STAT 3119

Week 15: 12/5/2019 @GWU

Outline

- Additional Design topics: Repeated Measures Design and split-plot design (Chapter 27)
- Part II: Discussion and Questions for the materials covered, quizzes/mid-term or final review concepts

Elements of Repeated Measures Designs (Ch 27.1)

- Repeated measures designs—designs that are widely used in the behavioral and biomedical sciences, including studies of persons, households, observers, and experimental animals.
- The study subject (e.g. patients/study participants) therefore serves as a block, and the same subject is measured repeatedly to study the treatment effects.
- A repeated measures study may involve several treatments or only a single treatment applied to the same subject that is evaluated at different points in time.

Examples of repeated measures designs:

- 1. Two hundred persons who have persistent migraine headaches are each to be given two different drugs and a placebo, for two weeks each, with the order of the drugs randomized for each person. The subjects in the study are the persons with migraine headaches. (This is also called "3 by 3 cross-over" design.)
- 2. In a weight loss study, 100 overweight persons are to be given the same diet and their weights measured at the end of each week for 12 weeks to assess the weight loss over time. Here the subjects are the overweight persons, who are observed repeatedly to provide information about the effects of a single treatment over time.

Advantages:

A principal advantage of repeated measures designs is that they provide good precision for comparing treatments because all sources of variability between subjects are excluded from the experimental error. Thus, one may view the subjects as serving as their own controls.

Disadvantages:

- Order effect: response depends on the position in the treatment order/sequence
- Carryover effect: response is affected by the preceding treatment
- Missing data: incomplete information for some treatments out of the entire treatment sequence for the same subject

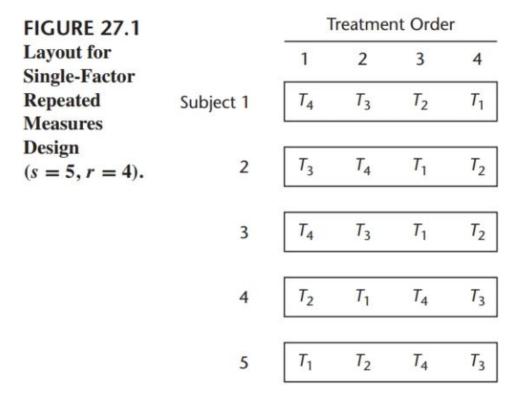
How to Randomize

The randomization of the order of the treatments assigned to a subject is straightforward. For each subject, a **random permutation** is used to define the treatment order (e.g. for three treatments, ABC, BAC, CBA, etc.), and independent permutations are selected for the different subjects. Some of the 'Latin square' with balanced treatment assignment that we discussed in the block design may be utilized.

Single-Factor Experiments with Repeated Measures on All Treatments (Ch 27.2)

- We first consider repeated measures designs where the treatments are based on a single factor.
- Almost always, the subjects in repeated measures designs (persons, stores, test markets, experimental animals) are viewed as a **random sample** from a population. Therefore, the effects of subjects will be viewed as random. This is the special case of randomized complete block design (RCBD) with the subject being the random *block*. The random effect assumption is also a way to introduce the within-subject correlation for modelling the data.

Example: the layout for a single-factor experiment with repeated measures on all treatments. Here, there are 5 subjects and 4 treatments, with the order of treatments independently randomized for each subject.



When treatment effects are fixed, we can use the model for RCBD design with random blocks (s random subjects):

$$Y_{ij} = \mu ... + \rho_i + \tau_j + \varepsilon_{ij} \tag{27.1}$$

where:

 μ .. is a constant ρ_i are independent $N(0, \sigma_\rho^2)$ τ_j are constants subject to $\sum \tau_j = 0$ ε_{ij} are independent $N(0, \sigma^2)$ ρ_i and ε_{ij} are independent $i = 1, \dots, s; j = 1, \dots, r$

Hence, we know from Section 25.5 that repeated measures model (27.1) assumes the following about the observations Y_{ij} :

$$E\{Y_{ij}\} = \mu.. + \tau_j$$
 (27.2a)

$$\sigma^{2}{Y_{ij}} = \sigma_{Y}^{2} = \sigma_{\rho}^{2} + \sigma^{2}$$
 (27.2b)

$$\sigma\{Y_{ij}, Y_{ij'}\} = \sigma_{\rho}^2 = \omega \sigma_Y^2 \qquad j \neq j'$$
 (27.2c)

$$\sigma\{Y_{ij}, Y_{i'j'}\} = 0$$
 $i \neq i'$ (27.2d)

where ω is the coefficient of correlation between any two observations for the same subject:

$$\omega = \frac{\sigma_{\rho}^2}{\sigma_{\nu}^2} \tag{27.2e}$$

Thus, this repeated measures model (27.1) assumes

- 1) In advance of the random trials, any two treatment observations for a given subject are correlated in the same fashion for all subjects. As we discussed in (25.71), that the variance-covariance matrix of the observations Y_{ij} for any given subject has compound symmetry. Any two observations from different subjects in advance of the random trials are independent.
- 2) There are no interference effects in the repeated measures study, such as order effects or carryover effects from one treatment to the next.

Analysis of Variance and Tests

The analysis of variance and the test for treatment effects will be the same, following the randomized complete block model with random block effects (25.67).

$$SSTO = SSS + SSTR + SSTR.S$$

where

- $SSS(block) = sum \ of \ squares \ for \ subjects$
- $SSTR.S = interaction \ sum \ of \ squares \ between \ treatments \ and \ subjects$ (used to estimate the error variance)

TABLE 27.1 ANOVA Table for Single-Factor Repeated Measures Design—ANOVA Model (27.1) with Subject Effects Random and Treatment Effects Fixed.

Source of Variation	SS	df	MS	E {MS}
Subjects	SSS	s — 1	MSS	$\sigma^2 + r\sigma_\rho^2$
Treatments	SSTR	r – 1	MSTR	$\sigma^2 + s \frac{\sum \tau_j^2}{r-1}$
Error	SSTR.S	(r-1)(s-1)	MSTR.S	σ^2
Total	SSTO	sr - 1		

where:

$$SSTO = \sum_{i} \sum_{j} (Y_{ij} - \overline{Y}_{.})^{2}$$
 (27.3a)

$$SSS = r \sum_{i} (\overline{Y}_{i}. - \overline{Y}.)^{2}$$
 (27.3b)

$$SSTR = s \sum_{j} (\overline{Y}_{j} - \overline{Y}_{.})^{2}$$
 (27.3c)

$$SSTR.S = \sum_{i} \sum_{i} (Y_{ij} - \overline{Y}_{i.} - \overline{Y}_{j} + \overline{Y}_{.})^{2}$$
 (27.3d)

To test treatment effects, we use

$$F^* = MSTR/MSTR.S$$

which follows a F(r-1, (r-1)(s-1)) distribution.

Note:

In repeated measures studies, SSTR and SSTR.S are sometimes combined into a within-subjects sum of squares SSW:

$$SSW = SSTR + SSTR.S$$

where

$$SSW = \sum_{i} \sum_{j} (Y_{ij} - \overline{Y}_{i.})^{2}$$
 (27.4a)

Hence, the ANOVA decomposition in (27.3) can also be expressed as follows:

Data analysis: Wine-Judging Example

- In a wine-judging competition, four red wines of the same vintage were judged by six experienced judges. Each judge tasted the wines in a blind fashion, i.e., without knowing their identities.
- The order of the wine presentation was randomized independently for each judge. To reduce carryover and other interference effects, there is *washout* period between tastings (e.g. same mouthwash may be used between and before each wine tasting).
- Each wine was scored on a 40-point scale; the higher the score, the greater is the excellence of the wine. The data for this competition are presented in Table 27.2.
- The six judges are considered to be a random sample from the population of possible judges, while the 4 wines tasted are of interest in themselves. Hence, single-factor repeated measures model (27.1) was expected to be appropriate, with the effects of subjects judges) considered random and the effects of treatments (wines) considered fixed.

TABLE 27.2 Data—Wine-Judging Example (ratings on a scale of 0 to 40).

Judge		Wine (j)			
i	1	2	3	4	\overline{Y}_i .
1	20	24	28	28	25
2	15	18	23	24	20
3	18	19	24	23	21
4	26	26	30	30	28
5	22	24	28	26	25
6	19	21	27	25	23
$\overline{Y}_{i,j}$	20.00	22.00	26.67	26.00	$23.67 = \overline{Y}.$

R analysis:

Step1: Read the data

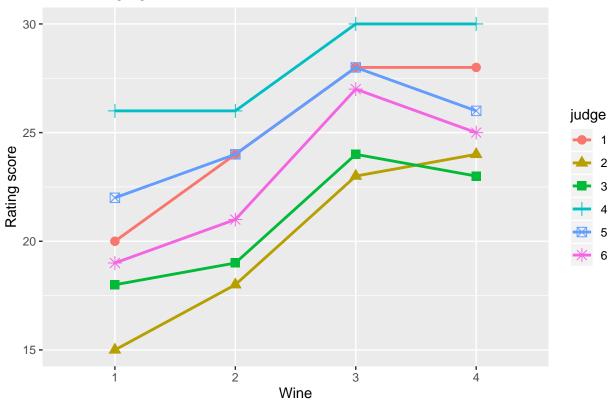
```
Wine =read.table(
          url("https://raw.githubusercontent.com/npmldabook/Stat3119/master/Week-15/CH27TA02.txt"))
names(Wine) = c("score", "judge", "wine")

# make categorical variables for factor A and B
Wine$judge = as.factor(Wine$judge)
Wine$wine = as.factor(Wine$wine)
str(Wine)

## 'data.frame': 24 obs. of 3 variables:
## $ score: int 20 24 28 28 15 18 23 24 18 19 ...
## $ judge: Factor w/ 6 levels "1","2","3","4",..: 1 1 1 1 2 2 2 2 3 3 ...
## $ wine : Factor w/ 4 levels "1","2","3","4": 1 2 3 4 1 2 3 4 1 2 ...
```

Step2: plot the data

Wine Judging



Results: We see that there are some distinct differences in ratings between judges but that the ratings for wine-3 and wine-4 are consistently best and for wine-1 generally worst. We also see that the rating curves for the judges do not appear to exhibit substantial departures from being parallel. Hence, an additive model appears to be appropriate.

Step3: ANOVA analysis

```
# Additive ANOVA
fit = aov(score ~ judge+ wine, data=Wine)
summary(fit)
##
               Df Sum Sq Mean Sq F value
                                            Pr(>F)
                  173.3
                           34.67
                                     32.5 1.55e-07 ***
## judge
## wine
                3
                  184.0
                           61.33
                                     57.5 1.85e-08 ***
## Residuals
                    16.0
                            1.07
               15
```

```
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Results: For random block additive model, tests for both judge (block) and wine (treatment) are the same as the fixed ANOVA. Therefore, both tests were significant, the mean wine ratings for the four wines differs and there are significant differences among the judges.

Step 4: estimate the fix effects and variance component

```
library(lme4)
## Loading required package: Matrix
library(lmerTest)
## Attaching package: 'lmerTest'
## The following object is masked from 'package:lme4':
##
##
       lmer
## The following object is masked from 'package:stats':
##
##
       step
fit.wine <- lmer(score ~ wine + (1 | judge) , data = Wine )
summary(fit.wine)
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: score ~ wine + (1 | judge)
##
     Data: Wine
##
## REML criterion at convergence: 82.6
##
## Scaled residuals:
      Min
               1Q Median
                                ЗQ
                                       Max
## -1.4002 -0.4022 -0.1514 0.6852 1.7429
##
## Random effects:
  Groups
                         Variance Std.Dev.
             (Intercept) 8.400
                                  2.898
##
   judge
##
   Residual
                         1.067
## Number of obs: 24, groups: judge, 6
## Fixed effects:
##
              Estimate Std. Error
                                        df t value Pr(>|t|)
## (Intercept) 20.0000 1.2561 5.9485 15.922 4.20e-06 ***
## wine2
                 2.0000
                            0.5963 15.0001
                                             3.354 0.00435 **
```

```
## wine3
                 6.6667
                            0.5963 15.0001 11.180 1.13e-08 ***
## wine4
                 6.0000
                            0.5963 15.0001 10.062 4.60e-08 ***
                   0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## Signif. codes:
##
## Correlation of Fixed Effects:
         (Intr) wine2 wine3
## wine2 -0.237
## wine3 -0.237
                0.500
                0.500 0.500
## wine4 -0.237
```

Results: From the random effects output, we find the $\sigma_{\rho}^2=8.400$, and $\sigma^2=1.067$, therefore, the within-subject (intra-class) correlation is 8.40/(8.40+1.067)=0.887, i.e., the rating for the same judges are positively correlation with high correlation. The total variances are mostly explained by the variability in the mean ratings by different judges.

From the fixed effects output, we can find that wines 2-4 are significantly better than wine-1 (the reference category). We can change the contrast options or use **vcov(fit.wine)** to get variance-covariance matrix of the fixed effects to make further inference about the differences or contrasts among the four wines.

Two-factor experiments with Repeated Measures on One Factor (ch 27.3)

In many two-factor studies, repeated measures can only be made on one of the two factors.

Example In an experiment,

- researcher wished to study the effects of two types of incentives (factor A) on a person's ability to solve problems.
- The researcher also wanted to study two types of problems (factor B)—abstract and concrete problems.
- Each experimental subject could be asked to do each type of problem, but could not be exposed to more than one type of incentive stimulus because of potential interference effects.

Thus, the design the experimenter utilized may be represented schematically as shown in Figure 27.5.

FIGURE 27.5 Layout for			Treatment Order	
Two-Factor	Incentive Stimulus	Subject	1	2
Design with Random Assignments of	-	1	A_1B_1	A ₁ B ₂
Factor A Level to Subjects and	A_1	i	:	
Repeated Measures on Factor B.	~	S	A_1B_1	A ₁ B ₂
ractor B.		s + 1	A_2B_2	A ₂ B ₁
	A_2	i	:	
		2 s	A_2B_1	A_2B_2

For such experiment of **two-factor experiment with repeated measures on one factor**, two randomizations generally need to be employed. First, the level of the non-repeated factor (A, in Figure 27.5) needs to be *randomly* assigned to the subjects. Second, the order of the levels of the **repeated** factor (B, in Figure 27.5) needs to be *randomized* independently for all subjects.

Note: In the experiment depicted in Figure 27.5, comparisons between factor A level means involve differences between groups of subjects as well as differences associated with the two factor A levels. The main effects of factor A are therefore are **confounded** with differences between groups of subjects, whereas the main effects of factor B (compared with subjects) are free of such confounding.

Statistical Model

Connecting with our earlier discussion:

- 1. two factor ANOVA (model effects of A, B, A:B),
- 2. random effects: subjects (block) is a random factor
- 3. nested factor: subjects are nested within A (different subjects in different levels of A)

Put everything together, we can use the following model:

$$Y_{ijk} = \mu ... + \rho_{i(j)} + \alpha_j + \beta_k + (\alpha \beta)_{jk} + \varepsilon_{ijk}$$
(27.11)

where:

```
\mu... is a constant \rho_{i(j)} are independent N(0, \sigma_{\rho}^2) \alpha_j are constants subject to \sum \alpha_j = 0 \beta_k are constants subject to \sum \beta_k = 0 (\alpha \beta)_{jk} are constants subject to \sum_j (\alpha \beta)_{jk} = 0 for all k and \sum_k (\alpha \beta)_{jk} = 0 for all j \varepsilon_{ijk} are independent N(0, \sigma^2) \rho_{i(j)} and \varepsilon_{ijk} are independent i = 1, \ldots, s; j = 1, \ldots, a; k = 1, \ldots, b
```

Analysis strategy

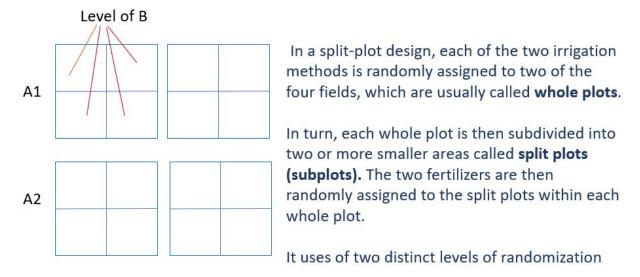
Given the experiment data, with the correct model specification such as the level of factors, random vs. fixed effects, nested vs. cross-factors, we already know how to set up a regression model (In R: lm() for fixed factor model and lmer() for model involving at least one random factor), then we can fit the appropriate model our data to test and estimate the factor effects. Regression models do not limit to the restriction of balanced observations (required for using a multi-factor ANOVA table for testing).

Split-Plot Design

- The so-called Split-Plot design is a two-factor experiments with repeated Measures on One Factor. Such design is frequently used in field, laboratory, industrial, and social science experiments. In some multifactor factorial experiments, we may be unable to completely randomize the order of the runs. This often results in a generalization of the factorial design called a **split-plot** design.
- Split-plot designs were originally developed for agricultural experiments. Consider an investigation to study the effects of two irrigation methods (factor A) and two fertilizers (factor B) on yield of a crop, using four available fields as experimental units. In a completely randomized design, four treatments (A1B1, A1B2, A2B1, A2B2) would then be assigned at random to the four fields. **Problem**: Since there are four treatments and just four experimental units, there will be no degrees of freedom for estimation of error.

	Source of Variation	Degrees of Freedom
	Factor A (irrigation methods)	1
		1
5	AB interactions	1
A2B2	Error	0
	Total	3
	A2B2	A2B2 Error

• If the fields could be subdivided into smaller experimental units, replicates of each factor-level combination could be obtained and the error variance could then be estimated. Unfortunately, in this investigation it is not possible to apply different irrigation methods (factor A) in areas smaller than a field, although different fertilizer types (factor B) could be applied in relatively small areas. A split-plot design can accommodate this situation.



Other example:

• Split-plot designs are useful in industrial experiments when one factor requires larger experimental units than another. Consider, for instance, a study of the effects of two additives (factor A) and two different containers (factor B) for prolonging the shelf life of a milk product. Here, it is easier to make larger batches of the milk product with a given additive (whole plot treatment), whereas the different containers (split-plot/Subplot treatment) can be used with smaller batches.

Split-plot model and ANOVA

We can then use the same model for the two-factor with repeated measures design on one factor (subject) for the **split-plot model**.

$$Y_{ijk} = \mu \dots + \rho_{i(j)} + \alpha_j + \beta_k + (\alpha\beta)_{jk} + \varepsilon_{ijk}$$
 (27.27)

For the split-plot agricultural experiment example, α_j denotes the main effect of the jth irrigation method (jth whole-plot treatment) and β_k denotes the main effect of the kth fertilizer type (kth split-plot treatment). Also, $\rho_{i(j)}$ denotes the effect of the ith whole plot, nested within the jth level of factor A (irrigation method).

For balanced studies, we have the following ANOVA Table to study the source of variation and test the factor effects.

TABLE 27.13 ANOVA Table for Two-Factor Split-Plot Experiment.

Source of Variation	SS	df	MS	F- Test
Whole plots Factor <i>A</i> Whole-plot error	SSA SSW(A)	<i>a</i> − 1 <i>a</i> (<i>s</i> − 1)	MSA — MSW(A)←	Factor A: F= MSA/MSW(A)
Split plots Factor B AB interactions Split-plot error Total	SSB SSAB SSB.W(A) SSTO	b-1 $(a-1)(b-1)$ $a(s-1)(b-1)$ $abs-1$	MSB MSAB MSB.W(A)	Factor B: F= MSB/MSB.W(A) Interaction A:B F= MSAB/MSB.W(A)

For unbalanced study, we rely on regression model for testing and estimation.

Split-plot example and analysis

We will Athletic Shoes Sales Example on page 1145-1146.

Example A national retail chain wanted to study the effects of two advertising campaigns (factor A) on the volume of sales of athletic shoes over time (factor B).

- Ten similar test markets (subjects, S) were chosen at random to participate in this study.
- The two advertising campaigns (A1 and A2) were similar in all respects except that a different national sports personality was used in each.
- Sales data were collected for three two-week periods (B1: two weeks prior to campaign; B2: two weeks during which campaign occurred; B3: two weeks after campaign was concluded).
- The experiment was conducted during a six-week period when sales of athletic shoes are usually quite stable. The data on sales (coded) are presented in Table 27.7.

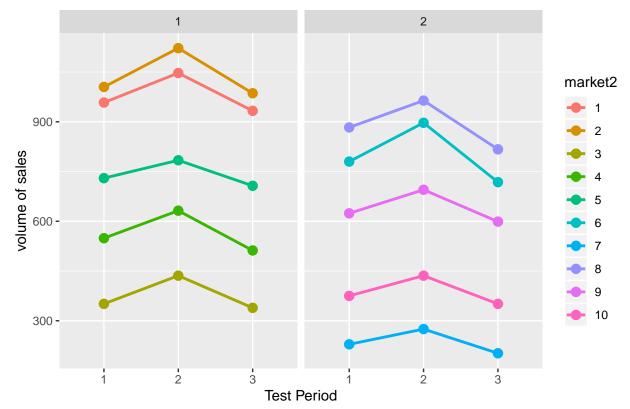
Step1: Read the data

```
Shoe$TestPeriod = as.factor(Shoe$TestPeriod)
Shoe$market2 = as.factor(Shoe$market2)

## 'data.frame': 30 obs. of 5 variables:
## $ sales : int 958 1005 351 549 730 1047 1122 436 632 784 ...
## $ market : Factor w/ 5 levels "1","2","3","4",..: 1 2 3 4 5 1 2 3 4 5 ...
## $ Campaign : Factor w/ 2 levels "1","2": 1 1 1 1 1 1 1 1 1 1 ...
## $ TestPeriod: Factor w/ 3 levels "1","2","3": 1 1 1 1 1 2 2 2 2 2 ...
## $ market2 : Factor w/ 10 levels "1","2","3","4",..: 1 2 3 4 5 1 2 3 4 5 ...
```

Step2: Plot the data by by test market for each advertising campaign

Shoe sales



Findings: There are 10 markets with 5 market nested with the Campaign methods. There is no evidence of any interactions between the test markets and the treatments. In general, sales tended to increase during each advertising campaign, and then tended to decline to previous or lower levels than just before the campaign.

Step 3. ANOVA analysis: specify the correct nested structure.

```
shoefit <- aov(sales ~ Campaign *TestPeriod + Error(Campaign/market),data=Shoe)
summary(shoefit)</pre>
```

```
##
## Error: Campaign
           Df Sum Sq Mean Sq
##
## Campaign 1 168151 168151
##
## Error: Campaign:market
                Sum Sq Mean Sq F value Pr(>F)
##
             Df
             8 1833681 229210
## Residuals
##
## Error: Within
##
                       Df Sum Sq Mean Sq F value
## TestPeriod
                          67073
                                   33537
                                          93.686 1.47e-09 ***
## Campaign:TestPeriod 2
                             391
                                     196
                                           0.547
                                                    0.589
## Residuals
                            5727
                                     358
                       16
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
Results (p.1147):
```

denominator, we recalculate the F-test and p-value.

1) To test the whole plot results, we use the whole plot error (Error: Campaign:market) = 229210 as the

```
MSA= 168151

MSW.inA = 229210

(FA= MSA/MSW.inA)

## [1] 0.7336111
```

```
(Pv= 1- pf(FA, 1,8))
```

[1] 0.4166317

So F-statistic =0.73 with p-value =0.42, we can't reject null (that no advertising campaign main effects exist).

2) To test the subplot (split-plots) results and we use residual errors within subjects. The F-test and p-values for the A:B interaction and effect of the TestPeriod are correct. We find there is a significant effects of test period. But the interaction effect is not significant.

Step 4. Evaluate the random market effect

```
library(lmerTest)
ranfit <- lmer(sales ~ Campaign * TestPeriod + (1 | market2), data = Shoe)
summary(ranfit)
## Linear mixed model fit by REML. t-tests use Satterthwaite's method [
## lmerModLmerTest]
## Formula: sales ~ Campaign * TestPeriod + (1 | market2)
##
     Data: Shoe
##
## REML criterion at convergence: 270.6
##
## Scaled residuals:
       Min
                 1Q
                      Median
                                    3Q
                                            Max
## -1.46621 -0.41184 -0.03545 0.50875 1.86359
##
## Random effects:
                         Variance Std.Dev.
## Groups
            Name
## market2 (Intercept) 76284
                                  276.20
## Residual
                           358
                                   18.92
## Number of obs: 30, groups: market2, 10
## Fixed effects:
##
                         Estimate Std. Error
                                                  df t value Pr(>|t|)
## (Intercept)
                          718.60
                                     123.81
                                               8.05
                                                      5.804 0.000394 ***
## Campaign2
                          -140.40
                                      175.09
                                               8.05 -0.802 0.445652
## TestPeriod2
                            85.60
                                       11.97
                                              16.00
                                                      7.154 2.29e-06 ***
## TestPeriod3
                           -23.20
                                       11.97
                                              16.00 -1.939 0.070370
## Campaign2:TestPeriod2
                                       16.92
                                              16.00 -0.615 0.547484
                          -10.40
## Campaign2:TestPeriod3
                           -17.60
                                              16.00 -1.040 0.313787
                                       16.92
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
               (Intr) Cmpgn2 TstPr2 TstPr3 C2:TP2
##
              -0.707
## Campaign2
## TestPeriod2 -0.048 0.034
## TestPeriod3 -0.048 0.034 0.500
## Cmpgn2:TsP2 0.034 -0.048 -0.707 -0.354
## Cmpgn2:TsP3 0.034 -0.048 -0.354 -0.707 0.500
```

Results: From the $random\ effects$ section, we find the variance due to variability of markets is 76284, which account for 76284/(76284+358)=99.5% of the total variance.

Summary

- Reading: Briefly for Chapter 27.1-27.3, 27.6 (this chapter will not be tested in the final)
- Final exam is Dec 12 (Thursday) at this classroom: 7:40 -9:40pm

Question and Office hours next week

• Additional o ice hours by the TA: 2-3 pm next Tuesday.

• No more class next Tuesday

I will hold **two office hours remotely on Monday and Wed evening by WebEx** (since I don't have office here and not sure which classroom is available after the class ends).

- \bullet Monday (Dec 9th) 7:30- 8:30 pm
- Wed (Dec 11th) 7:30- 8:30 pm
- Conference call-line (can host the whole class):
 - Log in with a computer to share screen/discuss your questions: https://nih.webex.com/join/tianxnih.gov
 - by phone: 1-650-479-3208
 - Access code: 623 734 702
 - attendee code : press '#' or use the code in login screen.

