**Assignment Topic #4**

**The assignment is due by Friday, February 26th at 10am EST. Please submit an electronic copy of your assignment through Blackboard.**

*Please present answers in the order the questions are asked and include your code as a separate file.*

The ANTI\_HYP data set comes from a parallel group, randomized, double-blind, placebo-controlled phase II clinical trial. The aim of the trial was to determine the effect of a new antihypertensive medication on systolic blood pressure (SBP) in patients with hypertension (i.e., high blood pressure). In this small trial, 46 patients were randomized to receive the experimental medication or a placebo in 1:1 manner. The two treatments were identical in appearance and taste. Three study centers were involved in the trial. Randomization was stratified by study center. Patients took their randomized medication for one year. The primary efficacy outcome of the trial on which treatments were compared was ‘change in systolic blood pressure from baseline to 12 months after baseline’. It is a continuous variable. A negative value indicates a decrease in blood pressure from baseline.

In the same Blackboard folder there is a SAS dataset called *anti\_htn.sas7bdat* for this assignment. The data consist of the following variables for the 46 patients:

TRT = Randomized Treatment (a character variable, entered as “Denerv2”, and “Placebo”, which stand for Denerv (the name of the treatment) dose 2 and placebo, respectively)

PT = Patient ID (a numeric variable that you can simply ignore)

FEMALE = Gender (0 = Male, 1=Female)

SITE = Study Center ID (there are 3 study centers; the numeric IDs given to the sites to uniquely identify them are 1, 10 and 50)

SBP\_BASE = Baseline SBP (the last SBP measured before randomized treatment started)

SBP\_REDUCTION\_12M = Change in SBP from baseline to 12 months (a negative value indicates a decrease from baseline)

HTN = A dichotomous efficacy outcome indicating whether patient had hypertension at end of study (0=No, 1=Yes). (ALL patients had hypertension at START of the study so this dichotomous outcome helps assess whether the experimental treatment is efficacious at study end).

Read in and explore the SAS data set. Then answer the following questions:

1. The study is considered a success if the experimental treatment has a significantly larger decrease than the placebo with respect to the outcome ‘change in SBP from baseline to 12 months’. With this in mind, please state the two sided null and alternative hypothesis of interest.
2. Provide appropriate descriptive statistics for site, sex, baseline SBP, change in SBP from baseline to month 12, and hypertension for the overall sample and by treatment group in a table. Please do NOT carry any formal statistical treatment comparison (i.e., no p-values and no confidence intervals) for this question. Present your results in a table using 1 decimal place.
3. Perform an appropriate formal statistical treatment group comparison on the mean of the primary outcome (change in SBP between at 12 months) and test the null hypothesis in question 1. Please adjust for site, the randomization stratification factor (Hint: include site in the class statement, otherwise SAS will treat site as continuous variable!). You can assume the variance of the primary outcome is equal between treatment groups. When writing your results, report and interpret your effect estimate reporting 95% confidence intervals and p-value. Explain how the conclusions from the confidence intervals match the conclusions from your formal test of the hypothesis.
4. Repeat question 3, adjusting for baseline SBP. As in question 3, report and interpret your treatment effect estimate. You should gain more significance than in the analysis in question 3. Inspect any relevant data to explain why this is.
5. Using the SAS output from question 4, write down the corresponding linear model with the parameter estimates. Interpret the intercept, the parameters for center and the parameter for baseline SBP.
6. Given the results your compiled above, is the study ‘successful’? Please explain briefly.
7. A secondary endpoint of this study is the binary outcome ‘hypertension by the end of the study at month 12’. The sponsor wants to show that the experimental mediation has lower percentage of individuals with hypertension than the placebo. With this in mind, please state the two-sided null and alternative hypothesis of interest for this secondary endpoint.
8. Use logistic regression to test the null hypothesis and present odds ratios for hypertension for the experimental treatment versus placebo with confidence intervals, while adjusting for site, the randomization stratification factor (Hint: again, remember to include site in the class statement of proc logistic!). Given these results, is the study ‘successful’ on this secondary outcome?
9. A colleague suggests to further adjust for baseline SBP, because baseline SBP is likely to be correlated with hypertension at the end of the study. Without running any further model, please explain if and why you agree or disagree with the suggestion.