BIOS6643. L13 Generalized Linear Mixed Models

GLMM for Seizure data

Epileptic Seizure Study of a randomized trial reported in Thall and Vail (1990).

- 59 subjects with epilepsy suffering from simple or partial seizures were assigned at random to receive either the progabide drug or a placebo
- Number of seizures suffered by each subject over the 8-week period prior to the start of study was also recorded
- After treatment initiation, the number of seizures for each subject was counted for each of 4 consecutive 2-week periods.

```
#  Read in the data

dat.sz <- read.table("../data/epilepsy.txt")
colnames(dat.sz) <- c("subj","seize","visit","trt","base","age")
## trt=0 corresponds to placebo
head(dat.sz,3)
```

```
##   subj seize visit trt base age
## 1  104    11     0   0   11  31
## 2  104     5     1   0   11  31
## 3  104     3     2   0   11  31
```

```
#  Create other covariates
dat.sz$o <- 8*(dat.sz$visit==0)+2*(dat.sz$visit>0)
dat.sz$logo <- log(dat.sz$o)
dat.sz$vm0 <- as.numeric(dat.sz$visit>0)
```

Investigate if there is a different different effect after baseline visit 0

This means include an interaction between the indicator variable for visit>0 and the treatment indicator.

```
fit.glmm <- glmer(seize ~ offset(logo) + vm0*trt + (1 + vm0 | subj),
    family=poisson, data=dat.sz)

summary(fit.glmm)
```

```
## Generalized linear mixed model fit by maximum likelihood (Laplace
##   Approximation) [glmerMod]
##  Family: poisson  ( log )
## Formula: seize ~ offset(logo) + vm0 * trt + (1 + vm0 | subj)
##    Data: dat.sz
##
##      AIC      BIC   logLik deviance df.resid
##   1863.3   1889.1   -924.7   1849.3      288
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.1388 -0.7118 -0.0607  0.5189  6.9652
##
## Random effects:
##  Groups Name        Variance Std.Dev. Corr
##  subj   (Intercept) 0.4999   0.7070
##         vm0         0.2319   0.4815   0.17
## Number of obs: 295, groups:  subj, 59
##
## Fixed effects:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)  1.071299   0.140267   7.638 2.21e-14 ***
## vm0         -0.002394   0.109092  -0.022   0.9825
## trt          0.049481   0.192716   0.257   0.7974
## vm0:trt     -0.307159   0.150452  -2.042   0.0412 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##         (Intr) vm0    trt
## vm0      0.016
## trt     -0.725 -0.017
## vm0:trt -0.018 -0.709  0.030
```

```
coef.glmm <-fixef(fit.glmm)
coef.glmm
```

```
##  (Intercept)          vm0          trt      vm0:trt
##  1.071298911 -0.002394417  0.049480730 -0.307158743
```

The model we are fitting is

$$\log(\mu_{ij}) = \log(t_{ij}) + (\beta_1 + b_{b=1i}) + (\beta_2 vm0_{ij} + b_{2i} vm0_{ij}) + \beta_3 trt_i + \beta_4 trt_i * vm0_i,$$

where t_{ij} = exposure time; $vm0$ = indicator for whether the visit is after baseline (1), $vm0 = 0$ for baseline visits; trt=1 if progabide and 0 if placebo.

Note interpretation of parameters is as follows

Placebo

- Baseline $\log(\mu_{ij}/T_{ij}) = \beta_1 + b_{1i}$
- Follow-up $\log(\mu_{ij}/T_{ij}) = (\beta_1 + b_{1i}) + (\beta_{vm0} + b_{2i})$

Progabide

- Baseline $\log(\mu_{ij}/T_{ij}) = \beta_1 + b_{1i} + \beta_{trt}$
- Follow-up $\log(\mu_{ij}/T_{ij}) = (\beta_1 + b_{1i}) + (\beta_{vm0} + b_{2i}) + \beta_{trt} + \beta_{vm0:trt}$

Results:

1. A patient treated with placebo has nearly the same expected seizure rate before and after randomization: exp ($\hat{\beta}_{vm0}$ =) 0.9976084
2. A patient treated with progabide has expected seizure rate reduced after treatment: $\exp(\hat{\beta}_{vm0} + \hat{\beta}_{vm0:trt})$ 0.7337748
3. Estimated variance of the random intercepts and slopes is relatively large

Marginal model

Interpret results of marginal model.

```
## AR1
ar1.gee <- geeglm(seize ~ vm0*trt,id=subj,family=poisson("log"),
             offset=logo, corstr="ar1",data=dat.sz)
summary(ar1.gee)
```

```
##
## Call:
## geeglm(formula = seize ~ vm0 * trt, family = poisson("log"),
##     data = dat.sz, offset = logo, id = subj, corstr = "ar1")
##
##  Coefficients:
##             Estimate  Std.err   Wald Pr(>|W|)
## (Intercept)  1.30885  0.16216 65.143 6.66e-16 ***
## vm0          0.15540  0.11405  1.856    0.173
## trt          0.01527  0.21183  0.005    0.943
## vm0:trt     -0.13064  0.26758  0.238    0.625
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation structure = ar1
## Estimated Scale Parameters:
##
##             Estimate Std.err
## (Intercept)    19.97   8.956
##   Link = identity
##
## Estimated Correlation Parameters:
##       Estimate Std.err
## alpha   0.8926 0.03877
## Number of clusters:   59  Maximum cluster size: 5
```

Investigate if there is a different effect after baseline visit 0 when adjusting for age in the model

```
## AR1
model1 = geeglm(
  seize ~ vm0*trt + age,
  id=subj,
  family=poisson("log"),
  offset=logo,
  corstr="ar1",
  data=dat.sz
)

summary(model1)
```

```
##
## Call:
## geeglm(formula = seize ~ vm0 * trt + age, family = poisson("log"),
##     data = dat.sz, offset = logo, id = subj, corstr = "ar1")
##
##  Coefficients:
##             Estimate Std.err  Wald Pr(>|W|)
## (Intercept)   2.5619  0.4823 28.21  1.1e-07 ***
## vm0           0.1551  0.1138  1.86   0.1731
## trt          -0.0471  0.2089  0.05   0.8216
## age          -0.0443  0.0162  7.45   0.0063 **
## vm0:trt      -0.1305  0.2670  0.24   0.6251
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation structure = ar1
## Estimated Scale Parameters:
##
##             Estimate Std.err
## (Intercept)     19.2    7.06
##   Link = identity
##
## Estimated Correlation Parameters:
##       Estimate Std.err
## alpha    0.886  0.0394
## Number of clusters:   59  Maximum cluster size: 5
```