>
</tbody>
</table>
Connection to Matching and Regression

- **Matching**: link “similar” cases in two samples, discard unmatched cases (bottom-up approach)

- **Weighting**: apply weights to entire samples, designed to create global balance (top-down approach)

- **Intrinsic connection**: Overlap weighting approaches many-to-many matching as the propensity score model becomes increasingly complex

- **Why?** The limit of a PS model is a saturated model with a fixed effect (dummy variable) for each design point (or small neighborhood, for continuous variables)
Connection to Matching and Regression

- Let the sample count for \( x_i \) in group \( z = 0, 1 \) be \( N_{zi} \), the estimated PS from the saturated model is \( \hat{e}(x_i) = \frac{N_{1i}}{N_{0i} + N_{1i}} \).

- The overlap weight for trt and con units is \( \frac{N_{0i}}{N_{0i} + N_{1i}} \) and \( \frac{N_{1i}}{N_{0i} + N_{1i}} \), respectively.

- In many-to-many matching: at each design point \( x \), each trt unit is matched to the \( N_{0i} \) controls at the same \( x \), each control to \( N_{1i} \) trt units – exactly the same as the overlap weighting.

- The total overlap weight for each design point \( x \) and hence of \( \hat{\tau}(x_i) \) is \( \frac{N_{0i}N_{1i}}{N_{0i} + N_{1i}} \).

- This is exactly the precision weight attached to \( \bar{y}_{1i} - \bar{y}_{0i} \) in the fixed-effects for each design point OLS outcome model:

\[ Y_{zi} = \alpha_i + z\tau + \epsilon_{zi} \]
Binary Outcomes: Estimands and Estimator

Recall $\tau_1 = \Pr_g[Y(1) = 1] = \mathbb{E}_g[Y(1)] = \frac{\mathbb{E}_f[h(X)\mu_1(X)]}{\mathbb{E}_f(h(X))}$, $\tau_0 = \Pr_g[Y(0) = 1] = \mathbb{E}_g[Y(0)] = \frac{\mathbb{E}_f[h(X)\mu_0(X)]}{\mathbb{E}_f(h(X))}$

$\tau_{ATO} = \tau_1 - \tau_0$ interpreted as the causal risk difference

We define the causal risk ratio and odds ratio among the overlap population as

$\tau_{RR} = \frac{\tau_1}{\tau_0}$, $\tau_{OR} = \frac{\tau_1/(1 - \tau_1)}{\tau_0/(1 - \tau_0)}$

Estimate PS, and use

$\hat{\tau}_1 = \frac{\sum_{i=1}^n Z_i Y_i (1 - \hat{e}_i)}{\sum_{i=1}^n Z_i (1 - \hat{e}_i)}$, $\hat{\tau}_0 = \frac{\sum_{i=1}^n (1 - Z_i) Y_i \hat{e}_i}{\sum_{i=1}^n (1 - Z_i) \hat{e}_i}$
M-estimator of Variance

- A closed-form consistent variance estimator for $\tau_h$ using the OW (i.e. ATO estimand) when the PS is estimated from a logistic regression is given in Li, Thomas, Li (2019)

- Based on M-estimation, account for the uncertainty in estimating the propensity scores, good finite sample coverage

- Attractive in studies with large sample size

- If the outcome is binary and the estimand is causal odds ratio or relative risk, we can also derive corresponding closed-form variance estimator using the Delta method
A Simulated Example

- Simulate \( n_0 = n_1 = 1000 \) units.
- A single covariate: \( X_i \sim N(0, 1) + 2Z_i \).
- Outcome model: \( Y_i(z) \sim N(X_i, 1) + \tau z \), and \( \tau = 1 \).
- Use the nonparametric estimator \( \hat{\tau}_h \) with different weights

**Figure:** Covariate distributions within each treatment group

<table>
<thead>
<tr>
<th></th>
<th>Unweighted</th>
<th>Overlap</th>
<th>HT</th>
<th>ATT</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \hat{\tau} )</td>
<td>2.945</td>
<td>1.000</td>
<td>0.581</td>
<td>0.640</td>
</tr>
<tr>
<td>( SE(\hat{\tau}) )</td>
<td>0.054</td>
<td>0.038</td>
<td>0.386</td>
<td>0.402</td>
</tr>
</tbody>
</table>
Framingham revisited
Weighted Distribution

All Patients

- Among Statins
- Among Control
- Overlap
- IPW

Propensity Score Across patients

Density
Weighted Distribution

All Patients

Density

Framingham Risk Score
Across patients

-10 0 10 20 30 40 50

0.00 0.02 0.04 0.06

Among Statins
Among Control
Overlap
IPW
Results: composite CV death
Results: all-cause mortality
PS Weighting for Covariate Adjustment in RCT

- PS weighting has been developed in the context of observational studies.
- PS can also be used for covariate adjustment in randomized trials.
- Chance imbalance is common in RCT; covariate adjustment improves precision.
- ANCOVA with covariate-treatment interaction model (Yang and Tsiatis, 2001; Lin, 2013) is widely used, but potential for "fishing expedition", also lose efficiency if ANCOVA is misspecified.
- In RCT, PS is known (often 1/2), how to do PS weighting?
PS Weighting for Covariate Adjustment in RCT

- PS weighting for covariate adjustment in RCT: procedure is no different from observational studies
  1. Specify a “working" PS model and obtain an estimated PS for each unit
  2. Use a PS weighting moment estimator based on the estimated PS as the covariate adjusted estimator

- Both IPW (Williamson et al., 2014; Shen et al., 2014) and OW (Zeng et al., 2020) works: asymptotically equivalent to the ANCOVA estimator, all belong to the same semiparametric family (Tsiatis et al. 2008)

- Key difference between RCT and observational studies: In RCT, PS is known and constant, so that the $h(x)$ for OW is constant, and thus IPW and OW corresponds to exact the same estimand - ATE
PS Weighting for Covariate Adjustment in RCT

- Finite sample performance: OW is more efficient than IPW, as good and sometimes even outperform an ANCOVA estimator with correct outcome model - the key is due to the exact balance property of OW

- PS weighting avoids outcome modeling, more objective and transparent for covariate adjustment

- This is an example of “estimated PS is better than true PS" (Rosenbaum, 1987)

- PS weighting methods with the family of balancing weights are implemented in the R package \texttt{PSweight} (available at CRAN) https://cran.r-project.org/web/packages/PSweight/index.html
Weighting vs. Balancing

- Balancing weights balance covariates in expectation, but do not balance in finite samples.

- A recent stream of research proposed estimators that directly balance covariates, bypassing estimating PS.

- **Goal**: find weights $w_i$ such that the weighted average of each covariate is approximately balanced:

  $$\frac{1}{N_1} \sum_{i=1}^{N} w_i Z_i X_i = \frac{1}{N_1} \sum_{i=1}^{N} w_i (1 - Z_i) X_i$$

- **General idea**: minimize variation of weights (e.g. entropy, coef of variation) subject to a set of balance constraints.

- Such weights are usually obtained via optimization algorithms.
Weighting vs. Balancing

- Literature
  - Entropy balancing (Hainmueller, 2011)
  - Covariate Balancing Propensity Score (CBPS) (Imai and Ratkovic, 2014)
  - Stabilized balancing weights (Zubizarreta, 2015)
  - Inverse probability tilting (Graham, Pinto, Egel, 2012; 2016, JEBS)
  - Approximate residual balancing (Athey, Imbens, Wager, 2016)

- These estimators sacrifice some efficiency for finite-sample balance

- Open question: How much are these estimators better than a DR estimator with a flexible logistic model (e.g. semiparametric with power series or splines) for PS?
Covariate Balancing Propensity Score (CBPS)

Imai and Ratkovic (2014)

- In traditional PS analysis, one fits a model (e.g. logistic) for PS and then check the resulting balance and iteratively improve the fit

- Imai and Ratkovic (2014) proposed the **Covariate Balancing Propensity Score (CBPS)** method

- **Core idea:** fit a logistic PS model—i.e. optimize the likelihood function of the logistic model—subject to covariate balancing constraints
Covariate Balancing Propensity Score (CBPS)
Imai and Ratkovic (2014)

Specifically, the logistic PS model is

$$\text{logit}\{e_\beta(X_i)\} = \beta_0 + X_i\beta',$$  \hspace{1cm} (6)

and the balancing conditions are

$$\mathbb{E}\left\{\frac{Z_i f(X_i)}{e_\beta(X_i)}\right\} = \mathbb{E}\left\{\frac{(1 - Z_i) f(X_i)}{1 - e_\beta(X_i)}\right\}$$

where $f(X_i)$ be an M-dim vector-valued function of $X_i$
Covariate Balancing Propensity Score (CBPS)

Imai and Ratkovic (2014)

▶ In implementation, CBPS obtains the PS that optimizes the likelihood function of model (6) subject to (sample) constraints

\[
\sum_{i=1}^{N} \left\{ \frac{Z_i f(X_i)}{e^{\beta}(X_i)} \right\} = \sum_{i=1}^{n} \left\{ \frac{(1 - Z_i)f(X_i)}{1 - e^{\beta}(X_i)} \right\}.
\]  

(7)

▶ When \( f(X_i) = e^{\prime}_{\beta}(X_i) = \partial e^{\beta}(X_i)/\partial \beta \), CBPS is exactly the MLE of the logistic model (6).

▶ Why? Look at the score functions of logistic model (6):

\[
\sum_{i=1}^{n} \left\{ \frac{Z_i e^{\prime}_{\beta}(X_i)}{e^{\beta}(X_i)} \right\} = \sum_{i=1}^{n} \left\{ \frac{(1 - Z_i)e^{\prime}_{\beta}(X_i)}{1 - e^{\beta}(X_i)} \right\}.
\]  

(8)

▶ Balancing constraints are placed on covariates predictive of PS
In the logistic model (6), we have $p + 1$ parameters and $p + 1$ constraints, the model is called “just-identified"

We can also add more constraints, say on higher moments of covariates

Then the PS model is over-identified: generally improve asymptotic efficiency at the cost of finite sample property – essentially a generalized method of moments (GMM) estimator (Newey and McFadden, 1994)
Covariate Balancing Propensity Score (CBPS)

Imai and Ratkovic (2014)

- Caveat: the PS model can be completely misspecified but the imposed moments are still balanced
- CBPS largely avoids extremely propensities, more robust and better balance
- Once CBPS is estimated, still apply to IPW to estimate ATE
- CBPS was extended to multiple and continuous treatments, longitudinal treatments (software and extension can be found on Kosuke Imai’s webpage)
What is balancing all about?

- All the above balancing methods are designed to balance the functions (e.g. moments) of $X$ that the analyst specifies.

- A thorny question: what if some functions of $X$ important (to the outcome model) are not specified?

- An example: if the true outcome model is $Y \sim X_1 + X_2 + X_1X_2$, whereas we balance $X_1, X_2, X_1^2, X_2^2$ (and higher order moments) but not the interaction $X_1X_2$, which may be severely imbalanced, then we will still end up with biased causal conclusion.
What is balancing all about?

- Ultimately the outcome model (or generating mechanism) is the most important thing

- Elephant in the room: Not “how to balance" but “what to balance."

- Balancing is a (implicit) form of adjustment

- My general view: in observational studies, we need to ensure covariate balance to a certain extent (e.g., via PS), and then proceed with flexible outcome models
Aside 1: Propensity Score with Clustered Data

- Health care and policy data are often clustered, e.g. patients clustered in hospitals, clinics, insurance plans

- We focus on the case of individual assigned treatments with individual covariates and outcome information

- Main points (Li, Zaslavsky, Landrum, 2013):
  - Necessary to incorporating clustering information into at least one of, preferably both, stages of PS analysis
  - Various version of the unconfoundedness assumption: depend on the different conditioning sets, e.g. with or without cluster-specific fixed/random effects (open question)
  - Special care in standard error estimation
Propensity Score with Clustered Data

Procedure of PS weighting with clustered data:

Stage 1: Estimate the propensity score using a fixed/random/mixed effects models with cluster-specific effects

Stage 2: Two methods

Method 1 (nonparametric): Calculate the cluster-specific treatment effect (using a selected weighting) within each cluster, and average these effects weighted by the total weights in each cluster

Methods 2 (augment by outcome model): augment weighting estimator by a multilevel (fixed/random/mixed effects) outcome model. Known as the double-robust estimator in the case of IPW

Standard errors: Two methods

Bootstrap: resample the clusters (not individuals)

Augmented weighting: sandwich estimator (Lunceford and Davidian, 2003), taking into account the uncertainty of estimating PS

Augmented estimators with both se methods are implemented in PSweight package for IPW, OW, MW
Aside 2: Propensity Score for Racial Disparities Analysis

- Causal studies: *no causation without manipulation* (Holland, 1986); a “cause” is at least hypothetically manipulable

- Race is obviously not manipulable

- Racial disparities in health care: not causal studies

- Question: Can propensity scores still be used for racial disparities? Hesitation and confusions among health service researchers

- Answer: Yes, with a few caveats.

- Key points:
  - The balancing property of PS does not involve potential outcomes nor imply causal interpretation
  - Racial disparities comparison requires weaker assumptions than causal comparisons
Controlled Descriptive Comparisons: Estimands

- Racial disparities comparison belongs to controlled descriptive comparisons:
  - Adjust for the difference in pre-specified covariates between two groups, rather than offer a causal interpretation
  - Other examples: different years, external vs. concurrent data (external controls)
- “Assignment”: a nonmanipulable state defining membership in one of two groups or populations
- Conditional average controlled difference (ACD):
  \[
  \tau(x) \equiv E(Y \mid Z = 1, X = x) - E(Y \mid Z = 0, X = x).
  \] (9)
- Estimand: average controlled difference on a target population
  \[
  \tau_h = E_g[\tau(X)] = \frac{E[h(X)\tau(X)]}{E[h(X)]}.
  \] (10)
- \(\tau_h\): average net difference in outcome \(Y\) between two groups with the covariate dist adjusted to be the same as in the target population \(g\)
Causal vs. Controlled Descriptive Comparisons
Li and Li (2022), Observational Studies

- Assumptions for causal comparisons:
  - (A1) Stable Unit Treatment Value Assumption (SUTVA): (i) no interference, (ii) no different versions of the treatment
    - Necessary for defining two potential outcomes for each unit
  - (A2) Unconfoundedness: no unmeasured confounder
    - Necessary for connecting potential outcomes to the observed outcomes and interpreting the difference in the observed outcomes as a causal effect
  - (A3) Overlap or positivity: each unit has non-zero probability of being in either group.

- Assumptions for controlled descriptive comparisons
  - ACD does not involve potential outcomes; thus not require SUTVA or unconfoundedness
  - Overlap is still needed, for operational reasons (large variance o.w.)
Propensity Score for Racial Disparities Analysis

- Racial disparities in health care: a special case of controlled descriptive comparisons
- Propensity score analysis of racial disparities
  - Yes, PS can be used: the balancing property of PS does not involve potential outcomes nor imply causal interpretation
  - PS is a one-dimensional summary score that helps to achieve balance between covariates
- The concept of target population is also important in racial disparities. Different weights lead to different target population:
  - IPW: the overall population combining the two racial groups under comparison (an union of two sets)
  - OW: overlap population – the subpopulation with the most similar covariate distribution between the two racial groups (an intersection of two sets)
  - ATT weight: a population with the same covariate distribution as one pre-specified racial group (e.g. White or Black).
References


References


References


