

# ST4241: Design and Analysis of Clinical Trials

2009/2010: Semester I

## Tutorial 8

1. Consider the study comparing two groups of subjects with respect to the temperature of the forehead (in degrees Celsius) measured at 30-minute intervals. The summary data of the two groups are given below:

| Group 1 |      |      |      |      |
|---------|------|------|------|------|
| Subject | Time |      |      |      |
|         | 1    | 2    | 3    | 4    |
| 1       | 30.9 | 30.7 | 30.9 | 30.9 |
| 2       | 31.9 | 31.6 | 31.6 | 31.7 |
| 3       | 31.3 | 31.1 | 31.0 | 31.3 |
| 4       | 32.1 | 31.0 | 31.7 | 31.3 |
| 5       | 30.9 | 31.2 | 30.5 | 30.8 |
| 6       | 31.3 | 31.7 | 31.4 | 31.2 |
| 7       | 31.3 | 31.8 | 31.8 | 31.7 |
| 8       | 32.1 | 33.0 | 31.7 | 31.5 |
| 9       | 30.3 | 30.9 | 30.8 | 30.6 |
| 10      | 32.2 | 32.1 | 32.2 | 32.4 |

  

| Group 2 |      |      |      |      |
|---------|------|------|------|------|
| Subject | Time |      |      |      |
|         | 1    | 2    | 3    | 4    |
| 1       | 31.5 | 30.6 | 30.8 | 31.0 |
| 2       | 31.2 | 31.2 | 31.1 | 31.3 |
| 3       | 31.3 | 31.3 | 31.5 | 31.4 |
| 4       | 30.4 | 30.8 | 30.4 | 30.2 |
| 5       | 30.7 | 30.9 | 30.9 | 30.9 |
| 6       | 29.8 | 30.8 | 30.9 | 30.8 |
| 7       | 31.4 | 32.0 | 31.7 | 31.6 |
| 8       | 30.9 | 32.4 | 31.8 | 31.9 |
| 9       | 31.1 | 31.3 | 31.2 | 31.2 |
| 10      | 31.5 | 31.5 | 31.6 | 31.7 |

- (i) Compute the estimates of the variance-covariance matrix of the repeated measurements over time: (a) separately for each group and (b) a pooled estimate assuming the variance-covariance matrices of the two groups are the same.

(ii) Compute the estimated correlation matrix based on the pooled estimate of the common variance-covariance matrix.

(iii) Compute the value of  $\epsilon$  as expressed below:

$$\epsilon = \frac{(t-1)(1-\bar{\rho}_{..})^2}{(t-1)(1-\bar{\rho}_{..})^2 - \frac{2(t-1)}{t} \sum (\bar{\rho}_{j\cdot} - \bar{\rho}_{..})^2 + \sum \sum_{j \neq j'} (\rho_{jj'} - \bar{\rho}_{..})^2}.$$

(iv) Give the adjusted degrees of freedom for the F-ratios  $F_2$  and  $F_3$  for testing the significance of time effect and time by group interaction effect respectively.

2. Calculate the value of  $C_i^{(k)} = -3X_{i1}^{(k)} - X_{i2}^{(k)} + X_{i3}^{(k)} + 3X_{i4}^{(k)}$  for each subject in the tables given in Problem 1 and confirms the values in the following table:

|         | $n$ | Mean  | sd     |
|---------|-----|-------|--------|
| Group 1 | 10  | -0.42 | 1.2943 |
| Group 2 | 10  | 0.63  | 1.3565 |

Compute the weighted average of the two means and the pooled standard deviation.

3. Apply the following two methods to the data in Problem 1 for testing whether the linear variation with time of the means in Group 1 is the same as in Group 2 ( the vector of constants defining the contrast is  $\mathbf{c} = (-3, 1, 1, 3)'$ ).

(i) Method 1: With  $\bar{\mathbf{X}}^{(1)}$  and  $\bar{\mathbf{X}}^{(2)}$  denoting the two vectors of mean responses and with  $\bar{\mathbf{S}}$  denoting the pooled covariance matrix, calculate  $C = \mathbf{c}'(\bar{\mathbf{X}}^{(1)} - \bar{\mathbf{X}}^{(2)})$  and  $\text{se}(C) = \sqrt{n \cdot \mathbf{c}' \bar{\mathbf{S}} \mathbf{c} / n_1 n_2}$ , and find the value of  $L = C / \text{se}(C)$ .

(ii) Method 2: With  $\mathbf{X}_i^{(k)}$  denoting the vector of  $t$  responses for Subject  $i$  in Group  $k$ , calculate the value of  $C_i^{(k)} = \mathbf{c}' \mathbf{X}_i^{(k)}$  separately for each subject and compare the resulting means in the straightforward way of two-sample  $t$  test.

Confirm that, no matter which method is employed, the same  $t$ -statistic value is found.