Practical 2

25/02/2022

Exercise 1

We will model the mean structure of the response in the TCL trial. We will use an unstructured covariance matrix and the gls function in the NMLE package for fitting the various models. Choose ML as method for estimation.

(a) Why using the ML and not REML?.

```
#clean the R environment
rm(list=ls())
#libraries to be installed
#ggplot2: producing nicer plots
if(!require(ggplot2)) {
  install.packages("ggplot2"); require(ggplot2)}
#tidyr: allows for easier data munipulation
if(!require(tidyr)) {
  install.packages("tidyr"); require(tidyr)}
#mvtnorm: allows to simulate from multivariate normal
if(!require(mvtnorm)) {
  install.packages("mvtnorm"); require(mvtnorm)}
#knitr: allows to produce nicer tables as summary
if(!require(knitr)) {
  install.packages("mvtnorm"); require(knitr)}
#nmle
if(!require(nlme)) {
  install.packages("nlme"); require(nlme)}
#nmle
if(!require(readstata13)) {
  install.packages("readstata13"); require(readstata13)}
#set your working directory
#use setwd()
```

(b) Give the difference in mean between the two groups at time point 1 and at time point 4 (second time point) according to this model? What are estimates of the correlations and the variances for each time point?

```
ds <- read.table("lead_trial.txt",header=T)
str(ds)
```

```
## 'data.frame':    100 obs. of  6 variables:
##  $ ID : int  1 2 3 4 5 6 7 8 9 10 ...
##  $ trt: chr  "P" "A" "A" "P" ...
##  $ Y0 : num  30.8 26.5 25.8 24.7 20.4 20.4 28.6 33.7 19.7 31.1 ...
##  $ Y1 : num  26.9 14.8 23 24.5 2.8 5.4 20.8 31.6 14.9 31.2 ...
##  $ Y4 : num  25.8 19.5 19.1 22 3.2 4.5 19.2 28.5 15.3 29.2 ...
##  $ Y6 : num  23.8 21 23.2 22.5 9.4 11.9 18.4 25.1 14.7 30.1 ...
```

```
#longformat
datalong <- reshape(ds, idvar="ID", varying=c("Y0","Y1","Y4","Y6"),v.names="Y",
                    timevar="time",time=c(0,1,4,6), direction="long")
#model time categorical. Test for treatment effect using ML.
week.f <- factor(datalong$time, c(0,1,4,6))
tt<-as.integer(week.f)
model1 <- gls(Y ~ trt*week.f, corr=corSymm(, form= ~ tt | ID),
              weights = varIdent(form = ~ 1 | week.f),data=datalong, method="ML")
model1
```

```
## Generalized least squares fit by maximum likelihood
##   Model: Y ~ trt * week.f
##   Data: datalong
##   Log-likelihood: -1212.684
##
## Coefficients:
##  (Intercept)         trtP      week.f1      week.f4      week.f6 trtP:week.f1
##       26.540       -0.268      -13.018      -11.026       -5.778       11.406
## trtP:week.f4 trtP:week.f6
##        8.824        3.152
##
## Correlation Structure: General
##  Formula: ~tt | ID
##  Parameter estimate(s):
##  Correlation:
##   1     2     3
## 2 0.571
## 3 0.570 0.775
## 4 0.577 0.582 0.581
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        1        4        6
## 1.000000 1.325866 1.370446 1.524806
## Degrees of freedom: 400 total; 392 residual
## Residual standard error: 4.972082
```

```
#time 1
#group A
cov_groupA_time1<-c(1,0,1,0,0,0,0,0)
```

```r
mean_groupA_time1<-t(cov_groupA_time1)%*%model1$coefficients
#group P
cov_groupP_time1<-c(1,1,1,0,0,1,0,0)
mean_groupP_time1<-t(cov_groupP_time1)%*%model1$coefficients
#difference at time 1
mean_time1<-mean_groupP_time1-mean_groupA_time1
print(mean_time1)
```

```
##        [,1]
## [1,] 11.138
```

```r
#time 4
#group A
cov_groupA_time4<-c(1,0,0,1,0,0,0,0)
mean_groupA_time4<-t(cov_groupA_time4)%*%model1$coefficients
#group P
cov_groupP_time4<-c(1,1,0,1,0,0,1,0)
mean_groupP_time4<-t(cov_groupP_time4)%*%model1$coefficients
#difference at time 1
mean_time4<-mean_groupP_time4-mean_groupA_time4
print(mean_time4)
```

```
##       [,1]
## [1,] 8.556
```

```r
#estimates of the correlations
model1$modelStruct
```

```
## corStruct  parameters:
## [1] -0.8168100 -0.8141441 -1.0064605 -0.8276375 -0.5012932 -0.2321765
## varStruct  parameters:
## [1] 0.2820661 0.3151360 0.4218671
```

```r
#the variances for each time point
diag(getVarCov(model1,individual=2))
```

```
## [1] 24.72160 43.45862 46.43016 57.47853
```

(c) Perform a likelihood ratio test to test the null hypothesis of no treatment effect.

```
#fit the nested model
model2 <- gls(Y ~ week.f, corr=corSymm(, form= ~ tt | ID),
              weights = varIdent(form = ~ 1 | week.f),data=datalong, method="ML")
#show the results
summary(model2)
```

```
## Generalized least squares fit by maximum likelihood
##   Model: Y ~ week.f
##   Data: datalong
##        AIC      BIC    logLik
##   2529.588 2585.469 -1250.794
##
## Correlation Structure: General
##  Formula: ~tt | ID
##  Parameter estimate(s):
##  Correlation:
##   1     2     3
## 2 0.419
## 3 0.468 0.845
## 4 0.562 0.557 0.583
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        1        4        6
## 1.000000 1.735035 1.617591 1.551579
##
## Coefficients:
##              Value Std.Error  t-value p-value
## (Intercept) 26.406 0.4998885 52.82378       0
## week.f1     -7.315 0.7993318 -9.15139       0
## week.f4     -6.614 0.7247895 -9.12541       0
## week.f6     -4.202 0.6448528 -6.51622       0
##
##  Correlation:
##         (Intr) wek.f1 wek.f4
## week.f1 -0.171
## week.f4 -0.167  0.814
## week.f6 -0.099  0.437  0.446
##
## Standardized residuals:
##         Min          Q1         Med          Q3         Max
## -2.34590240 -0.67640704 -0.02514904  0.62869300  5.40293563
##
## Residual standard error: 4.973828
## Degrees of freedom: 400 total; 396 residual
```

```
#perform the likelihood ratio test
anova(model1,model2)
```

```
##        Model df      AIC      BIC    logLik   Test  L.Ratio p-value
## model1     1 18 2461.368 2533.214 -1212.684
## model2     2 14 2529.588 2585.469 -1250.794 1 vs 2 76.22082  <.0001
```

```r
#model1 is preferable
#the treatment has a significant effect on the outcome
```

(d) Now fit a model with a linear trend for time. What are estimates of the correlations and the variances for each time point? Com- pare with model 1. Use a likelihood ratio statistic to test the null hypothesis of a linear trend versus the maximum model.

```
#fit the model
model3<-gls(Y ~ trt*time, corr=corSymm(, form= ~ tt | ID),
            weights = varIdent(form = ~ 1 | week.f),data=datalong, method="ML")
#show the results
summary(model3)
```

```
## Generalized least squares fit by maximum likelihood
##   Model: Y ~ trt * time
##   Data: datalong
##       AIC      BIC   logLik
##   2584.08 2639.961 -1278.04
##
## Correlation Structure: General
##  Formula: ~tt | ID
##  Parameter estimate(s):
##  Correlation:
##   1     2     3
## 2 0.124
## 3 0.264 0.846
## 4 0.541 0.403 0.489
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        1        4        6
## 1.000000 1.845124 1.557530 1.440191
##
## Coefficients:
##                 Value Std.Error  t-value p-value
## (Intercept) 24.101245 0.6905572 34.90116  0.0000
## trtP         1.938341 0.9765954  1.98479  0.0479
## time        -0.538283 0.1217232 -4.42219  0.0000
## trtP:time    0.169543 0.1721426  0.98490  0.3253
##
##  Correlation:
##           (Intr) trtP   time
## trtP      -0.707
## time      -0.077  0.054
## trtP:time  0.054 -0.077 -0.707
##
## Standardized residuals:
##        Min         Q1        Med         Q3        Max
## -2.3105492 -0.8006086 -0.2873596  0.3600192  5.6744198
##
## Residual standard error: 5.265193
## Degrees of freedom: 400 total; 396 residual
```

```
#estimates of the correlations
model3$modelStruct
```

```
## corStruct  parameters:
## [1] -0.1591711 -0.3436238 -1.5369202 -0.7629008 -0.5407147 -0.2247492
```

```
## varStruct  parameters:
## [1] 0.6125466 0.4431012 0.3647754
```

```r
#the variances for each time point
diag(getVarCov(model3, individual = 2))
```

```
## [1] 27.72226 94.37998 67.25142 57.50010
```

```r
#model 3 is nested in model 1
anova(model3,model1)
```

```
##        Model df      AIC      BIC    logLik   Test  L.Ratio p-value
## model3     1 14 2584.081 2639.961 -1278.040
## model1     2 18 2461.368 2533.214 -1212.684 1 vs 2 130.7129  <.0001
```

```r
#No significant evidence for the presence of a linear trend for time
```

(e) Now add the quadratic term to the model What are estimates of the correlations and the variances for each time point? Compare with model 1 and model 3. Use a likelihood ratio statistic to test the null hypothesis of a linear trend versus the quadratic model. What is your conclusion.

```
#add a quadratic term
timesq<-datalong$time^2
#fit the model
model4<-gls(Y ~ trt*time+trt*timesq, corr=corSymm(, form= ~ tt | ID),
            weights = varIdent(form = ~ 1 | week.f),data=datalong, method="ML")
#show the results
summary(model4)
```

```
## Generalized least squares fit by maximum likelihood
##   Model: Y ~ trt * time + trt * timesq
##   Data: datalong
##        AIC      BIC    logLik
##   2543.271 2607.134 -1255.635
##
## Correlation Structure: General
##  Formula: ~tt | ID
##  Parameter estimate(s):
##  Correlation:
##   1     2     3
## 2 0.377
## 3 0.553 0.671
## 4 0.476 0.646 0.560
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        1        4        6
## 1.000000 1.566820 1.352466 1.602547
##
## Coefficients:
##                 Value Std.Error   t-value p-value
## (Intercept) 25.351579 0.7009071  36.16967  0.0000
## trtP         0.780369 0.9912323   0.78727  0.4316
## time        -6.829683 0.5642678 -12.10362  0.0000
## timesq       1.120091 0.0980822  11.41992  0.0000
## trtP:time    5.996221 0.7979952   7.51411  0.0000
## trtP:timesq -1.037354 0.1387091  -7.47863  0.0000
##
##  Correlation:
##             (Intr) trtP   time   timesq trtP:tim
## trtP        -0.707
## time        -0.169  0.119
## timesq       0.156 -0.110 -0.976
## trtP:time    0.119 -0.169 -0.707  0.690
## trtP:timesq -0.110  0.156  0.690 -0.707 -0.976
##
## Standardized residuals:
##        Min         Q1        Med         Q3        Max
## -2.5483155 -0.7946336 -0.2660397  0.4392487  4.8503926
##
## Residual standard error: 5.043528
```

```
## Degrees of freedom: 400 total; 394 residual
```

```r
#estimates of the correlations
model4$modelStruct
```

```
## corStruct  parameters:
## [1] -0.5029664 -0.7846881 -0.8698819 -0.6533565 -0.8203975 -0.1199224
## varStruct  parameters:
## [1] 0.4490480 0.3019299 0.4715944
```

```r
#the variances for each time point
diag(getVarCov(model4,individual=2))
```

```
## [1] 25.43718 62.44634 46.52880 65.32668
```

```r
#model 3 is nested in model 1
anova(model4,model3)
```

```
##        Model df      AIC      BIC    logLik   Test  L.Ratio p-value
## model4     1 16 2543.271 2607.134 -1255.635
## model3     2 14 2584.081 2639.961 -1278.040 1 vs 2 44.80996  <.0001
```

```r
#No significant evidence for the presence of a linear trend for time
#Model with quadratic term should be chosen
```

(f) Finally fit a spline model

```
#specify the spline model with knot at week 1
#spline model with knot at week 1
week<-datalong$time
week1<-(week-1)*I(week>1)
model5<-gls(Y ~ week*trt+week1*trt, corr=corSymm(, form= ~ tt | ID),
            weights = varIdent(form = ~ 1 | week.f),data=datalong, method="ML")
summary(model5)
```

```
## Generalized least squares fit by maximum likelihood
##   Model: Y ~ week * trt + week1 * trt
##   Data: datalong
##        AIC      BIC    logLik
##   2468.205 2532.069 -1218.103
##
## Correlation Structure: General
##  Formula: ~tt | ID
##  Parameter estimate(s):
##  Correlation:
##   1     2     3
## 2 0.571
## 3 0.561 0.767
## 4 0.574 0.576 0.548
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        1        4        6
## 1.000000 1.325698 1.384878 1.540811
##
## Coefficients:
##                  Value Std.Error   t-value p-value
## (Intercept)  26.419408 0.7075719  37.33812  0.0000
## week        -12.898169 0.7890959 -16.34550  0.0000
## trtP         -0.146465 1.0006578  -0.14637  0.8837
## week1        14.032706 0.8851155  15.85410  0.0000
## week:trtP    11.285231 1.1159501  10.11267  0.0000
## trtP:week1  -12.620116 1.2517423 -10.08204  0.0000
##
##  Correlation:
##            (Intr) week   trtP   week1  wk:trP
## week       -0.216
## trtP       -0.707  0.153
## week1       0.207 -0.988 -0.146
## week:trtP   0.153 -0.707 -0.216  0.699
## trtP:week1 -0.146  0.699  0.207 -0.707 -0.988
##
## Standardized residuals:
##        Min         Q1        Med         Q3        Max
## -2.0220072 -0.6866121 -0.1136505  0.5501114  5.8347294
##
## Residual standard error: 4.972747
## Degrees of freedom: 400 total; 394 residual
```

```r
#Mean group A at time 1
cov_model5_groupA_time1<-c(1,1,0,0,0,0)
mean_model5_groupA_time1<-t(cov_model5_groupA_time1)%*%model5$coefficients
#Mean group P at time 1
cov_model5_groupP_time1<-c(1,1,1,0,1,0)
mean_model5_groupP_time1<-t(cov_model5_groupP_time1)%*%model5$coefficients
#difference between groups at time 1
mean_diff_time1_model5<-mean_model5_groupP_time1-mean_model5_groupA_time1
print(mean_diff_time1_model5)
```

```
##          [,1]
## [1,] 11.13877
```

```r
#Mean group A at time 4
cov_model5_groupA_time4<-c(1,4,0,3,0,0)
mean_model5_groupA_time4<-t(cov_model5_groupA_time4)%*%model5$coefficients
#Mean group P at time 4
cov_model5_groupP_time4<-c(1,4,1,3,4,3)
mean_model5_groupP_time4<-t(cov_model5_groupP_time4)%*%model5$coefficients
#difference between groups at time 4
mean_diff_time4_model5<-mean_model5_groupP_time4-mean_model5_groupA_time4
print(mean_diff_time4_model5)
```

```
##          [,1]
## [1,] 7.134112
```

```r
#estimates of the correlations
model5$modelStruct
```

```
## corStruct  parameters:
## [1] -0.8166528 -0.7986226 -0.9858602 -0.8208646 -0.4909220 -0.1654234
## varStruct  parameters:
## [1] 0.2819390 0.3256121 0.4323092
```

```r
#the variances for each time point
diag(getVarCov(model1,individual=2))
```

```
## [1] 24.72160 43.45862 46.43016 57.47853
```

```r
#Compare this model with the maximum model
anova(model1,model5)
```

```
##        Model df      AIC      BIC    logLik   Test  L.Ratio p-value
## model1     1 18 2461.368 2533.214 -1212.684
## model5     2 16 2468.205 2532.068 -1218.102 1 vs 2 10.83744  0.0044
```

(g) Compare the three models: linear trend, quadratic trend, splines usings AIC. What is your conclusion?

```r
#linear trend model3
aic_model3<-AIC(model3)
#quadratic trend model4
aic_model4<-AIC(model4)
#spline model5
aic_model5<-AIC(model5)
#print the results
print(c(aic_model3,aic_model4,aic_model5))
```

```
## [1] 2584.080 2543.271 2468.205
```

```r
#the spline model seems to be the best choice
```

(h) In the book they estimated this model under the constraint that the means in the two groups are the same at time point 0. Verify that you understand the code and the model. What is the difference between the two groups at time point 1 according to this model?

```r
trt.week<-week*I(datalong$trt=="A")
trt.week1<-week1*I(datalong$trt=="A")
model6<-gls(Y ~ week+trt.week+week1+trt.week1,corr=corSymm(, form= ~ tt | ID),
            weights = varIdent(form = ~ 1 | week.f),data=datalong, method="ML")
summary(model6)
```

```
## Generalized least squares fit by maximum likelihood
##   Model: Y ~ week + trt.week + week1 + trt.week1
##   Data: datalong
##        AIC      BIC    logLik
##   2466.226 2526.098 -1218.113
##
## Correlation Structure: General
##  Formula: ~tt | ID
##  Parameter estimate(s):
##  Correlation:
##   1     2     3
## 2 0.571
## 3 0.560 0.767
## 4 0.575 0.576 0.548
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        1        4        6
## 1.000000 1.325353 1.383210 1.541763
##
## Coefficients:
##                  Value Std.Error   t-value p-value
## (Intercept)  26.342207 0.4997473  52.71105  0.0000
## week         -1.629602 0.7788781  -2.09224  0.0371
## trt.week    -11.249996 1.0882964 -10.33725  0.0000
## week1         1.430494 0.8745148   1.63576  0.1027
## trt.week1    12.582258 1.2231834  10.28649  0.0000
##
##  Correlation:
##           (Intr) week   trt.wk week1
## week      -0.154
## trt.week   0.000 -0.699
## week1      0.148 -0.988  0.691
## trt.week1  0.000  0.690 -0.987 -0.699
##
## Standardized residuals:
##        Min         Q1        Med         Q3        Max
## -2.0147141 -0.6933102 -0.1142911  0.5550591  5.8379246
##
## Residual standard error: 4.974239
## Degrees of freedom: 400 total; 395 residual
```

```r
#Mean group A at time 1
cov_model6_groupA_time1<-c(1,1,1,0,0)
mean_model6_groupA_time1<-t(cov_model6_groupA_time1)%*%model6$coefficients
#Mean group P at time 1
cov_model6_groupP_time1<-c(1,1,0,0,0)
mean_model6_groupP_time1<-t(cov_model6_groupP_time1)%*%model6$coefficients
#difference between groups at time 1
mean_diff_time1_model6<-mean_model6_groupP_time1-mean_model6_groupA_time1
print(mean_diff_time1_model6)
```

```
##       [,1]
## [1,] 11.25
```

Exercise 2

We will model the covariance structure of a subset of the Data from Exercise Therapy Study. Reference: Freund, R.J., Littell, R.C. and Spector, P.C. (1986). SAS Systems for Linear Models, Cary, NC: SAS Institute Inc. The data are from a study of exercise therapies, where 37 patients were assigned to one of two weightlifting programs. In the first program (treatment 1), the number of repetitions 2 was increased as subjects became stronger. In the second program (treatment 2), the num- ber of repetitions was fixed but the amount of weight was increased as subjects became stronger. Measures of strength were taken at baseline (day 0), and on days 2, 4, 6, 8, 10, and 12. Variable List: ID, PROGRAM (1=Repetitions Increase; 2=Weights Increase), Response at Time 1, Re- sponse at Time 2, Response at Time 3, Response at Time 4, Response at Time 5, Response at Time 6, Response at Time 7.We will perform a simulation study to compare the performance of the OLS estimator and the GLS estimator for correlated data.

(a)Check the number of observed subjects. How many missing variables are there for each time point? Reshape the data in long format.

```
#read the data from STATA data set
dat <- read.dta13("exercise.dta")
#count missing variables per each time
count_NAs<-c(sum(is.na(dat$y0)),sum(is.na(dat$y2)),sum(is.na(dat$y4)),
             sum(is.na(dat$y6)),sum(is.na(dat$y8)),sum(is.na(dat$y10)),sum(is.na(dat$y12)))
names(count_NAs)<-colnames(dat)[3:9]
print(count_NAs)
```

```
##  y0  y2  y4  y6  y8 y10 y12
##   0   1   1   1   3   7   7
```

```
#read the data in long format
datalong <- reshape(dat, idvar="ID", varying=c("y0","y2","y4","y6","y8","y10","y12"),v.names="Y",
                    timevar="time",time=c(0,2,4,6,8,10,12), direction="long")
```

(b) Fit a model with an unstructured covariance matrix. Use REML for estimation of the parameters and use a maximal model for the mean structure.

```
#week.f as categorical version of week
week.f <- factor(datalong$time, c(0,2,4,6,8,10,12))
#assign tt to be the integer version of week.f
tt<-as.integer(week.f)
#fit the model
model1 <- gls(Y ~ group*week.f, corr=corSymm(, form= ~ tt | id),
  weights = varIdent(form = ~ 1 | week.f),data=datalong,
  method="REML",na.action=na.omit)
#correlation matrix for the second subject in your dataset
cov2cor(getVarCov(model1,individual=2))
```

```
## Marginal variance covariance matrix
##         [,1]    [,2]    [,3]    [,4]    [,5]    [,6]    [,7]
## [1,] 1.00000 0.96708 0.92446 0.88623 0.84955 0.81421 0.80700
## [2,] 0.96708 1.00000 0.93169 0.87255 0.84588 0.81578 0.79820
## [3,] 0.92446 0.93169 1.00000 0.96054 0.95027 0.90684 0.89154
## [4,] 0.88623 0.87255 0.96054 1.00000 0.95561 0.90752 0.90115
## [5,] 0.84955 0.84588 0.95027 0.95561 1.00000 0.95159 0.93422
## [6,] 0.81421 0.81578 0.90684 0.90752 0.95159 1.00000 0.95731
## [7,] 0.80700 0.79820 0.89154 0.90115 0.93422 0.95731 1.00000
##   Standard Deviations: 1 1 1 1 1 1 1
```

(c) Now fit also a model with an autoregressive correlation structure (corAR1). Note that ?corClasses will give you a list of all possible structures. Print the correlation matrix for subject 2. What is the estimate for the correlation parameter? And the variance?

```
?corClasses
#fit the model with autoregressive correlation structure
model1_AR1 <- gls(Y ~ group*week.f, corr=corAR1(, form= ~ tt | id),
  weights = varIdent(form = ~ 1 | week.f),data=datalong,
  method="REML",na.action=na.omit)
#correlation matrix for the second subject in your dataset
cov2cor(getVarCov(model1_AR1,individual=2))
```

```
## Marginal variance covariance matrix
##         [,1]    [,2]    [,3]    [,4]    [,5]    [,6]    [,7]
## [1,] 1.00000 0.95533 0.91265 0.87189 0.83294 0.79573 0.76019
## [2,] 0.95533 1.00000 0.95533 0.91265 0.87189 0.83294 0.79573
## [3,] 0.91265 0.95533 1.00000 0.95533 0.91265 0.87189 0.83294
## [4,] 0.87189 0.91265 0.95533 1.00000 0.95533 0.91265 0.87189
## [5,] 0.83294 0.87189 0.91265 0.95533 1.00000 0.95533 0.91265
## [6,] 0.79573 0.83294 0.87189 0.91265 0.95533 1.00000 0.95533
## [7,] 0.76019 0.79573 0.83294 0.87189 0.91265 0.95533 1.00000
##   Standard Deviations: 1 1 1 1 1 1 1
```

```
#variance estimates
variances<-diag(cov2cor(getVarCov(model1_AR1,individual=2)))
print(variances)
```

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

```
#covariance estimates are the off diagonal elements
covarinaces<-cov2cor(getVarCov(model1_AR1,individual=2))
covarinaces
```

```
## Marginal variance covariance matrix
##         [,1]    [,2]    [,3]    [,4]    [,5]    [,6]    [,7]
## [1,] 1.00000 0.95533 0.91265 0.87189 0.83294 0.79573 0.76019
## [2,] 0.95533 1.00000 0.95533 0.91265 0.87189 0.83294 0.79573
## [3,] 0.91265 0.95533 1.00000 0.95533 0.91265 0.87189 0.83294
## [4,] 0.87189 0.91265 0.95533 1.00000 0.95533 0.91265 0.87189
## [5,] 0.83294 0.87189 0.91265 0.95533 1.00000 0.95533 0.91265
## [6,] 0.79573 0.83294 0.87189 0.91265 0.95533 1.00000 0.95533
## [7,] 0.76019 0.79573 0.83294 0.87189 0.91265 0.95533 1.00000
##   Standard Deviations: 1 1 1 1 1 1 1
```

(d) Now fit also a model with an exponential correlation structure (corExp). Print the correlation matrix for subject 2. What is the estimate for the correlation parameter? And the variance?

```
#fit the model with autoregressive correlation structure
model1_Exp <- gls(Y ~ group*week.f, corr=corExp(, form= ~ tt | id),
  weights = varIdent(form = ~ 1 | week.f),data=datalong,
  method="REML",na.action=na.omit)
#correlation matrix for the second subject in your dataset
cov2cor(getVarCov(model1_Exp,individual=2))
```

```
## Marginal variance covariance matrix
##         [,1]    [,2]    [,3]    [,4]    [,5]    [,6]    [,7]
## [1,] 1.00000 0.95533 0.91265 0.87189 0.83294 0.79573 0.76018
## [2,] 0.95533 1.00000 0.95533 0.91265 0.87189 0.83294 0.79573
## [3,] 0.91265 0.95533 1.00000 0.95533 0.91265 0.87189 0.83294
## [4,] 0.87189 0.91265 0.95533 1.00000 0.95533 0.91265 0.87189
## [5,] 0.83294 0.87189 0.91265 0.95533 1.00000 0.95533 0.91265
## [6,] 0.79573 0.83294 0.87189 0.91265 0.95533 1.00000 0.95533
## [7,] 0.76018 0.79573 0.83294 0.87189 0.91265 0.95533 1.00000
##   Standard Deviations: 1 1 1 1 1 1 1
```

```
#variance estimates
print(diag(cov2cor(getVarCov(model1_Exp,individual=2))))
```

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

```
#covariance estimates are the off diagonal elements
```

(e) Compare the different models in terms of correlation matrices and model fit. When the models are nested use REML likelihoods and compute a p-value. For non nested models compare the AIC's of the models.

```
#we are comparing models with different covariance structures
#we can use AIC
#model1: varIdent
AIC_ident<-AIC(model1)
#model1: AR1
AIC_AR1<-AIC(model1_AR1)
#model1: corExp
AIC_Exp<-AIC(model1_Exp)
#store AICs in a vector
AIC<-c(AIC_ident,AIC_AR1,AIC_Exp)
names(AIC)<-c("Identity","AR1","Exponential")
print(AIC)
```

```
##    Identity         AR1 Exponential
##    843.5191    823.7970    823.7970
```

(f) For your favourite structure test whether there is a difference between the two groups using a likelihood ratio test.

```
#model1_Exp and model1_AR1 have the same AIC
#toss a coin to decide your favorite one
#model1_Exp
summary(model1_Exp)
```

```
## Generalized least squares fit by REML
##   Model: Y ~ group * week.f
##   Data: datalong
##       AIC      BIC    logLik
##   823.797 898.9512 -389.8985
##
## Correlation Structure: Exponential spatial correlation
##  Formula: ~tt | id
##  Parameter estimate(s):
##    range
## 21.88229
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        4        6        8       10       12        2
## 1.000000 1.152681 1.054478 1.208880 1.190584 1.165831 1.072751
##
## Coefficients:
##                   Value Std.Error  t-value p-value
## (Intercept)    78.32738 1.6938608 46.24192  0.0000
## group           1.36012 1.0303353  1.32007  0.1882
## week.f2         1.17783 0.5464546  2.15541  0.0322
## week.f4         1.35097 0.8037551  1.68083  0.0942
## week.f6         1.12106 0.8898872  1.25978  0.2091
## week.f8         1.73097 1.1411211  1.51691  0.1307
## week.f10        1.53937 1.2449580  1.23649  0.2176
## week.f12        0.89619 1.3152487  0.68138  0.4963
## group:week.f2  -0.27939 0.3308676 -0.84442  0.3993
## group:week.f4  -0.22597 0.4898016 -0.46136  0.6450
## group:week.f6   0.22519 0.5403908  0.41671  0.6773
## group:week.f8  -0.10237 0.6945824 -0.14738  0.8830
## group:week.f10  0.06644 0.7584332  0.08761  0.9303
## group:week.f12  0.58941 0.8093268  0.72828  0.4672
##
##  Correlation:
##                (Intr) group  wek.f2 wek.f4 wek.f6 wek.f8 wk.f10 wk.f12 grp:.2
## group          -0.954
## week.f2         0.077 -0.073
## week.f4         0.110 -0.104  0.682
## week.f6        -0.153  0.146  0.520  0.761
## week.f8         0.010 -0.010  0.455  0.666  0.823
## week.f10       -0.072  0.068  0.386  0.565  0.722  0.855
## week.f12       -0.146  0.140  0.336  0.491  0.653  0.751  0.864
## group:week.f2  -0.074  0.077 -0.954 -0.654 -0.498 -0.436 -0.370 -0.322
## group:week.f4  -0.104  0.109 -0.650 -0.953 -0.725 -0.634 -0.538 -0.468  0.684
## group:week.f6   0.147 -0.154 -0.497 -0.727 -0.954 -0.786 -0.690 -0.623  0.524
```

```
## group:week.f8  -0.010  0.010 -0.434 -0.634 -0.784 -0.953 -0.814 -0.715  0.457
## group:week.f10  0.068 -0.071 -0.368 -0.538 -0.688 -0.814 -0.953 -0.825  0.388
## group:week.f12  0.138 -0.145 -0.316 -0.463 -0.615 -0.707 -0.816 -0.952  0.333
##                grp:.4 grp:.6 grp:.8 gr:.10
## group
## week.f2
## week.f4
## week.f6
## week.f8
## week.f10
## week.f12
## group:week.f2
## group:week.f4
## group:week.f6   0.761
## group:week.f8   0.664  0.824
## group:week.f10  0.563  0.723  0.852
## group:week.f12  0.485  0.646  0.741  0.858
##
## Standardized residuals:
##         Min          Q1         Med          Q3         Max
## -2.26983905 -0.65948026 -0.03387948  0.61680917  2.52960695
##
## Residual standard error: 3.104898
## Degrees of freedom: 239 total; 225 residual
```

```
#look at the p-value for the effect of group 2 on the response
#p-value>0.05
#no significant difference between group 1 and group 2
summary(model1_AR1)
```

```
## Generalized least squares fit by REML
##   Model: Y ~ group * week.f
##   Data: datalong
##       AIC      BIC    logLik
##   823.797 898.9512 -389.8985
##
## Correlation Structure: ARMA(1,0)
##  Formula: ~tt | id
##  Parameter estimate(s):
##      Phi1
## 0.9553296
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##        0        4        6        8       10       12        2
## 1.000000 1.152673 1.054467 1.208863 1.190567 1.165803 1.072748
##
## Coefficients:
##                    Value Std.Error  t-value p-value
## (Intercept)     78.32738 1.6938805 46.24139  0.0000
## group            1.36012 1.0303473  1.32006  0.1882
## week.f2          1.17783 0.5464578  2.15539  0.0322
## week.f4          1.35097 0.8037559  1.68083  0.0942
## week.f6          1.12106 0.8898892  1.25977  0.2091
```

```
## week.f8          1.73097 1.1411159  1.51691  0.1307
## week.f10         1.53938 1.2449545  1.23649  0.2176
## week.f12         0.89619 1.3152359  0.68139  0.4963
## group:week.f2  -0.27939 0.3308696 -0.84442  0.3993
## group:week.f4  -0.22597 0.4898022 -0.46136  0.6450
## group:week.f6   0.22519 0.5403920  0.41671  0.6773
## group:week.f8  -0.10236 0.6945792 -0.14738  0.8830
## group:week.f10  0.06644 0.7584311  0.08760  0.9303
## group:week.f12  0.58941 0.8093188  0.72828  0.4672
##
##  Correlation:
##                (Intr) group  wek.f2 wek.f4 wek.f6 wek.f8 wk.f10 wk.f12 grp:.2
## group          -0.954
## week.f2         0.077 -0.073
## week.f4         0.110 -0.104  0.682
## week.f6        -0.153  0.146  0.520  0.761
## week.f8         0.010 -0.010  0.455  0.666  0.823
## week.f10       -0.072  0.068  0.386  0.565  0.722  0.855
## week.f12       -0.147  0.140  0.336  0.491  0.653  0.751  0.864
## group:week.f2  -0.074  0.077 -0.954 -0.654 -0.498 -0.436 -0.370 -0.322
## group:week.f4  -0.104  0.109 -0.650 -0.953 -0.725 -0.634 -0.538 -0.468  0.684
## group:week.f6   0.147 -0.154 -0.497 -0.727 -0.954 -0.786 -0.690 -0.623  0.524
## group:week.f8  -0.010  0.010 -0.434 -0.634 -0.784 -0.953 -0.814 -0.715  0.457
## group:week.f10  0.068 -0.071 -0.368 -0.538 -0.688 -0.814 -0.953 -0.825  0.388
## group:week.f12  0.138 -0.145 -0.316 -0.463 -0.615 -0.707 -0.816 -0.952  0.333
##                grp:.4 grp:.6 grp:.8 gr:.10
## group
## week.f2
## week.f4
## week.f6
## week.f8
## week.f10
## week.f12
## group:week.f2
## group:week.f4
## group:week.f6   0.761
## group:week.f8   0.664  0.824
## group:week.f10  0.563  0.723  0.852
## group:week.f12  0.485  0.646  0.741  0.858
##
## Standardized residuals:
##         Min          Q1         Med          Q3         Max
## -2.26981267 -0.65947260 -0.03387841  0.61681068  2.52959486
##
## Residual standard error: 3.104934
## Degrees of freedom: 239 total; 225 residual
```

```
#look at the p-value for the effect of group 2 on the response
#p-value>0.05
#no significant difference between group 1 and group 2
```

Exercise 3

We are now further with the dataset of tutorial 1 on data on serum cholesterol from the National Cooperative Gallstone Study. Remember this dataset is a subset of subjects with complete information.

(a) Compute the differences in mean between the two groups at time 0, 6 and 12 according to this model and compare the results with the figure of tutorial 1.

```
data<-read.table("dataex1.txt",header=T)

#Create data set for the treatment group
treat<-subset(data,data$grp==1)
#Create data set for the placebo group
plac<-subset(data,data$grp==2)
#reshape the data set for the treatment group
treatlong<-reshape(treat,varying=c("t1","t2","t3"),v.names="Y",
                   timevar="time",time=c(0,6,12),direction="long")
#reshape the data set for the placebo group
placlong<-reshape(plac,varying=c("t1","t2","t3"),v.names="Y",
                  timevar="time",time=c(0,6,12),direction="long")

#data in long format
datalong<-rbind(treatlong,placlong)
#treat week as factor
week.f <- factor(datalong$time, c(0,6,12))
tt<-as.integer(week.f)
#fit the model
model1 <- gls(Y ~ grp*week.f, corr=corSymm(, form= ~ tt | id),
           weights = varIdent(form = ~ 1 | week.f),
           data=datalong, method="ML")
summary(model1)
```

```
## Generalized least squares fit by maximum likelihood
##   Model: Y ~ grp * week.f
##   Data: datalong
##        AIC     BIC    logLik
##   2749.945 2793.52 -1362.973
##
## Correlation Structure: General
##  Formula: ~tt | id
##  Parameter estimate(s):
##  Correlation:
##   1     2
## 2 0.760
## 3 0.733 0.779
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##         0         6        12
## 1.0000000 0.9320475 0.8721908
##
## Coefficients:
##                    Value Std.Error   t-value p-value
## (Intercept)  216.93684 15.035363 14.428441  0.0000
## grp            9.66316 10.077904  0.958846  0.3385
```

```
## week.f6       33.06124 10.115074  3.268512  0.0012
## week.f12      42.33636 10.443993  4.053657  0.0001
## grp:week.f6  -13.18852  6.779932 -1.945228  0.0528
## grp:week.f12 -16.91818  7.000400 -2.416745  0.0163
##
##  Correlation:
##              (Intr) grp    wek.f6 wk.f12 grp:.6
## grp          -0.944
## week.f6      -0.434  0.410
## week.f12     -0.520  0.491  0.613
## grp:week.f6   0.410 -0.434 -0.944 -0.578
## grp:week.f12  0.491 -0.520 -0.578 -0.944  0.613
##
## Standardized residuals:
##         Min          Q1         Med          Q3         Max
## -2.29179545 -0.68324091 -0.03385625  0.61322084  3.84558013
##
## Residual standard error: 47.25863
## Degrees of freedom: 279 total; 273 residual
```

```
#mean differences for the two groups at time 0
cov_time0_grp0<-c(1,0,0,0,0,0)
mean_time0_grp0<-t(cov_time0_grp0)%*%model1$coefficients
cov_time0_grp1<-c(1,1,0,0,0,0)
mean_time0_grp1<-t(cov_time0_grp1)%*%model1$coefficients
diff_mean_time0<-mean_time0_grp1-mean_time0_grp0
print(diff_mean_time0)
```

```
##          [,1]
## [1,] 9.663158
```

```
#mean differences for the two groups at time 6
cov_time6_grp0<-c(1,0,1,0,0,0)
mean_time6_grp0<-t(cov_time6_grp0)%*%model1$coefficients
cov_time6_grp1<-c(1,1,1,0,1,0)
mean_time6_grp1<-t(cov_time6_grp1)%*%model1$coefficients
diff_mean_time6<-mean_time6_grp1-mean_time6_grp0
print(diff_mean_time6)
```

```
##           [,1]
## [1,] -3.525359
```

```
#mean differences for the two groups at time 6
cov_time12_grp0<-c(1,0,0,1,0,0)
mean_time12_grp0<-t(cov_time12_grp0)%*%model1$coefficients
cov_time12_grp1<-c(1,1,1,1,1,1)
mean_time12_grp1<-t(cov_time12_grp1)%*%model1$coefficients
diff_mean_time12<-mean_time12_grp1-mean_time12_grp0
print(diff_mean_time12)
```

```
##         [,1]
## [1,] 12.6177
```

(b) Now repeat the analysis of (a) for the whole dataset over 5 months. All data is in dataset "datachol.txt". Use na.action=na.omit to use all observed information. Compute again the differences in means between the two groups for the first three time points according to this model. Compare your results with (a). Any explanation for the differences?

```
data<-read.table("datachol.txt")
names(data)<-c("grp","id","t1","t2","t3","t4","t5")
#pay attention t3, t4, t5 must be treated as numeric
data$t3<-as.numeric(data$t3)
data$t4<-as.numeric(data$t4)
data$t5<-as.numeric(data$t5)
#reshape the data set for the placebo group
datalong<-reshape(data,idvar="ID",varying=c("t1","t2","t3","t4","t5"),v.names="Y",
                  timevar="time",time=c(0,6,12,20,24),direction="long")
#treat week as factor
week.f <- factor(datalong$time, c(0,6,12,20,24))
tt<-as.integer(week.f)
#fit the model
model2 <- gls(Y ~ grp*week.f, corr=corSymm(, form= ~ tt | id),
  weights = varIdent(form = ~ 1 | week.f),data=datalong,
  method="REML",na.action=na.omit)


summary(model2)
```

```
## Generalized least squares fit by REML
##   Model: Y ~ grp * week.f
##   Data: datalong
##       AIC      BIC   logLik
##   4315.08 4417.078 -2132.54
##
## Correlation Structure: General
##  Formula: ~tt | id
##  Parameter estimate(s):
##  Correlation:
##   1     2     3     4
## 2 0.770
## 3 0.732 0.775
## 4 0.737 0.796 0.725
## 5 0.589 0.669 0.680 0.626
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##          0         6        12        20        24
## 1.0000000 0.9322233 0.8798468 0.8962108 1.0303535
##
## Coefficients:
##                 Value Std.Error   t-value p-value
## (Intercept)  216.10543 13.942692 15.499548  0.0000
## grp            9.91070  9.412631  1.052915  0.2930
## week.f6       31.78836  9.174749  3.464766  0.0006
## week.f12      41.68341 10.027352  4.156971  0.0000
## week.f20      33.05677 10.526396  3.140369  0.0018
## week.f24      34.92999 14.849945  2.352197  0.0191
```

```
## grp:week.f6  -12.27223  6.193820 -1.981366  0.0482
## grp:week.f12 -16.41754  6.743416 -2.434603  0.0153
## grp:week.f20  -4.97699  6.982010 -0.712830  0.4763
## grp:week.f24  -6.90311  9.791181 -0.705034  0.4812
##
##  Correlation:
##              (Intr) grp    wek.f6 wk.f12 wk.f20 wk.f24 grp:.6 gr:.12 gr:.20
## grp          -0.944
## week.f6      -0.429  0.404
## week.f12     -0.495  0.468  0.579
## week.f20     -0.450  0.424  0.577  0.501
## week.f24     -0.369  0.349  0.454  0.490  0.406
## grp:week.f6   0.404 -0.429 -0.944 -0.547 -0.545 -0.429
## grp:week.f12  0.469 -0.497 -0.549 -0.944 -0.475 -0.464  0.582
## grp:week.f20  0.432 -0.458 -0.554 -0.481 -0.945 -0.388  0.587  0.512
## grp:week.f24  0.357 -0.378 -0.439 -0.474 -0.390 -0.945  0.465  0.504  0.419
##
## Standardized residuals:
##         Min          Q1         Med          Q3         Max
## -2.32089105 -0.68934569 -0.02685698  0.61014662  3.89372935
##
## Residual standard error: 46.76061
## Degrees of freedom: 447 total; 437 residual
```

```
#mean differences for the two groups at time 0
cov_time0_grp0_REML<-c(1,0,0,0,0,0,0,0,0,0)
mean_time0_grp0_REML<-t(cov_time0_grp0_REML)%*%model2$coefficients
cov_time0_grp1_REML<-c(1,1,0,0,0,0,0,0,0,0)
mean_time0_grp1_REML<-t(cov_time0_grp1_REML)%*%model2$coefficients
diff_mean_time0_REML<-mean_time0_grp1_REML-mean_time0_grp0_REML
print(diff_mean_time0_REML)
```

```
##        [,1]
## [1,] 9.9107
```

```
#mean differences for the two groups at time 6
cov_time6_grp0_REML<-c(1,0,1,0,0,0,0,0,0,0)
mean_time6_grp1_REML<-t(cov_time6_grp0_REML)%*%model2$coefficients
cov_time6_grp1_REML<-c(1,1,1,0,0,0,1,0,0,0)
mean_time6_grp1_REML<-t(cov_time6_grp1_REML)%*%model2$coefficients
diff_mean_time6_REML<-mean_time6_grp1_REML-mean_time6_grp1_REML
print(diff_mean_time6_REML)
```

```
##      [,1]
## [1,]    0
```

```
#mean differences for the two groups at time 12
cov_time12_grp0_REML<-c(1,0,0,1,0,0,0,0,0,0)
mean_time12_grp0_REML<-t(cov_time12_grp0_REML)%*%model2$coefficients
cov_time12_grp1_REML<-c(1,1,0,1,0,0,0,1,0,0)
mean_time12_grp1_REML<-t(cov_time12_grp1_REML)%*%model2$coefficients
diff_mean_time12_REML<-mean_time12_grp1_REML-mean_time12_grp0_REML
print(diff_mean_time12_REML)
```

```
##           [,1]
## [1,] -6.506844
```

(c) Now fit a model with the compound symmetry structure for the covariance matrix. For the mean structure use the maximal model. Use REML for estimation. Give the correlation parameter and the variance of the residuals.

```
?corClasses
model3 <- gls(Y ~ grp*week.f, corr=corCompSymm(, form= ~ tt | id),
  weights = varIdent(form = ~ 1 | week.f),data=datalong,
  method="REML",na.action=na.omit)
summary(model3)
```

```
## Generalized least squares fit by REML
##   Model: Y ~ grp * week.f
##   Data: datalong
##        AIC      BIC    logLik
##   4313.099 4378.378 -2140.549
##
## Correlation Structure: Compound symmetry
##  Formula: ~tt | id
##  Parameter estimate(s):
##       Rho
## 0.7217138
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##         0         6        12        20        24
## 1.0000000 0.9106329 0.8731184 0.8968869 1.0769694
##
## Coefficients:
##                  Value Std.Error   t-value p-value
## (Intercept)  216.10543 13.976882 15.461633  0.0000
## grp            9.91070  9.435712  1.050339  0.2941
## week.f6       31.78836 10.028543  3.169788  0.0016
## week.f12      41.81501 10.227304  4.088566  0.0001
## week.f20      33.04128 10.932072  3.022417  0.0027
## week.f24      36.04598 12.754290  2.826185  0.0049
## grp:week.f6  -12.27223  6.770211 -1.812680  0.0706
## grp:week.f12 -16.50600  6.876373 -2.400394  0.0168
## grp:week.f20  -4.88551  7.242599 -0.674552  0.5003
## grp:week.f24  -7.69810  8.391365 -0.917384  0.3594
##
##  Correlation:
##              (Intr) grp    wek.f6 wk.f12 wk.f20 wk.f24 grp:.6 gr:.12 gr:.20
## grp          -0.944
## week.f6      -0.478  0.451
## week.f12     -0.505  0.477  0.546
## week.f20     -0.451  0.426  0.508  0.517
## week.f24     -0.244  0.230  0.417  0.418  0.421
## grp:week.f6   0.451 -0.478 -0.944 -0.515 -0.479 -0.394
## grp:week.f12  0.479 -0.508 -0.517 -0.944 -0.490 -0.397  0.548
## grp:week.f20  0.434 -0.460 -0.488 -0.497 -0.945 -0.402  0.517  0.528
## grp:week.f24  0.236 -0.250 -0.404 -0.405 -0.404 -0.945  0.428  0.431  0.432
##
## Standardized residuals:
##         Min          Q1         Med          Q3         Max
```

```
## -2.37010552 -0.67290271 -0.02742649  0.61874449  3.88420457
##
## Residual standard error: 46.87528
## Degrees of freedom: 447 total; 437 residual
```

```r
#Rho is the estimated correlation parameter
summary(model3$modelStruct)
```

```
## Correlation Structure: Compound symmetry
##  Formula: ~tt | id
##  Parameter estimate(s):
##       Rho
## 0.7217138
## Variance function:
##  Structure: Different standard deviations per stratum
##  Formula: ~1 | week.f
##  Parameter estimates:
##         0         6        12        20        24
## 1.0000000 0.9106329 0.8731184 0.8968869 1.0769694
```

```r
#Variance function:
#variance at time point 0
sigma(model3)
```

```
## [1] 46.87528
```

```r
#relative increase or decrease in variance over time
#the estimates are present in the output
rel_var<-c(1,0.9106329,0.8731184,0.8968869,1.0769694)
#multiply the variance at time 0 by the previous vector
sigma(model3)*rel_var
```

```
## [1] 46.87528 42.68617 40.92767 42.04182 50.48324
```

```r
#these are the estimates for the variances of the residuals
```

(d) Now based on the output obtained in (b) which values would you expect for the variance of the estimators of the intercept and the variance of the residual when using a linear mixed model with a random intercept? Verify you result by fitting this model:

```r
#fit the linear mixed model with random intercept
model4 <- lme(Y ~ grp*week.f, random= ~1| id,data=datalong,method="REML",na.action=na.omit)
summary(model4)
```

```
## Linear mixed-effects model fit by REML
##   Data: datalong
##        AIC      BIC    logLik
##   4315.728 4364.688 -2145.864
##
## Random effects:
##  Formula: ~1 | id
##         (Intercept) Residual
## StdDev:    37.51785 23.71617
##
## Fixed effects:  Y ~ grp * week.f
##                  Value Std.Error  DF   t-value p-value
## (Intercept)  216.10543 13.234410 336 16.329056  0.0000
## grp            9.91070  8.934474 101  1.109265  0.2700
```

```
## week.f6       31.78836 10.000599 336  3.178645  0.0016
## week.f12      41.64067 10.385922 336  4.009338  0.0001
## week.f20      32.91190 11.079720 336  2.970463  0.0032
## week.f24      35.98146 11.627740 336  3.094450  0.0021
## grp:week.f6  -12.27223  6.751347 336 -1.817745  0.0700
## grp:week.f12 -16.42571  6.978203 336 -2.353860  0.0192
## grp:week.f20  -4.79793  7.324612 336 -0.655042  0.5129
## grp:week.f24  -7.59439  7.659611 336 -0.991485  0.3222
##  Correlation:
##              (Intr) grp    wek.f6 wk.f12 wk.f20 wk.f24 grp:.6 gr:.12 gr:.20
## grp          -0.944
## week.f6      -0.378  0.357
## week.f12     -0.364  0.343  0.481
## week.f20     -0.341  0.322  0.451  0.451
## week.f24     -0.325  0.307  0.430  0.427  0.428
## grp:week.f6   0.357 -0.378 -0.944 -0.454 -0.426 -0.406
## grp:week.f12  0.345 -0.366 -0.457 -0.944 -0.427 -0.405  0.484
## grp:week.f20  0.329 -0.348 -0.435 -0.434 -0.945 -0.409  0.461  0.462
## grp:week.f24  0.314 -0.333 -0.416 -0.413 -0.411 -0.945  0.441  0.440  0.440
##
## Standardized Within-Group Residuals:
##         Min          Q1         Med          Q3         Max
## -2.75298512 -0.57321896 -0.04586449  0.50818935  2.82120637
##
## Number of Observations: 447
## Number of Groups: 103
```

```
#Variance of intercept=(37.51785)^2
#Variance of the residual=(23.71617)^2
```