ST4241: Design and Analysis of Clinical Trials

2009/2010: Semester I

Tutorial 7

1. In a stratified study, the patients are stratified into three strata and three treatments are randomly assigned to patients in each stratum such that each treatment was administered to the same number of patients. The data is given below:

	Treatment		
Stratum	1	2	3
1	130	34	20
	155	40	70
	74	80	82
	180	75	58
2	150	126	25
	188	122	70
	159	106	58
	126	115	45
3	138	174	96
	110	120	104
	168	150	82
	160	139	60

The following R-codes can be used for the computation of the desired results:

```
x1 = c(130,155,74,180,34,40,80,75,20,70,82,58)
x2 = c(150,188,159,126,126,122,106,115,25,70,58,45)
x3 = c(138,110,168,160,174,120,150,139,96,104,82,60)
x=c(x1,x2,x3)
S = factor(c(rep(1,12),rep(2,12),rep(3,12)))
T = factor(rep(c(rep(1,4),rep(2,4),rep(3,4)),3))
options(contrasts=c("contr.treatment","contr.poly"))
lm.fit=lm(x~S*T)
```

Extract the relevant results from the fitted object `lm.fit` to do the following:

(i) Give the linear model behind the R code in terms of dummy variables.

(ii) Test the significance of stratum by treatment interaction at level $\alpha = 0.05$.

(iii) Suppose the interaction effect is significant, make pairwise comparisons within each of the three strata to find out how the treatment effects differ from stratum to stratum.

(iv) Regardless of the result in (ii), assume that there is no stratum by treatment interaction. Test the significance of the following contrasts: a) treatment 2 versus treatment 1, b) treatment 3 versus treatment 1, c) the average effect of treatment 2 and 3 versus treatment 1. (You need to refit the model without the interaction terms).

2. Consider the following model:

$$X_{ij} = \mu_i + \beta_i Z_{ij} + \epsilon_{ij},\ \ i = 1, \ldots, g; j = 1, \ldots, n_i.$$

(i) Derive the formula for the estimator of $\hat{\beta}_i$ and $\hat{\mu}_i$.

(ii) Show that the covariance of $\hat{\beta}_i$ and $\bar{X}_{i\cdot}$ equals zero.

(iii) Derive the formulas for the variances of $\hat{\beta}_i$ and $\hat{\mu}_i$.

(iv) Suppose $\beta_i = \beta$ for all i. Show that the least square estimate of β has the form

$$\hat{\beta} = \frac{\sum_i w_i \hat{\beta}_i}{\sum_i w_i},$$

for certain w_i's.

3. Consider the following summary data from Example 2 of Lecture notes 6:

Quantity	Treatment 1	Treatment 2	Treatment 3
n_i	19	20	20
$\bar{X}_{i\cdot}$	5.3158	8.3000	8.5500
$\sum(X_{ij} - \bar{X}_{i\cdot})^2$	67.1053	76.2000	139.9500
$\bar{Z}_{i\cdot}$	2.3158	2.4500	3.1500
$\sum(Z_{ij} - \bar{Z}_{i\cdot})^2$	23.1050	15.9500	22.5500
$\sum(X_{ij} - \bar{X}_{i\cdot})(Z_{ij} - \bar{Z}_{i\cdot})$	27.1053	18.3000	34.3500

Assume the model of non-parallel regression lines as described in Problem 2 above for the data.

(i) Compute the estimates $\hat{\mu}_i, \hat{\beta}_i$ for $i = 1, 2, 3$.

(ii) Test the following null hypothesis at level $\alpha = 0.05$.

$$H_0 : \beta_1 = \beta_2 = \beta_3.$$

(iii) Regardless of the result of (ii), assume that $\beta_1 = \beta_2 = \beta_3 = \beta$. Compute the estimate of $\hat{\beta}$ and the estimates of μ_i, $i = 1, 2, 3$, under this assumption.

(iv) Under assumption of (iii), test the following hypotheses simultaneously:

$$\mu_1 = \mu_2, \mu_1 = \mu_3, \mu_1 = \frac{1}{2}(\mu_2 + \mu_3).$$