STAT 495 FINAL EXAMINATION SOLUTION

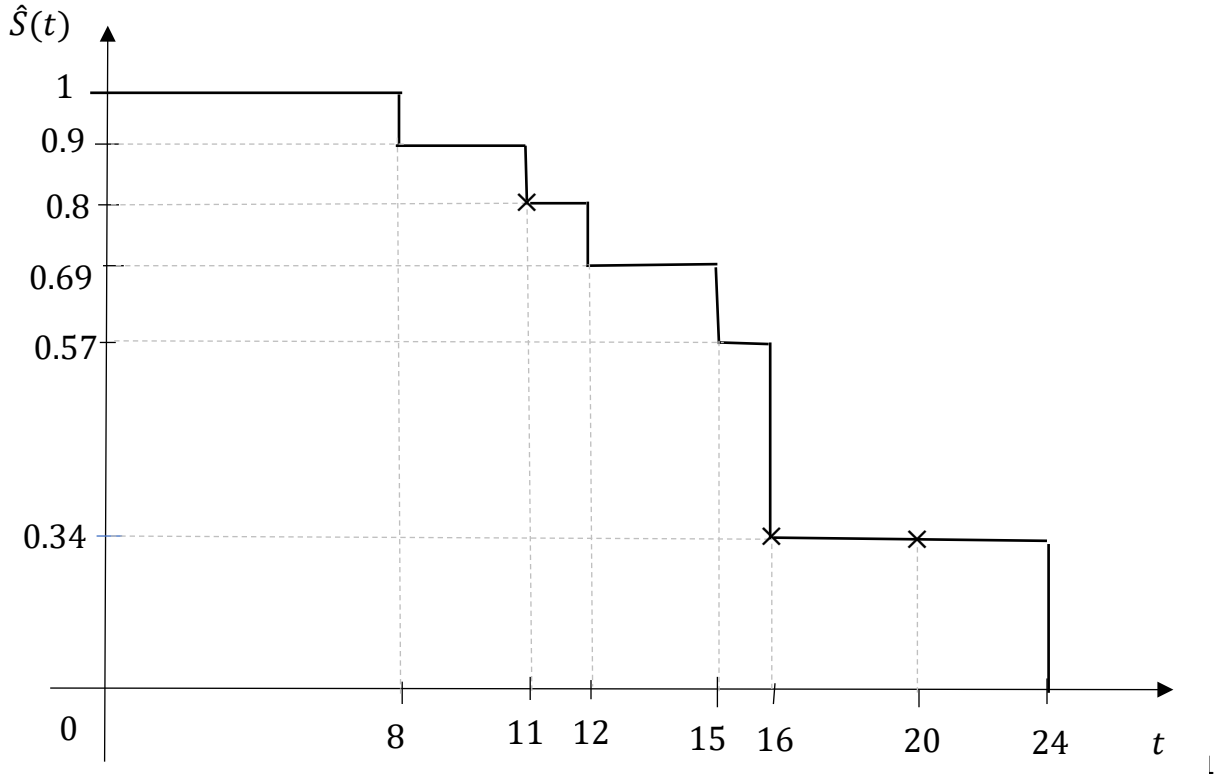
Problem 1. Dermatologists conducted a pilot clinical trial for Otezla, a medication for plaque psoriasis (a skin disease). Ten patients were given the medication and the times (in weeks) until remission were recorded. At the end of the study, the patients who had not experienced a remission were censored. The data are

8, 11, 11+ 12, 15, 16, 16, 16+, 20+, 24

(a) Compute by hand the Kaplan-Meier estimator of the survival function.

Time, t_i	**At risk, n_i**	**Died, d_i**	**Censored at time t_i**	**Survival Rate, $1-\frac{d_i}{n_i}$**	**Estimator $\widehat{S}(t), t_i \le t < t_{i+1}$**
0	**10**	**0**	**0**	**1**	**1**
8	**10**	**1**	**0**	**1-1/10=0.9**	**0.9**
11	**9**	**1**	**1**	**1-1/9=0.89**	**0.8**
12	**7**	**1**	**0**	**1-1/7=0.8571**	**0.6857**
15	**6**	**1**	**0**	**1-1/6=0.8333**	**0.5714**
16	**5**	**2**	**1**	**1-2/5=0.6**	**0.3429**
24	**1**	**1**	**0**	**1-1=0**	**0**

(b) Draw by hand the Kaplan-Meier survival curve.



(c) Estimate the survival function at 10, 15, and 20 weeks.

$\widehat{S}(10) = \widehat{S}(8) = 0.9, \widehat{S}(15) = 0.5714$, and $\widehat{S}(20) = \widehat{S}(16) = 0.3429$.

Problem 2. A study on pulmonary fibrosis was conducted in a specialized clinic. Gender, age at baseline, smoking status, time to relapse (in weeks), and censoring status were recorded. Use the accompanying SAS code and output to answer the following questions:

(a) Do times to relapse differ with respect to gender and smoking status? Support your arguments by giving the name of the test, hypotheses, and *p*-values. State your conclusion. Describe the relative position of the curves on the graphs.

Log-rank tests have been carried out to compare the survival curves by gender and by smoking status. The respective hypotheses are $H_0: S_{male}(t) = S_{female}(t)$ for all t vs. $H_2: S_{male}(t) \neq S_{female}(t)$ for some t, and $H_0: S_{ex\text{-}smoker}(t) = S_{never\ smoked}(t)$ for all t vs. $H_1: S_{ex\text{-}smoker}(t) \neq S_{never\ smoked}(t)$ for some t. In both tests, the p-value < 0.0001, thus, we accept the alternatives in each case, and conclude that the curves different by gender and smoking status. From the graphs, we see that the curve for males lies clearly below that for females, and that the curve for ex-smokers is lower than that for those who never smoked. The practical conclusion is that males and ex-smokers have shorter time to relapse of pulmonary fibrosis.

(b) Write down the fitted Cox proportional hazards model. What predictors are significant at the 5% level?

$\widehat{S}(t) = [\overline{S}(t)]^{\hat{r}}$ where the estimated relative risk is $\hat{r} = \exp(2.87723 \cdot male + 0.04459 \cdot (age - 67.2353) + 3.18595 \cdot ex\text{-}smoker)$. All three predictors (gender, age at baseline, and smoking status) are significant at the 5% level.

(c) Interpret the significant estimated regression coefficients.

For males, the estimated hazard of relapse of pulmonary fibrosis is $\exp(2.87723) \cdot 100\% = 1776.5\%$ of that for females.

As age at baseline increases by one year, the estimated hazard increases by $(\exp(0.04459) - 1) \cdot 100\% = 4.5599\%$.

For ex-smokers, the estimated hazard is $\exp(3.18595) \cdot 100\% = 2419.03\%$ of that for individuals who never smoked.

(d) Find the predicted probability that a 55-year-old female, ex-smoker, will not experience a relapse of pulmonary fibrosis for more than 35 weeks.

$S^0(35) = [0.77806]^{\exp(0.04459\cdot(55-67.2353)+3.18595)}$**=0.02966.**

Problem 3. A study on the efficacy of a biogel as a wound-healing substance is conducted on 85 subjects. Their gender (male/female), age at surgery (in years), surgery site (knee/ankle/shoulder), and score at 10 days post-surgery. The higher the score, the less pain and more joint mobility the subject experiences. The treatment group subjects were matched with historical control. Use the R codes and outputs to present your answers to the following questions:

(a) Compare the scores between the biogel and pre-matched control groups. Give the name of the test, hypotheses, and *p*-value, and state your conclusion. Describe the histograms in support of your conclusion.

Wilcoxon rank-sum test has been conducted to test $H_0: \theta_{biogel} = \theta_{Cx}$ against $H_1: \theta_{biogel} \neq \theta_{Cx}$ where θ represents a location parameter for the distribution of the score. The *p*-value is <0.0001 indicating that the location parameters for the biogel group and pre-matched control group are different. We can see on the histograms that the scores in the biogel group range roughly between 65 and 90, whereas, in the pre-matched control group, they range between about 20 and 90.

(b) Explain the process of matching step-by-step. What variables were used for matching? What type of matching has been conducted?

A binary logistic model is run by regressing variable group on gender, age, and site. The predicted probabilities (also termed propensity scores) are computed and ordered in decreasing order for the subjects in the control group. The individuals with the highest propensity scores are selected for the matched control group. There are 85 individuals in the biogel group and twice as many (170) are chosen for the matched set. This is a 2:1 matching.

(c) Compare the scores between the matched groups. Give a quantitative argument. Was it clever to match the data sets? Is biogel effective?

For the matched data, the Wilcoxon rank-sum test produces the *p*-value of 0.8285, leading to the conclusion that the location parameters of the score distribution don't differ between the biogel group and the matched control group. The histogram also supports this conclusion as the scores in the matched control group range between about 60 and 95.

The drawn conclusion means that it was a jolly good idea to do the matching and that biogel is not really effective.