BIOS6643. L14 Review exercises

Question 1. Models for Beta Carotene Data

Using the Beta carotene dataset, answer the following questions using a mixed model with no random effects but an unstructure covariance R.

a. Estimate the mean response (beta carotene level) at all weeks in Roche (group2) and BASF 30mg (group 3).

b. Test for an interaction between Roche (group2) and BASF 30mg (group 3).

c. Test the hypothesis that the 4 groups differ at 6 weeks

```
## import data beta
beta <- read.csv("/Users/juarezce/Documents/OneDrive - The University of Colorado Denver/BIOS6643/BIOS6
                 header=TRUE)
head(beta,3)
```

```
##   Prepar Id   y time
## 1      1 71 116    0
## 2      1 71 174    6
## 3      1 71 178    8
```

```
names(beta) <- c("prepar", "id", "y", "time")
#  mutate(time = as.integer(time))

mod1 <- gls(y ~ 1 + factor(time) * factor(prepar),
            ## UN for correlation! not covariance
            correlation = corSymm(form = ~1|id),
            ## for unequal variance over time
            weights = varIdent(form = ~1|time),
            method = "REML",
            data = beta)
```

a. Estimate the mean response (beta carotene level) at all weeks in group 2 and in group 3.

```
## fixed effects
# beta_hat <- fixed.effects(mod1)
beta_hat <- coef(mod1)
## fixed effects variance-covariance
covb <- vcov(mod1)

## mean group 2
mu2 <- matrix(NA, 5, 2)
## mean  group 3
mu3 <- matrix(NA, 5, 2)

##              int   time           prepar    prepar=2*ti    prepar=3*ti     prepar=4*ti
c21  <-     c( 1,   0, 0, 0, 0,   1, 0, 0,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c22  <-     c( 1,   1, 0, 0, 0,   1, 0, 0,    1, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
```

```
c23  <-     c( 1,   0, 1, 0, 0,   1, 0, 0,    0, 1, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c24  <-     c( 1,   0, 0, 1, 0,   1, 0, 0,    0, 0, 1, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c25  <-     c( 1,   0, 0, 0, 1,   1, 0, 0,    0, 0, 0, 1,    0, 0, 0, 0,     0, 0, 0, 0)

##             int   time          prepar    prepar=2*ti    prepar=3*ti     prepar=4*ti
c31  <-     c( 1,   0, 0, 0, 0,   0, 1, 0,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c32  <-     c( 1,   1, 0, 0, 0,   0, 1, 0,    0, 0, 0, 0,    1, 0, 0, 0,     0, 0, 0, 0)
c33  <-     c( 1,   0, 1, 0, 0,   0, 1, 0,    0, 0, 0, 0,    0, 1, 0, 0,     0, 0, 0, 0)
c34  <-     c( 1,   0, 0, 1, 0,   0, 1, 0,    0, 0, 0, 0,    0, 0, 1, 0,     0, 0, 0, 0)
c35  <-     c( 1,   0, 0, 0, 1,   0, 1, 0,    0, 0, 0, 0,    0, 0, 0, 1,     0, 0, 0, 0)

## calculating estimates of linear combination
## function to calculate linear combination  of beta parameters: est and SE (standard error)
## input: lvec, vector to calculate linear combination
## output: c(est, SE), point estimate and SE
f.lbeta <- function(lvec){
 est <- t(lvec) %*% beta_hat
 se <- sqrt(t(lvec) %*% covb %*% lvec)
 return(c(est, se))
}

mu2[1,] <- f.lbeta(c21)
mu2[2,] <- f.lbeta(c22)
mu2[3,] <- f.lbeta(c23)
mu2[4,] <- f.lbeta(c24)
mu2[5,] <- f.lbeta(c25)
## MEANs for group 2
mu2
```

```
##          [,1]     [,2]
## [1,] 120.3333 21.69787
## [2,] 202.6667 48.58312
## [3,] 209.3333 49.18307
## [4,] 179.0000 43.58040
## [5,] 186.6667 45.73887
```

```
mu3[1,] <- f.lbeta(c31)
mu3[2,] <- f.lbeta(c32)
mu3[3,] <- f.lbeta(c33)
mu3[4,] <- f.lbeta(c34)
mu3[5,] <- f.lbeta(c35)
## MEANs for group 3
mu3
```

```
##       [,1]     [,2]
## [1,] 163.2 23.76882
## [2,] 314.8 53.22015
## [3,] 280.0 53.87735
## [4,] 324.4 47.73993
## [5,] 360.0 50.10443
```

The means for group are higher. Note we could plot them and typically accompany the interaction test in b with a figure or table of these means (or the mean difference).

b. Test for an interaction between Roche (group2) and BASF 30mg. To answer this question we may think about the differences between each time point versus baseline and then the differences between groups.

```
contr0 <- cbind(c22-c21-(c32-c31), c23-c21-(c33-c31), c24-c21-(c34-c31), c25-c21-(c35-c31))
t(contr0)
```

```
##      [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8] [,9] [,10] [,11] [,12] [,13] [,14]
## [1,]    0    0    0    0    0    0    0    0    1     0     0     0    -1     0
## [2,]    0    0    0    0    0    0    0    0    0     1     0     0     0    -1
## [3,]    0    0    0    0    0    0    0    0    0     0     1     0     0     0
## [4,]    0    0    0    0    0    0    0    0    0     0     0     1     0     0
##      [,15] [,16] [,17] [,18] [,19] [,20]
## [1,]     0     0     0     0     0     0
## [2,]     0     0     0     0     0     0
## [3,]    -1     0     0     0     0     0
## [4,]     0    -1     0     0     0     0
```

```
## contrast point estimates to be
ce0 <- t(contr0) %*% beta_hat
## contrast variance covariance matrix
cov0 <- t(contr0) %*% covb %*% contr0

##
W0 <- t(ce0) %*% solve(cov0) %*% ce0
pchisq(W0, df = 4, lower.tail = FALSE)
```

```
##             [,1]
## [1,] 0.002353759
```

```
## emmeans is a package cover
test1 <- multcomp::glht(mod1, t(contr0))
summary(test1, test = Chisqtest())
```

```
##
##   General Linear Hypotheses
##
## Linear Hypotheses:
##        Estimate
## 1 == 0   -69.27
## 2 == 0   -27.80
## 3 == 0  -102.53
## 4 == 0  -130.47
##
## Global Test:
##   Chisq DF Pr(>Chisq)
## 1 16.56  4   0.002354
```

There is a significant interaction between Roche (group2) and BASF 30mg.

c. Conduct a test to compare if the 6 week - baseline value differs between the 4 *groups*.

```
##              int   time          prepar    prepar=2*ti    prepar=3*ti     prepar=4*ti
c11  <-     c( 1,   0, 0, 0, 0,   0, 0, 0,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c12  <-     c( 1,   1, 0, 0, 0,   0, 0, 0,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c13  <-     c( 1,   0, 1, 0, 0,   0, 0, 0,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c14  <-     c( 1,   0, 0, 1, 0,   0, 0, 0,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c15  <-     c( 1,   0, 0, 0, 1,   0, 0, 0,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
```

```
##             int   time           prepar    prepar=2*ti    prepar=3*ti     prepar=4*ti
c41  <-     c( 1,   0, 0, 0, 0,   0, 0, 1,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 0)
c42  <-     c( 1,   1, 0, 0, 0,   0, 0, 1,    0, 0, 0, 0,    0, 0, 0, 0,     1, 0, 0, 0)
c43  <-     c( 1,   0, 1, 0, 0,   0, 0, 1,    0, 0, 0, 0,    0, 0, 0, 0,     0, 1, 0, 0)
c44  <-     c( 1,   0, 0, 1, 0,   0, 0, 1,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 1, 0)
c45  <-     c( 1,   0, 0, 0, 1,   0, 0, 1,    0, 0, 0, 0,    0, 0, 0, 0,     0, 0, 0, 1)

## mean group 2
mu1 <- matrix(NA, 5, 2)
## mean  group 3
mu4 <- matrix(NA, 5, 2)

mu1[1,] <- f.lbeta(c11)
mu1[2,] <- f.lbeta(c12)
mu1[3,] <- f.lbeta(c13)
mu1[4,] <- f.lbeta(c14)
mu1[5,] <- f.lbeta(c15)
## MEANs for group 1
mu1
```

```
##          [,1]     [,2]
## [1,] 148.3333 21.69787
## [2,] 240.6667 48.58312
## [3,] 247.6667 49.18307
## [4,] 275.3333 43.58040
## [5,] 272.6667 45.73887
```

```
mu4[1,] <- f.lbeta(c41)
mu4[2,] <- f.lbeta(c42)
mu4[3,] <- f.lbeta(c43)
mu4[4,] <- f.lbeta(c44)
mu4[5,] <- f.lbeta(c45)
## MEANs for group 4
mu4
```

```
##          [,1]     [,2]
## [1,] 155.6667 21.69787
## [2,] 325.3333 48.58312
## [3,] 324.3333 49.18307
## [4,] 294.6667 43.58040
## [5,] 303.6667 45.73887
```

```
contr2 <- cbind(c25-c21 - (c15 -c11),
                c35-c31 - (c15 -c11),
                c45-c41 - (c15 -c11))
## contrast point estimates to be
(ce2 <- t(contr2) %*% beta_hat)
```

```
##           [,1]
## [1,] -58.00000
## [2,]  72.46667
## [3,]  23.66667
```

```
## contrast variance covariance matrix
cov2 <- t(contr2) %*% covb %*% contr2
```

```
## with both point estimates and standard deviation
## an anova or pairwise comparison can be performed
W2 <- t(ce2) %*% solve(cov2) %*% ce2
pchisq(W2, df = 3, lower.tail = FALSE)
```

```
##            [,1]
## [1,] 0.06575149
```

```
## emmeans is a package cover
test2 <- multcomp::glht(mod1, t(contr2))
summary(test2, test = Chisqtest())
```

```
##
##   General Linear Hypotheses
##
## Linear Hypotheses:
##        Estimate
## 1 == 0   -58.00
## 2 == 0    72.47
## 3 == 0    23.67
##
## Global Test:
##   Chisq DF Pr(>Chisq)
## 1 7.201  3    0.06575
```

Question 2. Models for Stepped Care Data

STEPPED-CARE randomized trial

The dataset we will use in class resembles the trial.

- A behavioral intervention was tested versus usual care in 286 patients with lung or head and neck cancer.

- Population: low income patients in the Denver area across 5 hospitals
- Primary outcomes: anxiety, depression and coping skills scores
- Outcomes were measured at baseline, and at 6, 12 and 24 weeks

Consider the stepped care data. Use a linear mixed model with time as continuous variable and random intercepts and random slopes. Assume there are no differences in coping self-efficacy score (CSES) at baseline.

a. Estimate the mean CSES at 6 weeks for both intervention groups.

b. Estimate the mean CSES difference at 6 weeks.

c. Test the hypothesis that the mean difference 12 weeks - baseline differs across the two treatment groups.

```
# Read in data
dat.step <- read.csv("/Users/juarezce/Documents/OneDrive - The University of Colorado Denver/BIOS6643/B

head(dat.step, 3)
```

```
##   id time   treat time6 time12 time24     cops
## 1  1    0 control     0      0      0 83.26686
## 2  1    6 control     1      0      0 81.52480
## 3  1   12 control     0      1      0 88.36082
```