**Assignment Topic # 8**

**Assessing interactions in clinical trials**

**The assignment is due Friday, March 26th at 10am. Please submit an electronic copy of your assignment through the blackboard. Out of 100 points.**

**Background.** Researchers investigated the effect of new medication in patients with high blood pressure in a two armed, placebo controlled, double-blinded, multisite Phase III clinical trial. Patients are randomized in a 1:1 allocation ratio to both treatment arms. The primary objective of this study is to see how the treatments differ on “change from baseline (month 0) to final systolic blood pressure (SBP)” at the end of the study (month 4). The sponsor is concerned that there may be some treatment-by-site interaction. As the lead biostatistician on the team, you are asked to assess any potential effect modification that may be present in the trial.

**Dataset.** The data are in the CSV file BPdata. The variables in the data set are:

|  |  |  |
| --- | --- | --- |
| **Variable** | **Label** | **Decode** |
| age | Age at baseline, years |  |
| change | Change from baseline to month 4 in systolic blood pressure (mmHg) |  |
| cvd | Indicator of cardiovascular disease | 0=No, 1=Yes |
| dbp0 | Diastolic blood pressure at baseline (mmHg) |  |
| dbp4 | Diastolic blood pressure at month 4 (mmHg) |  |
| patid | Patient ID number |  |
| sbp0 | Systolic blood pressure at baseline (mmHg) |  |
| sbp4 | Systolic blood pressure at month 4 (mmHg) |  |
| sex | Indicator of sex | 0=woman, 1=man |
| site | Indicator of site | 1=site 1, 2=site 2, 3=site 3 |
| trtgrp | Indicator of treatment | 0=Placebo, 1=new medication |

**Assignment**. When answering each question, (a) please provide final answers to the questions in the order in which they are asked; (b) for questions requiring SAS, please cut and paste the appropriate portion of the SAS output directly in the response to your question (i.e., please do not simply refer the reader to SAS output “at the end of the homework”) so that the reader does not have to flip pages back and forth to see the complete response to your question; (c) please provide the SAS code of your program in an appendix (no output or log files, please); and (d) please use the placebo as the referent in all analyses and interpretations.

1. Summarize the descriptive statistics (N, mean, and standard deviation) in each treatment group for change in SBP (overall and stratified by study site). Round to 1 decimal place (in PROC MEANS, you can use NDEC=1). Without performing any formal statistical testing, do you observe any potential interaction effect due to study site? Please provide numeric evidence.
2. Perform an unadjusted analysis of the effect of treatment on change in SBP. Do the results change when you adjust for site?
3. Use PROC GLM to assess if there is a significant treatment-by-site interaction on change in SBP using a 0.15 level of significance. Report the null and alternative hypotheses, the test statistic, and the p-value from the interaction test. Use an appropriate tabulation or graph to support your conclusion. If the interaction is significant, is it quantitative or qualitative? Summarize your conclusion in a sentence. (For interaction graphs, please provide site on the x-axis).
4. Re-code site with dummy variables and use PROC REG to test for treatment-by-site interaction. Report the test statistic and the p-value from the interaction test – they should match question 3.
5. Write the linear regression model relating expected change from baseline to final SBP and treatment for site 1, site 2, and site 3. Briefly explain how these results support your conclusion in question 1.
6. What is your final recommendation regarding treatment-by-site interaction? If interaction is not significant, please provide the overall measure of treatment effect and associated p-value. If the interaction is significant, please perform a subgroup analysis and report the stratified results (treatment effects and p-values).

The sponsor is also interested in knowing if this medication reduces the risk of CVD in the population under study. As a secondary analysis, you will investigate the effect of treatment on CVD. Previous Phase II trials have suggested that the medication may affect men and women differently. The sponsor would like you to explore possible effect modification due to sex.

1. Summarize the descriptive statistics (frequency and percent) of CVD in each treatment group (overall and stratified by sex). Do you observe any potential interaction effect due to sex?
2. Use PROC FREQ to evaluate treatment-by-sex interaction by performing a Breslow-Day test, adjusting the test if appropriate. Report the null and alternative hypotheses, the test statistic, degrees of freedom, and p-value. Interpret the results using a 0.15 significance level.
3. If the interaction is not significant, please report the overall, unadjusted treatment effect OR and p-value. If the interaction is significant, please provide the stratified ORs for men and women separately. Provide a sentence interpreting whichever OR(s) you report.
4. Using PROC LOGISTIC, evaluate interaction due to sex using a 0.15 significance level. Interpret the results and report the appropriate p-value.
5. When might you need to use PROC LOGISTIC instead of PROC FREQ?