## Inference about Mean Vectors

## Motivating Example: Iris Data

This data set consists of the measurements of the variables sepal length and width, and petal length and width (in centimeters), respectively, for 50 flowers from each of 3 species (setosa, versicolor and virginica) of iris.

- Source: Fisher, R. A. (1936) The use of multiple measurements in taxonomic problems. Annals of Eugenics, 7, Part II, 179-188.
- Dataset: Available in R as 'iris.'

## Motivating Example: Iris Data

The first few rows are given below

Sepal.Length	Sepal.Width	Petal.Length	Petal.Width	Species
5.1	3.5	1.4	0.2	setosa
4.9	3.0	1.4	0.2	setosa
4.7	3.2	1.3	0.2	setosa
4.6	3.1	1.5	0.2	setosa
5.0	3.6	1.4	0.2	setosa
5.4	3.9	1.7	0.4	setosa

- Q1: Estimate the mean of (SL, SW, PL, PW) for setosa flowers.
- Q2: Provide confidence intervals.
- Q3: Compare the mean of these characteristics across species.

#### Inference about Mean Vectors

Let  $\mu_1$  and  $\mu_2$  be two population mean vectors.

- ullet How to carry out inference about  $\mu_1$  (hypothesis testing & confidence intervals/regions)
- ullet How to formally assess a hypothesis of the form  $H_0$ :  $\mu_1=\mu_2$ .
- ullet How to formally assess a hypothesis of the form  $H_0$ : the change in the components of  $\mu_1=$  the change in the component of  $\mu_2=$
- How to construct confidence intervals/regions for the mean difference  $\mu_1 \mu_2$ .

## Inferences about a Vector of Population Means

- We will generalize t-tests to test hypotheses about a  $p \times 1$  vector of population means  $\boldsymbol{\mu} = (\mu_1, \mu_2, \dots, \mu_p)'$ .
- We could consider p hypothesis tests (one for each  $\mu_j$  in  $\mu$ ) but that would not take advantage of the correlations between the variables  $X_1, X_2, \ldots, X_p$ .
- We will consider applications to repeated measures (longitudinal) studies.
- We will also generalize the two-sample t-test to test the null hypothesis that vectors of population means are the same for two populations.

## Review of Univariate Hypothesis Testing

- Is  $\mu_0$  a plausible value for the population mean  $\mu$ ?
- We formulate the question as a hypothesis testing exercise. The competing hypotheses are

$$H_0: \mu = \mu_0$$
 and  $H_a: \mu \neq \mu_0$ .

• Given a sample  $x_1, ..., x_n$  from a normal population, we compute the  $test\ statistic$ 

$$t = \frac{(\bar{x} - \mu_0)}{s/\sqrt{n}}.$$

- If t is 'small', then  $\bar{x}$  is close enough to  $\mu_0$  to suggest that  $\mu_0$  is plausible and we fail to reject  $H_0$ .
- If t is "large" then  $\bar{x}$  is too far from  $\mu_0$  to believe that  $\mu_0$  is plausible and we reject  $H_0$ .

## **Univariate Hypothesis Testing**

- When  $H_0$  is true, the statistic t has a student t distribution with n-1 degrees of freedom. We reject the null hypothesis at significance level  $\alpha$  when  $|t| > t_{(n-1),1-\alpha/2}$ .
- Notice that rejecting  $H_0$  when t is large is equivalent to rejecting  $H_0$  when the squared standardized distance

$$t^{2} = \frac{(\bar{x} - \mu_{0})^{2}}{s^{2}/n} = n(\bar{x} - \mu_{0})(s^{2})^{-1}(\bar{x} - \mu_{0})$$

is large.

• We reject  $H_0$  when

$$n(\bar{x} - \mu_0)(s^2)^{-1}(\bar{x} - \mu_0) > t_{(n-1), 1-\alpha/2}^2$$

i.e., the squared standardized distance exceeds the  $1-\alpha$  percentile of a central F-distribution with (1, n-1) df.

## Univariate Hypothesis Testing

- If we fail to reject  $H_0$ , we conclude that  $\mu_0$  is close (in units of standard deviations of  $\bar{x}$ ) to  $\bar{x}$ , and thus is a plausible value for  $\mu$ .
- The set of plausible values for  $\mu$  is the set of all values that lie in the  $100(1-\alpha)\%$  confidence interval for  $\mu$ :

$$\bar{x} - t_{(n-1),1-\alpha/2} \frac{s}{\sqrt{n}} \le \mu_0 \le \bar{x} + t_{(n-1),1-\alpha/2} \frac{s}{\sqrt{n}}.$$

- Given the value of  $\bar{x}$ , a  $(1-\alpha)*100\%$  confidence interval consists of all the  $\mu_0$  values that would not be rejected by the  $\alpha$  level test of  $H_0: \mu = \mu_0$ .
- How to interpret confidence intervals?

## General Approach to Multivariate Inference

- Let  $\mathbf{x}'_i = (x_{i1}, x_{i2}, \dots, x_{ip})$  denote the *i*th observation.
- Compute summary statistics:

$$\bar{\mathbf{x}} = \frac{1}{n} \sum_{i=1}^{n} \mathbf{x}_i, \quad \text{and} \quad S = \frac{1}{n-1} \sum_{i=1}^{n} \mathbf{x}_i - \bar{\mathbf{x}}) (\mathbf{x}_i - \bar{\mathbf{x}})'.$$

- ullet When  $ar{\mathbf{x}}$  is too "far away" from the hypothesized vector of population means,  $\mu_0$ , there is evidence against the null hypothesis.
- ullet Otherwise, we will conclude that  $\mu_0$  is plausible.

## Problem with the Univariate Approach

• A naive approach for testing a multivariate hypothesis is to compute the *t*-test statistics for each individual variables, i.e.,

$$t_j = \frac{\bar{x}_j - \mu_{0j}}{\sqrt{s_j^2/n}}.$$

- We could reject  $H_0$ :  $\mu = \mu_0$  if  $|t_j| > t_{n-1,\alpha/2}$  for at least one variable  $j \in \{1, 2, ..., n\}$ .
- Family-wise error rate: Pr(rejecting at least one  $H_0$ :  $\mu_j = \mu_{0j}$  | all  $H_0$ 's are true).
- The naive approach implies that the family-wide error rate is

$$1 - (1 - \alpha)^p > \alpha.$$

• This approach is very conservative (i.e., tends to reject more null hypotheses than we should).

# Hotelling's $T^2$ Statistic

- Consider the question of whether the  $p \times 1$  vector  $\mu_0 = (\mu_{01}, \mu_{02}, ..., \mu_{0p})'$  is plausible for the unknown vector of population means  $\mu = (\mu_1, \mu_2, ..., \mu_p)'$ .
- The squared statistical distance between the vector of sample means and the hypothesized mean vector is

$$T^{2} = (\bar{\mathbf{x}} - \mu_{0})' \left(\frac{1}{n}S\right)^{-1} (\bar{\mathbf{x}} - \mu_{0}) = n(\bar{\mathbf{x}} - \mu_{0})'S^{-1}(\bar{\mathbf{x}} - \mu_{0})$$

is called the one-sample Hotelling's  $T^2$  statistic.

• In the expression above,

$$\bar{\mathbf{x}} = \frac{1}{n} \sum_{i=1}^{n} \mathbf{x}_i, \qquad S = \frac{1}{n-1} \sum_{i=1}^{n} (\mathbf{x}_i - \bar{\mathbf{x}}) (\mathbf{x}_i - \bar{\mathbf{x}})'.$$

# Hotelling's $T^2$ Statistic

- If the observed  $T^2$  value is 'large' we reject  $H_0: \mu = \mu_0$ .
- To decide how large is too large, we need the sampling distribution of  $T^2$  when the hypothesized mean vector is correct:

$$T^2 \sim \frac{(n-1)p}{(n-p)} F_{p,n-p}$$
 or  $\frac{n-p}{p(n-1)} T^2 \sim F_{p,n-p}$ 

• We reject the null hypothesis  $H_0$  :  $\mu=\mu_0$  for the p-dimensional vector  $\mu$  at level  $\alpha$  when

$$\frac{n-p}{p(n-1)}T^2 > F_{(p,n-p),1-\alpha}$$

where  $F_{(p,n-p),1-\alpha}$  is the upper  $1-\alpha$  percentile of the central F distribution with p and n-p degrees of freedom.

# Hotelling's $T^2$ Statistic

This result depends on the following conditions

- The vectors of observations  $x_1$ ,  $x_2$ , ...,  $x_n$  are independent, each randomly drawn from the same population (a simple random sample).
- Each  $\mathbf{x}_i$  is randomly selected from a population with a multivariate normal distribution with mean vector  $\boldsymbol{\mu}$  and covariance matrix  $\boldsymbol{\Sigma}$ .

When only p = 1 response is obtained from each subject

$$\frac{n-p}{p(n-1)}T^2 = \frac{n-1}{(1)(n-1)}T^2 = T^2$$

$$= (\bar{x} - \mu_0) \left(\frac{n}{s^2}\right) (\bar{x} - \mu_0) = \left(\frac{\bar{x} - \mu_0}{s/\sqrt{n}}\right)^2 = t^2$$

## Example: Female Sweat Data (J&W)

- Perspiration from a sample of 20 healthy females was analyzed. Three variables were measured for each woman:
  - $X_1$  =sweat rate
  - $X_2$  =sodium concentration
  - $X_3$  =potassium concentration
- The question is whether  $\mu_0 = [4, 50, 10]'$  is plausible for the population mean vector.
- $\bullet$  At level  $\alpha = 0.10$ , we reject the null hypothesis if

$$T^{2} = 20(\bar{\mathbf{x}} - \boldsymbol{\mu}_{0})'S^{-1}(\bar{\mathbf{x}} - \boldsymbol{\mu}_{0}) > \frac{(n-1)p}{(n-p)}F_{(p,n-p),0.9} = \frac{19(3)}{17}F_{(3,17),0.9} = 8.18.$$

The vector of sample means is

$$\bar{\mathbf{x}} = \begin{bmatrix} 4.64 \\ 45.4 \\ 9.96 \end{bmatrix}$$
 and  $\bar{\mathbf{x}} - \mu_0 = \begin{bmatrix} 4.64 - 4 \\ 45.4 - 50 \\ 9.96 - 10 \end{bmatrix} = \begin{bmatrix} 0.64 \\ -4.6 \\ -0.04 \end{bmatrix}$ .

## **Example: Sweat Data**

ullet After computing the inverse of the 3 imes 3 sample covariance matrix  $S^{-1}$  we can compute the value of the  $T^2$  statistic as

$$T^{2} = 20[0.64 -4.6 -0.04] \begin{bmatrix} 0.586 -0.022 & 0.258 \\ -0.022 & 0.006 & -0.002 \\ 0.258 & -0.002 & 0.402 \end{bmatrix} \begin{bmatrix} 0.64 \\ -4.60 \\ -0.04 \end{bmatrix}$$
$$= 9.74.$$

- ullet Because 9.74 > 8.18, we reject  $H_0$  and conclude that  $\mu_0$  is not a plausible value for  $\mu$  at the 10% level.
- At this point, we do not know which of the three hypothesized mean values is not supported by the data.

#### See R code for illustrations

# Confidence Region for a Vector of Population Means

A  $(1-\alpha) \times 100\%$  confidence region for the vector of population means  $\mu$  is the ellipsoid determined by all  $\mu$  such that

$$n(\bar{\mathbf{x}} - \boldsymbol{\mu})' S^{-1}(\bar{\mathbf{x}} - \boldsymbol{\mu}) \le \frac{(n-1)p}{(n-p)} F_{(p,n-p),1-\alpha}$$

This is a p-dimensional ellipsoid centered at  $ar{\mathbf{x}}$ 

- ullet The axes of the confidence ellipsoid are parallel to the eigenvectors of the sample covariance matrix S.
- ullet The lengths of the axes are proportional to the eigenvalues of S.

## **Confidence Regions**

• The distance from the center of the confidence ellipsoid at  $\bar{\mathbf{x}}$  to the edge of the ellipsoid along the *i*-th axis is

$$\pm\sqrt{\lambda_i}\sqrt{\frac{(n-1)p}{n(n-p)}F_{(p,n-p),1-\alpha}}.$$

- The directions of the the eigenvectors and sizes of the eigenvalues depend
  - The relative sizes of the variances of the measured variables
  - The sizes of the correlations between pairs of variables

- Data was collected on two measurements of radiation emitted from n=42 microwave ovens (J & W, Tables 4.1 and 4.5) Here,  $x_j$  denotes the transformed radiation measurements (fourth root)
- Sample statistics for the transformed data are:

$$\bar{\mathbf{x}} = \begin{bmatrix} 0.564 \\ 0.603 \end{bmatrix}, \quad S = \begin{bmatrix} 0.014 & 0.012 \\ 0.012 & 0.015 \end{bmatrix}, \quad S^{-1} = \begin{bmatrix} 203.02 & -163.39 \\ -163.39 & 200.23 \end{bmatrix}.$$

ullet Eigenvalue and eigenvector pairs for S are

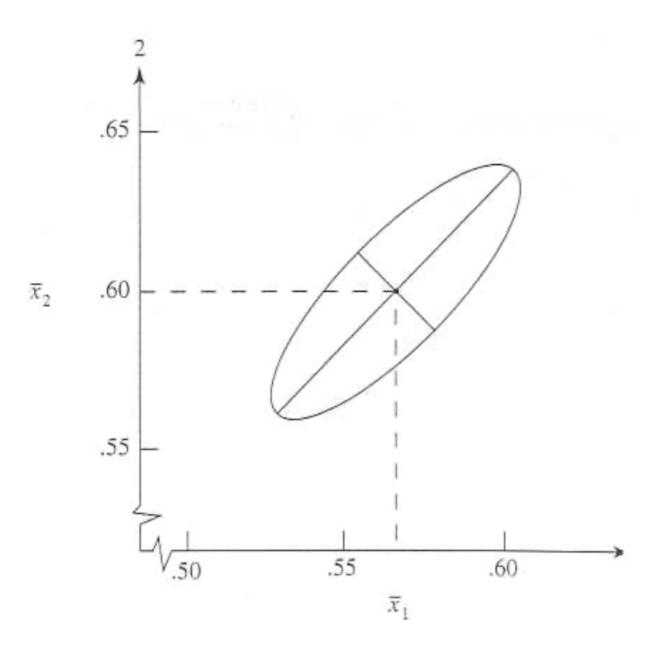
$$\lambda_1 = 0.026$$
  $e'_1 = [0.704, 0.710]$ 

$$\lambda_2 = 0.002$$
  $e'_2 = [-0.71, 0.704]$ 

• The 95% CR for the population mean vector is given by all vectors  $\mu = (\mu_1, \mu_2)'$  that satisfy:

$$42[0.564 - \mu_1 \quad 0.603 - \mu_2] \left[ \begin{array}{cc} 203.02 & -163.39 \\ -163.39 & 200.23 \end{array} \right] \left[ \begin{array}{c} 0.564 - \mu_1 \\ 0.603 - \mu_2 \end{array} \right] \leq 6.62,$$
 where 
$$\frac{2(41)}{40} F_{(2,40),0.95} = \frac{2(41)}{40} 3.23 = 6.62.$$

• Is  $\mu = [0.562 \quad 0.589]'$  a plausible value for the population mean vector? To check, plug  $\mu = [0.562 \quad 0.589]'$  into the expression above and see if it satisfies the inequality. In this case, we get 1.30 which is less than 6.62, and conclude that this is plausible at the 95% level.



• The joint confidence ellipsoid is centered at  $\bar{\mathbf{x}} = [0.564 \ 0.603]'$  and the half lengths of the two axes are

$$\sqrt{0.026}\sqrt{\frac{2(41)}{42(40)}}3.23 = 0.064, \quad \sqrt{0.002}\sqrt{\frac{2(41)}{42(40)}}3.23 = 0.018.$$

- ullet The axes are parallel to the two eigenvectors of S.
- The ratio of the square roots of the eigenvalues

$$\frac{\sqrt{0.026}}{\sqrt{0.002}} = 3.6$$

indicates that the major axis is 3.6 times longer than the minor axis.

#### **Simultaneous Confidence Statements**

- ullet Often we are interested in drawing inference about each  $\mu_j$ .
- One possibility is to construct ordinary confidence intervals

$$\bar{x}_j \pm t_{(n-1),1-\frac{\alpha}{2}} \sqrt{\frac{s_{jj}}{n}},$$

for each  $\mu_j$ . One problem is that the combined set of individual intervals result in a *simultaneous confidence level* that is less than the nominal  $1 - \alpha$ .

- There are various ways of constructing a collection of individual confidence intervals so that the joint confidence level for the family of parameters remains at  $1-\alpha$
- Intuitively, CI's that protect against erosion of the confidence level will be wider than the individual  $(1 \alpha) \times 100\%$  CI's.

#### **Simultaneous Confidence Statements**

• The following set of confidence intervals enclose the confidence ellipsoid and have at least probability  $1-\alpha$  of simultaneously containing all p of the population means.

$$\bar{x}_j \pm \sqrt{\frac{p(n-1)}{(n-p)}} F_{(p,n-p),1-\alpha} \sqrt{\frac{S_{jj}}{n}}$$
  $j = 1, 2, ..., p$ 

• These are called  $T^2$  confidence intervals.

- Compute simultaneous 95%  $T^2$  confidence intervals for  $\mu_1$  and  $\mu_2$ , the means of the fourth root of the amount of radiation with door closed and door open.
- First note that

$$\sqrt{\frac{p(n-1)}{n(n-p)}}F_{(p,n-p),0.95} = \sqrt{\frac{2(41)}{42(40)}}3.23 = 0.397.$$

is common to both intervals.

• For  $\mu_1$  and  $\mu_2$ :

$$\bar{x}_1 \pm 0.397 \sqrt{s_{11}} \Rightarrow 0.564 \pm (0.397 \times 0.12) \Rightarrow 0.564 \pm 0.0476$$
  
 $\bar{x}_2 \pm 0.397 \sqrt{s_{22}} \Rightarrow 0.603 \pm (0.397 \times 0.121) \Rightarrow 0.603 \pm 0.048.$ 

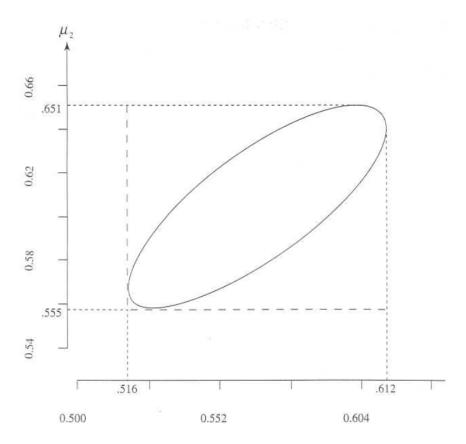
 For the difference between the means for the door closed and open:

$$\bar{x}_1 - \bar{x}_2 \pm 0.397 \sqrt{s_{11} - 2s_{12} + s_{22}} \Rightarrow -0.039 \pm (0.397 \times 0.0748)$$
  
 $\Rightarrow [-0.069, -0.009],$ 

suggesting that closing the door significantly reduces mean (fourth root) radiation emitted by the ovens.

ullet The  $T^2$  intervals are shadows or projections of the confidence ellipse onto the component axes.

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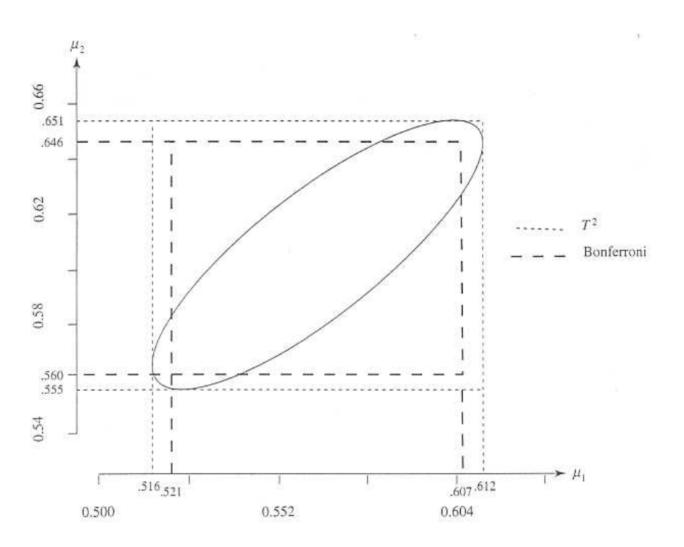
# The Bonferroni method for Simultaneous Confidence Intervals

• Simultaneous  $(1 - \alpha) \times 100\%$  Bonferroni confidence intervals for p population means are

$$\bar{X}_i \pm t_{(n-1),1-\frac{\alpha}{2p}} \sqrt{\frac{s_{ii}}{n}}$$

- The probability that all p of the confidence intervals simultaneously contain the corresponding population means is at least  $1-\alpha$
- ullet Microwave ovens: see  $T^2$  and Bonferroni intervals in the next figure.

# $T^2$ and Bonferroni Confidence Intervals



## $T^2$ and Bonferroni Confidence Intervals

Simultaneous confidence intervals can be made for any linear combination of the population means, say  $\mathbf{c}_k' \boldsymbol{\mu} = \sum_{j=1}^p c_{jk} \mu_j$  for k=1,2,...,m combinations. The k-th vector of coefficients is  $\mathbf{c}_k = (c_{1k}, c_{2k}, ... c_{pk})$ .

•  $T^2$  method

$$\left(\sum_{j=1}^{p} c_{jk}\bar{x}_{j}\right) \pm \sqrt{\frac{p(n-1)}{(n-p)}} F_{(p,n-p),1-\alpha} \sqrt{\frac{1}{n}} \mathbf{c}_{k}' S \mathbf{c}_{k} \qquad k = 1, 2, ..., m.$$

• Bonferroni method (these get wider as the number of combinations m gets bigger)

$$\left(\sum_{j=1}^{p} c_{jk}\bar{x}_{j}\right) \pm t_{(n-1),1-\frac{\alpha}{2m}}\sqrt{\frac{1}{n}\mathbf{c}_{k}'S\mathbf{c}_{k}} \qquad k=1,2,...,m.$$

- Hotelling's T-squared test for a single vector of population means has useful applications for studies with repeated measurements on each of the subjects in the study.
  - 1. Two treatments are applied to each sample unit and p variables are measured on each unit under each treatment.
  - 2. Studies in which the same variable is measured at a set of p time points on each subject in the study.

#### • Examples:

- We measure volumes of sales of a certain product in a certain market before and after an advertising campaign
- We measure blood pressure on a sample of individuals before receiving some drug and at monthly time intervals for one year after receiving the drug.

- One advantage of this type of study is that the differences in the outcome measures under one treatment or the other reflect only the effect of treatment because everything else about the subject receiving the treatments is identical.
- Using the  $T^2$  method allows us to account for correlations between responses provided by the same subject.
- Other things to worry about: In drug trials there may be carry-over effects to worry about and in 'before and after' experiments because conditions may change.

ullet Suppose now that p treatments are applied to each of the n sample units. Then

$$\mathbf{x}_j = [x_{j1}, X_{j2}, ..., x_{jp}]', \quad j = 1, ..., n.$$

ullet Of interest are contrasts of the elements of  $\mu=E(\mathbf{x}_j)$  such as

$$\begin{bmatrix} \mu_1 - \mu_2 \\ \mu_1 - \mu_3 \\ \vdots \\ \mu_1 - \mu_p \end{bmatrix} = \begin{bmatrix} 1 & -1 & 0 & \cdots & 0 \\ 1 & 0 & -1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 1 & 0 & 0 & \cdots & -1 \end{bmatrix} \mu = C\mu.$$

- The contrast matrix C has p-1 independent rows.
- If the null hypothesis that all treatments provide the same mean response is true, then  $C\mu=0$ .

# Testing Hypotheses in Repeated Measures Studies

• To test  $H_0: C\mu = 0$  we again use  $T^2$ :

$$T^{2} = n(C\bar{x} - 0)'(CSC')^{-1}(C\bar{x} - 0)$$

• The null hypothesis is rejected if

$$T^2 \ge \frac{(n-1)(p-1)}{(n-p+1)} F_{(p-1,n-p+1),1-\alpha}.$$

ullet Note that numerator degrees of freedom are p-1 instead of p because the null hypothesis puts only p-1 constraints on the means responses

## Example: Dog Anesthetics (J&W)

- A sample of 19 dogs were administered four treatments each:
  - (1) high  $CO_2$  pressure, (2) low  $CO_2$  pressure,
  - (3) high pressure + halothane, (4) low pressure + halothane.
- Outcome variable was milliseconds between heartbeats.
- Three possible contrasts that could be of interest:

 $(\mu_3 + \mu_4) - (\mu_1 + \mu_2)$  : Effect of halothane

averaging across  $CO_2$  pressure levels

 $(\mu_1 + \mu_3) - (\mu_2 + \mu_4)$  : Effect of  $CO_2$  pressure

averaging across levels of halothane

 $(\mu_1 - \mu_2) - (\mu_3 - \mu_4)$ : Interaction between halothane and  $CO_2$ .

## **Example: Dog Anesthetics**

• In class exercise: The  $3 \times 4$  contrast matrix C is

• The test of  $H_0: C\mu = 0$  rejects the null if

$$T^2 = n(C\bar{\mathbf{x}})'(CSC')^{-1}(C\bar{\mathbf{x}}) = 116 \ge \frac{(18)(3)}{(16)}F_{(3,16),0.95} = 10.94.$$

• We clearly reject the null, so the question now is whether there is a difference between  $CO_2$  pressure, between halothane levels or perhaps there is no main effect of treatment but there is still an interaction.

## **Example: Dog Anesthetics**

• Three simultaneous confidence intervals (one for each row of C). First consider the halothane effect, summing across  $CO_2$  pressure levels:  $(\mu_3 + \mu_4) - (\mu_1 + \mu_2)$ 

$$(\bar{x}_3 + \bar{x}_4) - (\bar{x}_1 + \bar{x}_2) \pm \sqrt{\frac{18(3)}{16}} F_{(3,16),0.95} \sqrt{\frac{c_1' S c_1}{19}}$$

$$\implies 209.31 \pm 73.70.$$

- For the effect of  $CO_2$  pressure and the interaction, we find respectively:  $-60.05 \pm 54.70$ ,  $-12.79 \pm 65.97$
- Use of halothane produces longer times between heartbeats. This effect is similar at *both* high and low  $CO_2$  pressure levels because the interaction is not significant (third contrast). Higher  $CO_2$  pressure produces shorter times between heartbeats.

## **Example: Dog Anesthetics**

- The same null hypothesis can be represented with different contrast matrices
- $\bullet$  For example, the null hypothesis that all four treatments have the same mean is also tested with  $H_0$ :  $C\mu=0$ , where

$$C = \begin{bmatrix} -1 & 1 & 0 & 0 \\ 0 & -1 & 1 & 0 \\ 0 & 0 & -1 & 1 \end{bmatrix} \quad \text{or} \quad C = \begin{bmatrix} 1 & 0 & 0 & -1 \\ 0 & 1 & 0 & -1 \\ 0 & 0 & 1 & -1 \end{bmatrix}$$

• The value of  $T^2$  is unchanged

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

- ullet The value of  $T^2$  will be the same for any set of contrasts that implies the same null hypothesis.
- R code demonstration