BIS 628 HW 5

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Q1-Q3:
Background for the data set:
Data are from a clinical trial comparing auranofin therapy (3 mg of oral gold, twice daily) and placebo for the treatment of rheumatoid arthritis (Bombardier et al., 1986). In this six-month, randomized, double-blind trial, 303 patients with classic or definite rheumatoid arthritis were randomized to one of the two treatment groups and followed over time. The outcome variable is a global impression scale (Arthritis Categorical Scale, ACS) measured at baseline (month 0), month 2, month 4, and month 6. This is a self-assessment of a patient's current arthritis, measured on a 5- level ordinal scale: (1) very good, (2) good, (3) fair, (4) poor, and (5) very poor. Baseline data on this outcome variable are available for 303 of the patients who participated in this trial; follow-up data at 6 months are available for 294 patients.
Dataset: arthritis-data.csv or arthritis-data.xlsx
The dataset is in a wide format. The variables are (in column order):
Variable List:
ID: participant ID number
Treatment: 0=Placebo, 1=Auranofin therapy Age: Patient's baseline age
Baseline: ACS at baseline
Month2: ACS at month 2
Month4: ACS at month 4
Month6: ACS at month 6

Question 1 (10 points):

(a) (5 points) Read the data file into SAS or R (depending upon your preference). The data already have a header. Restructure the data into a long format for the longitudinal analysis. Create a new ordinal outcome: 1="Very Good" or "Good" (combine original ACS categories 1 and 2), 2="Fair" (original ACS category 3), 3="Poor" or "Very Poor "(combine original ACS categories 4 and 5).

```
#setwd("~/Downloads/HW5")
library(readr)
library(data.table)
library(plyr)
library(ggplot2)
arthritis_data <- read_csv("arthritis-data.csv")
```

```
## Parsed with column specification:
## cols(
##   ID = col_double(),
##   Treatment = col_double(),
##   Age = col_double(),
##   Baseline = col_double(),
##   Month2 = col_double(),
##   Month4 = col_double(),
##   Month6 = col_double()
## )
```

```
dt = reshape2::melt(arthritis_data, id.vars = c("ID" ,"Treatment", "Age")) # reshape the data
setDT(dt)
dt$cTreatment <- factor(dt$Treatment, levels = c(0,1), labels = c("Placebo","Auranofin therapy"))
```

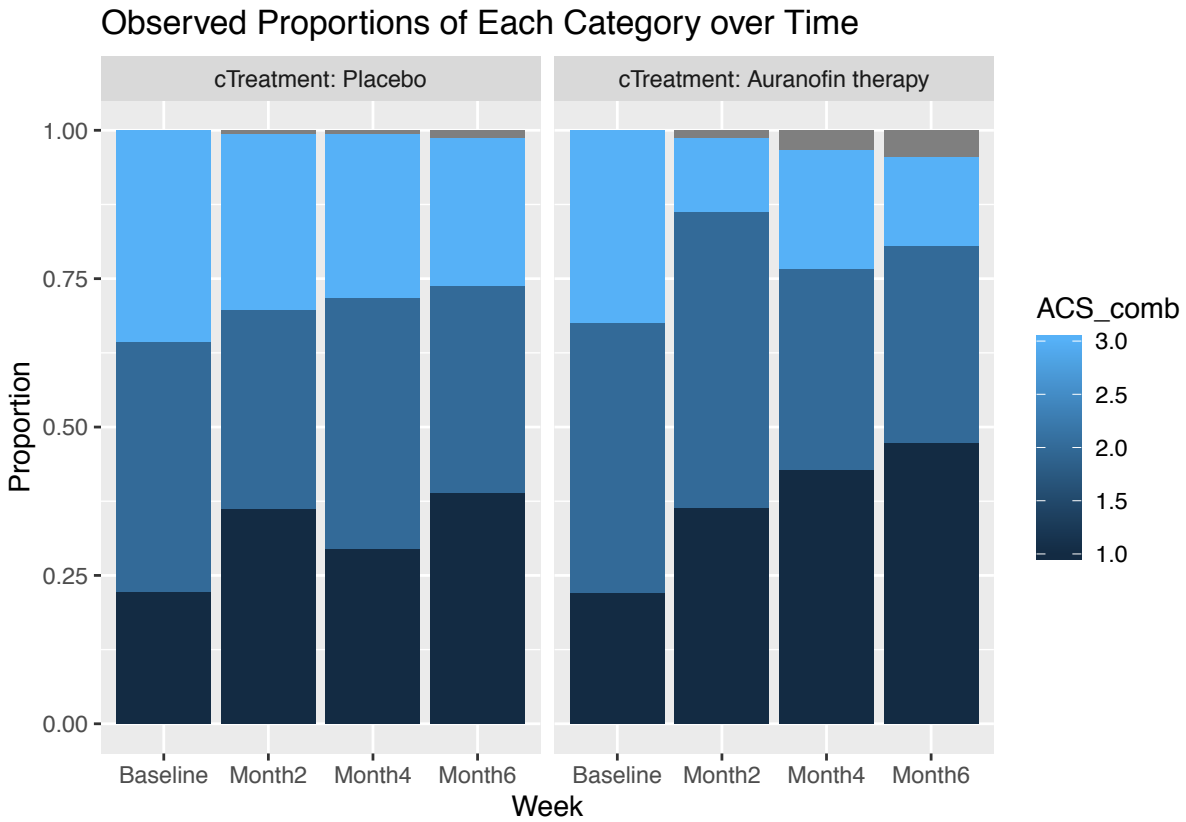
```r
setnames(dt,"value","ACS")
setnames(dt,"variable","month")
dt$cACS <- factor(dt$ACS, levels = c(1:5), labels = c("very good","good","fair","poor","very poor"))

dt[,ACS_comb:=ifelse(cACS == "very good"|cACS == "good",1, ifelse(cACS =="fair",2,ifelse(cACS =="poor"|
```

(b) (5 points) Figure 1: on a single graph, construct a time plot of the observed proportions of subjects with 3 categories of the new ordinal outcome across the months of follow up, stratified by the treatment group. You can either use lines or bars to show these proportions over time. Describe in a few sentences what you observe.

```r
t <- plyr::count(dt, c("cTreatment","month","ACS_comb"))

#Plot observed proportions of each category over time
p1 <- ggplot(data=t, aes(x=month, y=freq, fill=ACS_comb))
p1 + facet_wrap(~cTreatment, labeller=label_both) + geom_bar(position="fill", stat="identity") +
  labs(title="Observed Proportions of Each Category over Time", x="Week", y="Proportion")
```



The proportion of subjects in the Placebo group with the first category of new ordinal variable does not have a pattern (monotone increasing/decreasing) over the follow up time. Yet the proportion of subjects in the Auranofin therapy group with the first category of new ordinal variable is increasing over the follow up time. That makes sense because in the treatment group, more people get better (the number of people in the first new ACS category is increasing) over the time, but this might not hold in the Placebo group.

Question 2 (40 points):

Fit a generalized linear mixed effects model (GLMM) for the odds of a more favorable outcome, treating it as an ordinal response, with the following covariates: treatment, square root of month of follow-up (continuous

variable, starting with baseline month=0) and intervention by square-root of month of follow-up interaction, and a random intercept and a random slope for time for each subject. The random intercept and slope are assumed to be generated from a Normal distribution, each, with a mean of zero and a variance parameter for each, plus a covariance parameter (random intercept and slope are correlated).
Notes to myself: We can use either form (factor, numerical) for the outcome variable because mixor can regonize.

```
#install.packages("mixor")
library(mixor)
```

```
## Loading required package: survival
```

```
dt$month_num = dt[,ifelse(month == "Month6",6,ifelse(month == "Month4",4, ifelse(month == "Month2",2,if

dt$sqrt_month = sqrt(dt$month_num)
# Mixed effects proportional odds regression model with random intercept
# Outcome in descending order
dt<-dt[order(dt$ID),]
m1 <- mixor(ACS_comb ~ Treatment + sqrt_month + Treatment*sqrt_month, data=dt, id= ID, which.random.slo
```

```
## Warning in model.matrix.default(mt, mf, contrasts): non-list contrasts argument
## ignored
```

```
summary(m1)
```

```
##
## Call:
## mixor(formula = ACS_comb ~ Treatment + sqrt_month + Treatment *
##     sqrt_month, data = dt, id = ID, which.random.slope = 2, nAGQ = 20,
##     link = "logit")
##
## Deviance =          2216.627
## Log-likelihood =  -1108.313
## RIDGEMAX =          0
## AIC =              -1116.313
## SBC =              -1131.168
##
##                          Estimate Std. Error z value   P(>|z|)
## (Intercept)               2.01013    0.24289  8.2761  2.22e-16 ***
## sqrt_month               -0.40915    0.10932 -3.7426 0.0001821 ***
## Treatment                -0.17340    0.31849 -0.5445 0.5861276
## Treatment:sqrt_month     -0.33087    0.15404 -2.1479 0.0317187 *
## (Intercept) (Intercept)  3.55019    1.07986  3.2876 0.0010103 **
## (Intercept) sqrt_month   0.20260    0.32741  0.6188 0.5360541
## sqrt_month sqrt_month    0.29817    0.19387  1.5380 0.1240464
## Threshold2               3.06520    0.17602 17.4141 < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Note: I tried to add na.action=na.omit here, but it doesn't work in the mixor model.

(a) (10 points) Write out the subject-specific equations for this GLMM using the estimated parameters. If you are using R, go ahead and combine the intercept and the thresholds to get the appropriate 'new' combined intercepts. If you are using 'proc glimmix' in SAS, you do not need to do that because the output already gives you a new intercept for each relevant GLMM equation – pay attention to the 'descending' statement!

new var - 3 group => 2 equation(alpha) new intercept =alpha ASCENDING ORDER

```
alpha1 = -2.01013
alpha2 = -(2.01013 - 3.06520) # 1.055
```

Let Y_{ij} denote the ordinal response for the i^{th} subject at j^{th} occasion, we assume that the subject-specific log odds of a more favorable response at each occasion follows the proportional odds model

$$\log\left\{\frac{\Pr(Y_{ij}\leq 1|b_i)}{\Pr(Y_{ij}>1|b_i)}\right\} = \alpha_1+\beta_1\,\mathrm{Tr}\,t_i+\beta_2\sqrt{\mathrm{Month}_{ij}}+\beta_3\,\mathrm{Tr}_i\times\sqrt{\mathrm{Month}_{ij}}+b_{1i}+b_{2i}\sqrt{Month_{ij}}$$
$$= -2.01+0.17*\mathrm{Tr}\,t_i+0.41*\sqrt{\mathrm{Month}_{ij}}+0.33*\mathrm{Tr}_i\times\sqrt{\mathrm{Month}_{ij}}+b_{1i}+b_{2i}\sqrt{Month_{ij}}$$

$$\log\left\{\frac{\Pr(Y_{ij}\leq 2|b_i)}{\Pr(Y_{ij}>2|b_i)}\right\} = \alpha_2+\beta_1\,\mathrm{Tr}\,t_i+\beta_2\sqrt{\mathrm{Month}_{ij}}+\beta_3\,\mathrm{Tr}_i\times\sqrt{\mathrm{Month}_{ij}}+b_{1i}+b_{2i}\sqrt{Month_{ij}}$$
$$= 1.06+0.17*\mathrm{Tr}\,t_i+0.41*\sqrt{\mathrm{Month}_{ij}}+0.33*\mathrm{Tr}_i\times\sqrt{\mathrm{Month}_{ij}}+b_{1i}+b_{2i}\sqrt{Month_{ij}}$$

(b) Use SAS or R to fit this GLMM (try different number of quadrature points to improve precision of the estimates):

i. (2 points): test whether you need both, the random intercept and the random slope components in the model. What is the name of the test? What is your conclusion?

Likelihood ratio tests

```
full <- mixor(ACS_comb ~ Treatment + sqrt_month + Treatment*sqrt_month, data=dt, id= ID, which.random.sl
```

```
## Warning in model.matrix.default(mt, mf, contrasts): non-list contrasts argument
## ignored
```

```
reduced <- mixor(ACS_comb ~ Treatment + sqrt_month + Treatment*sqrt_month, data=dt, id= ID, link="logit
```

```
## Warning in model.matrix.default(mt, mf, contrasts): non-list contrasts argument
## ignored
```

```
LRtest = deviance(reduced) - deviance(full)
pchisq(LRtest, 2, lower.tail=FALSE)
```

```
## [1] 0.004790709
```

By comparing the deviances of the two models which is significant (LRT = 10.68 with p=0.004790709). Therefore we reject the null assumption that both the random intercept and the random slope components are needed in the model and conclude that the random slope is needed here (full model is better).

ii. (5 points) Test whether there is a significant effect of intervention group on the change in subject-specific odds of a more favorable response over the duration of the study. Write out your null and alternative hypotheses. Show which test you are using and interpret your findings in words. Please, do not just say 'we reject the null' or 'we have insufficient evidence to reject the null', also state your conclusion in a sentence relative to the research question raised here(i).

We only need to test the significance of the interaction term here. Null hypothesis: $\beta_3 = 0$ where β_3 is the coefficient of the interaction term
Alternative hypothesis: $\beta_3 \neq 0$
Use LRT.

```
full1 <- mixor(ACS_comb ~ Treatment + sqrt_month + Treatment*sqrt_month, data=dt, id= ID, which.random.
```

```
## Warning in model.matrix.default(mt, mf, contrasts): non-list contrasts argument
## ignored
```

```
reduce1 <- mixor(ACS_comb ~ Treatment + sqrt_month, data=dt, id= ID, which.random.slope=2, link="logit"
```

```
## Warning in model.matrix.default(mt, mf, contrasts): non-list contrasts argument
## ignored
```

```
LRtest1 = deviance(reduce1) - deviance(full1)
pchisq(LRtest1, 1, lower.tail=FALSE)
```

```
## [1] 0.03111199
```

-2log-lik = 4.64 with p = 0.031 < 0.5. Therefore we reject the null and conclude that there is a significant effect of intervention group on the change in subject-specific odds of a more favorable response over the duration of the study. The result indicate that the pattern of subject-specific changes over time in the odds of a more favorable response differs between treatment groups (interaction is significant and full model is better).

iii. (5 points) Interpret the estimates for the intercepts ('new' intercepts in R and the outputted intercepts in SAS) for each GLMM equation.

intercept1 = alpha1 = -2.01013. The first cumulative logit (1 vs.2-3) in placebo group's 'typical' patient in month 0 is -2.01013. intercept2 = alpha2 = -(2.01013 - 3.06520) = 1.055. The second cumulative logit (1-2 vs.3) in placebo group's 'typical' patient in month 0 is 1.055.

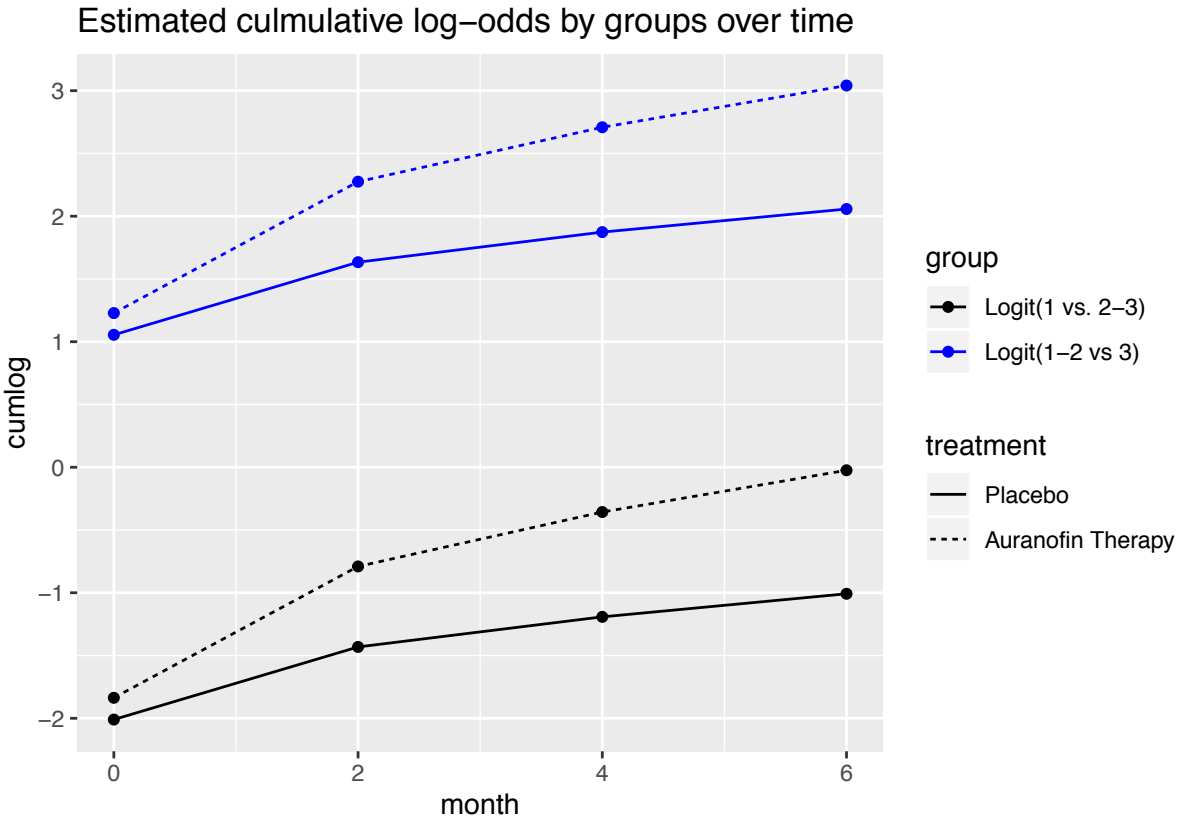
iv. (5points) Figure 2: create a plot that visually shows the "proportionality assumption". Explain what you plotted and interpret what the "proportionality assumption" means. Hint: see lecture 8 slides!

```
group = c(0, 0, 0, 0, 0, 0, 0, 0, 1, 1, 1, 1, 1, 1, 1, 1)
treatment = c(0, 0, 0, 0, 1, 1, 1, 1, 0, 0, 0, 0, 1, 1, 1, 1)
sqrt_time = c(0,sqrt(2),sqrt(4),sqrt(6))
month = c(rep(c(0,2,4,6),4))

# alpha group = 1, treatment = 0
cumlog1 = -2.01013 + 0.40915*sqrt_time
# alpha group = 1, treatment = 1
cumlog2 = -2.01013 + 0.17340 + 0.40915*sqrt_time + 0.33087*sqrt_time
# alpha group = 2, treatment = 0
cumlog3 = 1.05507 + 0.40915*sqrt_time
# alpha group = 2, treatment = 1
cumlog4 = 1.05507 + 0.17340 + 0.40915*sqrt_time + 0.33087*sqrt_time

cumlog = c(cumlog1,cumlog2,cumlog3,cumlog4)
df = as.data.frame(cbind(group, treatment, month, cumlog))
df$treatment = factor(df$treatment, levels = c(0,1),labels = c("Placebo","Auranofin Therapy"))

ggplot(df,aes(x=month,y = cumlog,color = factor(group),linetype = treatment, group = interaction(treatm
```



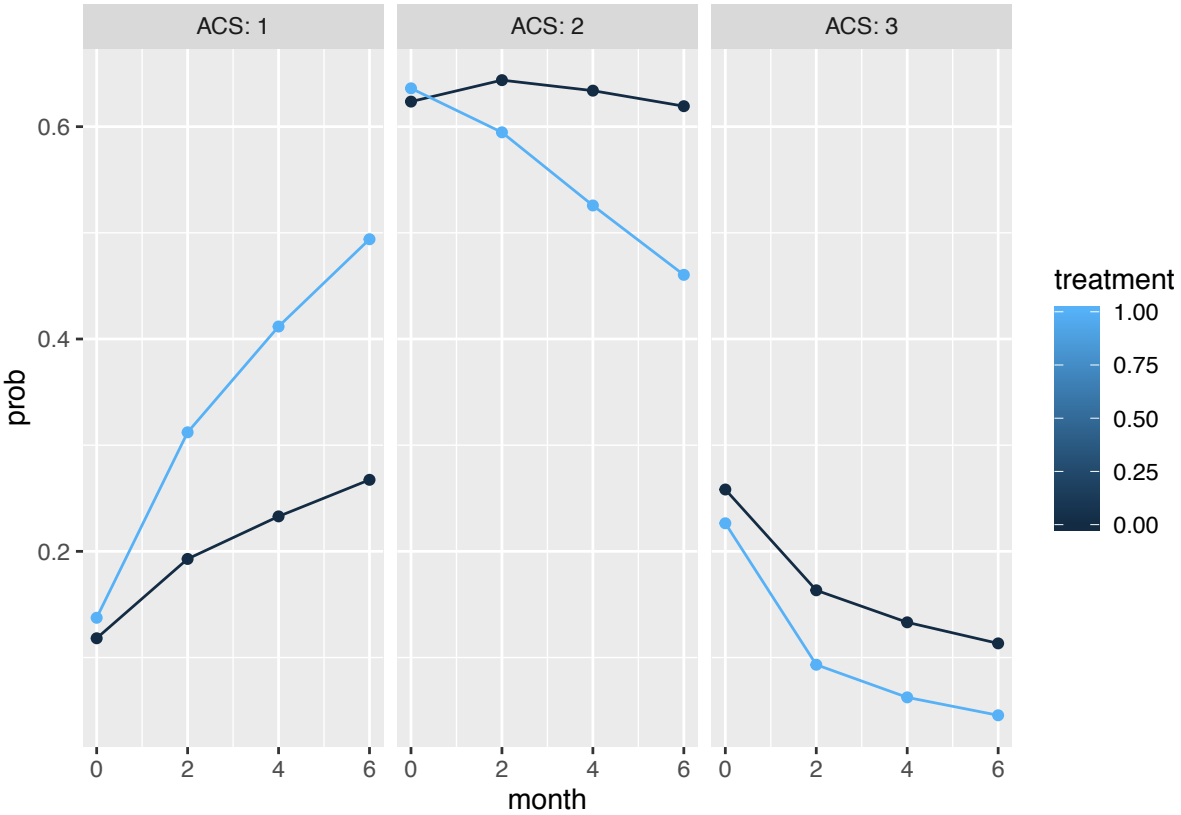
The plot shows the change of estimated cumulative log-odds of subject over time by treatment group for two different alphas. "Proportionality assumption" means that the slopes (beta) is the same and only the intercept is different. That is . Specifically, the slope of change in the cumulative log-odds for a subject response by treatment time over the followup time is the same across different cumulative log-odds (logits) within treatment and placebo groups. The log-odds are increasing proportionally across different logits, so that the ratios remain constant.

v. (5 points) Figure 3: Estimate probabilities of each of the 3 categories in the outcome of interest, and plot them over the study period by the treatment groups (months 0, 2,4,6). Plot everything on the same figure. Extra credit will be given for a creative representation! Describe what you observe in a few sentences. Compare what you see here to your findings in Q1 (b).

```
#.1 means for group 1, .2 means for group 2
p1.1 = 1/(1+exp(-cumlog1))
p1.2 = 1/(1+exp(-cumlog2))
p2.1 = 1/(1+exp(-cumlog3)) - 1/(1+exp(-cumlog1))
p2.2 = 1/(1+exp(-cumlog4)) - 1/(1+exp(-cumlog2))
p3.1 = 1 - 1/(1+exp(-cumlog3))
p3.2 = 1 - 1/(1+exp(-cumlog4))

prob = c(p1.1,p1.2,p2.1,p2.2,p3.1,p3.2)
treatment = rep(c(0,0,0,0,1,1,1,1),3)
ACS = c(rep(1,8),rep(2,8),rep(3,8))
month = rep(c(0,2,4,6),6)
df2 = as.data.frame(cbind(treatment,month,ACS,prob))
```

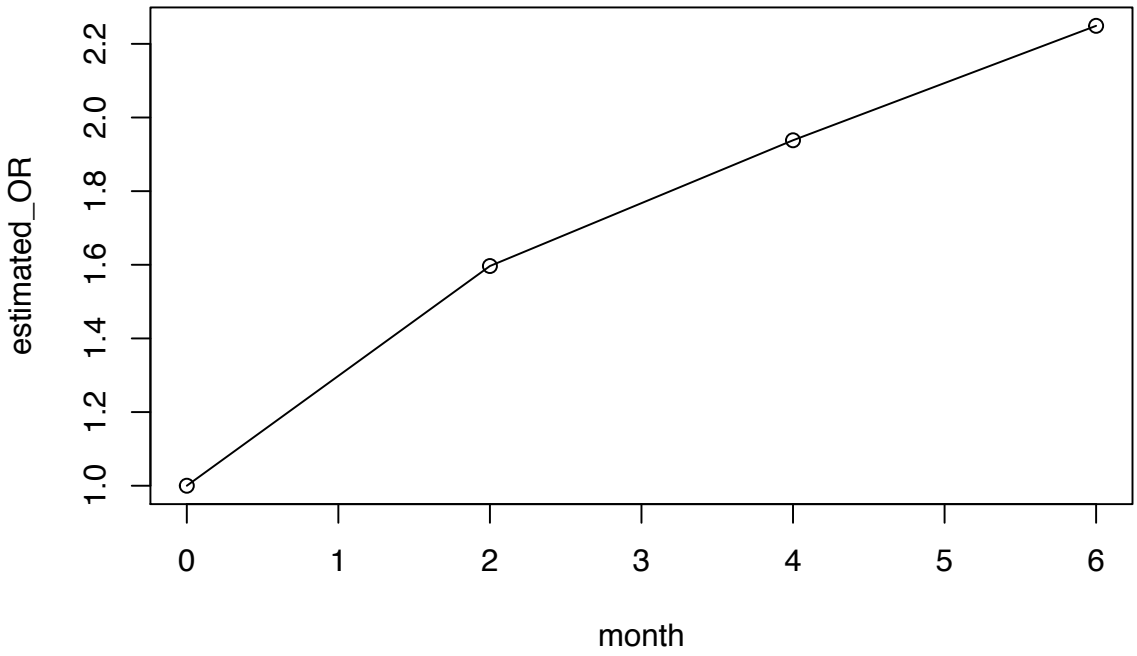
```
ggplot(df2,aes(x=month,y = prob, group = factor(treatment))) + geom_line(aes(color=treatment)) + geom_p
```



The figure shows that the probability increases along the month for ACS 1 (very good and good) for both groups but the probability from the treatment is faster than the placebo group. the probability decreases along the month for ACS 3 (very poor and poor) for both groups but the probability from the placebo is faster than the treatment group. The conclusion is concensus to the findings in Q1 (b).

vi. (5 points) Figure 5: Estimate subject-specific ratios of increased odds of a favorable outcome across time (months 0,2,4,6) in subjects randomized to the treatment relative to the subjects randomized to the placebo. Plot these estimated odds ratios across time. Interpret the estimated odds ratio at 4 months of follow up.

```
estimated_OR = c(exp(0.33087*sqrt(0)),exp(0.33087*sqrt(2)),exp(0.33087*sqrt(4)),exp(0.33087*sqrt(6)))
month = c(0,2,4,6)
plot(month,estimated_OR)
lines(month,estimated_OR)
```




```
exp(0.33087*sqrt(4))
```

```
## [1] 1.938162
```

At 4 months, a patient assigned to treatment is approximately 1.9 times more likely to have a favorable response when compared to a similar patient treated with placebo.

vii. (3 points) A similar analysis was reported on pages 427-429 of the "Applied Longitudinal Analysis, 2nd Edition" by Fitzmaurice, Laird, Ware (our main assigned book for the class). Compare your estimate to the book's estimate of the parameter for "Trt x sqrt(Month)". Are they similar? Why or Why not? Explain your finding.

The estimate in the textbook is 0.4005 which is slightly different from 0.33087. The reason is that, books use five ACS score as five different ordinal outcomes, while in the model we categorize three ACS scores as outcomes. So the proportionality assumption is different for our case and moreover we model different conditional mean response.

Question 3 (30 points):

Fit a generalized linear mixed effects model (GLMM) for the odds of a more favorable outcome, treating the outcome variable as a **nominal** response, with the following covariates: treatment, square root of month of follow-up (continuous variable, starting with baseline month=0) and intervention by square-root of month of follow-up interaction, and a random intercept for each subject that is assumed to be generated from a Normal distribution, with a mean of zero and a variance parameter.

(a) (8 points) Using "Poor or Very Poor" as the reference category, write out the subject-specific equations for this GLMM using the estimated parameters. What can you say about the random effect in each of the equation? How would you interpret it?

$$\log\left\{\frac{\Pr\left(Y_{ij}=1|b_i^{(c)}\right)}{\Pr\left(Y_{ij}=3|b_i^{(c)}\right)}\right\} = \beta_1^{(c)} + \beta_2^{(c)}\,\mathrm{Tr\,t}_i + \beta_3\sqrt{\mathrm{Month}_{ij}} + \beta_4\,\mathrm{Tr}_i \times \sqrt{\mathrm{Month}_{\ ij}} + b_{1i}^{(c)}$$
$$= -1.06262 + 0.27505 * \mathrm{Tr\,t}_i + 0.66196 * \sqrt{\mathrm{Month}_{ij}} + 0.54073 * \mathrm{Tr}_i \times \sqrt{\mathrm{Month}_{\ ij}} + b_{11i}$$

$$\log\left\{\frac{\Pr\left(Y_{ij}=2|b_i^{(c)}\right)}{\Pr\left(Y_{ij}=3|b_i^{(c)}\right)}\right\} = \beta_1^{(c)} + \beta_2^{(c)}\,\mathrm{Tr\,t}_i + \beta_3\sqrt{\mathrm{Month}_{ij}} + \beta_4\,\mathrm{Tr}_i \times \sqrt{\mathrm{Month}_{\ ij}} + b_{1i}^{(c)}$$
$$= 0.60832 + 0.41657 * \mathrm{Tr\,t}_i + 0.21839 * \sqrt{\mathrm{Month}_{ij}} + 0.17989 * \mathrm{Tr}_i \times \sqrt{\mathrm{Month}_{\ ij}} + b_{12i}$$

(b) Use SAS or R to fit this GLMM:

```
library(vcrpart)
```

```
## Loading required package: parallel
## Loading required package: partykit
## Loading required package: grid
## Loading required package: libcoin
## Loading required package: mvtnorm
```

```
dt$ACS_comb = factor(dt$ACS_comb)
dt$ID = factor(dt$ID)

m2 <- olmm(ACS_comb ~ Treatment + sqrt_month + Treatment*sqrt_month + re(1|ID), data=dt, family=baselin
summary(m2)
```

```
## Linear Mixed Model fit by Marginal Maximum
## Likelihood with Gauss-Hermite Quadrature
##
##  Family: baseline logit
## Formula: ACS_comb ~ Treatment + sqrt_month + Treatment * sqrt_month +
##     re(1 | ID)
##    Data: dt
##
## Goodness of fit:
##       AIC      BIC    logLik
##  2240.519 2296.454 -1109.259
##
## Random effects:
## Subject: ID
##                 Variance   StdDev     Corr
## 1|3:(Intercept) 11.5487403  3.3983438 1|3:(Intercept)
## 2|3:(Intercept)  2.3239756  1.5244591  0.9481255
## Number of obs: 1194, subjects: 303
## (18 observations deleted due to missingness)
##
## Category-specific fixed effects:
##                           Estimate Std. Error z value
## 1|3:(Intercept)          -1.06262    0.42922 -2.4757
```

```
## 1|3:Treatment              0.27505    0.57137  0.4814
## 1|3:sqrt_month             0.66196    0.16163  4.0955
## 1|3:Treatment:sqrt_month   0.54073    0.22620  2.3905
## 2|3:(Intercept)            0.60832    0.25207  2.4132
## 2|3:Treatment              0.41657    0.34823  1.1962
## 2|3:sqrt_month             0.21839    0.11731  1.8616
## 2|3:Treatment:sqrt_month   0.17989    0.17359  1.0363
```

i. (8 points) For each relevant equation from Q3(a) above, test whether there is a significant effect of intervention group on the change in subject-specific odds of a more favorable response over the duration of the study. Write out your null and alternative hypotheses. Show which test you are using and interpret your findings in words. Please, do not just say 'we reject the null' or 'we have insufficient evidence to reject the null', also state your conclusion in a sentence relative to the research question raised here(i).

Notes to my self: in the earlier case, we get rid of random slope (with the covariance related to random intercept, so there's 2 dof. Here the dof = 2 because of 2|3:Treatment:sqrt_month and 1|3:Treatment:sqrt_month

```
full2 <- olmm(ACS_comb ~ Treatment + sqrt_month + Treatment*sqrt_month + re(1|ID), data=dt, family=basel
reduce2 <- olmm(ACS_comb ~ Treatment + sqrt_month + re(1|ID), data=dt, family=baseline())

LRtest2 = deviance(reduce2) - deviance(full2)
pchisq(LRtest2, 2, lower.tail=FALSE)
```

```
## [1] 0.06962698
```

By comparing the deviances of the two models which is not significant (LRT = 5.33 with p=0.06962698). Therefore we fail to reject the null assumption and conclude that there is not a significant effect of intervention group on the change in subject-specific odds of a more favorable response over the duration of the study.

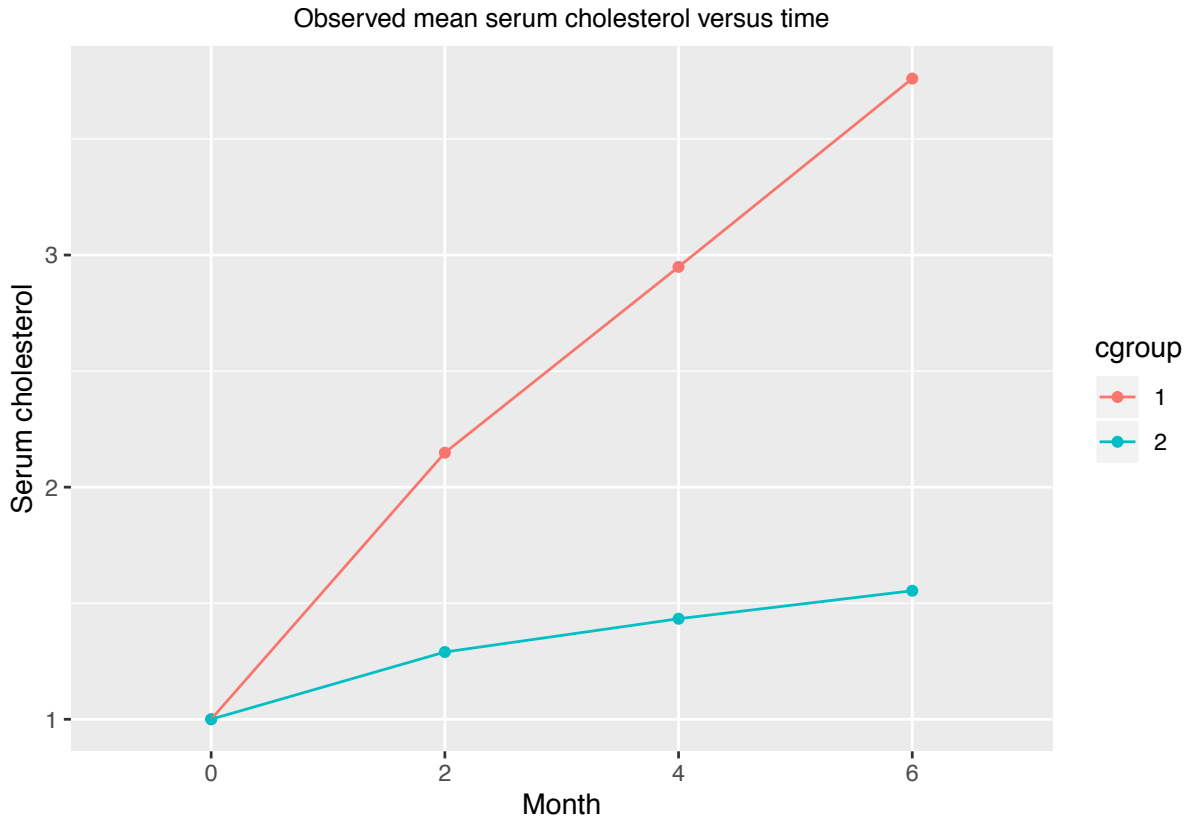
ii. (4 points) For each relevant equation from Q3(a) above, interpret the estimates for the intercepts when the response is nominal (the current model) and how are these interpretations different from Q2b(iii)?

Estimated $\beta_1 = -1.06262$ is the first logit for typical subject of outcome "1" compared to "3" for the reference category.
Estimated $\beta_2 = 0.60832$ is the second logit for typical subject of outcome "2" compared to "3" for the reference category.

iii. (5 points) Figure 5: For each relevant equation from Q3(a) above, estimate subject-specific ratios of increased odds of a favorable outcome across time (months 0, 2,4,6) in subjects randomized to the treatment relative to the subjects randomized to placebo. Plot these estimated odds ratios across time on one plot. Interpret the estimated odds ratios at 4 months of follow up for each specific equation.

```
estimated_OR = c(exp(0.54073*sqrt(0)),exp(0.54073*sqrt(2)),exp(0.54073*sqrt(4)),exp(0.54073*sqrt(6)),ex
month = factor(c(0,2,4,6,0,2,4,6))
group = factor(c(1,1,1,1,2,2,2,2))
for_plot = data.frame(month=month,estimated_OR=estimated_OR,group=group)


ggplot(for_plot, aes(x = month, y = estimated_OR, color = group, group = group )) + geom_point() +
geom_line() +
labs(title="Observed mean serum cholesterol versus time",
x="Month", y="Serum cholesterol", color = "cgroup") + theme(plot.title = element_text(size = 10, hjust
```




```
exp(0.54073*sqrt(4))
```

```
## [1] 2.948982
```

Estimated $OR_{t=4}$ = 2.948982. In other words, at 4 months, a patient assigned to treatment is approximately 2.94 times more likely to have a "Good/Very good" response when compared to a similar patient treated with placebo. But for NOT similar subjects at baseline in two groups, Estimated $OR_{t=4}$ = exp(0.27505+0.54073*sqrt(4))=3.88.

```
exp(0.17989*sqrt(4))
```

```
## [1] 1.433014
```

Estimated $OR_{t=4}$ =1.433014. In other words, at 4 months, a patient assigned to treatment is approximately 1.433014 times more likely to have a "Fair" response when compared to a similar patient treated with placebo. But for NOT similar subjects at baseline in two groups, Estimated $OR_{t=4}$ = exp(0.41657+0.17989*sqrt(4))=2.17.

iv. (5 points) Write out equations of how you would obtain estimated probabilities of each level of the nominal response for a typical subject in the study. Using the estimates from your model in Q3, what is the probability of having "Fair" response at 6 months of follow up for a patient randomized to the treatment group with a random intercept bi=-0.17?

$$\eta_{ij}^{(c)} = X'_{ij}\beta_1^{(c)} + Z'_{ij}b_i^{(c)}$$

Note that

$\eta_{ij}^{(1)*} = \beta_1^{(c)} + \beta_2^{(c)}\,\mathrm{Tr\,t}_i + \beta_3\sqrt{\mathrm{Month}_{ij}} + \beta_4\,\mathrm{Tr}_i \times \sqrt{\mathrm{Month}_{ij}} + b_{1i}^{(c)} = -1.06 + 0.28*(1) + 0.66*\mathrm{sqrt}(6) + 0.54*(1)\,\mathrm{sqrt}(6) - 0.17 = 1.9$

```
-1.06+0.28+0.66*sqrt(6)+0.54*sqrt(6)-0.17
```

```
## [1] 1.989388
```

$\eta_{ij}^{(2)*} = \beta_1^{(c)} + \beta_2^{(c)} \text{Tr t}_i + \beta_3 \sqrt{\text{Month}_{ij}} + \beta_4 \text{Tr}_i \times \sqrt{\text{ Month }_{ij}} + b_{1i}^{(c)} = 0.61 + 0.42 * (1) + 0.22 * \text{sqrt}(6) + 0.18 * (1) \, \text{sqrt}(6) - 0.17 = 1.83$

```
0.61+0.42+0.22*sqrt(6)+0.18*sqrt(6)-0.17
```

```
## [1] 1.839796
```

$\Pr\left(Y_{ij} = 2, \text{ "Fair" } | b_i, \text{ Trt=1, Time } = 6\right) = exp(1.839796)/(1 + exp(1.989388) + exp(1.839796)) = 0.4309954$