ST 520 Fall 2019 Homework 2 due Tuesday 9/17

Phase II study

1. In a small phase II clinical trial, 20 patients receive a new treatment and five have a complete response. Find the 80% confidence interval for the probability of a complete response π using

(a) normal approximation

(b) exact confidence intervals

(c) Compute the probability that the exact confidence interval covers the true value of π when (i) $\pi = .2$ and (ii) $\pi = .5$.

2. Suppose the minimal acceptable response rate in a phase II clinical trial is .25. Using Gehan's two-stage design, we will declare a new treatment a failure if there is little evidence (say .05) that this treatment will not have a response rate greater than or equal to .25. If we continue to the second stage, we want the 95% confidence interval for the probability of response to be within $\pm.10$.

How would you set up this phase II trial? i.e. how many individuals would you study in the first and second stage and what is the decision rule for continuing to the second stage?

3. Consider the following two stage decision rule:

Three patients are given a new drug. If none respond, the study is terminated and the drug is declared a failure. If all three respond then the study is terminated and the drug declared a success. Otherwise, an additional five patients are treated. If the total number of responses among all eight patients is less than or equal to four then the drug is declared ineffective; otherwise, it is considered a success.

(a) Using this decision rule, compute the probability that the drug will be considered a success if the true probability of response is (i) .25, (ii) .50, (iii) .75.

(b) For the same probabilities of response as in part (a), compute the expected number of patients to be studied using the above two-stage decision rule.

4. Suppose we are evaluating a new treatment in phase II. If the true response rate is .20 or less, then we want to declare the treatment a failure with at least 95% probability; whereas, if the true response rate is at least .35, then we want to declare the treatment a success with at least 90% probability. Describe the optimal two-stage design and the corresponding decision rule to achieve these goals. What is the expected sample size of this design when the true response rate is .20?

(Use the tables provided in the slides)