

ST520, Fall 2011

Homework 8, due: Wednesday, 11/30/2011

1. (5 pts) Suppose we conduct a group sequential test with 3 potential interim analyses where the accumulated information (for the parameter of interest, the treatment effect Δ) at those time points are $2I$, $3I$ and $5I$ where I represents some large information. What is the joint distribution of our potential test statistics $(T(t_1), T(t_2), T(t_3))^T$ calculated at those 3 interim analyses under the null hypothesis $H_0 : \Delta = 0$ and the alternative $H_0 : \Delta = \Delta_A$?

2. (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 60 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	30	116	112	60	115	120	90	113	114	120	115	122
treatment 0	30	122	110	60	120	112	90	121	113	120	122	124

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 with 4 maximum looks using Pocock boundaries at significance level $\alpha = 0.05$. What is your conclusion?
- (c) Conduct a (two-sided) group sequential test with 4 maximum looks using O'Brien-Fleming boundaries at significance level $\alpha = 0.05$. What is your conclusion?

3. (10 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 σ_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 test statistics will you calculate at each interim analysis and what boundary values you will compare the test statistics to. What is the maximum sample size required and how many patients will you assign to each treatment before you conduct an interim analysis?
- (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?
4. (10 pts) Suppose we want to detect a difference in mean response rates between a new treatment and the standard treatment where the outcome is whether or not a patient responds to the treatment. We would like to detect a 10% increase of response rate for the new treatment compared to the standard treatment with 90% power at the 0.05 level of significance. Assume 0.4 and 0.5 response rates for the new and standard treatments. 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 O'Brien-Fleming boundaries. How would you design such a study? What is the maximum sample size required? What is the cumulative information required at each interim analysis.
- (c) Suppose the true response rates for the new and standard treatments turn out to be 0.35 and 0.45. Do you have enough information at each interim analysis?