# Causal Inference: What If. Exercises – R code

Book by M. A. Hernán and J. M. Robins R code by Joy Shi and Sean McGrath
R Markdown code by Tom Palmer

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# Contents

# Preface

This book presents code examples from Hernán and Robins (2020), which is available in draft form from the following webpage.

https://www.hsph.harvard.edu/miguel-hernan/causal-inference-book/

The R code is based on the code by Joy Shi and Sean McGrath given here.

## Packages to install

To install the R packages required for this book please copy/fork the repository and run:

```
# install.packages('devtools') # uncomment if devtools not
# installed
devtools::install_deps()
```

## Downloading the datasets

We assume that you have downloaded the data from the Causal Inference Book website and saved it to a `data` subdirectory. You can do this manually or with the following code (nb. we use the `here` package to reference the data subdirectory).

```
library(here)
```

```
dataurls <- list()
dataurls[[1]] <- "https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1268/2012/10/nhefs_sas.zip"
dataurls[[2]] <- "https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1268/2012/10/nhefs_stata.zip"
dataurls[[3]] <- "https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1268/2017/01/nhefs_excel.zip"
dataurls[[4]] <- "https://cdn1.sph.harvard.edu/wp-content/uploads/sites/1268/1268/20/nhefs.csv"

temp <- tempfile()
for (i in 1:3) {
    download.file(dataurls[[i]], temp)
    unzip(temp, exdir = "data")
}

download.file(dataurls[[4]], here("data", "nhefs.csv"))
```

# R code

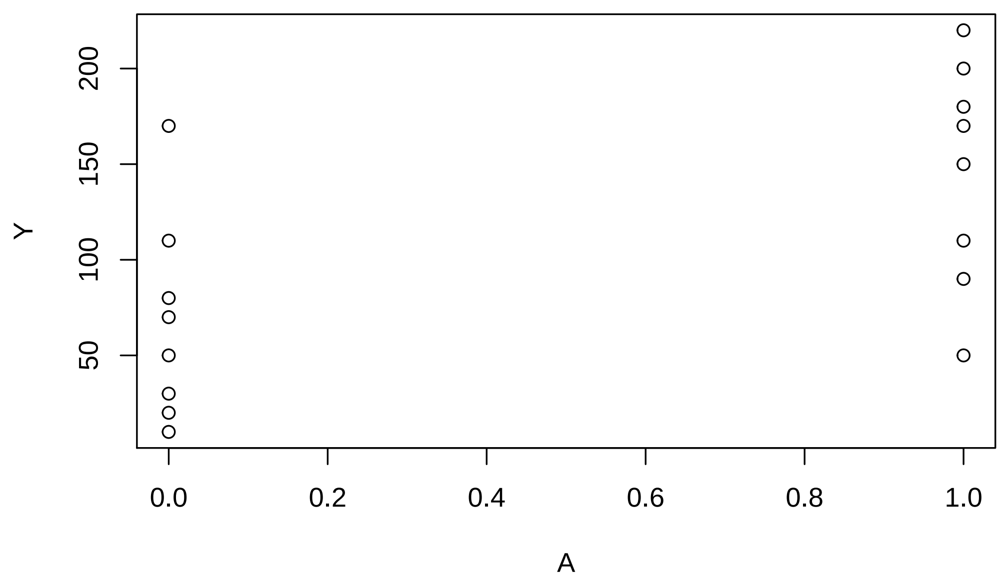
# 11. Why model?

## Program 11.1

- Sample averages by treatment level
- Data from Figures 11.1 and 11.2

```
A <- c(1, 1, 1, 1, 1, 1, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0)
Y <- c(200, 150, 220, 110, 50, 180, 90, 170, 170, 30,
       70, 110, 80, 50, 10, 20)

plot(A, Y)
```




```
summary(Y[A == 0])
```

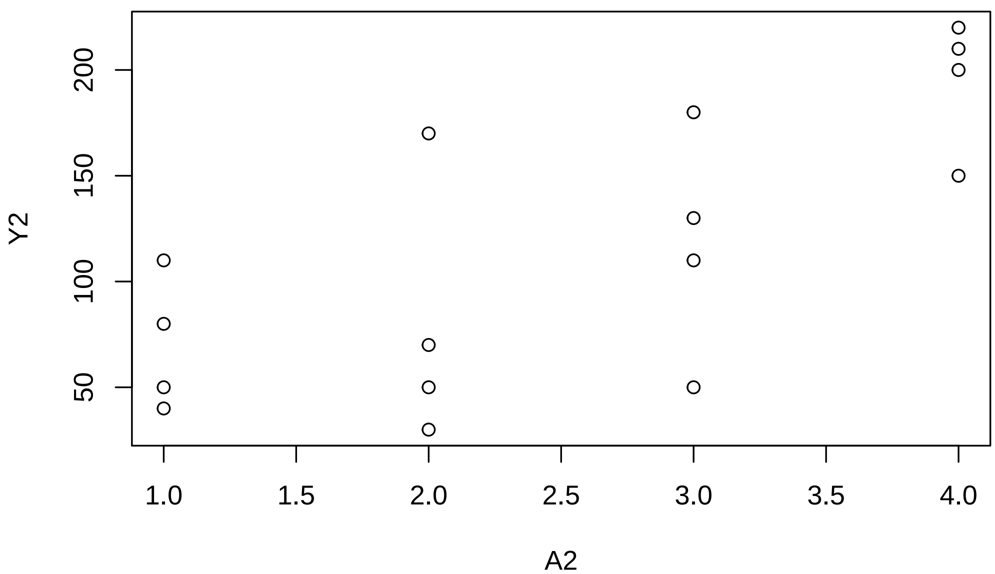
```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    10.0    27.5    60.0    67.5    87.5   170.0
```

```
summary(Y[A == 1])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    50.0   105.0   160.0   146.2   185.0   220.0
```

```r
A2 <- c(1, 1, 1, 1, 2, 2, 2, 2, 3, 3, 3, 3, 4, 4, 4, 4)
Y2 <- c(110, 80, 50, 40, 170, 30, 70, 50, 110, 50, 180,
        130, 200, 150, 220, 210)

plot(A2, Y2)
```




```r
summary(Y2[A2 == 1])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    40.0    47.5    65.0    70.0    87.5   110.0
```

```r
summary(Y2[A2 == 2])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##      30      45      60      80      95     170
```

```r
summary(Y2[A2 == 3])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    50.0    95.0   120.0   117.5   142.5   180.0
```

```r
summary(Y2[A2 == 4])
```

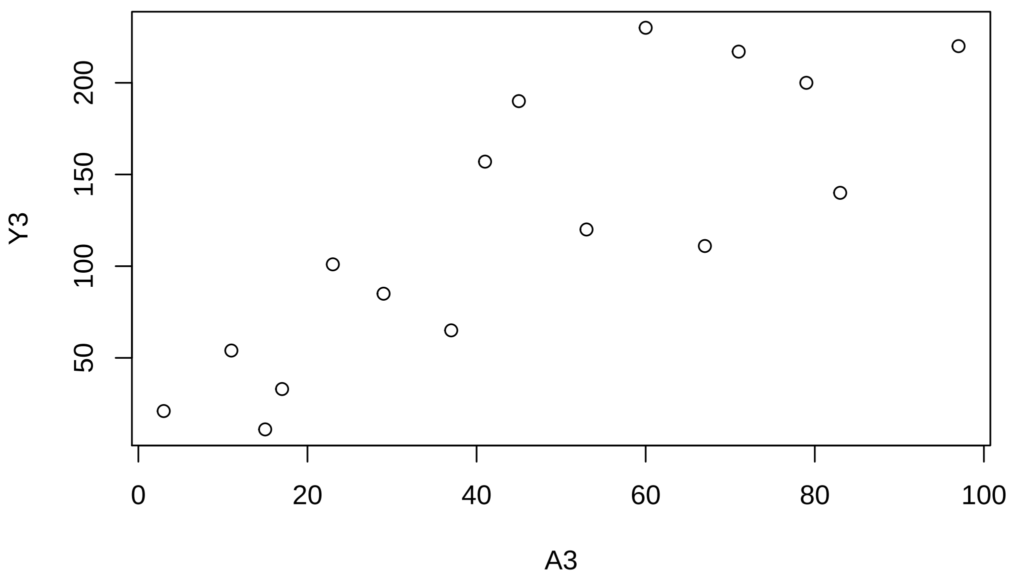
```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   150.0   187.5   205.0   195.0   212.5   220.0
```

## Program 11.2

- 2-parameter linear model
- Data from Figures 11.3 and 11.1

```
A3 <-
  c(3, 11, 17, 23, 29, 37, 41, 53, 67, 79, 83, 97, 60, 71, 15, 45)
Y3 <-
  c(21, 54, 33, 101, 85, 65, 157, 120, 111, 200, 140, 220, 230, 217,
    11, 190)

plot(Y3 ~ A3)
```




```
summary(glm(Y3 ~ A3))
```

```
##
## Call:
## glm(formula = Y3 ~ A3)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -61.930  -30.564   -5.741   30.653   77.225
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  24.5464    21.3300   1.151 0.269094
## A3            2.1372     0.3997   5.347 0.000103 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## (Dispersion parameter for gaussian family taken to be 1944.109)
##
##     Null deviance: 82800  on 15  degrees of freedom
## Residual deviance: 27218  on 14  degrees of freedom
## AIC: 170.43
##
## Number of Fisher Scoring iterations: 2
```

```
predict(glm(Y3 ~ A3), data.frame(A3 = 90))
```

```
##      1
## 216.89
```

```
summary(glm(Y ~ A))
```

```
##
## Call:
## glm(formula = Y ~ A)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -96.250  -40.000    3.125   35.938  102.500
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)    67.50      19.72   3.424  0.00412 **
## A              78.75      27.88   2.824  0.01352 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 3109.821)
##
##     Null deviance: 68344  on 15  degrees of freedom
## Residual deviance: 43538  on 14  degrees of freedom
## AIC: 177.95
##
## Number of Fisher Scoring iterations: 2
```

# Program 11.3

- 3-parameter linear model
- Data from Figure 11.3

```
Asq <- A3 * A3

mod3 <- glm(Y3 ~ A3 + Asq)
summary(mod3)
```

```
##
## Call:
```

```
## glm(formula = Y3 ~ A3 + Asq)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -65.27  -34.41   13.21   26.11   64.36
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) -7.40688   31.74777  -0.233   0.8192
## A3           4.10723    1.53088   2.683   0.0188 *
## Asq         -0.02038    0.01532  -1.331   0.2062
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 1842.697)
##
##     Null deviance: 82800  on 15  degrees of freedom
## Residual deviance: 23955  on 13  degrees of freedom
## AIC: 170.39
##
## Number of Fisher Scoring iterations: 2
```

```r
predict(mod3, data.frame(cbind(A3 = 90, Asq = 8100)))
```

```
##        1
## 197.1269
```

# 12. IP Weighting and Marginal Structural Models

## Program 12.1

- Descriptive statistics from NHEFS data (Table 12.1)

```
library(here)
```

```
# install.packages("readxl") # install package if required
library("readxl")

nhefs <- read_excel(here("data", "NHEFS.xls"))
nhefs$cens <- ifelse(is.na(nhefs$wt82), 1, 0)

# provisionally ignore subjects with missing values for weight in 1982
nhefs.nmv <-
  nhefs[which(!is.na(nhefs$wt82)),]

lm(wt82_71 ~ qsmk, data = nhefs.nmv)
```

```
##
## Call:
## lm(formula = wt82_71 ~ qsmk, data = nhefs.nmv)
##
## Coefficients:
## (Intercept)         qsmk
##       1.984        2.541
```

```
# Smoking cessation
predict(lm(wt82_71 ~ qsmk, data = nhefs.nmv), data.frame(qsmk = 1))
```

```
##        1
## 4.525079
```

```
# No smoking cessation
predict(lm(wt82_71 ~ qsmk, data = nhefs.nmv), data.frame(qsmk = 0))
```

```
##        1
## 1.984498
```

```r
# Table
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 0),]$age)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   25.00   33.00   42.00   42.79   51.00   72.00
```

```r
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 0),]$wt71)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   40.82   59.19   68.49   70.30   79.38  151.73
```

```r
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 0),]$smokeintensity)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    1.00   15.00   20.00   21.19   30.00   60.00
```

```r
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 0),]$smokeyrs)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    1.00   15.00   23.00   24.09   32.00   64.00
```

```r
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 1),]$age)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   25.00   35.00   46.00   46.17   56.00   74.00
```

```r
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 1),]$wt71)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   39.58   60.67   71.21   72.35   81.08  136.98
```

```r
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 1),]$smokeintensity)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##     1.0    10.0    20.0    18.6    25.0    80.0
```

```r
summary(nhefs.nmv[which(nhefs.nmv$qsmk == 1),]$smokeyrs)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    1.00   15.00   26.00   26.03   35.00   60.00
```

```r
table(nhefs.nmv$qsmk, nhefs.nmv$sex)
```

```
##
##       0   1
##   0 542 621
##   1 220 183
```

```r
prop.table(table(nhefs.nmv$qsmk, nhefs.nmv$sex), 1)
```

```
##
##             0         1
##   0 0.4660361 0.5339639
##   1 0.5459057 0.4540943
```

```r
table(nhefs.nmv$qsmk, nhefs.nmv$race)
```

```
##
##       0   1
##   0 993 170
##   1 367  36
```

```
prop.table(table(nhefs.nmv$qsmk, nhefs.nmv$race), 1)
```

```
##
##              0          1
##   0 0.85382631 0.14617369
##   1 0.91066998 0.08933002
```

```
table(nhefs.nmv$qsmk, nhefs.nmv$education)
```

```
##
##       1   2   3   4   5
##   0 210 266 480  92 115
##   1  81  74 157  29  62
```

```
prop.table(table(nhefs.nmv$qsmk, nhefs.nmv$education), 1)
```

```
##
##              1          2          3          4          5
##   0 0.18056750 0.22871883 0.41272571 0.07910576 0.09888220
##   1 0.20099256 0.18362283 0.38957816 0.07196030 0.15384615
```

```
table(nhefs.nmv$qsmk, nhefs.nmv$exercise)
```

```
##
##       0   1   2
##   0 237 485 441
##   1  63 176 164
```

```
prop.table(table(nhefs.nmv$qsmk, nhefs.nmv$exercise), 1)
```

```
##
##             0         1         2
##   0 0.2037833 0.4170249 0.3791917
##   1 0.1563275 0.4367246 0.4069479
```

```
table(nhefs.nmv$qsmk, nhefs.nmv$active)
```

```
##
##       0   1   2
##   0 532 527 104
##   1 170 188  45
```

```
prop.table(table(nhefs.nmv$qsmk, nhefs.nmv$active), 1)
```

```
##
##             0         1         2
##   0 0.4574377 0.4531384 0.0894239
##   1 0.4218362 0.4665012 0.1116625
```

## Program 12.2

- Estimating IP weights
- Data from NHEFS

```r
# Estimation of ip weights via a logistic model
fit <- glm(
  qsmk ~ sex + race + age + I(age ^ 2) +
    as.factor(education) + smokeintensity +
    I(smokeintensity ^ 2) + smokeyrs + I(smokeyrs ^ 2) +
    as.factor(exercise) + as.factor(active) + wt71 + I(wt71 ^ 2),
  family = binomial(),
  data = nhefs.nmv
)
summary(fit)
```

```
##
## Call:
## glm(formula = qsmk ~ sex + race + age + I(age^2) + as.factor(education) +
##     smokeintensity + I(smokeintensity^2) + smokeyrs + I(smokeyrs^2) +
##     as.factor(exercise) + as.factor(active) + wt71 + I(wt71^2),
##     family = binomial(), data = nhefs.nmv)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.5127  -0.7907  -0.6387   0.9832   2.3729
##
## Coefficients:
##                         Estimate Std. Error z value Pr(>|z|)
## (Intercept)           -2.2425191  1.3808360  -1.624 0.104369
## sex                   -0.5274782  0.1540496  -3.424 0.000617 ***
## race                  -0.8392636  0.2100665  -3.995 6.46e-05 ***
## age                    0.1212052  0.0512663   2.364 0.018068 *
## I(age^2)              -0.0008246  0.0005361  -1.538 0.124039
## as.factor(education)2 -0.0287755  0.1983506  -0.145 0.884653
## as.factor(education)3  0.0864318  0.1780850   0.485 0.627435
## as.factor(education)4  0.0636010  0.2732108   0.233 0.815924
## as.factor(education)5  0.4759606  0.2262237   2.104 0.035384 *
## smokeintensity        -0.0772704  0.0152499  -5.067 4.04e-07 ***
## I(smokeintensity^2)    0.0010451  0.0002866   3.647 0.000265 ***
## smokeyrs              -0.0735966  0.0277775  -2.650 0.008061 **
## I(smokeyrs^2)          0.0008441  0.0004632   1.822 0.068398 .
## as.factor(exercise)1   0.3548405  0.1801351   1.970 0.048855 *
## as.factor(exercise)2   0.3957040  0.1872400   2.113 0.034571 *
## as.factor(active)1     0.0319445  0.1329372   0.240 0.810100
## as.factor(active)2     0.1767840  0.2149720   0.822 0.410873
## wt71                  -0.0152357  0.0263161  -0.579 0.562625
## I(wt71^2)              0.0001352  0.0001632   0.829 0.407370
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1786.1  on 1565  degrees of freedom
## Residual deviance: 1676.9  on 1547  degrees of freedom
## AIC: 1714.9
##
## Number of Fisher Scoring iterations: 4
```

```
p.qsmk.obs <-
  ifelse(nhefs.nmv$qsmk == 0,
         1 - predict(fit, type = "response"),
         predict(fit, type = "response"))

nhefs.nmv$w <- 1 / p.qsmk.obs
summary(nhefs.nmv$w)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   1.054   1.230   1.373   1.996   1.990  16.700
```

```
sd(nhefs.nmv$w)
```

```
## [1] 1.474787
```

```
# install.packages("geepack") # install package if required
library("geepack")
msm.w <- geeglm(
  wt82_71 ~ qsmk,
  data = nhefs.nmv,
  weights = w,
  id = seqn,
  corstr = "independence"
)
summary(msm.w)
```

```
##
## Call:
## geeglm(formula = wt82_71 ~ qsmk, data = nhefs.nmv, weights = w,
##     id = seqn, corstr = "independence")
##
##  Coefficients:
##             Estimate Std.err  Wald Pr(>|W|)
## (Intercept)   1.7800  0.2247 62.73 2.33e-15 ***
## qsmk          3.4405  0.5255 42.87 5.86e-11 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)    65.06   4.221
##
## Correlation: Structure = independenceNumber of clusters:   1566   Maximum cluster size: 1
```

```r
beta <- coef(msm.w)
SE <- coef(summary(msm.w))[, 2]
lcl <- beta - qnorm(0.975) * SE
ucl <- beta + qnorm(0.975) * SE
cbind(beta, lcl, ucl)
```

```
##              beta   lcl  ucl
## (Intercept) 1.780 1.340 2.22
## qsmk        3.441 2.411 4.47
```

```r
# no association between sex and qsmk in pseudo-population
xtabs(nhefs.nmv$w ~ nhefs.nmv$sex + nhefs.nmv$qsmk)
```

```
##              nhefs.nmv$qsmk
## nhefs.nmv$sex     0     1
##             0 763.6 763.6
##             1 801.7 797.2
```

```r
# "check" for positivity (White women)
table(nhefs.nmv$age[nhefs.nmv$race == 0 & nhefs.nmv$sex == 1],
      nhefs.nmv$qsmk[nhefs.nmv$race == 0 & nhefs.nmv$sex == 1])
```

```
##
##       0  1
##   25 24  3
##   26 14  5
##   27 18  2
##   28 20  5
##   29 15  4
##   30 14  5
##   31 11  5
##   32 14  7
##   33 12  3
##   34 22  5
##   35 16  5
##   36 13  3
##   37 14  1
##   38  6  2
##   39 19  4
##   40 10  4
##   41 13  3
##   42 16  3
##   43 14  3
##   44  9  4
##   45 12  5
##   46 19  4
##   47 19  4
##   48 19  4
##   49 11  3
##   50 18  4
##   51  9  3
```

```
##    52 11  3
##    53 11  4
##    54 17  9
##    55  9  4
##    56  8  7
##    57  9  2
##    58  8  4
##    59  5  4
##    60  5  4
##    61  5  2
##    62  6  5
##    63  3  3
##    64  7  1
##    65  3  2
##    66  4  0
##    67  2  0
##    69  6  2
##    70  2  1
##    71  0  1
##    72  2  2
##    74  0  1
```

## Program 12.3

- Estimating stabilized IP weights
- Data from NHEFS

```r
# estimation of denominator of ip weights
denom.fit <-
  glm(
    qsmk ~ as.factor(sex) + as.factor(race) + age + I(age ^ 2) +
      as.factor(education) + smokeintensity +
      I(smokeintensity ^ 2) + smokeyrs + I(smokeyrs ^ 2) +
      as.factor(exercise) + as.factor(active) + wt71 + I(wt71 ^ 2),
    family = binomial(),
    data = nhefs.nmv
  )
summary(denom.fit)
```

```
##
## Call:
## glm(formula = qsmk ~ as.factor(sex) + as.factor(race) + age +
##     I(age^2) + as.factor(education) + smokeintensity + I(smokeintensity^2) +
##     smokeyrs + I(smokeyrs^2) + as.factor(exercise) + as.factor(active) +
##     wt71 + I(wt71^2), family = binomial(), data = nhefs.nmv)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.513  -0.791  -0.639   0.983   2.373
##
```

```
## Coefficients:
##                          Estimate Std. Error z value Pr(>|z|)
## (Intercept)             -2.242519   1.380836   -1.62  0.10437
## as.factor(sex)1         -0.527478   0.154050   -3.42  0.00062 ***
## as.factor(race)1        -0.839264   0.210067   -4.00  6.5e-05 ***
## age                      0.121205   0.051266    2.36  0.01807 *
## I(age^2)                -0.000825   0.000536   -1.54  0.12404
## as.factor(education)2 -0.028776   0.198351   -0.15  0.88465
## as.factor(education)3  0.086432   0.178085    0.49  0.62744
## as.factor(education)4  0.063601   0.273211    0.23  0.81592
## as.factor(education)5  0.475961   0.226224    2.10  0.03538 *
## smokeintensity          -0.077270   0.015250   -5.07  4.0e-07 ***
## I(smokeintensity^2)      0.001045   0.000287    3.65  0.00027 ***
## smokeyrs                -0.073597   0.027777   -2.65  0.00806 **
## I(smokeyrs^2)            0.000844   0.000463    1.82  0.06840 .
## as.factor(exercise)1     0.354841   0.180135    1.97  0.04885 *
## as.factor(exercise)2     0.395704   0.187240    2.11  0.03457 *
## as.factor(active)1       0.031944   0.132937    0.24  0.81010
## as.factor(active)2       0.176784   0.214972    0.82  0.41087
## wt71                    -0.015236   0.026316   -0.58  0.56262
## I(wt71^2)                0.000135   0.000163    0.83  0.40737
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1786.1  on 1565  degrees of freedom
## Residual deviance: 1676.9  on 1547  degrees of freedom
## AIC: 1715
##
## Number of Fisher Scoring iterations: 4
```

```r
pd.qsmk <- predict(denom.fit, type = "response")

# estimation of numerator of ip weights
numer.fit <- glm(qsmk ~ 1, family = binomial(), data = nhefs.nmv)
summary(numer.fit)
```

```
##
## Call:
## glm(formula = qsmk ~ 1, family = binomial(), data = nhefs.nmv)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.771   -0.771   -0.771    1.648    1.648
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -1.0598     0.0578   -18.3   <2e-16 ***
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1786.1  on 1565  degrees of freedom
## Residual deviance: 1786.1  on 1565  degrees of freedom
## AIC: 1788
##
## Number of Fisher Scoring iterations: 4
```

```
pn.qsmk <- predict(numer.fit, type = "response")

nhefs.nmv$sw <-
  ifelse(nhefs.nmv$qsmk == 0, ((1 - pn.qsmk) / (1 - pd.qsmk)),
         (pn.qsmk / pd.qsmk))

summary(nhefs.nmv$sw)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   0.331   0.867   0.950   0.999   1.079   4.298
```

```
msm.sw <- geeglm(
  wt82_71 ~ qsmk,
  data = nhefs.nmv,
  weights = sw,
  id = seqn,
  corstr = "independence"
)
summary(msm.sw)
```

```
##
## Call:
## geeglm(formula = wt82_71 ~ qsmk, data = nhefs.nmv, weights = sw,
##     id = seqn, corstr = "independence")
##
##  Coefficients:
##             Estimate Std.err Wald Pr(>|W|)
## (Intercept)    1.780   0.225 62.7  2.3e-15 ***
## qsmk           3.441   0.525 42.9  5.9e-11 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)     60.7    3.71
##
## Correlation: Structure = independenceNumber of clusters:   1566   Maximum cluster size: 1
```

```
beta <- coef(msm.sw)
SE <- coef(summary(msm.sw))[, 2]
lcl <- beta - qnorm(0.975) * SE
```

```r
ucl <- beta + qnorm(0.975) * SE
cbind(beta, lcl, ucl)
```

```
##             beta  lcl  ucl
## (Intercept) 1.78 1.34 2.22
## qsmk        3.44 2.41 4.47
```

```r
# no association between sex and qsmk in pseudo-population
xtabs(nhefs.nmv$sw ~ nhefs.nmv$sex + nhefs.nmv$qsmk)
```

```
##              nhefs.nmv$qsmk
## nhefs.nmv$sex   0   1
##             0 567 197
##             1 595 205
```

## Program 12.4

- Estimating the parameters of a marginal structural mean model with a continuous treatment Data from NHEFS

```r
# Analysis restricted to subjects reporting <=25 cig/day at baseline
nhefs.nmv.s <- subset(nhefs.nmv, smokeintensity <= 25)

# estimation of denominator of ip weights
den.fit.obj <- lm(
  smkintensity82_71 ~ as.factor(sex) +
    as.factor(race) + age + I(age ^ 2) +
    as.factor(education) + smokeintensity + I(smokeintensity ^ 2) +
    smokeyrs + I(smokeyrs ^ 2) + as.factor(exercise) + as.factor(active) + wt71 +
    I(wt71 ^ 2),
  data = nhefs.nmv.s
)
p.den <- predict(den.fit.obj, type = "response")
dens.den <-
  dnorm(nhefs.nmv.s$smkintensity82_71,
        p.den,
        summary(den.fit.obj)$sigma)

# estimation of numerator of ip weights
num.fit.obj <- lm(smkintensity82_71 ~ 1, data = nhefs.nmv.s)
p.num <- predict(num.fit.obj, type = "response")
dens.num <-
  dnorm(nhefs.nmv.s$smkintensity82_71,
        p.num,
        summary(num.fit.obj)$sigma)

nhefs.nmv.s$sw.a <- dens.num / dens.den
summary(nhefs.nmv.s$sw.a)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
```

```
##    0.19    0.89    0.97    1.00    1.05    5.10
```

```
msm.sw.cont <-
  geeglm(
    wt82_71 ~ smkintensity82_71 + I(smkintensity82_71 * smkintensity82_71),
    data = nhefs.nmv.s,
    weights = sw.a,
    id = seqn,
    corstr = "independence"
  )
summary(msm.sw.cont)
```

```
##
## Call:
## geeglm(formula = wt82_71 ~ smkintensity82_71 + I(smkintensity82_71 *
##     smkintensity82_71), data = nhefs.nmv.s, weights = sw.a, id = seqn,
##     corstr = "independence")
##
##  Coefficients:
##                                          Estimate  Std.err  Wald Pr(>|W|)
## (Intercept)                               2.00452  0.29512 46.13  1.1e-11 ***
## smkintensity82_71                        -0.10899  0.03154 11.94  0.00055 ***
## I(smkintensity82_71 * smkintensity82_71)  0.00269  0.00242  1.24  0.26489
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)     60.5     4.5
##
## Correlation: Structure = independenceNumber of clusters:   1162   Maximum cluster size: 1
```

```
beta <- coef(msm.sw.cont)
SE <- coef(summary(msm.sw.cont))[, 2]
lcl <- beta - qnorm(0.975) * SE
ucl <- beta + qnorm(0.975) * SE
cbind(beta, lcl, ucl)
```

```
##                                              beta      lcl      ucl
## (Intercept)                               2.00452  1.42610  2.58295
## smkintensity82_71                        -0.10899 -0.17080 -0.04718
## I(smkintensity82_71 * smkintensity82_71)  0.00269 -0.00204  0.00743
```

# Program 12.5

- Estimating the parameters of a marginal structural logistic model
- Data from NHEFS

```
table(nhefs.nmv$qsmk, nhefs.nmv$death)
```

```
##
```

```
##       0   1
##   0 963 200
##   1 312  91
```

```
# First, estimation of stabilized weights sw (same as in Program 12.3)
# Second, fit logistic model below
msm.logistic <- geeglm(
  death ~ qsmk,
  data = nhefs.nmv,
  weights = sw,
  id = seqn,
  family = binomial(),
  corstr = "independence"
)
```

```
## Warning in eval(family$initialize): non-integer #successes in a binomial glm!
```

```
summary(msm.logistic)
```

```
##
## Call:
## geeglm(formula = death ~ qsmk, family = binomial(), data = nhefs.nmv,
##     weights = sw, id = seqn, corstr = "independence")
##
##  Coefficients:
##             Estimate Std.err   Wald Pr(>|W|)
## (Intercept)  -1.4905  0.0789 356.50   <2e-16 ***
## qsmk          0.0301  0.1573   0.04     0.85
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)        1  0.0678
##
## Correlation: Structure = independenceNumber of clusters:   1566   Maximum cluster size: 1
```

```
beta <- coef(msm.logistic)
SE <- coef(summary(msm.logistic))[, 2]
lcl <- beta - qnorm(0.975) * SE
ucl <- beta + qnorm(0.975) * SE
cbind(beta, lcl, ucl)
```

```
##                beta    lcl    ucl
## (Intercept) -1.4905 -1.645 -1.336
## qsmk         0.0301 -0.278  0.338
```

# Program 12.6

- Assessing effect modification by sex using a marginal structural mean model
- Data from NHEFS

```r
table(nhefs.nmv$sex)
```

```
##
##   0   1
## 762 804
```

```r
# estimation of denominator of ip weights
denom.fit <-
  glm(
    qsmk ~ as.factor(sex) + as.factor(race) + age + I(age ^ 2) +
      as.factor(education) + smokeintensity +
      I(smokeintensity ^ 2) + smokeyrs + I(smokeyrs ^ 2) +
      as.factor(exercise) + as.factor(active) + wt71 + I(wt71 ^ 2),
    family = binomial(),
    data = nhefs.nmv
  )
summary(denom.fit)
```

```
##
## Call:
## glm(formula = qsmk ~ as.factor(sex) + as.factor(race) + age +
##     I(age^2) + as.factor(education) + smokeintensity + I(smokeintensity^2) +
##     smokeyrs + I(smokeyrs^2) + as.factor(exercise) + as.factor(active) +
##     wt71 + I(wt71^2), family = binomial(), data = nhefs.nmv)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.513  -0.791  -0.639   0.983   2.373
##
## Coefficients:
##                         Estimate Std. Error z value Pr(>|z|)
## (Intercept)            -2.242519   1.380836   -1.62  0.10437
## as.factor(sex)1        -0.527478   0.154050   -3.42  0.00062 ***
## as.factor(race)1       -0.839264   0.210067   -4.00  6.5e-05 ***
## age                     0.121205   0.051266    2.36  0.01807 *
## I(age^2)               -0.000825   0.000536   -1.54  0.12404
## as.factor(education)2 -0.028776   0.198351   -0.15  0.88465
## as.factor(education)3  0.086432   0.178085    0.49  0.62744
## as.factor(education)4  0.063601   0.273211    0.23  0.81592
## as.factor(education)5  0.475961   0.226224    2.10  0.03538 *
## smokeintensity         -0.077270   0.015250   -5.07  4.0e-07 ***
## I(smokeintensity^2)     0.001045   0.000287    3.65  0.00027 ***
## smokeyrs               -0.073597   0.027777   -2.65  0.00806 **
## I(smokeyrs^2)           0.000844   0.000463    1.82  0.06840 .
## as.factor(exercise)1    0.354841   0.180135    1.97  0.04885 *
## as.factor(exercise)2    0.395704   0.187240    2.11  0.03457 *
## as.factor(active)1      0.031944   0.132937    0.24  0.81010
## as.factor(active)2      0.176784   0.214972    0.82  0.41087
## wt71                   -0.015236   0.026316   -0.58  0.56262
## I(wt71^2)               0.000135   0.000163    0.83  0.40737
```

```
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1786.1  on 1565  degrees of freedom
## Residual deviance: 1676.9  on 1547  degrees of freedom
## AIC: 1715
##
## Number of Fisher Scoring iterations: 4
```

```
pd.qsmk <- predict(denom.fit, type = "response")

# estimation of numerator of ip weights
numer.fit <-
  glm(qsmk ~ as.factor(sex), family = binomial(), data = nhefs.nmv)
summary(numer.fit)
```

```
##
## Call:
## glm(formula = qsmk ~ as.factor(sex), family = binomial(), data = nhefs.nmv)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -0.825  -0.825  -0.719   1.576   1.720
##
## Coefficients:
##                 Estimate Std. Error z value Pr(>|z|)
## (Intercept)      -0.9016     0.0799  -11.28   <2e-16 ***
## as.factor(sex)1  -0.3202     0.1160   -2.76   0.0058 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1786.1  on 1565  degrees of freedom
## Residual deviance: 1778.4  on 1564  degrees of freedom
## AIC: 1782
##
## Number of Fisher Scoring iterations: 4
```

```
pn.qsmk <- predict(numer.fit, type = "response")

nhefs.nmv$sw.a <-
  ifelse(nhefs.nmv$qsmk == 0, ((1 - pn.qsmk) / (1 - pd.qsmk)),
         (pn.qsmk / pd.qsmk))

summary(nhefs.nmv$sw.a)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.29    0.88    0.96    1.00    1.08    3.80
```

```r
sd(nhefs.nmv$sw.a)
```

```
## [1] 0.271
```

```r
# Estimating parameters of a marginal structural mean model
msm.emm <- geeglm(
  wt82_71 ~ as.factor(qsmk) + as.factor(sex)
  + as.factor(qsmk):as.factor(sex),
  data = nhefs.nmv,
  weights = sw.a,
  id = seqn,
  corstr = "independence"
)
summary(msm.emm)
```

```
##
## Call:
## geeglm(formula = wt82_71 ~ as.factor(qsmk) + as.factor(sex) +
##     as.factor(qsmk):as.factor(sex), data = nhefs.nmv, weights = sw.a,
##     id = seqn, corstr = "independence")
##
##  Coefficients:
##                                  Estimate  Std.err  Wald Pr(>|W|)
## (Intercept)                       1.78445  0.30984 33.17  8.5e-09 ***
## as.factor(qsmk)1                  3.52198  0.65707 28.73  8.3e-08 ***
## as.factor(sex)1                  -0.00872  0.44882  0.00     0.98
## as.factor(qsmk)1:as.factor(sex)1 -0.15948  1.04608  0.02     0.88
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)     60.8    3.71
##
## Correlation: Structure = independenceNumber of clusters:   1566   Maximum cluster size: 1
```

```r
beta <- coef(msm.emm)
SE <- coef(summary(msm.emm))[, 2]
lcl <- beta - qnorm(0.975) * SE
ucl <- beta + qnorm(0.975) * SE
cbind(beta, lcl, ucl)
```

```
##                                      beta    lcl   ucl
## (Intercept)                       1.78445  1.177 2.392
## as.factor(qsmk)1                  3.52198  2.234 4.810
## as.factor(sex)1                  -0.00872 -0.888 0.871
## as.factor(qsmk)1:as.factor(sex)1 -0.15948 -2.210 1.891
```

## Program 12.7

- Estimating IP weights to adjust for selection bias due to censoring
- Data from NHEFS

```
table(nhefs$qsmk, nhefs$cens)
```

```
##
##        0    1
##   0 1163   38
##   1  403   25
```

```
summary(nhefs[which(nhefs$cens == 0),]$wt71)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    39.6    59.5    69.2    70.8    79.8   151.7
```

```
summary(nhefs[which(nhefs$cens == 1),]$wt71)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    36.2    63.1    72.1    76.6    87.9   169.2
```

```
# estimation of denominator of ip weights for A
denom.fit <-
  glm(
    qsmk ~ as.factor(sex) + as.factor(race) + age + I(age ^ 2) +
      as.factor(education) + smokeintensity +
      I(smokeintensity ^ 2) + smokeyrs + I(smokeyrs ^ 2) +
      as.factor(exercise) + as.factor(active) + wt71 + I(wt71 ^ 2),
    family = binomial(),
    data = nhefs
  )
summary(denom.fit)
```

```
##
## Call:
## glm(formula = qsmk ~ as.factor(sex) + as.factor(race) + age +
##     I(age^2) + as.factor(education) + smokeintensity + I(smokeintensity^2) +
##     smokeyrs + I(smokeyrs^2) + as.factor(exercise) + as.factor(active) +
##     wt71 + I(wt71^2), family = binomial(), data = nhefs)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.465  -0.804  -0.646   1.058   2.355
##
## Coefficients:
##                        Estimate Std. Error z value Pr(>|z|)
## (Intercept)           -1.988902   1.241279   -1.60  0.10909
## as.factor(sex)1       -0.507522   0.148232   -3.42  0.00062 ***
## as.factor(race)1      -0.850231   0.205872   -4.13  3.6e-05 ***
## age                    0.103013   0.048900    2.11  0.03515 *
## I(age^2)              -0.000605   0.000507   -1.19  0.23297
## as.factor(education)2 -0.098320   0.190655   -0.52  0.60607
```

```
## as.factor(education)3  0.015699   0.170714    0.09  0.92673
## as.factor(education)4 -0.042526   0.264276   -0.16  0.87216
## as.factor(education)5  0.379663   0.220395    1.72  0.08495 .
## smokeintensity        -0.065156   0.014759   -4.41  1.0e-05 ***
## I(smokeintensity^2)    0.000846   0.000276    3.07  0.00216 **
## smokeyrs              -0.073371   0.026996   -2.72  0.00657 **
## I(smokeyrs^2)          0.000838   0.000443    1.89  0.05867 .
## as.factor(exercise)1   0.291412   0.173554    1.68  0.09314 .
## as.factor(exercise)2   0.355052   0.179929    1.97  0.04846 *
## as.factor(active)1     0.010875   0.129832    0.08  0.93324
## as.factor(active)2     0.068312   0.208727    0.33  0.74346
## wt71                  -0.012848   0.022283   -0.58  0.56423
## I(wt71^2)              0.000121   0.000135    0.89  0.37096
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1876.3  on 1628  degrees of freedom
## Residual deviance: 1766.7  on 1610  degrees of freedom
## AIC: 1805
##
## Number of Fisher Scoring iterations: 4
```

```r
pd.qsmk <- predict(denom.fit, type = "response")

# estimation of numerator of ip weights for A
numer.fit <- glm(qsmk ~ 1, family = binomial(), data = nhefs)
summary(numer.fit)
```

```
##
## Call:
## glm(formula = qsmk ~ 1, family = binomial(), data = nhefs)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -0.781  -0.781  -0.781   1.635   1.635
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -1.0318     0.0563   -18.3   <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1876.3  on 1628  degrees of freedom
## Residual deviance: 1876.3  on 1628  degrees of freedom
## AIC: 1878
##
```

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

```r
pn.qsmk <- predict(numer.fit, type = "response")

# estimation of denominator of ip weights for C
denom.cens <- glm(
  cens ~ as.factor(qsmk) + as.factor(sex) +
    as.factor(race) + age + I(age ^ 2) +
    as.factor(education) + smokeintensity +
    I(smokeintensity ^ 2) + smokeyrs + I(smokeyrs ^ 2) +
    as.factor(exercise) + as.factor(active) + wt71 + I(wt71 ^ 2),
  family = binomial(),
  data = nhefs
)
summary(denom.cens)
```

```
##
## Call:
## glm(formula = cens ~ as.factor(qsmk) + as.factor(sex) + as.factor(race) +
##     age + I(age^2) + as.factor(education) + smokeintensity +
##     I(smokeintensity^2) + smokeyrs + I(smokeyrs^2) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71^2), family = binomial(),
##     data = nhefs)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.097  -0.287  -0.207  -0.157   2.996
##
## Coefficients:
##                        Estimate Std. Error z value Pr(>|z|)
## (Intercept)            4.014466   2.576106    1.56   0.1192
## as.factor(qsmk)1       0.516867   0.287716    1.80   0.0724 .
## as.factor(sex)1        0.057313   0.330278    0.17   0.8622
## as.factor(race)1      -0.012271   0.452489   -0.03   0.9784
## age                   -0.269729   0.117465   -2.30   0.0217 *
## I(age^2)               0.002884   0.001114    2.59   0.0096 **
## as.factor(education)2 -0.440788   0.419399   -1.05   0.2933
## as.factor(education)3 -0.164688   0.370547   -0.44   0.6567
## as.factor(education)4  0.138447   0.569797    0.24   0.8080
## as.factor(education)5 -0.382382   0.560181   -0.68   0.4949
## smokeintensity         0.015712   0.034732    0.45   0.6510
## I(smokeintensity^2)   -0.000113   0.000606   -0.19   0.8517
## smokeyrs               0.078597   0.074958    1.05   0.2944
## I(smokeyrs^2)         -0.000557   0.001032   -0.54   0.5894
## as.factor(exercise)1  -0.971471   0.387810   -2.51   0.0122 *
## as.factor(exercise)2  -0.583989   0.372313   -1.57   0.1168
## as.factor(active)1    -0.247479   0.325455   -0.76   0.4470
## as.factor(active)2     0.706583   0.396458    1.78   0.0747 .
## wt71                  -0.087887   0.040012   -2.20   0.0281 *
## I(wt71^2)              0.000635   0.000226    2.81   0.0049 **
```

```
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 533.36  on 1628  degrees of freedom
## Residual deviance: 465.36  on 1609  degrees of freedom
## AIC: 505.4
##
## Number of Fisher Scoring iterations: 7
```

```
pd.cens <- 1 - predict(denom.cens, type = "response")

# estimation of numerator of ip weights for C
numer.cens <-
  glm(cens ~ as.factor(qsmk), family = binomial(), data = nhefs)
summary(numer.cens)
```

```
##
## Call:
## glm(formula = cens ~ as.factor(qsmk), family = binomial(), data = nhefs)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -0.347  -0.254  -0.254  -0.254   2.628
##
## Coefficients:
##                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)        -3.421      0.165  -20.75   <2e-16 ***
## as.factor(qsmk)1    0.641      0.264    2.43    0.015 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 533.36  on 1628  degrees of freedom
## Residual deviance: 527.76  on 1627  degrees of freedom
## AIC: 531.8
##
## Number of Fisher Scoring iterations: 6
```

```
pn.cens <- 1 - predict(numer.cens, type = "response")

nhefs$sw.a <-
  ifelse(nhefs$qsmk == 0, ((1 - pn.qsmk) / (1 - pd.qsmk)),
         (pn.qsmk / pd.qsmk))
nhefs$sw.c <- pn.cens / pd.cens
nhefs$sw <- nhefs$sw.c * nhefs$sw.a

summary(nhefs$sw.a)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.33    0.86    0.95    1.00    1.08    4.21
```

```r
sd(nhefs$sw.a)
```

```
## [1] 0.284
```

```r
summary(nhefs$sw.c)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.94    0.98    0.99    1.01    1.01    7.58
```

```r
sd(nhefs$sw.c)
```

```
## [1] 0.178
```

```r
summary(nhefs$sw)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.35    0.86    0.94    1.01    1.08   12.86
```

```r
sd(nhefs$sw)
```

```
## [1] 0.411
```

```r
msm.sw <- geeglm(
  wt82_71 ~ qsmk,
  data = nhefs,
  weights = sw,
  id = seqn,
  corstr = "independence"
)
summary(msm.sw)
```

```
##
## Call:
## geeglm(formula = wt82_71 ~ qsmk, data = nhefs, weights = sw,
##     id = seqn, corstr = "independence")
##
##  Coefficients:
##             Estimate Std.err Wald Pr(>|W|)
## (Intercept)    1.662   0.233 51.0  9.3e-13 ***
## qsmk           3.496   0.526 44.2  2.9e-11 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)     61.8    3.83
##
## Correlation: Structure = independenceNumber of clusters:   1566   Maximum cluster size: 1
```

```r
beta <- coef(msm.sw)
SE <- coef(summary(msm.sw))[, 2]
lcl <- beta - qnorm(0.975) * SE
```

```r
ucl <- beta + qnorm(0.975) * SE
cbind(beta, lcl, ucl)
```

```
##             beta  lcl  ucl
## (Intercept) 1.66 1.21 2.12
## qsmk        3.50 2.47 4.53
```

# 13. Standardization and the parametric G-formula

## Program 13.1

- Estimating the mean outcome within levels of treatment and confounders
- Data from NHEFS

```
library(here)
```

```
#install.packages("readxl") # install package if required
library("readxl")
nhefs <- read_excel(here("data", "NHEFS.xls"))

# some preprocessing of the data
nhefs$cens <- ifelse(is.na(nhefs$wt82), 1, 0)

fit <-
  glm(
    wt82_71 ~ qsmk + sex + race + age + I(age * age) + as.factor(education)
    + smokeintensity + I(smokeintensity * smokeintensity) + smokeyrs
    + I(smokeyrs * smokeyrs) + as.factor(exercise) + as.factor(active)
    + wt71 + I(wt71 * wt71) + qsmk * smokeintensity,
    data = nhefs
  )
summary(fit)
```

```
##
## Call:
## glm(formula = wt82_71 ~ qsmk + sex + race + age + I(age * age) +
##     as.factor(education) + smokeintensity + I(smokeintensity *
##     smokeintensity) + smokeyrs + I(smokeyrs * smokeyrs) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71 * wt71) + qsmk * smokeintensity,
##     data = nhefs)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -42.056   -4.171   -0.343    3.891   44.606
##
```

```
## Coefficients:
##                                     Estimate Std. Error t value Pr(>|t|)
## (Intercept)                       -1.5881657  4.3130359  -0.368 0.712756
## qsmk                               2.5595941  0.8091486   3.163 0.001590 **
## sex                               -1.4302717  0.4689576  -3.050 0.002328 **
## race                               0.5601096  0.5818888   0.963 0.335913
## age                                0.3596353  0.1633188   2.202 0.027809 *
## I(age * age)                      -0.0061010  0.0017261  -3.534 0.000421 ***
## as.factor(education)2              0.7904440  0.6070005   1.302 0.193038
## as.factor(education)3              0.5563124  0.5561016   1.000 0.317284
## as.factor(education)4              1.4915695  0.8322704   1.792 0.073301 .
## as.factor(education)5             -0.1949770  0.7413692  -0.263 0.792589
## smokeintensity                     0.0491365  0.0517254   0.950 0.342287
## I(smokeintensity * smokeintensity) -0.0009907  0.0009380  -1.056 0.291097
## smokeyrs                           0.1343686  0.0917122   1.465 0.143094
## I(smokeyrs * smokeyrs)            -0.0018664  0.0015437  -1.209 0.226830
## as.factor(exercise)1               0.2959754  0.5351533   0.553 0.580298
## as.factor(exercise)2               0.3539128  0.5588587   0.633 0.526646
## as.factor(active)1                -0.9475695  0.4099344  -2.312 0.020935 *
## as.factor(active)2                -0.2613779  0.6845577  -0.382 0.702647
## wt71                               0.0455018  0.0833709   0.546 0.585299
## I(wt71 * wt71)                    -0.0009653  0.0005247  -1.840 0.066001 .
## qsmk:smokeintensity                0.0466628  0.0351448   1.328 0.184463
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 53.5683)
##
##     Null deviance: 97176  on 1565  degrees of freedom
## Residual deviance: 82763  on 1545  degrees of freedom
##   (63 observations deleted due to missingness)
## AIC: 10701
##
## Number of Fisher Scoring iterations: 2
```

```r
nhefs$predicted.meanY <- predict(fit, nhefs)

nhefs[which(nhefs$seqn == 24770), c(
  "predicted.meanY",
  "qsmk",
  "sex",
  "race",
  "age",
  "education",
  "smokeintensity",
  "smokeyrs",
  "exercise",
  "active",
  "wt71"
```

```
)]
```

```
## # A tibble: 1 x 11
##   predicted.meanY  qsmk   sex  race   age education smokeintensity smokeyrs
##             <dbl> <dbl> <dbl> <dbl> <dbl>     <dbl>          <dbl>    <dbl>
## 1           0.342     0     0     0    26         4             15       12
## # … with 3 more variables: exercise <dbl>, active <dbl>, wt71 <dbl>
```

```
summary(nhefs$predicted.meanY[nhefs$cens == 0])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## -10.876   1.116   3.042   2.638   4.511   9.876
```

```
summary(nhefs$wt82_71[nhefs$cens == 0])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## -41.280  -1.478   2.604   2.638   6.690  48.538
```

## Program 13.2

- Standardizing the mean outcome to the baseline confounders
- Data from Table 2.2

```
id <- c(
  "Rheia",
  "Kronos",
  "Demeter",
  "Hades",
  "Hestia",
  "Poseidon",
  "Hera",
  "Zeus",
  "Artemis",
  "Apollo",
  "Leto",
  "Ares",
  "Athena",
  "Hephaestus",
  "Aphrodite",
  "Cyclope",
  "Persephone",
  "Hermes",
  "Hebe",
  "Dionysus"
)
N <- length(id)
L <- c(0, 0, 0, 0, 0, 0, 0, 0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1)
A <- c(0, 0, 0, 0, 1, 1, 1, 1, 0, 0, 0, 1, 1, 1, 1, 1, 1, 1, 1, 1)
Y <- c(0, 1, 0, 0, 0, 0, 0, 1, 1, 1, 0, 1, 1, 1, 1, 1, 1, 0, 0, 0)
interv <- rep(-1, N)
observed <- cbind(L, A, Y, interv)
```

```r
untreated <- cbind(L, rep(0, N), rep(NA, N), rep(0, N))
treated <- cbind(L, rep(1, N), rep(NA, N), rep(1, N))
table22 <- as.data.frame(rbind(observed, untreated, treated))
table22$id <- rep(id, 3)

glm.obj <- glm(Y ~ A * L, data = table22)
summary(glm.obj)
```

```
##
## Call:
## glm(formula = Y ~ A * L, data = table22)
##
## Deviance Residuals:
##      Min        1Q    Median        3Q       Max
## -0.66667  -0.25000   0.04167   0.33333   0.75000
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)  2.500e-01  2.552e-01   0.980    0.342
## A           -4.164e-16  3.608e-01   0.000    1.000
## L            4.167e-01  3.898e-01   1.069    0.301
## A:L          3.237e-16  4.959e-01   0.000    1.000
##
## (Dispersion parameter for gaussian family taken to be 0.2604167)
##
##     Null deviance: 5.0000  on 19  degrees of freedom
## Residual deviance: 4.1667  on 16  degrees of freedom
##   (40 observations deleted due to missingness)
## AIC: 35.385
##
## Number of Fisher Scoring iterations: 2
```

```r
table22$predicted.meanY <- predict(glm.obj, table22)

mean(table22$predicted.meanY[table22$interv == -1])
```

```
## [1] 0.5
```

```r
mean(table22$predicted.meanY[table22$interv == 0])
```

```
## [1] 0.5
```

```r
mean(table22$predicted.meanY[table22$interv == 1])
```

```
## [1] 0.5
```

# Program 13.3

- Standardizing the mean outcome to the baseline confounders:
- Data from NHEFS

```r
# create a dataset with 3 copies of each subject
nhefs$interv <- -1 # 1st copy: equal to original one

interv0 <- nhefs # 2nd copy: treatment set to 0, outcome to missing
interv0$interv <- 0
interv0$qsmk <- 0
interv0$wt82_71 <- NA

interv1 <- nhefs # 3rd copy: treatment set to 1, outcome to missing
interv1$interv <- 1
interv1$qsmk <- 1
interv1$wt82_71 <- NA

onesample <- rbind(nhefs, interv0, interv1) # combining datasets

# linear model to estimate mean outcome conditional on treatment and confounders
# parameters are estimated using original observations only (nhefs)
# parameter estimates are used to predict mean outcome for observations with
# treatment set to 0 (interv=0) and to 1 (interv=1)

std <- glm(
  wt82_71 ~ qsmk + sex + race + age + I(age * age)
  + as.factor(education) + smokeintensity
  + I(smokeintensity * smokeintensity) + smokeyrs
  + I(smokeyrs * smokeyrs) + as.factor(exercise)
  + as.factor(active) + wt71 + I(wt71 * wt71) + I(qsmk * smokeintensity),
  data = onesample
)
summary(std)
```

```
##
## Call:
## glm(formula = wt82_71 ~ qsmk + sex + race + age + I(age * age) +
##     as.factor(education) + smokeintensity + I(smokeintensity *
##     smokeintensity) + smokeyrs + I(smokeyrs * smokeyrs) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71 * wt71) + I(qsmk * smokeintensity),
##     data = onesample)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -42.056   -4.171   -0.343    3.891   44.606
##
## Coefficients:
##                                        Estimate Std. Error t value Pr(>|t|)
## (Intercept)                          -1.5881657  4.3130359  -0.368 0.712756
## qsmk                                  2.5595941  0.8091486   3.163 0.001590 **
## sex                                  -1.4302717  0.4689576  -3.050 0.002328 **
## race                                  0.5601096  0.5818888   0.963 0.335913
## age                                   0.3596353  0.1633188   2.202 0.027809 *
```

```
## I(age * age)                       -0.0061010  0.0017261  -3.534 0.000421 ***
## as.factor(education)2               0.7904440  0.6070005   1.302 0.193038
## as.factor(education)3               0.5563124  0.5561016   1.000 0.317284
## as.factor(education)4               1.4915695  0.8322704   1.792 0.073301 .
## as.factor(education)5              -0.1949770  0.7413692  -0.263 0.792589
## smokeintensity                      0.0491365  0.0517254   0.950 0.342287
## I(smokeintensity * smokeintensity) -0.0009907  0.0009380  -1.056 0.291097
## smokeyrs                            0.1343686  0.0917122   1.465 0.143094
## I(smokeyrs * smokeyrs)             -0.0018664  0.0015437  -1.209 0.226830
## as.factor(exercise)1                0.2959754  0.5351533   0.553 0.580298
## as.factor(exercise)2                0.3539128  0.5588587   0.633 0.526646
## as.factor(active)1                 -0.9475695  0.4099344  -2.312 0.020935 *
## as.factor(active)2                 -0.2613779  0.6845577  -0.382 0.702647
## wt71                                0.0455018  0.0833709   0.546 0.585299
## I(wt71 * wt71)                     -0.0009653  0.0005247  -1.840 0.066001 .
## I(qsmk * smokeintensity)            0.0466628  0.0351448   1.328 0.184463
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 53.5683)
##
##     Null deviance: 97176  on 1565  degrees of freedom
## Residual deviance: 82763  on 1545  degrees of freedom
##   (3321 observations deleted due to missingness)
## AIC: 10701
##
## Number of Fisher Scoring iterations: 2
```

```r
onesample$predicted_meanY <- predict(std, onesample)

# estimate mean outcome in each of the groups interv=0, and interv=1
# this mean outcome is a weighted average of the mean outcomes in each combination
# of values of treatment and confounders, that is, the standardized outcome
mean(onesample[which(onesample$interv == -1), ]$predicted_meanY)
```

```
## [1] 2.56319
```

```r
mean(onesample[which(onesample$interv == 0), ]$predicted_meanY)
```

```
## [1] 1.660267
```

```r
mean(onesample[which(onesample$interv == 1), ]$predicted_meanY)
```

```
## [1] 5.178841
```

# Program 13.4

- Computing the 95% confidence interval of the standardized means and their difference
- Data from NHEFS

```r
#install.packages("boot") # install package if required
library(boot)
```

```r
# function to calculate difference in means
standardization <- function(data, indices) {
  # create a dataset with 3 copies of each subject
  d <- data[indices, ] # 1st copy: equal to original one`
  d$interv <- -1
  d0 <- d # 2nd copy: treatment set to 0, outcome to missing
  d0$interv <- 0
  d0$qsmk <- 0
  d0$wt82_71 <- NA
  d1 <- d # 3rd copy: treatment set to 1, outcome to missing
  d1$interv <- 1
  d1$qsmk <- 1
  d1$wt82_71 <- NA
  d.onesample <- rbind(d, d0, d1) # combining datasets

  # linear model to estimate mean outcome conditional on treatment and confounders
  # parameters are estimated using original observations only (interv= -1)
  # parameter estimates are used to predict mean outcome for observations with set
  # treatment (interv=0 and interv=1)
  fit <- glm(
    wt82_71 ~ qsmk + sex + race + age + I(age * age) +
      as.factor(education) + smokeintensity +
      I(smokeintensity * smokeintensity) + smokeyrs + I(smokeyrs *
                                                          smokeyrs) +
      as.factor(exercise) + as.factor(active) + wt71 + I(wt71 *
                                                           wt71),
    data = d.onesample
  )

  d.onesample$predicted_meanY <- predict(fit, d.onesample)

  # estimate mean outcome in each of the groups interv=-1, interv=0, and interv=1
  return(c(
    mean(d.onesample$predicted_meanY[d.onesample$interv == -1]),
    mean(d.onesample$predicted_meanY[d.onesample$interv == 0]),
    mean(d.onesample$predicted_meanY[d.onesample$interv == 1]),
    mean(d.onesample$predicted_meanY[d.onesample$interv == 1]) -
      mean(d.onesample$predicted_meanY[d.onesample$interv == 0])
  ))
}

# bootstrap
results <- boot(data = nhefs,
                statistic = standardization,
                R = 5)

# generating confidence intervals
se <- c(sd(results$t[, 1]),
```

```r
        sd(results$t[, 2]),
        sd(results$t[, 3]),
        sd(results$t[, 4]))
mean <- results$t0
ll <- mean - qnorm(0.975) * se
ul <- mean + qnorm(0.975) * se

bootstrap <-
  data.frame(cbind(
    c(
      "Observed",
      "No Treatment",
      "Treatment",
      "Treatment - No Treatment"
    ),
    mean,
    se,
    ll,
    ul
  ))
bootstrap
```

```
##                         V1             mean                se                ll
## 1                 Observed 2.56188497106103 0.239354808977166  2.09275816593932
## 2             No Treatment 1.65212306626746 0.421093323271437 0.826795318525161
## 3                Treatment 5.11474489549347 0.557051540774175  4.02294393804354
## 4 Treatment - No Treatment 3.46262182922601 0.860390023466464  1.77628837057416
##                 ul
## 1 3.03101177618274
## 2 2.47745081400976
## 3 6.20654585294339
## 4 5.14895528787785
```

# 14. G-estimation of Structural Nested Models

## Program 14.1

- Preprocessing, ranks of extreme observations, IP weights for censoring
- Data from NHEFS

```
library(here)
```

```
#install.packages("readxl") # install package if required
library("readxl")
nhefs <- read_excel(here("data", "NHEFS.xls"))

# some processing of the data
nhefs$cens <- ifelse(is.na(nhefs$wt82), 1, 0)

# ranking of extreme observations
#install.packages("Hmisc")
library(Hmisc)
```

```
## Loading required package: lattice

## Loading required package: survival

## Loading required package: Formula

## Loading required package: ggplot2

##
## Attaching package: 'Hmisc'

## The following objects are masked from 'package:base':
##
##     format.pval, units
```

```
describe(nhefs$wt82_71)
```

```
## nhefs$wt82_71
##        n  missing distinct     Info     Mean      Gmd      .05      .10
##     1566       63     1510        1    2.638    8.337   -9.752   -6.292
##      .25      .50      .75      .90      .95
##   -1.478    2.604    6.690   11.117   14.739
```

```
##
## lowest : -41.28047 -30.50192 -30.05007 -29.02579 -25.97056
## highest:  34.01780  36.96925  37.65051  47.51130  48.53839
```

```r
# estimation of denominator of ip weights for C
cw.denom <- glm(cens==0 ~ qsmk + sex + race + age + I(age^2)
                     + as.factor(education) + smokeintensity + I(smokeintensity^2)
                     + smokeyrs + I(smokeyrs^2) + as.factor(exercise)
                     + as.factor(active) + wt71 + I(wt71^2),
                     data = nhefs, family = binomial("logit"))
summary(cw.denom)
```

```
##
## Call:
## glm(formula = cens == 0 ~ qsmk + sex + race + age + I(age^2) +
##     as.factor(education) + smokeintensity + I(smokeintensity^2) +
##     smokeyrs + I(smokeyrs^2) + as.factor(exercise) + as.factor(active) +
##     wt71 + I(wt71^2), family = binomial("logit"), data = nhefs)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -2.9959   0.1571   0.2069   0.2868   1.0967
##
## Coefficients:
##                         Estimate Std. Error z value Pr(>|z|)
## (Intercept)           -4.0144661  2.5761058  -1.558  0.11915
## qsmk                  -0.5168674  0.2877162  -1.796  0.07242 .
## sex                   -0.0573131  0.3302775  -0.174  0.86223
## race                   0.0122715  0.4524887   0.027  0.97836
## age                    0.2697293  0.1174647   2.296  0.02166 *
## I(age^2)              -0.0028837  0.0011135  -2.590  0.00961 **
## as.factor(education)2  0.4407884  0.4193993   1.051  0.29326
## as.factor(education)3  0.1646881  0.3705471   0.444  0.65672
## as.factor(education)4 -0.1384470  0.5697969  -0.243  0.80802
## as.factor(education)5  0.3823818  0.5601808   0.683  0.49486
## smokeintensity        -0.0157119  0.0347319  -0.452  0.65100
## I(smokeintensity^2)    0.0001133  0.0006058   0.187  0.85171
## smokeyrs              -0.0785973  0.0749576  -1.049  0.29438
## I(smokeyrs^2)          0.0005569  0.0010318   0.540  0.58938
## as.factor(exercise)1   0.9714714  0.3878101   2.505  0.01224 *
## as.factor(exercise)2   0.5839890  0.3723133   1.569  0.11675
## as.factor(active)1     0.2474785  0.3254548   0.760  0.44701
## as.factor(active)2    -0.7065829  0.3964577  -1.782  0.07471 .
## wt71                   0.0878871  0.0400115   2.197  0.02805 *
## I(wt71^2)             -0.0006351  0.0002257  -2.813  0.00490 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
```

```
##     Null deviance: 533.36  on 1628  degrees of freedom
## Residual deviance: 465.36  on 1609  degrees of freedom
## AIC: 505.36
##
## Number of Fisher Scoring iterations: 7
```

```
nhefs$pd.c <- predict(cw.denom, nhefs, type="response")
nhefs$wc <- ifelse(nhefs$cens==0, 1/nhefs$pd.c, NA)  # observations with cens=1 only contribute to cens
```

# Program 14.2

- G-estimation of a 1-parameter structural nested mean model
- Brute force search
- Data from NHEFS

## G-estimation: Checking one possible value of psi

```
#install.packages("geepack")
library("geepack")

nhefs$psi <- 3.446
nhefs$Hpsi <- nhefs$wt82_71 - nhefs$psi*nhefs$qsmk

fit <- geeglm(qsmk ~ sex + race + age + I(age*age) + as.factor(education)
           + smokeintensity + I(smokeintensity*smokeintensity) + smokeyrs
           + I(smokeyrs*smokeyrs) + as.factor(exercise) + as.factor(active)
           + wt71 + I(wt71*wt71) + Hpsi, family=binomial, data=nhefs,
           weights=wc, id=seqn, corstr="independence")
```

```
## Warning in eval(family$initialize): non-integer #successes in a binomial glm!
```

```
summary(fit)
```

```
##
## Call:
## geeglm(formula = qsmk ~ sex + race + age + I(age * age) + as.factor(education) +
##     smokeintensity + I(smokeintensity * smokeintensity) + smokeyrs +
##     I(smokeyrs * smokeyrs) + as.factor(exercise) + as.factor(active) +
##     wt71 + I(wt71 * wt71) + Hpsi, family = binomial, data = nhefs,
##     weights = wc, id = seqn, corstr = "independence")
##
##  Coefficients:
##                                     Estimate    Std.err   Wald Pr(>|W|)
## (Intercept)                       -2.403e+00  1.329e+00  3.269 0.070604 .
## sex                               -5.137e-01  1.536e-01 11.193 0.000821 ***
## race                              -8.609e-01  2.099e-01 16.826 4.10e-05 ***
## age                                1.152e-01  5.020e-02  5.263 0.021779 *
## I(age * age)                      -7.593e-04  5.296e-04  2.056 0.151619
## as.factor(education)2             -2.894e-02  1.964e-01  0.022 0.882859
## as.factor(education)3              8.771e-02  1.726e-01  0.258 0.611329
```

```
## as.factor(education)4               6.637e-02  2.698e-01  0.061 0.805645
## as.factor(education)5               4.711e-01  2.247e-01  4.395 0.036036 *
## smokeintensity                     -7.834e-02  1.464e-02 28.635 8.74e-08 ***
## I(smokeintensity * smokeintensity)  1.072e-03  2.650e-04 16.368 5.21e-05 ***
## smokeyrs                           -7.111e-02  2.639e-02  7.261 0.007047 **
## I(smokeyrs * smokeyrs)              8.153e-04  4.490e-04  3.298 0.069384 .
## as.factor(exercise)1                3.363e-01  1.828e-01  3.384 0.065844 .
## as.factor(exercise)2                3.800e-01  1.889e-01  4.049 0.044187 *
## as.factor(active)1                  3.412e-02  1.339e-01  0.065 0.798778
## as.factor(active)2                  2.135e-01  2.121e-01  1.012 0.314308
## wt71                               -7.661e-03  2.562e-02  0.089 0.764963
## I(wt71 * wt71)                      8.655e-05  1.582e-04  0.299 0.584233
## Hpsi                               -1.903e-06  8.839e-03  0.000 0.999828
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)   0.9969 0.06717
##
## Correlation: Structure = independenceNumber of clusters:   1566   Maximum cluster size: 1
```

### G-estimation: Checking multiple possible values of psi

```r
#install.packages("geepack")
grid <- seq(from = 2,to = 5, by = 0.1)
j = 0
Hpsi.coefs <- cbind(rep(NA,length(grid)), rep(NA, length(grid)))
colnames(Hpsi.coefs) <- c("Estimate", "p-value")

for (i in grid){
  psi = i
  j = j+1
  nhefs$Hpsi <- nhefs$wt82_71 - psi * nhefs$qsmk

  gest.fit <- geeglm(qsmk ~ sex + race + age + I(age*age) + as.factor(education)
                  + smokeintensity + I(smokeintensity*smokeintensity) + smokeyrs
                  + I(smokeyrs*smokeyrs) + as.factor(exercise) + as.factor(active)
                  + wt71 + I(wt71*wt71) + Hpsi, family=binomial, data=nhefs,
                  weights=wc, id=seqn, corstr="independence")
  Hpsi.coefs[j,1] <- summary(gest.fit)$coefficients["Hpsi", "Estimate"]
  Hpsi.coefs[j,2] <- summary(gest.fit)$coefficients["Hpsi", "Pr(>|W|)"]
}
```

```
## Warning in eval(family$initialize): non-integer #successes in a binomial glm!

## Warning in eval(family$initialize): non-integer #successes in a binomial glm!

## Warning in eval(family$initialize): non-integer #successes in a binomial glm!
```

```
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```

```
## Warning in eval(family$initialize): non-integer #successes in a binomial glm!

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## Warning in eval(family$initialize): non-integer #successes in a binomial glm!
```

```
Hpsi.coefs
```

```
##         Estimate  p-value
##  [1,]  0.0267219 0.001772
##  [2,]  0.0248946 0.003580
##  [3,]  0.0230655 0.006963
##  [4,]  0.0212344 0.013026
##  [5,]  0.0194009 0.023417
##  [6,]  0.0175647 0.040430
##  [7,]  0.0157254 0.067015
##  [8,]  0.0138827 0.106626
##  [9,]  0.0120362 0.162877
## [10,]  0.0101857 0.238979
## [11,]  0.0083308 0.337048
## [12,]  0.0064713 0.457433
## [13,]  0.0046069 0.598235
## [14,]  0.0027374 0.755204
## [15,]  0.0008624 0.922101
## [16,] -0.0010181 0.908537
## [17,] -0.0029044 0.744362
## [18,] -0.0047967 0.592188
## [19,] -0.0066950 0.457169
## [20,] -0.0085997 0.342360
## [21,] -0.0105107 0.248681
## [22,] -0.0124282 0.175239
## [23,] -0.0143523 0.119841
## [24,] -0.0162831 0.079580
## [25,] -0.0182206 0.051347
## [26,] -0.0201649 0.032218
## [27,] -0.0221160 0.019675
## [28,] -0.0240740 0.011706
## [29,] -0.0260389 0.006792
## [30,] -0.0280106 0.003847
## [31,] -0.0299893 0.002129
```

# Program 14.3

- G-estimation for 2-parameter structural nested mean model
- Closed form estimator
- Data from NHEFS

## G-estimation: Closed form estimator linear mean models

```
logit.est <- glm(qsmk ~ sex + race + age + I(age^2) + as.factor(education)
                 + smokeintensity + I(smokeintensity^2) + smokeyrs
                 + I(smokeyrs^2) + as.factor(exercise) + as.factor(active)
                 + wt71 + I(wt71^2), data = nhefs, weight = wc,
                 family = binomial())
```

```
## Warning in eval(family$initialize): non-integer #successes in a binomial glm!
```

```
summary(logit.est)
```

```
##
## Call:
## glm(formula = qsmk ~ sex + race + age + I(age^2) + as.factor(education) +
##     smokeintensity + I(smokeintensity^2) + smokeyrs + I(smokeyrs^2) +
##     as.factor(exercise) + as.factor(active) + wt71 + I(wt71^2),
##     family = binomial(), data = nhefs, weights = wc)
##
## Deviance Residuals:
##    Min      1Q  Median      3Q     Max
## -1.529  -0.808  -0.650   1.029   2.417
##
## Coefficients:
##                        Estimate Std. Error z value Pr(>|z|)
## (Intercept)           -2.40e+00   1.31e+00   -1.83  0.06743 .
## sex                   -5.14e-01   1.50e-01   -3.42  0.00062 ***
## race                  -8.61e-01   2.06e-01   -4.18  2.9e-05 ***
## age                    1.15e-01   4.95e-02    2.33  0.01992 *
## I(age^2)              -7.59e-04   5.14e-04   -1.48  0.13953
## as.factor(education)2 -2.89e-02   1.93e-01   -0.15  0.88079
## as.factor(education)3  8.77e-02   1.73e-01    0.51  0.61244
## as.factor(education)4  6.64e-02   2.66e-01    0.25  0.80301
## as.factor(education)5  4.71e-01   2.21e-01    2.13  0.03314 *
## smokeintensity        -7.83e-02   1.49e-02   -5.27  1.4e-07 ***
## I(smokeintensity^2)    1.07e-03   2.78e-04    3.85  0.00012 ***
## smokeyrs              -7.11e-02   2.71e-02   -2.63  0.00862 **
## I(smokeyrs^2)          8.15e-04   4.45e-04    1.83  0.06722 .
## as.factor(exercise)1   3.36e-01   1.75e-01    1.92  0.05467 .
## as.factor(exercise)2   3.80e-01   1.82e-01    2.09  0.03637 *
## as.factor(active)1     3.41e-02   1.30e-01    0.26  0.79337
## as.factor(active)2     2.13e-01   2.06e-01    1.04  0.30033
## wt71                  -7.66e-03   2.46e-02   -0.31  0.75530
## I(wt71^2)              8.66e-05   1.51e-04    0.57  0.56586
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1872.2  on 1565  degrees of freedom
```

```
## Residual deviance: 1755.6  on 1547  degrees of freedom
##   (63 observations deleted due to missingness)
## AIC: 1719
##
## Number of Fisher Scoring iterations: 4
```

```
nhefs$pqsmk <- predict(logit.est, nhefs, type = "response")
describe(nhefs$pqsmk)
```

```
## nhefs$pqsmk
##        n  missing distinct     Info     Mean      Gmd      .05      .10
##     1629        0     1629        1   0.2622   0.1302   0.1015   0.1261
##      .25      .50      .75      .90      .95
##   0.1780   0.2426   0.3251   0.4221   0.4965
##
## lowest : 0.05145 0.05157 0.05438 0.05583 0.05931
## highest: 0.67208 0.68643 0.71391 0.73330 0.78914
```

```
summary(nhefs$pqsmk)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.0514  0.1780  0.2426  0.2622  0.3251  0.7891
```

```
# solve sum(w_c * H(psi) * (qsmk - E[qsmk | L]))  = 0
# for a single psi and H(psi) = wt82_71 - psi * qsmk
# this can be solved as psi = sum( w_c * wt82_71 * (qsmk - pqsmk)) / sum(w_c * qsmk * (qsmk - pqsmk))

nhefs.c <- nhefs[which(!is.na(nhefs$wt82)),]
with(nhefs.c, sum(wc*wt82_71*(qsmk-pqsmk)) / sum(wc*qsmk*(qsmk - pqsmk)))
```

```
## [1] 3.446
```

### G-estimation: Closed form estimator for 2-parameter model

```
diff = with(nhefs.c, qsmk - pqsmk)
diff2 = with(nhefs.c, wc * diff)

lhs = matrix(0,2,2)
lhs[1,1] = with(nhefs.c, sum(qsmk * diff2))
lhs[1,2] = with(nhefs.c, sum(qsmk * smokeintensity  * diff2))
lhs[2,1] = with(nhefs.c, sum(qsmk * smokeintensity * diff2))
lhs[2,2] = with(nhefs.c, sum(qsmk * smokeintensity * smokeintensity * diff2))

rhs = matrix(0,2,1)
rhs[1] = with(nhefs.c, sum(wt82_71 * diff2))
rhs[2] = with(nhefs.c, sum(wt82_71 * smokeintensity * diff2))

psi = t(solve(lhs,rhs))
psi
```

```
##       [,1]    [,2]
## [1,] 2.859 0.03004
```

# 15. Outcome regression and propensity scores

## Program 15.1

- Estimating the average causal effect within levels of confounders under the assumption of effect-measure modification by smoking intensity ONLY
- Data from NHEFS

```
library(here)
```

```
#install.packages("readxl") # install package if required
library("readxl")

nhefs <- read_excel(here("data", "NHEFS.xls"))
nhefs$cens <- ifelse(is.na(nhefs$wt82), 1, 0)

# regression on covariates, allowing for some effect modification
fit <- glm(wt82_71 ~ qsmk + sex + race + age + I(age*age) + as.factor(education)
           + smokeintensity + I(smokeintensity*smokeintensity) + smokeyrs
           + I(smokeyrs*smokeyrs) + as.factor(exercise) + as.factor(active)
           + wt71 + I(wt71*wt71) + I(qsmk*smokeintensity), data=nhefs)
summary(fit)
```

```
##
## Call:
## glm(formula = wt82_71 ~ qsmk + sex + race + age + I(age * age) +
##     as.factor(education) + smokeintensity + I(smokeintensity *
##     smokeintensity) + smokeyrs + I(smokeyrs * smokeyrs) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71 * wt71) + I(qsmk * smokeintensity),
##     data = nhefs)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -42.056   -4.171   -0.343    3.891   44.606
##
## Coefficients:
##                                      Estimate Std. Error t value Pr(>|t|)
## (Intercept)                        -1.5881657  4.3130359  -0.368 0.712756
```

```
## qsmk                               2.5595941  0.8091486   3.163 0.001590 **
## sex                               -1.4302717  0.4689576  -3.050 0.002328 **
## race                               0.5601096  0.5818888   0.963 0.335913
## age                                0.3596353  0.1633188   2.202 0.027809 *
## I(age * age)                      -0.0061010  0.0017261  -3.534 0.000421 ***
## as.factor(education)2              0.7904440  0.6070005   1.302 0.193038
## as.factor(education)3              0.5563124  0.5561016   1.000 0.317284
## as.factor(education)4              1.4915695  0.8322704   1.792 0.073301 .
## as.factor(education)5             -0.1949770  0.7413692  -0.263 0.792589
## smokeintensity                     0.0491365  0.0517254   0.950 0.342287
## I(smokeintensity * smokeintensity) -0.0009907  0.0009380  -1.056 0.291097
## smokeyrs                           0.1343686  0.0917122   1.465 0.143094
## I(smokeyrs * smokeyrs)            -0.0018664  0.0015437  -1.209 0.226830
## as.factor(exercise)1               0.2959754  0.5351533   0.553 0.580298
## as.factor(exercise)2               0.3539128  0.5588587   0.633 0.526646
## as.factor(active)1                -0.9475695  0.4099344  -2.312 0.020935 *
## as.factor(active)2                -0.2613779  0.6845577  -0.382 0.702647
## wt71                               0.0455018  0.0833709   0.546 0.585299
## I(wt71 * wt71)                    -0.0009653  0.0005247  -1.840 0.066001 .
## I(qsmk * smokeintensity)           0.0466628  0.0351448   1.328 0.184463
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 53.5683)
##
##     Null deviance: 97176  on 1565  degrees of freedom
## Residual deviance: 82763  on 1545  degrees of freedom
##   (63 observations deleted due to missingness)
## AIC: 10701
##
## Number of Fisher Scoring iterations: 2
```

```
# (step 1) build the contrast matrix with all zeros
# this function builds the blank matrix
# install.packages("multcomp") # install packages if necessary
library("multcomp")
```

```
## Loading required package: mvtnorm

## Loading required package: survival

## Loading required package: TH.data

## Loading required package: MASS

##
## Attaching package: 'TH.data'

## The following object is masked from 'package:MASS':
##
##     geyser
```

```r
makeContrastMatrix <- function(model, nrow, names) {
  m <- matrix(0, nrow = nrow, ncol = length(coef(model)))
  colnames(m) <- names(coef(model))
  rownames(m) <- names
  return(m)
}
K1 <- makeContrastMatrix(fit, 2, c('Effect of Quitting Smoking at Smokeintensity of 5',
                                   'Effect of Quitting Smoking at Smokeintensity of 40'))
# (step 2) fill in the relevant non-zero elements
K1[1:2, 'qsmk'] <- 1
K1[1:2, 'I(qsmk * smokeintensity)'] <- c(5, 40)

# (step 3) check the contrast matrix
K1
```

```
##                                                    (Intercept) qsmk sex race
## Effect of Quitting Smoking at Smokeintensity of 5            0    1   0    0
## Effect of Quitting Smoking at Smokeintensity of 40           0    1   0    0
##                                                    age I(age * age)
## Effect of Quitting Smoking at Smokeintensity of 5    0            0
## Effect of Quitting Smoking at Smokeintensity of 40   0            0
##                                                    as.factor(education)2
## Effect of Quitting Smoking at Smokeintensity of 5                      0
## Effect of Quitting Smoking at Smokeintensity of 40                     0
##                                                    as.factor(education)3
## Effect of Quitting Smoking at Smokeintensity of 5                      0
## Effect of Quitting Smoking at Smokeintensity of 40                     0
##                                                    as.factor(education)4
## Effect of Quitting Smoking at Smokeintensity of 5                      0
## Effect of Quitting Smoking at Smokeintensity of 40                     0
##                                                    as.factor(education)5
## Effect of Quitting Smoking at Smokeintensity of 5                      0
## Effect of Quitting Smoking at Smokeintensity of 40                     0
##                                                    smokeintensity
## Effect of Quitting Smoking at Smokeintensity of 5               0
## Effect of Quitting Smoking at Smokeintensity of 40              0
##                                                    I(smokeintensity * smokeintensity)
## Effect of Quitting Smoking at Smokeintensity of 5                                   0
## Effect of Quitting Smoking at Smokeintensity of 40                                  0
##                                                    smokeyrs
## Effect of Quitting Smoking at Smokeintensity of 5         0
## Effect of Quitting Smoking at Smokeintensity of 40        0
##                                                    I(smokeyrs * smokeyrs)
## Effect of Quitting Smoking at Smokeintensity of 5                       0
## Effect of Quitting Smoking at Smokeintensity of 40                      0
##                                                    as.factor(exercise)1
## Effect of Quitting Smoking at Smokeintensity of 5                     0
## Effect of Quitting Smoking at Smokeintensity of 40                    0
##                                                    as.factor(exercise)2
```

```
## Effect of Quitting Smoking at Smokeintensity of 5                         0
## Effect of Quitting Smoking at Smokeintensity of 40                        0
##                                                     as.factor(active)1
## Effect of Quitting Smoking at Smokeintensity of 5                       0
## Effect of Quitting Smoking at Smokeintensity of 40                      0
##                                                     as.factor(active)2 wt71
## Effect of Quitting Smoking at Smokeintensity of 5                       0    0
## Effect of Quitting Smoking at Smokeintensity of 40                      0    0
##                                                     I(wt71 * wt71)
## Effect of Quitting Smoking at Smokeintensity of 5                 0
## Effect of Quitting Smoking at Smokeintensity of 40                0
##                                                     I(qsmk * smokeintensity)
## Effect of Quitting Smoking at Smokeintensity of 5                          5
## Effect of Quitting Smoking at Smokeintensity of 40                        40
```

```
# (step 4) estimate the contrasts, get tests and confidence intervals for them
estimates1 <- glht(fit, K1)
  summary(estimates1)
```

```
##
##   Simultaneous Tests for General Linear Hypotheses
##
## Fit: glm(formula = wt82_71 ~ qsmk + sex + race + age + I(age * age) +
##     as.factor(education) + smokeintensity + I(smokeintensity *
##     smokeintensity) + smokeyrs + I(smokeyrs * smokeyrs) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71 * wt71) + I(qsmk * smokeintensity),
##     data = nhefs)
##
## Linear Hypotheses:
##                                                          Estimate Std. Error
## Effect of Quitting Smoking at Smokeintensity of 5 == 0    2.7929     0.6683
## Effect of Quitting Smoking at Smokeintensity of 40 == 0   4.4261     0.8478
##                                                          z value Pr(>|z|)
## Effect of Quitting Smoking at Smokeintensity of 5 == 0    4.179 5.84e-05 ***
## Effect of Quitting Smoking at Smokeintensity of 40 == 0   5.221 3.56e-07 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Adjusted p values reported -- single-step method)
```

```
  confint(estimates1)
```

```
##
##   Simultaneous Confidence Intervals
##
## Fit: glm(formula = wt82_71 ~ qsmk + sex + race + age + I(age * age) +
##     as.factor(education) + smokeintensity + I(smokeintensity *
##     smokeintensity) + smokeyrs + I(smokeyrs * smokeyrs) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71 * wt71) + I(qsmk * smokeintensity),
##     data = nhefs)
##
## Quantile = 2.2281
```

```
## 95% family-wise confidence level
##
##
## Linear Hypotheses:
##                                                         Estimate lwr    upr
## Effect of Quitting Smoking at Smokeintensity of 5 == 0  2.7929   1.3039 4.2819
## Effect of Quitting Smoking at Smokeintensity of 40 == 0 4.4261   2.5372 6.3151
```

```
# regression on covariates, not allowing for effect modification
fit2 <- glm(wt82_71 ~ qsmk + sex + race + age + I(age*age) + as.factor(education)
           + smokeintensity + I(smokeintensity*smokeintensity) + smokeyrs
           + I(smokeyrs*smokeyrs) + as.factor(exercise) + as.factor(active)
           + wt71 + I(wt71*wt71), data=nhefs)

summary(fit2)
```

```
##
## Call:
## glm(formula = wt82_71 ~ qsmk + sex + race + age + I(age * age) +
##     as.factor(education) + smokeintensity + I(smokeintensity *
##     smokeintensity) + smokeyrs + I(smokeyrs * smokeyrs) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71 * wt71), data = nhefs)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -42.332   -4.216   -0.318    3.807   44.668
##
## Coefficients:
##                                     Estimate Std. Error t value Pr(>|t|)
## (Intercept)                       -1.6586176  4.3137734  -0.384 0.700666
## qsmk                               3.4626218  0.4384543   7.897 5.36e-15 ***
## sex                               -1.4650496  0.4683410  -3.128 0.001792 **
## race                               0.5864117  0.5816949   1.008 0.313560
## age                                0.3626624  0.1633431   2.220 0.026546 *
## I(age * age)                      -0.0061377  0.0017263  -3.555 0.000389 ***
## as.factor(education)2              0.8185263  0.6067815   1.349 0.177546
## as.factor(education)3              0.5715004  0.5561211   1.028 0.304273
## as.factor(education)4              1.5085173  0.8323778   1.812 0.070134 .
## as.factor(education)5             -0.1708264  0.7413289  -0.230 0.817786
## smokeintensity                     0.0651533  0.0503115   1.295 0.195514
## I(smokeintensity * smokeintensity) -0.0010468  0.0009373  -1.117 0.264261
## smokeyrs                           0.1333931  0.0917319   1.454 0.146104
## I(smokeyrs * smokeyrs)            -0.0018270  0.0015438  -1.183 0.236818
## as.factor(exercise)1               0.3206824  0.5349616   0.599 0.548961
## as.factor(exercise)2               0.3628786  0.5589557   0.649 0.516300
## as.factor(active)1                -0.9429574  0.4100208  -2.300 0.021593 *
## as.factor(active)2                -0.2580374  0.6847219  -0.377 0.706337
## wt71                               0.0373642  0.0831658   0.449 0.653297
## I(wt71 * wt71)                    -0.0009158  0.0005235  -1.749 0.080426 .
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 53.59474)
##
##     Null deviance: 97176  on 1565  degrees of freedom
## Residual deviance: 82857  on 1546  degrees of freedom
##   (63 observations deleted due to missingness)
## AIC: 10701
##
## Number of Fisher Scoring iterations: 2
```

# Program 15.2

- Estimating and plotting the propensity score
- Data from NHEFS

```
fit3 <- glm(qsmk ~ sex + race + age + I(age*age) + as.factor(education)
            + smokeintensity + I(smokeintensity*smokeintensity) + smokeyrs
            + I(smokeyrs*smokeyrs) + as.factor(exercise) + as.factor(active)
            + wt71 + I(wt71*wt71), data=nhefs, family=binomial())
summary(fit3)
```

```
##
## Call:
## glm(formula = qsmk ~ sex + race + age + I(age * age) + as.factor(education) +
##     smokeintensity + I(smokeintensity * smokeintensity) + smokeyrs +
##     I(smokeyrs * smokeyrs) + as.factor(exercise) + as.factor(active) +
##     wt71 + I(wt71 * wt71), family = binomial(), data = nhefs)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.4646  -0.8044  -0.6460   1.0578   2.3550
##
## Coefficients:
##                                     Estimate Std. Error z value Pr(>|z|)
## (Intercept)                       -1.9889022  1.2412792  -1.602 0.109089
## sex                               -0.5075218  0.1482316  -3.424 0.000617 ***
## race                              -0.8502312  0.2058720  -4.130 3.63e-05 ***
## age                                0.1030132  0.0488996   2.107 0.035150 *
## I(age * age)                      -0.0006052  0.0005074  -1.193 0.232973
## as.factor(education)2             -0.0983203  0.1906553  -0.516 0.606066
## as.factor(education)3              0.0156987  0.1707139   0.092 0.926730
## as.factor(education)4             -0.0425260  0.2642761  -0.161 0.872160
## as.factor(education)5              0.3796632  0.2203947   1.723 0.084952 .
## smokeintensity                    -0.0651561  0.0147589  -4.415 1.01e-05 ***
## I(smokeintensity * smokeintensity)  0.0008461  0.0002758   3.067 0.002160 **
## smokeyrs                          -0.0733708  0.0269958  -2.718 0.006571 **
## I(smokeyrs * smokeyrs)             0.0008384  0.0004435   1.891 0.058669 .
## as.factor(exercise)1               0.2914117  0.1735543   1.679 0.093136 .
## as.factor(exercise)2               0.3550517  0.1799293   1.973 0.048463 *
```

```
## as.factor(active)1                  0.0108754  0.1298320   0.084 0.933243
## as.factor(active)2                  0.0683123  0.2087269   0.327 0.743455
## wt71                               -0.0128478  0.0222829  -0.577 0.564226
## I(wt71 * wt71)                      0.0001209  0.0001352   0.895 0.370957
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 1876.3  on 1628  degrees of freedom
## Residual deviance: 1766.7  on 1610  degrees of freedom
## AIC: 1804.7
##
## Number of Fisher Scoring iterations: 4
```

```r
nhefs$ps <- predict(fit3, nhefs, type="response")

summary(nhefs$ps[nhefs$qsmk==0])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.05298 0.16949 0.22747 0.24504 0.30441 0.65788
```

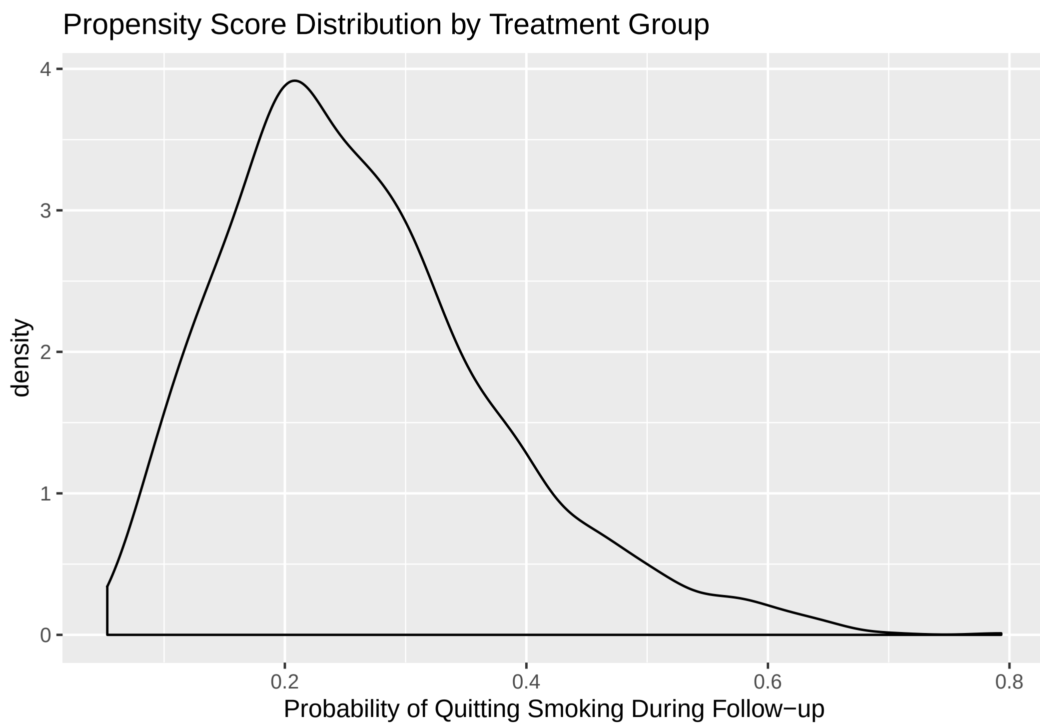
```r
summary(nhefs$ps[nhefs$qsmk==1])
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.06248 0.22046 0.28897 0.31240 0.38122 0.79320
```

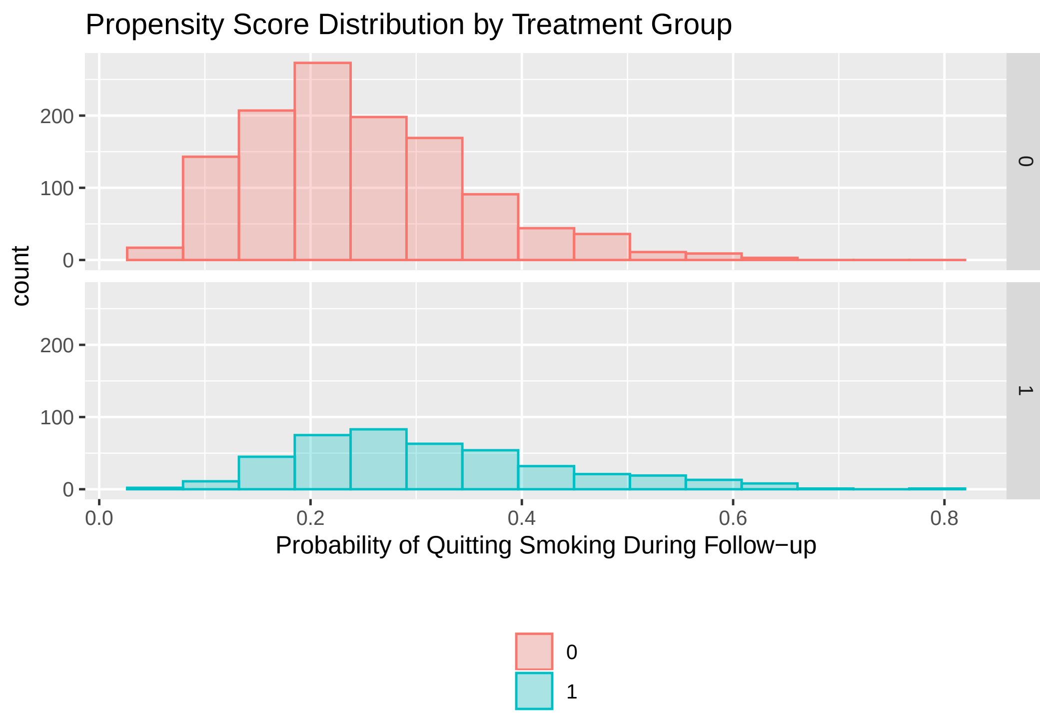
```r
# # plotting the estimated propensity score
# install.packages("ggplot2") # install packages if necessary
# install.packages("dplyr")
library("ggplot2")
library("dplyr")
```

```
##
## Attaching package: 'dplyr'

## The following object is masked from 'package:MASS':
##
##     select

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```r
ggplot(nhefs, aes(x = ps, fill = qsmk)) + geom_density(alpha = 0.2) +
  xlab('Probability of Quitting Smoking During Follow-up') +
  ggtitle('Propensity Score Distribution by Treatment Group') +
  scale_fill_discrete('') +
  theme(legend.position = 'bottom', legend.direction = 'vertical')
```




```
# alternative plot with histograms
nhefs <- nhefs %>% mutate(qsmklabel = ifelse(qsmk == 1,
                       yes = 'Quit Smoking 1971-1982',
                       no = 'Did Not Quit Smoking 1971-1982'))
ggplot(nhefs, aes(x = ps, fill = as.factor(qsmk), color = as.factor(qsmk))) +
  geom_histogram(alpha = 0.3, position = 'identity', bins=15) +
  facet_grid(as.factor(qsmk) ~ .) +
  xlab('Probability of Quitting Smoking During Follow-up') +
  ggtitle('Propensity Score Distribution by Treatment Group') +
  scale_fill_discrete('') +
  scale_color_discrete('') +
  theme(legend.position = 'bottom', legend.direction = 'vertical')
```




```
# attempt to reproduce plot from the book
nhefs %>%
  mutate(ps.grp = round(ps/0.05) * 0.05) %>%
  group_by(qsmk, ps.grp) %>%
  summarize(n = n()) %>%
  ungroup() %>%
  mutate(n2 = ifelse(qsmk == 0, yes = n, no =  -1*n)) %>%
  ggplot(aes(x = ps.grp, y = n2, fill = as.factor(qsmk))) +
  geom_bar(stat = 'identity', position = 'identity') +
  geom_text(aes(label = n, x = ps.grp, y = n2 + ifelse(qsmk == 0, 8, -8))) +
  xlab('Probability of Quitting Smoking During Follow-up') +
  ylab('N') +
  ggtitle('Propensity Score Distribution by Treatment Group') +
  scale_fill_discrete('') +
  scale_x_continuous(breaks = seq(0, 1, 0.05)) +
  theme(legend.position = 'bottom', legend.direction = 'vertical',
        axis.ticks.y = element_blank(),
        axis.text.y = element_blank())
```

# Program 15.3

- Stratification on the propensity score
- Data from NHEFS

```
# calculation of deciles
nhefs$ps.dec <- cut(nhefs$ps,
                    breaks=c(quantile(nhefs$ps, probs=seq(0,1,0.1))),
```

```
                     labels=seq(1:10),
                     include.lowest=TRUE)

#install.packages("psych") # install package if required
library("psych")
```

```
##
## Attaching package: 'psych'

## The following objects are masked from 'package:ggplot2':
##
##     %+%, alpha
```

```
describeBy(nhefs$ps, list(nhefs$ps.dec, nhefs$qsmk))
```

```
##
##  Descriptive statistics by group
## : 1
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range  skew kurtosis se
## X1    1 151  0.1 0.02   0.11     0.1 0.02 0.05 0.13  0.08 -0.55    -0.53  0
## ------------------------------------------------------------
## : 2
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range  skew kurtosis se
## X1    1 136 0.15 0.01   0.15    0.15 0.01 0.13 0.17  0.04 -0.04    -1.23  0
## ------------------------------------------------------------
## : 3
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range  skew kurtosis se
## X1    1 134 0.18 0.01   0.18    0.18 0.01 0.17 0.19  0.03 -0.08    -1.34  0
## ------------------------------------------------------------
## : 4
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range  skew kurtosis se
## X1    1 129 0.21 0.01   0.21    0.21 0.01 0.19 0.22  0.02 -0.04    -1.13  0
## ------------------------------------------------------------
## : 5
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 120 0.23 0.01   0.23    0.23 0.01 0.22 0.25  0.03 0.24    -1.22  0
## ------------------------------------------------------------
## : 6
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range  skew kurtosis se
## X1    1 117 0.26 0.01   0.26    0.26 0.01 0.25 0.27  0.03 -0.11    -1.29  0
## ------------------------------------------------------------
## : 7
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range  skew kurtosis se
```

```
## X1    1 120 0.29 0.01   0.29    0.29 0.01 0.27 0.31  0.03 -0.23    -1.19  0
## ------------------------------------------------------------
## : 8
## : 0
##    vars   n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 112 0.33 0.01   0.33    0.33 0.02 0.31 0.35  0.04 0.15     -1.1  0
## ------------------------------------------------------------
## : 9
## : 0
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 96 0.38 0.02   0.38    0.38 0.02 0.35 0.42  0.06 0.13    -1.15  0
## ------------------------------------------------------------
## : 10
## : 0
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis   se
## X1    1 86 0.49 0.06   0.47    0.48 0.05 0.42 0.66  0.24  1.1     0.47 0.01
## ------------------------------------------------------------
## : 1
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis   se
## X1    1 12  0.1 0.02   0.11     0.1 0.03 0.06 0.13  0.07 -0.5    -1.36 0.01
## ------------------------------------------------------------
## : 2
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range  skew kurtosis se
## X1    1 27 0.15 0.01   0.15    0.15 0.01 0.13 0.17  0.03 -0.03    -1.34  0
## ------------------------------------------------------------
## : 3
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 29 0.18 0.01   0.18    0.18 0.01 0.17 0.19  0.03 0.01    -1.34  0
## ------------------------------------------------------------
## : 4
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range  skew kurtosis se
## X1    1 34 0.21 0.01   0.21    0.21 0.01 0.19 0.22  0.02 -0.31    -1.23  0
## ------------------------------------------------------------
## : 5
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 43 0.23 0.01   0.23    0.23 0.01 0.22 0.25  0.03 0.11    -1.23  0
## ------------------------------------------------------------
## : 6
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 45 0.26 0.01   0.26    0.26 0.01 0.25 0.27  0.03  0.2    -1.12  0
## ------------------------------------------------------------
## : 7
## : 1
```

```
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 43 0.29 0.01   0.29    0.29 0.01 0.27 0.31  0.03 0.16    -1.25  0
## ------------------------------------------------------------
## : 8
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 51 0.33 0.01   0.33    0.33 0.02 0.31 0.35  0.04 0.11    -1.19  0
## ------------------------------------------------------------
## : 9
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis se
## X1    1 67 0.38 0.02   0.38    0.38 0.03 0.35 0.42  0.06 0.19    -1.27  0
## ------------------------------------------------------------
## : 10
## : 1
##    vars  n mean   sd median trimmed  mad  min  max range skew kurtosis   se
## X1    1 77 0.52 0.08   0.51    0.51 0.08 0.42 0.79  0.38 0.88     0.81 0.01
```

```r
# function to create deciles easily
decile <- function(x) {
  return(factor(quantcut(x, seq(0, 1, 0.1), labels = FALSE)))
}

# regression on PS deciles, allowing for effect modification
for (deciles in c(1:10)) {
  print(t.test(wt82_71~qsmk, data=nhefs[which(nhefs$ps.dec==deciles),]))
}
```

```
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = 0.0060506, df = 11.571, p-value = 0.9953
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -5.283903  5.313210
## sample estimates:
## mean in group 0 mean in group 1
##        3.995205        3.980551
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -3.1117, df = 37.365, p-value = 0.003556
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -6.849335 -1.448161
## sample estimates:
## mean in group 0 mean in group 1
```

```
##        2.904679        7.053426
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -4.5301, df = 35.79, p-value = 6.317e-05
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -9.474961 -3.613990
## sample estimates:
## mean in group 0 mean in group 1
##        2.612094        9.156570
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -1.4117, df = 45.444, p-value = 0.1648
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -5.6831731  0.9985715
## sample estimates:
## mean in group 0 mean in group 1
##        3.474679        5.816979
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -3.1371, df = 74.249, p-value = 0.002446
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -6.753621 -1.507087
## sample estimates:
## mean in group 0 mean in group 1
##        2.098800        6.229154
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -2.1677, df = 50.665, p-value = 0.0349
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -8.7516605 -0.3350127
## sample estimates:
## mean in group 0 mean in group 1
##        1.847004        6.390340
```

```
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -3.3155, df = 84.724, p-value = 0.001348
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -6.904207 -1.727590
## sample estimates:
## mean in group 0 mean in group 1
##        1.560048        5.875946
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -2.664, df = 75.306, p-value = 0.009441
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -6.2396014 -0.9005605
## sample estimates:
## mean in group 0 mean in group 1
##       0.2846851       3.8547661
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -1.9122, df = 129.12, p-value = 0.05806
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -4.68143608  0.07973698
## sample estimates:
## mean in group 0 mean in group 1
##      -0.8954482       1.4054014
##
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by qsmk
## t = -1.5925, df = 142.72, p-value = 0.1135
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -5.0209284  0.5404697
## sample estimates:
## mean in group 0 mean in group 1
##      -0.5043766       1.7358528
```

```r
# regression on PS deciles, not allowing for effect modification
fit.psdec <- glm(wt82_71 ~ qsmk + as.factor(ps.dec), data = nhefs)
summary(fit.psdec)
```

```
##
## Call:
## glm(formula = wt82_71 ~ qsmk + as.factor(ps.dec), data = nhefs)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -43.543   -3.932   -0.085    4.233   46.773
##
## Coefficients:
##                     Estimate Std. Error t value Pr(>|t|)
## (Intercept)           3.7505     0.6089   6.159 9.29e-10 ***
## qsmk                  3.5005     0.4571   7.659 3.28e-14 ***
## as.factor(ps.dec)2   -0.7391     0.8611  -0.858   0.3908
## as.factor(ps.dec)3   -0.6182     0.8612  -0.718   0.4730
## as.factor(ps.dec)4   -0.5204     0.8584  -0.606   0.5444
## as.factor(ps.dec)5   -1.4884     0.8590  -1.733   0.0834 .
## as.factor(ps.dec)6   -1.6227     0.8675  -1.871   0.0616 .
## as.factor(ps.dec)7   -1.9853     0.8681  -2.287   0.0223 *
## as.factor(ps.dec)8   -3.4447     0.8749  -3.937 8.61e-05 ***
## as.factor(ps.dec)9   -5.1544     0.8848  -5.825 6.91e-09 ***
## as.factor(ps.dec)10  -4.8403     0.8828  -5.483 4.87e-08 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 58.42297)
##
##     Null deviance: 97176  on 1565  degrees of freedom
## Residual deviance: 90848  on 1555  degrees of freedom
##   (63 observations deleted due to missingness)
## AIC: 10827
##
## Number of Fisher Scoring iterations: 2
```

```r
confint.lm(fit.psdec)
```

```
##                         2.5 %      97.5 %
## (Intercept)          2.556098  4.94486263
## qsmk                 2.603953  4.39700504
## as.factor(ps.dec)2  -2.428074  0.94982494
## as.factor(ps.dec)3  -2.307454  1.07103569
## as.factor(ps.dec)4  -2.204103  1.16333143
## as.factor(ps.dec)5  -3.173337  0.19657938
## as.factor(ps.dec)6  -3.324345  0.07893027
## as.factor(ps.dec)7  -3.688043 -0.28248110
## as.factor(ps.dec)8  -5.160862 -1.72860113
## as.factor(ps.dec)9  -6.889923 -3.41883853
```

```
## as.factor(ps.dec)10 -6.571789 -3.10873731
```

## Program 15.4

- Standardization using the propensity score
- Data from NHEFS

```r
#install.packages("boot") # install package if required
library("boot")
```

```
##
## Attaching package: 'boot'

## The following object is masked from 'package:psych':
##
##     logit

## The following object is masked from 'package:survival':
##
##     aml
```

```r
# standardization by propensity score, agnostic regarding effect modification
std.ps <- function(data, indices) {
  d <- data[indices,] # 1st copy: equal to original one`
  # calculating propensity scores
  ps.fit <- glm(qsmk ~ sex + race + age + I(age*age)
                + as.factor(education) + smokeintensity
                + I(smokeintensity*smokeintensity) + smokeyrs
                + I(smokeyrs*smokeyrs) + as.factor(exercise)
                + as.factor(active) + wt71 + I(wt71*wt71),
                data=d, family=binomial())
  d$pscore <- predict(ps.fit, d, type="response")

  # create a dataset with 3 copies of each subject
  d$interv <- -1 # 1st copy: equal to original one`
  d0 <- d # 2nd copy: treatment set to 0, outcome to missing
  d0$interv <- 0
  d0$qsmk <- 0
  d0$wt82_71 <- NA
  d1 <- d # 3rd copy: treatment set to 1, outcome to missing
  d1$interv <- 1
  d1$qsmk <- 1
  d1$wt82_71 <- NA
  d.onesample <- rbind(d, d0, d1) # combining datasets

  std.fit <- glm(wt82_71 ~ qsmk + pscore + I(qsmk*pscore), data=d.onesample)
  d.onesample$predicted_meanY <- predict(std.fit, d.onesample)

  # estimate mean outcome in each of the groups interv=-1, interv=0, and interv=1
  return(c(mean(d.onesample$predicted_meanY[d.onesample$interv==-1]),
           mean(d.onesample$predicted_meanY[d.onesample$interv==0]),
```

```r
           mean(d.onesample$predicted_meanY[d.onesample$interv==1]),
           mean(d.onesample$predicted_meanY[d.onesample$interv==1])-
             mean(d.onesample$predicted_meanY[d.onesample$interv==0])))
}

# bootstrap
results <- boot(data=nhefs, statistic=std.ps, R=5)

# generating confidence intervals
se <- c(sd(results$t[,1]), sd(results$t[,2]),
        sd(results$t[,3]), sd(results$t[,4]))
mean <- results$t0
ll <- mean - qnorm(0.975)*se
ul <- mean + qnorm(0.975)*se

bootstrap <- data.frame(cbind(c("Observed", "No Treatment", "Treatment",
                                "Treatment - No Treatment"), mean, se, ll, ul))
bootstrap
```

```
##                          V1             mean                 se               ll
## 1                  Observed 2.63384609228479 0.0507040735551285 2.53446793424727
## 2              No Treatment 1.71983636149843 0.0843031345589121 1.55460525397912
## 3                 Treatment 5.35072300362993  0.188364082722202 4.98153618551349
## 4 Treatment - No Treatment 3.63088664213151  0.218438975903448 3.20275411654093
##                 ul
## 1 2.73322425032232
## 2 1.88506746901773
## 3 5.71990982174637
## 4 4.05901916772208
```

```r
# regression on the propensity score (linear term)
model6 <- glm(wt82_71 ~ qsmk + ps, data = nhefs) # p.qsmk
summary(model6)
```

```
##
## Call:
## glm(formula = wt82_71 ~ qsmk + ps, data = nhefs)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -43.314   -4.006   -0.068    4.244   47.158
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)   5.5945     0.4831  11.581  < 2e-16 ***
## qsmk          3.5506     0.4573   7.765 1.47e-14 ***
## ps          -14.8218     1.7576  -8.433  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
```

```
## (Dispersion parameter for gaussian family taken to be 58.28455)
##
##     Null deviance: 97176  on 1565  degrees of freedom
## Residual deviance: 91099  on 1563  degrees of freedom
##   (63 observations deleted due to missingness)
## AIC: 10815
##
## Number of Fisher Scoring iterations: 2
```

```r
# standarization on the propensity score
# (step 1) create two new datasets, one with all treated and one with all untreated
treated <- nhefs
  treated$qsmk <- 1

untreated <- nhefs
  untreated$qsmk <- 0

# (step 2) predict values for everyone in each new dataset based on above model
treated$pred.y <- predict(model6, treated)
untreated$pred.y <- predict(model6, untreated)

# (step 3) compare mean weight loss had all been treated vs. that had all been untreated
mean1 <- mean(treated$pred.y, na.rm = TRUE)
mean0 <- mean(untreated$pred.y, na.rm = TRUE)
mean1
```

```
## [1] 5.250824
```

```r
mean0
```

```
## [1] 1.700228
```

```r
mean1 - mean0
```

```
## [1] 3.550596
```

```r
# (step 4) bootstrap a confidence interval
# number of bootstraps
nboot <- 100
# set up a matrix to store results
boots <- data.frame(i = 1:nboot,
                    mean1 = NA,
                    mean0 = NA,
                    difference = NA)
# loop to perform the bootstrapping
nhefs <- subset(nhefs, !is.na(ps) & !is.na(wt82_71)) # p.qsmk
for(i in 1:nboot) {
  # sample with replacement
  sampl <- nhefs[sample(1:nrow(nhefs), nrow(nhefs), replace = TRUE), ]

  # fit the model in the bootstrap sample
  bootmod <- glm(wt82_71 ~ qsmk + ps, data = sampl) # ps
```

```
  # create new datasets
  sampl.treated <- sampl %>%
    mutate(qsmk = 1)

  sampl.untreated <- sampl %>%
    mutate(qsmk = 0)

  # predict values
  sampl.treated$pred.y <- predict(bootmod, sampl.treated)
  sampl.untreated$pred.y <- predict(bootmod, sampl.untreated)

  # output results
  boots[i, 'mean1'] <- mean(sampl.treated$pred.y, na.rm = TRUE)
  boots[i, 'mean0'] <- mean(sampl.untreated$pred.y, na.rm = TRUE)
  boots[i, 'difference'] <- boots[i, 'mean1'] - boots[i, 'mean0']

  # once loop is done, print the results
  if(i == nboot) {
    cat('95% CI for the causal mean difference\n')
    cat(mean(boots$difference) - 1.96*sd(boots$difference),
        ',',
        mean(boots$difference) + 1.96*sd(boots$difference))
  }
}
```

```
## 95% CI for the causal mean difference
## 2.501167 , 4.558509
```

A more flexible and elegant way to do this is to write a function to perform the model fitting, prediction, bootstrapping, and reporting all at once.

# 16. Instrumental variables estimation

## Program 16.1

- Estimating the average causal using the standard IV estimator via the calculation of sample averages
- Data from NHEFS

```
library(here)
```

```
#install.packages("readxl") # install package if required
library("readxl")
nhefs <- read_excel(here("data", "NHEFS.xls"))

# some preprocessing of the data
nhefs$cens <- ifelse(is.na(nhefs$wt82), 1, 0)
summary(nhefs$price82)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.    NA's
##   1.452   1.740   1.815   1.806   1.868   2.103      92
```

```
# for simplicity, ignore subjects with missing outcome or missing instrument
nhefs.iv <- nhefs[which(!is.na(nhefs$wt82) & !is.na(nhefs$price82)),]
nhefs.iv$highprice <- ifelse(nhefs.iv$price82>=1.5, 1, 0)

table(nhefs.iv$highprice, nhefs.iv$qsmk)
```

```
##
##        0    1
##   0   33    8
##   1 1065  370
```

```
t.test(wt82_71 ~ highprice, data=nhefs.iv)
```

```
##
##  Welch Two Sample t-test
##
## data:  wt82_71 by highprice
## t = -0.10179, df = 41.644, p-value = 0.9194
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -3.130588  2.830010
## sample estimates:
```

```
## mean in group 0 mean in group 1
##        2.535729        2.686018
```

# Program 16.2

- Estimating the average causal effect using the standard IV estimator via two-stage-least-squares regression
- Data from NHEFS

```
#install.packages ("sem") # install package if required
library(sem)

model1 <- tsls(wt82_71 ~ qsmk, ~ highprice, data = nhefs.iv)
summary(model1)
```

```
##
##  2SLS Estimates
##
## Model Formula: wt82_71 ~ qsmk
##
## Instruments: ~highprice
##
## Residuals:
##      Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
## -43.34863  -4.00206  -0.02712   0.00000   4.17040  46.47022
##
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  2.068164   5.085098 0.40671  0.68428
## qsmk         2.396270  19.840037 0.12078  0.90388
##
## Residual standard error: 7.8561141 on 1474 degrees of freedom
```

```
confint(model1)  # note the wide confidence intervals
```

```
##                  2.5 %   97.5 %
## (Intercept)  -7.898445 12.03477
## qsmk        -36.489487 41.28203
```

# Program 16.3

- Estimating the average causal using the standard IV estimator via additive marginal structural models
- Data from NHEFS
- G-estimation: Checking one possible value of psi
- See Chapter 14 for program that checks several values and computes 95% confidence intervals

```
nhefs.iv$psi <- 2.396
nhefs.iv$Hpsi <- nhefs.iv$wt82_71-nhefs.iv$psi*nhefs.iv$qsmk

#install.packages("geepack") # install package if required
library("geepack")
```

```r
g.est <- geeglm(highprice ~ Hpsi, data=nhefs.iv, id=seqn, family=binomial(),
                corstr="independence")
summary(g.est)
```

```
##
## Call:
## geeglm(formula = highprice ~ Hpsi, family = binomial(), data = nhefs.iv,
##     id = seqn, corstr = "independence")
##
##  Coefficients:
##             Estimate   Std.err  Wald Pr(>|W|)
## (Intercept) 3.555e+00 1.652e-01 463.1   <2e-16 ***
## Hpsi        2.748e-07 2.273e-02   0.0        1
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Estimated Scale Parameters:
##             Estimate Std.err
## (Intercept)        1  0.7607
##
## Correlation: Structure = independenceNumber of clusters:   1476   Maximum cluster size: 1
```

```r
beta <- coef(g.est)
SE <- coef(summary(g.est))[,2]
lcl <- beta-qnorm(0.975)*SE
ucl <- beta+qnorm(0.975)*SE
cbind(beta, lcl, ucl)
```

```
##                  beta      lcl     ucl
## (Intercept) 3.555e+00  3.23152 3.87917
## Hpsi        2.748e-07 -0.04456 0.04456
```

# Program 16.4

- Estimating the average causal using the standard IV estimator with altnerative proposed instruments
- Data from NHEFS

```r
summary(tsls(wt82_71 ~ qsmk, ~ ifelse(price82 >= 1.6, 1, 0), data = nhefs.iv))
```

```
##
##  2SLS Estimates
##
## Model Formula: wt82_71 ~ qsmk
##
## Instruments: ~ifelse(price82 >= 1.6, 1, 0)
##
## Residuals:
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   -55.6   -13.5     7.6     0.0    12.5    56.4
##
```

```
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)    -7.89      42.25  -0.187    0.852
## qsmk           41.28     164.95   0.250    0.802
##
## Residual standard error: 18.6055 on 1474 degrees of freedom
```

```r
summary(tsls(wt82_71 ~ qsmk, ~ ifelse(price82 >= 1.7, 1, 0), data = nhefs.iv))
```

```
##
##  2SLS Estimates
##
## Model Formula: wt82_71 ~ qsmk
##
## Instruments: ~ifelse(price82 >= 1.7, 1, 0)
##
## Residuals:
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   -54.4   -13.4    -8.4     0.0    18.1    75.3
##
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)    13.16      48.08   0.274    0.784
## qsmk          -40.91     187.74  -0.218    0.828
##
## Residual standard error: 20.591 on 1474 degrees of freedom
```

```r
summary(tsls(wt82_71 ~ qsmk, ~ ifelse(price82 >= 1.8, 1, 0), data = nhefs.iv))
```

```
##
##  2SLS Estimates
##
## Model Formula: wt82_71 ~ qsmk
##
## Instruments: ~ifelse(price82 >= 1.8, 1, 0)
##
## Residuals:
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  -49.37   -8.31   -3.44    0.00    7.27   60.53
##
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)    8.086      7.288   1.110    0.267
## qsmk         -21.103     28.428  -0.742    0.458
##
## Residual standard error: 13.0188 on 1474 degrees of freedom
```

```r
summary(tsls(wt82_71 ~ qsmk, ~ ifelse(price82 >= 1.9, 1, 0), data = nhefs.iv))
```

```
##
##  2SLS Estimates
##
## Model Formula: wt82_71 ~ qsmk
##
## Instruments: ~ifelse(price82 >= 1.9, 1, 0)
```

```
##
## Residuals:
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  -47.24   -6.33   -1.43    0.00    5.52   54.36
##
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    5.963      6.067   0.983    0.326
## qsmk         -12.811     23.667  -0.541    0.588
##
## Residual standard error: 10.3637 on 1474 degrees of freedom
```

# Program 16.5

- Estimating the average causal using the standard IV estimator
- Conditional on baseline covariates
- Data from NHEFS

```
model2 <- tsls(wt82_71 ~ qsmk + sex + race + age + smokeintensity + smokeyrs +
                      as.factor(exercise) + as.factor(active) + wt71,
             ~ highprice + sex + race + age + smokeintensity + smokeyrs + as.factor(exercise) +
               as.factor(active) + wt71, data = nhefs.iv)
summary(model2)
```

```
##
##  2SLS Estimates
##
## Model Formula: wt82_71 ~ qsmk + sex + race + age + smokeintensity + smokeyrs +
##     as.factor(exercise) + as.factor(active) + wt71
##
## Instruments: ~highprice + sex + race + age + smokeintensity + smokeyrs + as.factor(exercise) +
##     as.factor(active) + wt71
##
## Residuals:
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  -42.23   -4.29   -0.62    0.00    3.87   46.74
##
##                        Estimate Std. Error t value Pr(>|t|)
## (Intercept)          17.280330   2.335402   7.399  2.3e-13 ***
## qsmk                 -1.042295  29.987369  -0.035   0.9723
## sex                  -1.644393   2.630831  -0.625   0.5320
## race                 -0.183255   4.650386  -0.039   0.9686
## age                  -0.163640   0.240548  -0.680   0.4964
## smokeintensity        0.005767   0.145504   0.040   0.9684
## smokeyrs              0.025836   0.161421   0.160   0.8729
## as.factor(exercise)1  0.498748   2.171239   0.230   0.8184
## as.factor(exercise)2  0.581834   2.183148   0.267   0.7899
## as.factor(active)1   -1.170145   0.607466  -1.926   0.0543 .
## as.factor(active)2   -0.512284   1.308451  -0.392   0.6955
## wt71                 -0.097949   0.036271  -2.701   0.0070 **
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 7.7162 on 1464 degrees of freedom
```

# 17. Causal survival analysis

## Program 17.1

- Nonparametric estimation of survival curves
- Data from NHEFS

```
library(here)
```

```
library("readxl")
nhefs <- read_excel(here("data","NHEFS.xls"))

# some preprocessing of the data
nhefs$survtime <- ifelse(nhefs$death==0, 120,
                         (nhefs$yrdth-83)*12+nhefs$modth) # yrdth ranges from 83 to 92

table(nhefs$death, nhefs$qsmk)
```

```
##
##       0   1
##   0 985 326
##   1 216 102
```

```
summary(nhefs[which(nhefs$death==1),]$survtime)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    1.00   35.00   61.00   61.14   86.75  120.00
```

```
#install.packages("survival")
#install.packages("ggplot2") # for plots
#install.packages("survminer") # for plots
library("survival")
library("ggplot2")
library("survminer")
```

```
## Loading required package: ggpubr
```

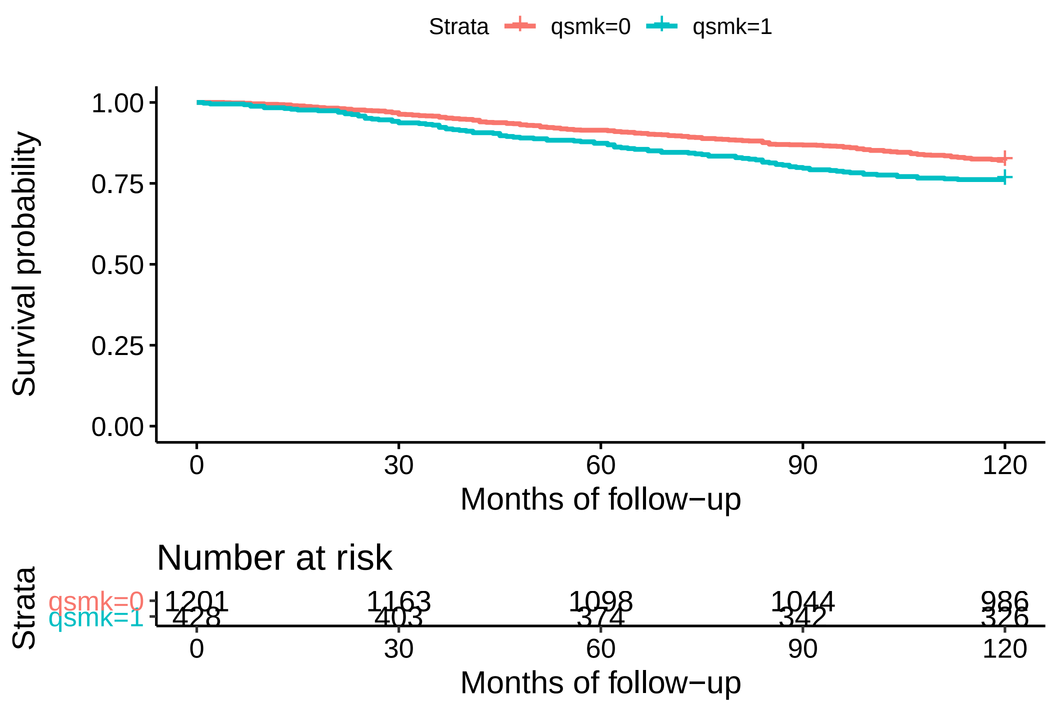
```
## Loading required package: magrittr
```

```
survdiff(Surv(survtime, death) ~ qsmk, data=nhefs)
```

```
## Call:
## survdiff(formula = Surv(survtime, death) ~ qsmk, data = nhefs)
##
```

```
##            N Observed Expected (O-E)^2/E (O-E)^2/V
## qsmk=0 1201      216    237.5      1.95      7.73
## qsmk=1  428      102     80.5      5.76      7.73
##
##  Chisq= 7.7  on 1 degrees of freedom, p= 0.005
```

```
fit <- survfit(Surv(survtime, death) ~ qsmk, data=nhefs)
ggsurvplot(fit, data = nhefs, xlab="Months of follow-up",
           ylab="Survival probability",
           main="Product-Limit Survival Estimates", risk.table = TRUE)
```




## Program 17.2

- Parametric estimation of survival curves via hazards model
- Data from NHEFS

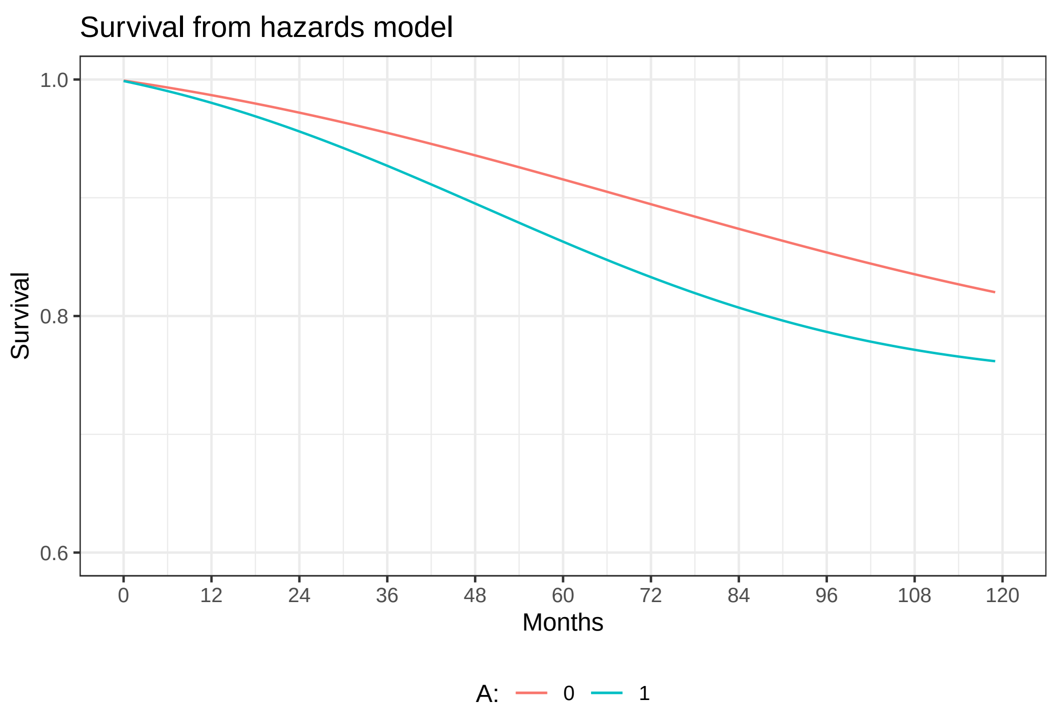
```
# creation of person-month data
#install.packages("splitstackshape")
library("splitstackshape")
nhefs.surv <- expandRows(nhefs, "survtime", drop=F)
nhefs.surv$time <- sequence(rle(nhefs.surv$seqn)$lengths)-1
nhefs.surv$event <- ifelse(nhefs.surv$time==nhefs.surv$survtime-1 &
                             nhefs.surv$death==1, 1, 0)
nhefs.surv$timesq <- nhefs.surv$time^2

# fit of parametric hazards model
hazards.model <- glm(event==0 ~ qsmk + I(qsmk*time) + I(qsmk*timesq) +
                       time + timesq, family=binomial(), data=nhefs.surv)
```

```r
summary(hazards.model)
```

```
##
## Call:
## glm(formula = event == 0 ~ qsmk + I(qsmk * time) + I(qsmk * timesq) +
##     time + timesq, family = binomial(), data = nhefs.surv)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -3.7253   0.0546   0.0601   0.0625   0.0783
##
## Coefficients:
##                    Estimate Std. Error z value Pr(>|z|)
## (Intercept)       6.996e+00  2.309e-01  30.292   <2e-16 ***
## qsmk             -3.355e-01  3.970e-01  -0.845   0.3981
## I(qsmk * time)   -1.208e-02  1.503e-02  -0.804   0.4215
## I(qsmk * timesq)  1.612e-04  1.246e-04   1.293   0.1960
## time             -1.960e-02  8.413e-03  -2.329   0.0198 *
## timesq            1.256e-04  6.686e-05   1.878   0.0604 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 4655.3  on 176763  degrees of freedom
## Residual deviance: 4631.3  on 176758  degrees of freedom
## AIC: 4643.3
##
## Number of Fisher Scoring iterations: 9
```

```r
# creation of dataset with all time points under each treatment level
qsmk0 <- data.frame(cbind(seq(0, 119),0,(seq(0, 119))^2))
qsmk1 <- data.frame(cbind(seq(0, 119),1,(seq(0, 119))^2))

colnames(qsmk0) <- c("time", "qsmk", "timesq")
colnames(qsmk1) <- c("time", "qsmk", "timesq")

# assignment of estimated (1-hazard) to each person-month */
qsmk0$p.noevent0 <- predict(hazards.model, qsmk0, type="response")
qsmk1$p.noevent1 <- predict(hazards.model, qsmk1, type="response")

# computation of survival for each person-month
qsmk0$surv0 <- cumprod(qsmk0$p.noevent0)
qsmk1$surv1 <- cumprod(qsmk1$p.noevent1)

# some data management to plot estimated survival curves
hazards.graph <- merge(qsmk0, qsmk1, by=c("time", "timesq"))
hazards.graph$survdiff <- hazards.graph$surv1-hazards.graph$surv0
```

```r
# plot
ggplot(hazards.graph, aes(x=time, y=surv)) +
  geom_line(aes(y = surv0, colour = "0")) +
  geom_line(aes(y = surv1, colour = "1")) +
  xlab("Months") +
  scale_x_continuous(limits = c(0, 120), breaks=seq(0,120,12)) +
  scale_y_continuous(limits=c(0.6, 1), breaks=seq(0.6, 1, 0.2)) +
  ylab("Survival") +
  ggtitle("Survival from hazards model") +
  labs(colour="A:") +
  theme_bw() +
  theme(legend.position="bottom")
```




# Program 17.3

- Estimation of survival curves via IP weighted hazards model
- Data from NHEFS

```r
# estimation of denominator of ip weights
p.denom <- glm(qsmk ~ sex + race + age + I(age*age) + as.factor(education)
               + smokeintensity + I(smokeintensity*smokeintensity)
               + smokeyrs + I(smokeyrs*smokeyrs) + as.factor(exercise)
               + as.factor(active) + wt71 + I(wt71*wt71),
               data=nhefs, family=binomial())
nhefs$pd.qsmk <- predict(p.denom, nhefs, type="response")

# estimation of numerator of ip weights
```

```r
p.num <- glm(qsmk ~ 1, data=nhefs, family=binomial())
nhefs$pn.qsmk <- predict(p.num, nhefs, type="response")

# computation of estimated weights
nhefs$sw.a <- ifelse(nhefs$qsmk==1, nhefs$pn.qsmk/nhefs$pd.qsmk,
                     (1-nhefs$pn.qsmk)/(1-nhefs$pd.qsmk))
summary(nhefs$sw.a)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.3312  0.8640  0.9504  0.9991  1.0755  4.2054
```

```r
# creation of person-month data
nhefs.ipw <- expandRows(nhefs, "survtime", drop=F)
nhefs.ipw$time <- sequence(rle(nhefs.ipw$seqn)$lengths)-1
nhefs.ipw$event <- ifelse(nhefs.ipw$time==nhefs.ipw$survtime-1 &
                            nhefs.ipw$death==1, 1, 0)
nhefs.ipw$timesq <- nhefs.ipw$time^2

# fit of weighted hazards model
ipw.model <- glm(event==0 ~ qsmk + I(qsmk*time) + I(qsmk*timesq) +
                   time + timesq, family=binomial(), weight=sw.a,
                 data=nhefs.ipw)
```

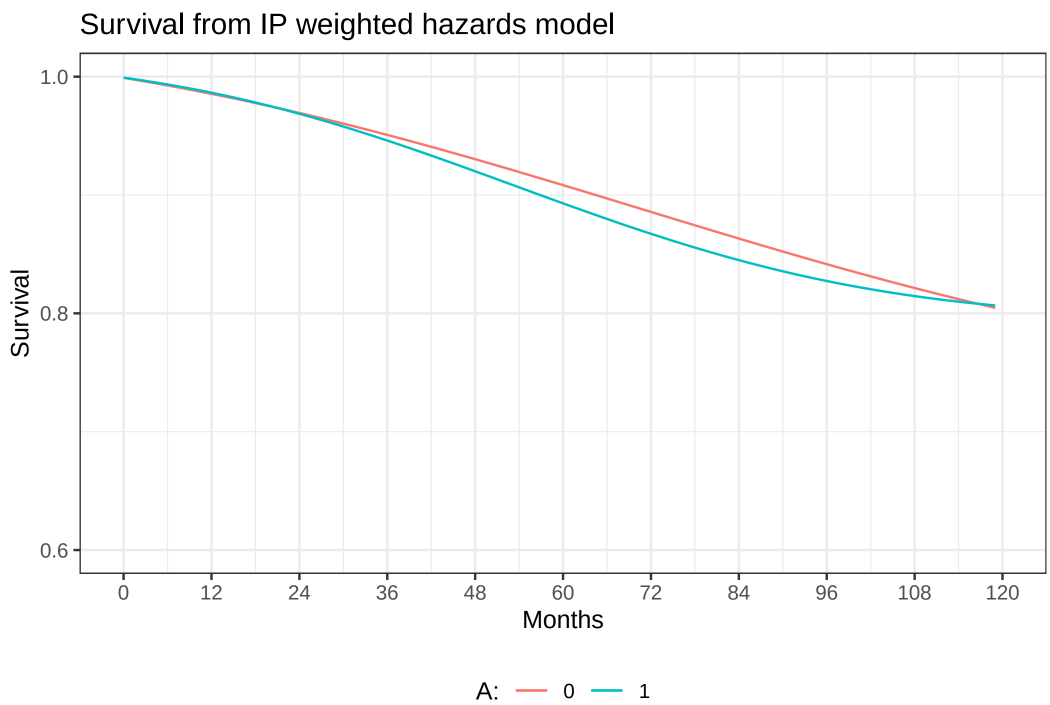
```
## Warning in eval(family$initialize): non-integer #successes in a binomial glm!
```

```r
summary(ipw.model)
```

```
##
## Call:
## glm(formula = event == 0 ~ qsmk + I(qsmk * time) + I(qsmk * timesq) +
##     time + timesq, family = binomial(), data = nhefs.ipw, weights = sw.a)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -7.1859   0.0528   0.0595   0.0640   0.1452
##
## Coefficients:
##                    Estimate Std. Error z value Pr(>|z|)
## (Intercept)       6.897e+00  2.208e-01  31.242   <2e-16 ***
## qsmk              1.794e-01  4.399e-01   0.408   0.6834
## I(qsmk * time)   -1.895e-02  1.640e-02  -1.155   0.2481
## I(qsmk * timesq)  2.103e-04  1.352e-04   1.556   0.1198
## time             -1.889e-02  8.053e-03  -2.345   0.0190 *
## timesq            1.181e-04  6.399e-05   1.846   0.0649 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 4643.9  on 176763  degrees of freedom
## Residual deviance: 4626.2  on 176758  degrees of freedom
```

```
## AIC: 4633.5
##
## Number of Fisher Scoring iterations: 9
```

```
# creation of survival curves
ipw.qsmk0 <- data.frame(cbind(seq(0, 119),0,(seq(0, 119))^2))
ipw.qsmk1 <- data.frame(cbind(seq(0, 119),1,(seq(0, 119))^2))

colnames(ipw.qsmk0) <- c("time", "qsmk", "timesq")
colnames(ipw.qsmk1) <- c("time", "qsmk", "timesq")

# assignment of estimated (1-hazard) to each person-month */
ipw.qsmk0$p.noevent0 <- predict(ipw.model, ipw.qsmk0, type="response")
ipw.qsmk1$p.noevent1 <- predict(ipw.model, ipw.qsmk1, type="response")

# computation of survival for each person-month
ipw.qsmk0$surv0 <- cumprod(ipw.qsmk0$p.noevent0)
ipw.qsmk1$surv1 <- cumprod(ipw.qsmk1$p.noevent1)

# some data management to plot estimated survival curves
ipw.graph <- merge(ipw.qsmk0, ipw.qsmk1, by=c("time", "timesq"))
ipw.graph$survdiff <- ipw.graph$surv1-ipw.graph$surv0

# plot
ggplot(ipw.graph, aes(x=time, y=surv)) +
  geom_line(aes(y = surv0, colour = "0")) +
  geom_line(aes(y = surv1, colour = "1")) +
  xlab("Months") +
  scale_x_continuous(limits = c(0, 120), breaks=seq(0,120,12)) +
  scale_y_continuous(limits=c(0.6, 1), breaks=seq(0.6, 1, 0.2)) +
  ylab("Survival") +
  ggtitle("Survival from IP weighted hazards model") +
  labs(colour="A:") +
  theme_bw() +
  theme(legend.position="bottom")
```




## Program 17.4

- Estimating of survival curves via g-formula
- Data from NHEFS

```
# fit of hazards model with covariates
gf.model <- glm(event==0 ~ qsmk + I(qsmk*time) + I(qsmk*timesq)
                + time + timesq + sex + race + age + I(age*age)
                + as.factor(education) + smokeintensity
                + I(smokeintensity*smokeintensity) + smkintensity82_71
                + smokeyrs + I(smokeyrs*smokeyrs) + as.factor(exercise)
                + as.factor(active) + wt71 + I(wt71*wt71),
                data=nhefs.surv, family=binomial())
summary(gf.model)
```

```
##
## Call:
## glm(formula = event == 0 ~ qsmk + I(qsmk * time) + I(qsmk * timesq) +
##     time + timesq + sex + race + age + I(age * age) + as.factor(education) +
##     smokeintensity + I(smokeintensity * smokeintensity) + smkintensity82_71 +
##     smokeyrs + I(smokeyrs * smokeyrs) + as.factor(exercise) +
##     as.factor(active) + wt71 + I(wt71 * wt71), family = binomial(),
##     data = nhefs.surv)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -4.3160   0.0244   0.0395   0.0640   0.3303
```

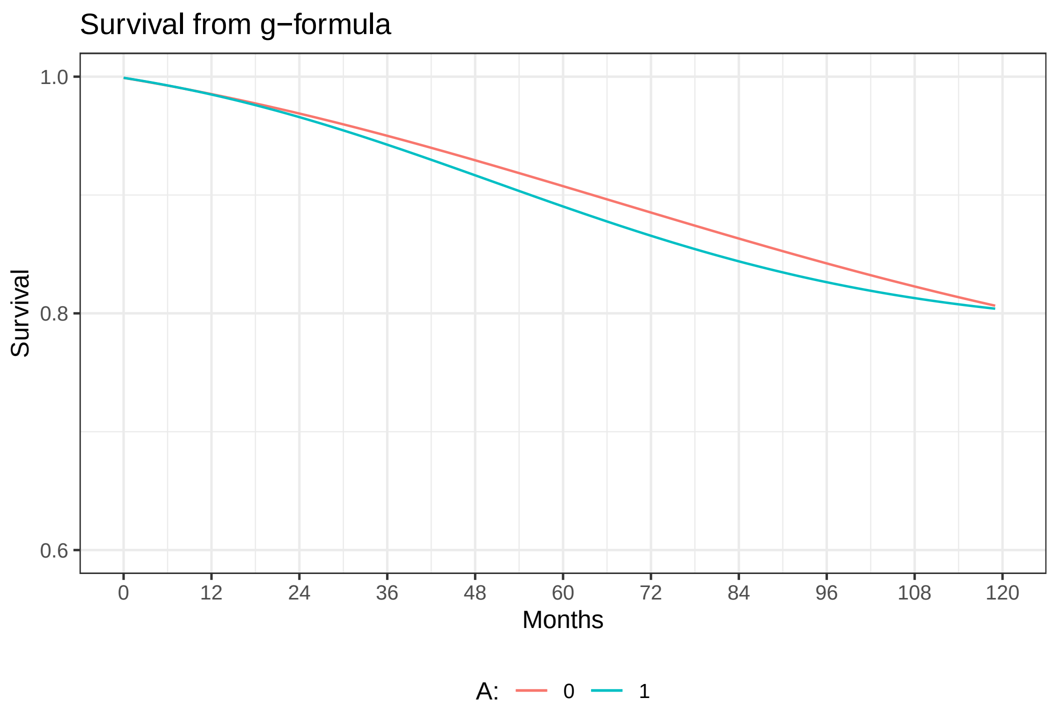
```
##
## Coefficients:
##                                      Estimate Std. Error z value Pr(>|z|)
## (Intercept)                         9.272e+00  1.379e+00   6.724 1.76e-11 ***
## qsmk                                5.959e-02  4.154e-01   0.143 0.885924
## I(qsmk * time)                     -1.485e-02  1.506e-02  -0.987 0.323824
## I(qsmk * timesq)                    1.702e-04  1.245e-04   1.367 0.171643
## time                               -2.270e-02  8.437e-03  -2.690 0.007142 **
## timesq                              1.174e-04  6.709e-05   1.751 0.080020 .
## sex                                 4.368e-01  1.409e-01   3.101 0.001930 **
## race                               -5.240e-02  1.734e-01  -0.302 0.762572
## age                                -8.750e-02  5.907e-02  -1.481 0.138536
## I(age * age)                        8.128e-05  5.470e-04   0.149 0.881865
## as.factor(education)2               1.401e-01  1.566e-01   0.895 0.370980
## as.factor(education)3               4.335e-01  1.526e-01   2.841 0.004502 **
## as.factor(education)4               2.350e-01  2.790e-01   0.842 0.399750
## as.factor(education)5               3.750e-01  2.386e-01   1.571 0.116115
## smokeintensity                     -1.626e-03  1.430e-02  -0.114 0.909431
## I(smokeintensity * smokeintensity) -7.182e-05  2.390e-04  -0.301 0.763741
## smkintensity82_71                  -1.686e-03  6.501e-03  -0.259 0.795399
## smokeyrs                           -1.677e-02  3.065e-02  -0.547 0.584153
## I(smokeyrs * smokeyrs)             -5.280e-05  4.244e-04  -0.124 0.900997
## as.factor(exercise)1                1.469e-01  1.792e-01   0.820 0.412300
## as.factor(exercise)2               -1.504e-01  1.762e-01  -0.854 0.393177
## as.factor(active)1                 -1.601e-01  1.300e-01  -1.232 0.218048
## as.factor(active)2                 -2.294e-01  1.877e-01  -1.222 0.221766
## wt71                                6.222e-02  1.902e-02   3.271 0.001073 **
## I(wt71 * wt71)                     -4.046e-04  1.129e-04  -3.584 0.000338 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 4655.3  on 176763  degrees of freedom
## Residual deviance: 4185.7  on 176739  degrees of freedom
## AIC: 4235.7
##
## Number of Fisher Scoring iterations: 10
```

```r
# creation of dataset with all time points for
# each individual under each treatment level
gf.qsmk0 <- expandRows(nhefs, count=120, count.is.col=F)
gf.qsmk0$time <- rep(seq(0, 119), nrow(nhefs))
gf.qsmk0$timesq <- gf.qsmk0$time^2
gf.qsmk0$qsmk <- 0

gf.qsmk1 <- gf.qsmk0
gf.qsmk1$qsmk <- 1

gf.qsmk0$p.noevent0 <- predict(gf.model, gf.qsmk0, type="response")
```

```r
gf.qsmk1$p.noevent1 <- predict(gf.model, gf.qsmk1, type="response")

#install.packages("dplyr")
library("dplyr")
```

```
##
## Attaching package: 'dplyr'
## The following objects are masked from 'package:stats':
##
##     filter, lag
## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```r
gf.qsmk0.surv <- gf.qsmk0 %>% group_by(seqn) %>% mutate(surv0 = cumprod(p.noevent0))
gf.qsmk1.surv <- gf.qsmk1 %>% group_by(seqn) %>% mutate(surv1 = cumprod(p.noevent1))

gf.surv0 <- aggregate(gf.qsmk0.surv, by=list(gf.qsmk0.surv$time), FUN=mean)[c("qsmk", "time", "surv0")]
gf.surv1 <- aggregate(gf.qsmk1.surv, by=list(gf.qsmk1.surv$time), FUN=mean)[c("qsmk", "time", "surv1")]

gf.graph <- merge(gf.surv0, gf.surv1, by=c("time"))
gf.graph$survdiff <- gf.graph$surv1-gf.graph$surv0

# plot
ggplot(gf.graph, aes(x=time, y=surv)) +
  geom_line(aes(y = surv0, colour = "0")) +
  geom_line(aes(y = surv1, colour = "1")) +
  xlab("Months") +
  scale_x_continuous(limits = c(0, 120), breaks=seq(0,120,12)) +
  scale_y_continuous(limits=c(0.6, 1), breaks=seq(0.6, 1, 0.2)) +
  ylab("Survival") +
  ggtitle("Survival from g-formula") +
  labs(colour="A:") +
  theme_bw() +
  theme(legend.position="bottom")
```




## Program 17.5

- Estimating of median survival time ratio via a structural nested AFT model
- Data from NHEFS

```
# some preprocessing of the data
nhefs <- read_excel(here("data", "NHEFS.xls"))
nhefs$survtime <- ifelse(nhefs$death==0, NA, (nhefs$yrdth-83)*12+nhefs$modth) # * yrdth ranges from 83

# model to estimate E[A|L]
modelA <- glm(qsmk ~ sex + race + age + I(age*age)
              + as.factor(education) + smokeintensity
              + I(smokeintensity*smokeintensity) + smokeyrs
              + I(smokeyrs*smokeyrs) + as.factor(exercise)
              + as.factor(active) + wt71 + I(wt71*wt71),
              data=nhefs, family=binomial())

nhefs$p.qsmk <- predict(modelA, nhefs, type="response")
d <- nhefs[!is.na(nhefs$survtime),] # select only those with observed death time
n <- nrow(d)

# define the estimating function that needs to be minimized
sumeef <- function(psi){

  # creation of delta indicator
  if (psi>=0){
    delta <- ifelse(d$qsmk==0 |
```

```r
                      (d$qsmk==1 & psi <= log(120/d$survtime)),
                    1, 0)
  } else if (psi < 0) {
    delta <- ifelse(d$qsmk==1 |
                      (d$qsmk==0 & psi > log(d$survtime/120)), 1, 0)
  }

  smat <- delta*(d$qsmk-d$p.qsmk)
  sval <- sum(smat, na.rm=T)
  save <- sval/n
  smat <- smat - rep(save, n)

  # covariance
  sigma <- t(smat) %*% smat
  if (sigma == 0){
    sigma <- 1e-16
  }
  estimeq <- sval*solve(sigma)*t(sval)
  return(estimeq)
}

res <- optimize(sumeef, interval = c(-0.2,0.2))
psi1 <- res$minimum
objfunc <- as.numeric(res$objective)


# Use simple bisection method to find estimates of lower and upper 95% confidence bounds
increm <- 0.1
for_conf <- function(x){
  return(sumeef(x) - 3.84)
}

if (objfunc < 3.84){
  # Find estimate of where sumeef(x) > 3.84

  # Lower bound of 95% CI
  psilow <- psi1
  testlow <- objfunc
  countlow <- 0
  while (testlow < 3.84 & countlow < 100){
    psilow <- psilow - increm
    testlow <- sumeef(psilow)
    countlow <- countlow + 1
  }

  # Upper bound of 95% CI
  psihigh <- psi1
  testhigh <- objfunc
```

```r
counthigh <- 0
while (testhigh < 3.84 & counthigh < 100){
  psihigh <- psihigh + increm
  testhigh <- sumeef(psihigh)
  counthigh <- counthigh + 1
}

# Better estimate using bisection method
if ((testhigh > 3.84) & (testlow > 3.84)){

  # Bisection method
  left <- psi1
  fleft <- objfunc - 3.84
  right <- psihigh
  fright <- testhigh - 3.84
  middle <- (left  + right) / 2
  fmiddle <- for_conf(middle)
  count <- 0
  diff <- right - left

  while (!(abs(fmiddle) < 0.0001 | diff < 0.0001 | count > 100)){
    test <- fmiddle * fleft
    if (test < 0){
      right <- middle
      fright <- fmiddle
    } else {
      left <- middle
      fleft <- fmiddle
    }
    middle <- (left + right) / 2
    fmiddle <- for_conf(middle)
    count <- count + 1
    diff <- right - left
  }

  psi_high <- middle
  objfunc_high <- fmiddle + 3.84

  # lower bound of 95% CI
  left <- psilow
  fleft <- testlow - 3.84
  right <- psi1
  fright <- objfunc - 3.84
  middle <- (left + right) / 2
  fmiddle <- for_conf(middle)
  count <- 0
  diff <- right - left

  while(!(abs(fmiddle) < 0.0001 | diff < 0.0001 | count > 100)){
```

```
      test <- fmiddle * fleft
      if (test < 0){
        right <- middle
        fright <- fmiddle
      } else {
        left <- middle
        fleft <- fmiddle
      }
      middle <- (left + right) / 2
      fmiddle <- for_conf(middle)
      diff <- right - left
      count <- count + 1
    }
    psi_low <- middle
    objfunc_low <- fmiddle + 3.84
    psi <- psi1
  }
}
c(psi, psi_low, psi_high)
```

```
## [1] -0.05041591 -0.22312099  0.33312901
```

# R session information

For reproducibility.

```r
# install.packages("sessioninfo")
sessioninfo::session_info()
```

```
## - Session info ----------------------------------------------------------------
##  setting  value
##  version  R version 3.6.1 (2019-07-05)
##  os       Windows 10 x64
##  system   x86_64, mingw32
##  ui       RTerm
##  language (EN)
##  collate  English_United Kingdom.1252
##  ctype    English_United Kingdom.1252
##  tz       Europe/London
##  date     2019-12-12
##
## - Packages --------------------------------------------------------------------
##  package     * version date       lib source
##  assertthat    0.2.1   2019-03-21 [1] CRAN (R 3.6.0)
##  bookdown      0.16.5  2019-12-09 [1] Github (rstudio/bookdown@70f9c07)
##  cli           2.0.0   2019-12-09 [1] CRAN (R 3.6.1)
##  crayon        1.3.4   2017-09-16 [1] CRAN (R 3.6.0)
##  digest        0.6.23  2019-11-23 [1] CRAN (R 3.6.1)
##  evaluate      0.14    2019-05-28 [1] CRAN (R 3.6.0)
##  fansi         0.4.0   2018-10-05 [1] CRAN (R 3.6.0)
##  glue          1.3.1   2019-03-12 [1] CRAN (R 3.6.0)
##  htmltools     0.4.0   2019-10-04 [1] CRAN (R 3.6.1)
##  knitr         1.26    2019-11-12 [1] CRAN (R 3.6.1)
##  magrittr      1.5     2014-11-22 [1] CRAN (R 3.6.0)
##  Rcpp          1.0.3   2019-11-08 [1] CRAN (R 3.6.1)
##  rlang         0.4.2   2019-11-23 [1] CRAN (R 3.6.1)
##  rmarkdown     1.18.7  2019-12-12 [1] Github (rstudio/rmarkdown@af6a777)
##  sessioninfo   1.1.1   2018-11-05 [1] CRAN (R 3.6.0)
##  stringi       1.4.3   2019-03-12 [1] CRAN (R 3.6.0)
##  stringr       1.4.0   2019-02-10 [1] CRAN (R 3.6.0)
##  withr         2.1.2   2018-03-15 [1] CRAN (R 3.6.0)
##  xfun          0.11    2019-11-12 [1] CRAN (R 3.6.1)
##  yaml          2.2.0   2018-07-25 [1] CRAN (R 3.6.0)
```

```
##
## [1] C:/Users/palmertm/library
## [2] C:/Program Files/R/R-3.6.1/library
```

# Bibliography

Miguel A Hernán and James M Robins. *Causal Inference: What If.* Boca Raton: Chapman & Hall/CRC, 2020.