STAT 486/886 (Winter 2022)

Assignment 3

The assignment is due on Mar. 20 (Sunday), 23:00 (time of Kingston Ontario Canada). Please submit to OnQ, the dropbox for this assignment.

Guidelines for Preparing Solutions:
For some problems in this course, complete code and output may be very long. Please only include important output and necessary results in the main text of your solutions.
Give descriptions and discussions for your important exploration and findings.
Put long, extra code and output in an **Appendix,** at the end of your assignment.
The Appendix will NOT be marked. Please include it as evidence of your independent work. Prepare your assignment solutions so that it is easy for readers to follow, without having to search everywhere for your answers from lengthy code and output.
Students submitting identical solutions (multiple sentences, derivation steps or code copied among students or from other resources) will be investigated for violations of academic integrity.

1. The dataset "p31.txt" contains the number of thousand cycles to failure for a type of spring tested under three load stresses 750, 850 and 950 N/mm^2. Fit a Weibull model for the data at stress level 750 N/mm^2 only. Answer the questions based on the fit.
(a) Find the 95% confidence interval for the median survival time (thousand cycles) at the stress level 750 N/mm^2.
(b) Find the 95% confidence interval for the probability that the type of spring survives over 6000 thousand cycles at the stress level 750 N/mm^2.

2. **Advanced non-Hodgkin's Lymphoma.** The data set is presented and studied in Examples 2.3.1 and 3.3.2.
a) As an initial exploration, plot a standard Q-Q plot ($\log(-\log \hat{S}_{KM}(t))$ versus $\log t$) and discuss if a Weibull (or exponential) model is suitable for the data.
b) Example 3.3.2 shows that Weibull model fits the data no better than the exponential model. But is exponential model good enough for the data? Check the fit of the exponential model by graphing a P-P plot (estimated survival function (s.f.) from exponential model versus K-M estimate of s.f.).
c) Fit a log normal model to the data. Draw a P-P plot to check if the log normal model fits the data well. Summarize your findings about the data based on your investigations in a), b) and c).

3. Consider the data in "p31.txt", described in Problem 1.
(a) Carry out a test of the equality of failure time distributions at stress levels 850 and 950 N/mm^2. Consider Weibull distributions only.
(b) Fit appropriate Weibull model or models to the data. Check the fit of the parametric models by comparing the estimated survival functions to the KM estimates. Discuss the differences in the failure time distributions for the three stress levels, and report the estimates of their location and scale parameters.

4. The dataset "p34.txt" arises from a study on bile duct cancer patients who took part in a study to determine whether a combination of radiation treatment (R_0R_x) and the drug 5-fluorouracil (5-FU) prolonged survival. Survival times, in days, are given for a group of patients given the radiation-drug therapy (denoted by "trt=1") and for a control group of patients (denoted by "trt=0").
(a) Plot the Kaplan-Meier estimates of the survivor functions for the two groups and comment on the form of the plot.

(b) Use the Wilcoxon and log-rank tests to test the hypothesis that the two survival time distributions are equal. Are these likely to be effective tests in this type of situation?
(c) Apply parametric methods to assess possible differences in the two distributions. Check if your parametric model is appropriate for the data.

5. *Weighted Log-Rank Test for Multiple Groups.* **This problem is for Stat 886 students only.**
In Section 4.2.2, we studied weighted log-rank test for comparing the distributions of 2 groups. More specifically, the section is about testing for
H_0: the 2 groups have the same survival time distribution, or equivalently
$H_0 : S_1(t) = S_2(t)$ for all t (or $H_0 : H_1(t) = H_2(t)$ for all t). The method is summarized below.

Let $t_1 < t_2 < \ldots < t_K$ be the distinct failure times of both groups. The weighted log-rank statistic for testing H_0 has the form

$$U = \sum_{j=1}^{K} w(t_j) \left[d_{1\cdot}(t_j) - \frac{Y_{1\cdot}(t_j)}{Y_{\cdot\cdot}(t_j)} d_{\cdot\cdot}(t_j) \right],$$

where $w()$ is the weight function, $d_{i\cdot}(t_j) = dN_{i\cdot}(t_j)$ is the number of failures at t_j in group i, $i = 1, 2$, $d_{\cdot\cdot}(t_j) = dN_{\cdot\cdot}(t_j)$ is the number of failures at t_j in both groups, $Y_{i\cdot}(t_j)$ is the number at risk at t_j in group i, $i = 1, 2$, and $Y_{\cdot\cdot}(t_j)$ is the number at risk at t_j in both groups (see the counting processes notation defined in this section). The variance estimator for U is

$$V = \widehat{Var}(U) = \sum_{j=1}^{K} [w(t_j)]^2 Y_{1\cdot}(t_j) \frac{d_{\cdot\cdot}(t_j)}{Y_{\cdot\cdot}(t_j)} \left[1 - \frac{d_{\cdot\cdot}(t_j)}{Y_{\cdot\cdot}(t_j)} \right] \frac{Y_{2\cdot}(t_j)}{Y_{\cdot\cdot}(t_j) - 1}.$$

Test of H_0 is based on the asymptotic result that

$$W^2 = U^{\mathrm{T}} V^{-1} U \approx \chi_1^2.$$

The notes (Klein and Moeschberger, 2003) posted below talk about testing for multiple groups, although in different notation. Text around Equations (7.3.3) to (7.3.6) on the notes are the most relevant for presenting the test method. Please describe the test following our notation as above and in Section 4.2.2 (so that your description can be added to the section as an extension of the weighted log-rank test to situations with multiple groups).

Suppose there are $i = 1, \ldots, G$ groups, and take group G as the reference. The weighted log rank statistic U takes a vector form, and V becomes a variance-covariance matrix. Please specify the expressions for U and V, and the asymptotic distribution for $W^2 = U^{\mathrm{T}} V^{-1} U$, for the purpose of testing the null hypothesis that all groups have the same survival time distribution.