Causal Inference Final Project: Effect of Smoking on 10-year Development of Cardiovascular Disease

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Data Exploration

```
fhs = read.csv('framingham.csv', header = T)
head(fhs)
```

```
##   male age education currentSmoker cigsPerDay BPMeds prevalentStroke
## 1    1  39         4             0          0      0               0
## 2    0  46         2             0          0      0               0
## 3    1  48         1             1         20      0               0
## 4    0  61         3             1         30      0               0
## 5    0  46         3             1         23      0               0
## 6    0  43         2             0          0      0               0
##   prevalentHyp diabetes totChol sysBP diaBP   BMI heartRate glucose
## 1            0        0     195 106.0    70 26.97        80      77
## 2            0        0     250 121.0    81 28.73        95      76
## 3            0        0     245 127.5    80 25.34        75      70
## 4            1        0     225 150.0    95 28.58        65     103
## 5            0        0     285 130.0    84 23.10        85      85
## 6            1        0     228 180.0   110 30.30        77      99
##   TenYearCHD
## 1          0
## 2          0
## 3          0
## 4          1
## 5          0
## 6          0
```

```
summary(fhs)
```

```
##       male             age          education     currentSmoker
##  Min.   :0.0000   Min.   :32.00   Min.   :1.000   Min.   :0.0000
##  1st Qu.:0.0000   1st Qu.:42.00   1st Qu.:1.000   1st Qu.:0.0000
##  Median :0.0000   Median :49.00   Median :2.000   Median :0.0000
##  Mean   :0.4292   Mean   :49.58   Mean   :1.979   Mean   :0.4941
##  3rd Qu.:1.0000   3rd Qu.:56.00   3rd Qu.:3.000   3rd Qu.:1.0000
##  Max.   :1.0000   Max.   :70.00   Max.   :4.000   Max.   :1.0000
##                                   NA's   :105
##    cigsPerDay         BPMeds        prevalentStroke     prevalentHyp
##  Min.   : 0.000   Min.   :0.00000   Min.   :0.000000   Min.   :0.0000
##  1st Qu.: 0.000   1st Qu.:0.00000   1st Qu.:0.000000   1st Qu.:0.0000
##  Median : 0.000   Median :0.00000   Median :0.000000   Median :0.0000
##  Mean   : 9.006   Mean   :0.02962   Mean   :0.005896   Mean   :0.3106
##  3rd Qu.:20.000   3rd Qu.:0.00000   3rd Qu.:0.000000   3rd Qu.:1.0000
##  Max.   :70.000   Max.   :1.00000   Max.   :1.000000   Max.   :1.0000
##  NA's   :29       NA's   :53
```

```
##     diabetes          totChol          sysBP           diaBP
##  Min.   :0.00000   Min.   :107.0   Min.   : 83.5   Min.   : 48.0
##  1st Qu.:0.00000   1st Qu.:206.0   1st Qu.:117.0   1st Qu.: 75.0
##  Median :0.00000   Median :234.0   Median :128.0   Median : 82.0
##  Mean   :0.02571   Mean   :236.7   Mean   :132.4   Mean   : 82.9
##  3rd Qu.:0.00000   3rd Qu.:263.0   3rd Qu.:144.0   3rd Qu.: 90.0
##  Max.   :1.00000   Max.   :696.0   Max.   :295.0   Max.   :142.5
##                    NA's   :50
##       BMI          heartRate         glucose         TenYearCHD
##  Min.   :15.54   Min.   : 44.00   Min.   : 40.00   Min.   :0.0000
##  1st Qu.:23.07   1st Qu.: 68.00   1st Qu.: 71.00   1st Qu.:0.0000
##  Median :25.40   Median : 75.00   Median : 78.00   Median :0.0000
##  Mean   :25.80   Mean   : 75.88   Mean   : 81.96   Mean   :0.1519
##  3rd Qu.:28.04   3rd Qu.: 83.00   3rd Qu.: 87.00   3rd Qu.:0.0000
##  Max.   :56.80   Max.   :143.00   Max.   :394.00   Max.   :1.0000
##  NA's   :19      NA's   :1        NA's   :388
```

```
table(fhs$TenYearCHD)
```

```
##
##    0    1
## 3596  644
```

```
table(fhs$currentSmoker)
```

```
##
##    0    1
## 2145 2095
```

```
table(fhs$cigsPerDay)
```

```
##
##    0    1    2    3    4    5    6    7    8    9   10   11   12   13   14
## 2145   67   18  100    9  121   18   12   11  130  143    5    3    3    2
##   15   16   17   18   19   20   23   25   29   30   35   38   40   43   45
##  210    3    7    8    2  734    6   55    1  218   22    1   80   56    3
##   50   60   70
##    6   11    1
```

```
dim(fhs)
```

```
## [1] 4240   16
```

Causal Roadmap

Step 0: Specify the Scientific Question

What is the effect of smoking on the ten-year development of Cardiovascular Disease? The target population is white middle-class men and women aged 30 to 62 (at baseline) in Framingham, Massachusetts. **Note: Professor Balzer's comment on our project description Google Document suggests this might be inadequate. Can we claim that our results generalize outside of Framingham? Why?**

Step 1: Specify a Causal Model

Step 2: Counterfactuals & Causal Parameter

$$\Psi^{*i}(\mathbb{P}^*) = \mathbb{E}^*[Y_i] \quad i \in \{1, ..., 14\}$$

$$\Psi_O(\mathbb{P}_O^i) = \mathbb{E}_o[\mathbb{E}_o[Y|A\text{in bin i}, \mathbb{W}]]$$

$$\Psi_n(\mathbb{P}_n^i) = \frac{1}{n}\sum_{j=1}^{n} E_n(Y|A = \text{ in bin i}, \mathbb{W})$$

Remove NA's (need something smarter later)

```
fhs <- fhs[complete.cases(fhs), ]
```

We first need to bin cigs per day

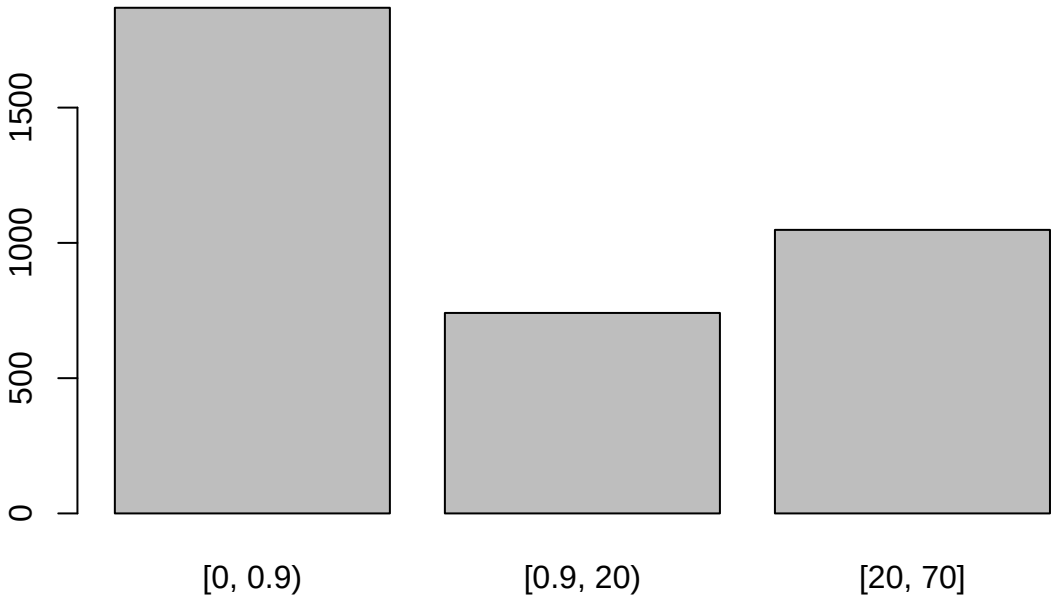
```
colnames(fhs)
```

```
##  [1] "male"            "age"             "education"
##  [4] "currentSmoker"   "cigsPerDay"      "BPMeds"
##  [7] "prevalentStroke" "prevalentHyp"    "diabetes"
## [10] "totChol"         "sysBP"           "diaBP"
## [13] "BMI"             "heartRate"       "glucose"
## [16] "TenYearCHD"
```

```
library(mltools)
```

```
## Warning: package 'mltools' was built under R version 3.4.4
```

```
## initalize empty binned dataframe
fhs_binned <- data.frame(i=1:nrow(fhs))


fhs_binned$cigsPerDay  <-bin_data(fhs$cigsPerDay,bins=c(0,.9,20,max(fhs$cigsPerDay)), binType = "explic
 plot(fhs_binned$cigsPerDay)
```




```
fhs_binned$diabetes <- fhs$diabetes
## Variables binned based on science!
fhs_binned$age  <- bin_data(fhs$age, bins=10, binType = "quantile")
fhs_binned$education  <- factor(fhs$education)
fhs_binned$sysBP  <- bin_data(fhs$sysBP, bins=c(0,120,140,max(fhs$sysBP)), binType = "explicit")
fhs_binned$diaBP  <- bin_data(fhs$diaBP, bins=c(0,80,90,max(fhs$diaBP)), binType = "explicit")
fhs_binned$totChol  <- bin_data(fhs$totChol, bins=c(0,80,90,max(fhs$totChol)), binType = "explicit")
fhs_binned$gender  <-factor(fhs$male)
fhs_binned$bmi  <- bin_data(fhs$BMI, bins=c(0,18.5,25,30,max(fhs$BMI)), binType = "explicit")
fhs_binned$glucose  <- bin_data(fhs$glucose, bins=c(0,78,max(fhs$glucose)), binType = "explicit")
fhs_binned$heartRate  <- bin_data(fhs$heartRate, bins=c(0,60,max(fhs$heartRate)), binType = "explicit")
fhs_binned$CHD <- factor(fhs$TenYearCHD)
## remove index created
fhs_binned <- subset(fhs_binned, select = -c(i))
```

Conditional Mean outcome

```
library(mgcv)
```

```
## Loading required package: nlme
```

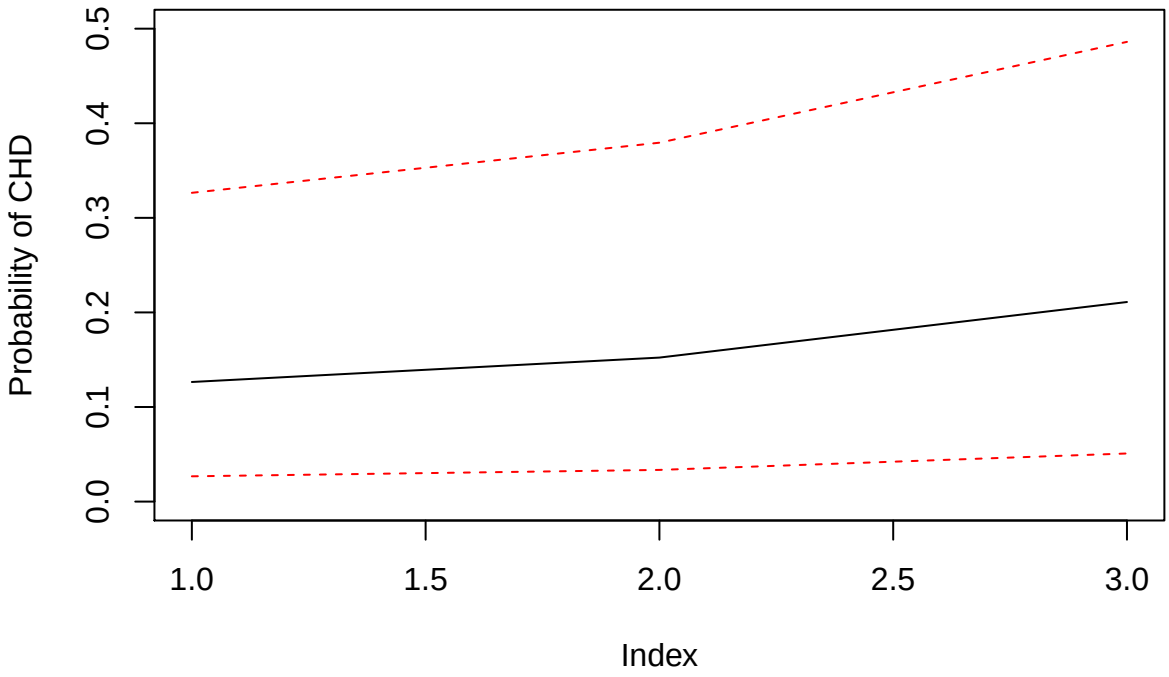
```
## This is mgcv 1.8-20. For overview type 'help("mgcv-package")'.
```

```
glm_fit <- glm( CHD ~ cigsPerDay + education + age + diabetes + bmi , data = fhs_binned, family = "bino
summary(glm_fit)
```

```
##
## Call:
## glm(formula = CHD ~ cigsPerDay + education + age + diabetes +
##     bmi, family = "binomial", data = fhs_binned)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.4081  -0.6352  -0.4508  -0.3031   2.7066
##
```

```
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)  -1.75474    0.12971 -13.528  < 2e-16 ***
## cigsPerDay.L  0.47268    0.08036   5.882 4.05e-09 ***
## cigsPerDay.Q  0.08321    0.10230   0.813 0.416017
## education2   -0.20096    0.12031  -1.670 0.094845 .
## education3   -0.24260    0.14561  -1.666 0.095693 .
## education4   -0.04079    0.16165  -0.252 0.800787
## age.L         2.28373    0.20094  11.365  < 2e-16 ***
## age.Q        -0.02872    0.18721  -0.153 0.878060
## age.C        -0.05312    0.18450  -0.288 0.773423
## age^4         0.10738    0.18026   0.596 0.551365
## age^5         0.05985    0.18796   0.318 0.750153
## age^6        -0.09165    0.17491  -0.524 0.600307
## age^7        -0.25058    0.16574  -1.512 0.130554
## age^8         0.13756    0.17141   0.803 0.422245
## age^9         0.14049    0.15857   0.886 0.375613
## diabetes      0.79005    0.22583   3.498 0.000468 ***
## bmi.L         0.21194    0.29804   0.711 0.477016
## bmi.Q         0.20046    0.22738   0.882 0.377988
## bmi.C        -0.14459    0.12156  -1.189 0.234267
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 3121.2  on 3657  degrees of freedom
## Residual deviance: 2855.0  on 3639  degrees of freedom
## AIC: 2893
##
## Number of Fisher Scoring iterations: 5
```

```r
intervene_on_bin <- function(i){
  fhs_binned_i <- fhs_binned
  fhs_binned_i$cigsPerDay <-levels(fhs_binned$cigsPerDay)[i]
  return (fhs_binned_i)
}


average_treatment_effect <- c()
average_treatment_effect_ci <- matrix(NA,nrow=length(levels(fhs_binned$cigsPerDay)),ncol=2)
for (i in 1:length(levels(fhs_binned$cigsPerDay))){
  average_treatment_effect[i] <- mean(predict(glm_fit, newdata=intervene_on_bin(i), type='response'))
  average_treatment_effect_ci[i,] <- quantile(predict(glm_fit, newdata=intervene_on_bin(i), type='respo

}

plot(average_treatment_effect,type='l',ylab="Probability of CHD",ylim=c(0,.5))
lines(average_treatment_effect_ci[,1],col='red',lty=2)
lines(average_treatment_effect_ci[,2],col='red',lty=2)
```



IPTW

```
### Create pairwise binary variables for each bin
fhs_binned$cigsPerDay_bin_1 <- ifelse(fhs_binned$cigsPerDay == "[0, 0.9)",1,0)
fhs_binned$cigsPerDay_bin_2 <- ifelse(fhs_binned$cigsPerDay == "[0.9, 20)",1,0)
fhs_binned$cigsPerDay_bin_3 <- ifelse(fhs_binned$cigsPerDay == "[20, 70]",1,0)

### BIN 2
glm_fit_iptw_bin_1 <- glm( cigsPerDay_bin_1 ~   education + age + diabetes + bmi , data = fhs_binned, fa
prob.1W <- predict(glm_fit_iptw_bin_1, type= "response")
wt_1<- 1/prob.1W
summary(wt_1)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   1.174   1.624   1.973   2.094   2.470   3.962
```

```
IPTW_bin_1<- mean( wt_1*as.numeric(fhs_binned$cigsPerDay_bin_1==1)*as.numeric(fhs_binned$CHD==1))

### BIN 2
glm_fit_iptw_bin_2 <- glm( cigsPerDay_bin_2 ~   education + age + diabetes + bmi , data = fhs_binned, fa
prob.1W <- predict(glm_fit_iptw_bin_2, type= "response")
wt_2<- 1/prob.1W
summary(wt_2)
```

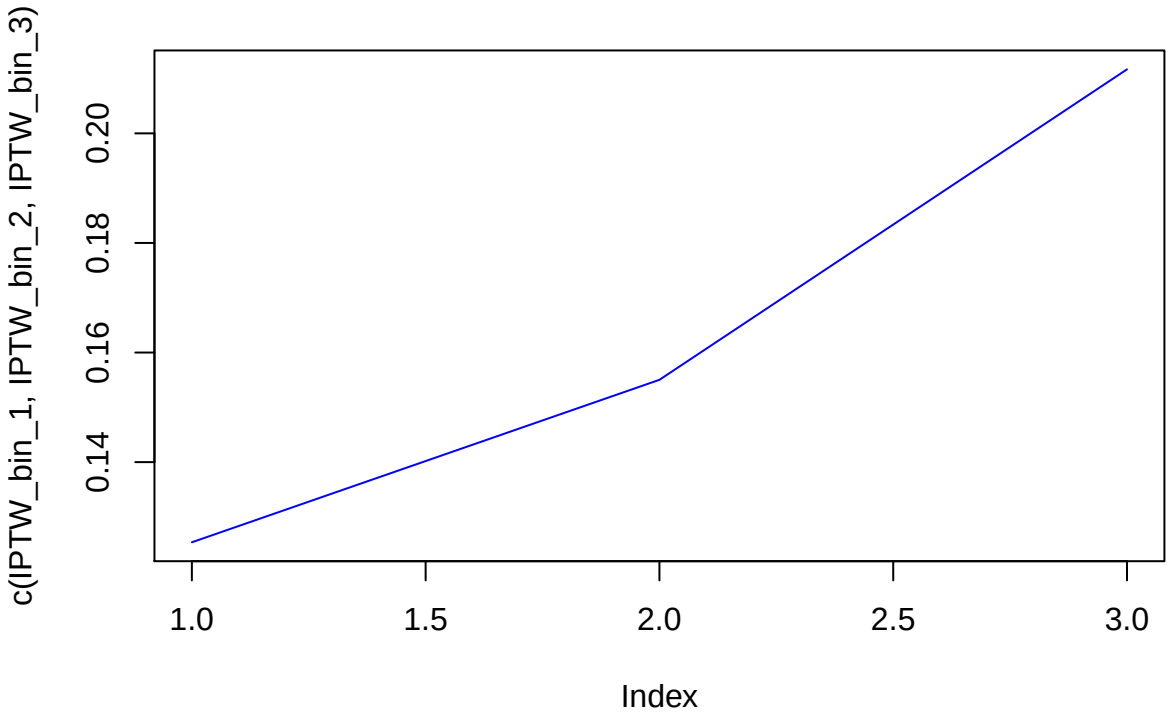
```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   2.476   3.895   5.272   5.445   6.456  12.287
```

```
IPTW_bin_2<- mean( wt_2*as.numeric(fhs_binned$cigsPerDay_bin_2==1)*as.numeric(fhs_binned$CHD==1))

### BIN 3
glm_fit_iptw_bin_3 <- glm( cigsPerDay_bin_3 ~   education + age + diabetes + bmi , data = fhs_binned, fa
prob.1W <- predict(glm_fit_iptw_bin_3, type= "response")
```

```r
wt_3<- 1/prob.1W
summary(wt_3)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   2.340   2.818   3.327   3.927   4.520  13.164
```

```r
IPTW_bin_3<- mean( wt_3*as.numeric(fhs_binned$cigsPerDay_bin_3==1)*as.numeric(fhs_binned$CHD==1))

plot(c(IPTW_bin_1,IPTW_bin_2,IPTW_bin_3),type='l',col='blue')
```



Superlearner/TMLE

Only confusing thing here is that we have to use the weights we estimated from the correct bin.

```r
library('SuperLearner')
```

```
## Warning: package 'SuperLearner' was built under R version 3.4.4
## Loading required package: nnls
## Super Learner
## Version: 2.0-24
## Package created on 2018-08-10
```

```r
SL.library<- c("SL.gam")


#### BIN 1 TMLE

X_minus_bin_1<- subset(fhs_binned, select= -CHD )

for (i in 1:ncol(X_minus_bin_1)){
```

```r
  X_minus_bin_1[,i] <- as.numeric(X_minus_bin_1[,i])
}

X_minus_bin_1_1 <- X_minus_bin_1



SL.outcome<- SuperLearner(Y=as.numeric(fhs_binned$CHD==1), X=X_minus_bin_1, SL.library=SL.library, famil
```

```
## Loading required package: gam

## Warning: package 'gam' was built under R version 3.4.4

## Loading required package: splines

## Loading required package: foreach

## Loaded gam 1.16

##
## Attaching package: 'gam'

## The following objects are masked from 'package:mgcv':
##
##     gam, gam.control, gam.fit, s

## Warning in (function (Y, X, newX, family, obsWeights, deg.gam = 2, cts.num
## = 4, : mgcv and gam packages are both in use. You might see an error
## because both packages use the same function names.

## Warning in predict.lm(object, newdata, se.fit, scale = 1, type =
## ifelse(type == : prediction from a rank-deficient fit may be misleading

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```

```
expY.givenAW <- predict(SL.outcome, newdata=X_minus_bin_1)$pred
```

```
## Warning in predict.lm(object, newdata, se.fit, scale = 1, type =
## ifelse(type == : prediction from a rank-deficient fit may be misleading
```

```
SL.exposure<- SuperLearner(Y=as.numeric(fhs_binned$CHD==1), X=subset(X_minus_bin_1, select= -c(cigsPerDa
```

```
## Warning in (function (Y, X, newX, family, obsWeights, deg.gam = 2, cts.num
## = 4, : mgcv and gam packages are both in use. You might see an error
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```

```r
probA1.givenW<- SL.exposure$SL.predict

probA0.givenW <- 1-probA1.givenW


H.AW<- as.numeric(fhs_binned$cigsPerDay_bin_1==1)/probA1.givenW# - as.numeric(fhs_binned$cigsPerDay_bin

logitUpdate<- glm(fhs_binned$CHD ~ -1 +offset(qlogis(expY.givenAW)) + H.AW, family='binomial')


epsilon<- logitUpdate$coef
expY.givenAW.star<- plogis(qlogis(expY.givenAW)+ epsilon*H.AW)


PsiHat.TMLE <- mean(expY.givenAW.star)#- expY.givenOW.star)
```