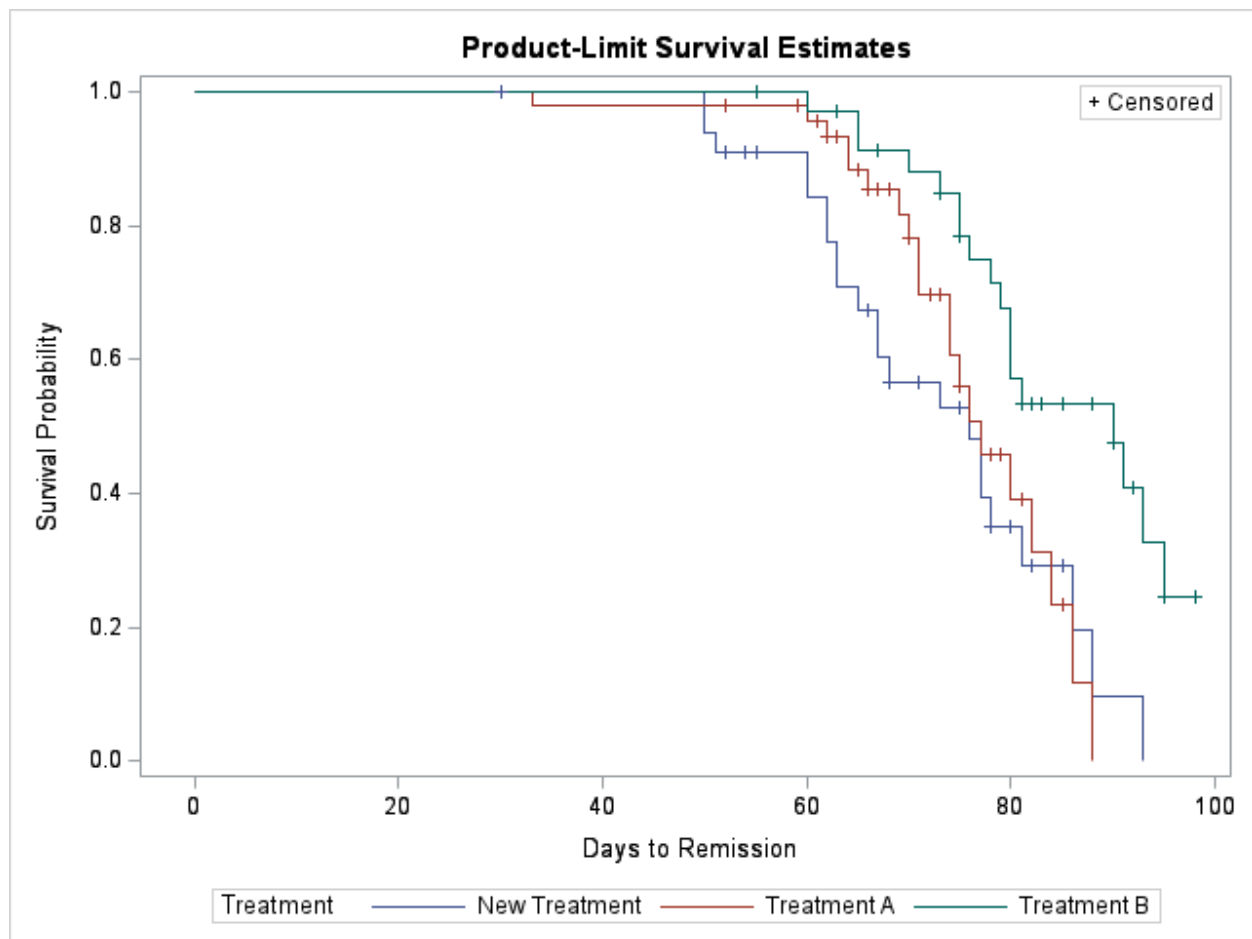


A phase III superiority study was conducted to determine if a new treatment for depression (treatment N) promotes remission better than *two* available standard of care therapies (treatment A and B). There is no placebo in this study due to the severity of the disease under study.

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  $<5$  and persistent depressive symptoms (PDSs; PHQ-9 score  $\geq 10$ ). 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.

The variables in the dataset are:

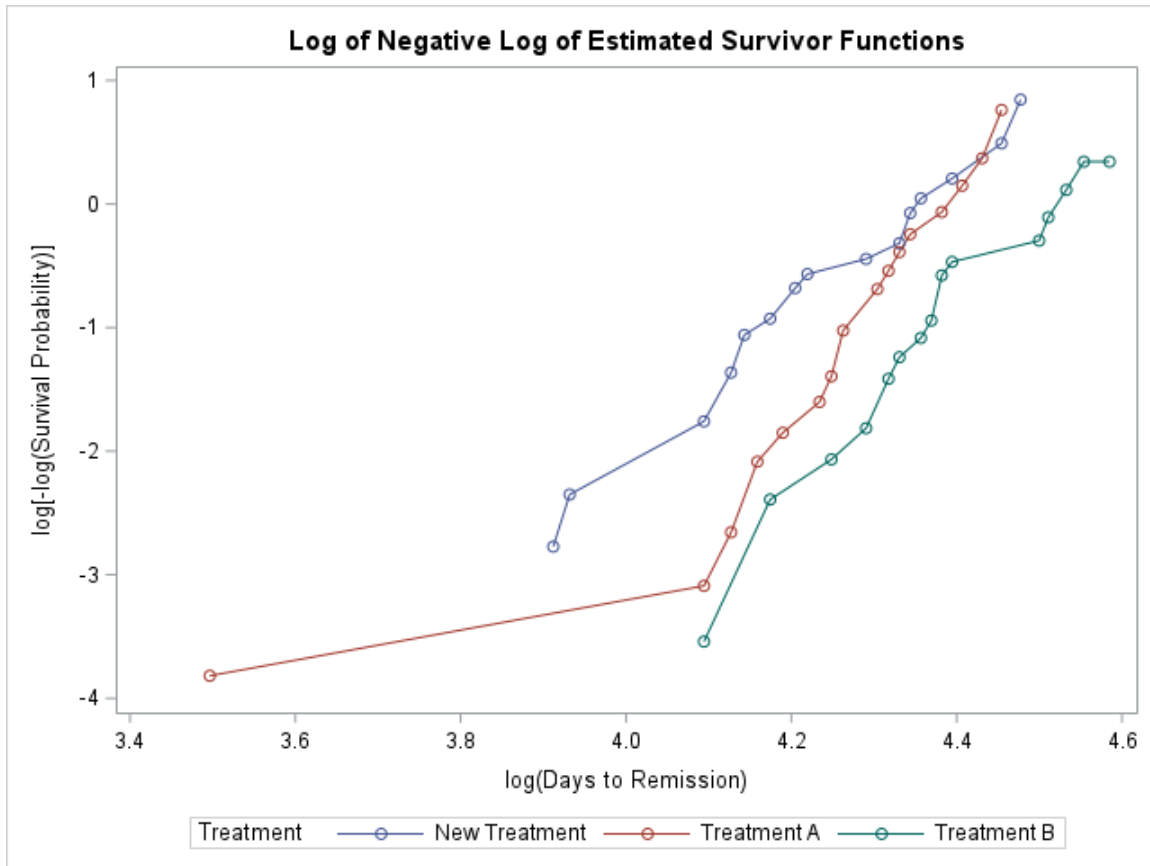
- REMISS indicates Remission Status (0=No,1=Yes)
- DEATH indicates Death (1=Died, 0=Lost to follow-up or had remission)
- DAYS indicates days to remission (if REMISS=1) or days until no longer in study (if REMISS=0 due to loss to follow-up or death)
- TRT indicates Treatment Group (N, A, B)
- AGEGRP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



**Kaplan-Meier Survival Plot for all Three Treatments**

Treatment	Median Time to Remission
A	77 days
B	90 days
N	76 days

Treatment N appears to be the most effective because it has the least time to depression remission.



Based on the log-log survival plots, the proportional hazards assumption is met between N and B, but not between N and A because the curves cross a couple of times.

$H_0: S_N(t) = S_A(t)$	The survival distribution for treatments N and A are the same.
$H_1: S_N(t) = (S_A(t))^\theta$	The survival distribution for one group is a power of the other.
$H_0: S_N(t) = S_B(t)$	The survival distribution for treatments N and B are the same.
$H_1: S_N(t) = (S_B(t))^\theta$	The survival distribution for one group is a power of the other.

A log-rank test was used to test whether the survival distributions for treatment groups N and A were different. The chi-squared statistic was 0.6112 and the resulting p-value was 0.4343. With a p-value greater than the  $\alpha=0.05$  significance level, the null hypothesis of there being a difference in the survival distributions between treatment groups N and A was not rejected. There is insufficient evidence to conclude that treatment N is more effective for depression remission than treatment A.

A log-rank test was used to test whether the survival distributions for treatment groups N and B were different. The chi-squared statistic was 10.4435 and the resulting p-value was 0.0012. With a p-value less than the  $\alpha=0.05$  significance level, the null hypothesis of there being a difference in the survival distributions between treatment groups N and B was rejected. There is evidence suggesting that treatment N is more effective for depression remission than treatment B.

$H_0: HR = 1, \beta = 1$

The hazard ratios for all treatments are the same.

$H_1: HR \neq 1, \beta \neq 1$

The hazard ratios for all the treatments are not the same.

A Cox proportional hazards regression analysis was used to test whether the hazard ratios for all the treatments were the same. Comparing treatments N and A, the chi-squared statistic was 0.6433 and the resulting p-value was 0.4225. With a p-value greater than the  $\alpha=0.05$  significance level, the null hypothesis of there being a difference in hazard ratios of treatments N and A was not rejected. The hazard of depression remission for treatment A is 0.778 of the hazard for treatment N (95% confidence interval: 0.421-1.437), but there is insufficient evidence to conclude that treatment N is more effective than treatment A.

Comparing treatments N and B, the chi-squared statistic was 10.7099 and the resulting p-value was 0.0011. With a p-value less than the  $\alpha=0.05$  significance level, the null hypothesis of there being a difference in hazard ratios of treatments N and B was rejected. There is evidence suggesting that the hazard of depression remission for treatment B is 0.338 of the hazard for treatment N (95% confidence interval: 0.177-0.647), making treatment N more effective at bringing about depression remission.