Chapter 6: Comparisons of Several Multivariate Means

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Chapter Objectives

- Extending on ideas in Chapter 5 to handle problems involving the comparison of several mean vectors
- Discuss the tenets of good experimental practice (i.e. repeated measure design) and look at the comparison of means
- Finally, discuss several comparisons among mean vectors (MANOVA)

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6.2: Paired Comparisons

- Measurements are often recorded under different sets of experimental conditions to see whether the responses differ significantly over these sets. (i.e. Efficacy of drug treatment)
- In some cases, we can compare **two or more** treatments and assess the **effects of those treatments**.
- One approach would be to assign both treatments to the **same or identical units**.
  - Compute the differences, thereby eliminating much of the influence of extraneous unit-to-unit variation.

6.2: Notation

- Let X_{j1} denote the response to *treatment 1*, and X_{j2} by the response to *treatment 2* for the jth trial. Let the n differences be,

$$D_j = X_{j1} - X_{j2} \tag{1}$$

- Let D_j represent independent observations from an $N(\delta, \sigma_d^2)$ distribution, and define t as,

$$t = \frac{\overline{D} - \delta}{s_d \sqrt{n}} \tag{2}$$

where,

$$\overline{D} = \frac{1}{n} \sum_{j=1}^{n} D_j \qquad\qquad s_d^2 = \frac{1}{n-1} \sum_{j=1}^{n} (D_j - \overline{D})^2$$

- Has a t-distribution with $n - 1$ d.f. Consequently an α-level test of the Hypothesis ($H_0 : \delta = 0$ and $H_1 : \delta \neq 0$) may be conducted.

Notation Cont.

- A $100(1-\alpha)\%$ **confidence interval** for the mean difference $\delta = E(X_{j1} - X_{j2})$ is provided as,

$$\bar{d} - t_{n-1}(\alpha/2)\frac{s_d}{\sqrt{n}} \le \delta \le \bar{d} + t_{n-1}(\alpha/2)\frac{s_d}{\sqrt{n}} \quad (3)$$

- For the **multivariate case** where we denote p responses, two treatments, and n experimental units.

$$X_{1jp} = \text{Variable p under treatment 1}$$
$$X_{2jp} = \text{variable p under treatment 2}$$

Notation Cont.

- The p paired difference random variables become $D_{jp} = X_{1jp} - X_{2jp}$. Let, $\mathbf{D}'_j = [D_{j1}, ..., D_{jp}]$ and assume for $j = 1, 2, ..., n$ $E(\mathbf{D}_j) = \delta$ and $Cov(\mathbf{D_j}) = \mathbf{\Sigma}_d$.
- If $\mathbf{D_n}$ are independent $N_p(\delta, \mathbf{\Sigma}_d)$ random vectors, inferences about the vector of mean differences δ can be based upon a T^2-Statistic.

$$T^2 = n(\overline{\mathbf{D}} - \delta)'\mathbf{S}_d^{-1}(\overline{\mathbf{D}} - \delta) \tag{4}$$

Result 6.1

Let the differences of $\mathbf{D}_n$ be a random sample from an $N_p(\delta, \mathbf{\Sigma}_d)$ population. Then equation (4) is distributed as an $[(n-1)p/(n-p)]F_{p,n-p}$ random variable, whatever the true δ and $\mathbf{\Sigma}_d$. If n and n - p are both large, T^2 is approximately distributed as a χ^2_p random variable.

Notation Cont.

- A $100(1-\alpha)\%$ **confidence region** for δ consists of all δ s.t.

$$(\overline{\mathbf{d}}-\delta)'\mathbf{S}_d^{-1}(\overline{\mathbf{d}}-\delta) \leq \frac{(n-1)p}{n(n-p)}F_{p,n-p}(\alpha) \tag{5}$$

- $100(1-\alpha)\%$ **simultaneous confidence intervals for the individual mean differences** δ_i are given by

$$\delta_i : \overline{d} \pm \sqrt{\frac{(n-1)p}{(n-p)}F_{p,n-p}(\alpha)}\sqrt{\frac{s_{d_i}^2}{n}} \tag{6}$$

- **Bonferroni** $100(1-\alpha)\%$ **simultaneous confidence intervals** for the individual mean differences are

$$\delta_i : \overline{d}_t \pm t_{n-1}\left(\frac{\alpha}{2p}\right)\sqrt{\frac{s_{d_i}^2}{n}} \tag{7}$$

where $t_{n-1}(\alpha/2p)$ is the upper $100(\alpha/2p)$th percentile of a t-distribution with $n-1$ d.f.

Example 6.1

Example 6.1 (Checking for a mean difference with paired observations) Municipal wastewater treatment plants are required by law to monitor their discharges into rivers and streams on a regular basis. Concern about the reliability of data from one of these self-monitoring programs led to a study in which samples of effluent were divided and sent to two laboratories for testing. One-half of each sample was sent to the Wisconsin State Laboratory of Hygiene, and one-half was sent to a private commercial laboratory routinely used in the monitoring program. Measurements of biochemical oxygen demand (BOD) and suspended solids (SS) were obtained, for $n = 11$ sample splits, from the two laboratories. The data are displayed in Table 6.1.

Table 6.1 Effluent Data

Sample j	Commercial lab x_{1j1} (BOD)	x_{1j2} (SS)	State lab of hygiene x_{2j1} (BOD)	x_{2j2} (SS)
1	6	27	25	15
2	6	23	28	13
3	18	64	36	22
4	8	44	35	29
5	11	30	15	31
6	34	75	44	64
7	28	26	42	30
8	71	124	54	64
9	43	54	34	56
10	33	30	29	20
11	20	14	39	21

Source: Data courtesy of S. Weber.

$d_{j1} = x_{1j1} - x_{2j1}$	−19	−22	−18	−27	−4	−10	−14	17	9	4	−19
$d_{j2} = x_{1j2} - x_{2j2}$	12	10	42	15	−1	11	−4	60	−2	10	−7

Here

$$\bar{\mathbf{d}} = \begin{bmatrix} \bar{d}_1 \\ \bar{d}_2 \end{bmatrix} = \begin{bmatrix} -9.36 \\ 13.27 \end{bmatrix}, \qquad \mathbf{S}_d = \begin{bmatrix} 199.26 & 88.38 \\ 88.38 & 418.61 \end{bmatrix}$$

and

$$T^2 = 11[-9.36, \ 13.27]\begin{bmatrix} .0055 & -.0012 \\ -.0012 & .0026 \end{bmatrix}\begin{bmatrix} -9.36 \\ 13.27 \end{bmatrix} = 13.6$$

Taking $\alpha = .05$, we find that $[p(n-1)/(n-p)]F_{p,n-p}(.05) = [2(10)/9]F_{2,9}(.05) = 9.47$. Since $T^2 = 13.6 > 9.47$, we reject H_0 and conclude that there is a nonzero mean difference between the measurements of the two laboratories. It appears, from inspection of the data, that the commercial lab tends to produce lower BOD measurements and higher SS measurements than the State Lab of Hygiene. The 95% simultaneous confidence intervals for the mean differences δ_1 and δ_2 can be computed using (6-10). These intervals are

$$\delta_1 : \bar{d}_1 \pm \sqrt{\frac{(n-1)p}{(n-p)} F_{p,n-p}(\alpha)} \sqrt{\frac{s^2_{d_1}}{n}} = -9.36 \pm \sqrt{9.47}\sqrt{\frac{199.26}{11}}$$

$$\text{or} \quad (-22.46, 3.74)$$

$$\delta_2 : 13.27 \pm \sqrt{9.47}\sqrt{\frac{418.61}{11}} \quad \text{or} \quad (-5.71, 32.25)$$

Figure 1: Checking for a mean Difference with paired observations (Effluent Data)

Example 6.1 Conclusions

- The T^2 statistic for testing $H_0 : \delta' = [\delta_1, \delta_2] = [0, 0]$ is constructed from the differences of paired observations.
- Since $T^2 = 13.6 > 9.47$ (Note: taking $\alpha = 0.5$) reject the H_0 and conclude that there is a non-zero mean difference between the measurements of the two laboratories.
- Compute the 95% simultaneous confidence intervals for the mean differences δ_1 and δ_2 can be computed using Equation (6).
  - 95% **simultaneous confidence coefficient** applies to the *entire* set of intervals that could be constructed by $a_1\delta_1 + a_2\delta_2$.
  - $\delta = 0$ falls outside the 95% **confidence region for** δ.
  - If $H_0 : \delta = \mathbf{0}$ were NOT rejected, then *all* **simultaneous intervals** would include **zero**.
  - **Bonferroni simultaneous intervals** also cover zero.

Paired Comparisons Continued

- Concluding paired comparisons by noting that $\overline{\mathbf{d}}$ and $\mathbf{S_d}$, and hence T^2, may be calculated from the full-sample quantities $\overline{\mathbf{x}}$ and $\mathbf{S}$. Where,

$$\mathbf{S}_{2p\times 2p} = \begin{bmatrix} \mathbf{S}_{11} & \mathbf{S}_{12} \\ \mathbf{S}_{21} & \mathbf{S}_{22} \end{bmatrix}$$

- After defining $\mathbf{S}$ we can define the following matrix $\mathbf{C}$ and verify $\mathbf{d_j} = \mathbf{C}\mathbf{x}_j$ and $\overline{\mathbf{d}} = \mathbf{C}\overline{\mathbf{x}}$ and $\mathbf{S_d} = \mathbf{CSC}'$. Thus,

$$T^2 = n\overline{\mathbf{x}}'\mathbf{C}'(\mathbf{CSC}')^{-\mathbf{1}}\mathbf{C}\overline{\mathbf{x}} \tag{8}$$

Each row of the matrix $\mathbf{C}$ is a **contrast vector** because its elements sum to zero. Each Contrast is perpendicular to the vector $\mathbf{1}'$ since $\mathbf{c_j'1} = 0$ the component $\mathbf{1}'\mathbf{x_j}$, representing the overall treatment sum, is ignored by T^2 presented in this section.

Notation

- Now we will observe situations where q treatments are compared w.r.t. a single response variable.
  - Each subject (or experimental unit) receives each treatment once over successive periods of time.
- Denote $\mathbf{X}_j$ for the jth observation where X_{ji} is the response to the ith treatments on the jth unit.

$$\mathbf{X}_j = \begin{bmatrix} X_{j1} \\ X_{j2} \\ \vdots \\ X_{jq} \end{bmatrix}$$

Consider the contrasts of the components of $\mu = E(\mathbf{X_j})$ these could be $\mathbf{C_1}\mu$ or $\mathbf{C_2}\mu$.

- When $\mathbf{C}_1\mu = \mathbf{C_2}\mu = 0$ the hypothesis that there are no differences in treatments becomes $\mathbf{C}\mu = 0$ for any choice $\mathbf{C}$.
- Test $\mathbf{C}\mu = 0$ using equation (8)

$$\begin{bmatrix} \mu_1 - \mu_2 \\ \mu_1 - \mu_3 \\ \vdots \\ \mu_1 - \mu_q \end{bmatrix} = \begin{bmatrix} 1 & -1 & 0 & \dots & 0 \\ 1 & 0 & -1 & \dots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & 0 & 0 & \dots & -1 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \\ \vdots \\ \mu_q \end{bmatrix} = \mathbf{C}_1\mu$$

Or,

$$\begin{bmatrix} \mu_2 - \mu_1 \\ \mu_3 - \mu_2 \\ \vdots \\ \mu_q - \mu_{q-1} \end{bmatrix} = \begin{bmatrix} -1 & 1 & 0 & \dots & 0 & 0 \\ 0 & -1 & 1 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \\ 1 & 0 & 0 & \dots & -1 & 1 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \\ \vdots \\ \mu_q \end{bmatrix} = \mathbf{C}_1\mu$$

Test for Equality of Treatments

- Consider $N_q(\mu, \mathbf{\Sigma})$ population and let $\mathbf{C}$ be a contrast matrix. An α-level test of $H_0 : \mathbf{C}\mu = \mathbf{0}$ versus $H_1 : \mathbf{C}\mu \neq \mathbf{0}$ is as follows: Reject H_0 if

$$T^2 = n(\mathbf{C}\overline{\mathbf{x}})'(\mathbf{CSC}')^{-1}\mathbf{C}\overline{\mathbf{x}} > \frac{(n-1)(q-1)}{(n-q+1)}F_{q-1,n-q+1}(\alpha) \tag{9}$$

- A confidence region for contrasts $\mathbf{C}\mu$ with μ the mean of a normal population is determined by the set of all $\mathbf{C}\mu$ s.t.

$$n(\mathbf{C}\overline{\mathbf{x}})'(\mathbf{CSC}')^{-1}\mathbf{C}\overline{\mathbf{x}} \leq \frac{(n-1)(q-1)}{(n-q+1)}F_{q-1,n-q+1}(\alpha) \tag{10}$$

- Simultaneous $100(1-)\%$ confidence intervals for single contrasts $\mathbf{c}'\mu$ for any contrast vectors of interest are given by,

$$\mathbf{c}'\mu : \mathbf{c}'\overline{\mathbf{x}} \pm \sqrt{\frac{(n-1)(q-1)}{(n-q+1)}F_{q-1,n-q+1}(\alpha)}\sqrt{\frac{\mathbf{c}'\mathbf{Sc}}{n}} \tag{11}$$

Example 6.2

Table 6.2 Sleeping-Dog Data

Dog	Treatment 1	2	3	4
1	426	609	556	600
2	253	236	392	395
3	359	433	349	357
4	432	431	522	600
5	405	426	513	513
6	324	438	507	539
7	310	312	410	456
8	326	326	350	504
9	375	447	547	548
10	286	286	403	422
11	349	382	473	497
12	429	410	488	547
13	348	377	447	514
14	412	473	472	446
15	347	326	455	468
16	434	458	637	524
17	364	367	432	469
18	420	395	508	531
19	397	556	645	625

Source: Data courtesy of Dr. J. Atlee.

With $\boldsymbol{\mu}' = [\mu_1, \mu_2, \mu_3, \mu_4]$, the contrast matrix $\mathbf{C}$ is

$$\mathbf{C} = \begin{bmatrix} -1 & -1 & 1 & 1 \\ 1 & -1 & 1 & -1 \\ 1 & -1 & -1 & 1 \end{bmatrix}$$

The data (see Table 6.2) give

$$\bar{\mathbf{x}} = \begin{bmatrix} 368.21 \\ 404.63 \\ 479.26 \\ 502.89 \end{bmatrix} \quad \text{and} \quad \mathbf{S} = \begin{bmatrix} 2819.29 & & & \\ 3568.42 & 7963.14 & & \\ 2943.49 & 5303.98 & 6851.32 & \\ 2295.35 & 4065.44 & 4499.63 & 4878.99 \end{bmatrix}$$

It can be verified that

$$\mathbf{C}\bar{\mathbf{x}} = \begin{bmatrix} 209.31 \\ -60.05 \\ -12.79 \end{bmatrix}; \quad \mathbf{CSC}' = \begin{bmatrix} 9432.32 & 1098.92 & 927.62 \\ 1098.92 & 5195.84 & 914.54 \\ 927.62 & 914.54 & 7557.44 \end{bmatrix}$$

and

$$T^2 = n(\mathbf{C}\bar{\mathbf{x}})'(\mathbf{CSC}')^{-1}(\mathbf{C}\bar{\mathbf{x}}) = 19(6.11) = 116$$

$$(\mu_3 + \mu_4) - (\mu_1 + \mu_2) = \begin{pmatrix} \text{Halothane contrast representing the} \\ \text{difference between the presence and} \\ \text{absence of halothane} \end{pmatrix}$$

$$(\mu_1 + \mu_3) - (\mu_2 + \mu_4) = \begin{pmatrix} \text{CO}_2 \text{ contrast representing the difference} \\ \text{between high and low CO}_2 \text{ pressure} \end{pmatrix}$$

$$(\mu_1 + \mu_4) - (\mu_2 + \mu_3) = \begin{pmatrix} \text{Contrast representing the influence} \\ \text{of halothane on CO}_2 \text{ pressure differences} \\ \text{(H–CO}_2 \text{ pressure "interaction")} \end{pmatrix}$$

Figure 2: Sleeping Dog Data & Computations

$$\frac{(19-1)(4-1)}{(19-4+1)} F_{3,16}(0.5) = 10.94 \quad \text{From (7) } T^2 = 116 > 10.94 \quad \text{Reject } H_0 : \mathbf{C}\mu = \mathbf{0}$$

6.3 Introduction

- This T^2 statistic is appropriate for comparing responses from one-set of experimental settings (population 1) with the independent responses from another set of experimental settings (population 2)
- Consider a random sample of size n_1 from population 1 and a sample of size n_2 from population 2. The observations on p variables are arranged as follows.

Sample		**Summary Statistics**
(population 1)	$\overline{\mathbf{x}}_1 = \frac{1}{n_1}\sum_{j=1}^{n_1} x_{1j}$	$\mathbf{S_1} = \frac{\mathbf{1}}{\mathbf{n_1-1}}\sum_{\mathbf{j=1}}^{\mathbf{n_1}}(\mathbf{x_{1j}} - \overline{\mathbf{x_1}})(\mathbf{x_{1j}} - \overline{\mathbf{x}}_1)'$
(population 1)	$\overline{\mathbf{x}}_1 = \frac{1}{n_2}\sum_{j=1}^{n_1} x_{2j}$	$\mathbf{S_1} = \frac{\mathbf{1}}{\mathbf{n_2-1}}\sum_{\mathbf{j=1}}^{\mathbf{n_2}}(\mathbf{x_{2j}} - \overline{\mathbf{x_2}})(\mathbf{x_{2j}} - \overline{\mathbf{x}}_2)'$

- Want to answer the question $\mu_1 = \mu_2$ and if $\boldsymbol{\mu_1} - \boldsymbol{\mu_2} \neq \mathbf{0}$ which component means are different?

Assumptions and Common Covariance

Assumptions Concerning the structure of the data:

1. The sample $\mathbf{X_{1n_1}}$ is a random sample size n_1 from a p-variate population with mean vector $\mu_\mathbf{1}$ and co variance matrix $\mathbf{\Sigma_1}$
2. The sample $\mathbf{X_{2n_2}}$ is a random sample of size n_2 from a p-variate population with mean vector $\mu_\mathbf{2}$ and co variance matrix $\mathbf{\Sigma_2}$
3. $\mathbf{X_{11}}, \mathbf{X_{12}}, ..., \mathbf{X_{1n_1}}$ are independent of $\mathbf{X_{21}}, \mathbf{X_{22}}, ..., \mathbf{X_{2n_2}}$

Assumptions When n_1 and n_2 are small:

1. Both populations are multivariate normal
2. $\mathbf{\Sigma_1} = \mathbf{\Sigma_2}$ (same co-variance matrix)

Here, we are assuming several pairs of variances and co variances are nearly equal. Consequently, we can *pool* the information in both samples to estimate the common co variance.

$$\mathbf{S}_{pooled} = \frac{n_1 - 1}{n_1 + n_2 - 2}\mathbf{S}_1 + \frac{n_2 - 1}{n_1 + n_2 - 2}\mathbf{S_2} \tag{12}$$

Assumptions Cont.

- By the independence assumption in slide (14) implies $\overline{\mathbf{X}}_1$ and $\overline{\mathbf{X}}_2$ are independent thus $COV(\overline{\mathbf{X_1}}, \overline{\mathbf{X_2}}) = 0$.Where

$$\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\mathbf{S}_{pooled} \tag{13}$$

is an estimator of $COV(\overline{\mathbf{X_1}} - \overline{\mathbf{X}}_2)$. The likelihood ratio test of $H_0 : \boldsymbol{\mu_1} - \boldsymbol{\mu_2} = \delta_0$ is base on T^2. Reject H_0 if,

$$T^2 = (\overline{\mathbf{x_1}} - \overline{\mathbf{x_2}} - \delta_{\mathbf{0}})' \left[\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\mathbf{S}_{pooled}\right]^{-1} (\overline{\mathbf{x_1}} - \overline{\mathbf{x_2}} - \delta_{\mathbf{0}}) > c^2 \tag{14}$$

Where the **critical distance** c^2 is determined from the distribution of the two-sample T^2 statistic.

Assumptions Cont.

Result 6.2

If $\mathbf{X_{11}}, \mathbf{X_{12}}, ..., \mathbf{X_{1n}}$ is a random sample of size n_1 from the $N_p(\mu_1, \Sigma)$ and $\mathbf{X_{21}}, \mathbf{X_{22}}, ..., \mathbf{X_{2n_2}}$ is an independent random sample of size n_2 from $N_P(\mu_2, \Sigma)$, then

$$P\left(\overline{\mathbf{X}} - \overline{\mathbf{X}} - (\mu_{\mathbf{1}} - \mu_{\mathbf{2}}))' \left[\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\right]^{-1} (\overline{\mathbf{X_1}} - \overline{\mathbf{X_2}} - (\mu_{\mathbf{1}} - \mu_{\mathbf{2}})) \leq c^2\right] = 1 - \alpha \tag{15}$$

Where,

$$c^2 = \frac{(n_1 + n_2 - 2)p}{(n_1 + n_2 - p - 1)} F_{p, n_1 + n_2 - p - 1}(\alpha)$$

We are interested in the confidence regions for $\mu_{\mathbf{1}} - \mu_{\mathbf{2}}$. From **Result 6.2** we conclude that all $\mu_1 - \mu_2$ within squared statistical distance c^2 of $\overline{\mathbf{x_1}} - \overline{\mathbf{x_2}}$ constitute the confidence region (forms an ellipse).

Simultaneous Confidence intervals

- Deriving simultaneous confidence intervals for the components of the vector $\boldsymbol{\mu_1} - \boldsymbol{\mu_2}$. We assume that parent multivariate populations are normal with a common co variance $\boldsymbol{\Sigma}$

Result 6.3

Let $c^2 = (n_1 + n_2 - 2)p/(n_1 + n_2 - p - 1)F_{p,n_1+n_2-p-1}(\alpha)$ with probability $1 - \alpha$

$$\mathbf{a}'(\overline{\mathbf{X}}_\mathbf{1} - \overline{\mathbf{X}}_\mathbf{2}) \pm c\sqrt{\mathbf{a}'\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\mathbf{S}_{pooled}\mathbf{a}}$$

will cover $\mathbf{a}(\boldsymbol{\mu_1} - \boldsymbol{\mu_2})$ for all $\mathbf{a}$. In particular $\mu_{1i} - \mu_{2i}$ will be covered by,

$$(\overline{X_{1i}} - \overline{X}_{2i}) \pm c\sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right)s_{ii,pooled}}$$

Example 6.4

Example 6.4 (Calculating simultaneous confidence intervals for the differences in mean components) Samples of sizes $n_1 = 45$ and $n_2 = 55$ were taken of Wisconsin homeowners with and without air conditioning, respectively. (Data courtesy of Statistical Laboratory, University of Wisconsin.) Two measurements of electrical usage (in kilowatt hours) were considered. The first is a measure of total *on*-peak consumption (X_1) during July, and the second is a measure of total *off*-peak consumption (X_2) during July. The resulting summary statistics are

$$\bar{\mathbf{x}}_1 = \begin{bmatrix} 204.4 \\ 556.6 \end{bmatrix}, \quad \mathbf{S}_1 = \begin{bmatrix} 13825.3 & 23823.4 \\ 23823.4 & 73107.4 \end{bmatrix}, \quad n_1 = 45$$

$$\bar{\mathbf{x}}_2 = \begin{bmatrix} 130.0 \\ 355.0 \end{bmatrix}, \quad \mathbf{S}_2 = \begin{bmatrix} 8632.0 & 19616.7 \\ 19616.7 & 55964.5 \end{bmatrix}, \quad n_2 = 55$$

$$\mathbf{S}_{\text{pooled}} = \frac{n_1 - 1}{n_1 + n_2 - 2}\mathbf{S}_1 + \frac{n_2 - 1}{n_1 + n_2 - 2}\mathbf{S}_2 = \begin{bmatrix} 10963.7 & 21505.5 \\ 21505.5 & 63661.3 \end{bmatrix}$$

and

$$c^2 = \frac{(n_1 + n_2 - 2)p}{n_1 + n_2 - p - 1} F_{p, n_1+n_2-p-1}(\alpha) = \frac{98(2)}{97} F_{2,97}(.05)$$
$$= (2.02)(3.1) = 6.26$$

With $\boldsymbol{\mu}_1' - \boldsymbol{\mu}_2' = [\mu_{11} - \mu_{21}, \mu_{12} - \mu_{22}]$, the 95% simultaneous confidence intervals for the population differences are

$$\mu_{11} - \mu_{21}: (204.4 - 130.0) \pm \sqrt{6.26}\sqrt{\left(\frac{1}{45} + \frac{1}{55}\right)10963.7}$$

or

$$21.7 \le \mu_{11} - \mu_{21} \le 127.1 \qquad \text{(on-peak)}$$

$$\mu_{12} - \mu_{22}: (556.6 - 355.0) \pm \sqrt{6.26}\sqrt{\left(\frac{1}{45} + \frac{1}{55}\right)63661.3}$$

or

$$74.7 \le \mu_{12} - \mu_{22} \le 328.5 \qquad \text{(off-peak)}$$

Figure 3: Constructing Simultaneous Confidence Intervals

- Using Equations (10) and Result 6.3. Note, the Bonferroni $100(1-\alpha)\%$ **simultaneous confidence intervals** for the p population mean differences

$$\mu_{1i} - \mu_{2i} : (\overline{x}_{1i} - \overline{x}_{2i}) \pm t_{n_1+n_2-2}\left(\frac{\alpha}{2p}\right)\sqrt{\frac{1}{n_1 + \frac{1}{n_2}} s_{ii,pooled}} \qquad (16)$$

The Two Sample Situation when $\mathbf{\Sigma} \neq \mathbf{\Sigma}$

- When $\mathbf{\Sigma} \neq \mathbf{\Sigma}$ we are unable to find the "distance" measure like T^2, whose distribution does not depend on the unknowns $\mathbf{\Sigma_1}, \mathbf{\Sigma_2}$.
  - Bartlett's test equality of $\mathbf{\Sigma_1}, \mathbf{\Sigma_2}$ in terms of generalized variances.
  - Misleading when populations non-normal
- Less Sensitive test, Tiku and Balakrishnan [23]
- Size of the discrepancies depend on number of p-variables

Result 6.4

Let the sample sizes be such that $n_1 - p$ and $n_2 - p$ are large. Then the approximate $100(1-\alpha)\%$ confidence ellipsoid (see slide 16) for $\boldsymbol{\mu_1} - \boldsymbol{\mu_2}$ is given by all $\boldsymbol{\mu_1} - \boldsymbol{\mu_2}$ satisfying,

$$[\overline{x}_1 - \overline{x}_2 - (\boldsymbol{\mu_1} - \boldsymbol{\mu_2})]' \left[\frac{1}{n_1}\mathbf{S}_1 + \frac{1}{n^2\mathbf{S}_2}\right]^{-1} [\overline{x}_1 - \overline{x}_2 - (\boldsymbol{\mu_1} - \boldsymbol{\mu_2})] \leq \chi_p^2(\alpha)$$

$$\mathbf{a}'(\overline{x}_1 - \overline{x}_2) \pm \sqrt{\chi_p^2(\alpha)}\sqrt{\mathbf{a}'\left(\frac{1}{n_1}\mathbf{S}_1 + \frac{1}{n_2}\mathbf{S}_2\right)\mathbf{a}}$$

Distribution of T^2

- We can test $H_0 : \boldsymbol{\mu_1} - \boldsymbol{\mu_2} = 0$ when population co-variance matrices are unequal even if the two sample sizes are not large provided the two populations are multivariate normal.
  - Behrens-Fisher Problem

$$T^2 = (\overline{\mathbf{X}}_\mathbf{1} - \overline{\mathbf{X}}_\mathbf{2} - (\boldsymbol{\mu_1} - \boldsymbol{\mu_2}))' \left[\frac{1}{n_1 \mathbf{S}_1 + \frac{1}{n_2}\mathbf{S_2}} \right]^{-1} (\overline{\mathbf{X}}_\mathbf{1} - \overline{\mathbf{X}}_\mathbf{2} - (\boldsymbol{\mu_1} - \boldsymbol{\mu_2})) \tag{17}$$

- recommended approximation for smaller samples is given by,

$$T^2 = \frac{\nu p}{\nu - p + 1} F_{p,\nu-p+1} \tag{18}$$

- For normal populations, the approximation to the distribution of T^2 given by (18) generates reasonable results.

Assumptions & Summary of ANOVA

Assumptions about the structure of the Data for One-Way MANOVA

1. $\mathbf{X}_{\ell 1}, X_{\ell 2}, ..., X_{\ell n_\ell}$ is a random sample of size n_ℓ from a population with mean μ_ℓ where $\ell = 1, 2, ..., g$. The random samples from different populations are independent.
2. All populations have a common co variance matrix $\mathbf{\Sigma}$.
3. Each population is multivariate normal

- Summary of ANOVA

$$\mu_\ell = \mu + \tau_\ell \tag{19}$$

$$\mathbf{X}_{\ell j} = \mu + \tau_\ell + e_{\ell j} \tag{20}$$

$$x_{\ell j} = \overline{x} + (\overline{x}_\ell - \overline{x}) + (x_{\ell j} - \overline{x}_\ell) \tag{21}$$

Comparing g population Mean Vectors

Paralleling the uni-variate reparameterization (see equation (16,17,18)) we specify the **MANOVA** model.

$$\mathbf{X}_{\ell \mathbf{j}} = \mu + \tau_\ell + e_{\ell j} \qquad j = 1, 2, ..., n_\ell \quad \text{and} \quad \ell = 1, 2, ..., g \tag{22}$$

$$\mathbf{x}_{\ell \mathbf{j}} = \overline{x} + (\overline{x}_\ell - \overline{x}) + x_\ell - \overline{x}_\ell) \tag{23}$$

- Decomposing Equation (20) leads t the multivariate analog of the uni-variate sum of squares breakup.
- Expanding $(\mathbf{x}_{\ell \mathbf{j}} - \overline{\mathbf{x}})(\mathbf{x}_{\ell \mathbf{j}} - \overline{\mathbf{x}})'$ leads to the **within sum of squares and cross product matrix**

$$\mathbf{W} = \sum_{\ell=1}^{g} \sum_{j=1}^{n_\ell} (\mathbf{x}_{\ell_\mathbf{j}} - \overline{\mathbf{x}}_\ell)(\mathbf{x}_{\ell \mathbf{j}} - \overline{\mathbf{x}}_\ell)' \tag{24}$$

$$= (n_1 - 1)\mathbf{S}_1 + (n_2 - 1)\mathbf{S}_2 + \ldots + (n_g - 1)\mathbf{S}_g \tag{25}$$

Comparing g population Mean Vectors Cont.

MANOVA table for Comparing Population Mean Vectors

Source of Variation	Matrix of SS and CP	d.f.
Treatment	B $= \sum_{\ell=1}^{g} n_\ell(\overline{\mathbf{x}}_\ell - \overline{\mathbf{x}})(\overline{\mathbf{x}}_\ell - \overline{\mathbf{x}})'$	g - 1
Residual (Error)	$\mathbf{W}$	$\sum_{\ell=1}^{g} n_\ell - g$
Total (corrected for the mean)	$\mathbf{B} + \mathbf{W}$	$\sum_{\ell=1}^{g} n_\ell - 1$

Comparing g population Mean Vectors Cont.

- One test of $H_0 : \tau_1 = \tau_g = \ldots = \tau_g = 0$ involves generalized variances and we reject H_0 if the ratio of generalized variances

$$\Lambda^* = \frac{|\mathbf{W}|}{|\mathbf{B} + \mathbf{W}|} \tag{26}$$

are too small. For large sample sizes, modifications to Λ^*, can be used to test H_0. (refer to §6.4, table 6.3, pg. 303 of textbook).

Simultaneous Confidence intervals for Treatment Effects

- Let τ_{ki} be the ith component of τ_k. Since τ_k is estimated by $\hat{\tau_{\mathbf{k}}} = \overline{\mathbf{x}}_{\mathbf{k}} - \overline{\mathbf{x}}$.

$$\hat{\tau}_{ki} = \overline{x}_{ki} - \overline{x}_i \tag{27}$$

- For p variables and $g(g-1)/2$ pairwise differences, so each two-sample t-interval will employ the critical value $t_{n-g}(\alpha/2m)$ where,

$$m = pg(g-1)/2 \tag{28}$$

  is the number of simultaneous confidence statements.

Result 6.5

Let $n = \sum_{k=1}^{g} n_k$. For the the model in **(19)** with confidence at least $(1-\alpha)$,

$$\tau_{ki} - \tau_{\ell i} \quad \text{belongs to} \quad \overline{x}_{ki} - \overline{x}_{\ell i} \pm t_{n-g}\left(\frac{\alpha}{pg(g-1)}\right)\sqrt{\frac{w_{ii}}{n-g}\left(\frac{1}{n_k} + \frac{1}{n_\ell}\right)}$$

for all components $i = 1, ..., p$ and all differences $\ell < k = 1, ..., g$. Here w_{ii} is the ith diagonal element of $\mathbf{W}$.

Testing for Equality of Covariance Matrices

- One assumption made when comparing two or more multivariate mean vectors is that the covariance matrices of the potentially different populations are the same.
- Test the equality of the population covariance matrices.
  - Box's M -test

$$H_0 : \mathbf{\Sigma_1} = \mathbf{\Sigma_2} = \ldots = \mathbf{\Sigma_g} = \mathbf{\Sigma} \tag{29}$$

$$\Lambda = \prod_{\ell} \left(\frac{|\mathbf{S}_\ell|}{|\mathbf{S}_{pooled}|} \right)^{(n_\ell - 1)/2} \tag{30}$$

$$M = [\mathbf{\Sigma}_\ell (n_\ell - 1)] \ln |\mathbf{S}_{pooled}| - \mathbf{\Sigma}[(n_{\ell-1}) \ln |\mathbf{S}_\ell|] \tag{31}$$

Box's Test for Equality of Covariance Matrices

Set,

$$u = \left[\boldsymbol{\Sigma}_\ell \frac{1}{(n_\ell - 1)} - \frac{1}{\boldsymbol{\Sigma}_\ell (n_\ell - 1)}\right] \left[\frac{2p^2 + 3p - 1}{6(p+1)(g-1)}\right] \tag{32}$$

then,

$$C = (1 - u)M \tag{33}$$

Has an approximate χ^2 distribution with

$$\nu = g\frac{1}{2}p(p+1) - \frac{1}{2}p(p+1) = \frac{1}{2}p(p+1)(g-1) \tag{34}$$

degrees of freedom at significance level α, reject H_0 if $C > \chi^2_{p(p+1)(g-1)/2}(\alpha)$

- Box's χ^2 approximation works well if each n_ℓ exceeds 20 and if p and g do not exceed 5.

Univariate Two-Way Fixed-Effects Model with Interaction

- Suppose there are g levels of factor 1 and b levels of factor 2, and that n independent obersevations can be observed at each of the gb combination levels.
- Denote the **univariate two way model** as

$$X_{\ell kr} = \mu + \tau_\ell + \beta_k + \gamma_{\ell k} + e_{\ell kr} \tag{35}$$

$$\begin{aligned} \ell &= 1, 2, \ldots, g \\ k &= 1, 2, \ldots, b \\ r &= 1, 2, \ldots, n \end{aligned}$$

Where the sums of the random variables and $e_{\ell kr}$ are independent $N(0, \sigma^2)$ random variables.

Multivariate Two-Way Fixed Effects Model with Interaction

- The two-way fixed effects model for a *vector* response consisting of p components.

$$\mathbf{X}_{\ell k r} = \mu + \tau_\ell + \beta_k + \gamma_{\ell k} + \mathbf{e}_{\ell k r} \tag{36}$$

$$\begin{aligned} \ell &= 1, 2, \dots, g \\ k &= 1, 2, \dots, b \\ r &= 1, 2, \dots, n \end{aligned}$$

- The vectors are all of order $p \times 1$, and the $\mathbf{e}_{\ell k r}$ are independent $N_p(\mathbf{0}, \mathbf{\Sigma})$ random vectors (MANOVA table for comparing Factors and their interaction in §6.7 page 316).

Multivariate Two-Way Fixed Effects Model with Interaction Cont.

- For the likelihood ratio test of $H_0 : \gamma_{11} = \gamma_{12} = \ldots = \gamma_{gb} = \mathbf{0}$ (no interaction effects versus H_1 : At least one $\gamma_{\ell\mathbf{k}} = \mathbf{0}$ is conducted by rejecting H_0 for small values of the ratio,

$$\Lambda^* = \frac{|\text{SSP}_{\text{res}}|}{|\text{SSP}_{\text{int}} + \text{SSP}_{\text{res}}|} \tag{37}$$

- p Univariate two-way analyses of variance (one for each variable) are often conducted to see whether the interaction appears in some responses not others.
- Consider $H_0 : \boldsymbol{\tau_1} = \boldsymbol{\tau_2} = \ldots = \boldsymbol{\tau_g} = \mathbf{0}$ and H_1 : at least one $\tau_\ell \neq \mathbf{0}$.

$$\Lambda^* = \frac{|\text{SSP}_{\text{res}}|}{|\text{SSP}_{\text{fac1}} + \text{SSP}_{\text{res}}|} \tag{38}$$

- For factor 2 effects, $H_0 : \boldsymbol{\beta_1} = \boldsymbol{\beta_1} = \ldots = \boldsymbol{\beta_1} = \mathbf{0}$ and H_1 : at least one $\beta_k \neq \mathbf{0}$

$$\Lambda^* = \frac{|\text{SSP}_{\text{res}}|}{|\text{SSP}_{\text{fac2}} + \text{SSP}_{\text{res}}|} \tag{39}$$

Multivariate Two-Way Fixed Effects Model with Interaction Cont.

Reject $H_0 : \gamma_{11} = \gamma_{12} = \ldots = \gamma_{gb} = 0$ **at level** α **if**

$$-\left[gb(n-1) - \frac{p+1-(g-1)(b-1)}{2}\right] \ln \Lambda^* > \chi^2_{(g-1)(b-1)p(\alpha)} \tag{40}$$

Reject $H_0 : \beta_1 = \tau_2 = \ldots = \tau_b = 0$ **at level** α **if** (no factor 1 effects)

$$-\left[gb(n-1) - \frac{p+1-(g-1)(b-1)}{2}\right] \ln \Lambda^* > \chi^2_{(g-1)p(\alpha)} \tag{41}$$

Reject $H_0 : \beta_1 = \beta_2 = \ldots = \beta_b = 0$ **at level** α **if** (no factor 2 effects)

$$-\left[gb(n-1) - \frac{p+1-(g-1)(b-1)}{2}\right] \ln \Lambda^* > \chi^2_{(g-1)(b-1)p(\alpha)} \tag{42}$$

Fixed Effects Model with Interaction Cont. Simultaneous Confidence Intervals

- **Simultaneous confidence intervals** for contrasts in the model parameters can provide insights into the nature of the factor effects.
- The **Bonferroni** approach applies to the components of the differences of the factor 1 effects and components of factor 2 effects, respectively.
- $100(1-\alpha)\%$ simultaneous confidence interval where $\nu = gb(n-1)$, E_{ii} is the ith diagonal element of $\mathbf{E} = SSP_{res}$ and $\overline{x}_{\ell i} - \overline{x}_{mi}$ is the ith component of $\overline{\mathbf{x}}_{\ell} - \overline{\mathbf{x}}_{m}$

$$\tau_{\ell i} - \tau_{mi} \quad \text{Belongs to} \quad (\overline{x}_{mi} - \overline{x}_{mi}) \pm t_{\nu}\left(\frac{\alpha}{pg(g-1)}\right)\sqrt{\frac{\mathbf{E}_{ii}}{\nu}\frac{2}{bn}} \tag{43}$$

- ν and E_{ii} are as just defined as $\overline{x}_{ki} - \overline{x}_{qi}$ is the ith component of $\overline{\mathbf{x}}_{k} - \overline{\mathbf{x}}_{q}$

$$\beta_{ki} - \beta_{qi} \quad \text{Belongs to} \quad (\overline{x}_{ki} - \overline{x}_{qi}) \pm t_{\nu}\left(\frac{\alpha}{pg(g-1)}\right)\sqrt{\frac{\mathbf{E}_{ii}}{\nu}\frac{2}{gn}} \tag{44}$$

Profile Analysis Introduction

- **Profile Analysis** pertains to situations in which a battery of p treatments are administered to *two or more groups of subjects*.
- Construct profiles for each **population** (group).
  - $\boldsymbol{\mu}_1' = [\mu_{11}, \mu_{12}, \ldots, \mu_{1p}]$ and $\mu_2' = [\mu_{21}, \mu_{22}, \ldots, \mu_{2p}]$ are the *mean responses* to p *treatments* for populations 1 and 2
- $H_0 : \boldsymbol{\mu}_1 = \boldsymbol{\mu}_2$ implies that the treatments have the **same (average) effect** on the two populations.

(Stage) Question?	Acceptable? Equivalently,
(1) Are the Profiles **Parallel**?	$H_{01} : \mu_{1i} - \mu_{1i-1} = \mu_{2i} - \mu_{2i-1}$ for $i = 2, 3, \ldots, p$
(2) Are the Profiles **Coincident**?	$H_{02} : \mu_{1i} = \mu_{2i}$ for $i = 1, 2, \ldots, p$
(3) Are the Profiles **Level**?	$H_{03} : \mu_{11} = \mu_{12} = \ldots = \mu_{1p} = \mu_{21} = \mu_{22} \ldots = \mu_{2p}$

Testing Profiles in Stages

Stage	Null Hypothesis	Reject at level α if
		Test for Parallel Profiles **(0)**
(1)	$H_{01} := \mathbf{C}\mu_\mathbf{1} = \mathbf{C}\mu_\mathbf{2}$	$(\overline{\mathbf{x}} - \overline{\mathbf{x}})'\mathbf{C}'[(\frac{1}{n_1} + \frac{1}{n_2})\mathbf{C}\mathbf{S}_\mathbf{p}\mathbf{C}']^{-1}\mathbf{C}(\overline{\mathbf{x}}_\mathbf{2} - \overline{\mathbf{x}}_\mathbf{2}) > \mathbf{c}^\mathbf{2}$
		Given Profiles are Parallel **(1)**
(2)	$H_{02} : \mathbf{1}'\mu_1 = \mathbf{1}'\mu_2$	$\left(\frac{\mathbf{1}'(\overline{\mathbf{x}_\mathbf{1}} - \overline{\mathbf{x}_\mathbf{2}})}{\sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right)\mathbf{1}'\mathbf{S}_\mathbf{p}\mathbf{1}}}\right)^2 > t^2_{n_1+n_2-2}\left(\frac{\alpha}{2}\right) = F_{1,n_1+n_2-2}(\alpha)$
		Given Profiles are Coincident **(2)**
(3)	$H_{03} : \mathbf{C}\mu = \mathbf{0}$	$(n_1 + n_2)\overline{\mathbf{x}}'\mathbf{C}'[\mathbf{C}\mathbf{S}\mathbf{C}']^{-1}\mathbf{C}\overline{\mathbf{x}} > c^2$

Last Remark

Remark 1:

When the Sample sizes are small, a profile analysis will depend on the normality assumption. This assumption can be checked, using methods discussed in Chapter 4, with the original observations $\mathbf{x}_{\ell \mathbf{j}}$ or the contrast observations $\mathbf{C}\mathbf{x}_{\ell \mathbf{j}}$. Moreover, **analysis of several populations** proceeds in much the *same fashion as that for two populations*.

Repeated Measures Introduction

- **Repeated measures** refers to situations where the same characteristic is observed, at different times or locations, on the same subject.
- The **Growth Model** measures a single treatment applied to each subject over a period of time.
- Consider the following example
    - *Question: Can the growth pattern be adequately represented by a polynomial in time?*

Table 6.5 Calcium Measurements on the Dominant Ulna; Control Group

Subject	Initial	1 year	2 year	3 year
1	87.3	86.9	86.7	75.5
2	59.0	60.2	60.0	53.6
3	76.7	76.5	75.7	69.5
4	70.6	76.1	72.1	65.3
5	54.9	55.1	57.2	49.0
6	78.2	75.3	69.1	67.6
7	73.7	70.8	71.8	74.6
8	61.8	68.7	68.2	57.4
9	85.3	84.4	79.2	67.0
10	82.3	86.9	79.4	77.4
11	68.6	65.4	72.3	60.8
12	67.8	69.2	66.3	57.9
13	66.2	67.0	67.0	56.2
14	81.0	82.3	86.8	73.9
15	72.3	74.6	75.3	66.1
Mean	72.38	73.29	72.47	64.79

Source: Data courtesy of Everett Smith.

Figure 4: **Table 6.5** Ca Measurements on the Dominant Ulna; Control Group

Theory & Notation

- When p measurements on all subjects are taken at time $t_1, t_2, \ldots, t_p$ the **Potthoff-Roy** model for quadratic growth becomes,
- **Assumptions:** All $\mathbf{X}_{\ell j}$ are independent and have the same covariance matrix $\mathbf{\Sigma}$. Under the **quadratic growth model** the mean vectors are

$$E[\mathbf{X}_{\ell j}] = \begin{bmatrix} \beta_0 + \beta_2 t_1 + \beta_2 t_1^2 \\ \beta_0 + \beta_2 t_2 + \beta_2 t_2^2 \\ \vdots \\ \beta_0 + \beta_2 t_p + \beta_2 t_p^2 \end{bmatrix} = \begin{bmatrix} 1 & t_1 & t_1^2 \\ 1 & t_2 & t_2^2 \\ \vdots & \vdots & \vdots \\ 1 & t_p & t_P^2 \end{bmatrix} \begin{bmatrix} \beta_{\ell 0} \\ \beta_{\ell 1} \\ \beta_{\ell 2} \end{bmatrix} = \mathbf{B}\beta_\ell$$

- Under the assumption of Multivariate normality, the **maximum likelihood estimators** of the β_ℓ are

$$\hat{\beta}_\ell = (\mathbf{B}'\mathbf{S}_p^{-1}\mathbf{B})^{-1}\mathbf{B}'\mathbf{S}_p^{-1}\overline{\mathbf{X}}_\ell \qquad \text{for} \qquad \ell = 1, 2, \ldots, g \qquad (45)$$

Theory & Notation Cont.

- Under a qth order polynomial, the error sum of squares and cross products (d.f: $n_g - g + p - q - 1$)

$$\mathbf{W}_q = \sum_{\ell=1}^{g} \sum_{j=1}^{n_\ell} (\mathbf{X}_{\ell \mathbf{j}} - \mathbf{B}\hat{\beta}_\ell)(\mathbf{X}_{\ell j} - \mathbf{B}\hat{\beta}_\ell)' \tag{46}$$

- The likelihood ratio test of the null hypothesis that the q-**order polynomial is adequate** can be based on *Wilk's lambda*.

$$\Lambda^* = \frac{|\mathbf{W}|}{|\mathbf{W}_q} \tag{47}$$

- For *large sample sizes*, the **null hypothesis** that the polynomial is adequate is **rejected** if

$$-\left(N - \frac{1}{2}(p - q + g)\right) \ln \Lambda^* > \chi^2_{(p-q-1)g}(\alpha) \tag{48}$$

A Strategy for the Multivariate Comparison of Treatments

1. **Try to identify Outliers:**
2. **Perform a multivariate test of Hypothesis:**
3. **Calculate the Bonferroni Simultaneous confidence intervals**

Remark 2:

In some cases, differences may appear in only one of the many characteristics, and hold for only a few treatment combinations. Therefore, these few active differences may become lost among all the inactive ones. That is, the overall test may not show significance whereas a univariate test restricted to the specific active variable would detect the difference.

Citations

1. Johnson, R. A., Wichern, D. W. (1992). Applied multivariate statistical analysis.Englewood Cliffs, N.J: Prentice Hall.