Case Study 1: National Collaborative Perinatal Project

Background

The data are taken from the National Collaborative Perinatal Project (CPP). Women were enrolled during pregnancy through different medical centers and then the kids were followed in order to collect both pregnancy and childhood development outcomes. We consider a subsample of 2380 women and children for this analysis, which was studied by [Longnecker et al., 2001]. A particular focus of the Longnecker et al substudy was in assaying serum samples from the original larger study to obtain information on exposures in order to assess the relationship between these exposures to the women and adverse pregnancy and developmental outcomes in their children. Two exposures of particular interest are Dichlorodiphenyldichloroethylene (DDE) and Polychlorinated Biphenyls (PCBs), which are breakdown products in the body of chemicals that have been historically used to treat crops to protect them from predation. These chemicals persist in the environment and are lipophilic, building up in fatty deposits in human tissues. Hence, each of us carries around our own body burden of these chemicals, potentially impacting our health.

The data

The dataset contains demographic variables, such as race, age, and socio-economic index, along with smoking status and concentration doses for DDE and PCBs. In addition, data are available on levels of cholesterol and triglycerides in serum; these variables are relevant since DDE/PCBs are stored in fat and cholesterol/triglycerides provide measurements of the levels of circulating fats (being somewhat informal) in serum.

Goal

The overarching goal of the analysis is to assess how DDE and PCBs relate to risk of premature delivery. Premature delivery is typically defined as a gestational age at delivery of 37 weeks or less, but it is important to note that deliveries occurring right at the cutoff have similar clinical outcomes to full term deliveries, while deliveries occurring substantially less than 37 weeks (early preterm) are associated with substantial risk of short and long term morbidity and mortality. Ideally we would like to infer a causal effect of these exposures on risk of premature deliveries of different severities, while investigating the dose response relationship. However, these data are not collected in a randomized trial but are the result of an observational epidemiology study. Hence, epidemiologists typically focus on assessing associations, while adjusting for covariates that may confound exposure-outcome relationships. In addressing the above interests, it is important to take into account heterogeneity across study centers.

Variable key

```
gestational_age = gestational age (in weeks)

dde = concentration of dde (ug/dL)

pcb_* = concentration of pcb_* (ng/dL)

albumin = concentration of albumin (g/dL)

cholesterol = concentration of cholesterol (g/dL)

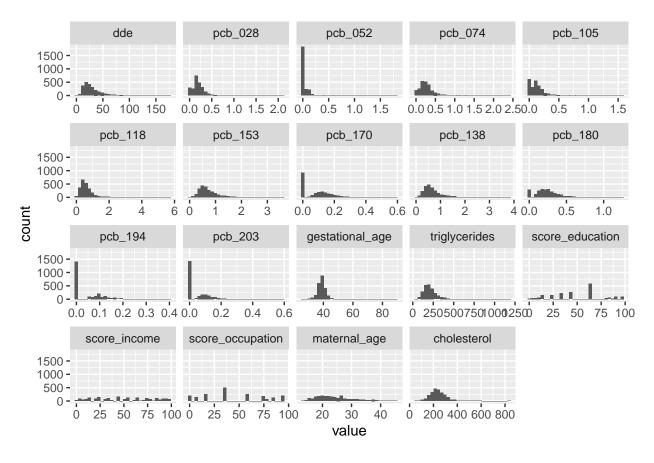
triglycerides = concentration of triglycerides (g/dL)

race

score_education

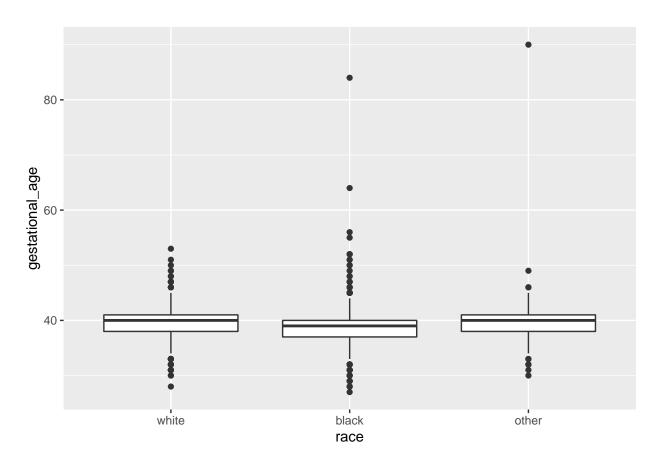
score income
```

```
score occupation
maternal\_age = age of mother
smoking\_status = mother smoking
center
# Load in data & remove data point with missing PCB information
dat <- readRDS("Longnecker.rds")</pre>
which(is.na(dat$pcb_028)==TRUE)
## [1] 1861
dat[1861,]
          dde pcb_028 pcb_052 pcb_074 pcb_105 pcb_118 pcb_153 pcb_170 pcb_138
##
                                  NA NA
## 1861 16.62 NA NA
                                                  NA NA
       pcb_180 pcb_194 pcb_203 albumin triglycerides race score_education
## 1861
           NA
                     NA
                             NA
                                     NA
                                                   145 black
        score_income score_occupation maternal_age smoking_status cholesterol
##
## 1861
                  15
                                    5
                                               14
                                                                 1
##
       gestational_age center
## 1861
                     42
dat <- dat[-1861,]</pre>
dat$race <- as.factor(dat$race)</pre>
dat$smoking_status <- as.factor(dat$smoking_status)</pre>
dat$center <- as.factor(dat$center)</pre>
attach(dat)
# Histograms
library(reshape2)
library(ggplot2)
d \leftarrow melt(dat[,c(1:12,22,14,16,17,18,19,21)])
## No id variables; using all as measure variables
ggplot(d,aes(x = value)) +
   facet_wrap(~variable,scales = "free_x") +
   geom_histogram()
## `stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
## Warning: Removed 1475 rows containing non-finite values (stat bin).
```

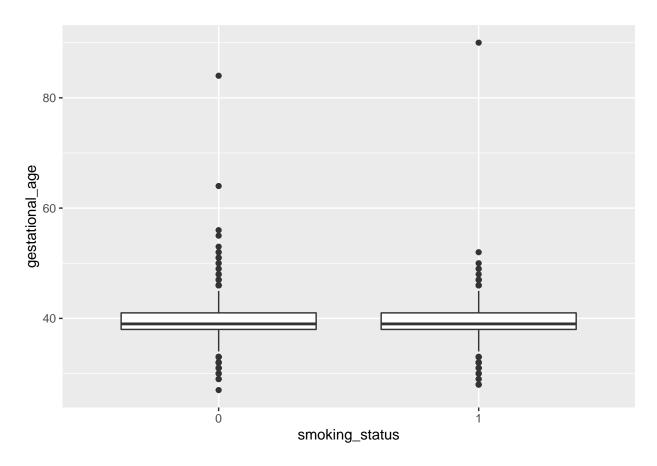


```
# # Log-transformation
# library(dplyr)
# log_d <- d
# log_d <- mutate(log_d,value = log(value))
# ggplot(log_d,aes(x = value)) +
# facet_wrap(~variable,scales = "free_x") +
# geom_histogram()

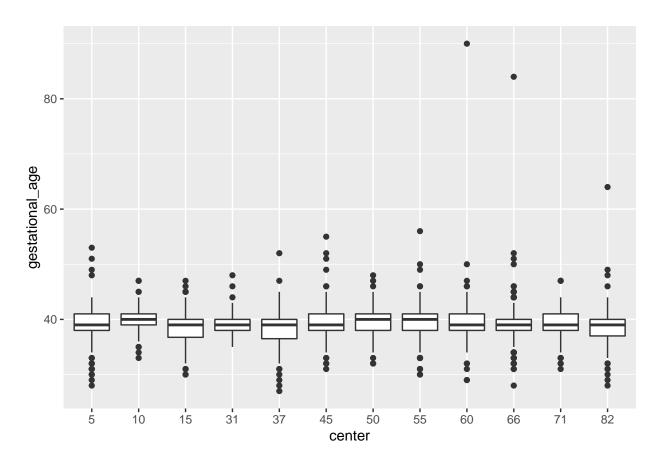
# Boxplots
ggplot(dat, aes(group=race, x=race, y=gestational_age)) +
geom_boxplot()</pre>
```



ggplot(dat, aes(group=smoking_status, x=smoking_status, y=gestational_age)) +
 geom_boxplot()

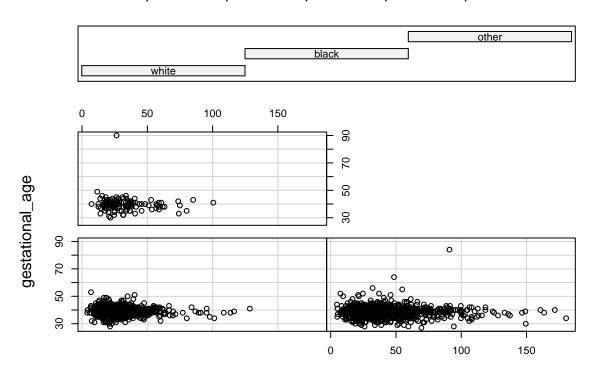


```
ggplot(dat, aes(group=center, x=center, y=gestational_age)) +
  geom_boxplot()
```



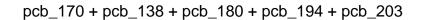
```
# Conditioning Plots
library(graphics)
coplot(gestational_age ~ dde + pcb_028 + pcb_052 + pcb_074 + pcb_105 + pcb_118 + pcb_153 + pcb_170 + pc
```

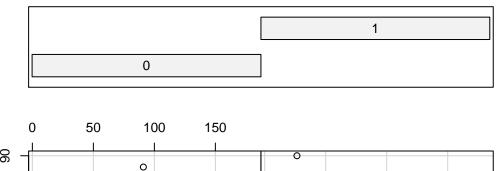
pcb_170 + pcb_138 + pcb_180 + pcb_194 + pcb_203

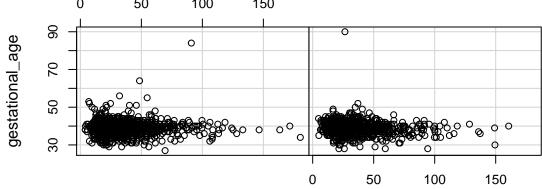


dde + pcb_028 + pcb_052 + pcb_074 + pcb_105 + pcb_118 + pcb_153 +

coplot(gestational_age ~ dde + pcb_028 + pcb_052 + pcb_074 + pcb_105 + pcb_118 + pcb_153 + pcb_170 + pc



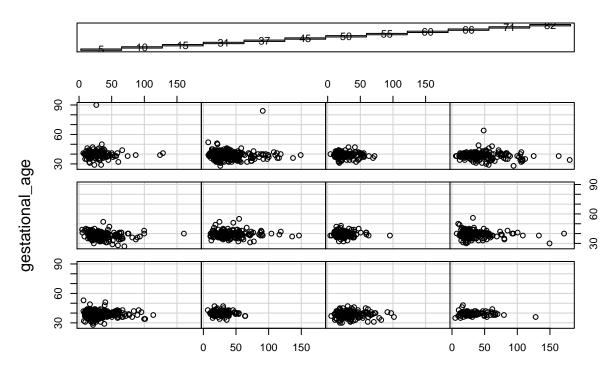




dde + pcb_028 + pcb_052 + pcb_074 + pcb_105 + pcb_118 + pcb_153 +

coplot(gestational_age ~ dde + pcb_028 + pcb_052 + pcb_074 + pcb_105 + pcb_118 + pcb_153 + pcb_170 + pc

pcb_170 + pcb_138 + pcb_180 + pcb_194 + pcb_203

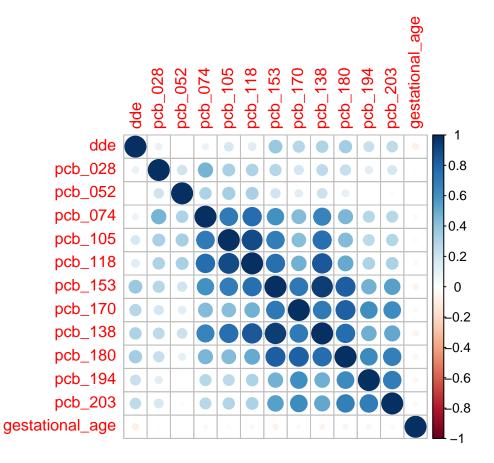


dde + pcb_028 + pcb_052 + pcb_074 + pcb_105 + pcb_118 + pcb_153 +

Correlation Plot
library(corrplot)

corrplot 0.84 loaded

corrplot(cor(dat[c(1:12,22)]))



Summary Statistics summary(dat)

| ## | dde | pcb_028 | pcb_052 | pcb_074 |
|----|----------------|----------------|-----------------|-----------------|
| ## | Min. : 2.50 | Min. :0.000 | Min. :0.00000 | Min. :0.0000 |
| ## | 1st Qu.: 17.10 | 1st Qu.:0.110 | 1st Qu.:0.00000 | 1st Qu.:0.1500 |
| ## | Median : 24.70 | Median :0.180 | Median :0.00000 | Median :0.2400 |
| ## | Mean : 30.19 | Mean :0.195 | Mean :0.03053 | Mean :0.2692 |
| ## | 3rd Qu.: 36.51 | 3rd Qu.:0.260 | 3rd Qu.:0.00000 | 3rd Qu.:0.3300 |
| ## | Max. :178.06 | Max. :2.100 | Max. :1.80000 | Max. :2.4000 |
| ## | | | | |
| ## | pcb_105 | pcb_118 | pcb_153 | pcb_170 |
| ## | Min. :0.00 | Min. :0.0000 | Min. :0.0000 | Min. :0.00000 |
| ## | 1st Qu.:0.00 | 1st Qu.:0.3500 | 1st Qu.:0.4500 | 1st Qu.:0.00000 |
| ## | Median :0.11 | Median :0.5400 | Median :0.6300 | Median :0.09000 |
| ## | Mean :0.13 | Mean :0.6575 | Mean :0.7255 | Mean :0.09591 |
| ## | 3rd Qu.:0.17 | 3rd Qu.:0.7900 | 3rd Qu.:0.8900 | 3rd Qu.:0.15000 |
| ## | Max. :1.57 | Max. :5.6900 | Max. :3.5900 | Max. :0.59000 |
| ## | | | | |
| ## | pcb_138 | pcb_180 | pcb_194 | pcb_203 |
| ## | Min. :0.0000 | Min. :0.0000 | Min. :0.00000 |) Min. :0.00000 |
| ## | 1st Qu.:0.4100 | 1st Qu.:0.1400 | 1st Qu.:0.00000 | 1st Qu.:0.00000 |
| ## | Median :0.5800 | Median :0.2200 | Median :0.00000 | Median :0.00000 |
| ## | Mean :0.6736 | Mean :0.2468 | Mean :0.04665 | Mean :0.04868 |
| ## | 3rd Qu.:0.8300 | 3rd Qu.:0.3300 | 3rd Qu.:0.09000 | 3rd Qu.:0.10000 |
| ## | Max. :3.8000 | Max. :1.2500 | Max. :0.40000 | Max. :0.59000 |

```
##
##
      albumin
                   triglycerides
                                               score_education score_income
                                     race
                   Min. : 51
                                                    : 0.00
##
  Min.
          :2.600
                                  white:1032
                                               Min.
                                                              Min. : 0.00
   1st Qu.:3.200
                   1st Qu.: 154
                                               1st Qu.:22.00
                                  black:1223
                                                              1st Qu.:22.00
## Median :3.500
                   Median: 195
                                  other: 124
                                               Median :43.00
                                                              Median :52.00
## Mean
          :3.522
                   Mean
                         : 209
                                               Mean
                                                      :48.96
                                                              Mean
                                                                     :49.62
## 3rd Qu.:3.700
                   3rd Qu.: 247
                                               3rd Qu.:64.00
                                                              3rd Qu.:75.00
                                                              Max.
## Max.
                   Max.
                                               Max.
                                                      :97.00
          :5.300
                          :1189
                                                                     :98.00
## NA's
           :2212
                                               NA's
                                                      :481
                                                              NA's
                                                                     :515
## score_occupation maternal_age
                                    smoking_status cholesterol
## Min. : 0.00
                    Min.
                           :13.00
                                    0:1327
                                                  Min.
                                                         : 55.0
## 1st Qu.:15.00
                                                   1st Qu.:195.0
                    1st Qu.:20.00
                                    1:1052
## Median :35.00
                    Median :23.00
                                                   Median :232.0
## Mean
          :44.44
                    Mean
                          :24.24
                                                   Mean
                                                         :237.5
## 3rd Qu.:73.00
                    3rd Qu.:28.00
                                                   3rd Qu.:274.0
## Max.
          :94.00
                    Max.
                           :45.00
                                                   Max.
                                                         :835.0
## NA's
          :479
## gestational_age
                       center
## Min.
          :27.00
                   5
                          :485
## 1st Qu.:38.00
                   66
                          :395
## Median :39.00
                   37
                          :207
## Mean
          :39.11
                   82
                          :192
## 3rd Qu.:41.00
                          :162
                   45
## Max. :90.00
                   15
                          :156
##
                   (Other):782
```

Binary outcomes

```
dat0 <- dat
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
# Indicator for preterm
dat <- dat %>%
       mutate(ind_gest37 = if_else(gestational_age<37,1,0))</pre>
# Combine all pcb columns
pcb_col <- grep("pcb", names(dat))</pre>
dat <- dat %>%
 mutate(pcb_total = apply(dat[,pcb_col], 1, sum))
library(mice)
```

```
## Loading required package: lattice
##
## Attaching package: 'mice'
   The following objects are masked from 'package:base':
##
##
       cbind, rbind
apply(is.na(dat), 2, sum)
##
                dde
                              pcb_028
                                                pcb_052
                                                                  pcb_074
##
                  0
                                                      0
                                                                        0
                                    0
##
            pcb_105
                              pcb_118
                                                pcb_153
                                                                  pcb_170
##
                  0
                                    0
                                                      0
                                                                        0
##
            pcb_138
                              pcb_180
                                                pcb_194
                                                                  pcb_203
##
                  0
                                    0
                                                      0
                                                                        0
                                                         score_education
##
            albumin
                        triglycerides
                                                   race
##
               2212
                                                      0
                                                                      481
                                    0
##
       score_income score_occupation
                                           maternal_age
                                                           smoking_status
##
                515
                                  479
                                                      0
                                                                        0
##
        cholesterol
                      gestational age
                                                 center
                                                               ind gest37
##
                  0
                                                      0
                                                                        0
##
          pcb_total
##
# remove albumin; impute score_education, score_income, score_occupation
dat_mice \leftarrow mice(dat[,-13], m=5, seed = 12345)
##
##
    iter imp variable
##
                              score_income
                                             score_occupation
           score_education
##
     1
            score_education
                              score_income
                                             score_occupation
##
     1
            score education
                              score income
                                             score occupation
##
         4
            score education
                              score income
     1
                                             score_occupation
##
     1
           score_education score_income
                                             score_occupation
##
     2
            score_education
                              score_income
                                             score_occupation
##
     2
         2
            score_education
                              score_income
                                             score_occupation
##
     2
           score_education
                              score_income
                                             score_occupation
##
     2
         4 score_education
                              score_income
                                             score_occupation
     2
##
         5 score_education
                              score_income
                                             score_occupation
##
     3
         1 score_education
                              score_income
                                             score_occupation
##
         2 score_education
     3
                              score_income
                                             score_occupation
##
     3
         3 score_education
                              score_income
                                             score_occupation
##
     3
            score_education
                              score_income
                                             score_occupation
     3
##
         5
           score_education
                              score_income
                                             score_occupation
##
           score education
                              score income
                                             score_occupation
```

score_occupation

score_occupation

score_occupation

score_occupation

score_occupation

score_income

score_income

score_income

score_income

##

##

##

##

##

4

4

4

5

3

2 score_education

4 score_education

5 score_education

score education

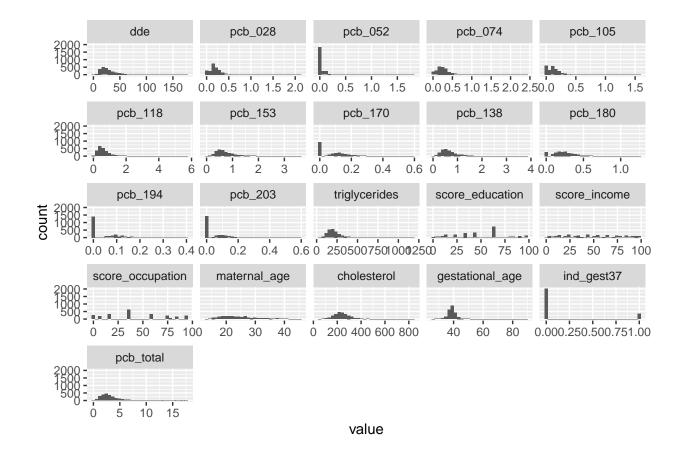
1 score_education score_income

```
##
        2 score_education score_income score_occupation
##
     5
        3 score_education score_income score_occupation
            score_education score_income score_occupation
##
##
     5
            score_education score_income score_occupation
## Warning: Number of logged events: 75
# complete(dat_mice)
# Further EDA
d <- melt(complete(dat_mice))</pre>
## Using race, smoking_status, center as id variables
ggplot(d,aes(x = value)) +
```

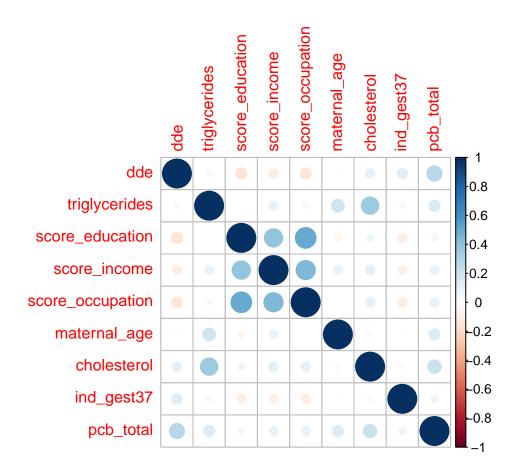
`stat_bin()` using `bins = 30`. Pick better value with `binwidth`.

facet_wrap(~variable,scales = "free_x") +

geom_histogram()



corrplot(cor(complete(dat_mice)[,c(1,13,15:18,20,23:24)]))

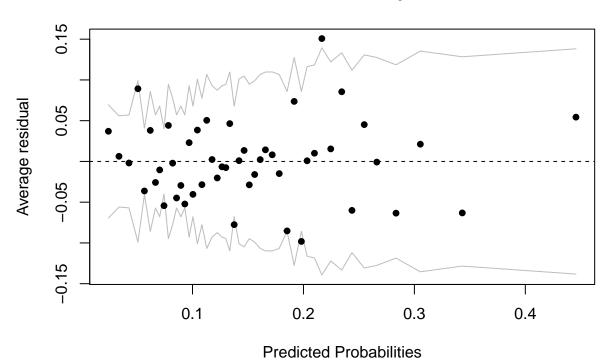


```
##
                        estimate
                                    std.error
                                                statistic
                                                                  df
                                                                           p.value
                    -2.239755968 0.4719387884 -4.74586116 2041.99229 2.220193e-06
## (Intercept)
## dde
                     0.007490606 0.0031118572 2.40711755 2336.58369 1.615610e-02
## pcb_028
                    -0.126581351 0.4815729206 -0.26284981 2340.35005 7.926895e-01
## pcb_052
                     0.509018177 0.7168979168 0.71002881 2340.34526 4.777570e-01
## pcb 074
                     0.734812378 0.4517821521 1.62647501 2343.62843 1.039831e-01
## pcb_105
                     0.021300182 1.0334150247 0.02061145 2342.86078 9.835574e-01
                    -0.343204070 0.4026407153 -0.85238292 2341.97938 3.940888e-01
## pcb 118
## pcb_153
                     0.465705447 0.5357793240 0.86921131 2324.34315 3.848213e-01
## pcb_170
                    -1.822419279 1.1089067905 -1.64343775 2331.46417 1.004272e-01
                     0.305790751 0.6642411201 0.46036107 2339.87581 6.452999e-01
## pcb_138
## pcb_180
                     0.237309610 0.8250023824 0.28764718 2334.22582 7.736424e-01
                     0.066119962 1.4551041269 0.04544002 2342.67402 9.637605e-01
## pcb_194
## pcb_203
                     0.789333584\ 1.3405109137\ 0.58883040\ 2335.93487\ 5.560320e-01
```

```
0.003129335 0.0007868986 3.97679636 2343.70817 7.196654e-05
## triglycerides
## raceblack
                     0.188839631 0.2167796416 0.87111331 2312.28039 3.837827e-01
## raceother
                     0.435603732 0.3544212907 1.22905633 2333.34254 2.191746e-01
## score_education -0.003027195 0.0028224103 -1.07255682 686.84343 2.838467e-01
## score income
                   -0.002161175 0.0029252033 -0.73881189
                                                           42.67258 4.640657e-01
## score occupation -0.002507316 0.0025958860 -0.96588069 351.43334 3.347681e-01
                 -0.013940566 0.0104642108 -1.33221379 2262.37222 1.829241e-01
## maternal age
## smoking status1 0.119949638 0.1253733922 0.95673919 2334.18475 3.387980e-01
## cholesterol
                   -0.002486336 0.0010208094 -2.43565141 2335.71180 1.493933e-02
## center10
                   -0.977967583 0.4938667403 -1.98022564 2343.48096 4.779497e-02
## center15
                     0.759236804 0.3370392947 2.25266554 1575.14139 2.441740e-02
## center31
                   -0.592244818 0.4912285156 -1.20564014 2340.46336 2.280781e-01
## center37
                    0.766897505 0.2828718986 2.71111238 2306.87144 6.755490e-03
                     0.085130009 0.3313721578 0.25690151 1978.93291 7.972815e-01
## center45
## center50
                   -0.041690474 0.3515749119 -0.11858205 2338.40269 9.056167e-01
## center55
                     0.313319819 0.3631964624 0.86267310 2229.59634 3.884100e-01
                     0.321783030 0.3232783089 0.99537464 2277.37226 3.196598e-01
## center60
## center66
                     0.202801829 0.2785524753 0.72805610 2248.59049 4.666551e-01
## center71
                    -0.085236955 0.3198593331 -0.26648262 2278.40847 7.898917e-01
                     0.549194229 0.3278861155 1.67495421 2101.88244 9.409197e-02
## center82
fit2 <- glm(full_formula_ind, data = complete(dat_mice),</pre>
            family = "binomial"(link="logit"))
dat2 <- complete(dat mice) %>%
        mutate(Residuals = residuals.glm(fit2,type="response"),
        Predicted = predict.glm(fit2,type="response"))
library(arm)
## Loading required package: MASS
##
## Attaching package: 'MASS'
## The following object is masked from 'package:dplyr':
##
##
       select
## Loading required package: Matrix
## Loading required package: lme4
##
## arm (Version 1.10-1, built: 2018-4-12)
## Working directory is /Users/yiji/Desktop/Duke Statistics PhD/2020 Spring Courses/STA 723 Case Studie
##
## Attaching package: 'arm'
## The following object is masked from 'package:corrplot':
##
##
       corrplot
```

summary(fit1.1_pool)

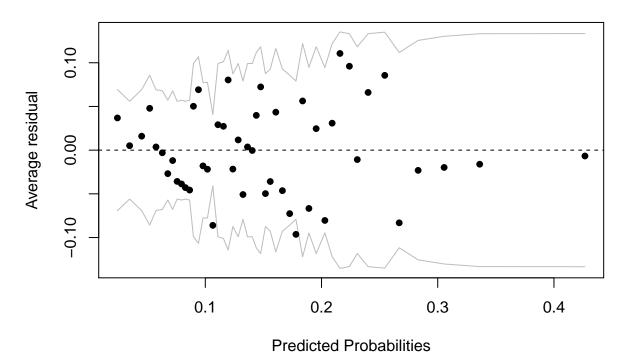
Binned residual plot



fit1.1 <- with(data = dat_mice, exp = glm(ind_gest37 ~ dde + pcb_total +
 triglycerides + race + score_education + score_income + score_occupation +
 maternal_age + smoking_status + cholesterol + center,
 family = "binomial"(link="logit")))
fit1.1_pool <- pool(fit1.1)</pre>

```
##
                        estimate
                                    std.error statistic
                                                                 df
                                                                         p.value
## (Intercept)
                    -2.233661833 0.4527310518 -4.9337500 2133.61921 8.690376e-07
## dde
                     0.008354011 0.0029340745 2.8472390 2341.32573 4.448463e-03
## pcb_total
                     0.107182020 0.0355175685 3.0177184 2348.15276 2.574220e-03
## triglycerides
                     0.003025333 0.0007760362 3.8984432 2353.75329 9.952008e-05
## raceblack
                     0.217699769 0.2117999856 1.0278554 2313.93649 3.041253e-01
## raceother
                     0.426033532 0.3525113865 1.2085667 2337.34617 2.269516e-01
## score_education
                   -0.003149136 0.0027970767 -1.1258669
                                                          764.76955 2.605750e-01
## score_income
                    -0.001964270 0.0028766801 -0.6828252
                                                           47.04292 4.980663e-01
## score_occupation -0.002566643 0.0025893157 -0.9912439
                                                         340.48404 3.222704e-01
                    -0.012675984 0.0100795515 -1.2575941 2241.50900 2.086696e-01
## maternal_age
## smoking_status1
                     0.156446431 0.1221493965 1.2807794 2341.29517 2.003980e-01
## cholesterol
                    -0.002449080 0.0010053749 -2.4359865 2343.96670 1.492527e-02
## center10
                    -0.942703324 0.4884588607 -1.9299544 2353.54627 5.373253e-02
                     0.812261072 0.3293132278 2.4665304 1742.92197 1.373851e-02
## center15
```

```
## center31
                    0.772226679 0.2658955417 2.9042483 2317.35271 3.716204e-03
## center37
## center45
                   0.113280953 0.3175432039 0.3567419 2054.29550 7.213217e-01
## center50
                   0.058826292 0.3387395831 0.1736623 2352.37884 8.621458e-01
                    0.365345112 0.3554367403 1.0278766 2246.13615 3.041185e-01
## center55
## center60
                   0.384293296 0.3160174231 1.2160510 2305.48688 2.240900e-01
## center66
                    0.229983177 0.2694263627 0.8536031 2271.21659 3.934150e-01
                  -0.045225559 0.3103564697 -0.1457213 2297.77329 8.841542e-01
## center71
## center82
                    0.518379911 0.3212681282 1.6135429 2119.22052 1.067755e-01
fit2.1 <- glm(ind_gest37 ~ dde + pcb_total +
   triglycerides + race + score_education + score_income + score_occupation +
   maternal_age + smoking_status + cholesterol + center, data = complete(dat_mice),
           family = "binomial"(link="logit"))
dat2.1 <- complete(dat_mice) %>%
       mutate(Residuals = residuals.glm(fit2.1,type="response"),
        Predicted = predict.glm(fit2.1,type="response"))
library(arm)
binnedplot(x=dat2.1$Predicted,y=dat2.1$Residuals,
          xlab="Predicted Probabilities")
```



Multi-level outcomes

```
dat0 <- dat
library(dplyr)
# Indicator for preterm
dat <- dat %>%
       mutate(preterm_ind = if_else(gestational_age<33,2,</pre>
                                      if_else(gestational_age<37 &</pre>
                                                 gestational_age>32,1,0)))
# Combine all pcb columns
pcb_col <- grep("pcb", names(dat))</pre>
dat <- dat %>%
  mutate(pcb_total = apply(dat[,pcb_col], 1, sum))
library(mice)
apply(is.na(dat), 2, sum)
##
                 dde
                              pcb_028
                                                 pcb_052
                                                                   pcb_074
##
                   0
                                     0
                                                       0
##
            pcb_105
                                                 pcb_153
                                                                   pcb_170
                               pcb_118
##
                   0
##
            pcb_138
                              pcb_180
                                                                   pcb_203
                                                 pcb_194
##
                                                       0
##
             albumin
                        triglycerides
                                                    race
                                                          score education
##
                2212
                                                       0
##
       score_income score_occupation
                                           maternal_age
                                                           smoking_status
##
                 515
                                                       0
##
        cholesterol
                      gestational_age
                                                                ind gest37
                                                  center
##
                                                       0
                   0
##
          pcb_total
                          preterm_ind
##
# remove albumin; impute score_education, score_income, score_occupation
dat_mice \leftarrow mice(dat[,-13], m=5, seed = 12345)
##
##
    iter imp variable
##
         1 score_education score_income
                                             score_occupation
##
            score education
                              score_income
                                             score occupation
##
         3 score_education score_income
     1
                                             score_occupation
##
         4 score_education
                              score_income
                                             score_occupation
```

```
##
        5 score education
                            score_income
                                           score_occupation
     1
     2
##
        1 score education
                            score income
                                           score occupation
##
     2
        2 score_education
                            score_income
                                           score_occupation
##
     2
        3 score_education
                            score_income
                                           score_occupation
     2
##
        4 score_education
                            score_income
                                           score_occupation
##
     2
        5 score_education
                            score_income
                                           score_occupation
##
     3
        1 score_education
                            score_income
                                           score_occupation
        2 score_education
##
     3
                            score_income
                                           score_occupation
        3 score_education
##
     3
                            score_income
                                           score_occupation
##
     3
        4 score_education
                            score_income
                                           score_occupation
##
     3
        5 score_education
                            score_income
                                           score_occupation
##
        1 score_education score_income
                                           score_occupation
```

```
##
     4
        2 score_education score_income
                                          score_occupation
##
     4
        3 score_education score_income
                                          score_occupation
##
        4 score_education score_income
                                          score_occupation
##
        5 score_education score_income
                                          score_occupation
##
     5
           score_education
                            score_income
                                          score_occupation
     5
        2 score_education score_income
                                          score_occupation
##
     5
           score_education
                            score income
                                          score_occupation
##
##
     5
           score_education
                            score_income
                                           score_occupation
##
     5
            score_education
                            score_income
                                          score_occupation
```

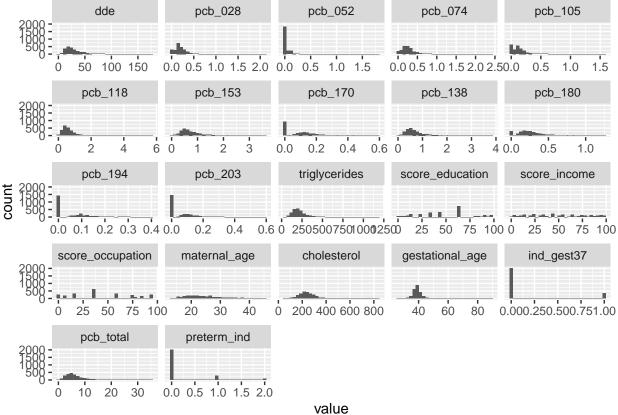
Warning: Number of logged events: 75

```
imp_dat <- complete(dat_mice)</pre>
# Further EDA
d <- melt(imp_dat)</pre>
```

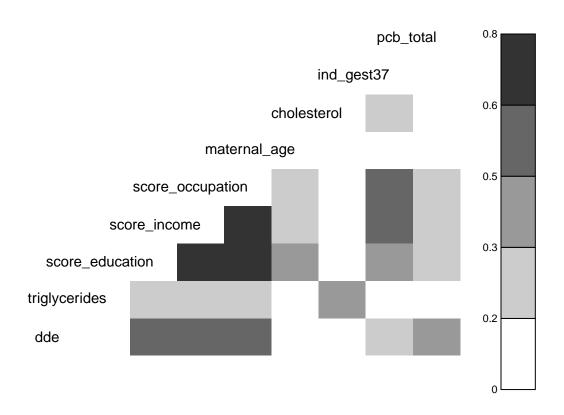
Using race, smoking_status, center as id variables

```
ggplot(d,aes(x = value)) +
    facet_wrap(~variable,scales = "free_x") +
    geom_histogram()
```

`stat_bin()` using `bins = 30`. Pick better value with `binwidth`.



```
corrplot(cor(imp_dat[,c(1,13,15:18,20,23:24)]))
```

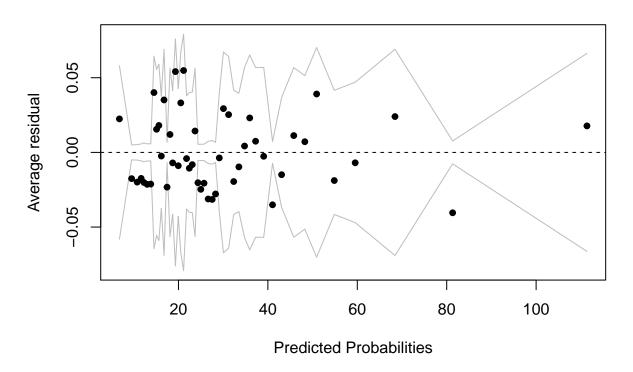


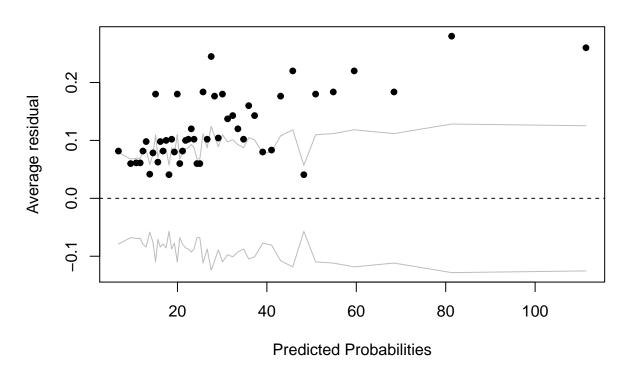
```
pcb_col <- grep("pcb", names(dat0))</pre>
pcb_colnames <- paste(colnames(dat0)[pcb_col], collapse = "+",sep = "")</pre>
confound_colnames <- paste(colnames(dat0[c(14:21,23)]),collapse = "+", sep = "")</pre>
full_formula_ind <- as.formula(paste("preterm_ind~dde+",pcb_colnames, "+", confound_colnames, seq = "")</pre>
library(nnet)
library(broom)
fit1 <- multinom(full_formula_ind, data = imp_dat)</pre>
## # weights: 105 (68 variable)
## initial value 2613.598635
## iter 10 value 1646.456174
## iter 20 value 1440.142645
## iter 30 value 1196.975770
## iter 40 value 1107.114988
## iter 50 value 1105.848056
## iter 60 value 1105.834184
## final value 1105.833634
## converged
```

20

tidy(fit1,exponentiate=FALSE) #display log-odds model

```
## # A tibble: 68 x 6
     y.level term
                                                       p.value
##
                        estimate std.error statistic
     <chr> <chr>
                           <dbl> <dbl>
                                                          <dbl>
##
                                             <dbl>
## 1 1
             (Intercept) -2.69
                                  0.508
                                             -5.29 0.000000121
                         0.00832 0.00329
                                                   0.0115
## 2 1
             dde
                                             2.53
                        -0.354
                                            -0.658 0.510
## 3 1
             pcb_028
                                  0.538
             pcb_052
## 4 1
                        0.428
                                  0.734
                                             0.583 0.560
## 5 1
                        0.596
                                  0.513
                                                    0.246
             pcb_074
                                             1.16
## 6 1
             pcb_105
                         0.683
                                   1.06
                                             0.645 0.519
## 7 1
                        -0.645
                                   0.514
                                             -1.25
                                                     0.210
             pcb_118
## 8 1
             pcb_153
                         0.539
                                   0.603
                                             0.893 0.372
## 9 1
                         -1.66
                                   1.16
                                             -1.43
                                                    0.154
             pcb_170
## 10 1
             pcb_138
                         0.0238
                                   0.734
                                             0.0324 0.974
## # ... with 58 more rows
# calculate predicted probabilities
pred.probs <- predict(fit1,type="probs")</pre>
# calculate residuals for category j
very_preterm <- if_else(imp_dat$preterm_ind==2,1,0)</pre>
residual_very_preterm <- very_preterm - pred.probs[,3]</pre>
preterm <- if_else(imp_dat$preterm_ind==1,1,0)</pre>
residual_preterm <- preterm - pred.probs[,2]</pre>
library(arm)
binnedplot(x=imp_dat$dde,y=residual_very_preterm,
          xlab="Predicted Probabilities")
```





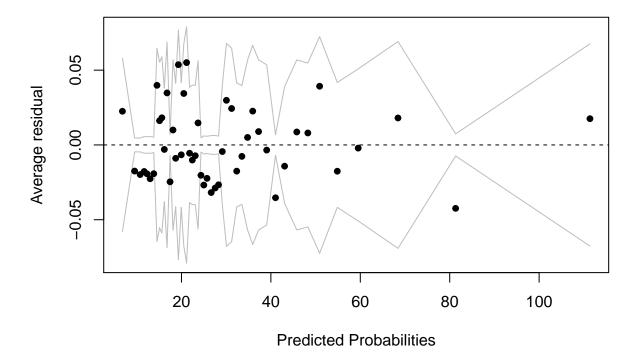
fit2 <- multinom(preterm_ind ~ dde + pcb_total + triglycerides + race + score_education + score_income
center, data = imp_dat)</pre>

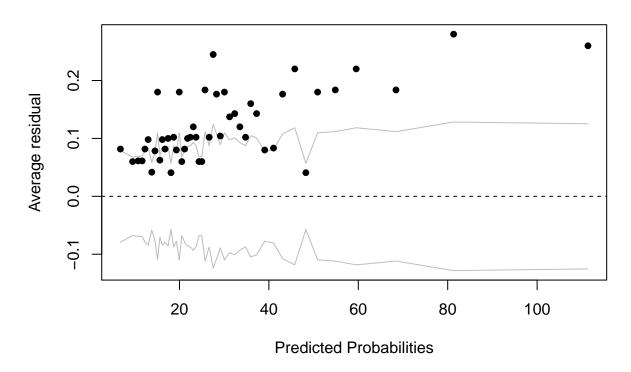
```
## # weights: 72 (46 variable)
## initial value 2613.598635
## iter 10 value 1646.474774
## iter 20 value 1425.439049
## iter 30 value 1184.777094
## iter 40 value 1112.982399
## iter 50 value 1112.343109
## final value 1112.342927
## converged
```

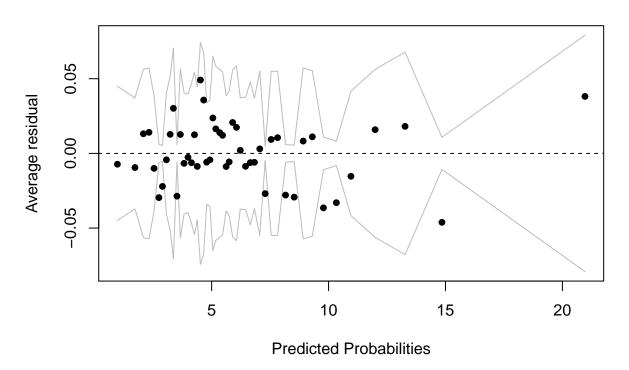
tidy(fit2,exponentiate=FALSE) #display log-odds model

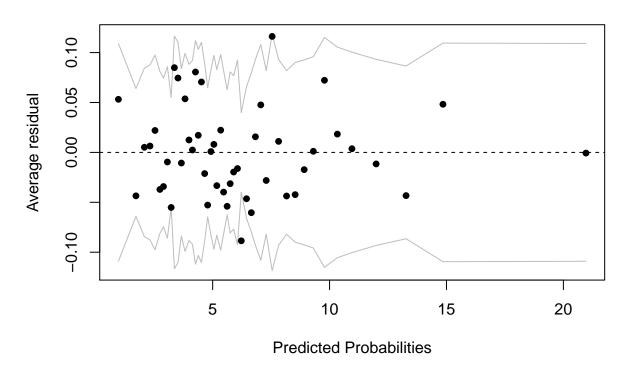
```
## # A tibble: 46 x 6
##
      y.level term
                                estimate std.error statistic
                                                                   p.value
      <chr>
                                             <dbl>
                                                                     <dbl>
##
              <chr>
                                   <dbl>
                                                        <dbl>
   1 1
              (Intercept)
                                -2.71
                                          0.492
                                                       -5.52 0.0000000343
                                 0.00955 0.00312
##
    2 1
              dde
                                                        3.07 0.00217
    3 1
              pcb_total
                                 0.0454
                                          0.0195
                                                        2.32 0.0201
    4 1
              triglycerides
                                 0.00311 0.000827
                                                        3.76 0.000170
##
    5 1
              raceblack
                                 0.0522
                                          0.229
                                                        0.228 0.819
##
## 6 1
              raceother
                                 0.144
                                          0.386
                                                       0.374 0.708
```

```
score_education -0.00379 0.00295
                                                       -1.28 0.199
                                 0.00237 0.00261
                                                        0.909 0.363
              score_income
              score_occupation -0.00290 0.00268
  9 1
                                                       -1.08 0.280
## 10 1
              maternal_age
                                -0.0140
                                           0.0110
                                                       -1.27 0.203
## # ... with 36 more rows
# calculate predicted probabilities
pred.probs <- predict(fit2,type="probs")</pre>
# calculate residuals for category j
very_preterm <- if_else(imp_dat$preterm_ind==2,1,0)</pre>
residual_very_preterm <- very_preterm - pred.probs[,3]</pre>
preterm <- if_else(imp_dat$preterm_ind==1,1,0)</pre>
residual_preterm <- preterm - pred.probs[,2]</pre>
library(arm)
binnedplot(x=imp_dat$dde,y=residual_very_preterm,
           xlab="Predicted Probabilities")
```









```
anova(fit1, fit2, test="Chisq")
```

```
## Likelihood ratio tests of Multinomial Models
## Response: preterm_ind
##
## 1
## 2 dde + pcb_028 + pcb_052 + pcb_074 + pcb_105 + pcb_118 + pcb_153 + pcb_170 + pcb_138 + pcb_180 + pcb
                                      Resid. df Resid. Dev
                                                                                                                                                                                                                    Test
                                                                                                                                                                                                                                                                                    Df LR stat.
                                                                                                                                                                                                                                                                                                                                                                                                Pr(Chi)
## 1
                                                                             4712
                                                                                                                                   2224.686
                                                                             4692
                                                                                                                                   2211.667 1 vs 2
                                                                                                                                                                                                                                                                                    20 13.01859 0.8765852
## 2
```

try ordinal logistic regression? (polr)

```
# # Extract PCB columns & Create full formula
# pcb_col <- grep("pcb", names(dat))
# pcb_colnames <- paste(colnames(dat)[pcb_col], collapse = "+", sep = "")
# confound_colnames <- paste(colnames(dat[c(14:21,23)]),collapse = "+", sep = "")
# full_formula <- as.formula(paste("gestational_age~dde+",pcb_colnames, "+", confound_colnames, seq = "
# # Remove pcb138 (collinearity)
# pcb_colnames_no138 <- gsub("\\+pcb_138", "", pcb_colnames)
# full_formula_no138 <- as.formula(paste("gestational_age~dde+",pcb_colnames_no138, "+", confound_colna</pre>
```