Propensity-Biased Treatment Allocation in Trials with Staggered Entry

Travis Loux

Department of Statistics and Applied Probability
University of California, Santa Barbara

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Outline

- The Propensity Score
- Randomization
- Propensity-Biased Allocation
- Simulations
- Application
- Conclusion
The propensity score (Rosenbaum and Rubin, 1983) is defined as the probability of exposure conditional on observed covariates:

\[ p(x) = P(T = 1 \mid X = x) \]

Exposed and unexposed populations with the same PS have the same distribution of observed covariates.

In this sense, we can think of the PS as a dimension-reduction which contains all the information about confounding due to \( X \).

- The PS does not balance unobserved covariates
Propensity Score
Estimation and uses

The most common method for estimating the PS is logistic regression

- Other methods include GAMs, CART, random forests, boosting, neural networks
- Essentially a classification problem

Once the PS is estimated, units can be matched or subclassified on the PS to reduce the bias

- Using as few as five subclasses is common and has been shown to work relatively well
- Also can be used as a weight or as a covariate in regression model
Randomization

In an experimental setting, treatment can be assigned to units under the control of the researcher.

- In a completely randomized study, $p(x) = p = 0.5$ for all subjects.

- R.A. Fisher called randomization “the reasoned basis for inference.”

Covariates are not balanced in every randomization, but only as an expectation over all possible randomizations.
Randomization

Issues

- Balance in expectation is of little comfort if given randomization yields poor balance
- Need to account for possibility of poor balance in inference
- Selection bias: if researchers know what treatment a subject is likely to receive, they may be more or less inclined to enroll subject into study or manipulate randomization procedure
- Subjects may enter study sequentially
  - Do not know covariate values at start of study
  - Do not know how many subjects will be recruited
Randomization
Restricting Treatment Allocation

- **Balance**
  - Efron's biased coin (Efron, 1971)
  - Wei's urn (Wei, 1977)
  - Minimization (Pocock and Simon, 1975)
  - Minimum likelihood allocation (Aickin, 1983)
  - Covariate-adaptive biased coin (Baldi Antognini and Zagoraiou, 2011)

- **Minimal variance of effect estimate**
  - Approximate variance minimization (Begg and Iglewicz, 1980)
  - $D_A$-Optimality (Atkinson, 1982)
Propensity-Biased Allocation

Algorithm

1. Before assigning subject $i$ to a group, model treatment allocation among first $i - 1$ units (i.e., logistic regression)

2. Let $p_i = \hat{p}(x_i)$ be the fitted probability of treatment for unit $i$ using the model from (1)

3. Assign subject $i$ to treatment with probability

$$\pi(p_i; k) = 0.5 + 0.5(1 - 2p_i)^{1/k}$$

where $k$ is the ratio of two positive odd integers

4. Repeat for subject $i + 1$, modeling treatment allocation among first $i$ units
Propensity-Biased Allocation
Balancing parameter

Treatment probability \( \pi(p; k) = 0.5 + 0.5(1 - 2p)^{1/k} \)

- For large values of \( k \), \( \pi \) favors covariate balance over randomization
- As \( k \to \infty \),
  \[ \pi(p; k) \to \begin{cases} 
    1, & p < 0.5 \\
    0.5, & p = 0.5 \\
    0, & p > 0.5 
  \end{cases} \]
- As \( k \to 0 \),
  \[ \pi(p; k) \to \begin{cases} 
    1, & p = 0 \\
    0.5, & 0 < p < 1 \\
    0, & p = 1 
  \end{cases} \]
Propensity-Biased Allocation

Balancing parameter

![Graph showing fitted propensity score and treatment assignment probability for different values of k. The graph includes lines for k = 5, k = 3, k = 5/3, k = 3/5, k = 1/3, and k = 1/5. The x-axis represents fitted propensity score, and the y-axis represents treatment assignment probability.]
Propensity-Biased Allocation

Comparison of methods

<table>
<thead>
<tr>
<th>Procedure</th>
<th>DISC</th>
<th>LIN</th>
<th>DET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covariate-adaptive biased coin Urn</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Approx variance minimization</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Minimum likelihood allocation</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>$D_A$-optimality</td>
<td></td>
<td>X</td>
<td>possible</td>
</tr>
<tr>
<td>PBA</td>
<td></td>
<td></td>
<td>possible</td>
</tr>
</tbody>
</table>

**DISC** = Discrete covariates; **LIN** = linear outcome model; **DET** = deterministic allocation.
Simulations
Methodology

Simulated 1000 samples of 200 units each. Each unit consisted of three mutually independent standard normal covariates.

- Pure randomization (RAND)
- Urn design with 2 (U2) and 3 (U3) strata per covariate
- Approximate variance minimization with two strata per covariate (APP)
- Minimum likelihood allocation (MLA)
- $D_A$-optimality with deterministic (OPT) and random (OPTRAND) assignment
- PBA with $k = 1$ (PBA1), $k = 3$ (PBA3), $k = 5$ (PBA5), and deterministic assignment (PBAINF)

For all methods but the urn design, a burn-in of 20 randomly assigned units was used.
Empirical 95% intervals for fitted propensity scores.
## Simulations

### Balance

Global and marginal balance.

<table>
<thead>
<tr>
<th>Method</th>
<th>$\text{range}(\sum t_i)$</th>
<th>$\text{sd}(\bar{x}_1^{(1)} - \bar{x}_1^{(0)})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAND</td>
<td>76 - 125</td>
<td>0.1391</td>
</tr>
<tr>
<td>U2</td>
<td>87 - 113</td>
<td>0.1067</td>
</tr>
<tr>
<td>U3</td>
<td>87 - 112</td>
<td>0.0959</td>
</tr>
<tr>
<td>PBA1</td>
<td>87 - 111</td>
<td>0.0834</td>
</tr>
<tr>
<td>OPTRAND</td>
<td>90 - 111</td>
<td>0.0647</td>
</tr>
<tr>
<td>PBA3</td>
<td>94 - 105</td>
<td>0.0375</td>
</tr>
<tr>
<td>PBA5</td>
<td>96 - 104</td>
<td>0.0274</td>
</tr>
<tr>
<td>PBA-INF</td>
<td>99 - 102</td>
<td>0.0134</td>
</tr>
<tr>
<td>MLA</td>
<td>99 - 102</td>
<td>0.0134</td>
</tr>
<tr>
<td>OPT</td>
<td>99 - 102</td>
<td>0.0133</td>
</tr>
<tr>
<td>APP</td>
<td>98 - 102</td>
<td>0.0131</td>
</tr>
</tbody>
</table>
Simulations
Loss function

薏 Atkinson (1999) and other authors taking a design-based approach (e.g., Atkinson 1982, Begg and Iglewicz 1980) use the loss function as a measure of assignment efficiency.

薏 Assuming the linear model \( Y = \beta X + \delta Z + \epsilon \), where \( Z = 2T - 1 \),

\[
\text{Var}(\hat{\delta}) = \frac{\sigma^2}{n - z^T X (X^T X)^{-1} X^T z}
\]

薏 The loss function after \( n \) allocations is then

\[
\mathcal{L}_n = z^T X (X^T X)^{-1} X^T z
\]

which can be interpreted as the number of units “lost” due to inefficiencies in treatment allocation.
Simulations

Average loss curves over 1000 simulations.
Simulations

Selection bias

- Selection bias measures the “predictability” of treatment assignments

- The proportion of correct guesses one would make having chosen the most likely treatment each time:

\[ S_n = n^{-1} \sum_{i=1}^{n} \frac{|\pi_i - 0.5|}{0.5} \]

where \( \pi_i = P(T_i = 1 \mid X_i, T_{i-1}, X_{i-1}) \)

(Heritier et al., 2005)
Simulations

Average selection bias curves

Average selection bias curves over 1000 simulations.
Study Details

Study: Pilot study to determine effect of diabetes prevention counseling on weight loss (Tsai et al., 2010)

- 50 subjects enrolled in study: 24 treated, 26 control by pure randomization
- Fourteen baseline variables measured
  - Race: 40 African American, 10 white
  - Correlations ranged from -0.53 to 0.95 (Q1: -0.12; Q3: 0.15)
  - $L_{50} = 10.25$
Average loss curves over 1000 simulations.
Application

Loss boxplots

Boxplots of $\mathcal{L}_{50}$. 
Conclusion
Propensity-Biased Allocation

- PBA is a flexible, easy to implement method for balancing covariates in a study with staggered entry
- Makes no assumptions about covariate structure or outcome model
- Comparable to $D_A$-optimal allocation in reducing loss
- Allows for trade off between covariate imbalance and selection bias on a case-by-case basis
Conclusion
Extensions and generalizations

▶ Choose to include/ exclude covariates throughout the trial (Aickin, 2001)

▶ Add time covariate to balance treatment through recruitment window (discussion following Atkinson, 1999)

▶ Other (nonparametric) propensity score models

▶ Adjust $k$ throughout trial: larger $k$ at start, relax restrictions as substantial imbalance becomes less of a concern
References