Problem 4.2

a) The survival functions and their standard errors for the AML low-risk and AML high-risk groups are on pages 1 and 2 of the output, respectively, in the columns labeled “surv” and “stderr”.

b) The cumulative hazard rates and their standard errors for the AML low-risk and AML high-risk groups are on pages 1 and 2 of the output, respectively, in the columns labeled “h” and “stderrh”.

c) Low-risk: \( h(2204) = 0.76206 - 0.01852 \times 30 \text{ days} \)
   \[ \frac{2204-10}{2204-10} \]
   \[ 0.01 \text{ deaths/month} \]

High-risk: \( h(677) = 1.37449 - 0.02222 \times 30 \text{ days/month} \)
   \[ \frac{677-2}{677-2} \]
   \[ 0.06 \text{ deaths/month} \]

Crude estimates of the hazard rate for each group based on the slope of the Nelson-Aalen estimator, are 0.01 disease deaths per month in the low-risk group and 0.06 disease deaths per month in the high-risk group. This is based on the linear assumption.

d) The mean time to death in the low-risk group is 1548.34 days, with a 95% confidence interval of (1248.21, 1849.47) (p.4 of the output).

The mean time to death in the high-risk group is 342.31 days, with a confidence interval of (480.19, 1043.41) (p.6 of the output).

For comparison purposes, it may be better to truncate at time...
e) Using a linear formula:
   For the low-risk group, the median time to death is 2204.00 with a 95% confidence interval of \((304.00, +\infty)\). (p.10 output)
   For the low-risk group, the median time to death is 183.00 with a 95% confidence interval of \((116.00, 390.00)\). (p.11 output)

Using a log-transformed formula:
   The low-risk group has a median time to death of 2204 with a 95% confidence interval of \((641.00, +\infty)\). (p.13 output)
   The high-risk group has a median time to death of 183.00 with a 95% confidence interval of \((113.00, 390.00)\). (p.19 output)

Using an arcsine formula:
   The low-risk group has a median time to death of 2204.00 with a 95% confidence interval of \((641.00, +\infty)\). (p.24 output)
   The high-risk group has a median time to death of 183.00 and a 95% confidence interval of \((115.00, 390.00)\). (p.26 output)

f) Using the log-transformed formula, the 95% confidence intervals for the survival functions at 300 days post-transplant are:
   \((0.646199, 0.863718)\) for the low-risk group (p.28 output) and \((0.27758, 0.55987)\) for the high-risk group (p.29 output).
   Using the arcsine formula, the 95% confidence intervals for the survival functions at 300 days post-transplant are:
   \((0.658838, 0.87753)\) for the low-risk group (p.18 output) and \((0.25328, 0.56798)\) for the high-risk group (p.19 output).
It may be good to plot them too since the tables are harder to read even though they are more informative.

The 95% EP confidence bands for the survival functions over the range 100-400 days post-transplant are on p. 30 of the output for the low-risk group and p. 31 for the high-risk group. The confidence bands using a linear formula are (linearL, linearU) or (leptinL, leptinU), using a log-transformed formula they are (logL, logU) or (leptlogL, leptlogU); using an arcsine formula they are (sinL, sinU) or (leptsinL, leptsinU).

The 95% HW confidence bands for the survival functions over the range 100-400 days post-transplant are on p. 32 for the low-risk group and p. 38 for the high-risk group. The confidence bands are (hwlinL, hwlinU) using the linear formula, (hwllogL, hwllogU) using the log-transformed formula, and (hwsinL, hwsinU) using the arcsine formula.

Calculations for confidence coefficients $cos(a, a_u)$:

**Low Risk**
- $\sigma^2(100) = 0.04277^2, 0.08889^2 = \sigma^2(80)
- $a_L = 0.1311 \approx 0.12$
- $a_U = 0.1654 \approx 0.16$
- $\cos(0.12, 0.26) = 2.5949$

**High Risk**
- $\sigma^2(100) = 0.06901^2, 0.13293^2 = \sigma^2(390)$
- $a_L = 0.1531 \approx 0.15$
- $a_U = 0.1855 \approx 0.18$
- $\cos(0.32, 0.64) = 1.68$

Calculations for confidence coefficients $k = (a, a_u)$:

Some $a, a_u$ as above => **Low Risk**: $k = (0.12, 0.26) = 1.0721$
- **High Risk**: $k = (0.32, 0.64) = 1.3155$
Based on the results above and those discussed in Example 4.2, the survival experience of the AML low-risk group is much more desirable than that of the high-risk group. At the beginning of the study, just a few days after transplant, there is not much difference between the survival functions for the groups. However, over time, the gap between them widens, and the further away from transplant the better chance of survival, the low-risk group has compared to the high-risk group. The median survival time is much higher significantly for the low-risk group than for the high-risk group or AML (2204 days compared to 183 and 418, respectively). The low-risk group clearly has the better prognosis, and the ALL group falls somewhere in the middle (though at times closer to the high-risk group).
Problem 4.6

a) The infection-free survival functions and their standard errors, labeled "Surv" and "SEsurv" respectively, are on p. 34 of the output for the Povidone-Iodine group and p. 35 of the output for the Chlorhexidine group.

b) The cumulative hazard rates and their standard errors, labeled "h" and "SEhazr" respectively, are on p. 34 of the output for the Povidone-Iodine (P-I) group and p. 35 of the output for the Chlorhexidine (Ch) group. The plot of the estimated cumulative hazard rates is on p. 81 of the output, Figure 1. It does not appear that the two cumulative hazard rates are proportional to each other because the hazard rate for the povidone-iodine group increases at a faster rate than that of the chlorhexidine group.

c) The median time to infection for the P-I group is 43.00 days using a log-transformed formula, 95% confidence interval (23.99, 72.98) (p. 38 output); the linear (p. 45 output) and arc-sine (p. 52 output) formulas gave the same results. For the Ch group, the log-transformed (p. 41 output), linear (p. 48 output), and arc-sine (p. 55 output) formulas all gave no point estimate for the median time to infection and gave only a lower limit of 42.00 for the 95% confidence interval.

d) The 95% confidence intervals for the infection-free survival functions at 10 days post-admission are on p. 57 of the output for the P-I group and p. 58 for the Ch group.
Using the log-transformed formula, the intervals are (log L, log U). Using the arcsine transformed formula, the intervals are (sin L, sin U).

c) The 95% EP confidence bands for the infection-free functions over the range 8–20 days post-infection are on p. 59 of the output for the P-I group and on p. 60 for the Ch group. The linear formula confidence bands are (linear L, linear U), the log transformed formula confidence bands are (log L, log U), and the arcsine formula confidence bands are (sin L, sin U) or (cos L, cos U).

Calculations for confidence coefficients \( \cos(\alpha, \omega) \):

\[
\begin{align*}
&\text{P-I: } \sigma^2(8) = 0.0493, \\
&\quad \alpha = \sqrt{\frac{8}{(8-3)}} = 0.213 = 0.22 \\
&\quad \alpha^2(10) = 0.0596, \\
&\quad \alpha^2(18) = 0.0630, \\
&\quad \text{U} = 0.368 = 0.36
\end{align*}
\]

\[\cos(0.22, 0.36) = 2.572\]

\[\text{Ch: } \sigma^2(8) = 0.0629, \\
\quad \alpha = \sqrt{\frac{8}{(8-3)}} = 0.30 \text{ (round)} \\
\quad \alpha^2(20) = 0.183 = 0.18 \\
\quad \alpha^2(18) = 0.1630, \\
\quad \text{U} = 0.3017 = 0.30
\]

\[\cos(0.18, 0.30) = 2.6000\]

d) The 95% HW confidence bands for the infection-free functions over the range 8–20 days post-infection are on p. 61 of the output for the P-I group and on p. 62 for the Ch group. The linear formula confidence bands are (HW lin L, HW lin U), the log transformed formula confidence bands are (HW log L, HW log U), and the arcsine formula confidence bands are (HW sin L, HW sin U).

Calculations for confidence coefficients \( \cos(\alpha, \omega) \):

Same as above:

\[\text{P-I: } \cos(0.22, 0.36) = 1.1444\]

\[\text{Ch: } \cos(0.14, 0.30) = 1.0843\]
Based on the results above, chlorhexidine group seems to have a more desirable infection experience. Both groups start off with about the same survival and hazard rate functioning, but the gap widens very quickly and the povidone-iodine group has lower survival probabilities than the chlorhexidine group. The hazard rate of the povidone-iodine group has a much higher upper limit (1.60865 compared to 0.40653). The confidence intervals for the survival functions at 10 days do overlap some for the two groups, so the finding that the chlorhexidine treatment is more effective may be inconclusive.

Problem 7.3 (p. 56 of output)

$H_0: h(t) = h_1(t)$ where $h_1(t)$ is for $z(t) = 0$, $h_2(t)$, $z(t) = 1$ vs. $H_0: h_1(t) \neq h_2(t)$

a) The log-rank chi-square test statistic is 3.7924 (p-value 0.0515). Since $p > 0.05$, we cannot reject the null hypothesis that there is no difference in rate of infection between patients with the povidone-iodine treatment and those with the chlorhexidine treatment.

b) The Gehan (aka Wilcoxon) chi-square test statistic is 2.8639 (p-value 0.0906). Since $p > 0.05$, we cannot reject the null hypothesis.
Problem 7.10 (p. 66 output)

\[ H_0 : h_1(t) = h_2(t) \text{ vs. } H_a : h_1(t) \neq h_2(t) \]

where \( h_1(t) \) represents the hazard rates for patients with treatment without Saquinavir and \( h_2(t) \) represents the hazard rates for patients receiving treatment with Saquinavir.

The log-rank test statistic is 2.0491, p-value 0.1523.

Since \( p > 0.05 \), we cannot reject the null hypothesis that there is no difference in the distribution of the times at which patient's CD4 reaches the prespecified level for the two treatments.

Problem 3.10, using \( \alpha = 0.05 / 3 = 0.0167 \)

\[ H_0 : h_1(t) = h_2(t) \text{ vs. } H_a : h_1(t) < h_2(t) \quad (p. 71 output) \]

The log-rank test statistic is 0.0283, p-value 0.8663.

Since \( p > 0.0167 \), we cannot reject the null hypothesis that Stage 1 and Stage 2 cancer patients have the same hazard rate.

\[ H_0 : h_1(t) = h_2(t) \text{ vs. } H_a : h_1(t) < h_2(t) \quad (p. 75 output) \]

The log-rank test statistic is 1.4683, p-value 0.2256 (0.1128 for a one-sided test).

Since \( p = 0.1128 > 0.0167 \), we cannot reject the null hypothesis that Stage 2 and Stage 3 cancer patients have the same hazard rate.

\[ H_0 : h_1(t) = h_2(t) \text{ vs. } H_a : h_1(t) < h_2(t) \quad (p. 80 output) \]

The log-rank test statistic is 5.1974, p-value 0.0226 (0.0113 for a one-sided test).

Since \( p = 0.0113 < 0.0167 \), we reject the null hypothesis and conclude that Stage 4 cancer patients have greater hazard rates than Stage 3 cancer patients.