

**ST520, Fall 2008**

**Homework 8, due: Tuesday, 12/2/2008**

1. (5 pts) Using the log-rank statistics and their variance-covariance estimates on slide 358, calculate the **Chi-Square** statistic on slide 359 for the log-rank test in 2 ways.
2. (5 pts) Suppose we conduct a group sequential test with 2 looks where the cumulative information at the second look is 3 times the information at the first look. What is the joint distribution of our test statistics ( $T(t_1)$  and  $T(t_2)$ ) under the null hypothesis?
3. (15 pts) The following data is from a traditional design comparing two treatments to lower blood pressures. The data is re-arranged in groups with every 30 patient increment (for a total of 4 groups):

|             | time 1 |           |       | time 2 |           |       | time 3 |           |       | time 4 |           |       |
|-------------|--------|-----------|-------|--------|-----------|-------|--------|-----------|-------|--------|-----------|-------|
|             | $n$    | $\bar{Y}$ | $S^2$ | $n$    | $\bar{Y}$ | $S^2$ | $n$    | $\bar{Y}$ | $S^2$ | $n$    | $\bar{Y}$ | $S^2$ |
| treatment 1 | 15     | 165       | 100   | 30     | 160       | 102   | 45     | 164       | 104   | 60     | 164       | 101   |
| treatment 0 | 15     | 172       | 101   | 30     | 171       | 100   | 45     | 170       | 102   | 60     | 171       | 100   |

where  $n$  is the total sample size available at each time point,  $\bar{Y}$  is the sample mean of the blood pressures and  $S^2$  is the sample variance. Do the following:

- (a) Use the (two-sided) two sample t-test at the last time point to test at the significance level 0.05 whether or not the mean blood pressures of the patients receiving treatment 1 and treatment 0 are the same.
  - (b) Conduct a (two-sided) group sequential test using Pocock boundaries at significance level  $\alpha = 0.05$ . What is your conclusion?
  - (c) Conduct a (two-sided) group sequential test using O'Brien-Fleming boundaries at significance level  $\alpha = 0.05$ . What is your conclusion?
4. (15 pts) Suppose we want to detect a difference in mean cholesterol values of 12 units between two treatments (new treatment and old treatment) with 95% power using the two-sample t-test (two-sided) at the 0.05 level of significance. Assume the standard deviation of the response  $\sigma_Y$  to be 60. Use equal allocation.
    - (a) Find the sample size for each treatment if a traditional design (analyze the data at the end of study) is used.

- (b) Suppose we plan to have a maximum of 5 analyses of the data after equal increments of information using Pocock boundaries. How would you design such a study? What is the maximum sample size required?
- (c) Repeat (b) using O'Brien-Fleming boundaries. If you have a strong belief that the new treatment will reduce 12 units of cholesterol more than the old treatment, which design do you prefer? If on the other hand there is a strong indication that there is no difference between these two treatments, which design do you prefer?