**Assignment Topic # 5**

**Survival analysis in clinical trials**

**The assignment is due Friday, March 5th at 10am. Please submit an electronic copy of your assignment through the blackboard. Out of 100 points.**

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

A phase III superiority study was conducted to determine if a new treatment for depression (treatment N) promotes remission better than *two* available standard of care therapies (treatment A and B). There is no placebo in this study due to the severity of the disease under study.

The study included 117 subjects with a recent diagnosis of depression were enrolled and treated in this study. The primary outcome was time to depression remission (9-item Patient Health Questionnaire [PHQ-9] score <5and persistent depressive symptoms (PDSs; PHQ-9 score ≥10). All patients were to be followed for a fixed time of 100 days, or until remission or loss to follow-up or death occurred. Note that here, the outcome is 1=“remission” (a positive outcome). Thus, “survival” actually means no remission and “failure” means depression remission; please keep this in mind as you interpret your results.

The data set and the SAS command to input the data are at the end of this assignment (please cut and paste into your SAS editor in order to read it in a SAS data step; if you have any problems, let the professors or TA know).

The variables in the dataset are:

* REMISS indicates Remission Status (0=No,1=Yes)
* DEATH indicates Death (1=Died, 0=Lost to follow-up or had remission)
* DAYS indicates days to remission (if REMISS=1) or days until no longer in study (if REMISS=0 due to loss to follow-up or death)
* TRT indicates Treatment Group (N, A, B)
* AGEGRP indicates Age Group (Young or Old)

1. Present a Kaplan-Meier survival plot for N vs. A vs. B (all 3 treatments should be on the same graph). Describe the nature of the survival experience in the 3 groups including timing of events and loss to follow-up, without any formal p-value. Which treatment appears to be best in promoting remission (15 points)?
2. What proportion of patients experienced depression remission by 70 days in each of the 3 groups (10 points)? (Remember that remission is a positive outcome: ‘Survival’ indicates that a patient did not experience remission.)
3. Report median time to remission (‘median survival’) for the three groups and discuss which treatment appears to be more effective (again, do not base your conclusions on p-values, this is subjective)(10 points).
4. Present the null hypothesis and p-value of separate pairwise log-rank tests of N vs. A and N vs. B. Do the results agree with your conclusion in part a (10 points)?   
   Note: Please ignore the issue of multiple testing due to multiple comparisons, we will cover that in a few weeks.
5. Present the log-log survival plot. Does the proportional hazards assumption appear to be met? Regardless of the answer to this question, continue with the remainder of the assignment, even if you would not in practice (15 points).
6. Assume that regulatory approval requires the new treatment to be more effective than both standard of care treatments A and B. Use one regression model to determine if the FDA would approve the new treatment. Present and interpret the hazard ratio and p-value for treatment A vs N and the hazard ratio and p-value for treatment B vs N (15 points).
7. Could differential competing risk due to death in the three treatment groups be biasing our results? Report the proportion who died in each treatment group, the appropriate statistical test to compare these proportions and its associated p-value, and your conclusions (10 points).
8. Write up the methodology and results of your Cox regression analyses, including confidence intervals, in a similar manner as discussed in the class notes in Class #5. Use one decimal place for hazard ratio and confidence interval, and 3 decimal places for p-values (15 points).

**SAS code to input the dataset:**

\*Read in data;

**data** one;

input trt $ agegrp $ days remiss death;

cards;

N Young 78.00 .00 1

N Young 80.00 .00 1

N Young 82.00 .00 1

N Young 71.00 .00 1

N Young 51.00 1.00 0

N Young 60.00 1.00 0

N Young 81.00 1.00 0

N Young 50.00 1.00 0

N Young 88.00 1.00 0

N Young 93.00 1.00 0

N Young 86.00 1.00 0

N Young 63.00 1.00 0

N Young 65.00 1.00 0

N Young 67.00 1.00 0

N Young 68.00 1.00 0

N Old 54.00 .00 1

N Old 30.00 .00 0

N Old 52.00 .00 0

N Old 68.00 .00 1

N Old 66.00 .00 0

N Old 75.00 .00 1

N Old 85.00 .00 0

N Old 55.00 .00 1

N Old 62.00 1.00 0

N Old 62.00 1.00 0

N Old 76.00 1.00 0

N Old 63.00 1.00 0

N Old 78.00 1.00 0

N Old 77.00 1.00 0

N Old 77.00 1.00 0

N Old 67.00 1.00 1

N Old 73.00 1.00 0

N Old 50.00 1.00 0

N Old 60.00 1.00 0

A Young 73.00 .00 1

A Young 79.00 .00 1

A Young 78.00 .00 1

A Young 81.00 .00 1

A Young 85.00 .00 1

A Young 80.00 1.00 0

A Young 88.00 1.00 0

A Young 76.00 1.00 0

A Young 71.00 1.00 0

A Young 70.00 1.00 0

A Young 71.00 1.00 0

A Young 77.00 1.00 0

A Young 75.00 1.00 0

A Young 62.00 1.00 0

A Young 64.00 1.00 0

A Young 69.00 1.00 0

A Young 66.00 1.00 0

A Young 84.00 1.00 0

A Young 60.00 1.00 0

A Old 65.00 .00 0

A Old 68.00 .00 1

A Old 66.00 .00 0

A Old 67.00 .00 0

A Old 62.00 .00 0

A Old 67.00 .00 0

A Old 61.00 .00 0

A Old 68.00 .00 1

A Old 65.00 .00 1

A Old 72.00 .00 1

A Old 65.00 .00 0

A Old 65.00 .00 0

A Old 52.00 .00 0

A Old 70.00 .00 1

A Old 70.00 .00 1

A Old 66.00 .00 0

A Old 68.00 .00 1

A Old 59.00 .00 0

A Old 65.00 .00 0

A Old 75.00 .00 1

A Old 63.00 .00 0

A Old 74.00 1.00 0

A Old 86.00 1.00 0

A Old 82.00 1.00 0

A Old 74.00 1.00 0

A Old 64.00 1.00 0

A Old 33.00 1.00 0

B Young 55.00 .00 0

B Young 88.00 .00 1

B Young 67.00 .00 1

B Young 88.00 .00 1

B Young 75.00 .00 0

B Young 55.00 .00 1

B Young 67.00 .00 1

B Young 85.00 .00 1

B Young 78.00 1.00 0

B Young 73.00 1.00 0

B Young 90.00 1.00 0

B Young 95.00 1.00 0

B Young 93.00 1.00 0

B Young 75.00 1.00 0

B Young 65.00 1.00 0

B Young 65.00 1.00 0

B Young 76.00 1.00 0

B Young 70.00 1.00 0

B Young 80.00 1.00 0

B Old 90.00 .00 0

B Old 98.00 .00 0

B Old 73.00 .00 1

B Old 63.00 .00 1

B Old 95.00 .00 0

B Old 83.00 .00 1

B Old 75.00 .00 1

B Old 81.00 .00 0

B Old 82.00 .00 0

B Old 95.00 .00 0

B Old 92.00 .00 0

B Old 80.00 1.00 0

B Old 81.00 1.00 0

B Old 79.00 1.00 0

B Old 75.00 1.00 0

B Old 80.00 1.00 0

B Old 91.00 1.00 0

B Old 60.00 1.00 0

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**run**;