

## Chapter 555

# Kaplan-Meier Curves (Logrank Tests)

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## Introduction

This procedure computes the nonparametric Kaplan-Meier and Nelson-Aalen estimates of survival and associated hazard rates. It can fit complete, right censored, left censored, interval censored (readout), and grouped data values. It outputs various statistics and graphs that are useful in reliability and survival analysis.

It also performs several logrank tests and provides both the parametric and randomization test significance levels. This procedure also computes restricted mean survival time (RMST) and restricted mean time lost (RMTL) statistics and associated between-group comparisons.

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## Overview of Survival Analysis

We will give a brief introduction to the subject in this section. For a complete account of survival analysis, we suggest the book by Klein and Moeschberger (2003).

Survival analysis is the study of the distribution of life times. That is, it is the study of the elapsed time between an initiating event (birth, start of treatment, diagnosis, or start of operation) and a terminal event (death, relapse, cure, or machine failure). The data values are a mixture of complete (terminal event occurred) and censored (terminal event has not occurred) observations. From the data values, the survival analyst makes statements about the survival distribution of the failure times. This distribution allows questions about such quantities as survivability, expected life time, and mean time to failure to be answered.

Let  $T$  be the elapsed time until the occurrence of a specified event. The event may be death, occurrence of a disease, disappearance of a disease, appearance of a tumor, etc. The probability distribution of  $T$  may be specified using one of the following basic functions. Once one of these functions has been specified, the others may be derived using the mathematical relationships presented.

1. Probability density function,  $f(t)$ . This is the probability that an event occurs at time  $t$ .
2. Cumulative distribution function,  $F(t)$ . This is the probability that an individual survives until time  $t$ .

$$F(t) = \int_0^t f(x)dx$$

3. Survival function,  $S(T)$ . This is the probability that an individual survives beyond time  $T$ . This is usually the primary quantity of interest. It is estimated using the nonparametric Kaplan-Meier curve.

$$\begin{aligned} S(T) &= \int_T^{\infty} f(x)dx \\ &= 1 - F(T) \end{aligned}$$

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$$S(T) = \exp\left[-\int_0^T h(x)dx\right]$$

$$= \exp[-H(T)]$$

4. Hazard rate,  $h(T)$ . This is the probability that an individual at time  $T$  experiences the event in the next instant. It is a fundamental quantity in survival analysis. It is also known as the conditional failure rate in reliability, the force of mortality in demography, the intensity function in stochastic processes, the age-specific failure rate in epidemiology, and the inverse of Mill's ratio in economics. The empirical hazard rate may be used to identify the appropriate probability distribution of a particular mechanism, since each distribution has a different hazard rate function. Some distributions have a hazard rate that decreases with time, others have a hazard rate that increases with time, some are constant, and some exhibit all three behaviors at different points in time.

$$h(T) = \frac{f(T)}{S(T)}$$

5. Cumulative hazard function,  $H(T)$ . This is integral of  $h(T)$  from 0 to  $T$ .

$$H(T) = \int_0^T h(x)dx$$

$$= -\ln[S(T)]$$

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## Nonparametric Estimators of Hazard and Survival

All of the following results are from Klein and Moeschberger (2003).

The recommended nonparametric estimator of the survival distribution,  $S(T)$ , is the Kaplan-Meier product-limit estimator. The recommended nonparametric estimator of the cumulative hazard function,  $H(T)$ , is the Nelson-Aalen estimator. Although each of these estimators could be used to estimate the other quantity using the relationship

$$H(T) = -\ln[S(T)]$$

or

$$S(T) = \exp[-H(T)]$$

this is not recommended.

The following notation will be used to define both of these estimators. Let  $t = 1, \dots, M$  index the  $M$  unique termination (failure or death) times  $T_1, T_2, \dots, T_M$ . Note that  $M$  does not include duplicate times or times at which only censored observations occur. Associated with each of these failure times is an entry time  $E_i$  at which the subject began to be observed. Usually, these entry times are taken to be zero. If positive entry times are specified, the data are said to have been *left truncated*. When data are left truncated, it is often necessary to define a minimum time,  $A$ , below which failures are not considered. When a positive  $A$  is used, the unconditional survival function  $S(T)$  is changed to a conditional survival function  $S(T|T>A)$ .

The set of all failures (deaths) that occur at time  $T_i$  is referred to as  $D_i$  and the number in this set is given by  $d_i$ . The *risk set* at  $t$ ,  $R_t$ , is the set of all individuals that are at risk immediately before time  $T_i$ . This set includes all individuals whose entry and termination times include  $T_i$ . That is,  $R_t$  is made up of all individuals with times such that  $E_j < T_i \leq T_j$  and  $A \leq T_i$ . The number of individuals in the risk set is given by  $r_i$ .

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**Kaplan-Meier Product-Limit Estimator**

Using the above notation, the Kaplan-Meier product-limit estimator is defined as follows in the range of time values for which there are data.

$$\hat{S}(T) = \begin{cases} 1 & \text{if } T_{\min} > T \\ \prod_{A \leq T_i \leq T} \left[ 1 - \frac{d_i}{r_i} \right] & \text{if } T_{\min} \leq T \end{cases}$$

The variance of  $S(T)$  is estimated by Greenwood's formula

$$\hat{V}[\hat{S}(T)] = \hat{S}(T)^2 \sum_{A \leq T_i \leq T} \frac{d_i}{r_i(r_i - d_i)}$$

**Pointwise Confidence Intervals of Survival**

A pointwise confidence interval for the survival probability at a specific time  $T_0$  of  $S(T_0)$  is represented by two confidence limits which have been constructed so that the probability that the true survival probability lies between them is  $1 - \alpha$ . Note that these limits are constructed for a single time point. Several of them cannot be used together to form a confidence band such that the entire survival function lies within the band. When these are plotted with the survival curve, these limits must be interpreted on an individual, point by point, basis.

Three difference confidence intervals are available. All three confidence intervals perform about the same in large samples. The linear (Greenwood) interval is the most commonly used. However, the log-transformed and the arcsine-square intervals behave better in small to moderate samples, so they are recommended.

**Linear (Greenwood) Pointwise Confidence Interval for S(T)**

This estimator may be used to create a confidence interval at a specific time point  $T_0$  of  $S(T_0)$  using the formula

$$\hat{S}(T_0) \pm z_{1-\alpha/2} \sigma_S(T_0)$$

where

$$\sigma_S^2(T_0) = \frac{\hat{V}[\hat{S}(T_0)]}{\hat{S}^2(T_0)}$$

and  $z$  is the appropriate value from the standard normal distribution.

**Log-Transformed Pointwise Confidence Interval for S(T)**

Better confidence limits may be calculated using the logarithmic transformation of the hazard functions. These limits are

$$\hat{S}(T_0)^{1/\theta}, \hat{S}(T_0)^\theta$$

where

$$\theta = \exp \left\{ \frac{z_{1-\alpha/2} \sigma_S(T_0)}{\log[\hat{S}(T_0)]} \right\}$$

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### ArcSine-Square Root Pointwise Confidence Interval for S(T)

Another set of confidence limits using an improving transformation is given by the formula

$$\sin^2 \left\{ \max \left[ 0, \arcsin \left\{ \hat{S}(T_0) \right\}^{1/2} - 0.5 z_{1-\alpha/2} \sigma_S(T_0) \left( \frac{\hat{S}(T_0)}{1 - \hat{S}(T_0)} \right)^{1/2} \right] \right\} \\ \leq S(T_0) \leq \\ \sin^2 \left\{ \min \left[ \frac{\pi}{2}, \arcsin \left\{ \hat{S}(T_0) \right\}^{1/2} + 0.5 z_{1-\alpha/2} \sigma_S(T_0) \left( \frac{\hat{S}(T_0)}{1 - \hat{S}(T_0)} \right)^{1/2} \right] \right\}$$

### Nelson-Aalen Hazard Estimator

The Nelson-Aalen estimator is recommended as the best estimator of the cumulative hazard function,  $H(T)$ . This estimator is given as

$$\tilde{H}(T) = \begin{cases} 0 & \text{if } T_{\min} > T \\ \sum_{A \leq T_i \leq T} \frac{d_i}{r_i} & \text{if } T_{\min} \leq T \end{cases}$$

Three estimators of the variance of this estimate are mentioned on page 34 of Therneau and Grambsch (2000). These estimators differ in the way they model tied event times. When there are no event time ties, they give almost identical results.

#### 1. Simple (Poisson) Variance Estimate

This estimate assumes that event time ties occur because of rounding and a lack of measurement precision. This estimate is the largest of the three, so it gives the widest, most conservative, confidence limits. The formula for this estimator, derived assuming a Poisson model for the number of deaths, is

$$\sigma_{\tilde{H}_1}^2(T) = \sum_{A \leq T_i \leq T} \frac{d_i}{r_i^2}$$

#### 2. Plug-in Variance Estimate

This estimate also assumes that event time ties occur because of rounding and a lack of measurement precision. The formula for this estimator, derived by substituting sample quantities in the theoretical variance formula, is

$$\sigma_{\tilde{H}_2}^2(T) = \sum_{A \leq T_i \leq T} \frac{d_i(r_i - d_i)}{r_i^3}$$

Note that when  $r_i = 1$ , a '1' is substituted for  $(r_i - d_i) / r_i$  in this formula.

#### 3. Binomial Variance Estimate

This estimate assumes that event time ties occur because the process is fundamentally discrete rather than due to lack of precision and/or rounding. The formula for this estimator, derived assuming a binomial model for the number of events, is

$$\sigma_{\tilde{H}_3}^2(T) = \sum_{A \leq T_i \leq T} \frac{d_i(r_i - d_i)}{r_i^2(r_i - 1)}$$

Note that when  $r_i = 1$ , a '1' is substituted for  $(r_i - d_i) / (r_i - 1)$  in this formula.

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**Which Variance Estimate to Use**

Therneau and Grambsch (2000) indicate that, as of the writing of their book, there is no clear-cut champion. The simple estimate is often suggested because it is always largest and thus gives the widest, most conservative confidence, confidence limits. In practice, there is little difference between them and the choice of which to use will make little difference in the final interpretation of the data. We have included all three since each occurs alone in various treatises on survival analysis.

**Pointwise Confidence Intervals of Cumulative Hazard**

A pointwise confidence interval for the cumulative hazard at a specific time  $T_0$  of  $H(T_0)$  is represented by two confidence limits which have been constructed so that the probability that the true hazard lies between them is  $1 - \alpha$ . Note that these limits are constructed for a single time point. Several of them cannot be used together to form a confidence band such that the entire hazard function lies within the band. When these are plotted with the hazard curve, these limits must be interpreted on an individual, point by point, basis.

Three difference confidence intervals are available. All three confidence intervals perform about the same in large samples. The linear (Greenwood) interval is the most commonly used. However, the log-transformed and the arcsine-square intervals behave better in small to moderate samples, so they are recommended.

**Linear Pointwise Confidence Interval for H(T)**

This estimator may be used to create a confidence interval at a specific time point  $T_0$  of  $H(T_0)$  using the formula

$$\tilde{H}(T_0) \pm z_{1-\alpha/2} \sigma_{\tilde{H}}(T_0)$$

where  $z$  is the appropriate value from the standard normal distribution.

**Log-Transformed Pointwise Confidence Interval for H(T)**

Better confidence limits may be calculated using the logarithmic transformation of the hazard functions. These limits are

$$\tilde{H}(T_0) / \phi, \tilde{H}(T_0)\phi$$

where

$$\phi = \exp\left\{\frac{z_{1-\alpha/2} \sigma_{\tilde{H}}(T_0)}{\tilde{H}(T_0)}\right\}$$

**ArcSine-Square Root Pointwise Confidence Interval for H(T)**

Another set of confidence limits using an improving transformation is given by the formula

$$\begin{aligned} & -2 \ln \left\{ \sin \left[ \min \left( \frac{\pi}{2}, \arcsin \left[ \exp \left\{ -\frac{\tilde{H}(T_0)}{2} \right\} \right] + \frac{z_{1-\alpha/2} \sigma_{\tilde{H}}(T_0)}{2\sqrt{\exp\{\tilde{H}(T_0)\} - 1}} \right) \right] \right\} \\ & \leq H(T_0) \leq \\ & -2 \ln \left\{ \sin \left[ \max \left( 0, \arcsin \left[ \exp \left\{ -\frac{\tilde{H}(T_0)}{2} \right\} \right] - \frac{z_{1-\alpha/2} \sigma_{\tilde{H}}(T_0)}{2\sqrt{\exp\{\tilde{H}(T_0)\} - 1}} \right) \right] \right\} \end{aligned}$$

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## Survival Quantiles

The median survival time is an example of a quantile of the survival distribution. It is the smallest value of  $T$  such that  $\hat{S}(T) = 0.50$ . In fact, more general results are available for any quantile  $p$ . The  $p$ th quantile is estimated by

$$T_p = \inf \left\{ T : \hat{S}(T) \leq 1 - p \right\}$$

In words,  $T_p$  is smallest time at which  $\hat{S}(T)$  is less than or equal to  $1 - p$ .

A  $100(1 - \alpha)\%$  confidence interval for  $T_p$  can be generated using each of the three estimation methods. These are given next.

Linear Pointwise Confidence Interval for  $T_p$ 

This confidence interval is given by the set of all times such that

$$-z_{1-\alpha/2} \leq \frac{\hat{S}(T) - (1-p)}{\sqrt{\hat{V}[\hat{S}(T)]}} \leq z_{1-\alpha/2}$$

where  $z$  is the appropriate value from the standard normal distribution.

Log-Transformed Pointwise Confidence Interval for  $T_p$ 

This confidence interval is given by the set of all times such that

$$-z_{1-\alpha/2} \leq \frac{\left[ \ln \left\{ -\ln[\hat{S}(T)] \right\} - \ln \left\{ -\ln[1-p] \right\} \right] \left[ \hat{S}(T) \ln[\hat{S}(T)] \right]}{\sqrt{\hat{V}[\hat{S}(T)]}} \leq z_{1-\alpha/2}$$

where  $z$  is the appropriate value from the standard normal distribution.

ArcSine-Square Root Pointwise Confidence Interval for  $T_p$ 

This confidence interval is given by the set of all times such that

$$-z_{1-\alpha/2} \leq \frac{2 \left\{ \arcsin \left[ \sqrt{\hat{S}(T)} \right] - \arcsin \left[ \sqrt{1-p} \right] \right\} \sqrt{\hat{S}(T) [1 - \hat{S}(T)]}}{\sqrt{\hat{V}[\hat{S}(T)]}} \leq z_{1-\alpha/2}$$

where  $z$  is the appropriate value from the standard normal distribution.

## Hazard Rate Estimation

The characteristics of the failure process are best understood by studying the hazard rate,  $h(T)$ , which is the derivative (slope) of the cumulative hazard function  $H(T)$ . The hazard rate is estimated using kernel smoothing of the Nelson-Aalen estimator as given in Klein and Moeschberger (2003). The formulas for the estimated hazard rate and its variance are given by

$$\hat{h}(T) = \frac{1}{b} \sum_{A \leq T_i \leq T} K \left( \frac{T - T_i}{b} \right) \Delta \tilde{H}(T_i)$$

$$\sigma^2[\hat{h}(T)] = \frac{1}{b^2} \sum_{A \leq T_i \leq T} K \left( \frac{T - T_i}{b} \right)^2 \Delta \hat{V}[\tilde{H}(T_i)]$$

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where  $b$  is the bandwidth about  $T$  and

$$\Delta\tilde{H}(T_k) = \tilde{H}(T_k) - \tilde{H}(T_{k-1})$$

$$\Delta\hat{V}[\tilde{H}(T_k)] = \hat{V}[\tilde{H}(T_k)] - \hat{V}[\tilde{H}(T_{k-1})]$$

Three choices are available for the kernel function  $K(x)$  in the above formulation. These are defined differently for various values of  $T$ . Note that the  $T_i$ 's are for failed items only and that  $T_{Max}$  is the maximum failure time. For the *uniform kernel* the formulas for the various values of  $T$  are

$$K(x) = \frac{1}{2} \quad \text{for } T - b \leq T \leq T + b$$

$$K_L(x) = \frac{4(1+q^3)}{(1+q)^4} + \frac{6(1-q)}{(1+q)^3}x \quad \text{for } T < b$$

$$K_R(x) = \frac{4(1+r^3)}{(1+r)^4} - \frac{6(1-r)}{(1+r)^3}x \quad \text{for } T_{Max} - b < T < T_{Max}$$

where

$$q = \frac{T}{b}$$

and

$$r = \frac{T_{Max} - T}{b}$$

For the *Epanechnikov kernel* the formulas for the various values of  $T$  are

$$K(x) = \frac{3}{4}(1-x^2) \quad \text{for } T - b \leq T \leq T + b$$

$$K_L(x) = K(x)(A + Bx) \quad \text{for } T < b$$

$$K_R(x) = K(-x)(A - Bx) \quad \text{for } T_{Max} - b < T < T_{Max}$$

where

$$A = \frac{64(2 - 4q + 6q^2 - 3q^3)}{(1+q)^4(19 - 18q + 3q^2)}$$

$$B = \frac{240(1-q)^2}{(1+q)^4(19 - 18q + 3q^2)}$$

$$q = \frac{T}{b}$$

$$r = \frac{T_{Max} - T}{b}$$

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For the *biweight kernel* the formulas for the various values of  $T$  are

$$K(x) = \frac{15}{16}(1-x^2)^2 \quad \text{for } T-b \leq T \leq T+b$$

$$K_L(x) = K(x)(A+Bx) \quad \text{for } T < b$$

$$K_R(x) = K(-x)(A-Bx) \quad \text{for } T_{Max} - b < T < T_{Max}$$

where

$$A = \frac{64(8 - 24q + 48q^2 - 45q^3 + 15q^4)}{(1+q)^5(81 - 168q + 126q^2 - 40q^3 + 5q^4)}$$

$$B = \frac{1120(1-q)^3}{(1+q)^5(81 - 168q + 126q^2 - 40q^3 + 5q^4)}$$

$$q = \frac{T}{b}$$

$$r = \frac{T_{Max} - T}{b}$$

Confidence intervals for  $h(T)$  are given by

$$\hat{h}(T) \exp \left[ \pm \frac{z_{1-\alpha/2} \sigma[\hat{h}(T)]}{\hat{h}(T)} \right]$$

Care must be taken when using this kernel-smoothed estimator since it is actually estimating a smoothed version of the hazard rate, not the hazard rate itself. Thus, it may be biased. Also, it is greatly influenced by the choice of the bandwidth  $b$ . We have found that you must experiment with  $b$  to find an appropriate value for each dataset.

## Hazard Ratio

Often, it will be useful to compare the hazard rates of two groups. This is most often accomplished by creating the *hazard ratio (HR)*. The hazard ratio is discussed in depth in Parmar and Machin (1995) and we refer you to this reference for details which we summarize here. The Cox-Mantel estimate of  $HR$  for two groups A and B is given by

$$\begin{aligned} HR_{CM} &= \frac{H_A}{H_B} \\ &= \frac{O_A / E_A}{O_B / E_B} \end{aligned}$$

where  $O_i$  is the observed number of events (deaths) in group  $i$ ,  $E_i$  is the expected number of events (deaths) in group  $i$ , and  $H_i$  is the overall hazard rate for the  $i$ th group. The calculation of the  $E_i$  is explained in Parmar and Machin (1995).

A confidence interval for  $HR$  is found by first transforming to the log scale which is better approximated by the normal distribution, calculating the limits, and then transforming back to the original scale. The calculation is made using

$$\ln(HR_{CM}) \pm z_{1-\alpha/2} (SE_{\ln HR_{CM}})$$



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where

$$SE_{\ln HR_{CM}} = \sqrt{\frac{1}{E_A} + \frac{1}{E_B}}$$

which results in the limits

$$\exp\left[\ln(HR_{CM}) - z_{1-\alpha/2}(SE_{\ln HR_{CM}})\right]$$

and

$$\exp\left[\ln(HR_{CM}) + z_{1-\alpha/2}(SE_{\ln HR_{CM}})\right]$$

An alternative estimate of  $HR$  that is sometimes used is the Mantel-Haenszel estimator which is calculated using

$$HR_{MH} = \exp\left(\frac{O_A - E_A}{V}\right)$$

where  $V$  is the hypergeometric variance. For further details, see Parmar and Machin (1995). A confidence interval for  $HR$  is found by first transforming to the log scale which is better approximated by the normal distribution, calculating the limits, and then transforming back to the original scale. The calculation is made using

$$\ln(HR_{MH}) \pm z_{1-\alpha/2}(SE_{\ln HR_{MH}})$$

where

$$SE_{\ln HR_{MH}} = \sqrt{\frac{1}{V}}$$

which results in the limits

$$\exp\left[\ln(HR_{MH}) - z_{1-\alpha/2}(SE_{\ln HR_{MH}})\right]$$

and

$$\exp\left[\ln(HR_{MH}) + z_{1-\alpha/2}(SE_{\ln HR_{MH}})\right]$$

### Restricted Mean Survival Time (RMST)

The mean survival time,  $\mu$ , is computed from the survival function,  $S(t)$ , as

$$\mu = \int_0^{\infty} S(t)dt.$$

This corresponds to the area under the survival curve and is only appropriate when the largest observation corresponds to a death. If we restrict the mean estimate to a time interval  $[0, \tau]$ , where  $\tau$  represents either the largest observed time (as in the case of Efron's tail correction) or a preassigned interval maximum time, then the mean survival time can be estimated using the nonparametric Kaplan-Meier curve as

$$\hat{\mu}_{\tau} = \int_0^{\tau} \hat{S}(t)dt.$$

This is called the Restricted Mean Survival Time (RMST) and corresponds to the area under the Kaplan-Meier survival curve up to time  $\tau$ . That is,

$$RMST_{\tau} = \hat{\mu}_{\tau}.$$

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The estimated variance of  $\hat{\mu}_\tau$  is

$$\hat{V}(\hat{\mu}_\tau) = \sum_{i=1}^D \left[ \int_{t_i}^{\tau} \hat{S}(t) dt \right]^2 \frac{d_i}{Y_i(Y_i - d_i)},$$

where  $D$  is the total number of events,  $Y_i$  is the number of subjects at risk at time  $t_i$ , and  $d_i$  is the number of subjects failing at time  $t_i$ . The standard error is

$$\widehat{SE}(\hat{\mu}_\tau) = \sqrt{\hat{V}(\hat{\mu}_\tau)}.$$

A  $100(1 - \alpha)\%$  confidence interval is given by

$$\hat{\mu}_\tau \pm \widehat{SE}(\hat{\mu}_\tau) Z_{1-\alpha/2}.$$

### Restricted Mean Time Lost (RMTL)

As described in Uno et al (2014), the Restricted Mean Time Lost (RMTL) corresponds to the area above the Kaplan-Meier survival curve up to time  $\tau$  and is computed as

$$RMTL_\tau = \tau - \hat{\mu}_\tau.$$

The variance and standard error estimates are the same as for  $\hat{\mu}_\tau$ . A  $100(1 - \alpha)\%$  confidence interval for  $RMTL_\tau$  is given by

$$\tau - \hat{\mu}_\tau \pm \widehat{SE}(\hat{\mu}_\tau) Z_{1-\alpha/2}.$$

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## Hypothesis Tests

This section presents methods for testing that the survival curves, and thus the hazard rates, of two or more populations are equal. The specific hypothesis set that is being tested is

$$H_0: h_1(T) = h_2(T) = \dots = h_K(T), \quad \text{for all } T \leq \tau.$$

$$H_A: h_i(T) \neq h_j(T) \text{ for at least one value of } i, j, \text{ and } T \leq \tau.$$

Here  $\tau$  is taken to be the largest observed time in the study.

In words, the null hypothesis is that the hazard rates of all populations are equal at all times less than the maximum observed time and the alternative hypothesis is that at least two of the hazard rates are different at some time less than the observed maximum time.

In the remainder of this section, we will present a general formulation that includes many of the most popular tests. We use the same notation as before, except that now we add an additional subscript,  $k$ , that represents one of the  $K$  populations. The test is formed by making a comparison of the actual versus the expected hazard rates. The various hazard rates may be weighted differently. These different weights result in different tests with different properties.

The test is based on the  $K-1$  statistics

$$Z_k(\tau) = \sum_{A \leq T_i \leq \tau} W(T_i) r_{ik} \left( \frac{d_{ik}}{r_{ik}} - \frac{d_i}{r_i} \right), \quad k = 1, 2, \dots, K-1$$

where

$$d_i = \sum_{k=1}^K d_{ik}$$

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$$r_i = \sum_{k=1}^K r_{ik}$$

The  $Z$ 's have a covariance matrix  $\Sigma$  with elements

$$\sigma_{kg} = \sum_{A \leq T_i \leq T} W(T_i)^2 \left( \frac{r_{ik}}{r_i} \right) \left( \delta_{kg} - \frac{r_{ig}}{r_i} \right) \left( \frac{r_i - d_i}{r_i - 1} \right) d_i$$

where

$$\delta_{kg} = \begin{cases} 1 & \text{if } k = g \\ 0 & \text{if } k \neq g \end{cases}$$

If we let  $Z$  represent the vector of  $K-1$  statistics and  $\Sigma$  represent the covariance matrix, the test statistic is given by

$$Q = Z' \Sigma^{-1} Z$$

In large samples,  $Q$  is approximately distributed as a chi-squared random variable with  $K-1$  degrees of freedom. Details of the above formulas can be found in Klein and Moeschberger (2003), pages 205-216 and Andersen, Borgan, Gill, and Keiding (1992), pages 345-356.

Ten different choices for the weight function,  $W(T)$ , result in the ten different tests that are available in NCSS. The most commonly used test is the logrank test which has equal weighting. The other nine tests shift the heaviest weighting to the beginning or end of the trial. This may be appropriate in some studies, but the use of one of these other weighting schemes should be designated before the data have been seen. Also, even though ten tests are displayed, you should only use one of them. Because of the different weighting patterns, they will often give quite different results. It is bad science to look at all the tests and pick the one that matches your own conclusions. That is why you must designate the test you will use before you have seen the data.

The following table describes each of these tests.

<u>Test</u>	<u>Weight</u>	<u>Comments</u>
Logrank	1	This is the most commonly used test and the one we recommend. Equal weights across all times. This test has optimum power when the hazard rates of the $K$ populations are proportional to each other.
Gehan	$r_i$	Places very heavy weight on hazards at the beginning of the study.
Tarone-Ware	$\sqrt{r_i}$	Places heavy weight on hazards at the beginning of the study.
Peto-Peto	$\tilde{S}(T_i)$	Places a little more weight on hazards at the beginning of the study.
Modified Peto-Peto	$\tilde{S}(T_i) r_i / (r_i + 1)$	Places a little more weight on hazards at the beginning of the study.
Fleming-Harrington (0,0)	$1 - \hat{S}(T_{i-1})$	Places heavy weight on hazards at the end of the study.
Fleming-Harrington (1,0)	$\hat{S}(T_{i-1})$	Places almost equal weight at all times.
Fleming-Harrington (1,1)	$\hat{S}(T_{i-1}) (1 - \hat{S}(T_{i-1}))$	Places heavy weight on hazards at the end of the study.

## Kaplan-Meier Curves (Logrank Tests)

<u>Test</u>	<u>Weight</u>	<u>Comments</u>
Fleming-Harrington (0.5,0.5)	$\sqrt{\hat{S}(T_{i-1})(1-\hat{S}(T_{i-1}))}$	Places a little more weight on hazards at the end of the study.
Fleming-Harrington (0.5,2)	$(1-\hat{S}(T_{i-1}))^2\sqrt{\hat{S}(T_{i-1})}$	Places very heavy weight on hazards at the end of the study.

This table uses the following definitions.

$$\hat{S}(T) = \prod_{T_i \leq T} \left(1 - \frac{d_i}{r_i}\right)$$

$$\tilde{S}(T) = \prod_{T_i \leq T} \left(1 - \frac{d_i}{r_i + 1}\right)$$

## Logrank Tests

The logrank test is perhaps the most popular test for testing equality of hazard functions. This test uses  $W(T) = 1$ , that is, equal weighting. This test has optimum power when the hazard rates of the  $K$  populations are proportional to each other.

Note that this version of the logrank test is different from the version used in NCSS's Logrank procedure. That procedure uses the permutation covariance matrix of Lee and Desu which is only valid for equal censoring. The covariance matrix used here is valid for any random censoring pattern, so it is much less restrictive.

### Cox-Mantel and Mantel-Haenszel Logrank Tests

When there are only two groups, two versions of the logrank test are commonly used. These tests test the hypothesis that the hazard ratio ( $HR$ ) is one; that is, that the two hazard rates being compared are zero. Note that these tests are equivalent except in small samples.

#### Cox-Mantel Logrank Test

Using the notation given above in the section on the hazard ratios, the *Cox-Mantel logrank test* statistic is computed using

$$\chi_{CM}^2 = \frac{(O_A - E_A)^2}{E_A} + \frac{(O_B - E_B)^2}{E_B}$$

This test statistic is approximately distributed as a chi-square random variable with one degree of freedom.

#### Mantel-Haenszel Logrank Test

The *Mantel-Haenszel logrank test* statistic is computed using

$$\chi_{CM}^2 = \frac{(O_A - E_A)^2}{V}$$

This test statistic is also approximately distributed as a chi-square random variable with one degree of freedom.

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### Randomization Probability Levels

Because of assumptions that must be made when using this procedure, NCSS also includes a randomization test as outlined by Edgington (1987). Randomization tests are becoming more and more popular as the speed of computers allows them to be computed in seconds rather than hours.

A randomization test is conducted by forming a Monte Carlo sampling of all possible permutations of the sample data, calculating the test statistic for each sampled permutation, and counting the number of permutations that result in a chi-square value greater than or equal to the actual chi-square value. Dividing this count by the number of permutations sampled gives the significance level of the test. Edgington suggests that at least 1,000 permutations be selected.

### Between-Group Mean Survival Comparisons

Restricted Mean Survival Time (RMST) and Restricted Mean Survival Time (RMSTL) comparisons between groups  $i$  and  $j$  that follow are described in Royston and Parmar (2013) and Uno et al. (2014) and summarized below.

#### Restricted Mean Survival Time (RMST) Difference

The RMST difference between groups  $i$  and  $j$  is calculated as

$$\widehat{D}_{RMST,ij} = \hat{\mu}_{\tau,i} - \hat{\mu}_{\tau,j},$$

and has estimated standard deviation

$$\widehat{SE}(\hat{\mu}_{\tau,i} - \hat{\mu}_{\tau,j}) = \sqrt{\widehat{V}(\hat{\mu}_{\tau,i}) + \widehat{V}(\hat{\mu}_{\tau,j})}.$$

A  $100(1 - \alpha)\%$  confidence interval for the difference is given by

$$\widehat{D}_{RMST,ij} \pm \widehat{SE}(\hat{\mu}_{\tau,i} - \hat{\mu}_{\tau,j})Z_{1-\alpha/2}.$$

A level  $\alpha$  test of the null hypothesis

$$H_0: \mu_{\tau,i} - \mu_{\tau,j} = 0$$

versus the alternative

$$H_A: \mu_{\tau,i} - \mu_{\tau,j} \neq 0$$

can be conducted using the test statistic

$$Z_{ij} = \frac{\hat{\mu}_{\tau,i} - \hat{\mu}_{\tau,j}}{\widehat{SE}(\hat{\mu}_{\tau,i} - \hat{\mu}_{\tau,j})},$$

which follows a standard normal distribution.

#### Restricted Mean Survival Time (RMST) Ratio

The RMST ratio of groups  $i$  and  $j$  is calculated as

$$\widehat{R}_{RMST,ij} = \frac{\hat{\mu}_{\tau,i}}{\hat{\mu}_{\tau,j}}.$$

The standard error of the ratio is estimated by first taking the log of  $\widehat{R}_{RMST,ij}$  and computing the standard error of the difference of logged means as

$$\widehat{SE}(\log(\hat{\mu}_{\tau,i}) - \log(\hat{\mu}_{\tau,j})) = \sqrt{\frac{\widehat{V}(\hat{\mu}_{\tau,i})}{\hat{\mu}_{\tau,i}^2} + \frac{\widehat{V}(\hat{\mu}_{\tau,j})}{\hat{\mu}_{\tau,j}^2}}.$$

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A  $100(1 - \alpha)\%$  confidence interval for the ratio is given by

$$\hat{R}_{RMST,ij} \pm e^{\widehat{SE}(\log(\hat{\mu}_{\tau,i}) - \log(\hat{\mu}_{\tau,j}))} Z_{1-\alpha/2}.$$

A level  $\alpha$  test of the null hypothesis

$$H_0: \frac{\mu_{\tau,i}}{\mu_{\tau,j}} = 1$$

versus the alternative

$$H_A: \frac{\mu_{\tau,i}}{\mu_{\tau,j}} \neq 1$$

can be conducted using the test statistic

$$Z_{ij} = \frac{\log(\hat{\mu}_{\tau,i}) - \log(\hat{\mu}_{\tau,j})}{\widehat{SE}(\log(\hat{\mu}_{\tau,i}) - \log(\hat{\mu}_{\tau,j}))},$$

which follows a standard normal distribution.

**Restricted Mean Time Lost (RMTL) Ratio**

The RMTL ratio of groups  $i$  and  $j$  is calculated as

$$\hat{R}_{RMTL,ij} = \frac{\tau - \hat{\mu}_{\tau,i}}{\tau - \hat{\mu}_{\tau,j}}.$$

The standard error of the ratio is estimated by first taking the log of  $\hat{R}_{RMTL,ij}$  and computing the standard error of the difference of logged means as

$$\begin{aligned} \widehat{SE}(\log(\tau - \hat{\mu}_{\tau,i}) - \log(\tau - \hat{\mu}_{\tau,j})) &= \widehat{SE}(\log(\hat{\mu}_{\tau,i}) - \log(\hat{\mu}_{\tau,j})) \\ &= \sqrt{\frac{\hat{V}(\hat{\mu}_{\tau,i})}{\hat{\mu}_{\tau,i}^2} + \frac{\hat{V}(\hat{\mu}_{\tau,j})}{\hat{\mu}_{\tau,j}^2}}. \end{aligned}$$

A  $100(1 - \alpha)\%$  confidence interval for the ratio is given by

$$\hat{R}_{RMTL,ij} \pm e^{\widehat{SE}(\log(\hat{\mu}_{\tau,i}) - \log(\hat{\mu}_{\tau,j}))} Z_{1-\alpha/2}.$$

A level  $\alpha$  test of the null hypothesis

$$H_0: \frac{\tau - \mu_{\tau,i}}{\tau - \mu_{\tau,j}} = 1$$

versus the alternative

$$H_A: \frac{\tau - \mu_{\tau,i}}{\tau - \mu_{\tau,j}} \neq 1$$

can be conducted using the test statistic

$$Z_{ij} = \frac{\log(\tau - \hat{\mu}_{\tau,i}) - \log(\tau - \hat{\mu}_{\tau,j})}{\widehat{SE}(\log(\hat{\mu}_{\tau,i}) - \log(\hat{\mu}_{\tau,j}))},$$

which follows a standard normal distribution.

## Data Structure

Survival data sets require up to three components for the survival time: the ending survival time, an optional beginning survival time during which the subject was not observed, and an indicator of whether an observation was censored or failed.

Based on these three components, various types of data may be analyzed. Right censored data are specified using only the ending time variable and the censor variable. Left truncated and Interval data are entered using all three variables.

### Sample Dataset

Most survival data sets require at least two variables: the failure time variable and a censor variable that indicates whether time is a failure or was censored. Optional variables include a count variable which gives the number of items occurring at that time and a group variable that identifies which group this observation belongs to. If the censor variable is omitted, all time values represent failed items. If the count variable is omitted, all counts are assumed to be one.

The table below shows a dataset reporting on a two-group time-to-tumor study. In this data set, time-to-tumor (in days) is given for twelve mice. The twelve mice were randomly divided into two groups. The first group served as a control group, while the second group received a dose of a certain chemical. These data are contained in the Survival dataset.

#### Survival dataset (subset)

Tumor6	Censor6	Trtmnt6
8	1	1
8	1	1
10	1	1
12	1	1
12	1	1
13	1	1
9	1	2
12	1	2

## Procedure Options

This section describes the options available in this procedure.

### Variables Tab

This panel specifies the variables used in the analysis.

#### Time Variables

##### (Elapsed) Time Variable

This variable contains the length of time that an individual was observed. This may represent a failure time or a censor time. Whether the subject actually died is specified by the Censor Variable. Since the values are elapsed times, they must be positive. Zeroes and negative values are treated as missing values.

During the maximum likelihood calculations, a risk set is defined for each individual. The risk set is defined to be those subjects who were being observed at this subject's failure and who lived as long or longer. It may take several rows of data to specify a subject's history.

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This variable and the Entry Time Variable define a period during which the individual was at risk of failing. If the Entry Time Variable is not specified, its value is assumed to be zero.

Several types of data may be entered. These will be explained next.

- **Failure**

This type of data occurs when a subject is followed from their entrance into the study until their death. The failure time is entered in this variable and the Censor Variable is set to the failed code, which is often a one.

The Entry Time Variable is not necessary. If an Entry Time Variable is used, its value should be zero for this type of observation.

- **Interval Failure**

This type of data occurs when a subject is known to have died during a certain interval. The subject may, or may not, have been observed during other intervals. If they were, they are treated as Interval Censored data. An individual may require several rows on the database to record their complete follow-up history.

For example, suppose the condition of the subjects is only available at the end of each month. If a subject fails during the fifth month, two rows of data would be required. One row, representing the failure, would have a Time of 5.0 and an Entry Time of 4.0. The Censor variable would contain the failure code. A second row, representing the prior periods, would have a Time of 4.0 and an Entry Time of 0.0. The Censor variable would contain the censor code.

- **Right Censored**

This type of data occurs when a subject has not failed up to the specified time. For example, suppose that a subject enters the study and does not die until after the study ends 12 months later. The subject's time (365 days) is entered here. The Censor variable contains the censor code.

- **Interval Censored**

This type of data occurs when a subject is known not to have died during a certain interval. The subject may, or may not, have been observed during other intervals. An individual may require several rows on the database to record their complete follow-up history.

For example, suppose the condition of the subjects is only available at the end of each month. If a subject fails during the fifth month, two rows of data would be required. One row, representing the failure, would have a Time of 5.0 and an Entry Time of 4.0. The Censor variable would contain the failure code. A second row, representing the prior periods, would have a Time of 4.0 and an Entry Time of 0.0. The Censor variable would contain the censor code.

### Entry Time Variable

This optional variable contains the elapsed time before an individual entered the study. Usually, this value is zero. However, in cases such as *left truncation* and *interval censoring*, this value defines a time period before which the individual was not observed.

Negative entry times are treated as missing values. It is possible for the entry time to be zero.

### Min Entry Time

When you have left truncation, this value gives the minimum entry time after which events are considered. When used, all survival and hazard rates are conditional on the subject reaching this age. When there is no left truncation (Entry Time Variable), this value is set to zero.

This value is necessary because with left truncation, it is possible for the Kaplan-Meier estimate to reach (and then stay at) zero too soon. Conditioning the probability statements so that this age must be reached in order for an individual to be in a risk set removes this zeroing out problem.



## Kaplan-Meier Curves (Logrank Tests)

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### Frequency Variable

#### Frequency Variable

This variable gives the count, or frequency, of the time displayed on that row. When omitted, each row receives a frequency of one. Frequency values should be positive integers. This is usually used to indicate the number of right censored values at the end of a study or the number of failures occurring within an interval. It may also be used to indicate ties for failure data.

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### Censor Variable

#### Censor Variable

The values in this variable indicate whether the value of the Time Variable represents a censored time or a failure time. These values may be text or numeric. The interpretation of these codes is specified by the Failed and Censored options to the right of this option.

Only two values are used, the Failure code and the Censor code. The Unknown Type option specifies what is to be done with values that do not match either the Failure code or the Censor code.

Rows with missing values (blanks) in this variable are omitted.

#### Failed

This value identifies those values of the Censor Variable that indicate that the Time Variable gives a failure time. The value may be a number or a letter.

We suggest the letter 'F' or the number '1' when you are in doubt as to what to use.

A failed observation is one in which the time until the event of interest was measured exactly; for example, the subject died of the disease being studied. The exact failure time is known.

#### (Left Censoring)

When the exact failure time is not known, but instead only an upper bound on the failure time is known, the time value is said to have been *left censored*. In this case, the time value is treated as if it were the true failure time, not just an upper bound. So left censored observations should be coded as failed observations.

#### Censored

This value identifies those values of the Censor Variable that indicate that the individual recorded on this row was censored. That is, the actual failure time occurs sometime after the value of the Time Variable.

We suggest the letter 'C' or the number '0' when you are in doubt as to what to use.

A censored observation is one in which the time until the event of interest is not known because the individual withdrew from the study, the study ended before the individual failed, or for some similar reason.

Note that it does not matter whether the censoring was Right or Interval. All you need to indicate here is that they were censored.

#### Unknown Censor

This option specifies what the program is to assume about rows whose censor value is not equal to either the Failed code or the Censored code. Note that observations with missing censor values are always treated as missing.

- **Censored**  
Observations with unknown censor values are assumed to have been censored.
- **Failed**  
Observations with unknown censor values are assumed to have failed.

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- **Missing**

Observations with unknown censor values are assumed to be missing and they are removed from the analysis.

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### Group Variable

#### Group Variable

An optional categorical (grouping) variable may be specified. If it is used, a separate analysis is conducted for each unique value of this variable and the log rank tests are performed. If it is not specified, the log rank tests cannot be generated.

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### Calculation Options – Kaplan-Meier Survival and Cumulative Hazard

#### Confidence Limits

This option specifies the method used to estimate the confidence limits of the Kaplan-Meier Survival and the Cumulative Hazard. The options are:

- **Linear**

This is the classical method which uses Greenwood's estimate of the variance.

- **Log Transform**

This method uses the logarithmic transformation of Greenwood's variance estimate. It produces better limits than the Linear method and has better small sample properties.

- **ArcSine**

This method uses the arcsine square-root transformation of Greenwood's variance estimate to produce better limits.

#### Variance

The option specifies which estimator of the variance of the Nelson-Aalen cumulative hazard estimate is to be used. Three estimators have been proposed. When there are no event-time ties, all three give about the same results.

We recommend that you use the Simple estimator unless ties occur naturally in the theoretical event times.

- **Simple**

This estimator should be used when event-time ties are caused by rounding and lack of measurement precision. This estimate gives the largest value and hence the widest, most conservative, confidence intervals.

- **Plug-in**

This estimator should be used when event-time ties are caused by rounding and lack of measurement precision.

- **Binomial**

This estimator should be used when ties occur in the theoretical distribution of event times.

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**Calculation Options – Restricted Mean Survival Time (RMST)****Interval Upper Limit ( $\tau$ )**

Specify what upper limit ( $\tau$ ) to use for Restricted Mean Survival Time (RMST) and Restricted Mean Time Lost (RMTL) calculations.

The choices are

- **Smallest Maximum Observed Time Among All Groups**

This option uses the smallest maximum observed time among all groups as the upper limit. For example, if there are 3 groups with maximum observed times (censored or uncensored) of 100, 110, and 120 days, the value for  $\tau$  would be set to 100 days.

- **Maximum Observed Time Among All Groups**

This option uses the maximum observed time among all groups as the upper limit. For example, if there are 3 groups with maximum observed times (censored or uncensored) of 100, 110, and 120 days, the value for  $\tau$  would be set to 120 days.

This option is not recommended since it may result in calculations based on upper limits that may be larger than the last observed time for some groups.

- **Maximum Observed Time Within Each Group (Variable)**

This option uses the maximum observed time as the upper limit within each group. This results in different upper limits for each group. For example, if there are 3 groups with maximum observed times (censored or uncensored) of 100, 110, and 120 days, the values for  $\tau$  would be set to 100, 110, and 120 days, respectively.

When two-group comparisons are calculated using this option, the smallest maximum observed time between the two groups is used in the calculation of the comparison.

- **Custom (User-Entered)**

Enter a custom value for  $\tau$ .

**Custom  $\tau$** 

Enter a custom value for  $\tau$ . Generally, you should enter a value for  $\tau$  that is less than or equal to the smallest maximum observed time among all groups.

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**Calculation Options – Hazard Rate**

The following options control the calculation of the hazard rate and cumulative hazard function.

**Bandwidth Method**

This option designates the method used to specify the smoothing bandwidth used to calculate the hazard rate. Specify an amount or a percentage of the time range. The default is to specify a percent of the time range.

**Bandwidth Amount**

This option specifies the bandwidth size used to calculate the hazard rate. If the Bandwidth Method was set to Amount, this is a value in time units (such as 10 hours). If Percentage of Time Range was selected, this is a percentage of the overall range of the data.

**Smoothing Kernel**

This option specifies the kernel function used in the smoothing to estimate the hazard rate. You can select uniform, Epanechnikov, or biweight smoothing. The actual formulas for these functions were provided above.

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## Reports Tab

The following options control which reports are displayed.

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### Select Reports

#### Data Summary – Hazard Rates

These options indicate whether to display the corresponding report.

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### Resampling

#### Run Logrank Randomization tests

Check this option to run randomization tests. Note that these tests are computer-intensive and may require a great deal of time to run.

#### Monte Carlo Samples

Specify the number of Monte Carlo samples used when conducting randomization tests. You also need to check the 'Run randomization tests' box to run these tests.

Somewhere between 1,000 and 100,000 Monte Carlo samples are usually necessary. We suggest the use of 10,000.

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### Alpha

#### Alpha Level

This is the value of alpha used in the calculation of confidence limits. For example, if you specify 0.04 here, then 96% confidence limits will be calculated.

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### Product-Limit Survival and Hazard Rate Calculation Values

#### Percentiles

This option specifies a list of percentiles (range 1 to 99) at which the reliability (survivorship) is reported. The values should be separated by commas.

You can specify sequences with a colon, putting the increment inside parentheses after the maximum in the sequence. For example: 5:25(5) means 5,10,15,20,25 and 1:5(2),10:20(2) means 1,3,5,10,12,14,16,18,20.

#### Times

This option specifies a list of times at which the percent surviving and cumulative hazard values are reported. Individual values are separated by commas. You can specify a sequence by specifying the minimum and maximum separate by a colon and putting the increment inside parentheses. For example: 5:25(5) means 5,10,15,20,25. Avoid 0 and negative numbers. Use '(10)' alone to specify ten values between zero and the maximum value found in the data.

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## Report Options Tab

The following options control the formatting of reports.

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### Report Options

#### Precision

Specify the precision of numbers in the report. A single-precision number will show seven-place accuracy, while a double-precision number will show thirteen-place accuracy. Note that the reports are formatted for single precision. If you select double precision, some numbers may run into others. Also note that all calculations are performed in double precision regardless of which option you select here. Single precision is for reporting purposes only.

#### Variable Names

This option lets you select whether to display only variable names, variable labels, or both.

#### Value Labels

This option lets you select whether to display only values, only value labels, or both for values of the group variable. Use this option if you want to automatically attach labels to the values of the group variable (like 1=Male, 2=Female, etc.). See the section on specifying *Value Labels* elsewhere in this manual.

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### Report Options – Decimal Places

#### Times

This option specifies the number of decimal places shown on reported time values.

#### Probabilities

This option specifies the number of decimal places shown on reported probability and hazard values.

#### Test Statistics

This option specifies the number of decimal places shown on reported test statistic values.

#### Ratios

This option specifies the number of decimal places shown on reported ratio values.

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## Plots Tab

The following options control the plots that are displayed.

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### Select Plots

These options specify which plots type of plots are displayed.

#### Kaplan-Meier Survival/Reliability Plot – Hazard Rate Plot

Specify whether to display each of these plots. Click the plot format button to change the plot settings.

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### Select Plots – Plots Displayed

#### Individual-Group Plots

When checked, this option specifies that a separate chart of each designated type is displayed.

## Kaplan-Meier Curves (Logrank Tests)

### Combined Plots

When checked, this option specifies that a chart combining all groups is to be displayed.

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### Plot Options – Plot Arrangement

These options control the size and arrangement of the plots.

#### Two Plots Per Line

When a man charts are specified, checking this option will cause the size of the charts to be reduced so that they can be displayed two per line. This will reduce the overall size of the output.

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## Storage Tab

These options let you specify if, and where on the dataset, various statistics are stored.

*Warning: Any data already in these columns are replaced by the new data. Be careful not to specify columns that contain important data.*

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### Data Storage Options

#### Storage Option

This option controls whether the values indicated below are stored on the dataset when the procedure is run.

- **Do not store data**  
No data are stored even if they are checked.
- **Store in empty columns only**  
The values are stored in empty columns only. Columns containing data are not used for data storage, so no data can be lost.
- **Store in designated columns**  
Beginning at the *First Storage Variable*, the values are stored in this column and those to the right. If a column contains data, the data are replaced by the storage values. Care must be used with this option because it cannot be undone.

#### Store First Item In

The first item is stored in this column. Each additional item that is checked is stored in the columns immediately to the right of this column.

Leave this value blank if you want the data storage to begin in the first blank column on the right-hand side of the data.

*Warning: any existing data in these columns is automatically replaced.*

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### Data Storage Options – Select Items to Store with the Dataset

#### Survival Group - Hazard Rate UCL

Indicate whether to store these values, beginning at the column indicated by the *Store First Item In* option.

## Example 1 – Kaplan-Meier Survival Analysis

This section presents an example of how to analyze a typical set of survival data. In this study, thirty subjects were watched to see how long until a certain event happened after the subject received a certain treatment. The study was terminated at 152.7 hours. At this time, the event had not occurred in eighteen of the subjects. The data used are recorded in the Weibull dataset.

You may follow along here by making the appropriate entries or load the completed template **Example 1** by clicking on Open Example Template from the File menu of the Kaplan-Meier Curves (Logrank Tests) window.

### 1 Open the Weibull dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **Weibull.NCSS**.
- Click **Open**.

### 2 Open the Kaplan-Meier Curves (Logrank Tests) window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Kaplan-Meier Curves (Logrank Tests)** procedure.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

### 3 Specify the variables.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Variables tab**.
- Set the **Time Variable** to **Time**.
- Set the **Censor Variable** to **Censor**.
- Set the **Frequency Variable** to **Count**.

### 4 Specify the reports.

- Select the **Reports tab**.
- Set the **Times** box to **10:150(10)**.

### 5 Specify the plots.

- Select the **Plots tab**.
- Check **Hazard Function Plot**.
- Check **Hazard Rate Plot**.
- Check **C.L. Lines** by clicking the format button and checking the **Confidence Limits** box.

### 6 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

## Data Summary

Type	Rows	Count	Percent (%)	Minimum	Maximum
Failed	12	12	40.00%	12.5	152.7
Censored	1	18	60.00%	152.7	152.7
Total	13	30	100.00%*	12.5	152.7

This report displays a summary of the amount of data that were analyzed. Scan this report to determine if there were any obvious data errors by double checking the counts and the minimum and maximum times.

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## Median and Mean Survival Estimates

Type	Failed	Total	Estimate	Standard Error	Lower 95% C.L.	Upper 95% C.L.
Median Survival Time	12	30			123.2	152.7
Restricted Mean Survival Time*	12	30	126.2	7.508	111.5	140.9
Restricted Mean Time Lost*	12	30	26.5	7.508	11.8	41.2

\* Estimates are based on an interval upper limit of  $\tau = 152.7$ , the maximum observed time.

This report displays point estimates for the median and restricted means, along with lower and upper confidence limits.

### Type

This is the statistic being reported on this line.

### Failed

This is the number of failed observations.

### Total

This is the total sample size.

### Estimate

This is the estimate of the corresponding statistic.

### Standard Error

This is the standard error of the estimate.

### Lower and Upper Confidence Limits

These are the lower and upper confidence limits for the estimate.

## Kaplan-Meier Product-Limit Survival Analysis

Event Time T	Cumulative Survival S(T)	Standard Error of S(T)	Lower 95% C.L. for S(T)	Upper 95% C.L. for S(T)	At Risk	Count	Total Events
12.5	0.9667	0.0328	0.9024	1.0000	30	1	1
24.4	0.9333	0.0455	0.8441	1.0000	29	1	2
58.2	0.9000	0.0548	0.7926	1.0000	28	1	3
68.0	0.8667	0.0621	0.7450	0.9883	27	1	4
69.1	0.8333	0.0680	0.7000	0.9667	26	1	5
95.5	0.8000	0.0730	0.6569	0.9431	25	1	6
96.6	0.7667	0.0772	0.6153	0.9180	24	1	7
97.0	0.7333	0.0807	0.5751	0.8916	23	1	8
114.2	0.7000	0.0837	0.5360	0.8640	22	1	9
123.2	0.6667	0.0861	0.4980	0.8354	21	1	10
125.6	0.6333	0.0880	0.4609	0.8058	20	1	11
152.7	0.6000	0.0894	0.4247	0.7753	19	1	12
152.7+					18	18	12

This report displays the Kaplan-Meier product-limit survival distribution along with confidence limits. The formulas used were presented earlier.

Also note that the sample size is given for each time period. As time progresses, participants are removed from the study, reducing the sample size. Hence, the survival results near the end of the study are based on only a few participants and are therefore less precise. This shows up as a widening of the confidence limits.



## Kaplan-Meier Curves (Logrank Tests)

### Event Time (T)

This is the time point being reported on this line. The time values are specific event times that occurred in the data.

Note that censored observations are marked with a plus sign on their time value. The survival functions are not calculated for censored observations.

### Cumulative Survival S(T)

This is the probability that a subject does not have the event until after the event time given on this line. This probability is estimated using the Kaplan-Meier product limit method. The estimate is given by the formula

$$\hat{S}(T) = \begin{cases} 1 & \text{if } T_{\min} > T \\ \prod_{A \leq T_i \leq T} \left[ 1 - \frac{d_i}{r_i} \right] & \text{if } T_{\min} \leq T \end{cases}$$

### Standard Error of S(T)

This is the estimated standard error of the Kaplan-Meier survival probability. The variance of  $S(T)$  is estimated by Greenwood's formula

$$\hat{V}[\hat{S}(T)] = \hat{S}(T)^2 \sum_{A \leq T_i \leq T} \frac{d_i}{r_i(r_i - d_i)}$$

The standard error is the square root of this variance.

### Lower and Upper Confidence Limits for S(T)

The lower and upper confidence limits provide a pointwise confidence interval for the survival probability at each time point. These limits are constructed so that the probability that the true survival probability lies between them is  $1 - \alpha$ . Note that these limits are constructed for a single time point. Several of them cannot be used together to form a confidence band such that the entire survival function lies within the band.

Three difference confidence intervals are available. All three confidence intervals perform about the same in large samples. The linear (Greenwood) interval is the most commonly used. However, the log-transformed and the arcsine-square intervals behave better in small to moderate samples, so they are recommended. The formulas for these limits were given at the beginning of the chapter and are not repeated here.

### At Risk

This value is the number of individuals at risk. The number at risk is all those under study who died or were censored at a time later than the current time. As the number of individuals at risk is decreased, the estimates become less reliable.

### Count

This is the number of individuals having the event (failing) at this time point.

### Total Events

This is the cumulative number of individuals having the event (failing) up to and including this time value.

## Kaplan-Meier Curves (Logrank Tests)

## Kaplan-Meier Product-Limit Survival Analysis at Specific Times

Time T	Cumulative Survival S(T)	Standard Error of S(T)	Lower 95% C.L. for S(T)	Upper 95% C.L. for S(T)	At Risk
10.0	1.0000	0.0000	1.0000	1.0000	30
20.0	0.9667	0.0328	0.9024	1.0000	29
30.0	0.9333	0.0455	0.8441	1.0000	28
40.0	0.9333	0.0455	0.8441	1.0000	28
50.0	0.9333	0.0455	0.8441	1.0000	28
60.0	0.9000	0.0548	0.7926	1.0000	27
70.0	0.8333	0.0680	0.7000	0.9667	25
80.0	0.8333	0.0680	0.7000	0.9667	25
90.0	0.8333	0.0680	0.7000	0.9667	25
100.0	0.7333	0.0807	0.5751	0.8916	22
110.0	0.7333	0.0807	0.5751	0.8916	22
120.0	0.7000	0.0837	0.5360	0.8640	21
130.0	0.6333	0.0880	0.4609	0.8058	19
140.0	0.6333	0.0880	0.4609	0.8058	19
150.0	0.6333	0.0880	0.4609	0.8058	19

This report displays the Kaplan-Meier product-limit survival probabilities at the specified time points. The formulas used were presented earlier.

**Event Time (T)**

This is the time point being reported on this line. The time values were specified in the Times box under the Report tab.

**Cumulative Survival S(T)**

This is the probability that a subject does not have the event until after the event time given on this line. This probability is estimated using the Kaplan-Meier product limit method. The estimate is given by the formula

$$\hat{S}(T) = \begin{cases} 1 & \text{if } T_{\min} > T \\ \prod_{A \leq T_i \leq T} \left[ 1 - \frac{d_i}{r_i} \right] & \text{if } T_{\min} \leq T \end{cases}$$

**Standard Error of S(T)**

This is the estimated standard error of the Kaplan-Meier survival probability. The variance of  $S(T)$  is estimated by Greenwood's formula

$$\hat{V}[\hat{S}(T)] = \hat{S}(T)^2 \sum_{A \leq T_i \leq T} \frac{d_i}{r_i(r_i - d_i)}$$

The standard error is the square root of this variance.

**Lower and Upper Confidence Limits for S(T)**

The lower and upper confidence limits provide a pointwise confidence interval for the survival probability at each time point. These limits are constructed so that the probability that the true survival probability lies between them is  $1 - \alpha$ . Note that these limits are constructed for a single time point. Several of them cannot be used together to form a confidence band such that the entire survival function lies within the band.

Three difference confidence intervals are available. All three confidence intervals perform about the same in large samples. The linear (Greenwood) interval is the most commonly used. However, the log-transformed and the arcsine-square intervals behave better in small to moderate samples, so they are recommended. The formulas for these limits were given at the beginning of the chapter and are not repeated here.

## Kaplan-Meier Curves (Logrank Tests)

**At Risk**

This value is the number of individuals at risk. The number at risk is all those under study who died or were censored at a time later than the current time. As the number of individuals at risk is decreased, the estimates become less reliable.

**Kaplan-Meier Quantiles of Survival Time**

Proportion Surviving	Proportion Failing	Survival Time	Lower 95% C.L. Survival Time	Upper 95% C.L. Survival Time
0.9500	0.0500	24.4	12.5	69.1
0.9000	0.1000	58.2	24.4	96.6
0.8500	0.1500	69.1	24.4	114.2
0.8000	0.2000	95.5	58.2	125.6
0.7500	0.2500	97.0	68.0	152.7
0.7000	0.3000	114.2	69.1	152.7
0.6500	0.3500	125.6	96.6	152.7
0.6000	0.4000	152.7	97.0	152.7
0.5500	0.4500		114.2	152.7
0.5000	0.5000		123.2	152.7
0.4500	0.5500		152.7	152.7
0.4000	0.6000			152.7
0.3500	0.6500			152.7
0.3000	0.7000			152.7
0.2500	0.7500			152.7
0.2000	0.8000			152.7
0.1500	0.8500			152.7
0.1000	0.9000			152.7
0.0500	0.9500			152.7

This report displays the estimated survival times for various survival proportions. For example, it gives the median survival time if it can be estimated.

**Proportion Surviving**

This is the proportion surviving that is reported on this line. The proportion values were specified in the Percentiles box under the Report tab.

**Proportion Failing**

This is the proportion failing. The proportion is equal to one minus the proportion surviving.

**Survival Time**

This is the time value corresponding to the proportion surviving. The  $p$ th quantile is estimated by

$$T_p = \inf \left\{ T : \hat{S}(T) \leq 1 - p \right\}$$

In words,  $T_p$  is smallest time at which  $\hat{S}(T)$  is less than or equal to  $1 - p$ .

For example, this table estimates that 95% of the subjects will survive longer than 24.4 hours.

**Lower and Upper Confidence Limits on Survival Time**

These values provide a pointwise  $100(1 - \alpha)\%$  confidence interval for  $T_p$ . For example, if  $p$  is 0.50, this provides a confidence interval for the median survival time.

Three methods are available for calculating these confidence limits. The method is designated under the Variables tab in the Confidence Limits box. The formulas for these confidence limits were given in the Survival Quantiles section. Note that because of censoring, estimates and confidence limits are not available for all survival proportions.

## Kaplan-Meier Curves (Logrank Tests)

## Nelson-Aalen Cumulative Hazard

Event Time T	Cumulative Hazard H(T)	Standard Error of H(T)	Lower 95% C.L. for H(T)	Upper 95% C.L. for H(T)	At Risk	Count	Total Events
12.5	0.0333	0.0333	0.0000	0.0987	30	1	1
24.4	0.0678	0.0480	0.0000	0.1618	29	1	2
58.2	0.1035	0.0598	0.0000	0.2207	28	1	3
68.0	0.1406	0.0703	0.0027	0.2784	27	1	4
69.1	0.1790	0.0802	0.0219	0.3362	26	1	5
95.5	0.2190	0.0896	0.0434	0.3946	25	1	6
96.6	0.2607	0.0988	0.0670	0.4544	24	1	7
97.0	0.3042	0.1079	0.0926	0.5158	23	1	8
114.2	0.3496	0.1171	0.1201	0.5792	22	1	9
123.2	0.3972	0.1264	0.1494	0.6451	21	1	10
125.6	0.4472	0.1360	0.1808	0.7137	20	1	11
152.7	0.4999	0.1458	0.2141	0.7856	19	1	12
152.7+					18	18	12

This report displays estimates of the cumulative hazard function at the time points encountered in the dataset. The formulas used were presented earlier.

**Event Time (T)**

This is the time point being reported on this line. The time values are specific event times that occurred in the data.

Note that censored observations are marked with a plus sign on their time value. The survival functions are not calculated for censored observations.

**Cumulative Hazard H(T)**

This is the Nelson-Aalen estimator of the cumulative hazard function,  $H(T)$ .

**Standard Error of H(T)**

This is the estimated standard error of the above cumulative hazard function. The formula used was specified under the Variables tab in the Variance box. These formulas were given above in the section discussing the Nelson-Aalen estimator.

The standard error is the square root of this variance.

**Lower and Upper Confidence Limits for H(T)**

The lower and upper confidence limits provide a pointwise confidence interval for the cumulative hazard at each time point. These limits are constructed so that the probability that the true cumulative hazard lies between them is  $1 - \alpha$ . Note that these limits are constructed for a single time point. Several of them cannot be used together to form a confidence band such that the entire cumulative hazard function lies within the band.

Three difference confidence intervals are available. All three confidence intervals perform about the same in large samples. The linear (Greenwood) interval is the most commonly used. However, the log-transformed and the arcsine-square intervals behave better in small to moderate samples, so they are recommended. The formulas for these limits were given at the beginning of the chapter and are not repeated here.

**At Risk**

This value is the number of individuals at risk. The number at risk is all those under study who died or were censored at a time later than the current time. As the number of individuals at risk is decreased, the estimates become less reliable.

**Count**

This is the number of individuals having the event (failing) at this time point.

## Kaplan-Meier Curves (Logrank Tests)

**Total Events**

This is the cumulative number of individuals having the event (failing) up to and including this time value.

**Nelson-Aalen Cumulative Hazard at Specific Times**

Event Time (T)	Cumulative Hazard H(T)	Standard Error of H(T)	Lower 95% C.L. for H(T)	Upper 95% C.L. for H(T)	At Risk
10.0	0.0000	0.0000	0.0000	0.0000	30
20.0	0.0333	0.0333	0.0000	0.0987	29
30.0	0.0678	0.0480	0.0000	0.1618	28
40.0	0.0678	0.0480	0.0000	0.1618	28
50.0	0.0678	0.0480	0.0000	0.1618	28
60.0	0.1035	0.0598	0.0000	0.2207	27
70.0	0.1790	0.0802	0.0219	0.3362	25
80.0	0.1790	0.0802	0.0219	0.3362	25
90.0	0.1790	0.0802	0.0219	0.3362	25
100.0	0.3042	0.1079	0.0926	0.5158	22
110.0	0.3042	0.1079	0.0926	0.5158	22
120.0	0.3496	0.1171	0.1201	0.5792	21
130.0	0.4472	0.1360	0.1808	0.7137	19
140.0	0.4472	0.1360	0.1808	0.7137	19
150.0	0.4472	0.1360	0.1808	0.7137	19

This report displays estimates of the cumulative hazard function at the specified time points. The formulas used were presented earlier.

**Event Time (T)**

This is the time point being reported on this line. The time values were specified in the Times box under the Report tab.

**Cumulative Hazard H(T)**

This is the Nelson-Aalen estimator of the cumulative hazard function,  $H(T)$ . This estimator is give by

$$\tilde{H}(T) = \begin{cases} 0 & \text{if } T_{\min} > T \\ \sum_{A \leq T_i \leq T} \frac{d_i}{r_i} & \text{if } T_{\min} \leq T \end{cases}$$

**Standard Error of H(T)**

This is the estimated standard error of the above cumulative hazard function. The formula used was specified under the Variables tab in the Variance box. These formulas were given above in the section discussing the Nelson-Aalen estimator.

The standard error is the square root of this variance.

**Lower and Upper Confidence Limits for H(T)**

The lower and upper confidence limits provide a pointwise confidence interval for the cumulative hazard at each time point. These limits are constructed so that the probability that the true cumulative hazard lies between them is  $1 - \alpha$ . Note that these limits are constructed for a single time point. Several of them cannot be used together to form a confidence band such that the entire cumulative hazard function lies within the band.

Three difference confidence intervals are available. All three confidence intervals perform about the same in large samples. The linear (Greenwood) interval is the most commonly used. However, the log-transformed and the arcsine-square intervals behave better in small to moderate samples, so they are recommended. The formulas for these limits were given at the beginning of the chapter and are not repeated here.

## Kaplan-Meier Curves (Logrank Tests)

**At Risk**

This value is the number of individuals at risk. The number at risk is all those under study who died or were censored at a time later than the current time. As the number of individuals at risk is decreased, the estimates become less reliable.

**Hazard Rates Section**

Failure Time	Nonparametric Hazard Rate	Std Error of Hazard Rate	95% Lower Conf. Limit of Hazard Rate	95% Upper Conf. Limit of Hazard Rate
10.0	0.0018	0.0014	0.0004	0.0085
20.0	0.0018	0.0013	0.0005	0.0073
30.0	0.0015	0.0010	0.0004	0.0055
40.0	0.0016	0.0009	0.0005	0.0047
50.0	0.0022	0.0012	0.0008	0.0063
60.0	0.0026	0.0015	0.0008	0.0080
70.0	0.0034	0.0016	0.0014	0.0084
80.0	0.0042	0.0017	0.0019	0.0095
90.0	0.0043	0.0019	0.0018	0.0101
100.0	0.0048	0.0021	0.0020	0.0111
110.0	0.0054	0.0022	0.0024	0.0121
120.0	0.0047	0.0021	0.0019	0.0113
130.0	0.0038	0.0020	0.0014	0.0105
140.0	0.0036	0.0025	0.0009	0.0143
150.0	0.0066	0.0066	0.0009	0.0468

This report displays estimates of the hazard rates at the specified time points. The formulas used were presented earlier.

**Failure Time**

This is the time point being reported on this line. The time values were specified in the Times box under the Report tab.

**Nonparametric Hazard Rate**

The characteristics of the failure process are best understood by studying the hazard rate,  $h(T)$ , which is the derivative (slope) of the cumulative hazard function  $H(T)$ . The hazard rate is estimated using kernel smoothing of the Nelson-Aalen estimator as given in Klein and Moeschberger (2003). The formulas used were given earlier and are not repeated here.

Care must be taken when using this kernel-smoothed estimator since it is actually estimating a smoothed version of the hazard rate, not the hazard rate itself. Thus, it may be biased. Also, it is greatly influenced by the choice of the bandwidth  $b$ . We have found that you must experiment with  $b$  to find an appropriate value for each dataset.

The values of the smoothing parameters are specified under the Hazards tab.

**Standard Error of Hazard Rate**

This is the estimated standard error of the above hazard rate. The formula used was specified under the Variables tab in the Variance box. These formulas were given above in the section discussing the Nelson-Aalen estimator.

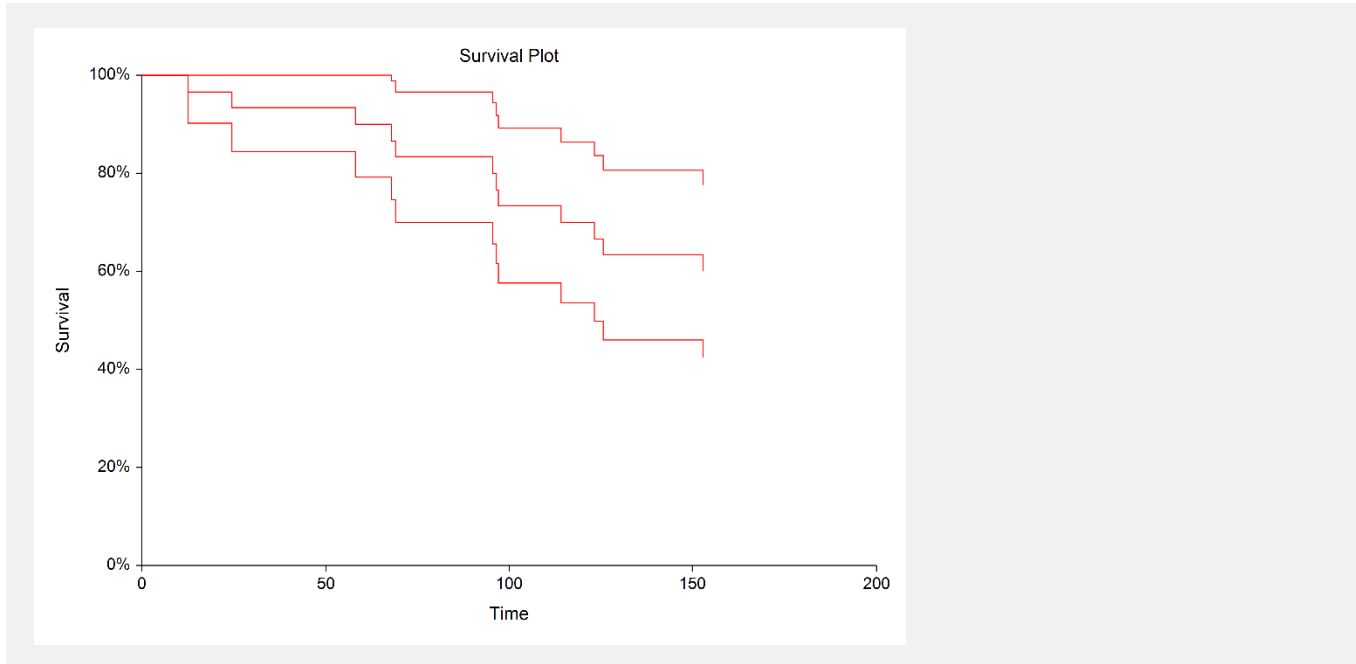
The standard error is the square root of this variance.

**Lower and Upper Confidence Limits of Hazard Rate**

The lower and upper confidence limits provide a pointwise confidence interval for the smoothed hazard rate at each time point. These limits are constructed so that the probability that the true hazard rate lies between them is  $1 - \alpha$ . Note that these limits are constructed for a single time point. Several of them cannot be used together to form a confidence band such that the entire hazard rate function lies within the band.

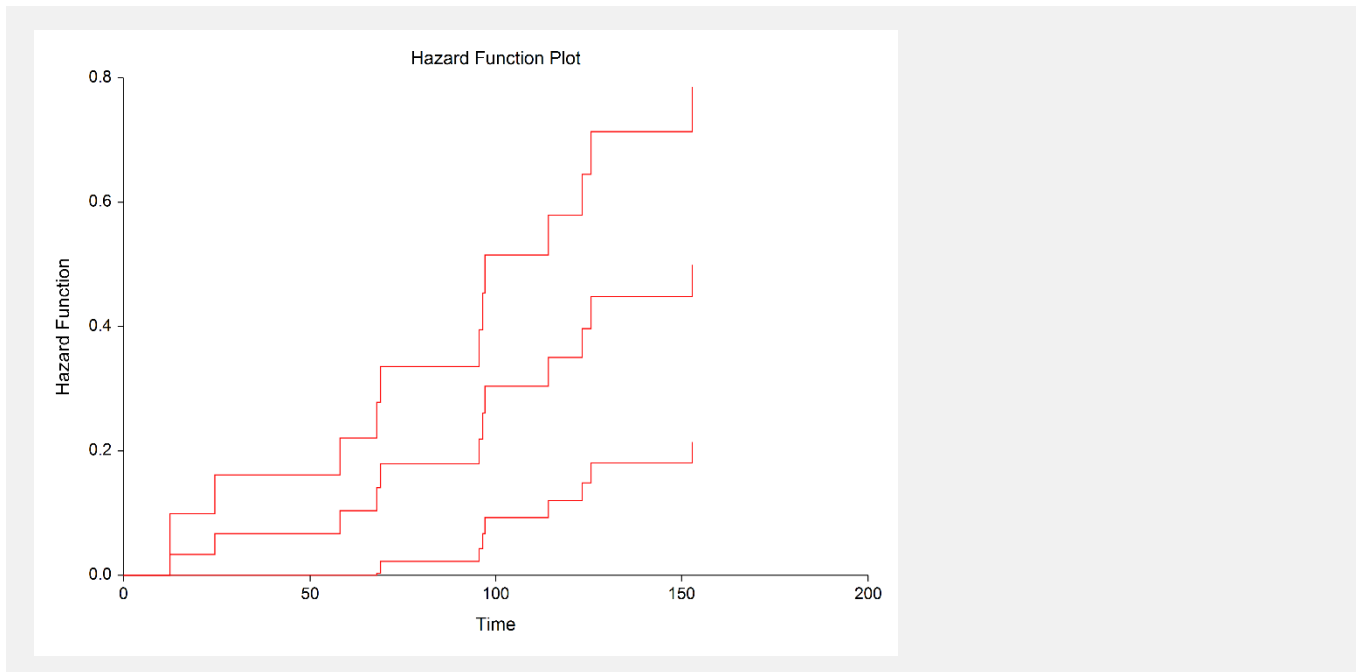
## Kaplan-Meier Curves (Logrank Tests)

## Kaplan-Meier Survival Curve(s)



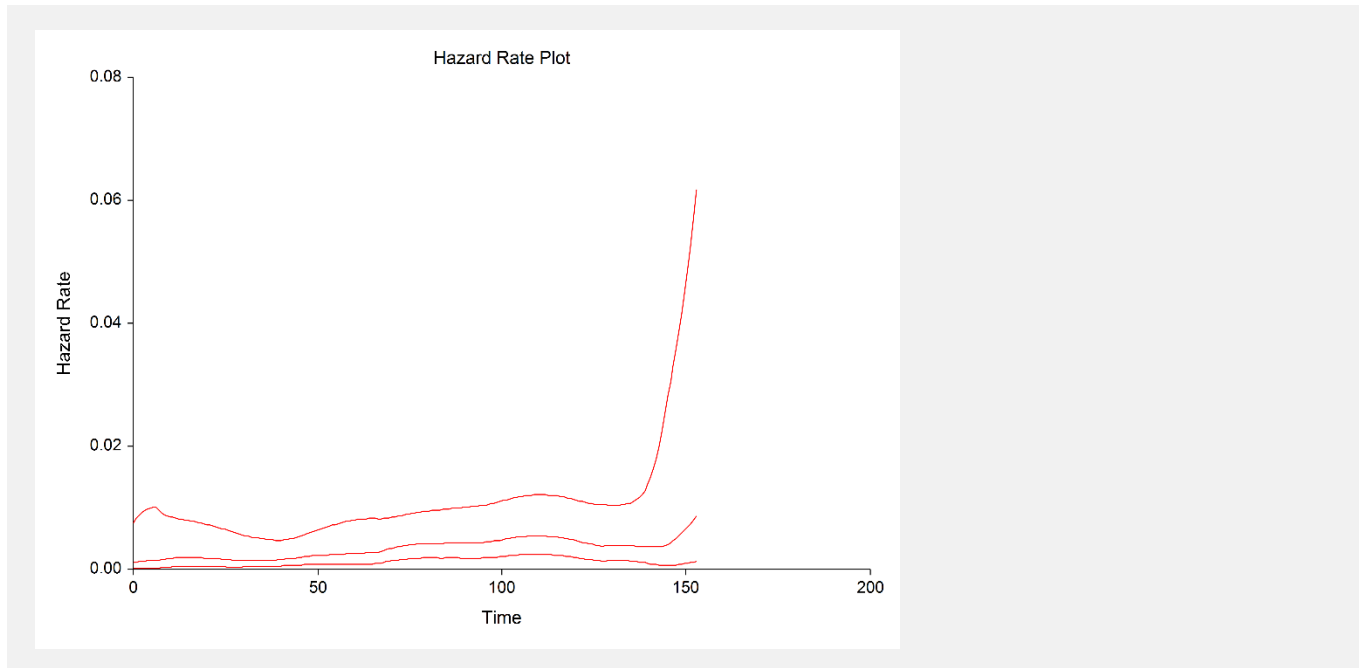
This plot shows the product-limit survivorship function as well as the pointwise confidence intervals. If there are several groups, a separate line is drawn for each group.

## Cumulative Hazard Function Plot(s)



This plot shows the Nelson-Aalen cumulative hazard function for the data analyzed. Confidence limits are also given. If you have several groups, then a separate line is drawn for each group.

## Kaplan-Meier Curves (Logrank Tests)

**Hazard Rate Plot(s)**

This plot shows the hazard rate with associated confidence limits.



## Kaplan-Meier Curves (Logrank Tests)

## Example 2 – Logrank Tests and Restricted Mean Survival Time (RMST) and Restricted Mean Time Lost (RMTL) Comparisons

This section presents an example of how to use a logrank test to compare the hazard rates of two or more groups. The data used are recorded in the variables Tumor6, Censor6, and Trtmnt6 of the Survival dataset.

You may follow along here by making the appropriate entries or load the completed template **Example 2** by clicking on Open Example Template from the File menu of the Kaplan-Meier Curves (Logrank Tests) window.

### 1 Open the Survival dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **Survival.NCSS**.
- Click **Open**.

### 2 Open the Kaplan-Meier Curves (Logrank Tests) window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Kaplan-Meier Curves (Logrank Tests)** procedure.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

### 3 Specify the variables.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Variables tab**.
- Set the **Time Variable** to **Tumor6**.
- Set the **Censor Variable** to **Censor6**.
- Set the **Group Variable** to **Trtmnt6**.

### 4 Specify the reports.

- Check the **Run Randomization Tests** box.
- Set the **Monte Carlo Samples** to **1000**.

### 5 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

## Data Summary

Group	Type	Rows	Count	Percent (%)	Minimum	Maximum
1	Failed	6	6	100.00%	8	13
	Censored	0	0	0.00%		
	Total	6	6	50.00%*	8	13
2	Failed	4	4	66.67%	9	20
	Censored	2	2	33.33%	30	30
	Total	6	6	50.00%*	9	30
Combined	Failed	10	10	83.33%	8	20
	Censored	2	2	16.67%	30	30
	Total	12	12	100.00%	8	30

\* Percent (%) of Combined Total

This report displays a summary of the amount of data that were analyzed. Scan this report to determine if there were any obvious data errors by double checking the counts and the minimum and maximum times.

## Kaplan-Meier Curves (Logrank Tests)

## Logrank Tests Summary

Test Name	Chi-Square	DF	Prob Level*	Randomization Test Prob Level*†	Weighting of Hazard Comparisons Across Time
Logrank	4.996	1	0.0254	0.0420	Equal
Gehan-Wilcoxon	3.956	1	0.0467	0.0500	High++ to Low++
Tarone-Ware	4.437	1	0.0352	0.0470	High to Low
Peto-Peto	3.729	1	0.0535	0.0700	High+ to Low+
Mod. Peto-Peto	3.618	1	0.0572	0.0770	High+ to Low+
F-H (1, 0)	3.956	1	0.0467	0.0500	Almost Equal
F-H (.5, .5)	3.507	1	0.0611	0.0970	Low+ to High+
F-H (1, 1)	4.024	1	0.0449	0.0820	Low to High
F-H (0, 1)	5.212	1	0.0224	0.0710	Low to High
F-H (.5, 2)	5.942	1	0.0148	0.0480	Low++ to High++

\*These probability levels are only valid when a single test was selected before this analysis is seen.

You cannot select a test to report after viewing this table without adding bias to the results.

Unless you have good reason to do otherwise, you should use the equal weighting (logrank) test.

† Randomization Test results are based on 1000 Monte Carlo samples.

This report gives the results of the ten logrank type tests that are provided by this procedure. We strongly suggest that you select the test that will be used before viewing this report. Unless you have a good reason for doing so, we recommend that you use the first (Logrank) test.

### Chi-Square

This is the chi-square value of the test. Each of these tests is approximately distributed as a chi-square in large samples.

### DF

This is the degrees of freedom of the chi-square distribution. It is one less than the number of groups.

### Prob Level

This is the significance level of the test. If this value is less than your chosen significance level (often 0.05), the test is significant, and the hazard rates of the groups are not identical at all time values.

### Randomization Test Prob Level

This is the significance level of the corresponding randomization test. This significance level is exact if the assumption that any censoring is independent of which group the subject was in.

In this example, several of the tests that were just significant at the 0.05 level are not significant using corresponding the randomization test. In cases like this, the randomization test should be considered more accurate than the chi-square test.

### Weighting of Hazard Comparisons Across Time

The type of weighting pattern that is used by this test is given here.

## Kaplan-Meier Curves (Logrank Tests)

## Logrank Tests Details

### Logrank Test

Chi-Square = 4.996, DF = 1, Probability Level = 0.0254  
 Randomization Test Probability Level = 0.0420 (1000 Monte Carlo Samples)  
 Weighting of Hazard Comparisons Across Time = Equal

Group	Z-Value	Standard Error	Standardized Z-Value
1	2.831	1.266	2.235
2	-2.831	1.266	-2.235

### Gehan-Wilcoxon Test

Chi-Square = 3.956, DF = 1, Probability Level = 0.0467  
 Randomization Test Probability Level = 0.0500 (1000 Monte Carlo Samples)  
 Weighting of Hazard Comparisons Across Time = High++ to Low++

Group	Z-Value	Standard Error	Standardized Z-Value
1	24.000	12.066	1.989
2	-24.000	12.066	-1.989

.  
.  
.

report continues for all ten tests.

This report gives the details of each of the ten logrank tests that are provided by this procedure. We strongly suggest that you select the test that will be used before viewing this report. Unless you have a good reason for doing so, we recommend that you use the first (Logrank) test.

### Group

This is the group reported about on this line.

### Z-Value

This is a weighted average of the difference between the observed hazard rates of this group and the expected hazard rates under the null hypothesis of hazard rate equality. The expected hazard rates are found by computing new hazard rates based on all that data as if they all came from a single group.

By considering the magnitudes of these values, you can determine which group (or groups) are different from the rest.

### Standard Error

This is the standard error of the above z-value. It is used to standardize the z-values.

### Standardized Z-Value

The standardized z-value is created by dividing the z-value by its standard error. This provides an index number that will usually vary between -3 and 3. Larger values represent groups that quite different from the typical group, at least at some time values.

## Kaplan-Meier Curves (Logrank Tests)

## Hazard Ratio Details

Group Ratio	Sample Size	Observed Events	Expected Events	Hazard Rates	Cox-Mantel Hazard Ratio	Hyper-geometric Variance
	n <sub>A</sub>   n <sub>B</sub>	O <sub>A</sub>   O <sub>B</sub>	E <sub>A</sub>   E <sub>B</sub>	H <sub>RA</sub>   H <sub>RB</sub>	HR	V
1/2	6   6	6   4	3.17   6.83	1.89   0.59	3.23	1.60
2/1	6   6	4   6	6.83   3.17	0.59   1.89	0.31	1.60

This report gives the details of the hazard ratio calculation. One line of the report is devoted to each pair of groups.

**Groups**

These are the two groups reported about on this line, separated by a slash.

**Sample Size**

These are the sample sizes of the two groups.

**Observed Events**

These are the number of events (deaths) observed in the two groups.

**Expected Events**

These are the number of events (deaths) expected in each group under the hypothesis that the two hazard rates are equal.

**Hazard Rates**

These are the hazard rates of the two groups. The hazard rate is computed as the ratio of the number of observed and expected events.

**Cox-Mantel Hazard Ratio**

This is the value of the Cox-Mantel hazard ratio. This is the ratio of the two hazard rates.

**Hypergeometric Variance**

This is the value of  $V$ , the hypergeometric variance. This value is used to compute the Mantel-Haenszel hazard ratio and confidence interval.

## Hazard Ratio Confidence Intervals

Group Ratio	Cox-Mantel Hazard Ratio	Log Hazard Ratio Value	Log Hazard Ratio SE	Lower 95% C.L. for HR	Upper 95% C.L. for HR
1/2	3.23	1.1733	0.6796	0.85	12.25
2/1	0.31	-1.1733	0.6796	0.08	1.17

This report gives the details of the Cox-Mantel confidence interval for the hazard ratio. The formulas for these quantities were given earlier in this chapter. One line of the report is devoted to each pair of groups.

**Groups**

These are the two groups reported about on this line, separated by a slash.

**Cox-Mantel Hazard Ratio (HR)**

This is the value of the Cox-Mantel hazard ratio.

## Kaplan-Meier Curves (Logrank Tests)

**Log Hazard Ratio Value**

This is the natural logarithm of the hazard ratio. The logarithmic transformation is applied because the distribution is better approximated by the normal distribution.

**Log Hazard Ratio S.E.**

This is the standard deviation of the log hazard ratio.

**Lower & Upper 95% C.L. for HR**

These are the lower and upper confidence limits of the Cox-Mantel confidence interval of the hazard ratio.

**Hazard Ratio Logrank Tests**

Group Ratio	Cox-Mantel Logrank Test			Mantel-Haenszel Logrank Test		
	Hazard Ratio	Chi-Square	Prob Level	Hazard Ratio	Chi-Square	Prob Level
1/2	3.23	3.701	0.0544	5.84	4.996	0.0254
2/1	0.31	3.701	0.0544	0.17	4.996	0.0254

This report gives the two logrank tests which test the null hypothesis that the hazard ratio is one (that is, that the hazard rates are equal). The formulas for these quantities were given earlier in this chapter. One line of the report is devoted to each pair of groups.

**Groups**

These are the two groups reported about on this line, separated by a slash.

**Cox-Mantel Hazard Ratio**

This is the value of the Cox-Mantel hazard ratio.

**Cox-Mantel Logrank Test Chi-Square**

This is the test statistic for the Cox-Mantel logrank test. This value is approximately distributed as a chi-square with one degree of freedom.

Note that this test is more commonly used than the Mantel-Haenszel test.

**Cox-Mantel Prob Level**

This is the significance level of the Cox-Mantel logrank test. The hypothesis of hazard rate equality is rejected if this value is less than 0.05 (or 0.01).

**Mantel-Haenszel Hazard Ratio**

This is the value of the Mantel-Haenszel hazard ratio.

**Mantel-Haenszel Logrank Test Chi-Square**

This is the test statistic for the Mantel-Haenszel logrank test. This value is approximately distributed as a chi-square with one degree of freedom.

**Mantel-Haenszel Prob Level**

This is the significance level of the Mantel-Haenszel logrank test. The hypothesis of hazard rate equality is rejected if this value is less than 0.05 (or 0.01).

Kaplan-Meier Curves (Logrank Tests)

Median and Mean Survival Estimates

Median Survival Time					
Group	Failed	Total	Median	Lower 95% C.L.	Upper 95% C.L.
1	6	6	10.0	8.0	10.0
2	4	6	15.0	12.0	20.0

Restricted Mean Survival Time (RMST)							
Group	Failed	Total	$\tau$	RMST( $\tau$ )*	Standard Error	Lower 95% C.L.	Upper 95% C.L.
1	6	6	13.0	10.5	0.808	8.9	12.1
2	4	6	13.0	12.2	0.597	11.0	13.3

\* Estimates are based on an interval upper limit of  $\tau = 13.0$ , the smallest maximum observed time among all groups.

Restricted Mean Time Lost (RMTL)							
Group	Failed	Total	$\tau$	RMTL( $\tau$ )*	Standard Error	Lower 95% C.L.	Upper 95% C.L.
1	6	6	13.0	2.5	0.808	0.9	4.1
2	4	6	13.0	0.8	0.597	-0.3	2.0

\* Estimates are based on an interval upper limit of  $\tau = 13.0$ , the smallest maximum observed time among all groups.

This report displays point estimates for the median and restricted means for each group, along with lower and upper confidence limits.

Between-Group Mean Survival Comparisons

**Restricted Mean Survival Time (RMST) Difference**  
Hypotheses:  $H_0: RMST_i(\tau) - RMST_j(\tau) = 0$  vs.  $H_1: RMST_i(\tau) - RMST_j(\tau) \neq 0$

Comparison	$\tau$	RMST( $\tau$ ) Difference*	Standard Error	Z-Value	Prob Level	Lower 95% C.L.	Upper 95% C.L.
1 - 2	13.0	-1.7	1.005	-1.659	0.0971	-3.6	0.3
2 - 1	13.0	1.7	1.005	1.659	0.0971	-0.3	3.6

\* Comparison estimates are based on an interval upper limit of  $\tau = 13.0$ , the smallest maximum observed time among all groups.

**Restricted Mean Survival Time (RMST) Ratio**  
Hypotheses:  $H_0: RMST_i(\tau)/RMST_j(\tau) = 1$  vs.  $H_1: RMST_i(\tau)/RMST_j(\tau) \neq 1$

Comparison	$\tau$	RMST( $\tau$ ) Ratio*	Standard Error	Z-Value	Prob Level	Lower 95% C.L.	Upper 95% C.L.
1/2	13.0	0.86	0.091	-1.614	0.1065	0.72	1.03
2/1	13.0	1.16	0.091	1.614	0.1065	0.97	1.39

\* Comparison estimates are based on an interval upper limit of  $\tau = 13.0$ , the smallest maximum observed time among all groups.

**Restricted Mean Time Lost (RMTL) Ratio**  
Hypotheses:  $H_0: RMTL_i(\tau)/RMTL_j(\tau) = 1$  vs.  $H_1: RMTL_i(\tau)/RMTL_j(\tau) \neq 1$

Comparison	$\tau$	RMTL( $\tau$ ) Ratio*	Standard Error	Z-Value	Prob Level	Lower 95% C.L.	Upper 95% C.L.
1/2	13.0	3.00	0.786	1.398	0.1622	0.64	14.00
2/1	13.0	0.33	0.786	-1.398	0.1622	0.07	1.56

\* Comparison estimates are based on an interval upper limit of  $\tau = 13.0$ , the smallest maximum observed time among all groups.

This report displays hypothesis tests for the RMST difference and ratio and RMTL ratio along with confidence limits. The three tests and confidence limits indicate that the two groups are not significantly different based on

## Kaplan-Meier Curves (Logrank Tests)

RMST difference and ratio and RMTL ratio. Note that the RMTL difference is not computed because it would be the same as the RMST difference.

### Comparison

This is the comparison (difference or ratio) being reported on this line.

### $\tau$

This is the value of the upper limit used in calculations.

### RMST( $\tau$ ) Difference, RMST( $\tau$ ) Ratio, RMTL( $\tau$ ) Ratio

This is estimated difference or ratio.

### Standard Error

This is the standard error of the comparison estimate.

### Z-value

This is the computed Z-statistic for the hypothesis test.

### Prob Level

This is the computed p-value for the hypothesis test.

### Lower and Upper Confidence Limits

These are the lower and upper confidence limits for the comparison estimate.

## Example 3 – Validation of Kaplan-Meier Product Limit Estimator using Collett (1994)

This section presents validation of the Kaplan-Meier product limit estimator and associated statistics. Collett (1994) presents an example on page 5 of the time to discontinuation of use of an IUD. The data are as follows: 10, 13+, 18+, 19, 23+, 30, 36, 38+, 54+, 56+, 59, 75, 93, 97, 104+, 107, 107+, 107+. These data are contained in the Collett dataset.

On page 26, Collett (1994) gives the product-limit estimator, its standard deviation, and 95% confidence interval. A partial list of these results is given here:

Time	S(T)	SE	95% C.I
10	0.9444	0.0540	(0.839, 1.000)
36	0.7459	0.1170	(0.529, 0.963)
93	0.4662	0.1452	(0.182, 0.751)
107	0.2486	0.1392	(0.000, 0.522)

We will now run these data through this procedure to see that NCSS gets these same results. You may follow along here by making the appropriate entries or load the completed template **Example 3** by clicking on Open Example Template from the File menu of the Kaplan-Meier Curves (Logrank Tests) window.

### 1 Open the Collett5 dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **Collett5.NCSS**.
- Click **Open**.

### 2 Open the Kaplan-Meier Curves (Logrank Tests) window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Kaplan-Meier Curves (Logrank Tests)** procedure.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

### 3 Specify the variables.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Variables tab**.
- Set the **Time Variable** to **Time**.
- Set the **Censor Variable** to **Censor**.

### 4 Specify the reports.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Reports tab**.
- Uncheck all reports except the **Kaplan-Meier Product-Limit Survival Analysis** report.

### 5 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.



## Kaplan-Meier Curves (Logrank Tests)

## Kaplan-Meier Product-Limit Survival Analysis Output

Event Time T	Cumulative Survival S(T)	Standard Error of S(T)	Lower 95% C.L. for S(T)	Upper 95% C.L. for S(T)	At Risk	Count	Total Events
10.0	0.9444	0.0540	0.8386	1.0000	18	1	1
13.0+					17	1	1
18.0+					16	1	1
19.0	0.8815	0.0790	0.7267	1.0000	15	1	2
23.0+					14	1	2
30.0	0.8137	0.0978	0.6220	1.0000	13	1	3
36.0	0.7459	0.1107	0.5290	0.9628	12	1	4
38.0+					11	1	4
54.0+					10	1	4
56.0+					9	1	4
59.0	0.6526	0.1303	0.3972	0.9081	8	1	5
75.0	0.5594	0.1412	0.2827	0.8361	7	1	6
93.0	0.4662	0.1452	0.1816	0.7508	6	1	7
97.0	0.3729	0.1430	0.0927	0.6532	5	1	8
104.0+					4	1	8
107.0	0.2486	0.1392	0.0000	0.5215	3	1	9
107.0+					2	2	9

You can check this table to see that the results are the same as Collett's.

## Example 4 – Validation of Nelson-Aalen Estimator using Klein and Moeschberger (2003)

This section presents validation of the Nelson-Aalen estimator and associated statistics. Klein and Moeschberger (2003) present an example of output for the cumulative hazard function on page 97. The data are available on their website. These data are contained in the BMT dataset.

A partial list of these results for the ALL group (our group 1) is given here:

<b>Time</b>	<b>H(T)</b>	<b>SE</b>
1	0.0263	0.0263
332	0.5873	0.1449
662	1.0152	0.2185

We will now run these data through this procedure to see that NCSS gets these same results. You may follow along here by making the appropriate entries or load the completed template **Example 4** by clicking on Open Example Template from the File menu of the Kaplan-Meier Curves (Logrank Tests) window.

### 1 Open the BMT dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **BMT.NCSS**.
- Click **Open**.

### 2 Open the Kaplan-Meier Curves (Logrank Tests) window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Kaplan-Meier Curves (Logrank Tests)** procedure.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

### 3 Specify the variables.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Variables tab**.
- Set the **Time Variable** to **Time**.
- Set the **Censor Variable** to **D3**.
- Set the **Group Variable** to **Group**.

### 4 Specify the reports.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Reports tab**.
- Uncheck all reports except the **Nelson-Aalen Cumulative Hazard** report.

### 5 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

## Kaplan-Meier Curves (Logrank Tests)

## Nelson-Aalen Cumulative Hazard Output

Nelson-Aalen Cumulative Hazard for Group = 1

Event Time (T)	Cumulative Hazard H(T)	Standard Error of H(T)	Lower 95% C.L. for H(T)	Upper 95% C.L. for H(T)	At Risk	Count	Total Events
<b>1.0</b>	<b>0.0263</b>	<b>0.0263</b>	<b>0.0000</b>	<b>0.0779</b>	<b>38</b>	<b>1</b>	<b>1</b>
55.0	0.0533	0.0377	0.0000	0.1273	37	1	2
74.0	0.0811	0.0468	0.0000	0.1729	36	1	3
86.0	0.1097	0.0549	0.0021	0.2172	35	1	4
104.0	0.1391	0.0623	0.0171	0.2611	34	1	5
107.0	0.1694	0.0692	0.0337	0.3051	33	1	6
109.0	0.2007	0.0760	0.0518	0.3495	32	1	7
110.0	0.2329	0.0825	0.0712	0.3947	31	1	8
122.0	0.2996	0.0950	0.1133	0.4859	30	2	10
129.0	0.3353	0.1015	0.1363	0.5343	28	1	11
172.0	0.3723	0.1081	0.1605	0.5842	27	1	12
192.0	0.4108	0.1147	0.1860	0.6356	26	1	13
194.0	0.4508	0.1215	0.2127	0.6889	25	1	14
226.0+					24	1	14
230.0	0.4943	0.1290	0.2414	0.7472	23	1	15
276.0	0.5397	0.1368	0.2716	0.8079	22	1	16
<b>332.0</b>	<b>0.5873</b>	<b>0.1449</b>	<b>0.3034</b>	<b>0.8713</b>	<b>21</b>	<b>1</b>	<b>17</b>
383.0	0.6373	0.1532	0.3370	0.9377	20	1	18
418.0	0.6900	0.1620	0.3724	1.0076	19	1	19
466.0	0.7455	0.1713	0.4098	1.0813	18	1	20
487.0	0.8044	0.1811	0.4494	1.1593	17	1	21
526.0	0.8669	0.1916	0.4913	1.2424	16	1	22
530.0+					15	1	22
609.0	0.9383	0.2045	0.5375	1.3390	14	1	23
<b>662.0</b>	<b>1.0152</b>	<b>0.2185</b>	<b>0.5870</b>	<b>1.4434</b>	<b>13</b>	<b>1</b>	<b>24</b>
996.0+					12	1	24
1111.0+					11	1	24
1167.0+					10	1	24
1182.0+					9	1	24
1199.0+					8	1	24
1330.0+					7	1	24
1377.0+					6	1	24
1433.0+					5	1	24
1462.0+					4	1	24
1496.0+					3	1	24
1602.0+					2	1	24
2081.0+					1	1	24

You can check this table to see that the results are the same as Klein and Moeschberger's.

## Example 5 – Validation of Logrank Tests using Klein and Moeschberger (2003)

This section presents validation of the logrank tests. Klein and Moeschberger (2003) present an example of output for the ten logrank tests on page 210. The data are available on their website. These data are contained in the Klein6 dataset.

A list of these results is given here:

Test	Chi-Square	P-Value
Logrank	2.53	0.112
Gehan	0.002	0.964
Tarone-Ware	0.40	0.526
Peto-Peto	1.40	0.237
Modified Peto-Peto	1.28	0.259
Fleming-Harrington(0,1)	9.67	0.002
Fleming-Harrington(1,0)	1.39	0.239
Fleming-Harrington(1,1)	9.83	0.002
Fleming-Harrington(0.5,0.5)	9.28	0.002
Fleming-Harrington(0.5,2)	8.18	0.004

We will now run these data through this procedure to see that **NCSS** gets these same results. You may follow along here by making the appropriate entries or load the completed template **Example 5** by clicking on Open Example Template from the File menu of the Kaplan-Meier Curves (Logrank Tests) window.

### 1 Open the Klein6 dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **Klein6.NCSS**.
- Click **Open**.

### 2 Open the Kaplan-Meier Curves (Logrank Tests) window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Kaplan-Meier Curves (Logrank Tests)** procedure.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

### 3 Specify the variables.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Variables tab**.
- Set the Time Variable to **Time**.
- Set the Censor Variable to **Censor**.
- Set the Group Variable to **Group**.

### 4 Specify the reports.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Reports tab**.
- Uncheck all reports except the **Logrank Tests Summary** report.

### 5 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

## Kaplan-Meier Curves (Logrank Tests)

**Logrank Tests Summary Output**

Test Name	Chi-Square	DF	Prob Level*	Weighting of Hazard Comparisons Across Time
Logrank	2.530	1	0.1117	Equal
Gehan-Wilcoxon	0.002	1	0.9636	High++ to Low++
Tarone-Ware	0.403	1	0.5257	High to Low
Peto-Peto	1.399	1	0.2369	High+ to Low+
Mod. Peto-Peto	1.276	1	0.2587	High+ to Low+
F-H (1, 0)	1.387	1	0.2390	Almost Equal
F-H (.5, .5)	9.285	1	0.0023	Low+ to High+
F-H (1, 1)	9.834	1	0.0017	Low to High
F-H (0, 1)	9.668	1	0.0019	Low to High
F-H (.5, 2)	8.179	1	0.0042	Low++ to High++

You can check this table to see that the results are the same as Klein and Moeschberger's. Note that the order of the tests is different.

## Example 6 – Validation of Restricted Mean Survival Time (RMST) Calculations using Klein and Moeschberger (2003)

This section presents validation of the RMST estimates. Klein and Moeschberger (2003) present an example of RMST calculations on pages 119 and 120. The data are available on their website. These data are contained in the BMT dataset. Group 1 is ALL, Group 2 is AML low risk, and Group 3 is AML high risk.

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Group	$\tau$	Mean	SE	95% Confidence Interval
1: ALL	2081	899.28	150.34*	(606.61, 1193.95)*
2: AML low risk	2569	1548.84	150.62	(1253.62, 1844.07)
3: AML high risk	2640	792.31	158.25	(482.15, 1102.5)

Page 120

Group	$\tau$	Mean	SE	95% Confidence Interval
1: ALL	2081	899.3	150.3*	(606.6, 1193.9)*
2: AML low risk	2081	1315.2	118.8	(1082.4, 1548.0)
3: AML high risk	2081	655.67	122.9	(414.8, 896.5)

\*The SE for the ALL group is incorrect as stated in the book. It should have been 146.13, which would have resulted in a confidence interval of (612.87, 1185.69). This can be verified by hand calculations.

We will now run these data through this procedure to see that NCSS gets these same results. You may follow along here by making the appropriate entries or load the completed template **Example 6 (a, b, and c)** by clicking on Open Example Template from the File menu of the Kaplan-Meier Curves (Logrank Tests) window.

### 1 Open the BMT dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **BMT.NCSS**.
- Click **Open**.

### 2 Open the Kaplan-Meier Curves (Logrank Tests) window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Kaplan-Meier Curves (Logrank Tests)** procedure.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

### 3 Specify the variables.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Variables tab**.
- Set the **Time Variable** to **Time**.
- Set the **Censor Variable** to **D3**.
- Set the **Group Variable** to **Group**.
- Set the **Interval Upper Limit ( $\tau$ )** to **Maximum Observed Time Within Each Group (Variable)**

### 4 Specify the reports.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Reports tab**.
- Uncheck all reports except the **Median and Mean Survival Estimates** report.

### 5 Run the procedure.

- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

## Kaplan-Meier Curves (Logrank Tests)

## Median and Mean Survival Estimates Output

## Median Survival Time

Group	Failed	Total	Median	Lower 95% C.L.	Upper 95% C.L.
1	24	38	418.0	194.0	662.0
2	25	54	2204.0	704.0	2204.0
3	34	45	183.0	115.0	363.0

## Restricted Mean Survival Time (RMST)

Group	Failed	Total	$\tau$	RMST( $\tau$ )*	Standard Error	Lower 95% C.L.	Upper 95% C.L.
1	24	38	2081.0	899.2	146.131	612.8	1185.6
2	25	54	2569.0	1548.8	150.625	1253.6	1844.1
3	34	45	2640.0	792.3	158.246	482.2	1102.5

\* Estimates are based on variable interval upper limits ( $\tau$ ) that equal the maximum observed time within each group.

## Restricted Mean Time Lost (RMTL)

Group	Failed	Total	$\tau$	RMTL( $\tau$ )*	Standard Error	Lower 95% C.L.	Upper 95% C.L.
1	24	38	2081.0	1181.8	146.131	895.4	1468.2
2	25	54	2569.0	1020.2	150.625	724.9	1315.4
3	34	45	2640.0	1847.7	158.246	1537.5	2157.8

\* Estimates are based on variable interval upper limits ( $\tau$ ) that equal the maximum observed time within each group.

These results are the same as Klein and Moeschberger's on page 119 (except for group 1, which matches the correct result, not the incorrect result in the book).

To match the results on page 120, change **Interval Upper Limit ( $\tau$ )** to **Smallest Maximum Observed Time Among All Groups** (Example 6b) or change **Interval Upper Limit ( $\tau$ )** to **Custom (User-Entered)** and enter **2081** for **Custom  $\tau$**  (Example 6c). Both give the same results since 2081 is the smallest

Example 6b**3 Specify the variables.**

- Set the **Interval Upper Limit ( $\tau$ )** to **Smallest Maximum Observed Time Among All Groups**

Example 6c**3 Specify the variables.**

- Set the **Interval Upper Limit ( $\tau$ )** to **Custom (User-Entered)**
- Set **Custom  $\tau$**  to **2081**

## Restricted Mean Survival Time (RMST)

Group	Failed	Total	$\tau$	RMST( $\tau$ )*	Standard Error	Lower 95% C.L.	Upper 95% C.L.
1	24	38	2081.0	899.2	146.131	612.8	1185.6
2	25	54	2081.0	1315.2	118.793	1082.3	1548.0
3	34	45	2081.0	655.7	122.895	414.8	896.5

\* Estimates are based on an interval upper limit of  $\tau = 2081.0$ , the smallest maximum observed time among all groups.

Again, these results are the same as Klein and Moeschberger's on page 120 (except for group 1, which matches the correct result, not the incorrect result in the book).

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## Example 7 – Adding an At-Risk Table to a Survival Plot and a Cumulative Hazard Plot

This section demonstrates how to add a table containing the number of subjects at risk, the cumulative number of censored observations, and the cumulative number of events to the bottom of a survival plot and a cumulative hazard plot. The cumulative hazard plot will be created with default settings, but we'll modify the survival plot to highlight some of the available options. The data used in this example are contained in the BMT dataset.

You may follow along here by making the appropriate entries or load the completed template **Example 7** by clicking on Open Example Template from the File menu of the Kaplan-Meier Curves (Logrank Tests) window.

### 1 Open the BMT dataset.

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **BMT.NCSS**.
- Click **Open**.

### 2 Open the Kaplan-Meier Curves (Logrank Tests) window.

- Using the Analysis menu or the Procedure Navigator, find and select the **Kaplan-Meier Curves (Logrank Tests)** procedure.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

### 3 Specify the variables.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Variables tab**.
- Set the **Time Variable** to **Time**.
- Set the **Censor Variable** to **D3**.
- Set the **Group Variable** to **Group**.

### 4 Specify the reports.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Reports tab**.
- Uncheck all reports.

### 5 Specify the report options.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Report Options tab**.
- Set **Value Labels** to **Value Labels**.

### 6 Specify the plots.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Plots tab**.
- Leave the **Kaplan-Meier Survival/Reliability Plot** checked.
- Check the **Cumulative Hazard Function Plot**.
- Under Plots Displayed, uncheck **Individual-Group Plots** so that only **Combined Plot(s)** is checked.

### 7 Modify the Kaplan-Meier Survival/Reliability plot.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Plots tab**.
- Click the **Kaplan-Meier Survival/Reliability Plot Format** button to edit the plot settings.

#### *Kaplan-Meier Survival/Reliability Plot Format Window*

- Click the **Survival** tab.
- Leave **Kaplan-Meier Survival Line** checked.
- Check **Tick Marks at Censor Points**.
- Click the **At-Risk Table** tab.
- At the top, select the **General** sub-tab.
- Check **Show At-Risk Table**.



## Kaplan-Meier Curves (Logrank Tests)

- Set **Display** to **Number At Risk (Number Censored) (Number of Events)**.
- At the top, select the **Layout** sub-tab.
- Set the **Top Outside Margin** to **0**.
- At the top, select the **Groups** sub-tab.
- Set **Display** to **Line + Symbol + Label**.
- Uncheck **Add a Label Prefix**.
- Click the **Value Layout** button and set **Alignment** to **Center**.
- Set **Label Colors From** to **Line Fill**.
- Set **Value Colors From** to **Line Fill**.
- Click **OK** to save the survival plot settings.

## 8 Modify the Cumulative Hazard Function plot.

- On the Kaplan-Meier Curves (Logrank Tests) window, select the **Plots** tab.
- Click the **Cumulative Hazard Function Plot Format** button to edit the plot settings.

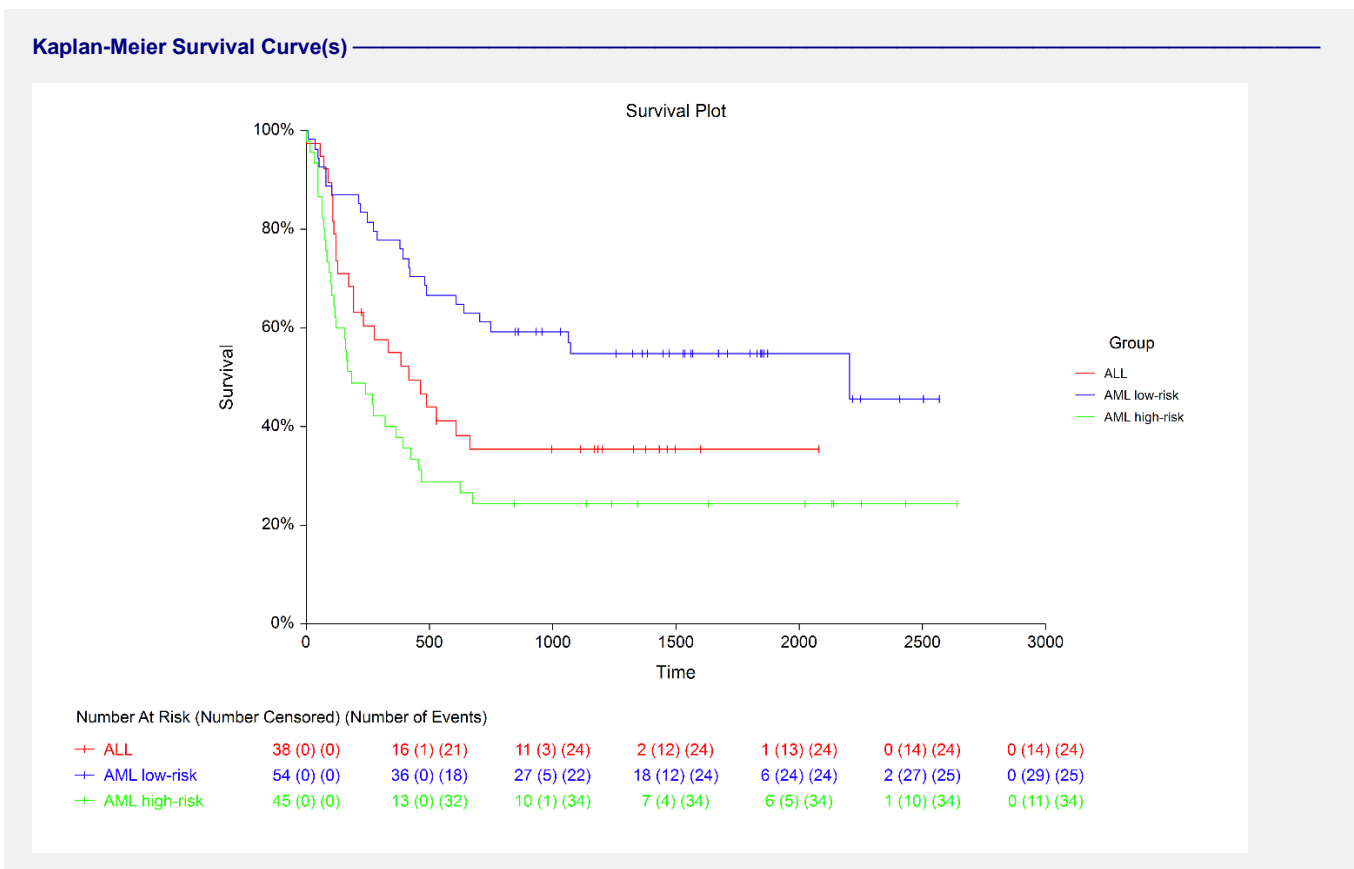
*Cumulative Hazard Function Plot Format Window*

- Click the **At-Risk Table** tab.
- At the top select the **General** sub-tab.
- Check **Show At-Risk Table** and click **OK** to save the hazard function plot settings.

## 9 Run the procedure.

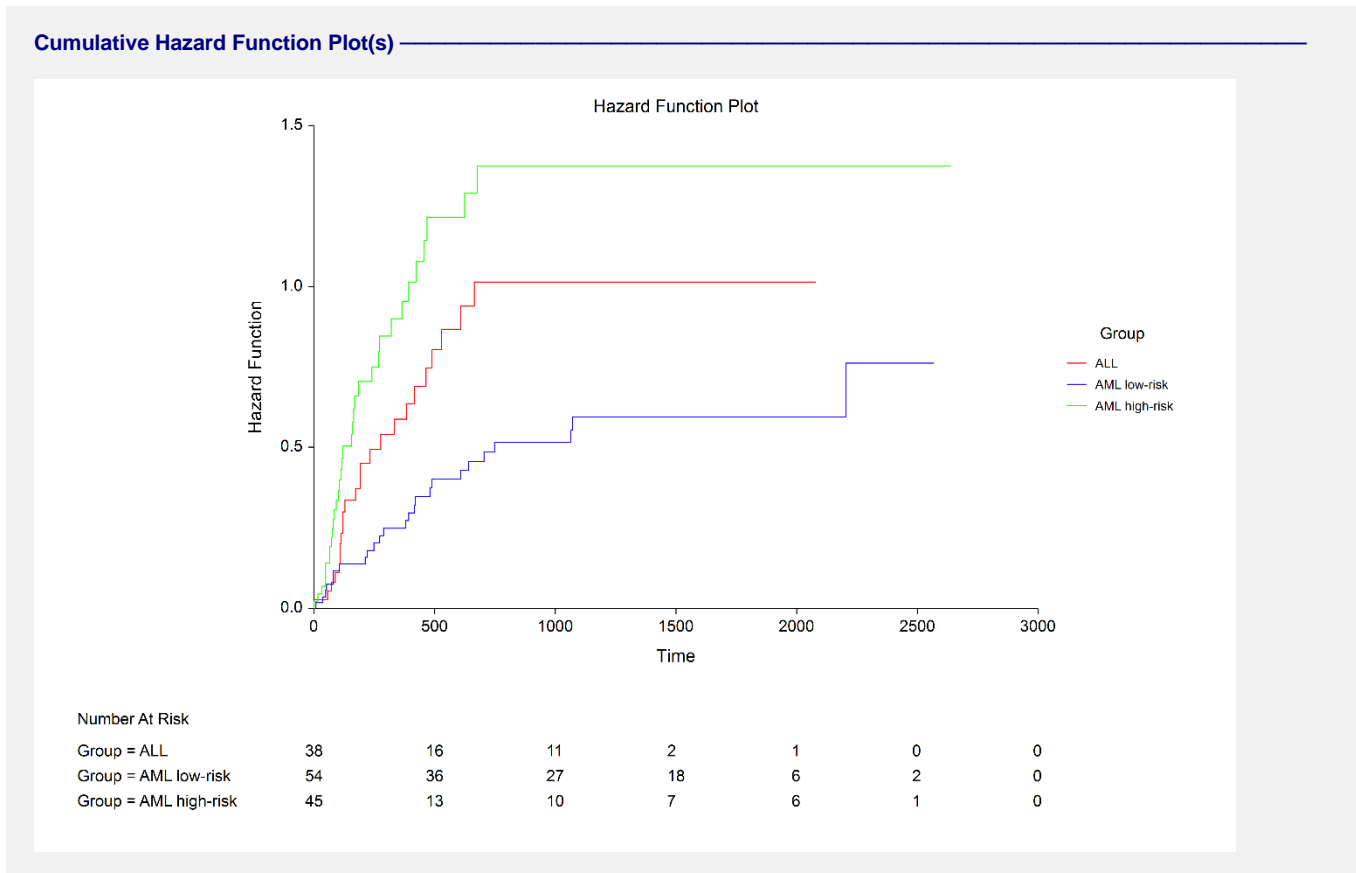
- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

## Output



The modified survival plot is displayed with numbers at risk, cumulative censoring, and cumulative events at each reference time point. You can further modify the plot as required to suit your needs.

### Kaplan-Meier Curves (Logrank Tests)



This plot is displayed with default at-risk table settings to give you an idea of what you get if you make no modifications to the table.