BIOS6643. L05: Full rank, Estimability and Contrasts

Notes

```
##
## Attaching package: 'dplyr'

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union

## -- Attaching packages --------------------------------------- tidyverse 1.3.0 --

## v ggplot2 3.3.3     v purrr   0.3.4
## v tibble  3.0.4     v stringr 1.4.0
## v tidyr   1.1.2     v forcats 0.5.1
## v readr   1.4.0

## -- Conflicts ------------------------------------------ tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()    masks stats::lag()

##
## Attaching package: 'nlme'

## The following object is masked from 'package:dplyr':
##
##     collapse
```

Example 5: Prospective randomized trial

STEPPED-CARE randomized trial. The dataset we will use the class resembles the trial.

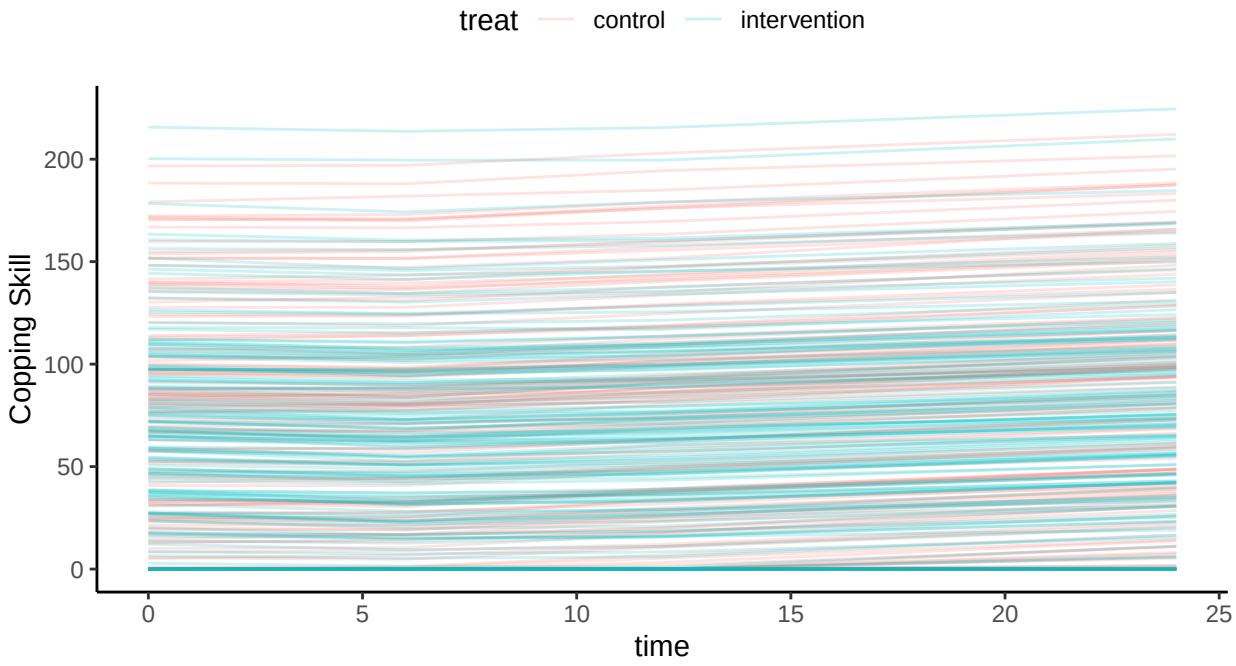
- A behavioral intervention was tested versus usual care in 286 patients with lung or head and neck cancer.

- 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

```
# 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
```



Tests using the Stepped Care data

1. Write a model that includes intervention arm and time as categorical/class variables, plus intervention × time interaction.
2. Provide estimates of means at 6 months for the control and intervention arms.
3. Provide a test for the mean difference at 6 months between the control and intervention arms.
4. Write a test to compare is if trends over time differ between intervention/treatment arms.
5. Write a test to compare changes from beginning to end among the 2 treatment arms.

1. Write a model that includes intervention arm and time as class variables, plus intervention × time interaction.

```
dat.step$time <- as.factor(dat.step$time)

## parameterization 1
fit1 <- lme(cops ~  treat*time,
            random= ~ 1 | id, data = dat.step)
summary(fit1)
```

```
## Linear mixed-effects model fit by REML
##   Data: dat.step
```

```
##        AIC      BIC    logLik
##   7287.948 7338.301 -3633.974
##
## Random effects:
##  Formula: ~1 | id
##         (Intercept) Residual
## StdDev:    51.26149 2.240207
##
## Fixed effects:  cops ~ treat * time
##                              Value Std.Error  DF   t-value p-value
## (Intercept)              65.26599  4.290793 852  15.21071  0.0000
## treatintervention         1.85187  6.068097 284   0.30518  0.7605
## time6                    -0.10908  0.264932 852  -0.41171  0.6807
## time12                    4.10350  0.264932 852  15.48885  0.0000
## time24                   12.40655  0.264932 852  46.82910  0.0000
## treatintervention:time6  -2.07341  0.374671 852  -5.53396  0.0000
## treatintervention:time12 -4.17650  0.374671 852 -11.14712  0.0000
## treatintervention:time24 -5.68776  0.374671 852 -15.18067  0.0000
##  Correlation:
##                          (Intr) trtntr time6  time12 time24 trtn:6 trt:12
## treatintervention        -0.707
## time6                    -0.031  0.022
## time12                   -0.031  0.022  0.500
## time24                   -0.031  0.022  0.500  0.500
## treatintervention:time6   0.022 -0.031 -0.707 -0.354 -0.354
## treatintervention:time12  0.022 -0.031 -0.354 -0.707 -0.354  0.500
## treatintervention:time24  0.022 -0.031 -0.354 -0.354 -0.707  0.500  0.500
##
## Standardized Within-Group Residuals:
##         Min          Q1         Med          Q3         Max
## -3.72260623 -0.35682499 -0.01061719  0.43666407  1.97296829
##
## Number of Observations: 1144
## Number of Groups: 286
```

```
## parameterization 1
fit2 <- lme(cops ~  time + treat:time-1,
            random= ~ 1 | id, data = dat.step)
summary(fit2)
```

```
## Linear mixed-effects model fit by REML
##   Data: dat.step
##        AIC      BIC    logLik
##   7287.948 7338.301 -3633.974
##
## Random effects:
##  Formula: ~1 | id
##         (Intercept) Residual
## StdDev:    51.26149 2.240207
##
## Fixed effects:  cops ~ time + treat:time - 1
##                              Value Std.Error  DF   t-value p-value
## time0                    65.26599  4.290793 851 15.210708  0.0000
## time6                    65.15692  4.290793 851 15.185287  0.0000
## time12                   69.36949  4.290793 851 16.167058  0.0000
```

```
## time24                   77.67254  4.290793 851 18.102143  0.0000
## time0:treatintervention   1.85187  6.068097 851  0.305181  0.7603
## time6:treatintervention  -0.22155  6.068097 851 -0.036510  0.9709
## time12:treatintervention -2.32464  6.068097 851 -0.383092  0.7017
## time24:treatintervention -3.83589  6.068097 851 -0.632140  0.5275
##  Correlation:
##                          time0  time6  time12 time24 tm0:tr tm6:tr tm12:t
## time6                     0.998
## time12                    0.998  0.998
## time24                    0.998  0.998  0.998
## time0:treatintervention  -0.707 -0.706 -0.706 -0.706
## time6:treatintervention  -0.706 -0.707 -0.706 -0.706  0.998
## time12:treatintervention -0.706 -0.706 -0.707 -0.706  0.998  0.998
## time24:treatintervention -0.706 -0.706 -0.706 -0.707  0.998  0.998  0.998
##
## Standardized Within-Group Residuals:
##         Min          Q1         Med          Q3         Max
## -3.72260623 -0.35682499 -0.01061719  0.43666407  1.97296829
##
## Number of Observations: 1144
## Number of Groups: 286
```

Estimating means in the control and intervention arm at 6 weeks

```
## estimate the means in the control and intervention arm at 6 weeks
coef2 <- summary(fit2)$coef$fixed
cov2 <- summary(fit2)$varFix

c6.c <- c(0, 1, 0, 0,
          0, 0, 0, 0)
c6.i <- c(0, 1, 0, 0,
          0, 1, 0, 0)
mu6.control <- c6.c %*% coef2
mu6.int <- c6.i %*% coef2

mu6.control
```

```
##          [,1]
## [1,] 65.15692
```

```
mu6.int
```

```
##          [,1]
## [1,] 64.93537
```

```
se6.control <- sqrt(c6.c %*% cov2  %*%  c6.c)
se6.int <- sqrt(c6.i %*% cov2  %*%  c6.i)
## mean, SE in control
c(mu6.control, se6.control)
```

```
## [1] 65.156917  4.290793
```

```
## mean, SE in intervention
c(mu6.int, se6.int)
```

```
## [1] 64.935372  4.290793
```

Estimating the mean difference in the control and intervention arm at 6 weeks

```
## estimate the difference between intervention and control arm
c6.dif <- c(0, 0, 0, 0,
            0, 1, 0, 0)
mu6.dif <- c6.dif %*% coef2
se6.dif <- sqrt(c6.dif %*% cov2  %*%  c6.dif)
c(mu6.dif, se6.dif)
```

```
## [1] -0.2215455  6.0680971
```

Test the hypothesis that there is an interaction between time and treatment arm

```
## reduced model
fit.red <- lme(cops ~  time -1,
            random= ~ 1 | id, data = dat.step)
summary(fit.red)
```

```
## Linear mixed-effects model fit by REML
##   Data: dat.step
##       AIC      BIC    logLik
##   7514.43 7544.662 -3751.215
##
## Random effects:
##  Formula: ~1 | id
##         (Intercept) Residual
## StdDev:    51.17085 2.558346
##
## Fixed effects:  cops ~ time - 1
##           Value Std.Error  DF  t-value p-value
## time0  66.19193  3.029575 855 21.84858       0
## time6  65.04614  3.029575 855 21.47039       0
## time12 68.20717  3.029575 855 22.51377       0
## time24 75.75460  3.029575 855 25.00502       0
##  Correlation:
##        time0 time6 time12
## time6  0.998
## time12 0.998 0.998
## time24 0.998 0.998 0.998
##
## Standardized Within-Group Residuals:
##         Min          Q1         Med          Q3         Max
## -2.73520594 -0.49225345  0.01599713  0.52439734  2.26092727
##
## Number of Observations: 1144
## Number of Groups: 286
```

```
anova.lme(fit2, fit.red)
```

```
## Warning in anova.lme(fit2, fit.red): fitted objects with different fixed
## effects. REML comparisons are not meaningful.
```

```
##         Model df      AIC      BIC    logLik   Test  L.Ratio p-value
## fit2        1 10 7287.948 7338.301 -3633.974
## fit.red     2  6 7514.430 7544.662 -3751.215 1 vs 2 234.4814  <.0001
```

```
fit2$logLik
```

```
## [1] -3633.974
```

```
fit.red$logLik
```

```
## [1] -3751.215
```

```
2*(fit2$logLik-fit.red$logLik)
```

```
## [1] 234.4814
```

```
pchisq(2*(fit2$logLik-fit.red$logLik), 4, ncp=0, lower.tail=FALSE, log.p=FALSE)
```

```
## [1] 1.431442e-49
```

Construct a wald-type test for the hypothesis that there is an interaction between time and treatment arm

```
##  testing all parameters corresponding to the diff in means are 0
c.w <- matrix(c(0, 0, 0, 0, 1, 0, 0, 0,
                0, 0, 0, 0, 0, 1, 0, 0,
                0, 0, 0, 0, 0, 0, 1, 0,
                0, 0, 0, 0, 0, 0, 0, 1), byrow=T, 4, 8)

c.wa <- c.w%*%coef2
## chisquare test value
chisq.v <- t(c.wa)%*%solve(c.w%*% cov2  %*%t(c.w)) %*% c.wa
pval.w <- pchisq(chisq.v, 4, ncp=0, lower.tail=FALSE, log.p=FALSE)
pval.w
```

```
##             [,1]
## [1,] 9.69305e-56
```