

# ST4241: Design and Analysis of Clinical Trials

2009/2010: Semester I

## Tutorial 3

1. The following table gives the summary data from a drug trial, with higher values being associated with better responses.

Drug A	Drug B	$n_i$	$\bar{X}_i$	$s_i$
no	no	15	12.2	6.66
yes	no	14	19.3	8.45
no	yes	13	20.6	11.39
yes	yes	15	38.5	9.72

It is required to test the effect of each drug (in the absence of the other) and the interaction effect.

- (i) Give the test statistics for the three tests (two for the effects of Drug A and B, one for the interaction).
- (ii) Conduct the three tests controlling the overall error rate at  $\alpha = 0.05$  by using an appropriate procedure. Give your conclusion of the tests.

2. Let  $Y_1, \dots, Y_m$  denote  $m$  independent estimators of the same underlying parameter, and suppose that  $\text{Var}(Y_j) = \sigma^2/w_j, j = 1, \dots, m$ , where  $w_j$ 's are known constants. Let  $\nu_1, \dots, \nu_m$  be any nonnegative weights satisfying  $\sum_{j=1}^m \nu_j = 1$ .

- (i) Prove that the weighted average  $\bar{Y}_{opt} = (\sum_{j=1}^m w_j Y_j) / \sum_{j=1}^m w_j$  has the smallest variance among all weighted averages of the form  $\bar{Y} = \sum_{j=1}^m \nu_j Y_j$ .
- (ii) Show that  $\text{Var}(\bar{Y}_{opt}) = \sigma^2 / \sum_{j=1}^m w_j$ .

3. In a  $2 \times 2$  factorial design, the test for interaction when  $\sigma^2$  is known and all four sample sizes are equal to  $n$  declares the interaction to be statistically significant if  $|\hat{E}_{AC}| / \sqrt{4\sigma^2/n} > z_{\alpha/2}$ , where  $\hat{E}_{AC}$  is the estimated interaction effect.

- (i) Suppose the true interaction effect  $E_{AC} = \Delta > 0$ . Show that the power of the above test is

$$Pr(Z > z_{\alpha/2} - \Delta / \sqrt{4\sigma^2/n}),$$

where  $Z$  is a standard normal random variable.

- (ii) Show that if the power of the above test is required to be  $1 - \beta$  then the required sample size is

$$n = \frac{4\sigma^2(z_{\alpha/2} + z_{\beta})^2}{\Delta^2}.$$

4. The following table gives the results of a reliability study comparing DMFS scores (number of decayed, missing, and filled surfaces of a patient's permanent teeth) by four examiners on ten patients.

Patient	Examiner			
	1	2	3	4
1	8	7	11	7
2	13	11	15	13
3	0	0	2	1
4	3	6	9	6
5	13	13	17	10
6	19	23	27	18
7	0	0	1	0
8	2	0	4	5
9	18	20	22	16
10	5	3	8	3

- (i) It is of concern whether or not each examiner's score is consistent with the other's. State the contrasts which are appropriate for testing the consistency of scores among examiners.
- (ii) Using Bonferroni's criterion to control overall error rate at level  $\alpha = 0.05$ , conduct the hypothesis testing of the contrasts you stated in part (i). Give your conclusion.
- (iii) If, instead of Bonferroni's criterion, you use other criterion such as Scheffe's, Tukey's and Dunnett's criterion to control the overall error rate at the same level, what will be your conclusion on the tests?