STAT 3119

Week 11: 11/5/2019 @GWU

Outline

- Two-way ANOVA model and equivalent regression formulation (unbalanced studies)
- Estimation and testing the model parameters
- Inference about factor effects
- Empty Cells in Two factor studies
- Missing values in RCBD design

Review ANCOVA : Quiz#4 This Thursday

- ANCOVA
  - Goal of ANCOVA
  - Single-factor ANCOVA factor effects model
  - Equivalent regression model: how to set the $r-1$ indicator functions to indicate r treatment levels
  - Two additional ANCOVA assumptions
  - How to test and estimate model parameters and treatment effects

Estimation of treatment effects (p.930-932)

Mean Response at $X = \bar{X}..$	Estimator	Variance
$\mu. + \tau_1$	$\hat{\mu}. + \hat{\tau}_1$	$\sigma^2\{\hat{\mu}.\} + \sigma^2\{\hat{\tau}_1\} + 2\sigma\{\hat{\mu}., \hat{\tau}_1\}$
$\mu. + \tau_2$	$\hat{\mu}. + \hat{\tau}_2$	$\sigma^2\{\hat{\mu}.\} + \sigma^2\{\hat{\tau}_2\} + 2\sigma\{\hat{\mu}., \hat{\tau}_2\}$
$\mu. + \tau_3$	$\hat{\mu}. - \hat{\tau}_1 - \hat{\tau}_2$	$\sigma^2\{\hat{\mu}.\} + \sigma^2\{\hat{\tau}_1\} + \sigma^2\{\hat{\tau}_2\} - 2\sigma\{\hat{\mu}., \hat{\tau}_1\} - 2\sigma\{\hat{\mu}., \hat{\tau}_2\} + 2\sigma\{\hat{\tau}_1, \hat{\tau}_2\}$

Comparison	Estimator	Variance
$\tau_1 - \tau_2$	$\hat{\tau}_1 - \hat{\tau}_2$	$\sigma^2\{\hat{\tau}_1\} + \sigma^2\{\hat{\tau}_2\} - 2\sigma\{\hat{\tau}_1, \hat{\tau}_2\}$
$\tau_1 - \tau_3 = 2\tau_1 + \tau_2$	$2\hat{\tau}_1 + \hat{\tau}_2$	$4\sigma^2\{\hat{\tau}_1\} + \sigma^2\{\hat{\tau}_2\} + 4\sigma\{\hat{\tau}_1, \hat{\tau}_2\}$
$\tau_2 - \tau_3 = \tau_1 + 2\tau_2$	$\hat{\tau}_1 + 2\hat{\tau}_2$	$\sigma^2\{\hat{\tau}_1\} + 4\sigma^2\{\hat{\tau}_2\} + 4\sigma\{\hat{\tau}_1, \hat{\tau}_2\}$

Note: For these treatment effects or other linear combinations with μ.,τ1, τ2, τ3

Use the facts (1) $\tau_3 = -\tau_1 - \tau_2$

(2) $\text{Var}(aX \pm bY) = a^2\text{Var}(X) + b^2\text{Var}(Y) \pm 2ab\ \text{cov}(X,Y)$

Two-Factor Studies with unequal sample size (Ch 23.1)

Our previous discussions (chapter 19-22) have restricted to equal treatment sample sizes ("balanced") for the two-factor ANOVA model

- ANOVA SS decomposition is orthogonal
- Computation is much easier

Often, two-factor studies involve unequal treatment sample sizes ("unbalanced")

- The experiment planned for a balanced design, but the observed data are unbalanced because of dropouts or missing data.
- In observation studies, the data were simply collected, and so the researchers had no complete control over the number of observations in each "treatment".
- Some factor levels may be more important or more prevalent than others, and the experimenter wishes these to be over-represented or sampled with certain proportions/distributions in the data.

Notation and Estimation

Most of the notations remain the same, unlike before (we used the same n within treatment),

- n_{ij}= sample size for the treatment consisting of the ith level of factor A and the jth level of factor B
- The total number of cases for the ith level of factor A: $n_{i.} = \sum_j n_{ij}$
- The total number of cases for the jth level of factor B: $n_{.j} = \sum_i n_{ij}$
- Total sample size for the study $n_T = \sum_i \sum_j n_{ij}$
- Estimate of treatment mean is still the sample mean:

$$\hat{\mu}_{ij} = \overline{Y}_{ij.} = \sum_k Y_{ijk}/n_{ij}$$

Two-way ANOVA model

- For unbalanced studies, we don't have the simple ANOVA SS partition, the factor effect component sums of squares (SSA, SSB, SSAB) are no longer orthogonal; that is, they do not sum to SSTR.
- For two-way (two-factor) ANOVA model, we will estimate the parameters and conduct the test of interactions and main effects through the regression approach.

Regression Approach to two-way ANOVA (Ch 23.1)

- Since no new principles are involved, we use an example to illustrate how ANOVA tests are conducted by means of the regression approach.
- As before, we have the standard two-way ANOVA factor effects model:

$$Y_{ijk} = \mu.. + \alpha_i + \beta_j + (\alpha\beta)_{ij} + \epsilon_{ijk}$$

Note:

1. Zero sum constraints: $\sum_i \alpha_i = 0$, we need only $a-1$ parameters α_i, the last α_a is equal to

$$\alpha_a = -(\alpha_1 + ... + \alpha_{a-1})$$

2. $\sum_j \beta_j = 0$, we need only $b-1$ parameters β_j, the last β_b is equal to

$$\beta_b = -(\beta_1 + ... + \beta_{b-1})$$

3. For interactions, we had

$$\sum_i (\alpha\beta)_{ij} = \sum_j (\alpha\beta)_{ij} = 0\,, \quad i = 1..., a\,;\; j = 1, ..., b$$

, therefore we only need $(a-1)(b-1)$ parameters in the regression model.

Example

- Synthetic growth hormone was administered at a clinical research center to growth hormone deficient, short children who had not yet reached puberty.
- The investigator was interested in the effects of a child's gender (factor A) and bone development (factor B: severely depressed, moderately depressed, mildly depressed) on the rate of growth induced by hormone administration.
- Three children were randomly selected for each gender-bone development group.
- The response variable (Y) of interest was the difference between the growth rate during growth hormone treatment and the normal growth rate prior to the treatment, expressed in cm per month.
- Four of the 18 children were unable to complete the year-long study, thus creating unequal treatment sample sizes.
- Note that this is an observational study. No randomization of treatments to subjects was employed.

TABLE 23.1 Sample Data and Notation—Growth Hormone Example (growth rate difference in centimeters per month).

Gender (factor A) i	Bone Development (factor B) j: Severely Depressed (B_1)	Moderately Depressed (B_2)	Mildly Depressed (B_3)
Male (A_1)	1.4 (Y_{111}) 2.4 (Y_{112}) 2.2 (Y_{113})	2.1 (Y_{121}) 1.7 (Y_{122})	.7 (Y_{131}) 1.1 (Y_{132})
Mean	2.0 ($\bar{Y}_{11\cdot}$)	1.9 ($\bar{Y}_{12\cdot}$)	.9 ($\bar{Y}_{13\cdot}$)
Female (A_2)	2.4 (Y_{211})	2.5 (Y_{221}) 1.8 (Y_{222}) 2.0 (Y_{223})	.5 (Y_{231}) .9 (Y_{232}) 1.3 (Y_{233})
Mean	2.4 ($\bar{Y}_{21\cdot}$)	2.1 ($\bar{Y}_{22\cdot}$)	.9 ($\bar{Y}_{23\cdot}$)

Data checking

1. read the data

```
Ex23  =read.table(
        url("https://raw.githubusercontent.com/npmldabook/Stat3119/master/Week-11/CH23TA01.txt"))
head(Ex23)
```

```
##    V1 V2 V3 V4
## 1 1.4  1  1  1
## 2 2.4  1  1  2
## 3 2.2  1  1  3
## 4 2.1  1  2  1
## 5 1.7  1  2  2
## 6 0.7  1  3  1
```

```r
names(Ex23) =  c("response", "Gender", "Bone", "units")

# make  categorical variables for factor A and B
Ex23$Gender =  as.factor(Ex23$Gender)
Ex23$Bone =  as.factor(Ex23$Bone)

levels(Ex23$Gender) = c("M", "F")
levels(Ex23$Bone) = c("Severe", "Moderate", "Mild")

str(Ex23)
```

```
## 'data.frame':    14 obs. of  4 variables:
##  $ response: num  1.4 2.4 2.2 2.1 1.7 0.7 1.1 2.4 2.5 1.8 ...
##  $ Gender  : Factor w/ 2 levels "M","F": 1 1 1 1 1 1 1 2 2 2 ...
##  $ Bone    : Factor w/ 3 levels "Severe","Moderate",..: 1 1 1 2 2 3 3 1 2 2 ...
##  $ units   : int  1 2 3 1 2 1 2 1 1 2 ...
```

```r
dim(Ex23)
```

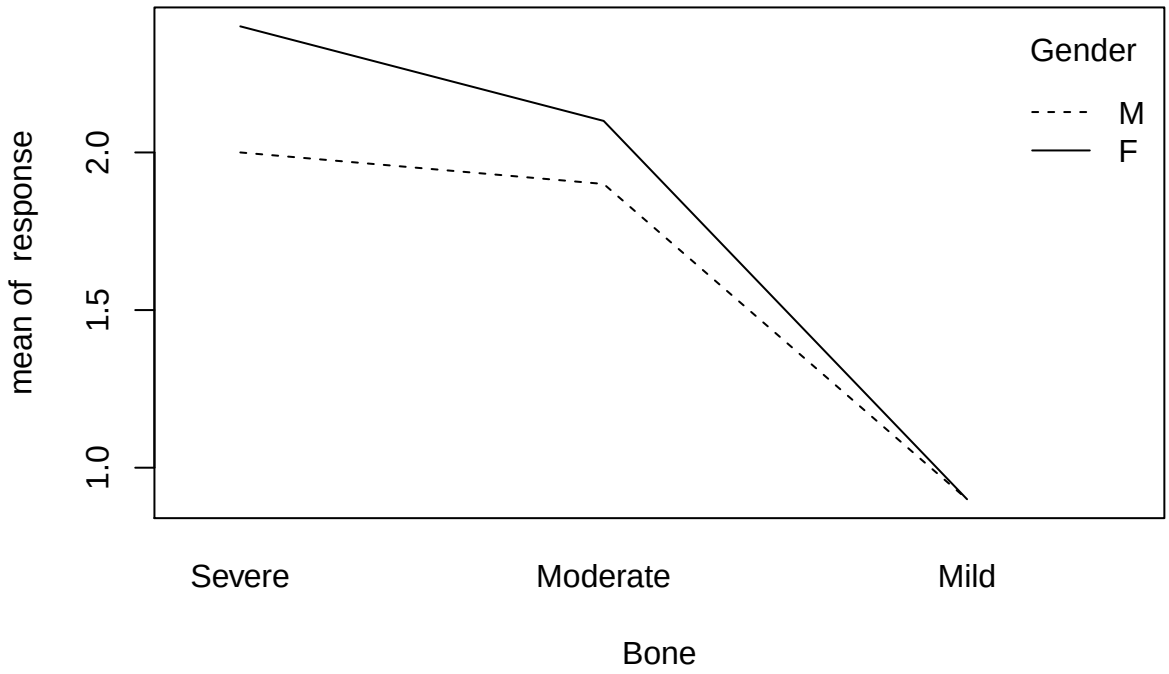
```
## [1] 14  4
```

```r
# check frequency within treatment => 'unbalanced studies'
with(Ex23, table( Gender, Bone))
```

```
##       Bone
## Gender Severe Moderate Mild
##      M      3        2    2
##      F      1        3    3
```

2. generate treatment mean (interaction) plot

```r
with(Ex23, interaction.plot(x.factor = Bone, trace.factor = Gender, response = response))
```



Note: Although the sample size is small (n=14), the analysis techniques are general and can be applied to much large studies with thousands of subjects.

Q: Based on 14 data points, we would like test whether there is a significant interaction, and whether the factor effects or treatment levels are significantly different given the test results for interaction.

Development the equivalent regression model

1. Two factor ANOVA model

$$Y_{ijk} = \mu.. + \alpha_i + \beta_j + (\alpha\beta)_{ij} + \epsilon_{ijk}, \quad i = 1, 2;\ j = 1, 2, 3$$

2. To set up the correct regression model, we use 1 indicator function for factor A and 2 for factor B; and the crossproduct terms for interaction. Then the equivalent regression model is (with regression coefficients corresponding to the ANOVA model parameters)

$$Y_{ijk} = \mu.. + \underbrace{\alpha_1 X_{ijk1}}_{\text{A main effect}} + \underbrace{\beta_1 X_{ijk2} + \beta_2 X_{ijk3}}_{\text{B main effect}}$$
$$+ \underbrace{(\alpha\beta)_{11} X_{ijk1} X_{ijk2} + (\alpha\beta)_{12} X_{ijk1} X_{ijk3}}_{\text{AB interaction effect}} + \varepsilon_{ijk} \qquad \text{Full model} \quad \textbf{(23.11)}$$

where:

$$X_1 = \begin{cases} 1 & \text{if case from level 1 for factor A} \\ -1 & \text{if case from level 2 for factor A} \end{cases}$$

$$X_2 = \begin{cases} 1 & \text{if case from level 1 for factor B} \\ -1 & \text{if case from level 3 for factor B} \\ 0 & \text{otherwise} \end{cases}$$

$$X_3 = \begin{cases} 1 & \text{if case from level 2 for factor B} \\ -1 & \text{if case from level 3 for factor B} \\ 0 & \text{otherwise} \end{cases}$$

3. From the regression fit, we can obtain the estimate for $\mu_{..}$, factor effects α_1, β_1 and β_2, and interaction effects $(\alpha\beta)_{11}$, $(\alpha\beta)_{12}$, then from their relationship, we can derive

$$\begin{aligned} \alpha_2 &= -\alpha_1 \\ \beta_3 &= -\beta_1 - \beta_2 \\ (\alpha\beta)_{13} &= -(\alpha\beta)_{11} - (\alpha\beta)_{12} \\ (\alpha\beta)_{21} &= -(\alpha\beta)_{11} \end{aligned} \qquad \textbf{(23.13)}$$

Implement the regression model

1. set the indicator function and obtain regression summary

```
IndicatorA1 = (Ex23$Gender =="M")*1 + (Ex23$Gender=="F")*(-1)

IndicatorB1 =  (Ex23$Bone=="Severe")*1  + (Ex23$Bone=="Mild")*(-1)
IndicatorB2 = (Ex23$Bone=="Moderate")*1 + (Ex23$Bone=="Mild")*(-1)


LM.full  =  lm( response~ IndicatorA1 + IndicatorB1 + IndicatorB2+
                  IndicatorA1:IndicatorB1 + IndicatorA1:IndicatorB2, data=Ex23 )
summary(LM.full)
```

```
##
## Call:
## lm(formula = response ~ IndicatorA1 + IndicatorB1 + IndicatorB2 +
##     IndicatorA1:IndicatorB1 + IndicatorA1:IndicatorB2, data = Ex23)
##
```

```
## Residuals:
##    Min     1Q Median     3Q    Max
##   -0.6   -0.2    0.0    0.2    0.4
##
## Coefficients:
##                            Estimate Std. Error t value Pr(>|t|)
## (Intercept)                1.700e+00  1.164e-01  14.609 4.73e-07 ***
## IndicatorA1               -1.000e-01  1.164e-01  -0.859   0.4152
## IndicatorB1                5.000e-01  1.778e-01   2.813   0.0227 *
## IndicatorB2                3.000e-01  1.576e-01   1.904   0.0934 .
## IndicatorA1:IndicatorB1 -1.000e-01  1.778e-01  -0.563   0.5891
## IndicatorA1:IndicatorB2  4.340e-17  1.576e-01   0.000   1.0000
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.4031 on 8 degrees of freedom
## Multiple R-squared:  0.7749, Adjusted R-squared:  0.6342
## F-statistic: 5.507 on 5 and 8 DF,  p-value: 0.01722
```

```
round(coef(LM.full),3)
```

```
##             (Intercept)             IndicatorA1             IndicatorB1
##                     1.7                    -0.1                     0.5
##             IndicatorB2 IndicatorA1:IndicatorB1 IndicatorA1:IndicatorB2
##                     0.3                    -0.1                     0.0
```

Results: We then obtain the full regression model as in Table 23.3:

$$\hat{Y} = 1.7 - 0.1X_{A_1} + 0.5X_{B_1} + 0.3X_{B_2} - 0.1X_{A_1}X_{B_1}0.0X_{A_1}X_{B_2}$$

where last term can be dropped since it's coefficient=0.

Testing the effects in unbalanced ANOVA model

Unlike the balanced case, we can run ANOVA SS decomposition with $SSTO = SSA + SSB + SSAB + SSE$ and construct the F-test from ANOVA table. In the unbalanced cases, we test different effects by appropriate model comparison approach.

1. Approach I: Compare the full model a reduced model (without interaction term; without factor A and without factor B, respectively) to test whether the interaction effects and factor effects are significant or not. (p.957-958)

1A. Testing interaction effects

```
Reduced.NoAB  =  lm( response~ IndicatorA1 + IndicatorB1 + IndicatorB2, data=Ex23 )

# anova to compare the two models
anova(Reduced.NoAB, LM.full)
```

```
## Analysis of Variance Table
##
```

```
## Model 1: response ~ IndicatorA1 + IndicatorB1 + IndicatorB2
## Model 2: response ~ IndicatorA1 + IndicatorB1 + IndicatorB2 + IndicatorA1:IndicatorB1 +
##     IndicatorA1:IndicatorB2
##   Res.Df    RSS Df Sum of Sq      F Pr(>F)
## 1     10 1.3754
## 2      8 1.3000  2  0.075429 0.2321  0.798
```

Results: The test statistic $F = 0.23 \sim F(2, 8)$*distribution* with a P-value=0.798, so we don't reject the corresponding null hypothesis (interaction effects are not present).

1B. Testing factor A

```
Reduced.NoA  =  lm( response~  IndicatorB1 + IndicatorB2 +
                   IndicatorA1:IndicatorB1 + IndicatorA1:IndicatorB2, data=Ex23 )

# anova to compare the two models
anova(Reduced.NoA, LM.full)
```

```
## Analysis of Variance Table
##
## Model 1: response ~ IndicatorB1 + IndicatorB2 + IndicatorA1:IndicatorB1 +
##     IndicatorA1:IndicatorB2
## Model 2: response ~ IndicatorA1 + IndicatorB1 + IndicatorB2 + IndicatorA1:IndicatorB1 +
##     IndicatorA1:IndicatorB2
##   Res.Df  RSS Df Sum of Sq      F Pr(>F)
## 1      9 1.42
## 2      8 1.30  1      0.12 0.7385 0.4152
```

Results: The test statistic $F = 0.74 \sim F(1, 8)$*distribution* with a P-value=0.42, so we don't reject the corresponding null hypothesis (factor A effects are not present).

1C. Testing factor B

```
Reduced.NoB  =  lm( response~  IndicatorA1 +
                   IndicatorA1:IndicatorB1 + IndicatorA1:IndicatorB2, data=Ex23 )

# anova to compare the two models
anova(Reduced.NoB, LM.full)
```

```
## Analysis of Variance Table
##
## Model 1: response ~ IndicatorA1 + IndicatorA1:IndicatorB1 + IndicatorA1:IndicatorB2
## Model 2: response ~ IndicatorA1 + IndicatorB1 + IndicatorB2 + IndicatorA1:IndicatorB1 +
##     IndicatorA1:IndicatorB2
##   Res.Df    RSS Df Sum of Sq      F   Pr(>F)
## 1     10 5.4897
## 2      8 1.3000  2    4.1897 12.891 0.003145 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Results: The test statistic $F = 12.89 \sim F(2, 8)$*distribution* with a P-value<0.01, so we reject the corresponding null hypothesis and conclude the factor B effects are significant.

2. Use R to generate the type III sum of squares.

- Type I (sequential): Sequentially build up model (depends on the "ordering" of the model terms!)
  - `SS(A | 1)`
  - `SS(B | 1, A)`
  - `SS(AB | 1, A, B)`
- Type II (hierarchical): Control for the influence of the largest *hierarchical* model not including the term of interest.
  - `SS(A | 1, B)`
  - `SS(B | 1, A)`
  - `SS(AB | 1, A, B)`
- Type III (fully adjusted): Control for *all* other terms.
  - `SS(A | 1, B, AB)`
  - `SS(B | 1, A, AB)`
  - `SS(AB | 1, A, B)`

The textbook suggests to test each factor while keeping all the other terms in the model (including those interactions terms involving the factor dropped), this corresponds to the type III sum of squares. *If you are not interested in testing the interactions while the factor main effect is dropped, then you can use type II sum of squares.*

```
options(contrasts = c("contr.sum", "contr.poly"))
library(car)
```

```
## Loading required package: carData
```

```
# Each factor is a categorical variable in the model
LM.full2  =  lm( response~  Gender*Bone, data=Ex23 )

# use Anova function in car package to get SS3
Anova(LM.full2, type="III")
```

```
## Anova Table (Type III tests)
##
## Response: response
##             Sum Sq Df  F value    Pr(>F)
## (Intercept) 34.680  1 213.4154 4.729e-07 ***
## Gender       0.120  1   0.7385  0.415160
## Bone         4.190  2  12.8914  0.003145 **
## Gender:Bone  0.075  2   0.2321  0.798034
## Residuals    1.300  8
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Results: This SS III table is the same as the Table 23.4. Therefore the conclusion of these tests: a child's bone development affects the change in growth rate during growth hormone treatment and that there are no gender and interaction effects.

At this point, the next step in the analysis of the study results is to examine the nature of the bone development effects.

Inferences about Factor Effects when Sample Sizes Are Unequal (Ch 23.3)

The estimation of factor effects when the treatment sample sizes are unequal is completely analogous to when the sample sizes are equal. The nature of the analysis depends on whether or not important interactions are present.

- When no important interactions are present, the analysis generally is concerned with the factor level means $\mu_{i.}$, and $\mu_{.j}$.
- when important interactions are present, the analysis usually focuses on the treatment means μ_{ij} .

We can derive similar formula for the least squares means with slight modification (involving $n_{ij} \neq n$). The main results are in Table 23.5 (p.961) for the point estimator and estimated variance when estimating factor level means, pairwise comparisons of factor level means, and contrasts or linear combinations of factor level means, when the sample sizes are unequal,together with the same three multiple comparison procedures with df $= n_T - ab$ for MSE.

TABLE 23.5 **Point Estimators and Estimated Variances for Two-Factor Analyses when Sample Sizes Are Unequal.**

(a) Factor Level Mean

$$\mu_{i\cdot} = \frac{\sum_j \mu_{ij}}{b} \qquad \mu_{\cdot j} = \frac{\sum_i \mu_{ij}}{a}$$

$$\hat{\mu}_{i\cdot} = \frac{\sum_j \overline{Y}_{ij\cdot}}{b} \qquad \hat{\mu}_{\cdot j} = \frac{\sum_i \overline{Y}_{ij\cdot}}{a} \qquad \textbf{(23.20)}$$

$$s^2\{\hat{\mu}_{i\cdot}\} = \frac{MSE}{b^2}\sum_j \frac{1}{n_{ij}} \qquad s^2\{\hat{\mu}_{\cdot j}\} = \frac{MSE}{a^2}\sum_i \frac{1}{n_{ij}}$$

(b) Pairwise Comparison of Factor Level Means

$$D = \mu_{i\cdot} - \mu_{i'\cdot} \qquad D = \mu_{\cdot j} - \mu_{\cdot j'}$$

$$\hat{D} = \hat{\mu}_{i\cdot} - \hat{\mu}_{i'\cdot} \qquad \hat{D} = \hat{\mu}_{\cdot j} - \hat{\mu}_{\cdot j'} \qquad \textbf{(23.21)}$$

$$s^2\{\hat{D}\} = \frac{MSE}{b^2}\sum_j \left(\frac{1}{n_{ij}} + \frac{1}{n_{i'j}}\right) \qquad s^2\{\hat{D}\} = \frac{MSE}{a^2}\sum_i \left(\frac{1}{n_{ij}} + \frac{1}{n_{ij'}}\right)$$

(c) Contrast or Linear Combination of Factor Level Means

$$L = \sum_i c_i \mu_{i\cdot} \qquad L = \sum_j c_j \mu_{\cdot j}$$

$$\hat{L} = \sum_i c_i \hat{\mu}_{i\cdot} \qquad \hat{L} = \sum_j c_j \hat{\mu}_{\cdot j} \qquad \textbf{(23.22)}$$

$$s^2\{\hat{L}\} = \frac{MSE}{b^2}\sum_i c_i^2 \sum_j \frac{1}{n_{ij}} \qquad s^2\{\hat{L}\} = \frac{MSE}{a^2}\sum_j c_j^2 \sum_i \frac{1}{n_{ij}}$$

(d) Confidence Interval Multiple

Single Estimate

$$t(1-\alpha/2; n_T - ab) \qquad t(1-\alpha/2; n_T - ab)$$

Multiple Comparisons

$$B = t(1-\alpha/2g; n_T - ab) \qquad B = t(1-\alpha/2g; n_T - ab)$$

$$T = \frac{1}{\sqrt{2}} q(1-\alpha; a, n_T - ab) \qquad T = \frac{1}{\sqrt{2}} q(1-\alpha; b, n_T - ab) \qquad \textbf{(23.23)}$$

$$S^2 = (a-1)F(1-\alpha; a-1, n_T - ab) \qquad S^2 = (b-1)F(1-\alpha; b-1, n_T - ab)$$

When treatment means are of interest to study, we also have the formula in part 2 of Table 23.5 (p.962)

TABLE 23.5 **Point Estimators and Estimated Variances for Two-Factor Analyses when Sample Sizes Are Unequal (concluded).**

(e) Treatment Mean

$$\mu_{ij}$$

$$\hat{\mu}_{ij} = \bar{Y}_{ij\cdot} \qquad (23.24)$$

$$s^2\{\hat{\mu}_{ij}\} = \frac{MSE}{n_{ij}}$$

(f) Pairwise Comparison of Treatment Means

$$D = \mu_{ij} - \mu_{i'j'}$$

$$\hat{D} = \bar{Y}_{ij\cdot} - \bar{Y}_{i'j'\cdot} \qquad (23.25)$$

$$s^2\{\hat{D}\} = MSE\left(\frac{1}{n_{ij}} + \frac{1}{n_{i'j'}}\right)$$

(g) Contrast or Linear Combination of Treatment Means

$$L = \sum\sum c_{ij}\mu_{ij}$$

$$\hat{L} = \sum\sum c_{ij}\bar{Y}_{ij\cdot} \qquad (23.26)$$

$$s^2\{\hat{L}\} = MSE\sum\sum\frac{c_{ij}^2}{n_{ij}}$$

(h) Confidence Interval Multiple

Single Estimate

$$t(1-\alpha/2;\, n_T - ab)$$

Multiple Comparisons

$$B = t(1-\alpha/2g;\, n_T - ab)$$

$$T = \frac{1}{\sqrt{2}}q(1-\alpha;\, ab,\, n_T - ab) \qquad (23.27)$$

$$S^2 = (ab-1)F(1-\alpha;\, ab-1,\, n_T - ab)$$

Example to illustrate the inferences in Unbalanced studies (p962-963)

Example 1: Pairwise comparison of factor level means

Continue with the growth hormone example. We found earlier

1. a child's gender and bone development do not interact in their effects on the change in the growth rate when growth hormone is administered.
2. no main gender (factor A) effects,
3. concluded that a child's bone development (factor B) does affect the change in growth rate. We shall now analyze the nature of the bone development effects by means of pairwise comparisons among the three bone development groups.

4. The **Tukey** multiple comparison procedure will be used. (This procedure is conservative when sample sizes are unequal. Use of the Bonferroni procedure would lead to wider confidence intervals here. The family confidence coefficient has been specified to be .90.

We got treatment means, then take the unweighted average to get the factor level means. The variance estimates depend on n_{ij}.

$$\hat{\mu}_{.1} = \frac{\overline{Y}_{11.} + \overline{Y}_{21.}}{2} = \frac{2.0 + 2.4}{2} = 2.2$$

$$\hat{\mu}_{.2} = \frac{\overline{Y}_{12.} + \overline{Y}_{22.}}{2} = \frac{1.9 + 2.1}{2} = 2.0$$

$$\hat{\mu}_{.3} = \frac{\overline{Y}_{13.} + \overline{Y}_{23.}}{2} = \frac{.9 + .9}{2} = .9$$

$$\hat{D}_1 = \hat{\mu}_{.1} - \hat{\mu}_{.2} = 2.2 - 2.0 = .2$$

$$\hat{D}_2 = \hat{\mu}_{.1} - \hat{\mu}_{.3} = 2.2 - .9 = 1.3$$

$$\hat{D}_3 = \hat{\mu}_{.2} - \hat{\mu}_{.3} = 2.0 - .9 = 1.1$$

$$s^2\{\hat{D}_1\} = \frac{.1625}{(2)^2}\left(\frac{1}{3} + \frac{1}{2} + \frac{1}{1} + \frac{1}{3}\right) = .0880 \qquad s\{\hat{D}_1\} = .297$$

$$s^2\{\hat{D}_2\} = \frac{.1625}{(2)^2}\left(\frac{1}{3} + \frac{1}{2} + \frac{1}{1} + \frac{1}{3}\right) = .0880 \qquad s\{\hat{D}_2\} = .297$$

$$s^2\{\hat{D}_3\} = \frac{.1625}{(2)^2}\left(\frac{1}{2} + \frac{1}{2} + \frac{1}{3} + \frac{1}{3}\right) = .0677 \qquad s\{\hat{D}_3\} = .260$$

Then with the point estimate and its standard error estimate, we can apply the Tukey procedure to get the simultaneously confidence interval with familywise confidence coefficient .90.

For a 90 percent family confidence coefficient, we require:

$$T = \frac{1}{\sqrt{2}} q(.90; 3, 8) = \frac{1}{\sqrt{2}}(3.37) = 2.38$$

Hence, we obtain the following confidence intervals:

$$-.51 = .2 - 2.38(.297) \le \mu_{.1} - \mu_{.2} \le .2 + 2.38(.297) = .91$$

$$.59 = 1.3 - 2.38(.297) \le \mu_{.1} - \mu_{.3} \le 1.3 + 2.38(.297) = 2.01$$

$$.48 = 1.1 - 2.38(.260) \le \mu_{.2} - \mu_{.3} \le 1.1 + 2.38(.260) = 1.72$$

R analysis

```
library(emmeans)

fit.emm <- emmeans( LM.full2, ~ Bone)
```

```
## NOTE: Results may be misleading due to involvement in interactions
```

```
# CI without adjustment for MCP
fit.emm
```

```
##  Bone     emmean    SE df lower.CL upper.CL
##  Severe      2.2 0.233  8    1.663     2.74
##  Moderate    2.0 0.184  8    1.576     2.42
##  Mild        0.9 0.184  8    0.476     1.32
##
## Results are averaged over the levels of: Gender
## Confidence level used: 0.95
```

```
# CI with adjustment for MCP
confint(pairs(fit.emm), adjust = "tukey", level=0.9)
```

```
##  contrast          estimate    SE df lower.CL upper.CL
##  Severe - Moderate      0.2 0.297  8   -0.508    0.908
##  Severe - Mild          1.3 0.297  8    0.592    2.008
##  Moderate - Mild        1.1 0.260  8    0.479    1.721
##
## Results are averaged over the levels of: Gender
## Confidence level used: 0.9
## Conf-level adjustment: tukey method for comparing a family of 3 estimates
```

So the conclusion from this pairwise analysis is:

1) $\mu_{.1}(severe\ depressed) \sim \mu_{.2}(moderate\ depressed)$
2) $\mu_{.1}(severe\ depressed) > \mu_{.3}(mild\ depressed)$
3) $\mu_{.2}(moderate\ depressed) > \mu_{.3}(mild\ depressed)$

So it suggests that the short children with mildly depressed bone development on the average have a substantially smaller increase in the growth rate than children with either moderately depressed or severely depressed bone development. Further, the latter two groups of children do not show significantly different mean changes in the growth rate.

Example 2: Testing

For ANOVA model, because we assume the observations are normally distributed, similar as before for each parameter of interest that we discussed, e.g. θ, we need to know what is the point estimator $\hat{\theta}$ and the estimator of the standard deviation $s(\hat{\theta})$, then we can make inference: (1- α) two-sided CI is

$$\hat{\theta} \pm t(1-\alpha/2, n_T - r)s(\hat{\theta})$$

The test statistic for the $H_0 : \theta = \theta_0$ would be

$$t^* = (\hat{\theta} - \theta_0)/s(\hat{\theta}) \sim t(n_T - r) \text{ distribution}$$

with $r = ab$ in a two factor study and the estimates are based on the appropriate formulas.

Empty Cells in Two factor studies (Ch 23.4)

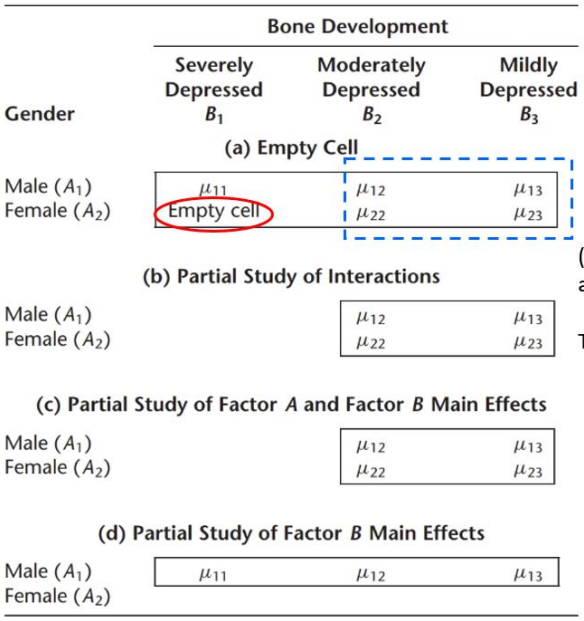
Occasionally after a two-factor study has been completed, it turns out that there are no cases in one or several treatment cells (empty cells) , e.g. due to missing data or dropout.

since certain cells are empty, the full regression models with all possible interactions are not good to use and we can't estimate certain interaction effects.

1. If the previous studies of similar problem suggest these two factors do not interact, then we can use the reduced regression model without interaction effects. Then the other model parameters are estimable. If without previous information, we should not partial analysis on the available data since we can't test the interaction with empty cells.
2. Partial Analysis (p. 965-966)

E.g. In the growth hormone example, suppose that there are no observations for female children with severely depressed bone development; i.e., $n_{21} = 0$. In that case no sample information is available about the treatment mean μ_{21}.

FIGURE 23.2 Schematic Representation of Growth Hormone Study with Empty Cell—Growth Hormone Example ($n_{21} = 0$).



Partial information about interactions can still be obtained by restricting attention to children with moderately depressed and mildly depressed bone development

(b) interactions are present if differences for M/F are not the same for two bone development groups.
i.e. $\mu12 - \mu22$ vs $\mu13 - \mu23$
Thus we may get CI or test for L
$L = \mu12 - \mu22 - \mu13 + \mu23$

(c) If interaction is not present, to test A or B without B1, we can use
For A: $\mu1. = (\mu12 + \mu13)/2$; $\mu2. = (\mu22 + \mu23)/2$
For B: $\mu.2 = (\mu12 + \mu22)/2$; $\mu.3 = (\mu13 + \mu23)/2$

(d) We can estimate the pairwise difference of effects of bone development on male by using estimate of $\mu11$, $\mu12$, and $\mu13$.

MSE can be estimated from the data $\Sigma\Sigma\Sigma(Y_{ijk} - \mu_{ij})/df$ with df= n_T-r* levels (r*=non-missing levels).

Missing value in a randomized complete block design

This means within certain blocks, we don't have a complete set of treatments. If two-way ANOVA without interaction model is appropriate,

- We can't run ANOVA SS partition (ANOVA table), loss the orthogonality due to missing, but we can use the equivalent regression model to estimate the model parameter.
- We use the full vs. reduced models or SS III to test the block and treatment effects.
- The estimation and inference of the treatment means are the same as before using regression model output for coefficient estimates and variance-covariance matrix.

R analysis

1. read the data

```
Ex23B  =read.table(
        url("https://raw.githubusercontent.com/npmldabook/Stat3119/master/Week-11/CH23TA06.txt"))
head(Ex23B)
```

```
##   V1 V2 V3
## 1 10  1  2
## 2  9  1  3
## 3 11  2  1
## 4 10  2  2
## 5  7  2  3
## 6  6  3  1
```

```
names(Ex23B) =  c("response", "Block", "Treatment")

# make  categorical variables
Ex23B$Block =  as.factor(Ex23B$Block)
Ex23B$Treatment =  as.factor(Ex23B$Treatment)


str(Ex23B)
```

```
## 'data.frame':    8 obs. of  3 variables:
##  $ response : int  10 9 11 10 7 6 4 3
##  $ Block    : Factor w/ 3 levels "1","2","3": 1 1 2 2 2 3 3 3
##  $ Treatment: Factor w/ 3 levels "1","2","3": 2 3 1 2 3 1 2 3
```

```
# check frequency within treatment => 'unbalanced studies'
with(Ex23B, table( Block))
```

```
## Block
## 1 2 3
## 2 3 3
```

2) Run regression and type 3 SS

```
Indicator.Block1 = (Ex23B$Block =="1")*1 + (Ex23B$Block=="3")*(-1)
Indicator.Block2 = (Ex23B$Block =="2")*1 + (Ex23B$Block=="3")*(-1)

Indicator.Trt1 = (Ex23B$Treatment =="1")*1 + (Ex23B$Treatment=="3")*(-1)
Indicator.Trt2 = (Ex23B$Treatment =="2")*1 + (Ex23B$Treatment=="3")*(-1)

LMex2.full  =  lm( response~ Indicator.Block1 + Indicator.Block2 +
                   Indicator.Trt1+ Indicator.Trt2, data=Ex23B )
summary(LMex2.full)
```

```
##
## Call:
## lm(formula = response ~ Indicator.Block1 + Indicator.Block2 +
##     Indicator.Trt1 + Indicator.Trt2, data = Ex23B)
##
## Residuals:
##          1          2          3          4          5          6
## -3.333e-01  3.333e-01  1.249e-16  6.667e-01 -6.667e-01 -4.302e-16
##          7          8
## -3.333e-01  3.333e-01
##
## Coefficients:
##                    Estimate Std. Error t value Pr(>|t|)
## (Intercept)       8.000e+00  2.485e-01  32.199 6.58e-05 ***
## Indicator.Block1  2.333e+00  3.849e-01   6.062  0.00901 **
## Indicator.Block2  1.333e+00  3.333e-01   4.000  0.02801 *
## Indicator.Trt1    1.667e+00  3.849e-01   4.330  0.02271 *
## Indicator.Trt2   -6.661e-16  3.333e-01   0.000  1.00000
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.6667 on 3 degrees of freedom
## Multiple R-squared:  0.9785, Adjusted R-squared:  0.9498
## F-statistic: 34.13 on 4 and 3 DF,  p-value: 0.007783
```

```
# coefficent and var-cov matrix
round(coef(LMex2.full),3)
```

```
##      (Intercept) Indicator.Block1 Indicator.Block2   Indicator.Trt1
##            8.000            2.333            1.333            1.667
##   Indicator.Trt2
##            0.000
```

```
vcov(LMex2.full)
```

```
##                  (Intercept) Indicator.Block1 Indicator.Block2
## (Intercept)       0.06172840       0.02469136      -0.01234568
## Indicator.Block1  0.02469136       0.14814815      -0.07407407
## Indicator.Block2 -0.01234568      -0.07407407       0.11111111
## Indicator.Trt1    0.02469136       0.04938272      -0.02469136
## Indicator.Trt2   -0.01234568      -0.02469136       0.01234568
##                  Indicator.Trt1 Indicator.Trt2
## (Intercept)          0.02469136    -0.01234568
## Indicator.Block1     0.04938272    -0.02469136
## Indicator.Block2    -0.02469136     0.01234568
## Indicator.Trt1       0.14814815    -0.07407407
## Indicator.Trt2      -0.07407407     0.11111111
```

```
# Each factor is a categorical variable in the model
LMex2.full2  =  lm( response~  Block+Treatment, data=Ex23B )

# use Anova function in car package to get SS3
Anova(LMex2.full2, type="III")
```

```
## Anova Table (Type III tests)
##
## Response: response
##             Sum Sq Df  F value    Pr(>F)
## (Intercept) 460.80  1 1036.800 6.583e-05 ***
## Block        53.83  2   60.562  0.003757 **
## Treatment    12.50  2   14.062  0.029924 *
## Residuals     1.33  3
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Summary this week

- Reading: Chapter 23.1-23.4
- Reminder:

1) The last homework (week 10 on ANCOVA) due on Thursday
2) Quiz this Thursday