**BS851 Assignment Topic 9 – Non Inferiority in Clinical Trials**

**Due April 2nd at 10am.** **Please submit an electronic copy of your assignment through blackboard. Out of 100 points.**

*Please present all answers and output in the order the questions are asked and include your SAS code as part of the answer.*

A Phase III trial examined the effectiveness of a new treatment (T) versus active control (C) in patients with head lice. Randomization to treatment is to be carried out in a 1:1 manner. Patients are to be given the treatment for one day and are to be checked once to see if the head lice still exists (a yes/no dichotomous outcome) 21 days after treatment. The main objective of the trial is to show that T is not inferior to C with respect to the proportion of patients who still have head lice 21 days after treatment.

a. Write the null and alternative hypothesis for this trial from a risk difference perspective, using a non-inferiority margin of 0.15 (or 15%).

b. Determine the sample size needed to conduct this non-inferiority trial with 80% power using a one-sided 0.025 level of significance and a Farrington-Manning test. Please assume that the expected proportion of patients with head lice in each of the treatment groups (T and C) 21 days after treatment is 0.40 (40%). Use the non-inferiority margin of 0.15 (15%). Calculate sample size from a risk difference perspective only.

c. Write an appropriate null and alternative hypothesis for this trial from a relative risk perspective. Determine the appropriate relative risk margin that is analogous to the risk difference information/margin in question a, assuming the true control group head lice rate after 21 days is 0.40 (40%).

d. Determine the sample size needed to conduct this non-inferiority trial from a relative risk perspective with 80% power, assuming a non-inferiority margin from part c and under the assumption that the proportion of patients still with head lice in each treatment group 21 days after treatment is 0.40 (40%). Use a one-sided 0.025 level of significance. How does the sample size compare to that from part b?

e. Suppose that after the study is over and 131 of 227 patients in the new drug group still had head lice after 21 days as compared to 100 of 217 patients in the active group.

Is non-inferiority of T versus C achieved at the one-sided 0.025 level of significance using a risk difference margin of 0.15 (or 15%)? Use the Farrington-Manning risk difference approach to test your hypotheses from question a.

(i) Rewrite your hypotheses from question a so that they match SAS (your margin should be negative). If they already do match SAS, please restate them.

(ii) Present the 95% confidence interval of the risk difference and the p-value.

(iii) Provide a concluding statement about whether you can reject the null hypothesis or not, explaining why based on the confidence interval as well as the p-value.

f. Repeat part e, but using the relative risk approach.