# 500 Homeworks 3 and 4 Answer Sketch

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# 1 Homework 3 Tasks

#### 1.0.1 Preliminaries

```
knitr::opts_chunk$set(comment=NA)

library(Hmisc)
library(tableone)
library(Matching)
library(twang)
```

```
library(cobalt)
library(broom)
library(survival)
library(arm)
library(tidyverse)

canc3 <- read.csv("canc3.csv") %>% tbl_df
```

#### 1.0.2 The Data

The canc3.csv data file is available at our Assignments page.

We have completed the data collection in a study of 400 subjects with cancer, where 150 have received an intervention, while the remaining 250 received usual care control. The primary aims of the study are to learn about the impact of the intervention on patient survival and whether or not the patient enters hospice.

#### 1.0.3 The Codebook

The data file includes 400 observations, on 12 variables. All values are measured at baseline except for the two outcomes: alive and hospice.

Variable	Description	Notes
id	Study ID #	1-250 control, 251-400 intervention
treated	Treatment status	1 = intervention, 0 = control
age	Age at study entry	range is 34-93 years
female	Sex	1 = female  (n = 258), 0 = male  (n = 142)
race	Race	1 = caucasian/white  (n = 317), 0 = not  (n = 83)
married	Marital status	1 = married  (n = 245), 0 = not  (n = 155)
typeca	Cancer type	1 = GI/colorectal (n = 177), 2 = Lung (n =
		129), $3 = GYN (n = 94)$
stprob	5-year survival	Model probability, based on type and stage of
	probability	cancer (range: $0.01, 0.72$ )
charlson	Charlson Comorbidity	Total score: higher indicates greater comorbidity
	index	(observed range: 0-7)
ecog	ECOG functional status	0 = fully active  (n = 155), 1 = restricted re:
		physically strenuous activity $(n = 201), 2 =$
		ambulatory, can self-care, otherwise limited ( $n =$
		31), $3 = \text{capable of only limited self-care } (n =$
		13)
alive	Alive at study conclusion	1 = alive  (n = 245), 0 = dead  (n = 155)
hospice	Entered hospice during study	1 = hospice  (n = 143), 0 = no hospice  (n = 257)

Note: In the answer sketch, I plan to treat ecog and typeca as categorical and charlson as quantitative.

#### 1.0.4 Data Management and Creation of New Formats

- For **binary** outcomes and treatments, we want both numerical (0/1) and factor (with meaningful names) versions, so that includes treatment status [in canc3, this is treated] or binary outcomes [in canc3, this includes alive and hospice]. For other binary variables (for instance, representing covariates), all we really need are the numeric (0/1) variables we already have, although I'll use a better name for race, so I can indicate what 1 means there.
- For categorical variables with more than two categories, we want factor (with meaningful names, especially for unordered categories) versions of the variable [in canc3, these are typeca and ecog], and we may also eventually need a series of numeric (0/1) indicators to represent the individual categories.
- For quantitative variables [in canc3, these will be age, stprob and charlson assuming that you, like me, are willing to treat charlson as quantitative], we just want the numerical representations we already have.

canc3

	#	Α	tibble:	400	х	12
--	---	---	---------	-----	---	----

	subject	treated	age	female	race	married	typeca	stprob	charlson	ecog	alive
	<int></int>	<dbl></dbl>	<int></int>	<int></int>	<int></int>						
1	1	0	59	1	1	1	1	0.07	1	3	1
2	2	0	58	1	1	1	3	0.16	0	0	1
3	3	0	71	1	1	1	3	0.72	1	0	1
4	4	0	64	0	1	1	2	0.16	1	2	1
5	5	0	56	1	1	1	1	0.07	0	1	1
6	6	0	79	0	1	1	1	0.09	0	0	1
7	7	0	69	0	1	1	2	0.16	1	0	1
8	8	0	62	0	1	1	1	0.07	0	0	1
9	9	0	71	0	1	1	1	0.07	1	1	1
10	10	0	52	1	0	0	1	0.07	1	0	0

# ... with 390 more rows, and 1 more variable: hospice <int>

So, our primary cleanup task will be to create factor versions of five of the variables (specifically, treated, alive and hospice on the binary side and typeca and ecog on the multi-categorical side), and numeric indicator variables for the multi-categorical variables, while the remaining variables can stay as they are.

```
treatment group = fct_relevel(treated f, "Intervention"),
alive f = factor(alive, levels = c(0,1),
                 labels = c("Dead", "Alive")),
hospice f = factor(hospice, levels = c(0, 1),
                   labels = c("No Hospice", "Hospice")),
caucasian = race,
typeca GI = as.numeric(typeca == 1),
typeca_Lung = as.numeric(typeca == 2),
typeca GYN = as.numeric(typeca == 3),
ecog = factor(ecog),
ecog_0 = as.numeric(ecog == 0),
ecog 1 = as.numeric(ecog == 1),
ecog 2 = as.numeric(ecog == 2),
ecog 3 = as.numeric(ecog == 3),
typeca = factor(typeca, levels = c(1, 2, 3),
                labels = c("GI/colorectal", "Lung", "GYN"))
```

#### 1.0.5 Table 1 to Check Results

I'll build a simple Table 1, without p values, to look over the results. We could easily leave off the two outcomes, but I'll keep them in for now.

```
Stratified by treatment_group
                         Intervention Control
                                          250
                           150
age (mean (SD))
                         63.76 (10.87) 62.56 (11.26)
female = 1 (\%)
                            93 (62.0)
                                         165 (66.0)
caucasian = 1 (\%)
                           109 (72.7)
                                         208 (83.2)
married = 1 (\%)
                            83 (55.3)
                                         162 (64.8)
typeca (%)
   GI/colorectal
                            68 (45.3)
                                         109 (43.6)
                            64 (42.7)
                                          65 (26.0)
   Lung
   GYN
                            18 (12.0)
                                          76 (30.4)
ecog (%)
   0
                            52 (34.7)
                                         103 (41.2)
   1
                            85 (56.7)
                                         116 (46.4)
```

```
2 9 (6.0) 22 (8.8)

3 4 (2.7) 9 (3.6)

alive_f = Alive (%) 82 (54.7) 163 (65.2)

hospice_f = Hospice (%) 62 (41.3) 81 (32.4)

rm(varlist, factorlist)
```

Everything looks reasonable to me.

#### 1.1 Task 1

Ignoring the covariate information, provide an appropriate (unadjusted) estimate (with point estimate and 95% confidence interval) of the effect of the intervention on each of the two binary outcomes; first survival, and then hospice entry. Be sure to describe the effect in English sentences, so that both the direction and magnitude are clear, and also be sure to specify the method you used in generating your estimates.

#### 1.1.1 Unadjusted Logistic Regression Model for Survival

We can obtain the odds ratio estimate uses logistic regression:

```
unadj.alive <- glm(alive ~ treated_f, data=canc3, family=binomial)</pre>
display(unadj.alive)
glm(formula = alive ~ treated f, family = binomial, data = canc3)
                      coef.est coef.se
                                 0.13
(Intercept)
                       0.63
treated_fIntervention -0.44
                                 0.21
  n = 400, k = 2
  residual deviance = 529.7, null deviance = 534.1 (difference = 4.4)
exp(coef(unadj.alive)) # odds ratio estimate
          (Intercept) treated fIntervention
            1.8735632
                                   0.6436305
exp(confint(unadj.alive)) # 95% CI for odds ratio
Waiting for profiling to be done...
                          2.5 %
                                    97.5 %
(Intercept)
                      1.4487048 2.4397580
treated_fIntervention 0.4252576 0.9733951
```

We have an odds ratio estimate for the intervention's impact on survival of **0.64** with 95% CI of (0.43, 0.97). This is just barely statistically significant at the 5% level.

### 1.1.2 Unadjusted logistic regression model for the hospice outcome

Waiting for profiling to be done...

```
2.5 % 97.5 % (Intercept) 0.3660984 0.6223179 treated fIntervention 0.9658958 2.2362360
```

Either way, we have an odds ratio estimate for the intervention's impact on hospice of 1.47 with 95% CI of (0.97, 2.24). So the odds of going to hospice are 1.47 times as large for intervention patients as compared to control patients. The confidence interval does include 1, so we cannot claim statistical significance (at a 5% significance level) in this unadjusted analysis for hospice.

#### 1.1.3 Final Answers for Task 1

Unadjusted Analyses Comparing the Intervention Group to the Control Group...

Outcome	Odds Ratio	95% CI
alive	0.64	(0.43, 0.97)
hospice	1.47	(0.97, 2.24)

#### 1.2 Task 2

Next, fit a propensity score model to the data, using the eight pieces of covariate information, including age, gender, race, marital status, cancer type (which must be treated in R as a factor rather than just a continuous predictor) the model survival probability, Charlson index and ECOG. Do not include interactions between terms.

#### 1.2.1 Fitting the Model and Saving Raw and Linear Propensity Scores

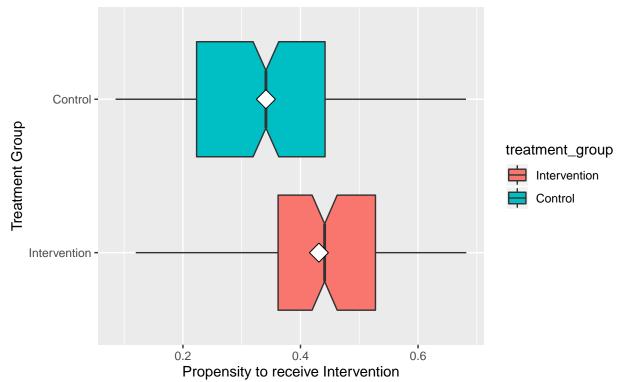
#### 1.2.2 Looking at the Overlap Numerically

```
canc3 %>%
  group_by(treated f) %>%
  summarise(mean.ps = mean(ps), sd.ps = sd(ps), median.ps = median(ps),
            mean.linps = mean(linps), sd.linps = sd(linps))
# A tibble: 2 x 6
               mean.ps sd.ps median.ps mean.linps sd.linps
  treated f
  <fct>
                 <dbl> <dbl>
                                  <dbl>
                                             <dbl>
                                                      <dbl>
1 Control
                 0.341 0.145
                                  0.341
                                            -0.735
                                                      0.705
2 Intervention
                 0.431 0.129
                                  0.441
                                            -0.308
                                                      0.585
```

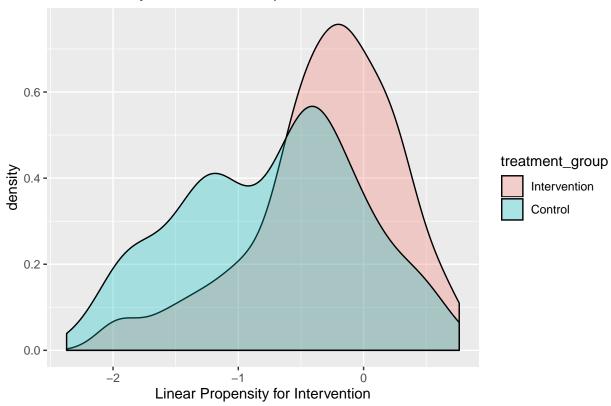
#### 1.2.3 Looking at the Overlap Graphically

### **Boxplot of Propensity Scores**

in the canc3 study



### Linear PS By Treatment Group



#### 1.3 Task 3

Evaluate Rubin's Rule 1 and Rubin's Rule 2 for the data taken as a whole. What can you conclude about the balance across the two exposure groups prior to using the propensity score? What do these results suggest about your model in Task 1?

#### 1.3.1 Rubin's Rule 1

First, the absolute value of the standardized difference of the linear propensity score, comparing the intervention group to the control group, should be close to 0, ideally below 10%, and in any case less than 50%. If so, we may move on to Rubin's Rule 2.

To evaluate this here, I'll use:

#### [1] 61.59673

Here, with a value of 62%, we cannot justify simply running an unadjusted regression model, be it a linear, logistic or Cox model. We have substantial observed selection bias, and need to further adjust for this using our propensity score before trusting that our comparisons will be fair. But we'll check Rule 2 anyway, as instructed.

#### 1.3.2 Rubin's Rule 2

Second, the ratio of the variance of the linear propensity score in the intervention group to the variance of the linear propensity score in the control group should be close to 1, ideally between 4/5 and 5/4, but certainly between 1/2 and 2. If so, we may move on to Rule 3.

To evaluate this here, I'll use:

#### [1] 0.6883501

Again, this is the ratio of variances of the linear propensity score comparing intervention patients to control patients. We want this value to be close to 1, and certainly between 0.5 and 2. In this case, we pass Rule 2, though not by much.

#### 1.3.3 Rubin's Rule 3 (not part of the assignment)

I didn't ask you to do this, but finding the Rubin's Rule 3 results prior to adjustment looks like this:

```
## General function rubin3 to help calculate Rubin's Rule 3
decim <- function(x, k) format(round(x, k), nsmall=k)
rubin3 <- function(data, covlist, linps) {
   covlist2 <- as.matrix(covlist)
   res <- NA
   for(i in 1:ncol(covlist2)) {
      cov <- as.numeric(covlist2[,i])
      num <- var(resid(lm(cov ~ data$linps))[data$exposure == 1])
      den <- var(resid(lm(cov ~ data$linps))[data$exposure == 0])
      res[i] <- decim(num/den, 3)
}</pre>
```

rubin3.unadj <- rubin3(data=canc3, covlist = cov.sub, linps = linps)</pre>

Warning: `data\_frame()` is deprecated, use `tibble()`. This warning is displayed once per session.

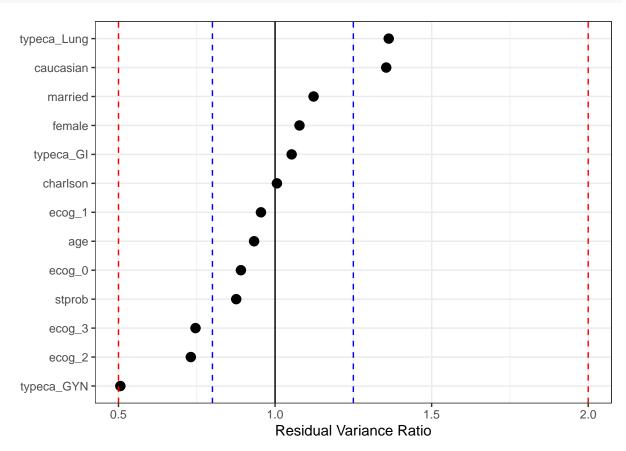
rubin3.unadj

```
# A tibble: 13 x 2
               resid.var.ratio
   name
   <chr>
                          <dbl>
                          0.933
 1 age
 2 female
                          1.08
 3 caucasian
                          1.36
 4 married
                          1.12
 5 stprob
                          0.876
 6 charlson
                          1.01
 7 typeca GI
                          1.05
 8 typeca_Lung
                          1.36
 9 typeca GYN
                          0.506
10 ecog 0
                          0.891
11 ecog 1
                          0.955
12 ecog 2
                          0.731
13 ecog_3
                          0.746
```

Some of these covariates look to have residual variance ratios near 1, while others are further away, but all are within the (0.5, 2.0) range. So we would pass Rule 3 here, although we would clearly like to see some covariates (typeca\_GYN, in particular) with ratios closer to 1. Here's a dotplot.

```
ggplot(rubin3.unadj, aes(x = resid.var.ratio, y = reorder(name, resid.var.ratio))) +
    geom_point(size = 3) +
    theme_bw() +
    xlim(0.5, 2.0) +
    geom_vline(xintercept = 1) +
```

```
geom_vline(xintercept = c(4/5,5/4), lty = "dashed", col = "blue") +
geom_vline(xintercept = c(0.5,2), lty = "dashed", col = "red") +
labs(x = "Residual Variance Ratio", y = "")
```



#### 1.4 Task 4

Use direct adjustment for the (logit of) the propensity score in a logistic regression model for the hospice outcome to evaluate the intervention's effect on hospice entry, developing a point estimate (this should be an odds ratio) and a 95% confidence interval.

#### 1.4.1 Fitting the Model

Recall that the unadjusted logistic regression model for the hospice outcome was:

```
unadj.hospice <- glm(hospice ~ treated, data=canc3, family=binomial)
```

This led to an unadjusted odds ratio estimate for the intervention's effect on hospice of 1.47 with 95% CI of (0.97, 2.24).

Our new model will add the linear propensity score on the right hand side...

```
adj.hospice <- glm(hospice ~ treated + linps, data=canc3, family=binomial)
display(adj.hospice)
glm(formula = hospice ~ treated + linps, family = binomial, data = canc3)
            coef.est coef.se
(Intercept) -0.20
                      0.17
             0.07
                      0.23
treated
             0.81
                      0.18
linps
  n = 400, k = 3
  residual deviance = 495.0, null deviance = 521.6 (difference = 26.6)
exp(coef(adj.hospice))
(Intercept)
                treated
                               linps
  0.8227802
                           2.2530282
              1.0736976
exp(confint(adj.hospice))
```

Waiting for profiling to be done...

```
2.5 % 97.5 % (Intercept) 0.5831353 1.159700 treated 0.6841785 1.676902 linps 1.6072543 3.211896
```

So, after direct adjustment for the linear propensity score, the odds ratio estimate for the impact of the intervention on hospice is 1.07 with 95% CI of (0.68, 1.68). In other words, we still see no significant treatment effect on the hospice outcome.

#### 1.4.2 Our results so far, for the hospice outcome

Estimating the intervention effect on the hospice outcome...

Analytic Approach	Odds Ratio	95% CI
Unadjusted		(0.97, 2.24)
Direct PS adjustment	1.07	(0.68, 1.68)

#### 1.5 Task 5

Use subclassification by quintile of the propensity score to estimate the effect of the intervention on hospice entry. Specifically, first report an odds ratio estimate (and confidence interval) for each individual stratum, then demonstrate a pooled estimate across all five strata, being sure to indicate whether you believe pooling to be appropriate in this setting.

#### 1.5.1 Subclassifying by Propensity Score Quintile

```
## cut2 requires the Hmisc library
canc3$stratum <- cut2(canc3$ps, g=5)
canc3$quintile <- factor(canc3$stratum, labels=1:5)

table(canc3$stratum, canc3$quintile) ## sanity check</pre>
```

```
1 2 3 4 5
[0.0854,0.229) 80 0 0 0 0
[0.2294,0.349) 0 80 0 0 0
[0.3493,0.419) 0 0 80 0 0
[0.4192,0.505) 0 0 0 80 0
[0.5046,0.682] 0 0 0 0 80

## semi-fancy summaries of PS by stratum using dplyr
canc3 %>% group by(stratum) %>%
```

```
# A tibble: 5 x 6
 stratum
                                sd
                                      min
                    n mean
                                            max
 <fct>
                <int> <dbl> <dbl> <dbl> <dbl>
1 [0.0854,0.229)
                   80 0.167 0.0382 0.0854 0.229
2 [0.2294,0.349)
                   80 0.284 0.0388 0.229 0.348
3 [0.3493, 0.419)
                   80 0.387 0.0188 0.349 0.419
4 [0.4192,0.505)
                   80 0.461 0.0257 0.419 0.505
                   80 0.576 0.0482 0.505 0.682
5 [0.5046,0.682]
```

Next, I'll create a separate subset of the data for each of the five quintiles.

```
quin1 <- subset(canc3, quintile==1)
quin2 <- subset(canc3, quintile==2)
quin3 <- subset(canc3, quintile==3)
quin4 <- subset(canc3, quintile==4)
quin5 <- subset(canc3, quintile==5)</pre>
```

#### 1.5.2 Fitting Logistic Regression Models

Given that we want an odds ratio estimate, we can focus on logistic regression modeling.

```
quin1.hospice <- glm(hospice ~ treated f, data=quin1, family=binomial)
quin2.hospice <- glm(hospice ~ treated f, data=quin2, family=binomial)
quin3.hospice <- glm(hospice ~ treated_f, data=quin3, family=binomial)</pre>
quin4.hospice <- glm(hospice ~ treated f, data=quin4, family=binomial)
quin5.hospice <- glm(hospice ~ treated f, data=quin5, family=binomial)</pre>
Let's start by looking closely at Quintile 1
display(quin1.hospice)
glm(formula = hospice ~ treated f, family = binomial, data = quin1)
                      coef.est coef.se
(Intercept)
                      -1.33
                                0.30
treated fIntervention -0.37
                                0.83
  n = 80, k = 2
  residual deviance = 79.8, null deviance = 80.1 (difference = 0.2)
exp(coef(quin1.hospice)[2]) # odds ratio estimate: Quintile 1
treated fIntervention
            0.6883117
exp(confint(quin1.hospice)[c(2,4)]) # 95% CI for OR in Quintile 1
[1] 0.09912283 2.96273415
```

#### 1.5.3 Quintile-Specific Logistic Regression Coefficients and Standard Errors

Here are the results for each Quintile...

(Intercept) treated fIntervention

```
0.3184537 -0.5095090
```

coef(quin5.hospice)

(Intercept) treated\_fIntervention -0.4054651 0.5389965

Quintile	Coefficient = $log(\hat{OR})$	Associated Standard Error
1	-0.374	0.825
2	0.762	0.598
3	-0.224	0.475
4	-0.51	0.452
5	0.539	0.456

#### 1.5.4 Odds Ratio Estimates and 95% CI within Quintiles

Quintile	Odds Ratio	95% CI
1	0.69	(0.1, 2.96)
2	2.14	(0.64, 6.87)
3	0.8	(0.31, 2.01)
4	0.6	(0.24, 1.45)
5	1.71	(0.71, 4.26)

Pooling doesn't look like a good idea here. The individual odds ratios vary substantially from quintile to quintile, even though none are statistically significantly different from 1.

#### 1.5.5 Producing a Pooled Estimate

That said, I asked you to produce a pooled estimate anyway. To do so, we first estimate the pooled log odds ratio, across the five quintiles:

```
treated_fIntervention 0.039
```

## And we exponentiate this to get the overall odds ratio estimate
round(exp(est.st),3)

```
treated_fIntervention 1.04
```

To get the combined standard error estimate, we have:

```
## Pooling the quintile-specific standard errors
se.q1 <- summary(quin1.hospice)$coefficients[2,2]
se.q2 <- summary(quin2.hospice)$coefficients[2,2]
se.q3 <- summary(quin3.hospice)$coefficients[2,2]
se.q4 <- summary(quin4.hospice)$coefficients[2,2]
se.q5 <- summary(quin5.hospice)$coefficients[2,2]
se.st <- sqrt((se.q1^2 + se.q2^2 + se.q3^2 + se.q4^2 + se.q5^2)*(1/25))</pre>
```

Of course, this standard error is also on the log odds ratio scale.

So the 95% Confidence Interval for the effect of the intervention on hospice (as an Odds Ratio) requires us to exponentiate again...

### 1.5.6 Our Results So Far, for the hospice Outcome

Estimating the intervention effect on the hospice outcome...

Analytic Approach	Odds Ratio	95% CI
Unadjusted Direct PS adjustment PS quintile subclassification	1.07	(0.97, 2.24) (0.68, 1.68) (0.63, 1.73)

#### 1.6 Task 6

In our first propensity score matching attempt with the canc3 data, we'll apply a 1:1 match without replacement. Do the matching, and then evaluate the balance associated with this approach, as follows.

#### 1.6.1 Do the matching

We'll do 1:1 greedy matching, without replacement.

```
## Use 1:1 greedy matching to match all treated to unique control patients
## on the linear propensity scores. We'll break ties at random, as well.
## requires Matching library
X <- psmodel$linear.predictors ## matching on the linear propensity score
Tr <- as.logical(canc3$treated)</pre>
set.seed(432)
# if we rerun Match, we want to get the same answer
# since we're breaking ties at random, we should set a seed
match1 <- Match(Tr=Tr, X=X, M = 1, replace=FALSE, ties=FALSE)</pre>
summary(match1)
Estimate... 0
SE....
T-stat.... NaN
p.val..... NA
Original number of observations.....
                                              400
Original number of treated obs.....
                                              150
Matched number of observations.....
                                              150
Matched number of observations (unweighted).
                                              150
## Finally, we'll create a new data frame, containing only the matched sample
matches <- factor(rep(match1$index.treated, 2))</pre>
canc3.matchedsample <-</pre>
  cbind(matches, canc3[c(match1$index.control, match1$index.treated),])
## Sanity Check
table(canc3.matchedsample$treated f)
1.6.1.1 Create Data Frame with Matched Sample After 1:1 Matching
     Control Intervention
        150
                     150
## should be 150 treated and 150 control patients
head(canc3.matchedsample,5)
```

```
matches subject treated age female race married
                                                                typeca stprob charlson
1
                              67
      251
               215
                                       0
                                             0
                                                      1 GI/colorectal
                                                                          0.02
2
      252
               191
                           0
                              51
                                       0
                                             0
                                                      0 GI/colorectal
                                                                                       0
                                                                          0.18
3
      253
                  6
                           0
                              79
                                       0
                                             1
                                                      1 GI/colorectal
                                                                          0.09
                                                                                       0
4
      254
                40
                              73
                           0
                                       0
                                             1
                                                      1 GI/colorectal
                                                                          0.04
                                                                                       0
5
      255
                              52
                                       1
                                             1
                                                      1
                44
                          0
                                                                  Lung
                                                                          0.16
                                                                                       6
  ecog alive hospice treated_f treatment_group alive_f
                                                              hospice f caucasian
                                                                 Hospice
     1
            0
                     1
                         Control
                                            Control
                                                        Dead
1
     0
                                                       Alive No Hospice
                                                                                   0
2
            1
                     0
                         Control
                                            Control
3
     0
                                                       Alive No Hospice
            1
                     0
                         Control
                                                                                   1
                                            Control
4
     1
            0
                     1
                         Control
                                            Control
                                                        Dead
                                                                 Hospice
                                                                                   1
     1
5
            1
                     0
                         Control
                                            Control
                                                       Alive No Hospice
                                                                                   1
  typeca GI typeca Lung typeca GYN ecog 0 ecog 1 ecog 2 ecog 3
                                                                              ps
1
                        0
                                     0
                                             0
                                                     1
                                                            0
                                                                    0 0.4915717
2
                                             1
                                                     0
                                                            0
           1
                        0
                                     0
                                                                    0 0.4607890
3
           1
                        0
                                     0
                                             1
                                                     0
                                                            0
                                                                    0 0.3519827
4
                        0
                                     0
                                             0
           1
                                                     1
                                                            0
                                                                    0 0.4036331
5
           0
                         1
                                     0
                                             0
                                                     1
                                                            0
                                                                    0 0.5403399
        linps exposure
                                 stratum quintile
1 -0.03371622
                       0 [0.4192,0.505)
2 -0.15716682
                       0 [0.4192,0.505)
                                                  4
                       0 [0.3493, 0.419)
3 -0.61033523
                                                  3
                       0 [0.3493, 0.419)
                                                  3
4 -0.39034963
 0.16171127
                       0 [0.5046,0.682]
                                                  5
```

#### 1.6.2 Task 6a.

Evaluate the degree of covariate imbalance before and after propensity score matching for each of the eight covariates and for the (linear and raw) propensity score. Do so by plotting the standardized differences. Your plot should include standardized differences that identify the three cancer types (one remaining as baseline) individually, one each for any other covariates you treat as quantitative, and an appropriate set of indicators for any others you treat as categorical, plus one for the linear propensity score, and one for the raw propensity score.

#### 1.6.2.1 Performing Task 6a with cobalt

#### Balance Measures

	Туре	${\tt Diff.Un}$	${\tt V.Ratio.Un}$	Diff.Adj	V.Ratio.Adj
age	Contin.	0.1101	0.9309	0.0595	0.9691
female	Binary	-0.0400		0.0067	
caucasian	Binary	-0.1053		-0.0333	
married	Binary	-0.0947		-0.0333	
<pre>typeca_GI/colorectal</pre>	Binary	0.0173		-0.0333	
typeca_Lung	Binary	0.1667		0.0267	
typeca_GYN	Binary	-0.1840		0.0067	
stprob	Contin.	-0.5473	0.6889	-0.0209	1.1205
charlson	Contin.	0.1286	0.9968	0.0117	0.7609
ecog_0	Binary	-0.0653		-0.0400	
ecog_1	Binary	0.1027		0.0467	
ecog_2	Binary	-0.0280		-0.0133	
ecog_3	Binary	-0.0093		0.0067	
ps	Contin.	0.7011	0.7859	0.0846	1.0746
linps	Contin.	0.7302	0.6884	0.0752	1.0687

#### Sample sizes

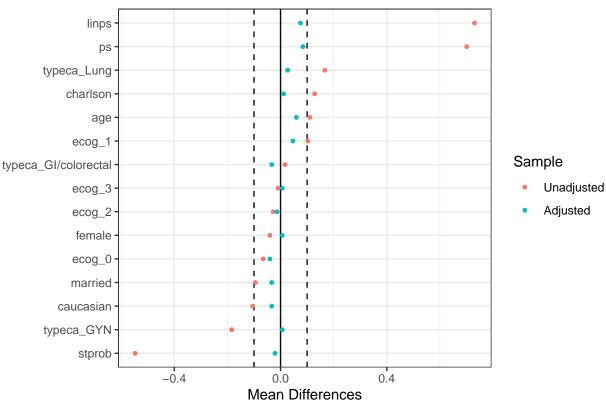
```
\begin{array}{ccc} & Control & Treated \\ All & 250 & 150 \\ Matched & 150 & 150 \\ Unmatched & 100 & 0 \\ \end{array}
```

## 1.6.2.1.1 Love Plot of Standardized Differences, via cobalt

Warning: Standardized mean differences and raw mean differences are present in the same Use the 'stars' argument to distinguish between them and appropriately label the x-axis.

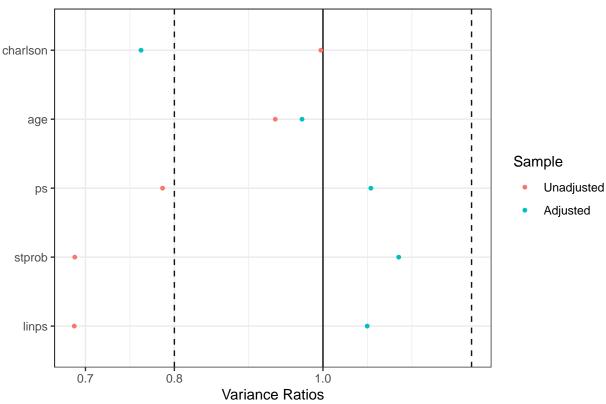
```
p + theme_bw()
```





1.6.2.1.2 Plot of Variance Ratios, via cobalt Note that by default in cobalt, this plot only compares variances for continuous predictors, and the linear and raw propensity scores.





#### 1.6.3 Task 6b.

rubin2.match

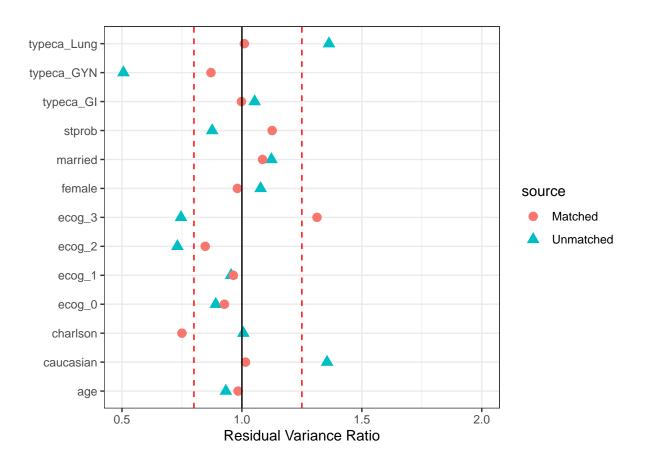
Evaluate the balance imposed by your 1:1 match via calculation of Rubin's Rule 1 and Rule 2 results, and comparing them to our results obtained prior to propensity adjustment in Task 3.

### 1.6.4 Evaluate the balance using Rubin's Rules after Matching

var(linps[treated==1])/
var(linps[treated==0]))

```
[1] 1.068696
```

```
cov.sub <- canc3.matchedsample %>% select(age, female, caucasian, married,
                             stprob, charlson, typeca_GI,
                             typeca_Lung, typeca_GYN, ecog_0,
                             ecog 1, ecog 2, ecog 3)
canc3.matchedsample$exposure <- canc3.matchedsample$treated</pre>
rubin3.match <- rubin3(data = canc3.matchedsample,</pre>
                         covlist = cov.sub, linps = linps)
rubin3.match
# A tibble: 13 x 2
             resid.var.ratio
  name
   <chr>
                         <dbl>
                         0.984
 1 age
 2 female
                         0.981
 3 caucasian
                        1.01
4 married
                        1.09
 5 stprob
                         1.13
 6 charlson
                        0.75
 7 typeca GI
                        0.998
 8 typeca_Lung
                        1.01
 9 typeca GYN
                        0.871
10 ecog 0
                        0.927
11 ecog 1
                        0.964
12 ecog 2
                         0.847
13 ecog 3
                         1.31
rubin3.match$source <- "Matched"</pre>
rubin3.unadj$source <- "Unmatched"</pre>
rubin3.both <- bind_rows(rubin3.unadj, rubin3.match)</pre>
ggplot(rubin3.both, aes(x = resid.var.ratio, y = name,
                        col = source, pch = source)) +
    geom_point(size = 3) +
    theme_bw() +
    xlim(0.5, 2.0) +
    geom_vline(aes(xintercept = 1)) +
    geom_vline(aes(xintercept = 4/5), linetype = "dashed", col = "red") +
    geom_vline(aes(xintercept = 5/4), linetype = "dashed", col = "red") +
  labs(x = "Residual Variance Ratio", y = "")
```



#### 1.6.4.1 Comparison of Results: Rubin's Rules

Setting	Rubin's Rule 1	Rubin's Rule 2	Rubin's Rule 3 Range
GOAL	0	near 1 $(4/5, 5/4)$	near 1 $(4/5, 5/4)$
PASS if	below 50	(1/2, 2)	(1/2, 2)
Prior to Matching	58.48	0.67	(0.53, 1.41)
After 1:1 Matching	7.65	1.07	(0.75, 1.31)

#### 1.6.5 Task 6c.

Finally, find a point estimate (and 95% confidence interval) for the effect of the treatment on the hospice outcome, based on your 1:1 match on the propensity score. Since the outcomes are binary, you should be using a conditional logistic regression to establish odds ratio estimates, while accounting for the pairs.

We'll run a conditional logistic regression (using the survival package) to estimate the intervention effect.

```
summary(model.hospice)
Call:
coxph(formula = Surv(rep(1, 300L), hospice) ~ treated + strata(matches),
    data = canc3.matchedsample, method = "exact")
 n= 300, number of events= 123
          coef exp(coef) se(coef)
                                    z Pr(>|z|)
treated 0.0339
                  1.0345
                           0.2604 0.13
                                           0.896
        exp(coef) exp(-coef) lower .95 upper .95
treated
            1.034
                      0.9667
                                 0.621
                                            1.723
Concordance= 0.508 (se = 0.092)
Likelihood ratio test= 0.02 on 1 df,
                                        p = 0.9
Wald test
                     = 0.02 on 1 df,
                                        p = 0.9
Score (logrank) test = 0.02 on 1 df,
                                        p = 0.9
```

This model estimates the Odds Ratio as OR = 1.03, with 95% CI (0.62, 1.72).

#### 1.7 Task 7

Compare your unadjusted (Task 1), propensity score-adjusted (by regression: Task 4), propensity score subclassification (Task 5) and propensity matching (Task 6) estimates of the effect of the intervention on the hospice outcome in a table (or better, graph.) What can you conclude?

Estimating the **intervention effect** on the **hospice** outcome, we have yet to find a statistically significant result at the 5% significance level.

Analytic Approach	Odds Ratio	95% CI
Unadjusted	1.47	(0.97, 2.24)
Direct PS adjustment	1.07	(0.68, 1.68)
PS quintile subclassification	1.04	(0.63, 1.73)
1:1 propensity score matching	1.03	(0.62, 1.72)

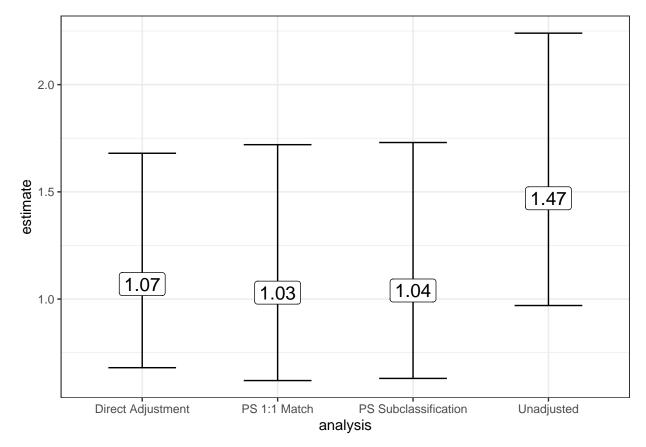
#### 1.7.1 Building a Data Frame of the Results

To make a nice plot, I'll want a data frame of the hospice results.

```
res_hospice <- data_frame(
    analysis = c("Unadjusted", "Direct Adjustment",</pre>
```

```
"PS Subclassification", "PS 1:1 Match"),
estimate = c(1.47, 1.07, 1.04, 1.03),
conf.low = c(0.97, 0.68, 0.63, 0.62),
conf.high = c(2.24, 1.68, 1.73, 1.72))

ggplot(res_hospice, aes(x = analysis, y = estimate)) +
    geom_errorbar(aes(ymax = conf.high, ymin = conf.low), width = 0.5) +
    geom_label(aes(label = estimate), size = 5) +
    theme_bw()
```

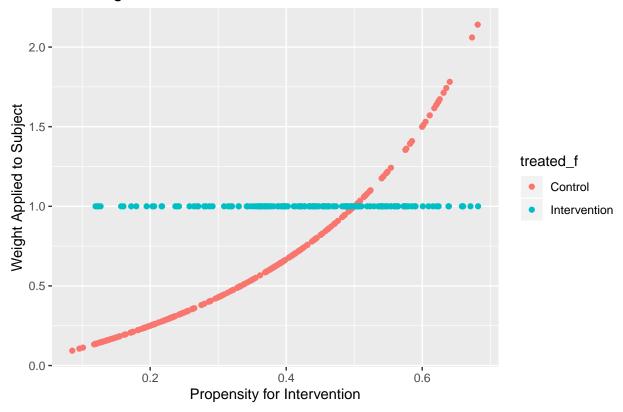


### 2 Homework 4 Tasks

#### 2.1 Task 1.

Execute weighting by the inverse propensity score, using the ATT approach (weight 1 for all intervention patients and weight ps/(1-ps) for all controls.) Plot the weights you applied within the intervention and control groups. Briefly explain what's happening.

### ATT weights for canc3 data



The intervention patients are each weighted at 1, while the control patients weights vary, as a function of their propensity score. Control patients with unusual combinations of predictors among the controls (and thus relatively high propensity for the intervention) are weighted more than more typical controls (with low propensity scores.)

#### 2.2 Task 2.

Use the twang package's dx.wts function to start assessing balance after weighting. What is the effective sample size within the control group after weighting? Can you explain what this value means, briefly?

```
type n.treat n.ctrl ess.treat ess.ctrl
                                               max.es
                                                          mean.es
                                                                     max.ks
                             150 250.0000 0.73020532 0.30820291 0.3120000
1
  unw
           150
                   250
2
           150
                   250
                             150 170.3926 0.05904512 0.02398123 0.1712779
     mean.ks iter
1 0.14225641
               NA
2 0.04613121
               NΑ
```

The effective sample size within the control group after ATT weighting by the inverse propensity score is 170.3926248, which implies that about 170 of the 250 control patients are comparable to the treatment group. This implies that the results we'll see will have similar power to an observational comparative effectiveness study done with 150 treated and 170 unweighted control subjects.

Quoting the TWANG vignette:

The ESS is approximately the number of observations from a simple random sample that yields an estimate with sampling variation equal to the sampling variation obtained with the weighted comparison observations. Therefore, the ESS will give an estimate of the number of comparison participants that are comparable to the treatment group when estimand = "ATT".

#### 2.3 Task 3.

Use the bal.table function to list (among other things) the standardized effect sizes for your covariate list. What can you conclude about the standardized differences (i.e. 100\* the standardized effect sizes) across our covariates? Plot these standardized differences in a Love plot, along with the standardized differences prior to propensity adjustment that you developed in Assignment 3. Are you satisfied with the balance after weighting here?

#### bal.table(bal.wts) \$unw ct.sd std.eff.sz tx.sd ct.mn stat ks ks.pval tx.mn р 0.431 0.129 0.341 0.145 0.701 6.476 0.000 0.300 0.000 ps 0.585 - 0.7356.547 0.000 0.300 -0.308 0.705 0.730 0.000 linps 1.053 0.293 0.097 age 63.760 10.866 62.564 11.262 0.110 0.313 female 0.620 0.487 0.660 0.475 -0.082 -0.804 0.422 0.040 0.996 0.832 -0.236 -2.424 0.016 0.105 caucasian 0.727 0.447 0.375 0.230 0.553 0.499 0.648 0.479 -0.190 -1.869 0.062 0.095 0.345 married 0.427 0.496 0.260 0.440 0.336 3.398 0.001 0.167 0.010 typeca Lung typeca\_GYN 0.120 0.326 0.304 0.461 -0.564 -4.667 0.000 0.184 0.003 ecog 1 0.567 0.497 0.464 0.500 0.206 1.999 0.046 0.103 0.256 ecog 2 0.060 0.238 0.088 0.284 -0.118 -1.059 0.290 0.028 1.000 ecog\_3 0.027 0.162 0.036 0.187 -0.058 -0.528 0.598 0.009 1.000 0.220 0.280 -0.547 -4.907 0.000 0.312 stprob 0.160 0.265 0.000 charlson 0.727 1.140 0.580 1.142 0.129 1.246 0.213 0.109 0.196 [[2]] ct.sd std.eff.sz tx.mn tx.sd ct.mn stat p ks ks.pval 0.431 0.129 0.436 0.138 -0.040 -0.341 0.733 0.103 0.342 ps linps -0.308 0.585 - 0.2880.621 -0.035 -0.309 0.757 0.103 0.342 -0.014 -0.115 0.908 0.086 age 63.760 10.866 63.909 11.734 0.556 female 0.620 0.487 0.642 0.480 -0.046 -0.419 0.675 0.022 1.000 0.447 0.451 0.160 0.873 0.009 caucasian 0.727 0.718 0.019 1.000 0.059 0.524 0.601 0.029 married 0.553 0.499 0.524 0.500 1.000 0.427 0.496 0.438 0.497 -0.024 -0.208 0.835 0.012 typeca Lung 1.000 typeca\_GYN 0.120 0.326 0.122 0.328 -0.007 -0.077 0.939 0.002 1.000 ecog 1 0.567 0.497 0.561 0.497 0.010 0.094 0.925 0.005 1.000 0.238 ecog 2 0.060 0.054 0.227 0.024 0.238 0.812 0.006 1.000 ecog\_3 0.027 0.162 0.025 0.158 0.008 0.076 0.939 0.001 1.000 -0.006 -0.058 0.954 0.171 stprob 0.160 0.220 0.161 0.201 0.016 0.727 1.140 0.751 1.349 -0.021 -0.156 0.876 0.050 charlson 0.979

To build a standardized difference plot, we'll first collect the standardized effect sizes, and multiply them by 100 to produce estimated standardized differences. Then, we'll sort the results by the pre-weight standardized differences, to yield the table we'll need.

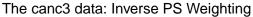
```
szd.weight1 <- data.frame(names=rownames(bal.table(bal.wts)[[2]]),
prew.szd = 100*bal.table(bal.wts)[[1]]$std.eff.sz,
postw.szd = 100*bal.table(bal.wts)[[2]]$std.eff.sz)
szd.weights <- szd.weight1[with(szd.weight1, order(prew.szd)),]
szd.weights</pre>
```

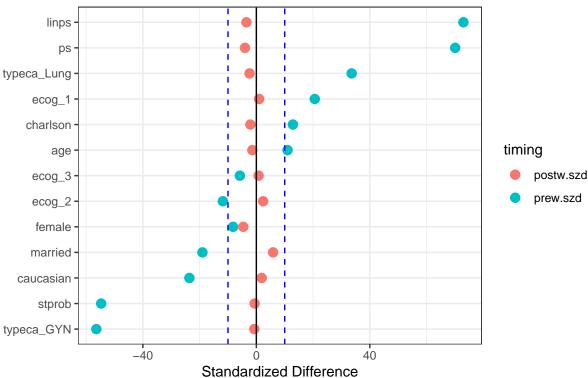
```
names prew.szd postw.szd 8 typeca GYN -56.4 -0.7
```

```
12
                             -0.6
        stprob
                  -54.7
5
     caucasian
                  -23.6
                               1.9
6
       married
                  -19.0
                               5.9
                               2.4
10
        ecog_2
                  -11.8
                             -4.6
4
        female
                   -8.2
                   -5.8
                              0.8
11
        ecog 3
                             -1.4
3
                   11.0
           age
                             -2.1
13
      charlson
                   12.9
                              1.0
9
        ecog_1
                   20.6
7 typeca_Lung
                   33.6
                             -2.4
1
            ps
                   70.1
                             -4.0
2
                   73.0
                             -3.5
         linps
```

And now, we can generate the plot, either through base graphics, or, as shown below, with ggplot2.

# Standardized Difference before and after ATT Weighting





#### 2.4 Task 4.

Evaluate Rubin's Rule 1 and Rule 2 for the post-weighting covariate distributions. Do the results seem satisfactory?

In a word, yes.

#### 2.4.1 Rubin's Rule 1

From the bal.table output above, the std.eff.sz for linps after the weighting is -0.035, so that's a standardized difference of  $100 \times -0.035 = -3.5\%$ , which is well below Rubin's maximum tolerable level in Rule 1 of 50%, so we pass Rule 1.

#### 2.4.2 Rubin's Rule 2

From that same table, the post-weighting *treatment* standard deviation for linps is 0.585 and so, squaring the SD, we find the variance is 0.342225.

The post-weighting *control* standard deviation for linps is 0.621 and so the variance is 0.385641.

So that's a variance ratio for linps of 0.342225 / 0.385641 = 0.887, which is well within the maximum tolerable range of 0.5 to 2, and even within the tighter range we typically try to achieve of 0.8 to 1.25, so we also pass Rule 2.

#### 2.5 Task 5.

Now use the twang package to create both the propensity scores (using generalized boosted modeling) and the ATT weights. Compare your results from 1-5 to your result here in terms of the following measures.

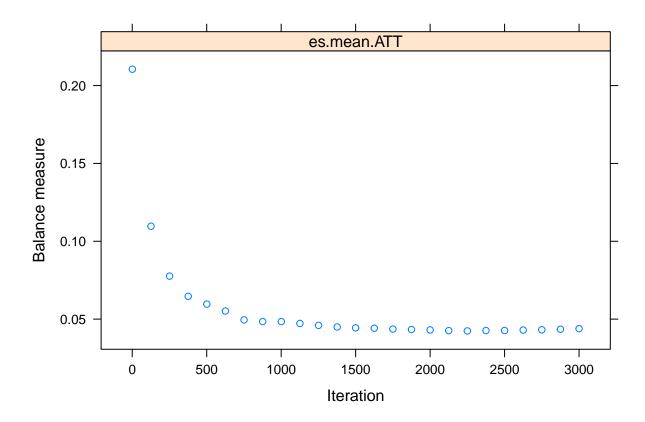
- effective sample size
- Love plot and standardized differences
- Rubin's first two rules

#### 2.5.1 Creating the weights with twang

Start by estimating the propensity score using the twang function ps.

Does 3000 look like a long enough simulation run?

```
plot(ps_canc3)
```



#### 2.5.2 Effective Sample Size

What is the effective sample size of these weighted results?

```
summary(ps_canc3)
            n.treat n.ctrl ess.treat ess.ctrl
                                                    max.es
                                                               mean.es
                                                                           max.ks
                 150
                        250
                                  150 250.0000 0.56622086 0.21167255 0.31200000
unw
es.mean.ATT
                150
                        250
                                  150 133.2961 0.08773735 0.04233414 0.05048702
            max.ks.p
                         mean.ks iter
                  NA 0.10246154
unw
                                   NA
                  NA 0.02469004 2291
es.mean.ATT
```

The effective sample size in the control group is now 133.2961035, which is considerably smaller than we saw previously. Perhaps the balance of covariates will be better?

#### 2.5.3 Standardized Differences / Love Plot

```
bal.tab(ps_canc3, full.stop.method = "es.mean.att")
```

Call

```
ps(formula = treated ~ age + female + caucasian + married + typeca +
    stprob + charlson + ecog, data = canc3_df, n.trees = 3000,
    interaction.depth = 2, verbose = FALSE, estimand = "ATT",
    stop.method = c("es.mean"))
```

#### Balance Measures

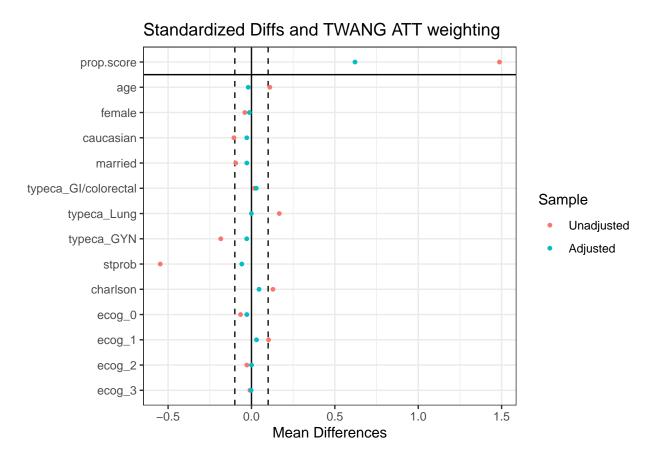
```
Type Diff.Adj
                    Distance
prop.score
                               0.6210
                     Contin.
                              -0.0196
age
female
                      Binary -0.0124
caucasian
                      Binary -0.0281
married
                      Binary -0.0278
typeca_GI/colorectal
                      Binary 0.0289
                      Binary -0.0004
typeca_Lung
typeca_GYN
                      Binary -0.0285
                     Contin. -0.0580
stprob
                     Contin.
charlson
                              0.0453
ecog 0
                      Binary -0.0281
                      Binary 0.0301
ecog_1
ecog 2
                      Binary
                               0.0004
                      Binary -0.0024
ecog_3
```

#### Effective sample sizes

```
Control Treated Unadjusted 250.000 150 Adjusted 133.296 150
```

Warning: Standardized mean differences and raw mean differences are present in the same Use the 'stars' argument to distinguish between them and appropriately label the x-axis.

```
p + theme_bw()
```



The Love plot looks meaningfully worse on the propensity score in the ATT weights approach, and the two strategies also yield different effective sample sizes.

#### 2.6 Task 6.

Select the weighting approach (of the two you have developed) that you prefer, and use it to find propensity-weighted estimates of the intervention effect on survival and on hospice. Your results should include a properly labeled point estimate and associated confidence interval for each outcome.

I'll go with the ATT weights I generated from the same propensity score model we've been using for matching, etc., because the balance of the propensity score is better, and the effective sample size is larger.

#### 2.6.1 Analysis of survival using propensity score generated ATT weights

For *survival*, we fit a logistic regression model, and exponentiate the log odds ratio treatment effect estimate to obtain an odds ratio estimate of the average causal effect of treatment on the treated.

```
canc3wt.design <- svydesign(ids=~1, weights=~wts, data=canc3)</pre>
survadj.wt <- svyglm(alive ~ treated, design=canc3wt.design,</pre>
                     family=quasibinomial())
summary(survadj.wt)
Call:
svyglm(formula = alive ~ treated, design = canc3wt.design, family = quasibinomial())
Survey design:
svydesign(ids = ~1, weights = ~wts, data = canc3)
Coefficients:
            Estimate Std. Error t value Pr(>|t|)
              0.3560
                         0.1574
                                   2.261
                                           0.0243 *
(Intercept)
                         0.2275 - 0.742
                                           0.4586
treated
             -0.1688
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
(Dispersion parameter for quasibinomial family taken to be 1.002506)
Number of Fisher Scoring iterations: 4
exp(summary(survadj.wt)$coef)
             Estimate Std. Error t value Pr(>|t|)
(Intercept) 1.4275635 1.170469 9.5974418 1.024564
            0.8447136
                        1.255425 0.4762198 1.581858
treated
exp(confint(survadj.wt))
                2.5 %
                        97.5 %
(Intercept) 1.0486069 1.943471
treated
            0.5408578 1.319277
Our odds ratio estimate for the intervention's effect on survival is 0.84 and our 95% CI is
(0.54, 1.32).
2.6.2
      Analysis of hospice using propensity score generated ATT weights
For hospice, we adopt the same approach...
```

```
Estimate Std. Error t value Pr(>|t|)

(Intercept) 0.6313001 1.172317 0.0553959 1.004030

treated 1.1160231 1.258427 1.6121247 1.883686

exp(confint(hospadj.wt))

2.5 % 97.5 %
```

```
2.5 % 97.5 % (Intercept) 0.4622855 0.8621074 treated 0.7112362 1.7511869
```

Our odds ratio estimate for the intervention's effect on *hospice* is 1.12 and our 95% CI is (0.71, 1.75).

#### 2.7 Task 7.

Next, run an analysis that combines weighting (either approach is OK) with regression adjustment for the linear propensity score to obtain a "doubly robust" set of estimates. Use this approach to again find estimates of the intervention effect on survival and hospice.

#### 2.7.1 Double Robust Analysis of survival via usual ATT weights

For *survival*, we simply fit the same logistic regression model but now add in the linear propensity score as a predictor, then exponentiate the log odds ratio treatment effect estimate to obtain an odds ratio estimate of the average causal effect of treatment on the treated.

```
(Intercept) 0.1591 0.1883 0.845 0.398438

treated -0.1937 0.2330 -0.831 0.406481

linps -0.7651 0.1955 -3.913 0.000107 ***

---
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

(Dispersion parameter for quasibinomial family taken to be 0.9983068)

```
Number of Fisher Scoring iterations: 4
```

exp(summary(survadj.dr)\$coef)

```
Estimate Std. Error t value Pr(>|t|)
(Intercept) 1.1725063 1.207151 2.32873880 1.489496
treated 0.8239451 1.262429 0.43561950 1.501525
linps 0.4653067 1.215945 0.01998238 1.000107
```

```
exp(confint(survadj.dr))
```

```
2.5 % 97.5 % (Intercept) 0.8107101 1.6957616 treated 0.5218384 1.3009499 linps 0.3171836 0.6826025
```

Our odds ratio estimate for the intervention's effect on survival is 0.82 and our 95% CI is (0.52, 1.3).

#### 2.7.2 Analysis of hospice using propensity score generated ATT weights

For *hospice*, we adopt the same approach...

```
Estimate Std. Error t value Pr(>|t|)
(Intercept) 0.7574157 1.208647 0.2308066 1.154182
treated 1.1398428 1.265925 1.7420856 1.784522
linps 2.0549502 1.216629 39.3767866 1.000272
```

```
exp(confint(hospadj.dr))
```

```
2.5 % 97.5 % (Intercept) 0.5224323 1.098092 treated 0.7180074 1.809510 linps 1.3992464 3.017925
```

Our odds ratio estimate for the intervention's effect on hospice is 1.14 and our 95% CI is  $(0.72,\,1.81)$ .

## 2.8 Task 8.

Finally, compare your results in Tasks 6 and 7 here to those obtained in Assignment 3 for the hospice outcome. What conclusions can you draw?

Estimating the **intervention effect** on the hospice outcome, we have yet to find a statistically significant result at the 5% significance level.

Analytic Approach	Odds Ratio	95% CI
Unadjusted	1.47	(0.97, 2.24)
Direct PS adjustment	1.07	(0.68, 1.68)
PS quintile subclassification	1.04	(0.63, 1.73)
1:1 propensity score matching	1.03	(0.62, 1.72)
ATT weights from usual PS	1.12	(0.71, 1.75)
Double Robust from usual PS	1.14	(0.72, 1.81)