Practice Survival Analysis Questions

1) (10 points) Sixteen patients with advanced stomach carcinoma were randomized to receive one of two chemotherapies (Group A or Group B). The survival times from treatment (in weeks) are (+ denotes a censored observation):

Group A: 63+, 59+, 57+, 40, 37, 33, 21+, 11
Group B: 57+, 51+, 44+, 32, 27, 27+, 10+, 6

a) (2 points) Two reasons why an observation might be censored include:
(i) administrative: study closes before patient dies;
(ii) loss to follow-up during study due to patient leaving the area.
State for each whether the assumption of statistical independence with survival time is plausible or not and the basis for your statement.

b) (3 points) Construct (arithmetically) and plot (very roughly) the Kaplan-Meier survival curve for Group B.

c) (3 points) Construct the risk sets of patients still alive and on-study in each group at t = 32 weeks and show (arithmetically) the contribution to the observed and expected number of deaths in Group A at that time using the log-rank procedure.

d) (2 points) For each group, total observed and expected deaths were calculated using the log-rank procedure, with the following results:

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed deaths</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Expected deaths</td>
<td>4.03</td>
<td>2.97</td>
</tr>
</tbody>
</table>

What is the null hypothesis $H_0$ under which the row of expected numbers of deaths is calculated? In particular, if $S_A(t)$ and $S_B(t)$ denote the survival probabilities in the two groups at time $t$, what is assumed about these probabilities under $H_0$?
2) (8 points) A group of 101 leukemia patients who received allogeneic vs autologous (type) transplants were followed up from transplant until death or relapse (Klein & Moeschberger, 1997). Time was recorded in months. The figure below shows the Kaplan-Meier estimates of the corresponding survival functions:

![Kaplan-Meier survival estimates](image)

a) (2 points) Label the hazards as “allogeneic” or “autologous” in the plot below.

![Smoothed hazard estimates, by type](image)
b) (2 points) Klein and Moschberger state that “In studies of the efficacy of allogeneic vs autologous transplants for acute myelogenous leukemia, it is well known that patients tend to have more complications early in their recovery process. Of primary interest to investigators in this area is comparing the failure rate (death or relapse) among longterm survivors”.

Of the tests you have learned for comparing survival curves, the best test for addressing this scientific question is the (choose one):

i. Log-rank test
ii. Tarone-Ware test
iii. Wilcoxon-Gehan-Breslow test.

Motivate your choice of test.

c) (2 points) Consider the following plot which provides a graphical means of assessing the proportional hazards assumption in the model:

\[ \log(h(t;X)) = \log(h_0(t)) + \beta \text{ type} \]

Based on this plot, comment on the validity of the proportional hazards assumption.

d) (2 points) Suppose we write a hazard model for type (0 = allogeneic; 1 = autologous) as

\[ \log(h(t;X)) = \log(h_0(t)) + \beta_1(t) \text{ type} \]

Consider the Stata output labeled “Question 2d”. In terms of \( \beta_1(t) \) from the model above, what null hypothesis is being tested in this output? What is the conclusion?
3) (20 points) These data come from a follow-up study of larynx cancer. Refer to the Stata output labeled “Question 3”.

a) (3 points) What is the interpretation of the regression coefficient in “model1”? What (quantitative) effect does stage34 appear to have on the instantaneous death rate? Is the effect statistically significant at the 5% level?

b) (2 points) What is the interpretation of the regression coefficient for stage34 in “model2”?

c) (2 points) Is there evidence that age confounds the effect of stage34? Justify your response.

d) (2 points) Suppose that, for model 2, the baseline survival at 6 months \( \hat{S}_b(6) \) is 0.714. What is the predicted survival at 6 months for a 55 year old individual with stage3 or 4 cancer based on this model?

e) (2 points) The third model, “model3” involves the interaction between stage34 and age50. Write down the Cox PH model (using \( \beta \)’s) that corresponds to “model3”.

f) (2 points) What is the interpretation of the coefficient of age50 in “model3”?

g) (2 points) For patients with stage 3 or 4 cancer, if age increases from 55 to 65, by what multiplicative factor does the fitted model3 estimate that their death rate increases?

h) (5 points) Is there evidence that the hazard ratio for stage34 varies by age? Write a null and alternative hypothesis to address this question in terms of the model written down in part (e). Give the name of a test that can be used to test the null hypothesis. Carry out the test using \( \alpha = 0.05 \). Be sure to provide the value of the test statistic, the reference distribution (with degrees of freedom, if appropriate) and state your conclusion. (The 95th percentile of a Chi-squared distribution with 1 degree of freedom is 3.84, of a Chi-squared distribution with 2 degrees of freedom is 5.99.)
Question 2d

The variables represented in the dataset are as follows:
- Time to death or relapse, months
- Type of transplant (0=allogeneic, 1=autologous)
- Leukemia-free survival indicator (0=alive without relapse, 1=dead or relapse)

\[ stcox \) type, scaledsch(SCA*) \]
\[ stptest, detail \]

Test of proportional hazards assumption

<table>
<thead>
<tr>
<th>rho</th>
<th>chi2</th>
<th>df</th>
<th>Prob&gt;chi2</th>
</tr>
</thead>
<tbody>
<tr>
<td>type</td>
<td>0.38366</td>
<td>7.62</td>
<td>1</td>
</tr>
</tbody>
</table>

Question 3

Stage 34 Stage of disease (0=stage 1, 2 1=stage 3, 4)
Time Time to death or on-study time, months
Age 50 (Age at diagnosis of larynx cancer - 50)
Status Death indicator (0=alive, 1=dead)

Model 1:

\[ stcox stage34, nohr \]

No. of subjects = 90  Number of obs = 90
No. of failures = 50
Time at risk = 377.8000028
LR chi2(1) = 9.43
Prob > chi2 = 0.0021

| _t | Coef.  | Std. Err. | z     | P>|z| | [95% Conf. Interval] |
|----|--------|-----------|------|------|----------------------|
| stage34 | .879474 | .286939 | 3.07 | 0.002 | .3170838 - 1.441864 |

Model 2:

\[ stcox stage34 age50, nohr \]

No. of subjects = 90  Number of obs = 90
No. of failures = 50
Time at risk = 377.8000028
LR chi2(2) = 11.90
Prob > chi2 = 0.0026

| _t | Coef.  | Std. Err. | z     | P>|z| | [95% Conf. Interval] |
|----|--------|-----------|------|------|----------------------|
| stage34 | .879474 | .286939 | 3.07 | 0.002 | .3170838 - 1.441864 |
Model 3:

\[ . \text{xi: stcox i.stage34*age50, nohr} \]

|               | Coef.   | Std. Err. | z     | P>|z|   |  [95% Conf. Interval] |
|---------------|---------|-----------|-------|-------|-----------------------|
| _Istage34_1   | 1.087132| 0.5725228 | 1.90  | 0.058 | -.0349917 2.209256    |
| age50         | .0297464| 0.0219454 | 1.36  | 0.175 | -.0132658 .0727587   |
| _IstaXage5~1| -.0127367| 0.0293888 | -0.43 | 0.665 | -.0703378 .0448644   |