

Comparative Effectiveness and Personalized Medicine Research Using Real-World Data

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Preface

This is a Quarto book.

To learn more about Quarto books visit <https://quarto.org/docs/books>.

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1 Dealing with missing data

In this example, we consider the estimation of comparative treatment effects in the absence of treatment-effect heterogeneity.

1.0.1 Prepare R environment

```
library(mice)
library(dplyr)
library(ggmice)
library(MatchThem)
```

1.0.2 Generating an observational dataset

We can simulate an observational dataset of $N = 3000$ patients as follows:

```
data_noHTE <- generate_data(n = 3000, seed = 1234)
```

This dataset does not (yet) contain any missing values;

The simulated dataset contains two treatment groups with differences in baseline characteristics. For example, the figure below shows that we have baseline imbalance in age.

1.0.3 Generating missing values

Missing values can be generated using the function `getmissdata()`, which considers the following patterns of missingness for the previous number of relapses (`prerelapse_num`):

1. MAR: missingness depends on `age` and `sex`
2. MART: missingness depends on `age`, `sex` and the treatment variable `treatment`
3. MARTY: missingness depends on `age`, `sex`, `treatment` and the outcome variable `y`
4. MNAR: missingness depends on `age`, `sex` and `prerelapse_num`

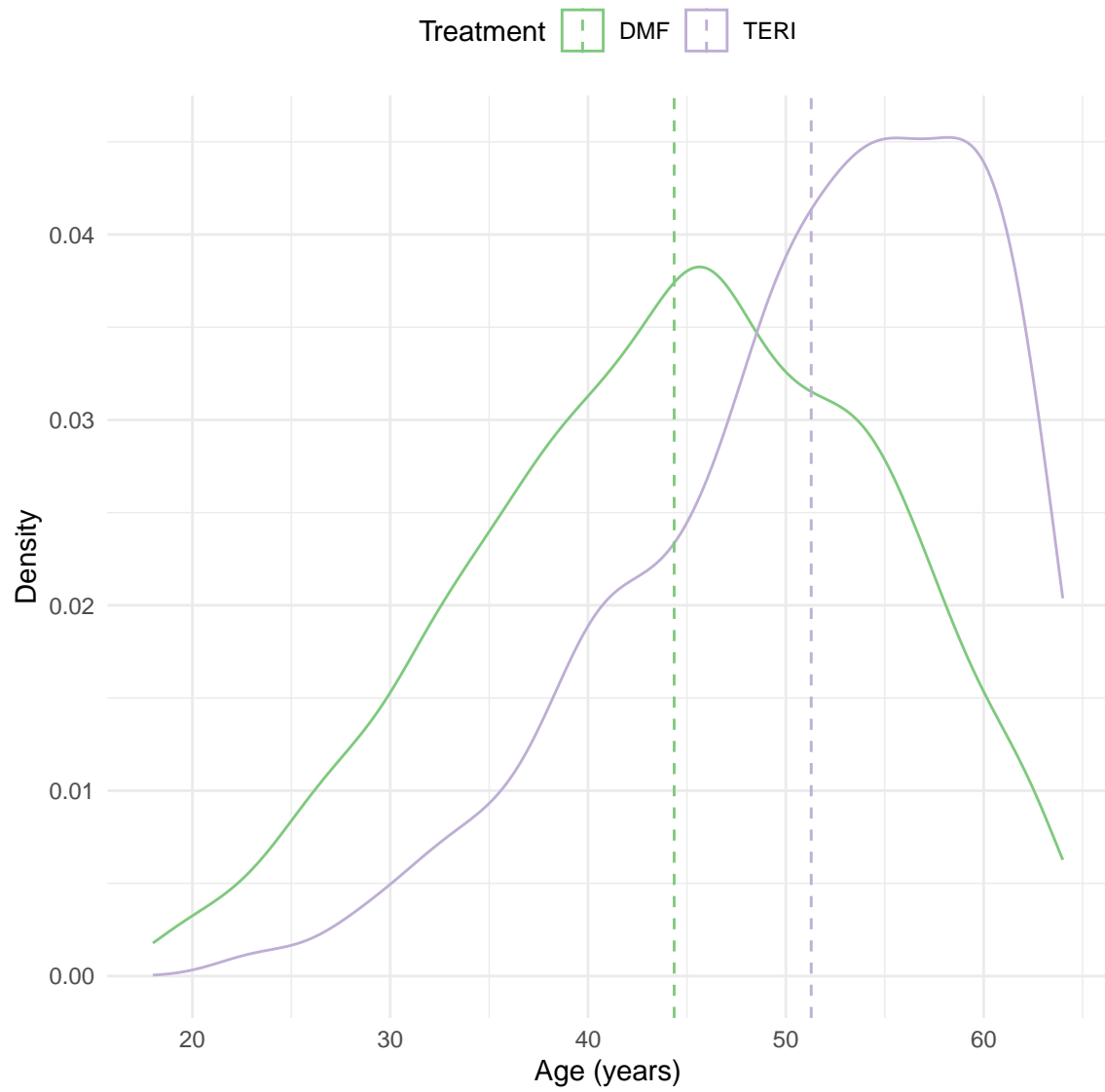


Figure 1.1: Distribution of confounders and outcome variable

```
mdata_noHTE <- getmissdata(data_noHTE, "MART")
```

After introducing missing values, we only have complete data for $N = 946$ patients.

1.1 Analysis of incomplete data

1.1.1 Complete Case Analysis

Below, we describe how to estimate the ATE using propensity score matching.

```
impdata <- mdata_noHTE[complete.cases(mdata_noHTE), ]

# Apply Matching
mout <- matchit(DMF ~ age + female + prevDMTefficacy + premedicalcost + prerelapse_num,
               data = impdata,
               family = binomial,
               method = "full",
               caliper = 0.2,
               estimand = "ATE",
               replace = FALSE)

mdata <- as.data.table(match.data(mout))
match_mod <- glm("y ~ DMF + offset(log(years))",
               family = poisson(link = "log"),
               data = mdata,
               weights = weights)

# Estimate robust variance-covariance matrix
tx_var <- vcovCL(match_mod, cluster = ~ subclass, sandwich = TRUE)
```

We can extract the treatment effect estimate as follows:

```
# Treatment effect estimate (log rate ratio)
coef(match_mod)["DMF"]
```

```
      DMF
-0.3524863
```

Table 1.1: Baseline characteristics of the incomplete dataset.

	DMF	TERI	Overall
	(N=2265)	(N=735)	(N=3000)
Age (years)			
Mean (SD)	44.4 (10.0)	51.3 (8.72)	46.2 (10.1)
Median [Min, Max]	45.0 [18.0, 64.0]	53.0 [23.0, 64.0]	47.0 [18.0, 64.0]
Missing	248 (10.9%)	57 (7.8%)	305 (10.2%)
Female Sex			
Yes	1740 (76.8%)	526 (71.6%)	2266 (75.5%)
No	525 (23.2%)	209 (28.4%)	734 (24.5%)
Efficacy of previous DMT			
None	740 (32.7%)	325 (44.2%)	1065 (35.5%)
Low	190 (8.4%)	59 (8.0%)	249 (8.3%)
Medium or High	830 (36.6%)	246 (33.5%)	1076 (35.9%)
Missing	505 (22.3%)	105 (14.3%)	610 (20.3%)
Prior medical costs			
Mean (SD)	9970 (10700)	25500 (35400)	13900 (21200)
Median [Min, Max]	6530 [164, 102000]	12500 [259, 337000]	7450 [164, 337000]
Missing	257 (11.3%)	52 (7.1%)	309 (10.3%)
Number of prior symptoms			
0	157 (6.9%)	58 (7.9%)	215 (7.2%)
1	1169 (51.6%)	411 (55.9%)	1580 (52.7%)
>=2	435 (19.2%)	159 (21.6%)	594 (19.8%)
Missing	504 (22.3%)	107 (14.6%)	611 (20.4%)
Number of prior relapses			
Mean (SD)	0.453 (0.671)	0.408 (0.646)	0.436 (0.662)
Median [Min, Max]	0 [0, 4.00]	0 [0, 3.00]	0 [0, 4.00]
Missing	1365 (60.3%)	152 (20.7%)	1517 (50.6%)


```
# Standard error
sqrt(tx_var["DMF", "DMF"])
```

```
[1] 0.1498211
```

1.1.2 Multiple Imputation (within method)

In this approach, we will generate $m = 5$ imputed datasets and perform matching within each imputed dataset. We first need to specify how the variables `prevDMTefficacy`, `premedicalcost`, `numSymptoms`, `prerelapse_num` and `age` will be imputed:

```
# We add a covariate for log(years)
impdata <- mdata_noHTE %>% mutate(logyears = log(years))

# Specify the conditional imputation models
form_y <- list(prevDMTefficacy ~ age + female + logyears + premedicalcost + numSymptoms +
               treatment + prerelapse_num + y,
               premedicalcost ~ age + female + logyears + prevDMTefficacy + numSymptoms +
               treatment + prerelapse_num + y,
               numSymptoms ~ age + female + premedicalcost + logyears + prevDMTefficacy +
               prerelapse_num + treatment + y,
               prerelapse_num ~ age + female + premedicalcost + logyears + prevDMTefficacy +
               numSymptoms + treatment + y,
               age ~ prerelapse_num + female + premedicalcost + logyears + prevDMTefficacy +
               numSymptoms + treatment + y)
form_y <- name.formulas(form_y)

# Adopt predictive mean matching for imputing the incomplete variables
imp0 <- mice(impdata, form = form_y, maxit = 0)
method <- imp0$method
method["numSymptoms"] <- "pmm"
method["prevDMTefficacy"] <- "pmm"

# Generate 5 imputed datasets
imp <- mice(impdata, form = form_y, method = method, m = 5, maxit = 100)
```

We can now estimate the ATE using propensity score analysis in each of the imputed datasets. We here adopt full matching without replacement.

```
# Matching based on PS model
mout <- matchthem(DMF ~ age + female + prevDMTefficacy + premedicalcost + prerelapse_num,
  datasets = imp,
  approach = "within",
  method = "full",
  caliper = 0.2,
  family = binomial,
  estimand = "ATE",
  distance = "glm",
  link = "logit",
  replace = FALSE)
```

The results are then combined using Rubin's rules. We adopt robust standard errors to account for clustering of matched individuals.

```
match_mod <- summary(pool(with(mout, svyglm(y ~ DMF + offset(log(years)),
  family = poisson(link = "log")),
  cluster = TRUE)), conf.int = TRUE)
```

We can extract the treatment effect estimate and corresponding standard error as follows:

```
# Treatment effect estimate (log rate ratio)
(match_mod %>% filter(term == "DMF"))$estimate
```

```
[1] -0.1172783
```

```
# Standard error
(match_mod %>% filter(term == "DMF"))$std.error
```

```
[1] 0.1895277
```

1.1.3 Multiple Imputation (across method)

```
# Matching based on PS model
mout <- matchthem(DMF ~ age + female + prevDMTefficacy + premedicalcost + prerelapse_num,
  datasets = imp,
  approach = "across",
  method = "full",
  caliper = 0.2,
```

```
family = binomial,
estimand = "ATE",
distance = "glm",
link = "logit",
replace = FALSE)
```

The results are then combined using Rubin's rules. We adopt robust standard errors to account for clustering of matched individuals.

```
match_mod <- summary(pool(with(mout, svyglm(y ~ DMF + offset(log(years)),
                                          family = poisson(link = "log")),
                          cluster = TRUE)), conf.int = TRUE)
```

We can extract the treatment effect estimate and corresponding standard error as follows:

```
# Treatment effect estimate (log rate ratio)
(match_mod %>% filter(term == "DMF"))$estimate
```

```
[1] -0.2838299
```

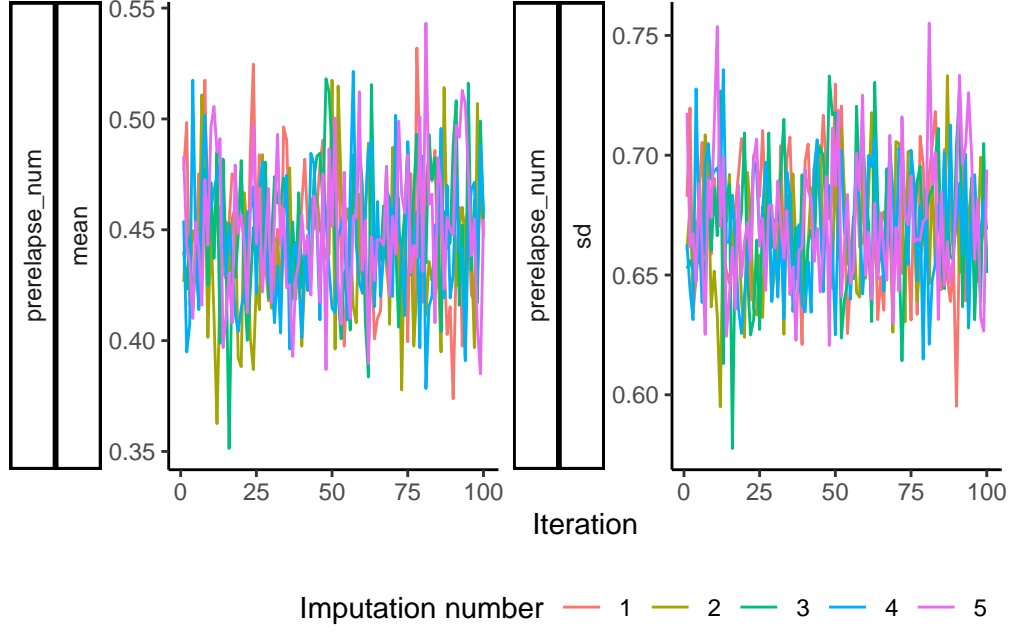
```
# Standard error
(match_mod %>% filter(term == "DMF"))$std.error
```

```
[1] 0.1221876
```

1.2 Convergence checking

We can inspect convergence for the imputed variable `prerelapse_num` using a trace plot:

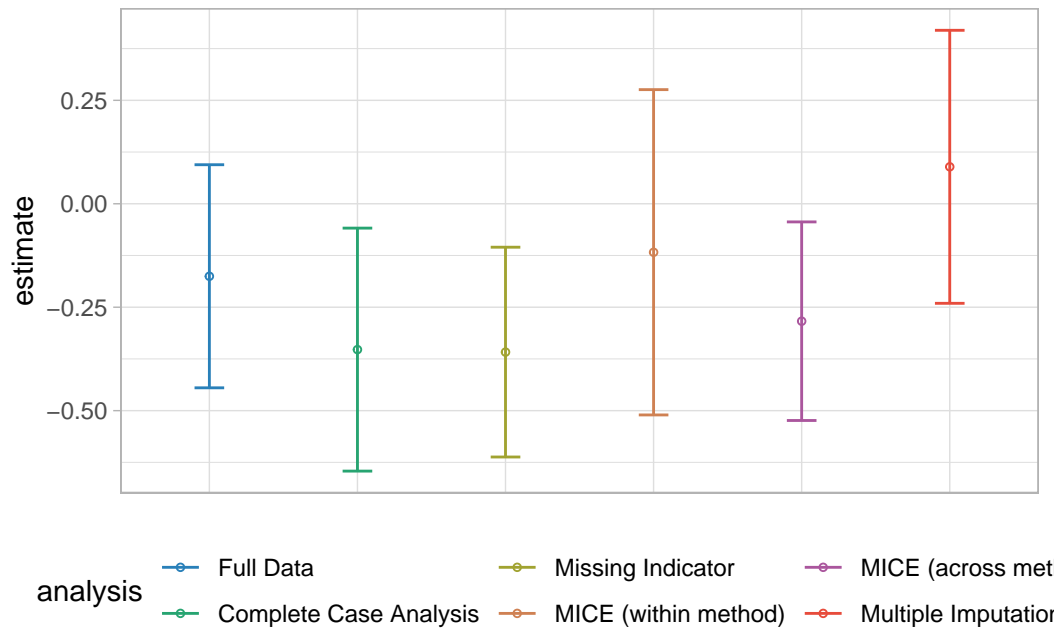
```
plot_trace(imp, vrb = "prerelapse_num")
```



1.3 Results

Analysis methods:

- **Full Data:** The treatment effect is estimated in the original data of $N = 3000$ patients where no missing values are present. This estimate can be used as a benchmark to compare the missing data methods.
- **Complete Case Analysis:** The treatment effect is estimated using all data from $N = 946$ patients that do not have any missing values.
- **Missing Indicator:** The treatment effect is estimated in the incomplete dataset of $N = 3000$ patients. The propensity score model includes a missing indicator variable for each incomplete covariate.
- **MICE (within method):** A treatment effect is estimated within each imputed dataset using propensity score analysis. Using Rubin's rule, the five treatment effects are combined into a single treatment effect.
- **MICE (ITE method):** The missing covariates and potential outcomes are imputed simultaneously. Treatment effect estimates are derived by taking the average of the individualized treatment effect estimates $Y|DMF - Y|TERI$.



2 Confounding adjustment using propensity score methods

The purpose of this document is to provide example R code that demonstrates how to estimate the propensity score and implement matching, stratification, weighting, and regression adjustment for the continuous propensity score. In this example using simulated data, we have two disease modifying therapies (DMT1 and DMT0) and the outcome is the number of post-treatment multiple sclerosis relapses during follow-up. We will estimate the average treatment effect in the treated (ATT) using propensity score matching, stratification, and weighting. We will estimate the average treatment effect in the population (ATE) using regression adjustment for the continuous propensity score. The treatment effects can be interpreted as annualized relapse rate ratios (ARR).

We consider an example dataset with the following characteristics:

```
head(dat)
```

	age	female	prevDMTefficacy	premedicalcost	numSymptoms	prerelapse_num
1:	50	1	None	3899.61	1	1
2:	51	0	None	9580.51	1	0
3:	56	0	None	4785.89	1	0
4:	44	1	None	8696.80	1	1
5:	63	0	None	2588.03	1	0
6:	28	1	None	5435.57	1	0

	treatment	y	years	Iscore
1:	DMT1	0	1.78507871	Moderate A1
2:	DMT1	0	0.01368925	High A1
3:	DMT1	2	3.25530459	High A1
4:	DMT1	2	5.73853525	Neutral
5:	DMT1	0	1.31143053	High A1
6:	DMT1	0	0.59137577	Moderate A0

3 Comparing baseline characteristics

- DMT1 is the treatment group and DMT0 is the control group
- `prevDMTefficacy` is previous DMT efficacy (none, low efficacy, and medium/high efficacy)
- `prerelapse_num` is the number of previous MS relapses

	DMT0	DMT1
n	2300	7700
age (mean (SD))	51.39 (8.32)	44.25 (9.79)
female = 1 (%)	1671 (72.65)	5915 (76.82)
prevDMTefficacy (%)		
None	1247 (54.22)	3171 (41.18)
Low_efficacy	261 (11.35)	858 (11.14)
Medium_high_efficacy	792 (34.43)	3671 (47.68)
prerelapse_num (mean (SD))	0.39 (0.62)	0.46 (0.68)

4 Estimating the propensity score

4.1 Logistic regression

We sought to restore balance in the distribution of baseline covariates in patients treated with DMT1 (index treatment) and DMT0 (control treatment). We fit a multivariable logistic regression model in which treatment was regressed on baseline characteristics including age, sex, previous DMT efficacy, and previous number of relapses.

```
# Fit logistic regression model
ps.model <- glm(treatment ~ age + female + prevDMTefficacy + prerelapse_num,
               data = dat, family = binomial())

# Summary of logistic regression model
summary(ps.model)
```

Call:

```
glm(formula = treatment ~ age + female + prevDMTefficacy + prerelapse_num,
    family = binomial(), data = dat)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-2.7949	0.2585	0.5220	0.7478	1.5033

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	4.809473	0.157127	30.609	< 2e-16 ***
age	-0.086708	0.002996	-28.939	< 2e-16 ***
female1	0.253611	0.057664	4.398	1.09e-05 ***
prevDMTefficacyLow_efficacy	0.310394	0.083022	3.739	0.000185 ***
prevDMTefficacyMedium_high_efficacy	0.660266	0.054393	12.139	< 2e-16 ***
prerelapse_num	0.156318	0.039288	3.979	6.93e-05 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 10786 on 9999 degrees of freedom
Residual deviance: 9597 on 9994 degrees of freedom
AIC: 9609

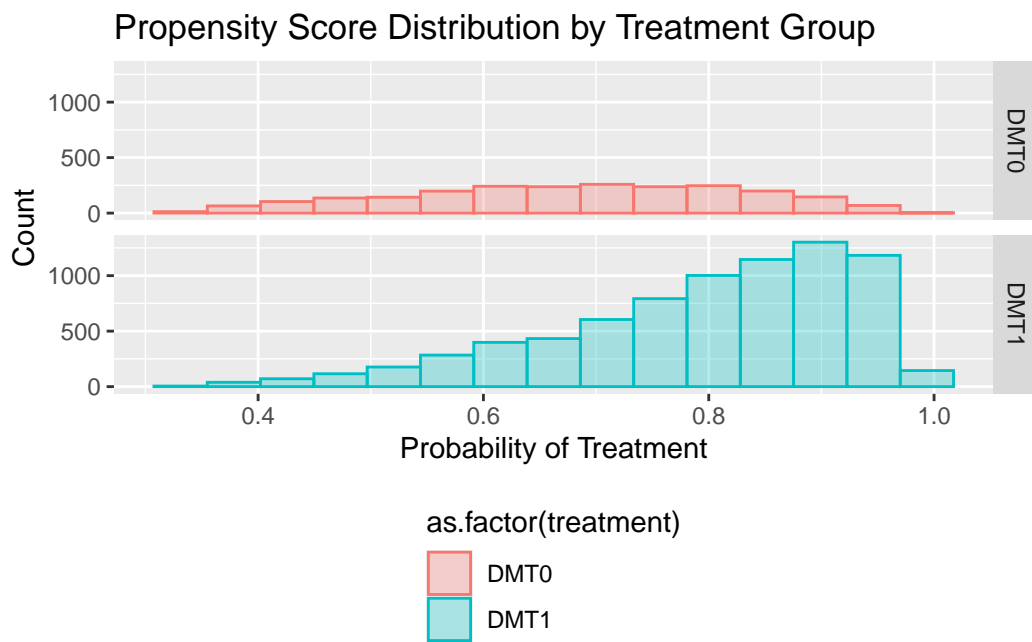
Number of Fisher Scoring iterations: 5

```
# Extract propensity scores  
dat$ps <- predict(ps.model, data = dat, type = "response")
```

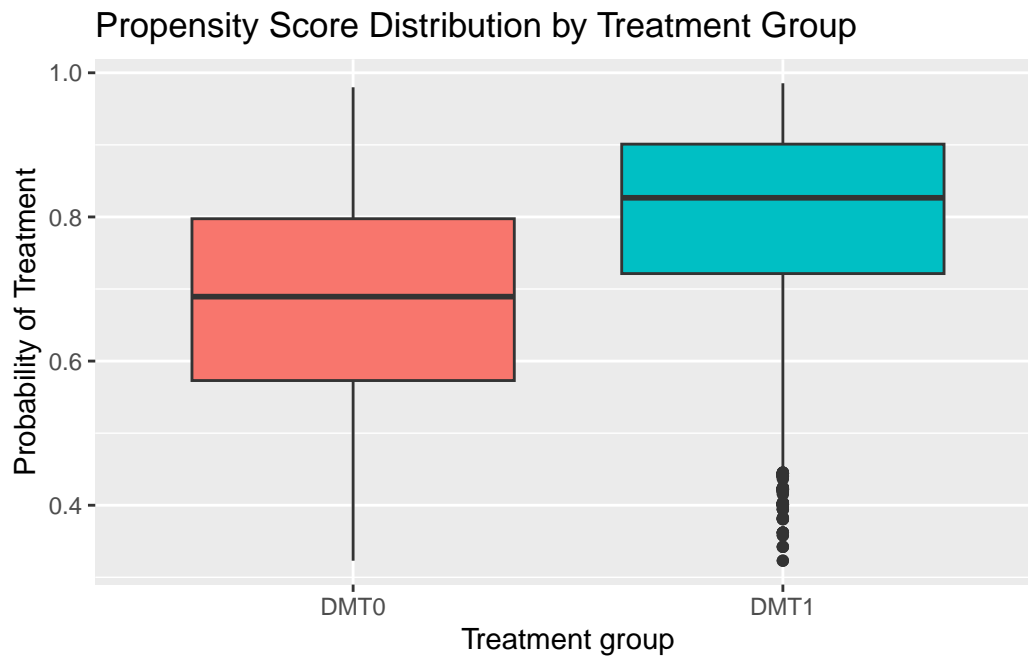
4.2 Assessing overlap

We examined the degree of overlap in the distribution of propensity scores across treatment groups using histograms and side-by-side box plots.

```
# Histogram  
ggplot(dat, aes(x = ps, fill = as.factor(treatment), color = as.factor(treatment))) +  
  geom_histogram(alpha = 0.3, position='identity', bins = 15) +  
  facet_grid(as.factor(treatment) ~ .) +  
  xlab("Probability of Treatment") +  
  ylab("Count") +  
  ggtitle("Propensity Score Distribution by Treatment Group") +  
  theme(legend.position = "bottom", legend.direction = "vertical")
```



```
# Side-by-side box plots
ggplot(dat, aes(x=as.factor(treatment), y=ps, fill=as.factor(treatment))) +
  geom_boxplot() +
  ggtitle("Propensity Score Distribution by Treatment Group") +
  ylab("Probability of Treatment") +
  xlab("Treatment group") +
  theme(legend.position = "none")
```



```
# Distribution of propensity scores by treatment groups
summary(dat$ps[dat$treatment == "DMT1"])
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.3230  0.7214  0.8265  0.7970  0.9010  0.9854
```

```
summary(dat$ps[dat$treatment == "DMT0"])
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.3230  0.5730  0.6894  0.6795  0.7975  0.9799
```

5 Propensity score matching

5.1 1:1 Optimal full matching without replacement

```
library(MatchIt)

# Use MatchIt package for PS matching
opt <- matchit(treatment ~ age + female + prevDMTefficacy + prerelapse_num,
              data = dat,
              method = "full",
              estimand = "ATT")

opt
```

A matchit object

- method: Optimal full matching
- distance: Propensity score
 - estimated with logistic regression
- number of obs.: 10000 (original), 10000 (matched)
- target estimand: ATT
- covariates: age, female, prevDMTefficacy, prerelapse_num

5.2 Assess balance after matching

```
summary(opt)
```

Call:

```
matchit(formula = treatment ~ age + female + prevDMTefficacy +
        prerelapse_num, data = dat, method = "full", estimand = "ATT")
```

Summary of Balance for All Data:

	Means Treated	Means Control	Std. Mean Diff.
distance	0.7970	0.6795	0.8943
age	44.2496	51.3883	-0.7289
female0	0.2318	0.2735	-0.0987
female1	0.7682	0.7265	0.0987
prevDMTefficacyNone	0.4118	0.5422	-0.2649
prevDMTefficacyLow_efficacy	0.1114	0.1135	-0.0065
prevDMTefficacyMedium_high_efficacy	0.4768	0.3443	0.2651
prerelapse_num	0.4595	0.3930	0.0976

	Var. Ratio	eCDF Mean	eCDF Max
distance	0.7873	0.1917	0.3379
age	1.3868	0.1519	0.3085
female0	.	0.0417	0.0417
female1	.	0.0417	0.0417
prevDMTefficacyNone	.	0.1304	0.1304
prevDMTefficacyLow_efficacy	.	0.0020	0.0020
prevDMTefficacyMedium_high_efficacy	.	0.1324	0.1324
prerelapse_num	1.1990	0.0133	0.0383

Summary of Balance for Matched Data:

	Means Treated	Means Control	Std. Mean Diff.
distance	0.7970	0.7970	0.0001
age	44.2496	44.1364	0.0116
female0	0.2318	0.2517	-0.0470
female1	0.7682	0.7483	0.0470
prevDMTefficacyNone	0.4118	0.4157	-0.0079
prevDMTefficacyLow_efficacy	0.1114	0.1224	-0.0347
prevDMTefficacyMedium_high_efficacy	0.4768	0.4619	0.0297
prerelapse_num	0.4595	0.4654	-0.0087

	Var. Ratio	eCDF Mean	eCDF Max
distance	0.9955	0.0012	0.0116
age	1.0161	0.0076	0.0260
female0	.	0.0199	0.0199
female1	.	0.0199	0.0199
prevDMTefficacyNone	.	0.0039	0.0039
prevDMTefficacyLow_efficacy	.	0.0109	0.0109
prevDMTefficacyMedium_high_efficacy	.	0.0148	0.0148
prerelapse_num	0.9530	0.0057	0.0110

	Std. Pair Dist.
distance	0.0022
age	0.1688
female0	0.5149
female1	0.5149

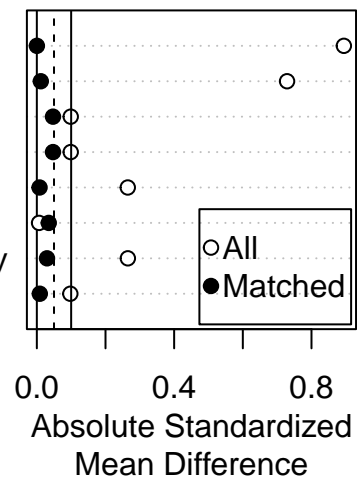
prevDMTefficacyNone	0.1816
prevDMTefficacyLow_efficacy	0.5944
prevDMTefficacyMedium_high_efficacy	0.4731
prerelapse_num	0.3893

Sample Sizes:

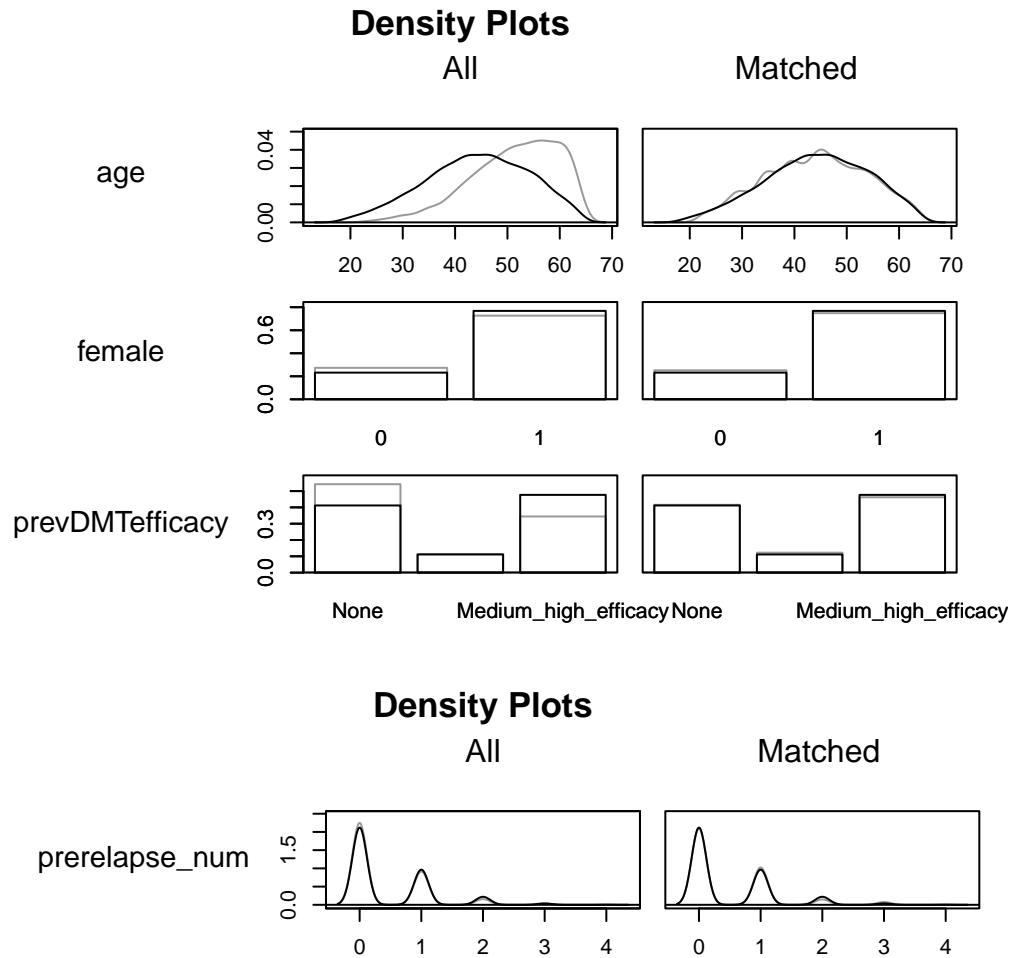
	Control	Treated
All	2300.	7700
Matched (ESS)	198.89	7700
Matched	2300.	7700
Unmatched	0.	0
Discarded	0.	0

```
plot(summary(opt))
```

distance
age
female0
female1
prevDMTefficacyNone
prevDMTefficacyLow_efficacy
prevDMTefficacyMedium_high_efficacy
prerelapse_num



```
# black line is treated group, grey line is control group
plot(opt, type = "density", which.xs = vars)
```



5.3 Estimating the ATT

We can estimate the ATT in the matched sample using Poisson regression in which the number of post-treatment relapses is regressed on treatment status and follow-up time for each patient (captured by the variable `years`). More details are provided at <https://cran.r-project.org/web/packages/MatchIt/vignettes/estimating-effects.html>.

```
# Matched data
matched.data <- match.data(opt)

# Poisson regression model
opt.fit <- glm(y ~ treatment + offset(log(years)),
              family = poisson(link = "log"),
```

```

      data = matched.data,
      weights = weights)

# Treatment effect estimation
opt.comp <- comparisons(opt.fit,
                        variables = "treatment",
                        vcov = ~subclass,
                        newdata = subset(matched.data, treatment == "DMT1"),
                        wts = "weights",
                        transform_pre = "ratio")

opt.comp |> tidy()

```

```

# A tibble: 1 x 9
  type      term      contrast  estim~1 std.e~2 stati~3 p.value conf.~4 conf.~5
<chr>   <chr>    <chr>      <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>
1 response treatment mean(DMT1~  0.761   0.100    7.59 3.21e-14  0.564   0.958
# ... with abbreviated variable names 1: estimate, 2: std.error, 3: statistic,
# 4: conf.low, 5: conf.high

```

As indicated in the summary output above, the annualized relapse rate ratio for DMT1 vs DMT0 among patients treated with DMT0 (ATT) is given as 0.76 with a 95% confidence interval ranging from 0.56 to 0.96.

6 Propensity score stratification

6.1 Divide sample into quintiles of propensity scores

We will form five mutually exclusive groups of the estimated propensity score.

```
# Create five strata
dat <- dat %>% mutate(ps.strata = cut(ps,
                                     breaks = c(quantile(ps, probs=seq(0,1,0.2))),
                                     labels = seq(1:5),
                                     include.lowest = TRUE))

# Number of patients in each stratum
table(dat$ps.strata)
```

```
1      2      3      4      5
2002 2015 1991 1997 1995
```

6.2 Assess balance within each propensity score stratum

Within each propensity score stratum, treated and control patients should have similar values of the propensity score and the distribution of baseline covariates should be approximately balanced between treatment groups.

6.2.1 Propensity Score Stratum #1

```
tab1.strata1 <- CreateTableOne(vars, data = dat %>% filter(ps.strata == 1),
                              factorVars = c("female", "prevDMTefficacy"),
                              strata = "treatment", test = FALSE)

tab1.strata1.print <- print(tab1.strata1, catDigits = 2, contDigits = 2,
                           smd = TRUE)
```

	DMT0	DMT1	SMD
n	901	1101	
age (mean (SD))	58.38 (3.67)	57.45 (3.73)	0.251
female = 1 (%)	605 (67.15)	775 (70.39)	0.070
prevDMTefficacy (%)			0.056
None	650 (72.14)	771 (70.03)	
Low_efficacy	106 (11.76)	130 (11.81)	
Medium_high_efficacy	145 (16.09)	200 (18.17)	
prerelapse_num (mean (SD))	0.29 (0.53)	0.33 (0.56)	0.074

6.2.2 Propensity Score Stratum #2

```
tab1.strata2 <- CreateTableOne(vars, data = dat %>% filter(ps.strata == 2),
                              factorVars = c("female", "prevDMTefficacy"),
                              strata = "treatment", test = FALSE)

tab1.strata2.print <- print(tab1.strata2, catDigits = 2, contDigits = 2,
                             smd = TRUE)
```

	DMT0	DMT1	SMD
n	617	1398	
age (mean (SD))	52.18 (4.35)	51.97 (4.22)	0.049
female = 1 (%)	458 (74.23)	1048 (74.96)	0.017
prevDMTefficacy (%)			0.054
None	292 (47.33)	624 (44.64)	
Low_efficacy	69 (11.18)	162 (11.59)	
Medium_high_efficacy	256 (41.49)	612 (43.78)	
prerelapse_num (mean (SD))	0.40 (0.64)	0.41 (0.66)	0.004

6.2.3 Propensity Score Stratum #3

```
tab1.strata3 <- CreateTableOne(vars, data = dat %>% filter(ps.strata == 3),
                              factorVars = c("female", "prevDMTefficacy"),
                              strata = "treatment", test = FALSE)

tab1.strata3.print <- print(tab1.strata3, catDigits = 2, contDigits = 2,
                             smd = TRUE)
```

	DMT0	DMT1	SMD
n	392	1599	
age (mean (SD))	46.73 (4.06)	46.36 (4.08)	0.092
female = 1 (%)	305 (77.81)	1193 (74.61)	0.075
prevDMTefficacy (%)			0.041
None	168 (42.86)	687 (42.96)	
Low_efficacy	52 (13.27)	191 (11.94)	
Medium_high_efficacy	172 (43.88)	721 (45.09)	
prerelapse_num (mean (SD))	0.49 (0.68)	0.47 (0.66)	0.031

6.2.4 Propensity Score Stratum #4

```
tab1.strata4 <- CreateTableOne(vars, data = dat %>% filter(ps.strata == 4),
                              factorVars = c("female", "prevDMTefficacy"),
                              strata = "treatment", test = FALSE)

tab1.strata4.print <- print(tab1.strata4, catDigits = 2, contDigits = 2,
                             smd = TRUE)
```

	DMT0	DMT1	SMD
n	269	1728	
age (mean (SD))	41.07 (4.11)	40.88 (4.29)	0.046
female = 1 (%)	203 (75.46)	1356 (78.47)	0.071
prevDMTefficacy (%)			0.084
None	105 (39.03)	634 (36.69)	
Low_efficacy	22 (8.18)	181 (10.47)	
Medium_high_efficacy	142 (52.79)	913 (52.84)	
prerelapse_num (mean (SD))	0.50 (0.69)	0.51 (0.71)	0.012

6.2.5 Propensity Score Stratum #5

```
tab1.strata5 <- CreateTableOne(vars, data = dat %>% filter(ps.strata == 5),
                              factorVars = c("female", "prevDMTefficacy"),
                              strata = "treatment", test = FALSE)

tab1.strata5.print <- print(tab1.strata5, catDigits = 2, contDigits = 2,
                             smd = TRUE)
```

	DMT0	DMT1	SMD
n	121	1874	
age (mean (SD))	33.26 (4.95)	32.04 (5.58)	0.233
female = 1 (%)	100 (82.64)	1543 (82.34)	0.008
prevDMTefficacy (%)			0.050
None	32 (26.45)	455 (24.28)	
Low_efficacy	12 (9.92)	194 (10.35)	
Medium_high_efficacy	77 (63.64)	1225 (65.37)	
prerelapse_num (mean (SD))	0.52 (0.66)	0.52 (0.73)	0.004

6.3 Estimating and pooling of stratum-specific treatment effects

The overall ATT across strata can be estimated by weighting stratum-specific estimates by the proportion of treated patients in each stratum over all treated patients in the sample.

We first define a function `att.strata.function()` to calculate stratum-specific estimates of the treatment effect:

```
att.strata.function <- function(data, stratum, confint = TRUE) {

  fit <- glm("y ~ treatment + offset(log(years))",
    family = poisson(link = "log"),
    data = data %>% filter(ps.strata == stratum))

  arr <- round(as.numeric(exp(coef(fit)["treatmentDMT1"])), digits = 3)
  ll <- ul <- NA

  if (confint) {
    ll <- round(exp(confint(fit))["treatmentDMT1",1], digits = 3)
    ul <- round(exp(confint(fit))["treatmentDMT1",2], digits = 3)
  }

  return(c("stratum" = stratum,
    "arr" = arr,
    "ci_lower" = ll,
    "ci_upper" = ul))
}

arr.strata <- as.data.frame(t(apply(1:5, att.strata.function, data = dat)))
arr.strata
```

	stratum	arr	ci_lower	ci_upper
1	1	0.904	0.760	1.076
2	2	0.822	0.696	0.975
3	3	0.798	0.666	0.961
4	4	0.716	0.587	0.881
5	5	0.589	0.463	0.761

Subsequently, we define a function `weights.strata.function()` to calculate the weights for each stratum. The weight is the proportion of treated patients in each stratum over all treated patients in the sample:

```
weights.strata.function <- function(data, stratum) {
  n_DMT1_stratum <- nrow(data %>% filter(ps.strata == stratum & treatment == "DMT1"))
  n_DMT1_all <- nrow(data %>% filter(treatment == "DMT1"))
  weight <- n_DMT1_stratum/n_DMT1_all
  return(c("stratum" = stratum, "weight" = weight))
}

weights.strata <- as.data.frame(t(apply(1:5, weights.strata.function, data = dat)))
weights.strata
```

	stratum	weight
1	1	0.1429870
2	2	0.1815584
3	3	0.2076623
4	4	0.2244156
5	5	0.2433766

```
# Create table with ARRs and weights for each PS stratum
arr.weights.merged <- merge(arr.strata, weights.strata, by = "stratum")

# Calculate the weighted ARR for each stratum
arr.weights.merged <- arr.weights.merged %>%
  mutate(weighted.arr = as.numeric(arr) * weight)

# Sum the weighted ARRs across strata to get the overall ATT
sum(arr.weights.merged$weighted.arr)
```

```
[1] 0.7482462
```

We now define a new function `ps.stratification.bootstrap()` that integrates estimation of the ATT and the PS weights for bootstrapping purposes:

```
ps.stratification.bootstrap <- function(data, inds) {
  d <- data[inds,]

  d$ps.strata <- cut(d$ps,
                    breaks = c(quantile(dat$ps, probs = seq(0, 1, by = 0.2))),
                    labels = seq(5),
                    include.lowest = TRUE)

  arr.strata <- as.data.frame(t(sapply(1:5, att.strata.function,
                                     data = d, confint = FALSE)))

  weights.strata <- as.data.frame(t(sapply(1:5, weights.strata.function, data = d)))

  return(arr.strata$arr[1] * weights.strata$weight[1] +
         arr.strata$arr[2] * weights.strata$weight[2] +
         arr.strata$arr[3] * weights.strata$weight[3] +
         arr.strata$arr[4] * weights.strata$weight[4] +
         arr.strata$arr[5] * weights.strata$weight[5])
}
```

We can now estimate the treatment effect and its confidence interval using the bootstrap procedure:

```
library(boot)
```

Attaching package: 'boot'

The following object is masked from 'package:survival':

```
aml

set.seed(1854)
arr.stratification.boot <- boot(data = dat,
                              statistic = ps.stratification.bootstrap,
                              R = 1000)

# Bootstrapped ARR
```

```
median(arr.stratification.boot$t)
```

```
[1] 0.7558609
```

```
# Bootstrapped ARR 95% CI
```

```
quantile(arr.stratification.boot$t[,1], c(0.025, 0.975))
```

2.5%	97.5%
0.6835885	0.8362947

7 Propensity score weighting

7.1 Calculate propensity score weights for ATT

Propensity score weighting reweights the study sample to generate an artificial population (i.e., pseudo-population) in which the covariates are no longer associated with treatment, thereby removing confounding by measured covariates. For the ATT, the weight for all treated patients is set to one. Conversely, the weight for patients in the control group is set to the propensity score divided by one minus the propensity score, that is, $(PS/(1 - PS))$. We estimated stabilized weights to address extreme weights.

```
library(WeightIt)

w.out <- weightit(treatment ~ age + female + prevDMTefficacy + prerelapse_num,
                  data = dat,
                  method = "ps",
                  estimand = "ATT")
                  #stabilize = TRUE)

w.out
```

A weightit object

- method: "ps" (propensity score weighting)
- number of obs.: 10000
- sampling weights: none
- treatment: 2-category
- estimand: ATT (focal: DMT1)
- covariates: age, female, prevDMTefficacy, prerelapse_num

```
summary(w.out)
```

Summary of weights

- Weight ranges:

	Min		Max
DMT0	0.4772	-----	48.6856
DMT1	1.0000		1.0000

- Units with 5 most extreme weights by group:

	9492	8836	6544	9610	4729
DMT0	32.1027	32.1027	34.3126	38.1817	48.6856
	6	4	3	2	1
DMT1	1	1	1	1	1

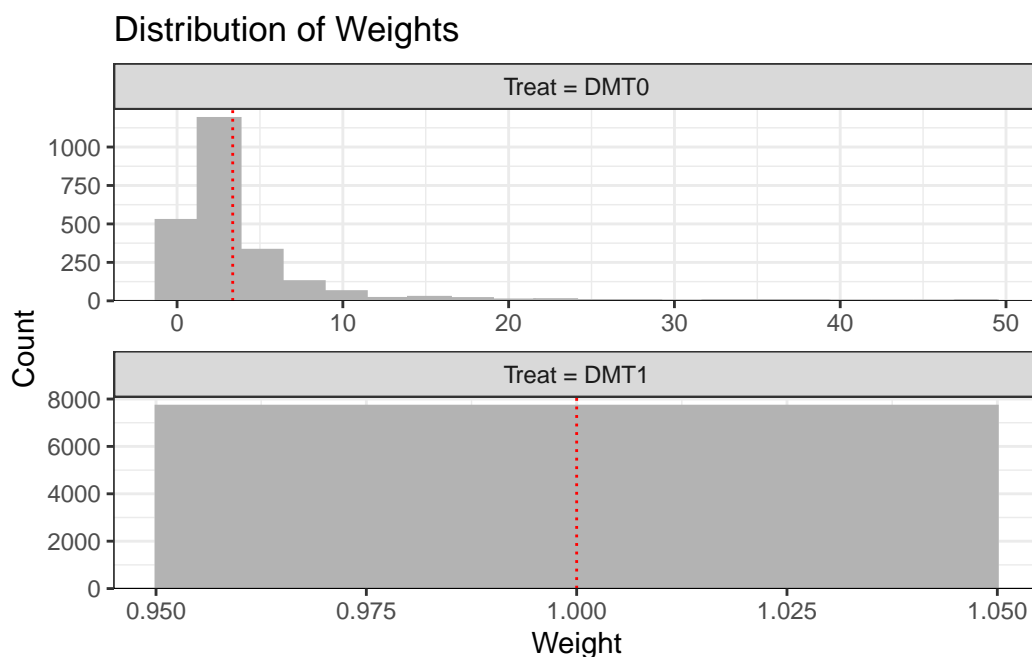
- Weight statistics:

	Coef of Var	MAD	Entropy	# Zeros
DMT0	1.098	0.673	0.383	0
DMT1	0.000	0.000	-0.000	0

- Effective Sample Sizes:

	DMT0	DMT1
Unweighted	2300.	7700
Weighted	1043.16	7700

```
plot(summary(w.out))
```



7.2 Assess balance in the weighted sample

```
bal.tab(w.out, stats = c("m", "v"), thresholds = c(m = .05))
```

Balance Measures

	Type	Diff.Adj	M.Threshold
prop.score	Distance	-0.0045	Balanced, <0.05
age	Contin.	0.0054	Balanced, <0.05
female	Binary	0.0005	Balanced, <0.05
prevDMTefficacy_None	Binary	-0.0003	Balanced, <0.05
prevDMTefficacy_Low_efficacy	Binary	0.0023	Balanced, <0.05
prevDMTefficacy_Medium_high_efficacy	Binary	-0.0020	Balanced, <0.05
prerelapse_num	Contin.	-0.0034	Balanced, <0.05
	V.Ratio.Adj		
prop.score		0.9926	
age		1.0102	
female		.	
prevDMTefficacy_None		.	
prevDMTefficacy_Low_efficacy		.	
prevDMTefficacy_Medium_high_efficacy		.	
prerelapse_num		1.0941	

Balance tally for mean differences

	count
Balanced, <0.05	7
Not Balanced, >0.05	0

Variable with the greatest mean difference

Variable	Diff.Adj	M.Threshold
age	0.0054	Balanced, <0.05

Effective sample sizes

	DMT0	DMT1
Unadjusted	2300.	7700
Adjusted	1043.16	7700

7.3 Estimate the ATT

One way to estimate the ATT is to use the survey package. The function `svyglm()` generates model-robust (Horvitz-Thompson-type) standard errors by default, and thus does not require additional adjustments.

```
library(survey)

weighted.data <- svydesign(ids = ~1, data = dat, weights = ~w.out$weights)

weighted.fit <- svyglm(y ~ treatment + offset(log(years)),
                      family = poisson(link = "log"),
                      design = weighted.data)

exp(coef(weighted.fit)["treatmentDMT1"])
```

```
treatmentDMT1
0.7083381
```

```
exp(confint(weighted.fit))["treatmentDMT1",]
```

```
2.5 %    97.5 %
0.6245507 0.8033662
```

As indicated above, propensity score weighting yielded an ATT estimate of 0.71 (95% CI: 0.62; 0.8).

An alternative approach is to use `glm()` to estimate the treatment effect and calculate robust standard errors.

```
# Alternative way to estimate treatment effect
weighted.fit2 <- glm(y ~ treatment + offset(log(years)),
  family = poisson(link = "log"),
  data = dat,
  weights = w.out$weights)

# Extract the estimated ARR
exp(coef(weighted.fit2))["treatmentDMT1"]
```

```
treatmentDMT1
0.7083381
```

```
# Calculate robust standard error and p-value of the log ARR
coeftest(weighted.fit2, vcov. = vcovHC)["treatmentDMT1",]
```

Estimate	Std. Error	z value	Pr(> z)
-3.448337e-01	6.442745e-02	-5.352280e+00	8.685284e-08

```
# Derive 95% confidence interval of the ARR
exp(lmtest::coefci(weighted.fit2,
  level = 0.95, # 95% confidence interval
  vcov. = vcovHC)["treatmentDMT1",])
```

2.5 %	97.5 %
0.6243094	0.8036767

Using this approach, the ATT estimate was 0.71 (95% CI: 0.62; 0.8).

8 Regression adjustment for the propensity score for the ATE

In this approach, a regression model is fitted to describe the observed outcome as a function of the received treatment and the estimated propensity score:

```
ps.reg.fit <- glm(y ~ treatment + ps + offset(log(years)),  
                  family = poisson(link = "log"),  
                  data = dat)  
  
summary(ps.reg.fit)
```

Call:

```
glm(formula = y ~ treatment + ps + offset(log(years)), family = poisson(link = "log"),  
     data = dat)
```

Deviance Residuals:

Min	1Q	Median	3Q	Max
-2.0160	-0.7336	-0.4441	-0.1352	4.2634

Coefficients:

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-1.99585	0.10359	-19.266	< 2e-16 ***
treatmentDMT1	-0.25598	0.04431	-5.777	7.60e-09 ***
ps	1.07521	0.13878	7.748	9.36e-15 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for poisson family taken to be 1)

Null deviance: 7514.7 on 9999 degrees of freedom
Residual deviance: 7443.0 on 9997 degrees of freedom
AIC: 12378

Number of Fisher Scoring iterations: 6

```
# ATE
exp(coef(ps.reg.fit))["treatmentDMT1"]
```

```
treatmentDMT1
0.7741606
```

Waiting for profiling to be done...

Waiting for profiling to be done...

Bootstrapped confidence intervals can be obtained as follows:

```
# Function to bootstrap for 95% CIs
ps.reg.bootstrap <- function(data, inds) {
  d <- data[inds,]

  fit <- glm(y ~ treatment + ps + offset(log(years)),
            family = poisson(link = "log"),
            data = d)

  return(exp(coef(fit))["treatmentDMT1"])
}

set.seed(1854)

# Generate 1000 bootstrap replicates
arr.boot <- boot(dat, statistic = ps.reg.bootstrap, R = 1000)

# Extract the median annualized relapse rate across 1000 bootstrap replicates
median(arr.boot$t)
```

```
[1] 0.7750426
```

```
# Take 2.5th and 97.5th percentiles to be 95% CI
quantile(arr.boot$t[,1], c(0.025, 0.975))
```

```
      2.5%      97.5%
0.7010540 0.8545169
```

9 Overview

Method	Estimand	Estimate	95% CI (lower)	95% CI (upper)
Optimal full matching	ATT	0.7610138	0.5644807	0.9575469
Propensity score stratification	ATT	0.7482462	NA	NA
Propensity score stratification (with bootstrapping)	ATT	0.7558609	0.6835885	0.8362947
Propensity score weighting	ATT	0.7083381	0.6245507	0.8033662
Propensity score weighting (robust SE)	ATT	0.7083381	0.6243094	0.8036767
PS regression adjustment	ATE	0.7741606	0.7101080	0.8448218
PS regression adjustment (bootstrapping)	ATE	0.7750426	0.7010540	0.8545169

10 Effect Modification Analysis within the Propensity score Framework

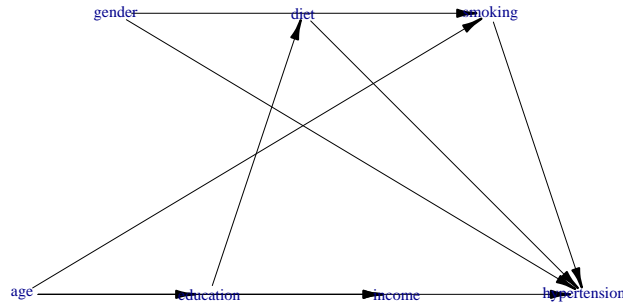
First, we need to install the R package `simcausal`, which can be obtained from GitHub:

```
devtools::install_github('oso/r/simcausal', build_vignettes = FALSE)
```

We will use the following data-generation model:

```
require(simcausal)
D <- DAG.empty()
D <- D +
  node("age", distr = "rnorm",
        mean = 2, sd = 4) +
  node("gender", distr = "rbern",
        prob = plogis(4)) +
  node("education", distr = "rbern",
        prob = plogis(3 + 5 * age)) +
  node("diet", distr = "rbern",
        prob = plogis(1 - 3 * education)) +
  node("income", distr = "rbern",
        prob = plogis(2 - 5 * education - 4 * age)) +
  node("smoking", distr = "rbern",
        prob = plogis(1 + 1.2 * gender + 2 * age)) +
  node("hypertension", distr = "rbern",
        prob = plogis(1 + log(3) * diet +
                      log(1.3) * age +
                      log(3.5) * smoking +
                      log(0.5) * gender))

Dset <- set.DAG(D)
plotDAG(Dset)
```

We can now generate an example dataset:

```
Obs.Data <- sim(DAG = Dset, n = 50000, rndseed = 123)

Obs.Data$smoking <- as.character(Obs.Data$smoking)
Obs.Data$income <- as.factor(Obs.Data$income)
Obs.Data$income <- relevel(Obs.Data$income, ref = "1")
```

Sample data from the hypothetical example of association between hypertension and smoking, where other variables such as income, age [centered], gender, education and diet also plays a role in the data generation process.

	age	gender	education	diet	income	smoking	hypertension
34901	12.288936	1	1	1	0	1	1
149	10.400436	1	1	0	0	1	1
10060	2.991820	1	1	0	0	1	0
22220	-4.311952	0	0	0	1	0	1
9979	-6.435549	0	0	0	1	0	1

10.1 Effect measure assessment via adding interaction term

Below, we estimate a logistic regression model to assess whether the effect of smoking (the exposure) on hypertension is modified by income. The covariates age and gender are confounders.

```
fit.w.em <- glm(hypertension ~ smoking * income + age + gender,
               family = binomial(link = "logit"), data = Obs.Data)

require(jtools)
results.model <- summ(fit.w.em, model.info = FALSE,
                    model.fit = FALSE,
```

```
exp = TRUE)
results.model
```

	exp(Est.)	2.5%	97.5%	z val.	p
(Intercept)	5.46	4.37	6.82	14.97	0.00
smoking1	2.93	2.60	3.30	17.69	0.00
income0	0.48	0.41	0.57	-8.28	0.00
age	1.29	1.27	1.31	36.77	0.00
gender	0.54	0.43	0.67	-5.55	0.00
smoking1:income0	1.27	1.04	1.56	2.33	0.02

Standard errors: MLE

The interaction term in `results.model` is statistically significant.

Presentation of effect measures

We can generate a summary report from aforementioned effect modification analysis. The table below depicts the adjusted odds ratios for income levels (`high = 0`, and `low = 1`)

```
require(interactionR)
em.object <- interactionR(fit.w.em,
                          exposure_names = c("income0", "smoking1"),
                          ci.type = "mover", ci.level = 0.95,
                          em = TRUE, recode = FALSE)

em.object$dframe[,1:4]
```

	Measures	Estimates	CI.l1	CI.ul
1	OR00	1.0000000	NA	NA
2	OR01	2.9301604	2.6010653	3.3008937
3	OR10	0.4832932	0.4068652	0.5740780
4	OR11	1.7997639	1.6334908	1.9829619
5	OR(smoking1 on outcome [income0==0])	2.9301604	2.6010653	3.3008937
6	OR(smoking1 on outcome [income0==1])	3.7239584	3.1434919	4.4116118
7	Multiplicative scale	1.2709060	1.0385052	1.5553143
8	RERI	-0.6136898	-0.9754808	-0.2905171

10.2 Effect measure assessment via stratified approach

This approach involves estimating a regression model in different strata of the effect modifier income:

```
fit.income1 <- glm(hypertension ~ smoking + age + gender,
  family = binomial(link = "logit"),
  data = subset(Obs.Data, income == 1))
fit.income0 <- glm(hypertension ~ smoking + age + gender,
  family=binomial(link = "logit"),
  data= subset(Obs.Data, income == 0))
```

The table below summarizes the adjusted odds ratios for smoking across the different income levels (low = 1, and high = 0) as obtained using the stratified approach.

	Value of income	exp(Est.)	2.5%	97.5%	z val.	p
[1,]	1	3.066878	2.707961	3.473366	17.64728	1.067842e-69
[2,]	0	3.590260	3.023124	4.263792	14.57113	4.287200e-48

Note that we can obtain the same results by estimating a regression model with an interaction term between the modifier and all covariates:

```
fit.all.int <- glm(hypertension ~ income * (smoking + age + gender),
  family = binomial(link = "logit"), data = Obs.Data)
```

	Variable	Units	OddsRatio	CI.95	p-value
1	income(1): smoking(1 vs 0)		3.07	[2.71;3.47]	< 1e-04
2	income(0): smoking(1 vs 0)		3.59	[3.02;4.26]	< 1e-04

10.3 Interaction

Assessment of interaction between smoking and income. We estimate a logistic regression model where

- Outcome: hypertension
- Exposure variables: smoking and income
- Confounders: age, gender, and education

An interaction term of smoking and income is added.

```
fit.w.int <- glm(hypertension ~ smoking * income + age + gender +
                 education, family = binomial(link = "logit"),
                 data = Obs.Data)
results.int.model <- summ(fit.w.int, model.info = FALSE, model.fit = FALSE,
                          exp = TRUE)
results.int.model$coeftable
```

	exp(Est.)	2.5%	97.5%	z val.	p
(Intercept)	5.6937765	4.5570175	7.1141027	15.3077121	6.791105e-53
smoking1	3.3452459	2.9505339	3.7927612	18.8503257	2.920389e-79
income0	1.0908060	0.8506311	1.3987941	0.6849951	4.933470e-01
age	1.2981524	1.2804814	1.3160673	37.3150071	9.371499e-305
gender	0.5366777	0.4313229	0.6677666	-5.5815569	2.383750e-08
education	0.4233969	0.3502014	0.5118909	-8.8749618	6.995745e-19
smoking1:income0	1.1022535	0.8968615	1.3546825	0.9253438	3.547871e-01

The interaction term between income and smoking is, however, not statistically significant.

Presentation of effect measures

```
int.object = interactionR(fit.w.int,
                          exposure_names = c("smoking1", "income0"),
                          ci.type = "mover", ci.level = 0.95,
                          em = FALSE, recode = FALSE)
```

Summary report from an interaction analysis when investigating association between two exposure variables (smoking and income) and hypertension. Below, CI.l1 and CI.u1 depict the lower and upper limits of the 95 percent confidence intervals, $OR_{11} = OR_{A=1, M=1}$, $OR_{10} = OR_{A=1, M=0}$, $OR_{01} = OR_{A=0, M=1}$ and OR_{00} captures the reference.

	Measures	Estimates	CI.l1	CI.u1
1	OR00	1.0000000	NA	NA
2	OR01	1.0908060	0.850631061	1.3987941
3	OR10	3.3452459	2.950533888	3.7927612
4	OR11	4.0221386	3.287881778	4.9203713
5	OR(income0 on outcome [smoking1==0])	1.0908060	0.850631061	1.3987941
6	OR(income0 on outcome [smoking1==1])	1.2023447	0.997265811	1.4495962
7	OR(smoking1 on outcome [income0==0])	3.3452459	2.950533888	3.7927612
8	OR(smoking1 on outcome [income0==1])	3.6873089	3.112335708	4.3685026
9	Multiplicative scale	1.1022535	0.896861546	1.3546825

10	RERI	0.5860867	0.029944164	1.2657133
11	AP	0.1457152	-0.004274684	0.2598376
12	SI	1.2405887	1.008364517	1.5262937

11 Dealing with irregular and informative visits

We first load the required packages

```
library(dplyr)
library(broom)
library(ggplot2)
library(mice)
```

11.1 Example dataset

In this example dataset, we have a discrete outcome `y` that is affected by its baseline value `edss`, age, sex, and the treatment duration `time`.

```
set.seed(9843626)

dataset <- sim_data_EDSS(npatients = 500,
  ncenters = 10,
  follow_up = 12*5, # Total follow-up (number of months)
  sd_a_t = 0.5,    # DGM - Within-visit variation in EDSS scores
  baseline_EDSS = 1.3295,    # DGM - Mean baseline EDDS score
  sd_alpha_ij = 1.46,    # DGM - Between-subject variation in base
  sd_beta1_j = 0.20,    # DGM - Between-site variation in baseline
  mean_age = 42.41,
  sd_age = 10.53,
  min_age = 18,
  beta_age = 0.05, # DGM - prognostic effect of age
  beta_t = 0.014, # DGM - prognostic effect of time
  beta_t2 = 0,    # DGM - prognostic effect of time squared
  delta_xt = 0, # DGM - interaction treatment time
  delta_xt2 = 0, # 0.0005    # DGM - interaction treatment time2
  p_female = 0.75,
  beta_female = -0.2, ## DGM - prognostic effect of male sex
  delta_xf = 0,      ## DGM - interaction sex treatment
```

```

rho = 0.8,                # DGM - autocorrelation of between alpha_
corFUN = corAR1,          # DGM - correlation structure of the late
tx_alloc_FUN = treatment_alloc_confounding_v2 ) ## or treatment_

```

We remove `y` according to the informative visit process that depends on the received treatment, gender, and age.

```

dataset_visit <- censor_visits_a5(dataset, seed = 12345) %>%
  dplyr::select(-y) %>%
  mutate(time_x = time*x)

```

In the censored data, a total of 17 out of 5000 patients have a visit at `time=60`.

11.2 Estimation of treatment effect

We will estimate the marginal treatment effect at time `time=60`.

11.2.1 Original data

```

origdat60 <- dataset %>% filter(time == 60)

# Predict probability of treatment allocation
fitps <- glm(x ~ age + sex + edss, family = 'binomial',
            data = origdat60)

# Derive the propensity score
origdat60 <- origdat60 %>% mutate(ipt = ifelse(x == 1, 1/predict(fitps, type = 'response')
                                             1/(1-predict(fitps, type = 'response'))))

# Estimate
fit_ref_m <- tidy(lm(y ~ x, weight = ipt, data = origdat60), conf.int = TRUE)

```

11.2.2 Doubly-weighted marginal treatment effect

```

obsdat60 <- dataset_visit %>% mutate(visit = ifelse(is.na(y_obs),0,1)) %>% filter(time ==

gamma <- glm(visit ~ x + sex + age + edss, family = 'binomial', data = obsdat60)$coef

```

```

obsdat60 <- obsdat60 %>% mutate(rho_i = 1/exp(gamma["(Intercept)"] +
                                             gamma["x"]*x +
                                             gamma["sex"]*sex +
                                             gamma["age"]*age))

# Predict probability of treatment allocation
fitps <- glm(x ~ age + sex + edss, family='binomial', data = obsdat60)

# Derive the propensity score
obsdat60 <- obsdat60 %>% mutate(ipt = ifelse(x==1, 1/predict(fitps, type='response'),
                                             1/(1-predict(fitps, type='response'))))

fit_w <- tidy(lm(y_obs ~ x, weights = ipt*rho_i, data = obsdat60), conf.int = TRUE)

```

11.2.3 Multilevel multiple imputation

We impute the entire vector of `y_obs` for all 61 potential visits and generate 10 imputed datasets. Note: `mlmi` currently does not support imputation of treatment-covariate interaction terms.

```

imp <- impute_y_mice_3l(dataset_visit, seed = 12345)

```

We can now estimate the treatment effect in each imputed dataset

```

# Predict probability of treatment allocation
fitps <- glm(x ~ age + sex + edss, family='binomial', data = dataset_visit)

# Derive the propensity score
dataset_visit <- dataset_visit %>% mutate(ipt = ifelse(x==1, 1/predict(fitps, type='response'),
                                             1/(1-predict(fitps, type='response'))))

Q <- U <- rep(NA, 10) # Error variances

for (i in seq(10)) {
  dati <- cbind(dataset_visit[,c("x","ipt","time")], y_imp = imp[,i]) %>% filter(time == 6)

  # Estimate
  fit <- tidy(lm(y_imp ~ x, weight = ipt, data = dati), conf.int = TRUE)
}

```



```

Q[i] <- fit %>% filter(term == "x") %>% pull(estimate)
U[i] <- (fit %>% filter(term == "x") %>% pull(std.error))**2
}

fit_mlmi <- pool.scalar(Q = Q, U = U)

```

11.3 Reproduce the results using all data to compute the marginal effect with IIV-weighted

11.3.1 Doubly -weighted marginal treatment effect total

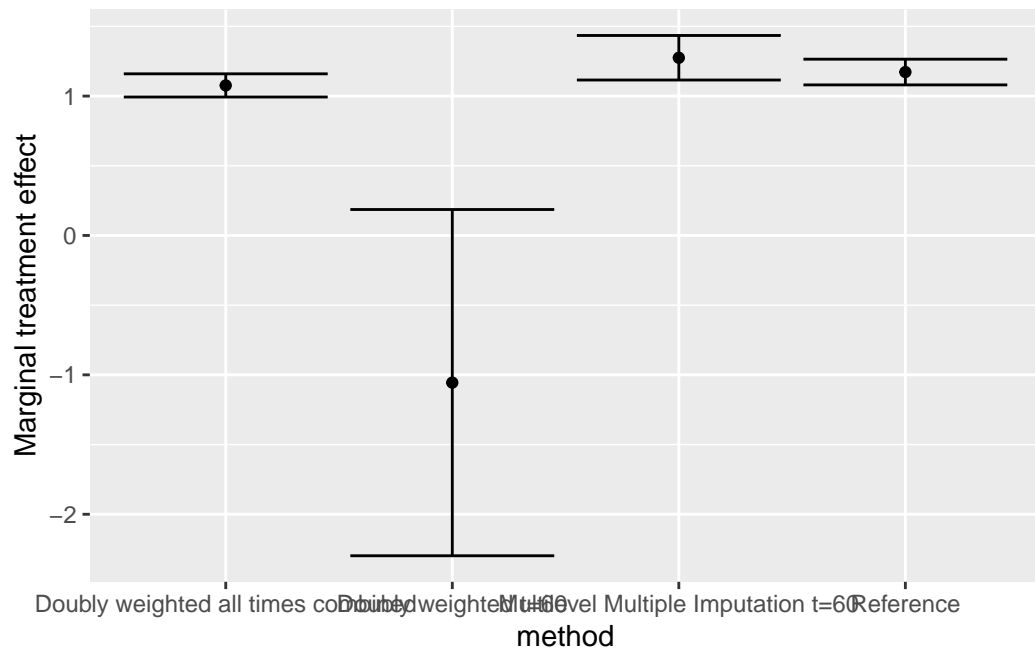
```

obsdatall <- dataset_visit %>% mutate(visit = ifelse(is.na(y_obs),0,1))
gamma <- glm(visit ~ x + sex + age + edss, family = 'binomial', data = obsdatall)$coef
obsdatall <- obsdatall %>% mutate(rho_i = 1/exp(gamma["(Intercept)"] +
                                             gamma["x"]*x +
                                             gamma["sex"]*sex +
                                             gamma["age"]*age))

# Predict probability of treatment allocation
fitps <- glm(x ~ age + sex + edss, family='binomial', data = obsdatall)
# Derive the propensity score
obsdatall <- obsdatall %>% mutate(ipt = ifelse(x==1, 1/predict(fitps, type='response'),
                                             1/(1-predict(fitps, type='response'))))
fit_w <- tidy(lm(y_obs ~ x, weights = ipt*rho_i, data = obsdatall), conf.int = TRUE)

```

11.4 Results



References