Epilepsy Clinical Trial

STAT 222
Week 5

```
> install.packages("HSAUR2")
package 'HSAUR2' successfully unpacked and MD5 sums checked
> library(HSAUR2)
> data(epilepsy)
> dim(epilepsy)
[1] 236   6   > 236/4  [1] 59   > #patients
> library(lattice)
> dotplot(I(seizure.rate/base)~period|subject,data=epilepsy,subset=treatment=="Progabide")
> dotplot(I(seizure.rate/base)~period|subject,data=epilepsy,subset=treatment=="placebo")
> head(epilepsy)
    treatment base age seizure.rate period subject
1     placebo   11  31             5      1       1
110   placebo   11  31             3      2       1
112   placebo   11  31             3      3       1
114   placebo   11  31             3      4       1
2     placebo   11  30             3      1       2
210   placebo   11  30             5      2       2

> itp<-interaction(epilepsy$treatment,epilepsy$period)
> tapply(epilepsy$seizure.rate,itp,mean)  #get cell means
  placebo.1 Progabide.1   placebo.2 Progabide.2   placebo.3 Progabide.3   placebo.4
   9.357143    8.580645    8.285714    8.419355    8.785714    8.129032    7.964286
Progabide.4
   6.709677
> # some small advantage for drug

> #boxplots of log-seizure
> layout(matrix(1:2,nrow=1))
> ylim<-range(log(epilepsy$seizure.rate+1))
> boxplot(log(seizure.rate+1)~period,data=placebo,main="Placebo",ylab="Lognumberofseizures", xlab=
> boxplot(log(seizure.rate+1)~period,data=progabide, main="Progabide",ylab="Lognumberofseizures",
```

see HSAUR chap for plots and code

```
> per<-rep(log(2),nrow(epilepsy)) # if don't do this offset  Intercept doesn't match
> epilepsy_glm <- glm(seizure.rate ~ base + age + treatment + offset(per), data = epilepsy,
                family = "poisson")
> summary(epilepsy_glm)
Call:
glm(formula = seizure.rate ~ base + age + treatment + offset(per),
    family = "poisson", data = epilepsy)
Deviance Residuals:
    Min       1Q   Median       3Q      Max
-4.4360  -1.4034  -0.5029   0.4842  12.3223
Coefficients:
                      Estimate Std. Error z value Pr(>|z|)
(Intercept)         -0.1306156  0.1356191  -0.963   0.3355
base                 0.0226517  0.0005093  44.476  < 2e-16 ***
age                  0.0227401  0.0040240   5.651 1.59e-08 ***
treatmentProgabide -0.1527009  0.0478051  -3.194   0.0014 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
(Dispersion parameter for poisson family taken to be 1)
    Null deviance: 2521.75  on 235  degrees of freedom
Residual deviance:  958.46  on 232  degrees of freedom
AIC: 1732.5
```

glm model ignores indiv trajectories linked, conditions on covariates

```
# if don't use covariates, then can't find sig treatment effect
> epilepsy_glma <- glm(seizure.rate ~ treatment + offset(per), data = epilepsy, family = "poisson
> summary(epilepsy_glma)
Call: glm(formula = seizure.rate ~ treatment + offset(per), family = "poisson",
    data = epilepsy)
Coefficients:
                    Estimate Std. Error z value Pr(>|z|)
(Intercept)          1.45841    0.03222  45.258   <2e-16 ***
treatmentProgabide -0.07717    0.04529  -1.704   0.0884 .
---
```

```
> install.packages("gee")
```

Try

Generalized Estimating Eqs gee
Liang-Zeger

Epilepsy p.2

STAT722
week 5

```
> library(gee)

> fm <- seizure.rate ~ base + age + trt + offset(per)
> epilepsy_gee1 <- gee(fm, data = epilepsy, family = "poisson",
+  id = subject, corstr = "independence", scale.fix = TRUE,
+  scale.value = 1)
Beginning Cgee S-function, @(#) geeformula.q 4.13 98/01/27
running glm to get initial regression estimate
       (Intercept)               base                age treatmentProgabide
       -0.13061561         0.02265174          0.02274013        -0.15270095
> summary(epilepsy_gee1)
 GEE:  GENERALIZED LINEAR MODELS FOR DEPENDENT DATA
 gee S-function, version 4.13 modified 98/01/27 (1998)
Model:
 Link:                      Logarithm
 Variance to Mean Relation: Poisson
 Correlation Structure:     Independent
Call:
gee(formula = fm, id = subject, data = epilepsy, family = "poisson",
    corstr = "independence", scale.fix = TRUE, scale.value = 1)
Summary of Residuals:
       Min         1Q     Median         3Q        Max
-4.9195387  0.1808059  1.7073405  4.8850644 69.9658560
Coefficients:
                      Estimate  Naive S.E.    Naive z Robust S.E.   Robust z
(Intercept)        -0.13061561 0.1356191185 -0.9631062 0.365148155 -0.3577058
base                0.02265174 0.0005093011 44.4761250 0.001235664 18.3316325
age                 0.02274013 0.0040239970  5.6511312 0.011580405  1.9636736
treatmentProgabide -0.15270095 0.0478051054 -3.1942393 0.171108915 -0.8924196
```

"glm" "gee"

not sig

```
> epilepsy_lmer <- lmer(seizure.rate ~ base + age + treatment + offset(per) +(period|subject),
          data = epilepsy, family = "poisson")
> summary(epilepsy_lmer)
Generalized linear mixed model fit by the Laplace approximation
Formula: seizure.rate ~ base + age + treatment + offset(per) + (period | subject)
   Data: epilepsy
   AIC BIC logLik deviance
 505.5 554 -238.8    477.5
Random effects:
 Groups  Name        Variance Std.Dev. Corr
 subject (Intercept) 0.27139  0.52095
         period.L    0.11981  0.34613   0.034
         period.Q    0.14247  0.37746  -0.494 -0.593
         period.C    0.11981  0.34613  -0.274 -0.178  0.098
Number of obs: 236, groups: subject, 59
Fixed effects:
                    Estimate Std. Error z value Pr(>|z|)
(Intercept)        -0.215683   0.373725  -0.577   0.5639
base                0.026197   0.002374  11.035   <2e-16 ***
age                 0.016859   0.011476   1.469   0.1418
treatmentProgabide -0.306282   0.140690  -2.177   0.0295 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr) base   age
base        -0.401
age         -0.939  0.201
trtmntPrgbd -0.304 -0.002  0.130
```

try lmer "poisson"
no time trend, just level effect of treatment (1|subject)

gee

```
> exp(-.1527)
[1] 0.8583872
```

lmer

```
> exp(-.3063)
[1] 0.7361657
```

CI by exp(confint(?))

```
# Laird-Ware ALA p.349 "patient treated with progabide the expected decrease in seizures
is approx 26% (exp(-.3069) ~ .74)"
```

Ch.12 b/an Laird uses diff model
period effects, no covariates
same result as