Marginal effects for time-fixed treatments: model construction and checking

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Session goals

- How can we fit a propensity score?
- How can we check balance?
- How can we fit an ATE or ATT?

Road map

1. Fitting a propensity score

- ▶ Logistic regression
- ► Checking balance
- ► Alternatives to logistic regression

2. Fitting an ATE

- ► Traditional regression (G-computation)
- ▶ PS stratification
- PS matching
- ▶ PS regression
- inverse probability of treatment weighting

3. Fitting an ATT

- ▶ PS matching
- inverse probability of treatment weighting

Recall: Average Potential Outcomes

The *causal* (unconfounded) *effect* of exposure Z on outcome Y is a measure of how much Y changes as Z is manipulated.

- Here *Z* is not treated as a random variable, but a manipulable quantity that may influence *Y*.
- Other variables (confounders), *X*, may also influence *Y*.
- Y(z) denotes the outcome if the exposure Z is set equal to z:
 - ightharpoonup Y(z) is termed a counterfactual or potential outcome.
- A causal quantity of interest is then

$$\mathbb{E}[Y(\mathbf{z})] = \int y f_{Y(\mathbf{z}),X}(y,x) \, \mathrm{d}y \mathrm{d}x$$

that is, an average potential outcome (APO).

Recall: Aim

Estimate $\mathbb{E}[Y(z)]$ using a random sample of data

$$(x_i, z_i, y_i), i = 1, \ldots, n$$

for z in the set of values $\{0, 1\}$.

Confounder balance

- In PS-based methods, the goal of the treatment model is to eliminate imbalance in the distribution of covariates between treatment and untreated subjects.
 - Achieving balance on other covariates (particularly strong predictors of treatment) is unhelpful.
- The goal is *not* to build an excellent predictive model for the treatment.
- Some methods to avoid:
 - ► C-statistic (AUC),
 - significance tests.

Confounder balance

Common measures of balance:

• Standardized mean difference or proportion:

$$\frac{\bar{x}^{1,w} - \bar{x}^{0,w}}{\sqrt{0.5(v^{1,w} + v^{0,w})}}$$

where $\bar{x}^{z,w} = \frac{1}{n} \sum_{i=1}^{n} \frac{\mathbb{1}_{z(Z_i)X_i}}{f_{Z|X}^{\mathcal{O}}(Z_i|X_i)}$, i.e. the weighted sample mean of variable X among those with treatment value z, and similarly $v^{z,w}$ is the weighted variance estimate.

- ► For all methods of analysis other than IPW, the weights are taken to be 1 for all subjects.
- ▶ SMD of 0.1 or less typically considered reasonable.
- Visual examination of weighted empirical CDFs among the treated and untreated (for binary or categorical treatment).

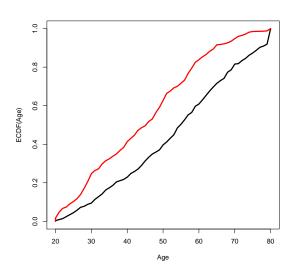
- In this example, we will explore propensity score based analyses using the publicly available (U.S.) National Health and Nutrition Examination Survey (NHANES). For this, I installed NHANES, tableone, and Matching in R.
- We will focus our analysis on the question of whether currently smoking affects average systolic blood pressure. The variables we will need are: BPSysAve, SmokeNow, Gender, Age, Race3, Education, MaritalStatus, and Poverty where the first two are the outcome and exposure of interest and the remaining are potential confounders.
- Additionally, we will restrict our attention to adults (> 17 years old) in the second wave of the survey.

```
> library(NHANES)
> library(tableone)
> library(Matching)
>
> NHANES$SmokeNow <- as.numeric(NHANES$SmokeNow)-1</p>
> small.nhanes <- na.omit(NHANES[NHANES$SurveyYr=="2011_12"
    & NHANES$Age > 17,c(3,4,8:11,13,25,61)])
> dim(small.nhanes) ## 1377
>
> vars <- c("Gender", "Age", "Race3", "Education",
    "MaritalStatus", "Poverty")
> tabUnmatched <- CreateTableOne(vars = vars,
    strata = "SmokeNow", data = small.nhanes,
    test = FALSE)
```

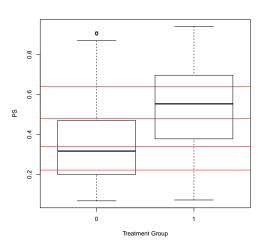
>	print(tabUnmatched	, smd =	TRUE)			
		Stratif	ied by	SmokeNo	W	
		0		1		SMD
	n	782		595		
	<pre>Gender = male (%)</pre>	432	(55.2)	369	(62.0)	0.138
	Age (mean (sd))	54.33	(16.52)	44.96	(15.11)	0.592
	Race3 (%)					0.31
	Asian	25	(3.2)	15	(2.5)	
	Black	43	(5.5)	64	(10.8)	
	Hispanic	26	(3.3)	38	(6.4)	
	Mexican	45	(5.8)	35	(5.9)	
	White	630	(80.6)	416	(69.9)	
	Other	13	(1.7)	27	(4.5)	

Education (%)					0.512
8th Grade	59	(7.5)	33	(5.5)	
9 - 11th Grade	71	(9.1)	120	(20.2)	
High School	152	(19.4)	151	(25.4)	
Some College	256	(32.7)	210	(35.3)	
College Grad	244	(31.2)	81	(13.6)	
MaritalStatus (%)					0.488
Divorced	85	(10.9)	77	(12.9)	
LivePartner	61	(7.8)	96	(16.1)	
Married	453	(57.9)	240	(40.3)	
NeverMarried	108	(13.8)	142	(23.9)	
Separated	6	(0.8)	14	(2.4)	
Widowed	69	(8.8)	26	(4.4)	
Poverty (mean (sd))	3.11	(1.65)	2.38	(1.58)	0.453

Assessing balance – original sample eCDFs in smokers and non-smokers for age:



Assessing overlap – boxplots of propensity scores estimated via logistic regression by treatment group (red lines indicate quintiles of the estimated PS distribution):

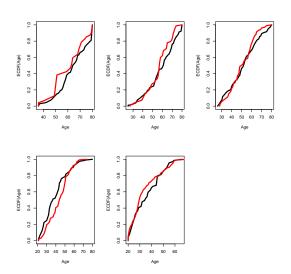


The overlap is a bit better than the boxplots suggest:

We can therefore proceed to check for balance knowing we have sufficient numbers of smokers and non-smokers in each quintile to ensure the stratum-specific estimates are not too unstable.

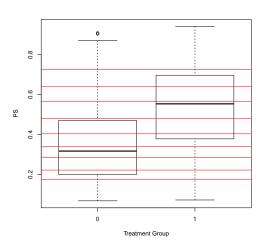
Table 1. Standardized mean differences: NHANES.										
Var.	PS Quintiles									
	Orig. Q1 Q2 Q3 Q4 Q5									
Gender	0.138	0.102	0.104	0.029	0.200	0.031				
Age	0.592	0.257	0.171	0.099	0.311	0.164				
Race	0.315	0.317	0.112	0.344	0.415	0.287				
Educ.	0.512	0.538	0.417	0.280	0.238	0.302				
Marital	0.488	0.432	0.239	0.272	0.233	0.261				
Poverty	0.453	0.087	0.126	0.114	0.004	0.146				

Assessing balance – eCDFs within quintiles of PS in smokers and non-smokers for age:



- Balance does not appear to have been achieved:
 - ► SMDs > 0.1 for at least three quintiles for all variables.
 - ► The empirical CDFs of age do not overlap in several quintiles.
- Should we try for finer strata?

Assessing overlap – boxplots of propensity scores estimated via logistic regression by treatment group (red lines indicate *deciles* of the estimated PS distribution):



First decile has 20 smokers: still reasonable overlap.

```
Is balance improved?
```

Most variables still showing significant imbalance. What if we were to use the PS in another way?

0.01194 0.12220 0.31360 0.31570 0.47980 0.78460

Let's look at matching and IPW.

match.out=ps.lr.match)

```
> ps.lr.match <- Match(Tr=small.nhanes$SmokeNow,
      X=small.nhanes$ps.lr,estimand="ATE",ties=FALSE)
> matched.samp <- small.nhanes[c(ps.lr.match$index.control,
      ps.lr.match$index.treated),]
> table(table(c(ps.lr.match$index.control,
     ps.lr.match$index.treated)))
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 851 246 131 47 42 18 7 5 2 4 5 4 3 3 5
>
> tabMatched <- CreateTableOne(vars = vars, strata = "SmokeNow",</pre>
      data = matched.samp, test = FALSE)
> MatchBalance(SmokeNow~Gender+Age+Race3+Education+
      MaritalStatus+HHIncome+Poverty, data=small.nhanes,
```

The function MatchBalance from the Matching library provides many more details than CreateTableOne, including:

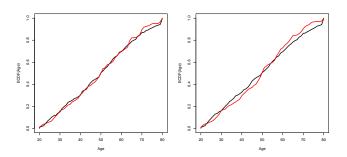
- mean, median, and maximum difference in empirical CDF plots,
- mean, median, and maximum difference in empirical QQ plots,
- Kolmogorov-Smirnov statistics,
- ratio of variances,
- p-value for t-test.
- Note that SMDs are $\times 100$.
- > temp0 <- Ecdf(matched.samp\$Age[matched.samp\$SmokeNow==0])</pre>
- > temp1 <- Ecdf(matched.samp\$Age[matched.samp\$SmokeNow==1])</pre>
- > lines(temp1\$x,temp1\$y,col="red",lwd=3)

```
> ps.lr.weight <- small.nhanes$SmokeNow/ps.lr +
     (1-small.nhanes$SmokeNow)/(1-ps.lr)
>
> nhanes.IPW.lr <- svydesign(ids=~0, data=small.nhanes,</pre>
     weights=ps.lr.weight)
> tabIPW <- svyCreateTableOne(vars = vars, strata = "SmokeNow",</pre>
     data = nhanes.IPW.lr, test = FALSE)
> print(tabIPW, smd = TRUE)
>
> temp0 <- Ecdf(small.nhanes$Age[small.nhanes$SmokeNow==0],</pre>
     weights=ps.lr.weight[small.nhanes$SmokeNow==0])
> temp1 <- Ecdf(small.nhanes$Age[small.nhanes$SmokeNow==1],</pre>
     weights=ps.lr.weight[small.nhanes$SmokeNow==1])
> plot(temp0$x,temp0$y,ylab="ECDF(Age)",xlab="Age",main="",
     type="1", lwd=3)
> lines(temp1$x,temp1$y,col="red",lwd=3)
```

Table 1, con't. Standardized mean differences: NHANES.

,									
PS Quintiles									
Orig.	Q1	Q2	Q3	Q4	Q5	Match	IPW		
0.138	0.102	0.104	0.029	0.200	0.031	0.006	0.023		
0.592	0.257	0.171	0.099	0.311	0.164	0.002	0.014		
0.315	0.317	0.112	0.344	0.415	0.287	0.120	0.052		
0.512	0.538	0.417	0.280	0.238	0.302	0.133	0.029		
0.488	0.432	0.239	0.272	0.233	0.261	0.094	0.023		
0.453	0.087	0.126	0.114	0.004	0.146	0.049	0.000		
	Orig. 0.138 0.592 0.315 0.512 0.488	Orig. Q1 0.138 0.102 0.592 0.257 0.315 0.317 0.512 0.538 0.488 0.432	Orig. Q1 Q2 0.138 0.102 0.104 0.592 0.257 0.171 0.315 0.317 0.112 0.512 0.538 0.417 0.488 0.432 0.239	Orig. Q1 Q2 Q3 0.138 0.102 0.104 0.029 0.592 0.257 0.171 0.099 0.315 0.317 0.112 0.344 0.512 0.538 0.417 0.280 0.488 0.432 0.239 0.272	PS Quintiles Orig. Q1 Q2 Q3 Q4 0.138 0.102 0.104 0.029 0.200 0.592 0.257 0.171 0.099 0.311 0.315 0.317 0.112 0.344 0.415 0.512 0.538 0.417 0.280 0.238 0.488 0.432 0.239 0.272 0.233	PS Quintiles Orig. Q1 Q2 Q3 Q4 Q5 0.138 0.102 0.104 0.029 0.200 0.031 0.592 0.257 0.171 0.099 0.311 0.164 0.315 0.317 0.112 0.344 0.415 0.287 0.512 0.538 0.417 0.280 0.238 0.302 0.488 0.432 0.239 0.272 0.233 0.261	Orig. Q1 Q2 Q3 Q4 Q5 Match 0.138 0.102 0.104 0.029 0.200 0.031 0.006 0.592 0.257 0.171 0.099 0.311 0.164 0.002 0.315 0.317 0.112 0.344 0.415 0.287 0.120 0.512 0.538 0.417 0.280 0.238 0.302 0.133 0.488 0.432 0.239 0.272 0.233 0.261 0.094		

Assessing balance – eCDFs in smokers and non-smokers for age, matched and IPW:



Assessing balance: alternative PS fits

Some authors have argued in favour of more complex or flexible methods of estimating the PS. Ridgeway and McCaffrey (2007), for example, recommend generalized boosted models (GBM):

Let us check balance and overlap using this fit.

Using GBM: boxplots of propensity scores estimated via logistic regression by treatment group (red lines indicate quintiles of the estimated PS distribution, 1st quintile has 17 smokers):

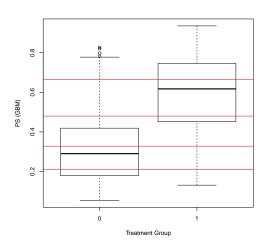


Table 2. Standardized mean differences using PS estimated by GBM.

					0		,		
Var.	PS Quintiles								
	Orig.	Q1	Q2	Q3	Q4	Q5	Match	IPW	
Gender	0.138	0.040	0.168	0.055	0.262	0.109	0.108	0.065	
Age	0.592	0.027	0.450	0.258	0.301	0.142	0.211	0.168	
Race	0.315	0.512	0.434	0.166	0.308	0.693	0.304	0.116	
Educ.	0.512	0.576	0.267	0.369	0.440	0.702	0.253	0.153	
Marital	0.488	0.716	0.682	0.652	0.323	0.499	0.144	0.156	
Poverty	0.453	0.372	0.118	0.193	0.556	0.099	0.237	0.096	

Balance is noticeably worse than under a PS estimated by logistic regression.

Assessing balance: alternative PS fits

We shall try one additional approach, Super Learning (SL):

Let us again check balance and overlap using this fit.

Using SL: boxplots of propensity scores estimated via logistic regression by treatment group (red lines indicate quintiles of the estimated PS distribution):

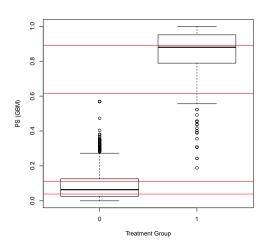


Table 3. Standardized mean differences using PS estimated by SL.

PS Quintiles									
Orig.	Q1	Q5	Match	IPW					
0.138	-	-	0.539	-	-	1.123	0.116		
0.592	-	-	0.507	-	-	0.174	0.488		
0.315	-	-	1.061	-	-	0.131	0.249		
0.512	-	-	1.142	-	-	1.551	0.408		
0.488	-	-	0.789	-	-	0.218	0.382		
0.453	-	-	1.719	-	-	0.004	0.293		
	0.138 0.592 0.315 0.512 0.488	0.138 - 0.592 - 0.315 - 0.512 - 0.488 -	Orig. Q1 Q2 0.138 0.592 0.315 0.512 0.488	Orig. Q1 Q2 Q3 0.138 - - 0.539 0.592 - - 0.507 0.315 - - 1.061 0.512 - - 1.142 0.488 - - 0.789	Orig. Q1 Q2 Q3 Q4 0.138 - - 0.539 - 0.592 - - 0.507 - 0.315 - - 1.061 - 0.512 - - 1.142 - 0.488 - - 0.789 -	Orig. Q1 Q2 Q3 Q4 Q5 0.138 - - 0.539 - - 0.592 - - 0.507 - - 0.315 - - 1.061 - - 0.512 - 1.142 - - 0.488 - - 0.789 - -	Orig. Q1 Q2 Q3 Q4 Q5 Match 0.138 - - 0.539 - - 1.123 0.592 - - 0.507 - - 0.174 0.315 - - 1.061 - - 0.131 0.512 - - 1.142 - - 1.551 0.488 - - 0.789 - - 0.218		

Assessing balance: summary

Key ideas:

- Creating or restoring confounder balance is essential to estimating a causal effect.
- It can be hard to assess overlap or achieve balance in high dimensions.
- The propensity score, a scalar summary of confounding variables, simplifies this task.
- However:
 - fitting a model for treatment does not guarantee balance,
 - fitting a model that predicts treatment with a high degree of precision can be unhelpful.

Estimating the ATE

Let's proceed now to estimating the ATE, using:

- outcome regression,
- PS stratification,
- PS matching,
- PS regression,
- IPW.

We will use the PS estimated via logistic regression, as this provided the best balance.

Linear regression

Let us first look at regression coefficients:

The naive conditional effect estimate is more than 3 times greater than its condounder-adjusted counterpart.

ATE: outcome regression

Now let's use the regression to obtain the ATE:

```
> nhanes.allsmoke <- small.nhanes</pre>
> nhanes.allsmoke$SmokeNow <- 1</pre>
> nhanes.nosmoke <- small.nhanes</pre>
> nhanes.nosmoke$SmokeNow <- 0</pre>
> mod1.lm <- lm(BPSysAve~SmokeNow+Gender+Age+Race3+
      Education+MaritalStatus+HHIncome+Poverty,
      data=small.nhanes)
> APO.lm.1 <- mean(predict(mod1.lm,nhanes.allsmoke))</pre>
> APO.lm.0 <- mean(predict(mod1.lm,nhanes.nosmoke))</pre>
> APO.lm.1 - APO.lm.0
[1] -1.097768
```

Conditional and marginal effect are the same in a linear model with no interaction!

ATE: outcome regression

With interactions:

ATE: PS stratification

```
> ps.lr.quints <- cut(ps.lr,quints,labels=1:5)</pre>
> p.strat <- table(ps.lr.quints)/length(ps.lr.quints)</pre>
> p.strat
ps.lr.quints
                             3
0.2018882 0.2004357 0.1975309 0.2018882 0.1982571
> ATE.strat <- rep(NA,5)
> for(j in 1:5) {
    ATE.strat[i] <-
       mean(BPSysAve[SmokeNow == 1 & ps.lr.quints==j]) -
      mean(BPSysAve[SmokeNow == 0 & ps.lr.quints==j])
  }
> ATE.strat
[1] -8.1736207 -2.2701785 -0.2062732 -1.1820287 2.8633845
> sum(ATE.strat*p.strat)
[1] -1.816879
```

ATE: PS matching

```
> ps.lr.match <- Match(Tr=small.nhanes$SmokeNow,
     X=small.nhanes$ps.lr,estimand="ATE",ties=FALSE)
> matched.samp <- small.nhanes[c(ps.lr.match$index.control,
     ps.lr.match$index.treated),]
> dim(matched.samp)
[1] 2754
         13
> mean(matched.samp$BPSysAve[matched.samp$SmokeNow == 1]) -
   mean(matched.samp$BPSysAve[matched.samp$SmokeNow == 0])
[1] -0.4705882
```

ATE: PS regression

```
> mod1.PSlm1 <- lm(BPSysAve~SmokeNow+ps.lr,data=small.nhanes)</pre>
> APO.PSlm1.1 <- mean(predict(mod1.PSlm1,nhanes.allsmoke))</pre>
> APO.PSlm1.0 <- mean(predict(mod1.PSlm1,nhanes.nosmoke))</pre>
> APO.PSlm1.1 - APO.PSlm1.0
[1] -1.10791
> mod1.PSlm2 <- lm(BPSysAve~SmokeNow+ps.lr+I(ps.lr^2),
     data=small.nhanes)
> APO.PSlm2.1 <- mean(predict(mod1.PSlm2,nhanes.allsmoke))</pre>
> APO.PSlm2.0 <- mean(predict(mod1.PSlm2,nhanes.nosmoke))</pre>
> APO.PSlm2.1 - APO.PSlm2.0
\lceil 1 \rceil - 1.110337
> mod1.PSlm3 <- lm(BPSysAve~SmokeNow+bs(ps.lr,df=4),</pre>
     data=small.nhanes)
> APO.PSlm3.1 <- mean(predict(mod1.PSlm3,nhanes.allsmoke))</pre>
> APO.PSlm3.0 <- mean(predict(mod1.PSlm3,nhanes.nosmoke))</pre>
> APO.PSlm3.1 - APO.PSlm3.0
[1] -1.133493
```

ATE: IPW

Table 4. Balance and ATE: a comparison across approaches.

	Outcome reg.	PS quints.	PS match	PS reg.	IPW
Max SMD	-	0.538	0.133		0.052
Mean SMD	_	0.221	0.067	_	0.024
Med. SMD	_	0.236	0.007	_	0.021
	_1 ∩98			_1 133	
ATE	-1.098	-1.817	-0.471	-1.133	-1.929

ATT: PS matching

For the ATT, we simply need to ensure that only the *exposed* our matched. This will, of course, reduce the sample size.

```
> matched.ATT <- Match(Y=small.nhanes$BPSysAve,
     Tr=small.nhanes$SmokeNow,X=ps.lr,
     estimand = "ATT", ties=FALSE)
> matched.samp.ATT <-
       small.nhanes[c(matched.ATT$index.control,
      matched.ATT$index.treated),]
> dim(matched.samp.ATT)
Γ1] 1190
         13
> mean(BPSysAve[SmokeNow == 1], data=matched.samp.ATT) -
   mean(BPSysAve[SmokeNow == 0], data=matched.samp.ATT)
Γ1 0.6756303
```

ATT: PS matching

Alternatively, we can estimate the ATT by re-weighting only the *unexposed* individuals by Pr(Z = 1|x)/Pr(Z = 0|x):

```
> ATT.lr.weight <- small.nhanes$SmokeNow +
          (1-small.nhanes$SmokeNow)*ps.lr/(1-ps.lr)
> mean(SmokeNow*BPSysAve*ATT.lr.weight) -
          mean((1-SmokeNow)*BPSysAve*ATT.lr.weight)
[1] -0.3895692
```

Note that the estimated ATT under IPW is in the same direction as for the estimated ATE using all methods. The ATT has the opposite sign, and estimates vary considerably from one analysis to another (0.24-1.28).

Table 5. SMDs for estimation of the ATT.

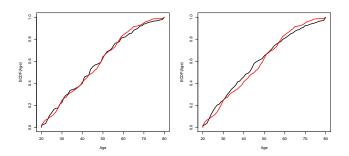
Var.	Orig.	Match	IPW
Gender	0.138	0.110	0.016
Age	0.592	0.002	0.031
Race	0.315	0.158	0.110
Educ.	0.512	0.067	0.065
Marital	0.488	0.192	0.034
Poverty	0.453	0.064	0.006

Note that only the untreated are weighted:

```
> print(ATT.IPW, smd = TRUE)
                    Stratified by SmokeNow
                    0
                                                 SMD
                                    595.0
                     597.0
 n
                     365.4 (61.2) 369.0 (62.0)
                                                  0.016
 Gender = male (%)
                     44.46 (16.35) 44.96 (15.11)
 Age (mean (sd))
                                                  0.031
 Race3 (%)
                                                  0.110
                      15.4 ( 2.6)
                                     15.0 (2.5)
    Asian
                      76.0 (12.7)
                                     64.0 (10.8)
    Black
                      49.5 (8.3)
                                     38.0 (6.4)
    Hispanic
                      36.2 (6.1)
                                     35.0 (5.9)
    Mexican
    White
                      389.8 (65.3)
                                    416.0 (69.9)
    Other
                      30.0 (5.0)
                                     27.0 (4.5)
```

Education (%)					0.065
8th Grade	30.4	(5.1)	33.0	(5.5)	
9 - 11th Grade	113.6	(19.0)	120.0	(20.2)	
High School	141.9	(23.8)	151.0	(25.4)	
Some College	226.7	(38.0)	210.0	(35.3)	
College Grad	84.4	(14.1)	81.0	(13.6)	
MaritalStatus (%)					0.034
Divorced	76.0	(12.7)	77.0	(12.9)	
LivePartner	93.6	(15.7)	96.0	(16.1)	
Married	242.0	(40.5)	240.0	(40.3)	
NeverMarried	141.9	(23.8)	142.0	(23.9)	
Separated	17.1	(2.9)	14.0	(2.4)	
Widowed	26.4	(4.4)	26.0	(4.4)	
Poverty (mean (sd))	2.39	(1.60)	2.38	(1.58)	0.006

Assessing balance – eCDFs in smokers and non-smokers for age, matched and IPW:



Estimating the ATE (ATT): summary

Key ideas:

- From a coding perspective, all approaches to estimating the ATE are straightforward.
- All approaches are not, however, equally likely to satisfy the assumption of correct model specification.
- Using a PS, it is much easier to assess balance prior to computing the ATE.
- How the PS is then used in the analysis should be carefully considered and cannot be judged based on concordance between observed estimates, as all are subject to differing degrees of variability and bias.

Additional considerations: SEs and CIs

- All of the PS approaches considered rely on substitution estimators.
 - ▶ In PS regression, we plug in an estimated PS as a covariate.
 - ▶ In IPW, we plug in estimated weights.
- We need to account for this when estimating standard errors and/or confidence intervals.
- Analytically derived asymptotic variances can be used, but are not provided in many standard software packages.
- The easiest approach is to bootstrap.
- Note, however, that the bootstrap is *not* valid for matching.

Additional considerations: missing data

- If data are missing, one can either impute or (if only missing the outcome but not covariates), "censor" the individual.
- Censored data can easily be handled by incorporating weights for censoring into estimator or the regression model for any of the approaches that we have considered.

Key points: Summary

- In a real-data setting, caution must be taken to ensure balance is acheived.
- Model choices should be based on subject-matter knowledge to the greatest extent possible.
- Many subtle and not-so-subtle issues remain, and must be accounted for carefully.