Pharm 3011 - Fall 19 - Assignment 4 Solutions

(Out of 45 points)

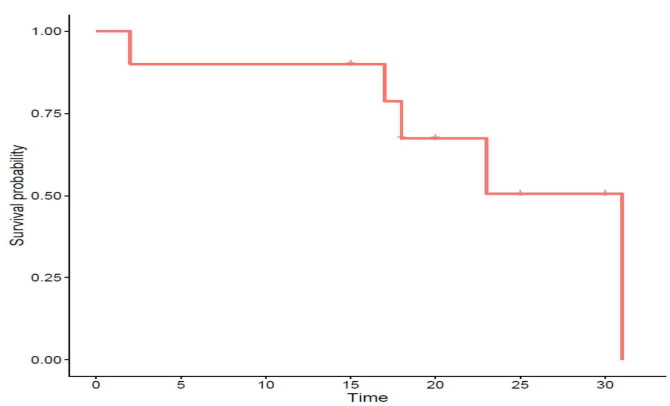
1. The times until recurrence of headaches following treatment for ten subjects are listed below, with "+" indicating censored observations.
2, 15+, 17, 18, 18+, 20+, 23, 25+, 30+, 31

   Calculate and plot the Kaplan Meier estimate of the survival curve.

   - the calculations are shown in the following table, where
     - t are the times at which failures occur,
     - r is the number at risk at that time,
     - f is the number of failures (recurrence of headaches) at that time,
     - sp is the proportion surviving that time period, and
     - s is the value of the survival curve

t	r	f	sp	s
2	10	1	9/10	.9
17	8	1	7/8	63/80=.7875
18	7	1	6/7	54/80=.675
23	4	1	3/4	81/160=.5063
31	1	1	0	0

   - The plot is shown below. Drops occur at the failure times, and ticks show the censored values.



(15 points total. 1 point each for the numbers at risk $(10, 8, 7, 4, 1)$ and the survival function estimates $\approx (.9, .79, .68, .51, 0)$ in the table. Deduct 1 point for each error, but don't accumulate errors. Give 5 points if the plot of the survival curve matches the estimates from the table. No penaly for not including tick marks at censored times, or for drawing the curve without the vertical drop lines - which is, in fact, the correct way to draw a Kaplan Meier estimate.)

2. The following table shows survival times (in weeks) for a control group (Group 0) and a Treatment group (Group 1):

Group 0	15	18	19	19	
Group 1	16+	18+	20+	23	24+

Compare the two survival curves using the Cochran-Mantel-Haenszel test (also known as the log rank test).

(2) (a) State the hypotheses.

$H_0 : S_T(t) = S_C(t)$ for all $t > 0$. $H_A : S_T(t)! = S_C(t)$ for some $t > 0$.

or

H_0: the survival functions are the same for each time. H_A: the survival functions differ at some time.

(2 points for one of these, or something similar)

(b) Calculate the test statistic, showing your work in a table similar to that on page 3 of the class notes.

	Num at Risk		Num of Deaths			
	Treat	Total	Treat	Total		
t_i	M_i	T_i	a_i	N_i	E_i	V_i
15	5	9	0	1	0.556	0.247
18	4	7	0	1	0.571	0.245
19	3	5	0	2	1.200	0.360
23	2	2	1	1	1.000	0.000
			1		3.327	0.852

(9)

(9 points for a table with entries as above. Deduct 1 point for each incorrect entry, but don't accumulate errors. For example, if the 1st entry in the T_i column is 8 rather than 9, deduct only 1 point, even though the first entry in the E_i and V_i columns will be wrong, as will the cumulative sums of those columns.)

(2) $Z_{obs} \approx \frac{1-3.327}{\sqrt{.852}} \approx -2.52$ (2 points for observed Z)

(Some students may have focused on a cell other than deaths in the treatment group. In that case, the table entries will be different, except for the V_i column, but the value of the test statistic will be the same. Give full marks in that case.)

(c) Determine the P value as accurately as possible.

$$2P(Z > |-2.52|) = 2P(Z < -2.52) \approx .012$$

(2)

3. A Cox proportional hazards model for survival time of ovarian cancer patients was fit. Where $X = 1$ for a subject in the treatment group, and $X = 0$ for the control group, and AGE is the age of the subject in years, the model had estimated hazard function

$$h_{X,AGE}(t) = h_{0,0}(t)e^{-.8X+.2AGE}$$

Also, it was determined that the baseline hazard at 20 months was $h_{0,0}(20) = .01$.

(2) (a) What is the hazard at 20 months for a 40 year old in the control group?

$$.01e^{.2(40)} = .01e^{8} \approx 29.8$$

(2) (b) What is the hazard at 20 months for a 40 year old in the treatment group?

$$.01e^{-.8+.2(40)} = .01e^{-.8+8} \approx 13.4$$

(2) (c) What is the ratio of the hazards at 20 months for a 40 year old in the treatment group relative to (over) a 40 year old in the control group.

$$e^{-.8} \approx .45$$

(2) (d) What is the hazard ratio at 10 months for a patient aged 50 relative to (over) a patient aged 30 in the treatment group?

$$e^{-.8+.2*50}/e^{-.8+.2*30} = e^{.2*20} \approx 54.6$$

(2) (e) What is the hazard ratio at 15 months for a patient aged 50 relative to (over) a patient aged 30 in the treatment group?

$$\approx 54.6$$

4. A sample of size 10 was taken. The sample values were 1,2,3,4,5,6,7,8,9,10, giving a sample average $\bar{X} = 5.5$.

Imagine taking a bootstrap sample, meaning a sample of size 10 with replacement, from these data.

(a) What is the smallest possible mean of the bootstrap sample?

(2) 1

(b) What is the largest possible mean of the bootstrap sample?

(1) 10

(c) What is the probability that the value 10 does NOT occur in this bootstrap sample?

$$(9/10)^{10} \approx 0.35$$

(2)