

**BIOST/EPI 357**  
**SURVIVAL DATA ANALYSIS IN EPIDEMIOLOGY**

**Winter 2020**  
**Instructor: Marco Carone**

PROBLEM SET 2  
due on Feb 5th, 2020 at 11:59pm

**PROBLEM 1.**

Consider the following trial data on time until relapse (in months) for patients in remission of acute myelogenous leukemia administered a maintenance chemotherapeutic agent or not:

maintenance group: 9, 12, 13+, 18, 23, 28+, 31, 34, 45, 45+, 48, 161+  
control group: 4, 5, 8, 8, 10+, 12, 16+, 23, 27, 30, 38, 43, 45

(a) Compute the Kaplan-Meier and Nelson-Aalen estimators by filling the following tables:

maintenance group

time t	# at risk (n)	# events (d)	d/n	1-d/n	$S_{KM}(t)$	$H_{NA}(t)$
0						
9						
...						

control group

time t	# at risk (n)	# events (d)	d/n	1-d/n	$S_{KM}(t)$	$H_{NA}(t)$
0						
4						
...						

(b) For each group, what is the estimated probability that no relapse will occur by 36 months?

**PROBLEM 2.**

In this problem, you will revisit the dataset on methadone maintenance for heroin addicts, as studied in Problem Set 1. Please refer to that homework for a description of the relevant variables.

- (a) Plot the Kaplan-Meier estimator of the survival function of the time until exit from maintenance along with pointwise 95% confidence intervals. What is the estimated probability that no exit will occur by one year? Provide a 95% confidence interval for your answer.
- (b) Provide the estimated median time until exit from maintenance and associated 95% confidence interval by:
- scrutinizing values of the Kaplan-Meier estimator and associated confidence intervals (explain how you obtain your answer);
  - using the median estimate and confidence intervals provided by the `survfit` command.
- (c) In this part, you will investigate differences between patients with and without a history of incarceration.
- On the same graph, plot the Kaplan-Meier estimator of the survival function of the time until exit from maintenance for patients with a history of incarceration and for patient without.
  - Does the probability that no exit occurred by 8 months differ significantly between these two groups?
  - Based on the logrank test, does the distribution of time until exit from maintenance differ significantly by history of incarceration?

- iv. Based on the Wilcoxon-Gehan-Breslow test, does the distribution of time until exit from maintenance differ significantly by history of incarceration?
  - v. Plot estimated hazard functions for patients with and without a history of incarceration. Briefly indicate how this plot may inform you regarding the power of the logrank test as well as expected differences in the magnitude of the chi-square statistics from the logrank and Wilcoxon-Gehan-Breslow tests.
- (d) Repeat (c) but substituting history of incarceration by methadone dosage dichotomized at 60mg/day (i.e., compare the subpopulation of patients administered more than 60mg/day of methadone to the subpopulation of patients administered no more than 60 mg/day).
- (e) Based on a stratified logrank test, does the time until exit from maintenance differ by history of previous incarceration adjusting for clinic membership? State explicitly what the null and alternative hypotheses are and contrast with what they are in a standard logrank test.
- (f) What is the estimated median residual time until exit from maintenance at 4, 8 and 12 months? Calculate these estimates using only values of the Kaplan-Meier estimator. Verify your answer using the R function provided for this purpose, and obtain 95% confidence intervals to accompany your estimates.