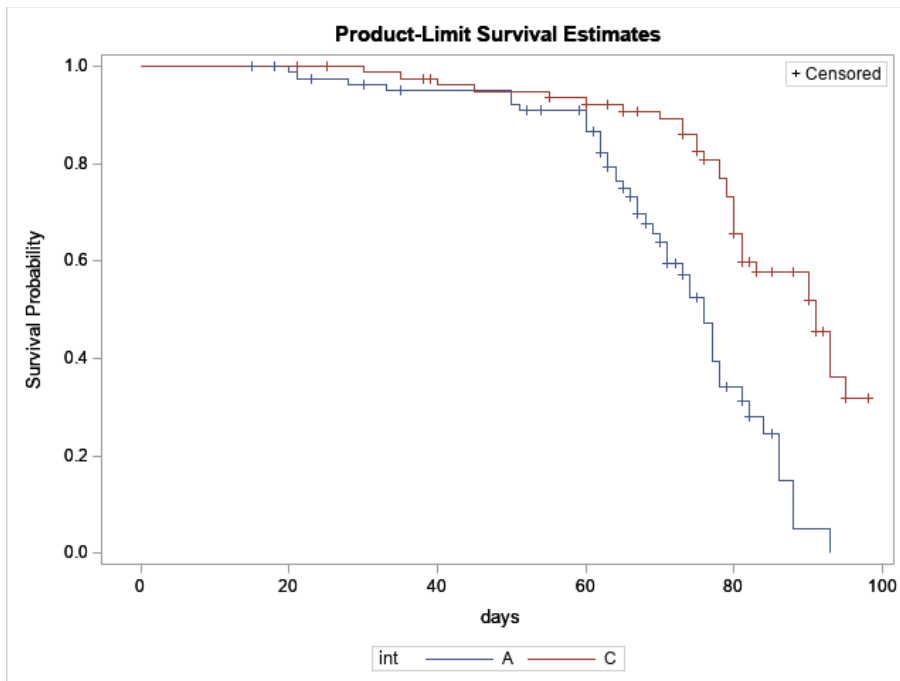


A clinical trial was conducted among patients who experienced a recent drug overdose. The treated group (A=active) underwent an economic incentive intervention plus standard of care. Patients in the treated group were incentivized for presenting a negative urine toxicology. In contrast, the control group (C=control) underwent standard of care alone. The primary objective was to determine if the intervention promotes linkage to primary care (outcome) better than standard of care alone.

The study included 161 subjects who were enrolled and randomized to receive the economic incentive intervention plus standard of care or standard of care alone. The primary outcome was time to first outpatient linkage with a primary care addiction provider. After subjects were randomized, individuals were followed until they had linkage to care, loss-to-follow-up, or died. Note here that the outcome is LINK=1 (a positive outcome). Thus, “survival” actually means “no linkage” and “failure” means “linkage” to care in the SAS Kaplan-Meier output label; please keep this in mind as you interpret your results.

The SAS data set *overdose.sas7bdat* contains the following variables:

- LINKAGE indicates linkage status (0=No, 1=Yes)
 - DEATH indicates death (1=Died, 0=Lost to follow or linked to care)
 - DAYS indicates days to linkage to care (if LINKAGE=1) or days until no longer in study (if LINKAGE=0 due to loss to follow-up or death)
 - INT indicates the intervention group (A=economic incentive + standard of care, C=standard of care only)
 - DRUG_TYPE indicates the type of drug that caused overdose (Heroin or Cocaine) – the randomization stratification factor
1. Present a Kaplan-Meier survival plot for economic incentive versus standard of care only on the time to linkage to care. Describe the survival curve in the 2 groups including timing of events and loss to follow-up, without any formal p-value. Which intervention appears best in promoting linkage to healthcare?



Since our outcome is time to linkage (LINK=1) is a positive outcome, the y-axis represents “no linkage” probability. The interventions are similar in the first 60 days. However, after that we observe a noticeable separation in the curves between the intervention groups. The intervention group (blue line, ‘A’) is experiencing greater frequency and speed in linkage to an addiction provider compared to the control group (red line, ‘C’). Since the blue line is lower, patients are experiencing the event, linkage to a provider, at earlier times in the intervention group compared to those in the standard of care alone. The intervention appears best in promoting linkage to a provider. The lines overlap in the beginning, the survival experience is not significantly different in the beginning. Here, survival is the negative outcome so the standard of care group does not link to care frequently and has less probability of linkage to care as compared to the economic incentive group. Between day 60 to day 95 there is a higher probability of linkage to care in economic incentive group compared to the standard of care group. Patients are experiencing more event and linkage to care in intervention group compared to the standard of care group.

2. What proportion of patients link to care by 60 days in each of the 2 groups? What proportion of patients link to care by 80 days in the two groups? (Remember that linkage to care is a positive outcome: ‘Survival’ indicates that a patient did not link to care)

Intervention A: $P(T < 60) = 0.1338$

Intervention C: $P(T < 60) = 0.0789$

0.1338 (13%) patients link to care by 60 days in economic incentive group whereas 0.0789 (7%) patients link to care by 60 days in standard of care incentive group.

Intervention A: $P(T < 80) = 0.6591$

Intervention C: $P(T < 80) = 0.3426$

0.3426 (34%) patients link to care by 80 days in economic incentive group whereas 0.0622 (6%) patients link to care by 80 days in standard of care incentive group

- Report median time to linkage to care for the two intervention groups and discuss which intervention appears to be more effective (again, do not base your conclusions on p-values, this is subjective).

Quartile Estimates for Intervention Group ('A')				
Percent	Point Estimate	95% Confidence Interval		
		Transform	[Lower	Upper)
75	84.0000	LOGLOG	78.0000	88.0000
50	76.0000	LOGLOG	71.0000	78.0000
25	65.0000	LOGLOG	62.0000	70.0000

Quartile Estimates for Control Group ('C')				
Percent	Point Estimate	95% Confidence Interval		
		Transform	[Lower	Upper)
75	.	LOGLOG	93.0000	.
50	91.0000	LOGLOG	81.0000	95.0000
25	79.0000	LOGLOG	75.0000	81.0000

Median time to linkage to care for economic incentive group is 76 days and Median time to linkage to care for standard of care group is 91 days, hence the economic incentive is clearly more effective than the standard of care.

- Present the null hypothesis and p-value of the log-rank test for economic incentive versus standard of care for time to linkage to care. Do the results agree with your conclusion in part 1? (2 points)

$$H_0: S_A(t) = S_C(t) \text{ vs. } H_1: S_A(t) \neq S_C(t)$$

Null hypothesis: No difference in survival between the two treatments.

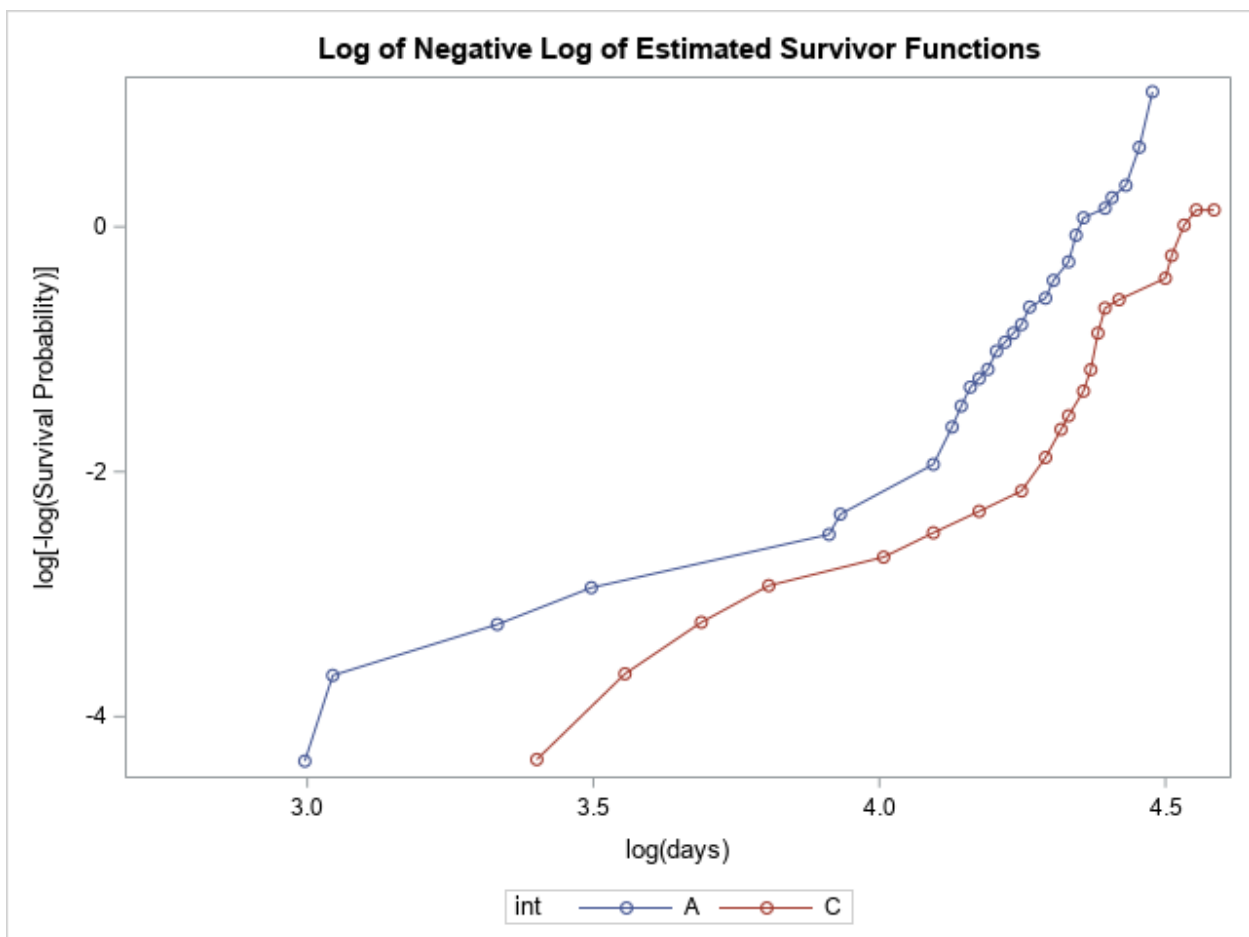
Alternative hypothesis: Difference in survival between the two treatments

The log-rank test comparing the intervention ('A') and control ('C') is show below. Our p-value is <.0001 and we reject the null hypothesis at alpha level 0.05. We have sufficient evidence of a difference in the survival curves between the intervention groups.

Test of Equality over Strata			
Test	Chi-Square	DF	Pr > Chi-Square
Log-Rank	25.1323	1	<.0001
Wilcoxon	16.6322	1	<.0001
-2Log(LR)	3.9601	1	0.0466

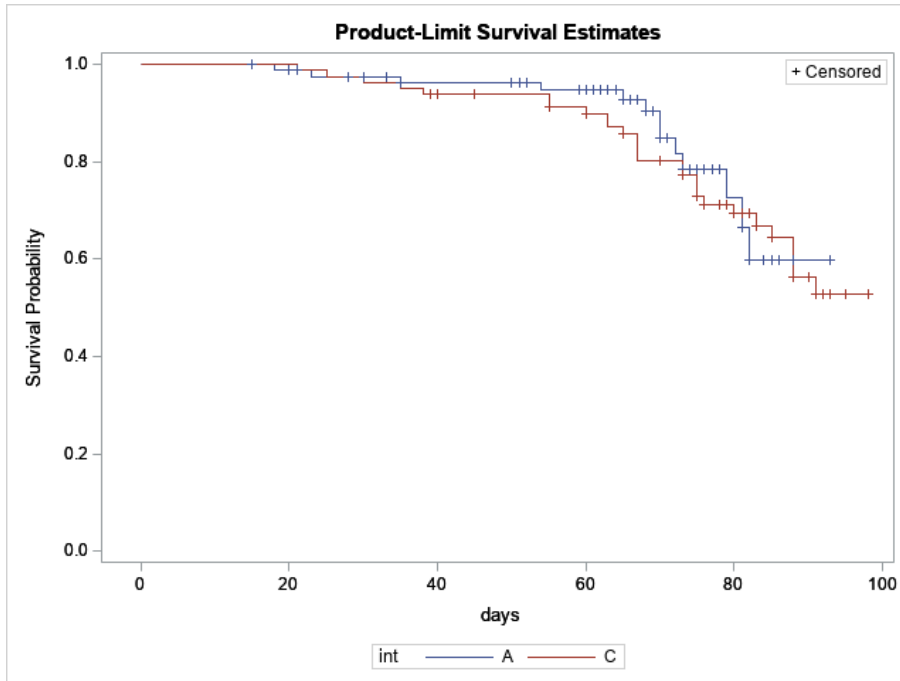
Yes, the results correspond with our observation of the curves in part 1.

- 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. (2 points)



Based on the log-log plot the proportional hazards assumptions appears to be met.

6. Suppose we are also interested in time to death comparing between intervention groups (secondary outcome). Present a Kaplan-Meier survival plot for economic incentive versus standard of care only with death as the outcome. Which intervention (if any) appears to be associated with the higher risk of mortality? (4 points)



Based on the plot, both curves are overlapping, crossing, and are similar over the course of the study. Thus, neither intervention appears to be higher than the other in the risk of mortality as measured by the time to death. Death is more common in the standard of care group as compared to the incentive group. There are more frequent events i.e. death in the standard of care group as compared to the incentive group. The lines overlap a few times so there is not very significant difference in the rates of death in both the group.